REGULAR CALENDAR

March 7, 2022

HOUSE OF REPRESENTATIVES

REPORT OF COMMITTEE

The Majority of the Committee on Health, Human Services and Elderly Affairs to which was referred HB 1022,

AN ACT permitting pharmacists to dispense the drug ivermectin by means of a standing order. Having considered the same, report the same with the following amendment, and the recommendation that the bill OUGHT TO PASS WITH AMENDMENT.

Rep. Leah Cushman

FOR THE MAJORITY OF THE COMMITTEE

Original: House Clerk
Cc: Committee Bill File

MAJORITY
COMMITTEE REPORT

Committee:	**Health, Human Services and Elderly Affairs**
Bill Number:	**HB 1022**
Title:	**permitting pharmacists to dispense the drug ivermectin by means of a standing order.**
Date:	**March 7, 2022**
Consent Calendar:	**REGULAR**
Recommendation:	**OUGHT TO PASS WITH AMENDMENT 2022-0964h**

STATEMENT OF INTENT

This bill as amended permits Ivermectin to be dispensed via a standing order at a pharmacy. A standing order is a specific prescriptive protocol written by a physician or advanced practice registered nurse (APRN), issued to a participating pharmacy, which enables the pharmacist to dispense a medication when it is requested by a patron. Ivermectin is a drug that has been used in humans globally for the treatment of parasites since 1988 and over 6 billion doses have been administered. It has a robustly safe drug profile, demonstrated over the three decades it has been utilized. Ivermectin is available over-the-counter in many other countries. In New Hampshire, hormonal contraceptives and Narcan are available at pharmacies via a standing order, both which carry greater risk than Ivermectin. This bill was modeled after the hormonal contraceptives standing order legislation that became law in 2018. It requires the standing order to "specify a screening protocol for each patient, specify a requirement to document screening performed and the prescription in the patient's medical record, and include a plan for evaluation and treatment of adverse events." It also requires that an information sheet be given to the patient which includes "potential adverse effects, drug interactions, Food and Drug Administration (FDA) approved indications for Ivermectin use, the importance of follow-up care, and health care referral information." Ivermectin has been shown to be helpful in reducing the severity and duration of infection of COVID-19, as well as other viruses. People will resort to purchasing it from questionable sources when they are trying to help themselves or their family members fight illness. Currently, people are buying Ivermectin over-the-counter in other countries like Mexico and bringing it to the US, purchasing it online from countries such as India, or resorting to getting Ivermectin formulated for livestock from farm stores. This bill enables easier access to an exceptionally safe medication, supplied by FDA-regulated and inspected drug manufacturing facilities, formulated for humans. There is great potential public benefit and minimal potential risk of making this medication available via the mechanisms in this bill as amended.

Vote 11-9.

Rep. Leah Cushman
FOR THE MAJORITY

Original: House Clerk
Cc: Committee Bill File

REGULAR CALENDAR

Health, Human Services and Elderly Affairs

HB 1022, permitting pharmacists to dispense the drug ivermectin by means of a standing order. **MAJORITY: OUGHT TO PASS WITH AMENDMENT. MINORITY: INEXPEDIENT TO LEGISLATE.**

Rep. Leah Cushman for the **Majority** of Health, Human Services and Elderly Affairs. This bill as amended permits Ivermectin to be dispensed via a standing order at a pharmacy. A standing order is a specific prescriptive protocol written by a physician or advanced practice registered nurse (APRN), issued to a participating pharmacy, which enables the pharmacist to dispense a medication when it is requested by a patron. Ivermectin is a drug that has been used in humans globally for the treatment of parasites since 1988 and over 6 billion doses have been administered. It has a robustly safe drug profile, demonstrated over the three decades it has been utilized. Ivermectin is available over-the-counter in many other countries. In New Hampshire, hormonal contraceptives and Narcan are available at pharmacies via a standing order, both which carry greater risk than Ivermectin. This bill was modeled after the hormonal contraceptives standing order legislation that became law in 2018. It requires the standing order to "specify a screening protocol for each patient, specify a requirement to document screening performed and the prescription in the patient's medical record, and include a plan for evaluation and treatment of adverse events." It also requires that an information sheet be given to the patient which includes "potential adverse effects, drug interactions, Food and Drug Administration (FDA) approved indications for Ivermectin use, the importance of follow-up care, and health care referral information." Ivermectin has been shown to be helpful in reducing the severity and duration of infection of COVID-19, as well as other viruses. People will resort to purchasing it from questionable sources when they are trying to help themselves or their family members fight illness. Currently, people are buying Ivermectin over-the-counter in other countries like Mexico and bringing it to the US, purchasing it online from countries such as India, or resorting to getting Ivermectin formulated for livestock from farm stores. This bill enables easier access to an exceptionally safe medication, supplied by FDA-regulated and inspected drug manufacturing facilities, formulated for humans. There is great potential public benefit and minimal potential risk of making this medication available via the mechanisms in this bill as amended. **Vote 11-9.**

Original: House Clerk
Cc: Committee Bill File

REGULAR CALENDAR

March 7, 2022

HOUSE OF REPRESENTATIVES

REPORT OF COMMITTEE

The Minority of the Committee on Health, Human Services and Elderly Affairs to which was referred HB 1022,

AN ACT permitting pharmacists to dispense the drug ivermectin by means of a standing order. Having considered the same, and being unable to agree with the Majority, report with the following resolution: RESOLVED, that it is INEXPEDIENT TO LEGISLATE.

Rep. Gary Merchant

FOR THE MINORITY OF THE COMMITTEE

Original: House Clerk
Cc: Committee Bill File

MINORITY
COMMITTEE REPORT

Committee:	**Health, Human Services and Elderly Affairs**
Bill Number:	**HB 1022**
Title:	**permitting pharmacists to dispense the drug ivermectin by means of a standing order.**
Date:	**March 7, 2022**
Consent Calendar:	**REGULAR**
Recommendation:	**INEXPEDIENT TO LEGISLATE**

STATEMENT OF INTENT

A standing order requires a well-evaluated protocol established through consensus of physicians, nurse practitioners, and pharmacists. The lack of a well-defined protocol built on broad consensus of a wide range of clinicians may expose a pharmacist and a prescriber to undue legal liability, to the potential loss of liability insurance coverage, and to potential patient harm.

Rep. Gary Merchant
FOR THE MINORITY

Original: House Clerk
Cc: Committee Bill File

REGULAR CALENDAR

Health, Human Services and Elderly Affairs
HB 1022, permitting pharmacists to dispense the drug ivermectin by means of a standing order. **INEXPEDIENT TO LEGISLATE.**
Rep. Gary Merchant for the **Minority** of Health, Human Services and Elderly Affairs. A standing order requires a well-evaluated protocol established through consensus of physicians, nurse practitioners, and pharmacists. The lack of a well-defined protocol built on broad consensus of a wide range of clinicians may expose a pharmacist and a prescriber to undue legal liability, to the potential loss of liability insurance coverage, and to potential patient harm.

Original: House Clerk
Cc: Committee Bill File

Rep. Cushman, Hills. 2
March 4, 2022
2022-0964h
12/08

Amendment to HB 1022

Amend the bill by replacing all after the enacting clause with the following:

1 New Section; Ivermectin; Dispensing. Amend RSA 318 by inserting after section 47-m the following new section:

318:47-n Ivermectin; Dispensing.

I. In this section, "standing order" means a written and signed protocol authored by one or more physicians licensed under RSA 329:12 or one or more advanced practice registered nurses licensed under RSA 326-B:18. Such agreement shall specify a protocol allowing the pharmacist licensed under RSA 318:18 to dispense ivermectin under the delegated prescriptive authority of the physician or advanced practice registered nurse, specify a screening protocol for each patient, specify a requirement to document screening performed and the prescription in the patient's medical record, and include a plan for referring for evaluation and treatment of adverse events. Any such prescription shall be regarded as being issued for a legitimate medical purpose in the usual course of professional practice.

II. Licensed pharmacists following standing orders may dispense ivermectin to persons in this state without a prior prescription. Pharmacies may charge a fee for consultation with the patient.

III. A pharmacist, pharmacy, physician, advanced practice registered nurse, or a medical facility that employs a pharmacist, physician, or advanced practice registered nurse issuing or following standing orders shall be prohibited from seeking personal financial benefit by participating in any incentive-based program or accepting any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

IV. A pharmacist, physician, or advanced practice registered nurse shall be held to the same standard of care as when prescribing and dispensing any other medication.

V. The pharmacist shall provide each recipient of ivermectin pursuant to this section with an information sheet written in plain language, which shall include, but is not limited to, potential adverse effects, drug interactions, Food and Drug Administration-approved indications for ivermectin use, the importance of follow-up care, and health care referral information.

VI. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of this section are satisfied. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an advanced practice registered nurse based on a

pharmacist's failure to follow standing orders provided the provisions of this section are satisfied. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of this section are satisfied.

2 New Section; Prescription and Administration of Ivermectin. Amend RSA 329 by inserting after section 1-h the following new section:

329:1-i Prescription and Administration of Ivermectin. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of RSA 318:47-n are satisfied.

3 New Section; Prescription and Administration of Ivermectin. Amend RSA 326-B by inserting after section 37 the following new section:

326-B:37-a Prescription and Administration of Ivermectin. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an advanced practice registered nurse based on a pharmacist's failure to follow standing orders provided the provisions of RSA 318:47-n are satisfied. .

4 New Section; Prescription and Administration of Ivermectin. Amend RSA 318 by inserting after section 16-f the following new section:

318:16-g Prescription and Administration of Ivermectin. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of RSA 318:47-n are satisfied.

5 Effective Date. This act shall take effect 60 days after its passage.

HOUSE COMMITTEE ON HEALTH, HUMAN SERVICES AND ELDERLY AFFAIRS

EXECUTIVE SESSION on Bill # __HB1022____

BILL TITLE: **An Act permitting pharmacists to dispense the drug Ivermectin by means of a standing order.**

DATE: **3/7/2022**

LOB ROOM: 210-11

MOTION: (Please check one box)

Adoption of Amendment # 2022-0964h

Moved by Rep. ___Cushman___ Seconded by Rep. ___Folsom_____ Vote: 11-9

MOTION: (Please check one box)

OTP/A

Moved by Rep. ____Cushman_____ Seconded by Rep. ____Delemus___ Vote: 11-9

CONSENT CALENDAR: _____ YES __X___ NO

Minority Report? ___X___ Yes _____ No If yes, author, Rep: _Merchant_ Motion ITL

Respectfully submitted: _____baf_____
Rep. Beth Folsom, Clerk

STATE OF NEW HAMPSHIRE
OFFICE OF THE HOUSE CLERK

9/28/2021 11:15:01 AM
Roll Call Committee Registers Report

2022 SESSION

Health, Human Services and Elderly Affairs

Bill #: HB1022 **Motion:** _____ **AM #:** 2022-0964h **Exec Session Date:** 3/7/2022

Members	YEAS	Nays	NV
Pearson, Mark A. Chairman	Y		
Layon, Erica J. Vice Chairman	Y		
McMahon, Charles E.	Y		
Acton, Dennis F.	Y		
Gay, Betty I.	Y		
Cushman, Leah P.	Y		
Folsom, Beth A. Clerk	Y		
Kelsey, Niki	Y		
King, Bill C.	Y		
Kofalt, Jim	Y		
DeLemus, Susan	Y		
Weber, Lucy M.		N	
~~MacKay, James R.~~ Rep. Freitas		N	
Snow, Kendall A.			A
Knirk, Jerry L.		N	
~~Salloway, Jeffrey C.~~ Rep Query		N	
Cannon, Gerri D.		N	
Nutter-Upham, Frances E.		N	
Schapiro, Joe		N	
Woods, Gary L.		N	
Merchant, Gary		N	
TOTAL VOTE:	11	9	

Rep. Cushman, Hills. 2
March 4, 2022
2022-0964h
12/08

Amendment to HB 1022

Amend the bill by replacing all after the enacting clause with the following:

1 New Section; Ivermectin; Dispensing. Amend RSA 318 by inserting after section 47-m the following new section:

318:47-n Ivermectin; Dispensing.

I. In this section, "standing order" means a written and signed protocol authored by one or more physicians licensed under RSA 329:12 or one or more advanced practice registered nurses licensed under RSA 326-B:18. Such agreement shall specify a protocol allowing the pharmacist licensed under RSA 318:18 to dispense ivermectin under the delegated prescriptive authority of the physician or advanced practice registered nurse, specify a screening protocol for each patient, specify a requirement to document screening performed and the prescription in the patient's medical record, and include a plan for referring for evaluation and treatment of adverse events. Any such prescription shall be regarded as being issued for a legitimate medical purpose in the usual course of professional practice.

II. Licensed pharmacists following standing orders may dispense ivermectin to persons in this state without a prior prescription. Pharmacies may charge a fee for consultation with the patient.

III. A pharmacist, pharmacy, physician, advanced practice registered nurse, or a medical facility that employs a pharmacist, physician, or advanced practice registered nurse issuing or following standing orders shall be prohibited from seeking personal financial benefit by participating in any incentive-based program or accepting any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

IV. A pharmacist, physician, or advanced practice registered nurse shall be held to the same standard of care as when prescribing and dispensing any other medication.

V. The pharmacist shall provide each recipient of ivermectin pursuant to this section with an information sheet written in plain language, which shall include, but is not limited to, potential adverse effects, drug interactions, Food and Drug Administration-approved indications for ivermectin use, the importance of follow-up care, and health care referral information.

VI. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of this section are satisfied. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an advanced practice registered nurse based on a

pharmacist's failure to follow standing orders provided the provisions of this section are satisfied. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of this section are satisfied.

2 New Section; Prescription and Administration of Ivermectin. Amend RSA 329 by inserting after section 1-h the following new section:

329:1-i Prescription and Administration of Ivermectin. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of RSA 318:47-n are satisfied.

3 New Section; Prescription and Administration of Ivermectin. Amend RSA 326-B by inserting after section 37 the following new section:

326-B:37-a Prescription and Administration of Ivermectin. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an advanced practice registered nurse based on a pharmacist's failure to follow standing orders provided the provisions of RSA 318:47-n are satisfied. .

4 New Section; Prescription and Administration of Ivermectin. Amend RSA 318 by inserting after section 16-f the following new section:

318:16-g Prescription and Administration of Ivermectin. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of RSA 318:47-n are satisfied.

5 Effective Date. This act shall take effect 60 days after its passage.

STATE OF NEW HAMPSHIRE
OFFICE OF THE HOUSE CLERK

9/28/2021 11:15:01 AM
Roll Call Committee Registers Report

2022 SESSION

Health, Human Services and Elderly Affairs

Bill #: HB1022 **Motion:** OTPA **AM #:** 2022-0964h **Exec Session Date:** 3/7/2022

Members	YEAS	Nays	NV
Pearson, Mark A. Chairman	Y		
Layon, Erica J. Vice Chairman	Y		
McMahon, Charles E.	Y		
Acton, Dennis F.	Y		
Gay, Betty I.	Y		
Cushman, Leah P.	Y		
Folsom, Beth A. Clerk	Y		
Kelsey, Niki	Y		
King, Bill C.	Y		
Kofalt, Jim	Y		
DeLemus, Susan	Y		
Weber, Lucy M.		N	
~~MacKay, James R.~~ Rep. Freitas		N	
Snow, Kendall A.			A
Knirk, Jerry L.		N	
~~Salloway, Jeffrey C.~~ Rep Query		N	
Cannon, Gerri D.		N	
Nutter-Upham, Frances E.		N	
Schapiro, Joe		N	
Woods, Gary L.		N	
Merchant, Gary		N	
TOTAL VOTE:	11	9	

Rep. Cushman, Hills. 2
March 4, 2022
2022-0964h
12/08

Amendment to HB 1022

Amend the bill by replacing all after the enacting clause with the following:

1 New Section; Ivermectin; Dispensing. Amend RSA 318 by inserting after section 47-m the following new section:

318:47-n Ivermectin; Dispensing.

I. In this section, "standing order" means a written and signed protocol authored by one or more physicians licensed under RSA 329:12 or one or more advanced practice registered nurses licensed under RSA 326-B:18. Such agreement shall specify a protocol allowing the pharmacist licensed under RSA 318:18 to dispense ivermectin under the delegated prescriptive authority of the physician or advanced practice registered nurse, specify a screening protocol for each patient, specify a requirement to document screening performed and the prescription in the patient's medical record, and include a plan for referring for evaluation and treatment of adverse events. Any such prescription shall be regarded as being issued for a legitimate medical purpose in the usual course of professional practice.

II. Licensed pharmacists following standing orders may dispense ivermectin to persons in this state without a prior prescription. Pharmacies may charge a fee for consultation with the patient.

III. A pharmacist, pharmacy, physician, advanced practice registered nurse, or a medical facility that employs a pharmacist, physician, or advanced practice registered nurse issuing or following standing orders shall be prohibited from seeking personal financial benefit by participating in any incentive-based program or accepting any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

IV. A pharmacist, physician, or advanced practice registered nurse shall be held to the same standard of care as when prescribing and dispensing any other medication.

V. The pharmacist shall provide each recipient of ivermectin pursuant to this section with an information sheet written in plain language, which shall include, but is not limited to, potential adverse effects, drug interactions, Food and Drug Administration-approved indications for ivermectin use, the importance of follow-up care, and health care referral information.

VI. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of this section are satisfied. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an advanced practice registered nurse based on a

pharmacist's failure to follow standing orders provided the provisions of this section are satisfied. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of this section are satisfied.

2 New Section; Prescription and Administration of Ivermectin. Amend RSA 329 by inserting after section 1-h the following new section:

329:1-i Prescription and Administration of Ivermectin. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of RSA 318:47-n are satisfied.

3 New Section; Prescription and Administration of Ivermectin. Amend RSA 326-B by inserting after section 37 the following new section:

326-B:37-a Prescription and Administration of Ivermectin. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an advanced practice registered nurse based on a pharmacist's failure to follow standing orders provided the provisions of RSA 318:47-n are satisfied. .

4 New Section; Prescription and Administration of Ivermectin. Amend RSA 318 by inserting after section 16-f the following new section:

318:16-g Prescription and Administration of Ivermectin. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of RSA 318:47-n are satisfied.

5 Effective Date. This act shall take effect 60 days after its passage.

HOUSE COMMITTEE ON HEALTH, HUMAN SERVICES AND ELDERLY AFFAIRS

PUBLIC HEARING on Bill # HB1022

BILL TITLE: **An Act permitting pharmacists to dispense the drug Ivermectin by means of a standing order.**

DATE: **02/18/2022**

ROOM: **LOB 210-11** **Time Public Hearing Called to Order: 3:30pm**
Time Adjourned: 5:30pm

Committee Members: Reps. M. Pearson, Layon, Folsom, Acton, Cushman, Kelsey, B. King, Kofalt, MacKay, DeLemus, Wallner, Knirk, Salloway, Cannon, Schapiro, Woods and Merchant, Query

TESTIMONY

Representative Cushman introduced the bill.
- Safe use since 1988.
- multiple applications
- safer than any of the other drugs being used, even Tylenol
- covers more of the health issues related to Covid 19.

Dr. Paul Marik, Front Line Covid-19 Critical Care Alliance, support
- reviewed the prophylaxis & treatment protocols for Covid-19 - handout of slide presentation
- reviewed WHO uses of Ivermectin as an essential medicine
- discoverers of Ivermectin were awarded Nobel Prize in 2015 for their 1975 discovery
- FDA & CDC & Media wove a web of lies around Ivermectin
- Safe in 79 countries
- kills the covid19 virus
- is standing order the best vehicle to handle this
- pharmacist standing order with protocols set by physician is the safest way to obtain ivermectin
- safer than veterinarian grade
- safer than obtaining out of country
- who paid for you to come - self
- expand on the data from WHO
- discussion on validity of studies

Nick Perencevich, MD - opposed, self and NH Medical Society
- the protocols set in the law are good and signed consent
- concerned possible increase in complaints and lawsuits
- better standard of care
- would like to see these patients as part of a supervised study
- why have protocols for early treatment not been developed in NH
- Swedish model of registry

Rep. Nuniz, Pelham, self , support,
- Personal story, told to go home by dr and take Tylenol, telemedicine avenue used to get prescription and order filled and mailed to him.

Rep Knirk, Carroll 3, oppose

- disagrees with the validity of studies
- disagrees with masking problems
- what is the downside of the patient taking and it not working since there are no other early treatment protocols except Tylenol.
- If it is safe, shouldn't we leave it up to the patient.
- "standing order" medical provider writes an order that can be filled anytime during a set period of time, often 1 year.
- owners of pharmacy may choose not to stock
- there have been no safety signals in the studies as compared to other more common over the counter medications.
- no other alternatives being offered
- shouldn't those who can't take the vaccine for medical reasons have this as an option

Hon. Linda Rea Camarota, Bedford, self, support,
- Registered nurse, personal story, her physician was threatened with disciplinary action if he wrote script for ivermectin

Courtney Tanner, Dartmouth Hitchcock, opposed
- have not seen an internal policy not to prescribe
- since vaccines were rushed and long-term effects not known why not try something already proven safe - could not answer because she was a lawyer not a doctor

Paula Minnehan, NH Hospital Association, opposed
- medicare funds for covid patients
- wouldn't alternatives help lessen hospital overcrowding

Erin Fallon, Wolfeburo Falls, self, support
- this process is reminiscent of the work establishing treatment protocols for Lyme Disease
- ivermectin has a low risk profile and high efficacy

David DeWitt, Dublin, self, support,
- He is vaccinated as we are encouraged to do, but would still like to have the option because of the inefficiency of the vaccine

Ed Groves, Hookset, self, support
- Follow the money

Heather Mullens, Bennington, support
- Reporter - there is suppression of information in the media

Clara Combalisty, Rochester, self, support
- Project Veritas Reports

Karne Sweeting, Sanbornton, self, support
- COVID, Daystar.com

Dr. Nicole Schernell, Naturopath, support
- patient needs drove her to research, not confident in FDA

Respectfully submitted,

Rep. Beth Folsom, Clerk

SIGN UP SHEET

To Register Opinion If Not Speaking

Bill # HB1022 Date 1/18/22

Committee HHS

**** Please Print All Information ****

Name	Address	Phone	Representing	Pro	Con
Rep. Jeanine Notter			Hills 21	X	
Rep. Susan C. DeLemus			Rochester 24	X	
Rep Glenn Cordelli			Carroll 4	✓	
REP TONY LEKAS			HILLS 37	✓	
REP ALICIA LEKAS			HILLS 37	✓	
Rep Aidan Ankarberg			Strafford 10	✓	
Rep Marsh			Carroll 8		X
Alvin See	London		Self	✓	
Laura El-Azem	Londonderry			✓	
Hon Linda Rea Camarota			Self	✓	
REP. JOHN POTUCEK			Rock 6	X	
Rosemary Landry			Meredith	✓	
Betty Gay				✓	
Deb Hobson			Rock 35	✓	
CHAU KELLEY	Hooksett		Self	✓	
DAVID DEWITT	22 GREENWOOD RD. DUBLIN NH		SELF	✓	
Elizabeth Sargent, NH Pharmacists Association					X
Elizabeth Sargent, NH Society Health System Pharmacists					X
Pam DiNapoli	NH Nurses Association				X
Melissa Blasek			Hills 21	✓	
Hon Linda Rea Camarota			Self	✓	
Julie Smith			Self	X	

JERRY BRUNELL London Self X

(OVER)

HB 1022

			Favor	Con
Rep Jess Edwards Rock Dist 4				
Shannon McGinley	4 Balsam Court, Bedford	Self	✓	
Gary York, MD	Hopkinton		X	
Tony Fallon (Anthony)	Wolfeboro Falls PO Box 407	03896 (603) 269-3206	✓	

House Remote Testify

Health, Human Services and Elderly Affairs Committee Testify List for Bill HB1022 on 2022-01-18

Support: 389 Oppose: 323 Neutral: 1 Total to Testify: 0

Export to Excel

Name	City, State Email Address	Title	Representing	Position	Testifying	Non-Germane	Signed Up
Plummer, Cassie	Nashua, NH casplummer9@gmail.com	A Member of the Public	Myself	Support	No	No	1/14/2022 9:50 AM
Anastasia, Patricia	Londonderry, NH patti.anastasia@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/14/2022 4:02 PM
Smith, Julie	Nashua, NH cantdog@comcast.net	A Member of the Public	Myself	Support	No	No	1/14/2022 4:50 PM
White, Robert	Merrimack, NH white14@comcast.net	A Member of the Public	Myself	Support	No	No	1/14/2022 6:04 PM
Griffin, Amy	Loudon, NH Nhkick@aol.com	A Member of the Public	Myself	Support	No	No	1/14/2022 8:30 PM
Mercer, Jennifer	Loudon, NH cjmercer@myfairpoint.net	A Member of the Public	Myself	Support	No	No	1/14/2022 8:32 PM
Courchaine, Sarah	SANBORNTON, NH simplybalanced@yahoo.com	A Member of the Public	Myself	Support	No	No	1/14/2022 11:29 PM
Cembalisty, Clara	Rochester, NH Cqsc43@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 2:02 AM
Cavaretta, John	Chester, NH Johncav@comcast.net	A Member of the Public	Myself	Support	No	No	1/15/2022 5:54 AM
Lupoli, Shawna	Milford, NH shawna75@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 6:26 AM
McDowell, Karen	Gilford, NH Karen.l.mcdowell66@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 9:04 AM
Weston, Joyce	Plymouth, NH jweston14@roadrunner.com	An Elected Official	Myself	Oppose	No	No	1/15/2022 9:53 AM
Neskey, Jessica	Raymond, NH Jmneskey@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 10:47 AM

Manney, Jeanne	Goffstown, NH Thekingswife@comcast.net	A Member of the Public	Myself	Support	No	No	1/15/2022 10:58 AM
Smith, Edward	Hillsborough, NH edsplace5@tds.net	A Member of the Public	Myself	Support	No	No	1/15/2022 11:26 AM
Tower, Sharon	Litchfield, NH Shoosh414@comcast.net	A Member of the Public	Myself	Support	No	No	1/15/2022 12:28 PM
Hohmeister, Julie	Bethlehem, NH jhohmeister@roadrunner.com	A Member of the Public	Myself	Oppose	No	No	1/15/2022 12:30 PM
Romano, Leane	Litchfield, NH Leaneari@hotmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 3:00 PM
Romano, Stephen	Litchfield, NH Allpro@allpromoversnh.com	A Member of the Public	Myself	Support	No	No	1/15/2022 3:45 PM
Riel, Jennifer	Barnstead, NH Jenniferlriel@yahoo.com	A Member of the Public	Myself	Support	No	No	1/15/2022 3:51 PM
Brisson, Angel	Manchester, NH Angelbrisson72@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 4:52 PM
Brisson, David	Manchester, NH Overmann@comcast.net	A Member of the Public	Myself	Support	No	No	1/15/2022 4:54 PM
Sartin, Marty	Nottingham, NH Martysartin@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 4:59 PM
Glass, Jonathan	Cornish, NH jglass1063@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/15/2022 5:01 PM
Potter, Karen	Concord, NH j_k_potter@comcast.net	A Member of the Public	Karen Potter	Oppose	No	No	1/15/2022 5:04 PM
Anderson, Shayla	Merrimack, NH Shaylan85@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 6:26 PM
Carignan, Sherry	Derry, NH Sherrycarignan@yahoo.com	A Member of the Public	Myself	Support	No	No	1/15/2022 6:46 PM
Pepin, Maurene	Pelham, NH Mpepin1031@yahoo.com	A Member of the Public	Myself	Support	No	No	1/15/2022 6:55 PM
Camarota, Hon. Linda Rea	Bedford, NH repcamarota@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 7:01 PM
Hall, Hilary	Salem, NH Hil.faye@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 7:08 PM
Neskey, Aaron	Raymond, NH Alneskey@gmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 7:41 PM

West, Daniele	Wakefield, NH danielebardsley@yahoo.com	A Member of the Public	Myself	Support	No	No	1/15/2022 8:48 PM
Whissel, Michele	Merrimack, NH Shellytal@hotmail.com	A Member of the Public	Myself	Support	No	No	1/15/2022 9:10 PM
Imgrund, Steve	Hopkinton, NH s.imgrund@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:13 AM
Bannister, Kristen	Manchester, NH klb5551@msn.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:16 AM
Kneissl, Ursula	Bedford, NH Ursula.kneissl@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:18 AM
Dewar Lane, Jennifer	Bow, NH dewarj2003@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:18 AM
Schwarz, Adam	Etna, NH Adam.schwarz@hanovercontinuityclinic.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:21 AM
Nackman, Louis	Londonderry, NH lnackman@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:23 AM
Payton, Jessica	Keene, NH, NH jpayton@cheshire-med.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:26 AM
Medlicott, Alex	Piermont, NH ampluskm1@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:27 AM
Tedcastle, Jennifer	Barnstead, NH jtedcastle@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:28 AM
Young-xu, Sarah	Haverhill, NH Syoungxu@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:29 AM
DiSilva, Allyson	Amherst, NH allysondisilva@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:31 AM
Grady, Samuel	Brentwood, NH Samuel.r.grady@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:40 AM
Peck, Brandon	Stratham, NH brandonwpeck@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:44 AM
Langerman, Fawn	North Conway, NH bikecamphikegirl@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:55 AM
Hou, Irene	Bow, NH iorzano@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:03 AM
Evans, Jenny	Fremont, NH jamoulton23@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:06 AM

Flanigan, Dr Alan	Manchester, NH aflanigan@usacs.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:13 AM
Hamer, Heidi	Manchester, NH heidi.hamer@leg.state.nh.us	An Elected Official	Myself	Oppose	No	No	1/16/2022 8:14 AM
Maxwell, leisa	Hudson, NH leisa03@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:35 AM
Clem, Kathleen	Lebanon, NH drkclem@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:36 AM
Stabile, Jonathan	East Kingston, NH Jonathan.stabile@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:38 AM
Eddinger, Jonathan	Amherst, NH eddinj@msn.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:43 AM
Levy, Campbell	Hanover, NH lcampbelllevy@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:46 AM
Fernandez, Angel	Bedford, NH aaf.segura@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:48 AM
Hamer, Gary	Manchester, NH ghamer@mansd.org	An Elected Official	Myself	Oppose	No	No	1/16/2022 8:51 AM
Hamer, Geoff	Manchester, NH geoffh87@aol.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:52 AM
Hofley, Pamela	Bow, NH hofley@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:53 AM
Dupuis, Keren	Gilford, NH Kd_nh17@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 8:55 AM
Calderwood, Audrey	Hanovet, NH Audrey.h.calderwood@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:56 AM
Ullal, Ritu	Hollis, NH Rituguptaullal@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:58 AM
Rothstein, Richard	Hanover, NH Richard.I.Rothstein@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:00 AM
Drinane, Mary	Hanover, NH drinamvt@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:02 AM
Parker, Siddhartha	Hanover, NH syparker@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:10 AM
Jones, MD, MPH, Steven	Exeter, NH stevenclarkjones@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:11 AM

Winter, Michael	Etna, NH mwinter21@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:12 AM
Smith, Michael	Windham, NH medic218@hotmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 9:42 AM
Sandberg, Betsy	Durham, NH bsandberg@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:51 AM
Crocker, Nancy	Grantham, NH NancyCrocker79@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:04 AM
Mitchell, Margaret	Concord, NH Mamitchell9@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:05 AM
Iber, Leigh	Manchester, NH Leigh.iber@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:10 AM
Williams, Linda	Bedford, NH linda.williams@snhhs.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:21 AM
Atwell, Alex	Bedford, NH alexandjune@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:30 AM
Gordon, Stuart	Lebanon, NH stuart.r.gordon@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:44 AM
Cullen, Mary	Manchester, NH mcullen@amoskeaghealth.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:54 AM
Siegel, Corey	Hanover, NH Corey.a.siegel@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 11:26 AM
Sturgis, Cheryl	East Thetford, VT cheryl.a.sturgis@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 11:42 AM
Korn, Leonard	New Castle, NH lenkorn.md@gmail.com	A Member of the Public	Myself and the New Hampshire Medical Society	Oppose	No	No	1/16/2022 11:51 AM
Sarkis, Marlene	North Haverhill, NH msarkis55@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 12:21 PM
Lamb, Ashley	Durham, NH campioa@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 12:27 PM
Klunk, L. John	Bow, NH lklunk@elliot-hs.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 12:46 PM
Licciardi, Kimberly	Bedford, NH truaxk@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 1:00 PM
Neilley, Dr. Gregory	Francestown, NH neilley@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 1:18 PM

Dunlap, Elisabeth	Lisbon, NH dunlapme@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 1:41 PM
Thomas, Elaine	Nashua, NH thomas.marshall@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 1:42 PM
Palmer, William	Cornish, NH wspalmer56@gmail.com	A Member of the Public	Myself and the New Hampshire Chapter of the American Vollege of Physicisns	Oppose	No	No	1/16/2022 2:05 PM
Kaploe, Michael	Milford, NH Michael.D.Kaploe@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/16/2022 2:09 PM
Fisk, Marianne	Concord, NH venus3463@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 2:16 PM
Matos, Michael	Wolfeboro, NH mikematos1969@yahoo.com	A Member of the Public	Myself and my patients at Wolfeboro Pediatrics in Wolfeboro	Oppose	No	No	1/16/2022 2:29 PM
Martin, Anysia	Amherst, NH nysi.martin@me.com	A Member of the Public	Myself	Support	No	No	1/16/2022 3:44 PM
Manuse, Andrew J	Derry, NH amanuse@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 3:50 PM
Berg, Angela	Manchester, NH apalm12@aol.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:00 PM
Pouliot, Cheryl	West Lebanon, NH pouliotcheryl@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:01 PM
Grenier, J	Nashua, NH Jgren124@icloud.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:10 PM
Takekoshi, Christy	Manchester, NH cetakekoshi@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:14 PM
kirsch, walter	warner, NH kirschwalterf@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:15 PM
Schultze, Pamela	Dover, NH Schultzep@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 4:16 PM
Beatrice, Donna	Nashua, NH dbjb1314@comcast.net	A Member of the Public	Myself	Support	No	No	1/16/2022 4:17 PM
Brown, Kathleen	Acworth, NH brown57kat@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:23 PM
Pumilia, MaryAnn	Laconia, NH mpumilia@frontiernet.net	A Member of the Public	Myself	Support	No	No	1/16/2022 4:25 PM
Jellison, Catherine	Amherst, NH cathyjello@comcast.net	A Member of the Public	Myself	Support	No	No	1/16/2022 4:27 PM

Beatrice, John	Nashua, NH starkave1964@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:35 PM
Fenner-Lukaitis, Elizabeth	Warner, NH glukaitis@mcttelecom.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 4:37 PM
Doughty, Patrick	Bethlehem, NH patrickdoughty@roadrunner.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:42 PM
Ward, Deborah	Monroe, NH hdward@hotmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:46 PM
Ward, Bryan	Monroe, NH mtvfarm75@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:46 PM
DeBourke, Sheana	Merrimack, NH sheanaalanna@hotmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 4:47 PM
Fleischman, Marianne	Concord, NH marianne@fleischman.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 4:48 PM
SKIDMORE, CLARENCE	BROOKLINE, NH ashskidmore@charter.net	A Member of the Public	Myself	Support	No	No	1/16/2022 4:53 PM
Collison, Daniel	Hanover, NH dan.collison@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 5:04 PM
Pollak, Tracy	Northwood, NH tpollak@metrocast.net	A Member of the Public	Myself	Support	No	No	1/16/2022 5:04 PM
Loew, jenny	Windham, NH jeloew@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:06 PM
Rearick, Ellen	NASHUA, NH emrearick@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 5:07 PM
Howland, Curtis	Manchester, NH howland@priss.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:14 PM
Williams, Bill	Tilton, NH pb@pagweb.org	A Member of the Public	Myself	Support	No	No	1/16/2022 5:17 PM
Rivera, Marilyn	Strafford, NH mari0831@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:35 PM
Rivera, Jose	Strafford, NH marilyn.serviceprovider@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:36 PM
Kaminski, Marie	Bridgewater, NH Martkam4492@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:42 PM
O'Connell, Sabrina	Nashua, NH thelightindarkness@msn.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:44 PM

Enos, Liz	Litchfield, NH pwrmine@aol.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:45 PM
O'Connell, Caley	Nashua, NH cs3vcz@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:47 PM
Guven, Taci	Windham, NH taci.guven@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:58 PM
Leggett, Liz	Litchfield, NH pwrmine@aol.com	A Member of the Public	Myself	Support	No	No	1/16/2022 5:58 PM
Howes, Linda	Springfield, NH 4lindahowes@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 6:08 PM
Tyszka, Matthew	Newport, NH mattcol@aol.com	A Member of the Public	Myself	Support	No	No	1/16/2022 6:18 PM
Womack, Kevin	Concord, NH Hislighthouse77@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 6:22 PM
Leone, John	Danbury, NH FreeLion2@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 6:53 PM
Fraysse, Michael	Epsom, NH mikefraysse@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:00 PM
Couture, Geraldine	RYE, NH gacouture@aol.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:12 PM
Richard, Mark	Hampstead, NH mbrichard@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:14 PM
Leone, Rose	Danbury, NH rosurple50@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 7:15 PM
Hanley, Thea	Raymond, NH thea_beans@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 7:25 PM
Lamalfa, Paul	Londonderry, NH pslamalfa@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 7:26 PM
Darrow, Linda	Ctr. Barnstead, NH lindard.1956@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 7:28 PM
Goldblatt, Warren	Dover, NH wgoldblatt@eyesightnh.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 7:42 PM
Finke, Erin	Greenville, NH finkee@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 7:50 PM
Leavitt, Mary	Strafford, NH Leavittmary91@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 7:51 PM

Schertell-Crigger, Nicole	Stratham, NH Drschertell@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 8:15 PM
Haidaichuk, Cheri	Goffstown, NH cheri@bmhitsolutions.com	A Member of the Public	Myself	Support	No	No	1/16/2022 8:16 PM
Peters, Newton	Portsmouth, NH paean.handsaw_0z@icloud.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:16 PM
Edwards, Patricia	Bow, NH drpatedwards@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 8:24 PM
Gamache, Julia	Londonderry, NH baumshel1@aol.com	A Member of the Public	Myself	Support	No	No	1/16/2022 8:31 PM
Donovan, Barbara	Deerfield, NH bjdonovan@metrocast.net	A Member of the Public	Myself	Support	No	No	1/16/2022 8:33 PM
graustein, alan	Sanbornton, NH alangraustein@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 8:34 PM
Wuelper, Rep Kurt	Strafford, NH kurt.wuelper@leg.state.nh.us	An Elected Official	Strafford 3	Support	No	No	1/16/2022 8:48 PM
Husarik, Nancy	Candia, NH nhusarik@me.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:02 PM
Faulkner, Nathan	Hopkinton, NH Natty8788@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/16/2022 9:15 PM
Gladstone, Gwendolyn	Exeter, NH WAGladstone@comcast.net	A Member of the Public	The New Hampshire Chapter of the American Academy of Pediatrics	Oppose	No	No	1/16/2022 9:44 PM
Schertell, John	Hampton, NH johnschertell@aol.com	A Member of the Public	Myself	Support	No	No	1/16/2022 9:46 PM
Haas, Amy	Nashua, NH amylouisehaas@hotmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 9:48 PM
Tuthill, Jennifer	Somersworth, NH Psychokatz@comcast.net	A Member of the Public	Myself	Support	No	No	1/16/2022 10:13 PM
Stuart, Andrea	Hampton, NH Andilandangel@icloud.com	A Member of the Public	Myself	Support	No	No	1/16/2022 10:16 PM
Tuthill, William	Somersworth, NH Wtuthill@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 10:20 PM
Katz, Aaron	Somersworth, NH Katza9961@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 10:34 PM
Stevenson, Janet	Gilsum, NH Janet.Stevenson50@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 10:36 PM

Smith, Ken	Strafford, NH kens7454@gmail.com	A Member of the Public	Myself	Support	No	No	1/16/2022 10:44 PM
Dolkart, Kenneth	Grantham, NH kenneth.dolkart@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/16/2022 10:48 PM
Cooper, Carlton	Rochester, NH cwcooper20@yahoo.com	A Member of the Public	Myself	Support	No	No	1/16/2022 10:50 PM
Delano, Janie	hudson, NH tadandpole4@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 2:52 AM
Skinner, Paula	Hudson, NH pskinforte@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:27 AM
Hubbard, Samantha	Lyman, NH Shubbard2819@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:59 AM
Bettencourt, Nicole	Northwood, NH Nicolebettencourt@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:34 AM
Miller, Rebecca	Albany, NH Rebeccamillernh@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:46 AM
glidden, deborah	alexandria, NH moosepathfarmstainedglass@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:59 AM
Connelly, Dianne	Merrimack, NH di.connelly@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 6:52 AM
Connelly, James	Merrimack, NH jim_connelly@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 6:56 AM
Fetter, Jeffrey	Concord, NH Jfettermd@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:06 AM
Wazir, Safiya	Concord, NH S.wazir@leg.state.nh.us	An Elected Official	Myself and my constituents	Oppose	No	No	1/17/2022 7:09 AM
Burt, Phyllis	Goffstown, NH pmburt@yahoo.com	A Member of the Public	myself	Support	No	No	1/17/2022 7:14 AM
Taylor, Holly	Hanover, NH holly.a.taylor@dartmouth.edu	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:16 AM
Goodhue, Susan	Barrington, NH Sgoodhue94@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:24 AM
Mazur, Brian	Goffstown, NH bmazur1776@protonmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:44 AM
Pschirrer, Elizabeth	Hanover, NH e.rebecca.pschirrer@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:49 AM

Barber, Pamela	Dover, NH Pfrenchbarber@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:53 AM
Boos, Susan	Dover, NH susanboos@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 7:54 AM
McGinley, Shannon	Bedford, NH s.mcginley@icloud.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:55 AM
Avery, Tara	Hill, NH tavery313@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:11 AM
Berling, Mark	Auburn, NH MB58197@protonmaill.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:12 AM
Beaudoin, Bret	Concord, NH bret8888@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:23 AM
ANGELIS, CHERYL	SALEM, NH cangelis_alt@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:33 AM
CONCORDIA, NICOLE	TEMPLE, NH nconcordia@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:35 AM
Swain, Christine	Chichester, NH Christined3071@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:35 AM
Doherty, David	Pembroke, NH ddoherty0845@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:36 AM
Higgins, Sandra	Windham, NH Slhiggins@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 8:38 AM
Noyes, Cynthia	Chichester, NH Cnoyes212@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:43 AM
Funnell, Margaret	Grantham, NH mfunnell62@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:47 AM
Manning, Trish	Hampton, NH tmanning3@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:58 AM
Foss, Darlene	CHICHESTER, NH darlenemarie@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 9:02 AM
Stone, Jennifer	Dover, NH jenstone01@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:12 AM
Hatfield, Tara	Dover, NH tlhatfield@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:17 AM
Carlson, Helen	Exeter, NH Watercolorist2@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 9:19 AM

DiNapoli, Pamela	Concord, NH nhna.ned@gmail.com	A Member of the Public	NH Nurses Association	Oppose	No	No	1/17/2022 9:19 AM
Whitcomb, Jon	Chichester, NH Jon.whitcomb@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:19 AM
Cooper, Levi	Chichester, NH Clevi5384@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:20 AM
Hodges, Amanda	Milford, NH Hodges_a@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:23 AM
Zabkar, Debbie	Milton, NH Luvnituphere@msn.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:27 AM
Bates, David	Warner, NH dbates3@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:30 AM
Gladders, Barbara	NEW LONDON, NH bharriso98363@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:37 AM
Roy, Lucy	North Hampton, NH Bikeerz@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 9:39 AM
Millet, Daniel	Berlin, NH dan@ipodfixit.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:45 AM
Sylvain, Barbara	Tilton, NH Brbsalem@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:48 AM
Young, Susan	Alton Bay, NH snewco@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:48 AM
Stone, Richard	Dover, NH scottandjen99@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:51 AM
DONOFRIO, JENNIFER	MANCHESTER, NH jdonofrio@manchesterob.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 10:05 AM
Perkins, Caryn	Derry, NH carynperkins6@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:07 AM
harris III, delbert	bradford, NH sonny@thecblife.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:07 AM
Gagner, Tracey	Albany, NH traceyap@twc.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:09 AM
S, Julie	Newport, NH Jpmom39@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:09 AM
Trexler, Larisa	Stoddard, NH trexlah@icloud.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:22 AM

Dewey, Karen	NEWPORT, NH pkdewey@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 10:23 AM
Trexler, Ryan	Stoddard, NH trexlers@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:23 AM
Pedone, Jennifer	Manchester, NH jennapedone@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:24 AM
Cumbee, Lydia	FRANCONIA, NH lydiac7@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:40 AM
Rousseau, Michael	North Hampton, NH Mike@mrhomeimprovements.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:42 AM
Thyng, Jonathan	Hollis, NH jonthyng@charter.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 11:02 AM
Gibadlo, Robert	Farmington, NH bobbyg89@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:07 AM
Rosentrater, Donna	Salem, NH donna.rosentrater@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:09 AM
Rosentrater, Robert	Salem, NH bob.rosentrater@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:10 AM
Smith, Carla	Fremont, NH tsmith1992@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 11:13 AM
Lindpaintner, Lyn	Concord, NH lynlin@bluewin.ch	A Member of the Public	Myself	Oppose	No	No	1/17/2022 11:13 AM
Blanchard, Sandra	Loudon, NH sandyblanchard3@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 11:19 AM
Brock, Mary	Laconia, NH mbrock1660@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:29 AM
winter, nitzah	Etna, NH nitzah.winter@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 11:34 AM
Cambrils, Jose	Loudon, NH Jose4NH@comcast.net	An Elected Official	Myself	Support	No	No	1/17/2022 11:37 AM
Heath, Mary	Manchester, NH m.heath@comcast.net	An Elected Official	Myself	Oppose	No	No	1/17/2022 11:43 AM
Saba, Robin	Candia, NH rbrooks230@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:51 AM
harris, delbert	bradford, NH sonny@thecblife.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:01 PM

Cedolin, Alexandra	Epping, NH Ahwhyte@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:05 PM
Fogel, Erin	Bow, NH esfogel@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 12:05 PM
Cedolin, Bradley	Epping, NH Bbcedolin@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:05 PM
Brock, Kennith	Laconia, NH kbrock2638@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:08 PM
Lorette, Connie	Derry, NH conniechris1212@icloud.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 12:10 PM
Stoddard, Kristine	Bow, NH kstoddard@bistatepca.org	A Lobbyist	Bi-State Primary Care Association	Oppose	No	No	1/17/2022 12:21 PM
Torpey, Jeanne	Concord, NH jtorp51@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 12:21 PM
Wilson, Audra	Alstead, NH h3islife@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:23 PM
Wilson, Rock	Alstead, NH fullermachine@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 12:24 PM
Salamanca, David	Salem, NH pzzboy1@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 12:26 PM
LOZITO, PATRICK	Claremont, NH patlozito@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:31 PM
LOZITO, Viola Marie	Claremont, NH vmarielozito@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:33 PM
Weber, Jill	Mont Vernon, NH jill@frajilfarms.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 12:42 PM
Clough, Julie	Nashua, NH clough.julie@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 12:57 PM
Beltre, Jo Ann	Brentwood, NH jo.beltre@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 12:58 PM
Clough, Scott	Nashua, NH scottrangerclough@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:00 PM
Cerrato, Kerri	Bedford, NH Klcerrato16@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:00 PM
LaPointe, Susan	Epping, NH suelap16@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:05 PM

Whitaker, Frances	Manchester, NH fmwhitaker@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 1:09 PM
Hayward, Marcia	Laconia, NH mjhayward131@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 1:10 PM
Oxenham, Lee	Plainfield, NH leeoxenham@comcast.net	An Elected Official	Myself	Oppose	No	No	1/17/2022 1:16 PM
Salemi, Heather	Nashua, NH Hjksalemi@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:23 PM
Preston, Patricia	Nashua, NH prestonpatty15@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:33 PM
Zeichick, Angela	Nashua, NH Amzeichick3@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:35 PM
schade, catherine	Bedford, NH kate.schade5@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:37 PM
Carpenter, Penny	Raymond, NH pcarp2627@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:48 PM
Collins, Kelly	Hancock, NH kellyanncollins@live.com	A Member of the Public	Myself	Support	No	No	1/17/2022 1:51 PM
DHemecourt MD, Andre	Concord, NH adhemecour@aol.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 1:53 PM
Szal, Mark	Bow, NH mszal@cecnh.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 1:55 PM
heath, harley	wolfeboro, NH hheath@hugginshospital.org	A Member of the Public	Myself	Oppose	No	No	1/17/2022 1:58 PM
Imgrund, Donna	Hopkinton, NH dimgrundrn@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 2:00 PM
Windt,MD, Mark	East Kngston, NH mwindtmd@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 2:05 PM
Almy, Susan	Lebanon, NH susan.almy@comcast.net	An Elected Official	Myself	Oppose	No	No	1/17/2022 2:11 PM
Timmins, Courtney	Belmont, NH cst610@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 2:19 PM
Timmins, Jeremiah	Belmont, NH kaiheitai@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 2:20 PM
Hillis, John	Hooksett, NH jhillis@BasicISP.net	A Member of the Public	Myself	Support	No	No	1/17/2022 2:20 PM

Hillis, Rebecca	Hooksett, NH jhillis@basicISP.net	A Member of the Public	Myself	Support	No	No	1/17/2022 2:22 PM
Campion, Polly	Etna, NH pollykcampion@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 2:28 PM
Carter, Kathleen	Meredith, NH kcarter52@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 2:29 PM
Kishinevsky, Rebecca	Wilton, NH rp.kishinevsky@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 2:46 PM
kelleher, Laurie	North Hampton, NH laurie.kelleher@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 2:57 PM
Maguire, Donna	North Hampton, NH dmaguire100@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 2:59 PM
Salafia, Matthew	Bedford, NH msalafia@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:03 PM
McClennen, Sarah P	North Woodstock, NH sarah@feelpeaceful.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:08 PM
Dyer, John	Stratham, NH jock1943@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:11 PM
Mahoney, Elisabeth	North Haverhill, NH Calgonnow13@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:30 PM
Chuk, Amanda	Enfield, NH acchuk@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 3:42 PM
Kepich, Jenna	Manchester, NH jkepich@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:47 PM
Carlton, Tonya	Lee, NH tonya@mvst.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 3:48 PM
Burris, David	Center Barnstead, NH davidburris79@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:52 PM
Noyes Jr, Charles	Nottingham, NH rote.that_0q@icloud.com	A Member of the Public	Myself	Support	No	No	1/17/2022 3:57 PM
Dontonville, Roger	Enfield, NH rdontonville@gmail.com	An Elected Official	Myself	Oppose	No	No	1/17/2022 4:00 PM
Paladino, Mina	Sunapee, NH mina.paladino@luxsci.net	A Member of the Public	Myself	Support	No	No	1/17/2022 4:03 PM
Hagenow, Janice	Warner, NH lovestodance40@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:15 PM

Reed, Sarah	Concord, NH stubbs.saraha@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:17 PM
White, Melissa	Peterborough, NH marino_melissa@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:18 PM
Marino, John	PETERBOROUGH, NH techlon11@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:18 PM
Reed, William	Concord, NH willie.b.reed@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:19 PM
Porter, Jandee	Acworth, NH jandeeporter@live.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:19 PM
Dudak, Breanna	Marlow, NH bdudak8820@icloud.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:20 PM
Dudak, Colemann	Marlow, NH dudak93@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:20 PM
Davidson, Suellen	Hollis, NH suellendavidson@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 4:22 PM
Kingsley, Christine and Scott	Gilford, NH chris0605@metrocast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 4:24 PM
Lord, Mark	Raymond, NH sirmalord-1@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 4:38 PM
Dolpies, Michael	Northfield, NH mdolpies@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:45 PM
Miller, MPH, Patrick	Campton, NH perogroup@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 4:45 PM
Thibodeau, Marie	Nashua, NH scr.hrt4me@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:48 PM
Ferrantello, Anthony	Keene, NH ajfnino@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 4:54 PM
Smith, Sara	Pembroke, NH sara.rose.ssmith@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 4:58 PM
Theriault, Robert	Barrington, NH rhtheriaultjr@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 5:02 PM
Ballentine, John	Nashua, NH mikeb@btine.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 5:10 PM
Wooten, Kristine	New London, NH kwooten@kearsarge.org	A Member of the Public	Myself	Support	No	No	1/17/2022 5:15 PM

Sheehan, Vanessa	Milford, NH vanessa@vanessa4nh.com	An Elected Official	Hillsborough 23 (Milford)	Support	No	No	1/17/2022 5:24 PM
Janiak, Stephanie	Hollis, NH woodsorrel07@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:31 PM
Dyer, Jane	Stratham, NH Janed1947@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:38 PM
Thibodeau, Frank	Nashua, NH frankthibodeau79@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:40 PM
Schwab, Rebecca	Concord, NH rebecca.schwab@protonmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:44 PM
Fontaine, Leandra	Pittsfield, NH angovemom4@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:44 PM
Griffin, Lee	Hampton, NH lgriffin236@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:44 PM
Early, Robert	Amherst, NH b_early@myfairpoint.net	A Member of the Public	Myself	Support	No	No	1/17/2022 5:45 PM
Aranzabal, Luis	Milford, NH Luisaranzabal40@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 5:46 PM
Hardy, Maureen	Londonderry, NH Meaux61@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 5:49 PM
perez, maria	milford, NH mariaeli63@gmail.com	An Elected Official	Myself	Oppose	No	No	1/17/2022 5:50 PM
STARRING, JAN	LITTLETON, NH janstarring70@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 5:57 PM
McBride, Rose	MEREDITH, NH mcbdrose@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:00 PM
Mohan, Kim	Meredith, NH kimmohan@nhnpa.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 6:01 PM
Marshall, Greg	Seabrook, NH g.37.marshall@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:07 PM
Francoeur, David	Bedford, NH Twbridge@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 6:07 PM
Forbes, Alan	Portsmouth, NH alanforbes@outlook.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:13 PM
Francoeur, Karin	Bedford, NH Livinglifeopps@ymail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:14 PM

Brough, J	New Hampton, NH mmiw@live.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:22 PM
Griffin, Sylvia	Hampton, NH Sylviaandleegriffin@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:22 PM
McClure, Dawn	Amherst, NH jdmacnh@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:40 PM
Odom, Judith	Bow, NH judyodom@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 6:40 PM
Rigazio, Sandra	Goffstown, NH newbeginning2@hushmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:45 PM
Mayo, Kathy	NOTTINGHAM, NH kathymayo2013@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 6:58 PM
Lafferty, Nancy	Windham, NH Nancymgr8ce@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:00 PM
Lalone, Edward	Epping, NH LaLone.Edward@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 7:02 PM
Tucker, Katherine	Wilmot, NH katherine.s.tucker@valley.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:13 PM
Tyner, Robin	Exeter, NH rd.tyner88@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:13 PM
Oxenham, Evan	Plainfield, NH evan.oxenham@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:15 PM
Desmarais, Diane	Goffstown, NH dianedes2565@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:17 PM
Dignam, Mike	Hampton, NH mgd7474@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:20 PM
Nelson, Elizabeth	Derry, NH BethDavid@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:26 PM
Dontonville, Anne	Enfield, NH Ardontonville@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:28 PM
Gamache, Beverly	Hampton, NH bkgamache@outlook.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:30 PM
Cushman, Stephen	Weare, NH cstephen521@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:36 PM
Brennan, Nancy	Weare, NH burningnan14@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:38 PM

Corell, Elizabeth	Concord, NH Elizabeth.j.corell@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:39 PM
Allard, David	Exeter, NH Daveallard@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:40 PM
Fleming, Jennifer	Dunbarton, NH Jlfaesthetics@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:45 PM
Jorgensen, Patricia	NORTHFIELD, NH yellaboat@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:46 PM
Preble, Melissa	Antrim, NH mdnatr@tds.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:49 PM
Pauer, Rep. Diane	Brookline, NH diane.pauer@leg.state.nh.us	An Elected Official	Myself	Support	No	No	1/17/2022 7:53 PM
Allard, Linda	Exeter, NH Lindaallard@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:54 PM
Arcaro, Harold	Portsmouth, NH judge@nesystems.us	A Member of the Public	Myself	Support	No	No	1/17/2022 7:55 PM
Thompson, Janna	Loudon, NH Jannathompson2001@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:55 PM
Wood, Sarah	Stratham, NH Sarah.Elizabeth.lennon@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 7:57 PM
Scammon, Lara	Dover, NH dscammon@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 7:58 PM
Towle, Jennifer	Bow, NH jennifer.towle@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:00 PM
Wolfe, Melinda	Dunbarton, NH wolferatt@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:03 PM
Garland, Ann	LEBANON, NH annhgarland@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:06 PM
Wright, Jennifer	Rumney, NH Jennifer.a.wright@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:06 PM
Deschenes, Susan	Loudon, NH Susan.deschenes79@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:06 PM
Genovese, Kristina	Swanzey, NH Tghiker@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:06 PM
O'CONNOR, Patricia	New London, NH patkatiejesskev@msn.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:06 PM

Rojas, Cali	Manchester, NH Calianne321@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:07 PM
Pappal, Patricia	Hudson, NH pat@pappals.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:07 PM
Walston, Robin	Stratham, NH Robinwalston@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 8:08 PM
sullivan-congdon, Scott	merrimack, NH smcongdon@crimson.ua.edu	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:09 PM
Jankins, Christine	Portsmouth, NH christinejankins@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:09 PM
Prazar, Karen	Nottingham, NH kprazar@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:09 PM
Wilson, Nancy	Concord, NH nancawilson@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:09 PM
Pierce, Stephanie	Webster, NH stephanie_pierce@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:09 PM
Dombrowski, Roxanne	Concord, NH roxyski@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:10 PM
Fay, Chris	Litchfield, NH loyalx3@aol.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:13 PM
Surman, Janet	Spofford, NH vjsblues@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:13 PM
Rojas, Emily	Manchester, NH Emilyrojas27@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:15 PM
Ainslie, Marcy	Wilton, NH marcy.ainslie@unh.edu	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:17 PM
Saracino, Pharm.D, Dr. Michael	Claremont, NH drchike@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:18 PM
Avard, Paul	Wolfboro, NH pavard1@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:18 PM
LaBrie, Pierre	Hooksett, NH Pitlabrie@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:21 PM
Cool, Michelle	Nashua, NH michellecool.nh@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:21 PM
Hauschel, Acksone	Newmarket, NH acksones@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:22 PM

Coffey, Courtney	Hampton, NH Courtgould91@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:24 PM
Tamposi, Robert	Nashua, NH tamposirobert@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:24 PM
DeCaprio, Mike	Kensington, NH Mikedecaprio@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 8:25 PM
Brennan-Mungovan, Brooke	Nashua, NH Bam.mungo@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:28 PM
Grant, Donna	Manchester, NH dgrant282325@msn.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:28 PM
Lev Hod, Hila	Goffstown, NH hilalh@hushmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:29 PM
Sheldon, Lisa	Center Harbor, NH lisakennedysheldon@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:30 PM
Napoli, Jonathan	Goffstown, NH Napolirx@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:32 PM
Smith, Megan	lebanon, NH megan@themonahans.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:35 PM
Moulton, Amanda	Sandown, NH Balancedmamaof2@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:37 PM
Newman, Rick	Nottingham, NH rick@ricknewman.com	A Lobbyist	NH Independent Pharmacy Association	Support	No	No	1/17/2022 8:37 PM
Yehling, Hilary	Auburn, NH hilary.yehling@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:38 PM
Lambert, Angela	Portsmouth, NH drangela@mac.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:39 PM
Nadreau, Courtney	Deering, NH teetsiecat@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:42 PM
Centra, Tania	Merrimack, NH tcentra@me.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:43 PM
Charest (Ret NP), Jeanne	Berlin, NH nhwoodduck@myfairpoint.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:44 PM
Sullivan, Kathryn	Newton, NH kebruck@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:48 PM
Caswell, Paul F.	Portsmouth, NH pfcaswell@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:50 PM

Nadreau, Todd	Deering, NH toddraymond@mail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:50 PM
MacGregor, Leslie	Grantham, NH lsmacgregor@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:52 PM
MacDonald, Carrie	Wolfeboro, NH camsmom629@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:54 PM
Surber, Gloria	Langdon, NH gsurber@ hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 8:54 PM
Davis, Kathryn	Windham, NH katkala@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:55 PM
Moser, Leah	Westminster, CO Leah.moser1@gmail.com	A Member of the Public	Myself	Neutral	No	No	1/17/2022 8:56 PM
Winslow, Dalton	Grantham, NH dwinslow04736@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:58 PM
Condodemetraky, Stephanie	Bedford, NH Snicolepappas229@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:58 PM
Kadic, Lejla	Manchester, NH Drlejlakadic@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 8:59 PM
Smith, Rosemary	Dover, NH roses12@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:00 PM
McCartney, Michelle	Concord, NH Michelleredmond2000@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:01 PM
Towne, Brenda	Stratham, NH Btowne@protonmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:02 PM
Bujno, Lisa	North Woodstock, NH lbujno@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:03 PM
Godin, Justin	Merrimack, NH justin.j.godin@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:03 PM
McCartney, Evan	Concord, NH bebop0505@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:05 PM
doherty, jane	hopkinton, NH hannon.jane@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:12 PM
Sharp, Dayle	Rochester, NH daylesharp@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:13 PM
Dukelow, Gayle	New Boston, NH Gayle.sukelow@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:15 PM

Petrusewicz, Carol	rochester, NH clmcc2befree@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:16 PM
Levesque, Jan	Hopkinton, NH janjuma@tds.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:17 PM
Wilson, Priscilla	Wilton, NH Priscillanichole@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:18 PM
Stark, Ann	Holderness, NH annjohnsonstark@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:24 PM
Stark, Robert	Holderness, NH starkelectric2002@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:25 PM
Stark, Theadora	Holderness, NH tstark855@Anselm.Edu	A Member of the Public	Myself	Support	No	No	1/17/2022 9:27 PM
Stark, Adeline	Holderness, NH adelinemstark@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:28 PM
Allard, Margaret	Portsmouth, NH peggyallard41@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:34 PM
Goodman, Daisy	Hanover, NH daisy.j.goodman@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:34 PM
Wilmot, Kyle	Nashua, NH Kywilmot92@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:36 PM
Richman, Susan	Durham, NH susan7richman@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:38 PM
Rettew, Annie	Concord, NH abrettew@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:39 PM
Godin, PharmD, BCIDP, Jamie	Merrimack, NH Funnypharm08@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:42 PM
Peschiera, Alyssa	Bedford, NH Alycatmmc@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:43 PM
Lewis, Alice	Hollis, NH majmwlewis@msn.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:44 PM
Peschiera, Rafael	Bedford, NH Rpeschiera@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:44 PM
Damon, Claudia	Concord, NH cordsdamon@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:44 PM
Matta, Sarah	Manchester, NH SJmatta@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:45 PM

Torrice, Paula	Windham, NH wynntorrice@icloud.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:51 PM
Wood, James	Merrimack, NH fairlanejim@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 9:52 PM
Schertell, Christine	Hampton, NH clsylvester06@comcast.net	A Member of the Public	Myself	Support	No	No	1/17/2022 9:53 PM
Freund, Tiffany	Lee, NH thisishowtosave@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:54 PM
Nault, Shane	Lee, NH pestocake@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 9:57 PM
perencevich, ruth	concord, NH rperence@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 9:59 PM
Methot, Jennifer	Milford, NH jennifer.s.methot@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:08 PM
Merner, Kelly	Wilton, NH kellyamerner@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:16 PM
Trudel, Anita	Atkinson, NH Aetrudel@aol.com	A Member of the Public	My self	Support	No	No	1/17/2022 10:18 PM
Minehart, Will	Wilton, NH sylvandream@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:19 PM
McClure, Kevin	Amherst, NH kevkevmc02@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:25 PM
Hammerman, Samuel	Goffstown, NH samjh@hushmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:29 PM
chapman, kevin	marlborough, NH denoct103@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:48 PM
Aronson, Laura	MANCHESTER, NH laura@mlans.net	A Member of the Public	Myself	Oppose	No	No	1/17/2022 10:49 PM
Sylvia, Elizabeth	Nashua, NH elizabethlidman@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 10:51 PM
Martin, Andrea	Sandwich, NH andi_t_martin@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:01 PM
Tavanyar, Yvonne	Nashua, NH ytavanyar@yahoo.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:01 PM
Nichols, Robin	Newbury, NH Robinnichols59@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/17/2022 11:02 PM

Tavanyar, Simon	NASHUA, NH jlsharvester@hotmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:11 PM
Kopacz, Jennifer	Franklin, NH Jennifermkopacz@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:26 PM
Gilman, Representative Julie	Exeter, NH julie.gilman@leg.state.nh.us	An Elected Official	Town of Exeter	Oppose	No	No	1/17/2022 11:30 PM
Wood, Zephan	Pembroke, NH zephanw@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:36 PM
Dekle, Marcus	Waterford, VT Northeasternkingdomrn@gmail.com	A Member of the Public	Myself	Support	No	No	1/17/2022 11:38 PM
Seaman, Jessicah	Derry, NH Ajseaman@myfairpoint.net	A Member of the Public	Myself	Support	No	No	1/17/2022 11:39 PM
Raspiller, Cindy	Mont Vernon, NH raspicl@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:05 AM
Clark, Denise	Milford, NH denise.m.clark03055@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:18 AM
Meyer, Joanne	Rye, NH jomeyer777@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 12:23 AM
Brown, Howard	Mont Vernon, NH hobro39@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:25 AM
Richardson, Bryan	Alexandria, NH marks-dad@ipatriots.us	A Member of the Public	Myself	Support	No	No	1/18/2022 12:50 AM
Wied, Alex	Manchester, NH nh.gencourt@centromere.net	A Member of the Public	Myself	Support	No	No	1/18/2022 1:14 AM
landry, rosemary	meredith, NH rkqueenie@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:25 AM
Wink, Margaret	Brookline, NH Mwinky1@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:01 AM
Woods, Renia	Bow, NH renia.woods1@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:51 AM
Elliott, Jacqueline	Chester, NH jacqueline.elliott85@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 4:58 AM
Aiston, Tricia	Mont Vernon, NH tricia@aiston.net	A Member of the Public	Myself	Support	No	No	1/18/2022 5:00 AM
Meyer, Pamela	Goffstown, NH MeyerPamelaJ@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 5:14 AM

Abrams, Patricia	Swanzey, NH keeganmo44@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:31 AM
Abrams, Denis	Swanzey, NH keeganmo44@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:32 AM
Wolcott, Rochelle	Hampton, NH Shelly@shelwood.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:33 AM
O'Mahoney, Kim	Newmarket, NH Kimo@lampreyhealth.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 5:35 AM
Wolcott, Sherwood	Hampton,, NH wwolcott@shelwood.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:37 AM
Morrow, Eric	Derry, NH Shoearl@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:53 AM
Sklencar, Todd	Deerfield, NH tezrazeek@aol.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:00 AM
Lloyd, Gisela	East Kingston, NH haus@onepinewoods.us	A Member of the Public	Myself	Support	No	No	1/18/2022 6:01 AM
Lewis, Elizabeth	Nashua, NH ecop.lewis@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:01 AM
Jeffers, Rachel	Etna, NH jeffers.rachel@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:02 AM
Zadounaev, Ivan	Berlin, NH ivan.zadounaev@avhnh.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:08 AM
Ebert, James	North Hampton, NH James.b.Ebert.jr@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:10 AM
Hnizdor, Randal	Sutton, NH rlhnizdor@tds.net	A Member of the Public	Myself	Support	No	No	1/18/2022 6:13 AM
Moschetto, Grace	Derry, NH gracemariestyle@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:13 AM
Devine, Chris	Hampton Falls, NH c.devine12@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:14 AM
Buckley, DNP, APRN, Holly	North Sutton, NH Hbbarnp@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:14 AM
Bettencourt, Don	Sunapee, NH Don.Bettencourt@GMail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:21 AM
Mirzoeff, Joseph	Keene, NH mrzvyp@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:21 AM

Zaenglein, Barbara	Amherst, NH bzaenglein@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:25 AM
Foster, Keith	Henniker, NH pdceta26@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:25 AM
Zaenglein, Eric	Amherst, NH henley11@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:26 AM
Sherwood, Mallory	Dover, NH mal.sherwood1@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:28 AM
Broze, Renee	Manchester, NH Reneebroze@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:29 AM
Filiatrault, Christie	Nashua, NH Ckxapa@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:40 AM
Matta, Susan	Goffstown, NH susanmatta44@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:40 AM
Milliard, Carl	Goffstown, NH thecycleshed@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 6:42 AM
Buchanan, Elizabeth	Chester, NH buchanan40@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:43 AM
Selleck, Stephanie	Goffstown, NH sbselleck@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:44 AM
vanderheiden, nicole	Hampton Falls, NH coleyv4@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:45 AM
Gendron, Deborah	Hampton Falls, NH Gendrond@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 6:50 AM
Gendron, John	Hampton Falls, NH Gendrond@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 6:51 AM
Bender, Lorie	Hopkinton, NH lorie.bender@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 6:54 AM
Ellermann, Maureen	Concord, NH ellermannf@aol.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 6:59 AM
Dekle, Ericka	Waterford, VT Dekledg@gmail.com	A Member of the Public	Myself (Ericka Dekle)	Support	No	No	1/18/2022 7:01 AM
Crosier, Marinda	Stratham, NH marinda.crosier@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:02 AM
Lacey, Elisha	Pembroke, NH elisha.lacey@alumni.acphs.edu	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:05 AM

Goddard, Sandra	Hampton, NH Sandra.Goddard@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:05 AM
Hayes, Randy	Canterbury, NH rcompostr@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:09 AM
Moore, Kristen	Milford, NH kristen_Cotsifas@hotmail.com	An Elected Official	Myself	Support	No	No	1/18/2022 7:10 AM
Bowers, Danielle	Acworth, NH bktime777@protonmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:10 AM
Morton, Jon	Weare, NH Livingwell247@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:20 AM
Bidgood-Wilson, Mary	Moultonboro, NH mary.bidgood@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:21 AM
Bemis, ashley	manchester, NH abemis427@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:23 AM
Cushman, Leah	Weare, NH leah.cushman@leg.state.nh.us	An Elected Official	Myself	Support	No	No	1/18/2022 7:24 AM
McLellan, MD,MPH, Robert	Lebanon, NH Robert.K.McLellan@dartmouth.Edu	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:24 AM
Spring, Bridget	Concord, NH Bridgetcardin@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:28 AM
MacMonagle, John	Bedford, NH pat@jpmacmonagle.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:29 AM
Comstock, Nancy	Litchfield, NH njcomstock@protonmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:30 AM
Bowers, Steven	Acworth, NH cpcliberty70@protonmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:31 AM
Lloyd, E.A.	East Kingston, NH House@onepinewoods.us	A Member of the Public	Myself	Support	No	No	1/18/2022 7:33 AM
Peters, Dr. Katherine	Manchester, NH katepetersdo@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:36 AM
Owens, Brady	Nashua, NH brady.owens@pm.me	A Member of the Public	Myself	Support	No	No	1/18/2022 7:36 AM
Walsh, Lynne	Melvin Village, NH lynnewalsh14@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:37 AM
Owens, Kimberly	Nashua, NH tiptoeskst@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:38 AM

Desmond, RPh, Dennis	Shelburne, NH dez366@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:39 AM
Harris, Stephen	Amherst, NH steveharris1978@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:39 AM
Joyce, Michele	Bath, NH mjdigspigs@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 7:52 AM
Marx, Jessica	Exeter, NH Jessica.marx@hcahealthcare.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:54 AM
Anania, Peter	Portsmouth, NH peteanania@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:55 AM
Martin, Ashley	Northwood, NH admart@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:57 AM
Peternel, Catherine	Wolfeboro, NH katypeternel@pm.me	A Member of the Public	Myself	Support	No	No	1/18/2022 8:01 AM
bowley, bonnie	Danville, NH, NH gracepaul517@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:06 AM
Thomas, Janet	Laconia, NH janetthomas7@icloud.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:06 AM
Thompson, Kisha	Westmoreland, NH kisha.lifgren@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:10 AM
Robinson, Ellis	Grantham, NH ellismmrobinson@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:10 AM
Piehl, Emily	Proctor, VT ec.piehl@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:11 AM
Bittner, Bonnie	Dover, NH Bonniebitt@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:13 AM
Hill, Marilyn	Lebanon, NH mghill3527@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:16 AM
Gowen, Jaclynne	Rochester, NH jrgowen@partners.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:16 AM
Grinnell, Terese	Loudon, NH Teresegrinnell@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:17 AM
Greene, Bob	Hudson, NH Bob.Greene@leg.state.nh.us	An Elected Official	Myself	Support	No	No	1/18/2022 8:18 AM
Kelley, BaoChau	Hooksett, NH chaukelley@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:18 AM

McMullen, Maria	Lebanon, NH maria.p.mcmullen@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:19 AM
Le Doux, Julie	Holllis, NH jbizzbuzz@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:20 AM
LeDoux, Mark	Hollis, NH markledoux@me.com	An Elected Official	Myself	Support	No	No	1/18/2022 8:20 AM
Parry, Nancy	Hollis, NH njparry@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:23 AM
Carraher, Melanie	Boscawen, NH MLCarraher@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:23 AM
Smith, Brian	Hampton, NH bps123@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 8:23 AM
Foss, Lauren	Hopkinton, NH vieira.lauren@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:24 AM
Pelchat, Randy	Washington, NH Nhyankee24@yahoo.com	A Member of the Public	My self	Support	No	No	1/18/2022 8:24 AM
Burrill, Susan	Plainfield, NH sueburrill@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:25 AM
Priam, Nwando	Manchester, NH Npriam@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:26 AM
Pelchat, Linda J	Washington, NH Nhyankee24@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:26 AM
Overbagh, Meg	Campton, NH meg.overbagh@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:27 AM
Case, Barbara	Windham, NH bacrx21@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:27 AM
Feng, Henry	Lebanon, NH jhfeng3@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:29 AM
Michaud, Karen	Dover, NH Kmichaud92@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:29 AM
Burnap, Linda	Wolfeboro, NH 54able@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:33 AM
Cahill, Michael	Newmarket, NH michael.cahill@leg.state.nh.us	An Elected Official	Myself	Oppose	No	No	1/18/2022 8:34 AM
Couture, Laurie A.	Newmarket, NH LAC@LaurieACouture.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:35 AM

Elliott, Maria	Portsmouth, NH BEEMEE@COMCAST.NET	A Member of the Public	Myself	Support	No	No	1/18/2022 8:36 AM
Griffin, Anthony	Hampton, NH Tgriffin149@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:41 AM
Morse, Kristen	Washington, NH jamkam86@hotmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:44 AM
McKinney, Carolyn	Amherst, NH carolyn.mckinney@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:45 AM
Snarr, Elizabeth	Barrington, NH esnarr@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:48 AM
Heckman, James	Lebanon, NH james.a.heckman@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:50 AM
Vieira, Nancy	Milford, NH Nancy.vieira@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:51 AM
Gauthier, Melissa	Merrimack, NH Mapster81@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:52 AM
Pastel, Lisa	Lebanon, NH lisa.c.pastel@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:52 AM
Warren, Thomas	Hampton, NH thowarren94@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:53 AM
Carroll, Robyn	Portsmouth, NH robyn.bruce@hcahealthcare.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:53 AM
Shippee-Rice, Raelene	nottingham, NH dwrice73@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:53 AM
Prisch, Stephanie	Etna, NH Stephanie.b.prisch@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:54 AM
Vieira, James	Milford, NH Javieira@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:54 AM
Bailey, Alicia	Exeter, NH ambaile85@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:54 AM
O'Neill, Nan	Salisbury, NH Raptorko@gmail. Com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:55 AM
Johnson, Debra	Grantham, NH debjohnsondjj@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:56 AM
Desrosiers, Kevin	Bedford, NH kdesrosiers@elliot-hs.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:56 AM

Robinson, Sara	Stratham, NH sararobinson.np@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:56 AM
O'Neill, Kevin	Salisbury, NH raptornan@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 8:58 AM
Powell, Kenton	Lebanon, NH Kenton.e.powell@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:00 AM
Brady, Maureen	Dover, NH maureen.brady@wdhospital.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:01 AM
Crockett, Melissa	Strafford, NH mbrewer84@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:01 AM
Padmore, Michael	Manchester, NH michael.padmore@nhms.org	A Lobbyist	NH Medical Society	Oppose	No	No	1/18/2022 9:03 AM
Tracey, Patricia	Milford, NH pattytracey@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:07 AM
Sindelar, Reid	Claremont, NH reid.sindelar@vrh.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:08 AM
Levine, David	Lebanon, NH David.A.Levine@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:12 AM
LaClair, Donna	Loudon, NH alleycat9801@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 9:14 AM
Doucette, Margaret	Hanover, NH megdoucette11@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:14 AM
Findley, Sally	Grantham, NH findley.se@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:14 AM
Naylor, Claire	Peterborough, NH cnaylor714@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:14 AM
Stone, Lynne	Wilton, NH lynne@tellink.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:16 AM
Whitson, Abby	Concord, NH suroise@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:17 AM
Christen, Brennan	Farmington, NH brencode@outlook.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:19 AM
Robinson, Amy	HAMPTON, NH amyrobinsonnh@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:19 AM
Matta, Luisa	Bedford, NH luisa.matta123@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:20 AM

Devine, Haley	Hampton Falls, NH haleydevine95@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:21 AM
Morrill, Amanda	Hudson, NH morrill.amanda.m@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:22 AM
Cauley, Elizabeth	Milford, NH b.cauley@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 9:23 AM
Sawyer, Linda	Lyme, NH linda.m.sawyer@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:24 AM
Horman, Heidi	Sanbornton, NH hhorman@proton.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:26 AM
Robertson, Elizabeth	Gilford, NH Elizuhbethr@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:27 AM
Anan, Jimmy	Littleton, NH jimmyanan1@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:29 AM
Bangiolo, Lois	Enfield, NH lbangiolo@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:30 AM
Drye, Melissa	Cornish, NH melissa.drye@vrh.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:30 AM
Mahoney, Brittany	Manchester, NH brittany.mahoney@pm.me	A Member of the Public	Myself	Support	No	No	1/18/2022 9:32 AM
Parrish, Laura	Hollis, NH lparrish28@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:35 AM
Gray, Stacy	Kingston, NH sskafas@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:35 AM
Matta, Mauretta	Bedford, NH mauretta.matta@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:40 AM
Matta, Jonathan	Bedford, NH Wathencontracting@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:41 AM
Juilfs, Alyssa	Whitefield, NH amjuilfs07@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:51 AM
Brackett, Charles	Lebanon, NH cdb@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:51 AM
Sweeney, Margaret	Campton, NH ms975@protonmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 9:56 AM
Roberts, Alexandra	Portsmouth, NH arobnh@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:56 AM

Paschell, Susan	Bow, NH spaschell@dupontgroup.com	A Lobbyist	NH Nurse Practitioner Association	Oppose	No	No	1/18/2022 9:57 AM
Cooper, Maryann	Windham, NH maryann.cooper32@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:57 AM
Bal, MD, Simrun	Hanover, NH simrun.k.bal@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:57 AM
DiNubila, Jennifer	Keene, NH jdinubila@cheshire-med.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 9:58 AM
Istel, Claudia	Acworth, NH cistel79@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:01 AM
Guerin, Richard	Auburn, NH rcharlesguerin@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:01 AM
Ketteler, Claire	Newbury, NH cketteler@tds.net	A Member of the Public	Myself	Support	No	No	1/18/2022 10:06 AM
Black, Martin	Concord, NH mdblackmd@netscape.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:06 AM
Williams, Tyler	Thetford, VT tylerwms14@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:11 AM
Harding, Laurie	Lebanon, NH lharding0625@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:11 AM
VanPatten, Emily	Deering, NH Emily.b.vanpatten@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:12 AM
Apicelli, Adriane	Rochester, NH adrianeapicelli@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:14 AM
Cecchetti, Lynda	Strafford, NH lcecc92017@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:15 AM
Avallon, James	North Hampton, NH jimavallon@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:25 AM
Druckenmiller, Samantha	Warren, NH samantha.b.druckenmiller@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:25 AM
Boucher, Elizabeth	Bow, NH eboucher@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:25 AM
cormier, Julia	Salisbury, NH addisongregory@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:25 AM
Elsasser, Karen	Dunbarton, NH kelsasse@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:26 AM

Capriotti, Joseph	Nashua, NH Jmc62190@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:28 AM
Mather, Cheri	Lebanon, NH Cheri.c.mather@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:30 AM
Corey, William	Maidstone, VT Maidmac@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:31 AM
Spratt, Greg	Concord, NH gspratt@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:33 AM
Elliott, John	Manchester, NH Tyre1@verizon.net	A Member of the Public	Myself	Support	No	No	1/18/2022 10:39 AM
Bergevin, Leslie	Loudon, NH Leslie.bergevin@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:41 AM
Tanner, Courtney	Bedford, NH Courtney.Tanner@hitchcock.org	A Lobbyist	Dartmouth-Hitchcock Health	Oppose	No	No	1/18/2022 10:44 AM
Erlebacher, Frances	Rye, NH creatives@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:46 AM
Keeler, Margaret	New London, NH peg5keeler@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:53 AM
Avery, Jenna	Brentwood, NH misbhvnprincess@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:53 AM
Erickson, Amy	Wolfeboro, NH ableacres@outlook.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 10:54 AM
Moulton, Sue	Hampton, NH suevaliq@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:55 AM
nason, anne	webster, NH nasonanne0@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:00 AM
aylesworth, annie	New Boston, NH aaylesworth@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 11:01 AM
haywood, judith	nashua, NH jhaywd@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:03 AM
Mezzetti, Jamie	Concord, NH Mezzettijamie@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:05 AM
Condon, Laura	Bedford, NH vaxchoicenh@gmailcom	A Member of the Public	Myself	Support	No	No	1/18/2022 11:06 AM
Gendre, Michael	North Hampton, NH Michael.gendre@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:24 AM

Glowa, Patricia	Hanover, NH patricia.t.glowa@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:31 AM
Forbes, Thais	Nashua, NH thaisrforbes@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:33 AM
Thomas, Cynthia	Belmont, NH Cindyathomas56@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:37 AM
Brady, Stephanie	Brentwood, NH stephanie.megan.brady@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:38 AM
Olson, Stephanie	Bristol, NH stephanieqolson@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:38 AM
Beaudoin, Sherry	Rochester, NH sherrybeaudoin@metrocast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 11:40 AM
Beaudoin, Steve	Rochester, NH stevebeaudoin@metrocast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 11:40 AM
Olson, William	Bristol, NH md88driver@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:41 AM
Romito, Susan	Hollis, NH susanromito@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:44 AM
Degnan, Peter	Newmarket, NH ahpd@hotmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:45 AM
Lewis, Kelly	Enfield, NH kelly.t.lewis@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:46 AM
Garboski, Jordan	Weare, NH jgarb1@stu.mcphs.edu	A Member of the Public	Myself	Oppose	No	No	1/18/2022 11:51 AM
Geyer, Alberta	Merrimack, NH Alberta@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 12:11 PM
Murray, Elizabeth	Canaan, NH Elizabeth.T.Murray@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:18 PM
Covey, Starr	Hillsboro, NH allxforxjesus@aol.com	A Member of the Public	Myself	Support	No	No	1/18/2022 12:18 PM
Lee, Colleen	Lebanon, NH colleen.e.lee@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:32 PM
Lawrence, Johanna	Rye, NH johannalawrence@verizon.net	A Member of the Public	Myself	Support	No	No	1/18/2022 12:35 PM
Kuemmerle, Nancy	Enfield, NH nkuemmerle@une.edu	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:35 PM

Yip, Kerry	Londonderry, NH kyip@crhc.org	State Agency Staff	Myself	Oppose	No	No	1/18/2022 12:36 PM
Beaurivage, Scott	Hooksett, NH sbeauriv@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:36 PM
Gabris, Sadie	Weare, NH sgabris@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:37 PM
Jones, Katharine	Goffstown, NH kmjones@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 12:40 PM
Morgan, Melissa	Raymond, NH Coachmelissa.morgan@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 12:45 PM
hadley, craig	keene, NH 333cra2@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 12:49 PM
Barth, Katherine	Berlin, NH booblue39@yahoo.com	A Member of the Public	Myself	Support	No	No	1/18/2022 12:58 PM
Richardson, Jennifer	DOVER, NH jennifer.richardson@advancedconceptsinsurance.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 1:00 PM
Hamel, Madeleine	Exeter, NH mserpahamel@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:03 PM
Cates, Tammy	Nashua, NH tjcates@eagleswind.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:11 PM
Cates, William	Nashua, NH wcatesjr@eagleswind.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:11 PM
Cates, Bethany	Nashua, NH brcates99@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:12 PM
Cates, Tyler	Nashua, NH xtylercatesx@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:12 PM
Cates, Sahriah	Nashua, NH sahriah@sahriah.com	A Member of the Public	Myself	Support	No	No	1/18/2022 1:12 PM
Wade, Elizabeth	Amherst, NH ewade@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 1:15 PM
Fitzgerald, Kathryn	Manchester, NH katefitzy@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 1:24 PM
Lasell, Kerrie	Grafton, NH Kerrie.Lasell@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 1:48 PM
Sorber, Anne	Exeter, NH anne@sorber.us	A Member of the Public	Myself	Support	No	No	1/18/2022 1:49 PM

Labbe, Sarah	Epping, NH Scj3890@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 2:01 PM
McAlary, Eileen	Exeter, NH emcalary@crhc.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 2:03 PM
Kras, Alison	Exeter, NH akras@massagechairsgiveback.com	A Member of the Public	Myself	Support	No	No	1/18/2022 2:30 PM
Farrell, Courtney	Hanover, NH courtneyraefarrell@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 2:40 PM
Comeau, Olga	Nashua, NH olgacomeau@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 2:45 PM
Von Ahn, Andrew	Merrimack, NH andrewvonahn@protonmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 2:53 PM
Pastel, David	Etna, NH david.a.pastel@hitchcock.org	A Member of the Public	Myself	Oppose	No	No	1/18/2022 2:55 PM
Cormier, Jennifer	Dunbarton, NH nhgencourt@jcsmotif.com	A Member of the Public	Myself	Support	No	No	1/18/2022 3:01 PM
Jones, Andrew	Pembroke, NH arj11718@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:09 PM
benham, siobhan	Peterborough, NH skieranb@yahoo.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:18 PM
Booth, Andrew	Nashua, NH andrewbo623@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:24 PM
Morin, Jennifer	Plainfield, NH Jennifer.morin@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 3:27 PM
Winkler, AnneMarie	Dover, NH Amwinkler81@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:28 PM
Craigue, Emily	Boscawen, NH em10marden@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:32 PM
McGonagle, Jan	Stoddard, NH mcgonaglejan@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:34 PM
Downs, Nathan	Dover, NH nathan.a.downs@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 3:42 PM
Cappiello, Joyce	Barrington, NH cappiellojoyce@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 4:03 PM
Cody, John	Epping, NH Spmedicrn@gmail.com	An Elected Official	Myself	Support	No	No	1/18/2022 4:47 PM

Van Arsdale, Linda	Wolfeboro, NH Lynjenks@hotmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:01 PM
Van Arsdale, Joel	North Hampton, NH Lynjenks@hotmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:01 PM
Jenkins, Cynthia	North Hampton, NH Cynjenks@comcast.net	A Member of the Public	Myself	Support	No	No	1/18/2022 5:02 PM
Jenkins, Isabel	Exeter, NH Isajenks@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:03 PM
Weihrauch, Lynne	Merrimack, NH nhbuckeye@comcast.net	A Member of the Public	Myself	Oppose	No	No	1/18/2022 5:47 PM
Dusute, Kelly	Hopkinton, NH kdepiero79@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 5:56 PM
Goodwin, Kendra	Sandown, NH kenj86rdcs@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 5:58 PM
M Macpherson, Christine	Chesterfield, NH Christine.macpherson@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:07 PM
May, Tracy	Northwood, NH Tracymay69@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:31 PM
Kono, Jacqueline	Peterborough, NH jacquelinekono@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:32 PM
Waitte, Kelly	Northwood, NH mkwaitte@protonmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 6:37 PM
McLeod, Thomas	Mont Vernon, NH contact@ldfnh.org	A Member of the Public	Myself	Support	No	No	1/18/2022 7:24 PM
Gould, Matthew	Litchfield, NH mgould3090@gmail.com	A Member of the Public	Myself	Oppose	No	No	1/18/2022 7:35 PM
Wade, Linda F	North Hampton, NH enh314nw@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 8:01 PM
Stevens, Susan	Union, NH Stevenssusantim@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 10:13 PM
McGuinness, Martha	Bedford, NH mmcguinness45@gmail.com	A Member of the Public	Myself	Support	No	No	1/18/2022 11:32 PM

Archived: Thursday, February 10, 2022 11:12:05 AM
From: Kathleen Lutter
Sent: Wednesday, January 26, 2022 9:49:46 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022 - very important
Importance: Normal

Dear HHSEA Committee Members ,

My name is Kathleen Lutter . I am a retired dietitian from Ashland , NH and I am a registered Independent voter.

HB 1022 is am immensely important bill to allow access to the very safe and highly effective , 40 year old, FDA approved , Nobel Prize winning drug named Ivermectin. This is NOT horse paste and should NEVER be a political issue . It is too important . Many lives could have been saved me (and can be saved) if Ivermectin had been used in early treatment but it was disallowed and is essentially banned from sale throughout the country because it is a very cheap drug that competes with the profits of the powerful pharmaceutical companies . Always “follow the money” .

I am forwarding the link to the FLCCC (Front Line Covid-19 Critical Care Alliance) which provides extensive information and references on Ivermectin as well as suggested treatment protocols and the potential means by which to acquire Ivermectin. I have some in my own medicine cabinet and it provides a great sense of comfort and freedom to me. My adult son took this recently when he acquired a cold that tested positive for Covid. He was well within days.

You can access an incredible 11 minute documentary on the story of Ivermectin from the FLCCC website under the Ivermectin tab at the top of the home page but I will also forward it directly to you as well . If you do nothing else , please watch this important information so that you are well informed before voting on HB 1022

Thank you all for your service ,
Kathleen Lutter

https://us-east-2.protection.sophos.com?d=covid19criticalcare.com&u=aHR0cHM6Ly9jb3ZpZDE5Y3JpdGljYWxjYXJlLmNvbS9hYm91dC8=&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=bWQydzJwRVFBdDk0TFdDZUR5VDZ5YXphY2lFWVlUZVRhc3hOWm1OKytxTT0=&h=d17ba1cd20f040f091720c497398538e

Supplementary Appendix). Among adults who tested positive, those who were unvaccinated tended to be much younger, to have fewer coexisting conditions, and to have a lower socioeconomic status and were more likely to be men than those who were vaccinated; these differences tended to be especially pronounced in comparison with those who received the ChAdOx1 nCoV-19 vaccine (Table S2).

Overall, 201 deaths from Covid-19 were caused by SARS-CoV-2 that had been tested and found to be *S*-positive or *S*-negative (Table 1). Among persons 18 to 39 years of age who had infections for which data on *S* gene status were available, no deaths occurred among those who were fully vaccinated, as compared with 17 deaths among those who were unvaccinated. Among those who were 40 to 59 years of age, vaccine effectiveness against death from Covid-19 was 88% (95% confidence interval [CI], 76 to 93) for ChAdOx1 nCoV-19 and 95% (95% CI, 79 to 99) for BNT162b2; vaccine effectiveness was 90% (95% CI, 84 to 94) and 87% (95% CI, 77 to 93), respectively, among those 60 years of age or older. Overall, vaccine effectiveness against death from the delta variant 14 or more days after the second vaccine dose was 90% (95% CI, 83 to 94) for BNT162b2 and 91% (95% CI, 86 to 94) for ChAdOx1 nCoV-19 (Table S3).

A limitation of this study is the fact that it was based on an analysis of community samples. In addition, 1.8% of samples did not yield *S* gene categorization because of missing data in the Ct fields.

In summary, we found that the BNT162b2 and ChAdOx1 nCoV-19 vaccines offered substantial protection against death from Covid-19 caused by the delta variant.

Aziz Sheikh, M.D.
University of Edinburgh
Edinburgh, United Kingdom
aziz.sheikh@ed.ac.uk

Chris Robertson, Ph.D.
University of Strathclyde
Glasgow, United Kingdom

Bob Taylor, Ph.D.
Public Health Scotland
Glasgow, United Kingdom

Supported by a grant (MR/R008345/1) from the Medical Research Council; a grant (MC_PC_19004) from BREATHE–The Health Data Research Hub for Respiratory Health, funded through the U.K. Research and Innovation Industrial Strategy Challenge Fund and delivered through Health Data Research UK; Public Health Scotland; and the Scottish Government Director General for Health and Social Care.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

The data used to undertake this analysis are not publicly available because they are based on deidentified national clinical records. These data are available, subject to approval by the NHS Scotland Public Benefit and Privacy Panel, by application through the Scotland National Safe Haven. The R code used to perform this analysis is available from https://github.com/EAVE-II.

This letter was published on October 20, 2021, and updated on October 25, 2021, at NEJM.org.

1. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet 2021;397:2461-2.
2. Simpson CR, Robertson C, Vasileiou E, et al. Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II): protocol for an observational study using linked Scottish national data. BMJ Open 2020;10(6):e039097.
3. Mulholland RH, Vasileiou E, Simpson CR, et al. Cohort profile: Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) database. Int J Epidemiol 2021;50:1064-74.
4. Vasileiou E, Simpson CR, Shi T, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet 2021;397:1646-57.
5. Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020;371:m3731.

DOI: 10.1056/NEJMc2113864

Toxic Effects from Ivermectin Use Associated with Prevention and Treatment of Covid-19

TO THE EDITOR: Ivermectin is approved by the Food and Drug Administration as an oral treatment for intestinal strongyloidiasis and onchocerciasis and as a topical treatment for pediculosis and rosacea. It is also used as a treatment for parasites in pets and livestock. Ivermectin may decrease severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication in vitro,[1,2] but randomized, controlled trials have shown no clinical benefit in the prevention or treatment of coronavirus disease 2019 (Covid-19).[3] Veterinary use of ivermectin has increased, and the number of prescriptions for use by humans in the United States is 24 times as high as the number before

the pandemic. Moreover, the number of such prescriptions in August 2021 was 4 times as high as the number in July 2021.[3,4]

The Oregon Poison Center is a telephone consultative center staffed by specialty-trained nurses, pharmacists, and physicians who provide treatment advice for the public and comprehensive treatment consultation for health care workers caring for patients in Oregon, Alaska, and Guam. The center has recently received an increasing number of calls regarding ivermectin exposure related to Covid-19. The rate of calls regarding ivermectin had been 0.25 calls per month in 2020 and had increased to 0.86 calls per month from January through July 2021; in August 2021, the center received 21 calls. Monthly total call volumes for all poison exposures were stable throughout 2020 and 2021.

Of the 21 persons who called in August, 11 were men, and most were older than 60 years of age (median age, 64; range, 20 to 81). Approximately half (11 persons) were reported to have used ivermectin to prevent Covid-19, and the remaining persons had been using the drug to treat Covid-19 symptoms. Three persons had received prescriptions from physicians or veterinarians, and 17 had purchased veterinary formulations; the source of ivermectin for the remaining person was not confirmed. Symptoms had developed in most persons within 2 hours after a large, single, first-time dose. In 6 persons, symptoms had developed gradually after several days to weeks of repeated doses taken every other day or twice weekly. One person had also been taking vitamin D to treat or prevent Covid-19. Reported doses ingested by the persons who had been using veterinary products ranged from 6.8 mg to 125 mg of 1.87% paste and 20 to 50 mg of the 1% solution. The dose of the human-use tablets was 21 mg per dose twice weekly for prevention.

Six of the 21 persons were hospitalized for toxic effects from ivermectin use; all 6 reported preventive use, including the 3 who had obtained the drug by prescription. Four received care in an intensive care unit, and none died. Symptoms were gastrointestinal distress in 4 persons, confusion in 3, ataxia and weakness in 2, hypotension in 2, and seizures in 1. Of the persons who were not admitted to a hospital, most had gastrointestinal distress, dizziness, confusion, vision symptoms, or rash.

These cases illustrate the potential toxic effects of ivermectin, including severe episodes of confusion, ataxia, seizures, and hypotension, and the increasing frequency of inappropriate use. There is insufficient evidence to support the use of ivermectin to treat or prevent Covid-19,[3] and improper use, as well as the possible occurrence of medication interactions,[5] may result in serious side effects requiring hospitalization.

Courtney Temple, M.D.
Ruby Hoang, D.O.
Robert G. Hendrickson, M.D.
Oregon Health and Science University
Portland, OR

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on October 20, 2021, at NEJM.org.

1. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res 2020;178:104787.
2. Lehrer S, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor-binding domain attached to ACE2. In Vivo 2020;34:3023-6.
3. Centers for Disease Control and Prevention. Rapid increase in ivermectin prescriptions and reports of severe illness associated with use of products containing ivermectin to prevent or treat COVID-19. CDC Health Alert Network no. CDCHAN-00449. August 26, 2021 (https://emergency.cdc.gov/han/2021/han00449.asp).
4. Lind JN, Lovegrove MC, Geller AI, Uyeki TM, Datta SD, Budnitz DS. Increase in outpatient ivermectin dispensing in the US during the COVID-19 pandemic: a cross-sectional analysis. J Gen Intern Med 2021;36:2909-11.
5. Edwards G. Ivermectin: does P-glycoprotein play a role in neurotoxicity? Filaria J 2003;2:Suppl 1:S8.

DOI: 10.1056/NEJMc2114907

Benefits and Risks of Iron Interventions in Infants in Bangladesh

TO THE EDITOR: The randomized, placebo-controlled trial Benefits and Risks of Iron Interventions in Young Children (BRISC) (September 9 issue)[1] showed that 3 months of iron supplementation in infants reduced the prevalence of anemia but did not improve infant develop-

318:16-a Standards for Collaborative Pharmacy Practice. –

I. For a pharmacist to participate in a collaborative pharmacy practice agreement, the pharmacist shall:

(a) Hold an unrestricted and current license to practice as a pharmacist in New Hampshire.

(b) Have at least $1,000,000 of professional liability insurance coverage.

(c) Have the knowledge base necessary for proper monitoring, including, but not limited to, associated disease states, relevant laboratory tests, adverse events, drug and food interactions, safety, and efficacy. Depending upon the complexity of the services being provided, the pharmacist may be required to have additional credentials or training and shall demonstrate the receipt of approval by the board of pharmacy.

II. Any practitioner with prescriptive authority who holds an active, unrestricted license in the state of New Hampshire may enter into a collaborative pharmacy practice agreement. A service authorized by a practitioner to be performed by a pharmacist under a collaborative pharmacy practice agreement must be within the practitioner's current scope of practice.

III. Collaborative pharmacy practice agreements may be between single or multiple pharmacists and a single or multiple practitioners.

IV. Collaborative pharmacy practice agreements shall meet the following general requirements:

(a) Each protocol developed pursuant to the collaborative pharmacy practice agreement shall contain detailed direction concerning the services that the pharmacist may perform for patients. The protocol shall include, but not be limited to:

(1) The specific drug or drugs to be managed by the pharmacist.

(2) The terms and conditions under which drug therapy may be implemented, modified, or discontinued.

(3) The conditions and events upon which the pharmacist is required to notify the collaborating practitioner and the manner and time frame in which notification will occur.

(4) The laboratory tests that may be ordered in accordance with medication therapy management.

(5) Activities which may be performed by the pharmacist in conjunction with the protocol, which shall be documented as specified in the protocol.

(6) A statement of the expected amount of time the pharmacist will dedicate to performing duties specified under the protocol.

(b) Collaborative pharmacy practice agreements shall state the beginning and ending dates of the period of time during which the agreement is in effect, and may be terminated, in writing, by either party at any time. Collaborative pharmacy practice agreements shall be renewed at a minimum every 2 years. When collaborative pharmacy practice agreements are terminated, the patient shall be informed and provided with details to allow for the uninterrupted continuation of their medication therapy management regimen.

(c) Ongoing metrics for quality assurance and safety monitoring shall be agreed upon by the practitioner and pharmacist and shall be included in the collaborative practice agreement. These metrics shall be consistent with metrics adopted or enforced by regulatory bodies.

V. Supervision of the collaborative pharmacy practice agreement shall include:

(a) Protocols developed based on evidence-based guidelines for best practices.

(b) The referring practitioner receiving progress visit notes from each patient encounter in a time specified in the agreement.

(c) The referring practitioner providing supervision for the treatment management of the referred patient.

(d) The retention on file of the collaborative pharmacy practice agreement and protocols at the pharmacist's place of practice and at the practitioner's administrative office or place of practice, which shall be available upon request.

VI. Neither the attending practitioner nor the pharmacist in a collaborative practice pharmacy agreement may seek to gain personal financial benefit by participating in any incentive-based program or accept any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

Source. 2020, 27:29, eff. July 21, 2020

318:47-l Hormonal Contraceptives; Dispensing. –

I. In this section, "standing order" means a written and signed protocol authored by one or more physicians licensed under RSA 329:12 or one or more advanced practice registered nurses licensed under RSA 326-B:18. Such agreement shall specify a protocol allowing the pharmacist licensed under RSA 318:18 to dispense hormonal contraceptives under the delegated prescriptive authority of the physician or APRN, specify a mechanism to document screening performed and the prescription in the patient's medical record, and include a plan for evaluating and treating adverse events. Any such prescription shall be regarded as being issued for a legitimate medical purpose in the usual course of professional practice.

II. Licensed pharmacists following standing orders may dispense hormonal contraceptives to persons in this state without a prior prescription.

III. A pharmacist, pharmacy, physician, or APRN issuing or following standing orders shall be prohibited from seeking personal financial benefit by participating in any incentive-based program or accepting any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

IV. Prior to dispensing hormonal contraceptives under this section, a pharmacist shall complete an Accreditation Council for Pharmacy Education (ACPE) accredited educational training program related to hormonal contraceptives. In addition, pharmacists shall comply with the most current United States Medical Eligibility Criteria (USMEC) for Contraceptive Use as adopted by the Centers for Disease Control and Prevention.

V. The pharmacist shall provide each recipient of hormonal contraceptives pursuant to this section with a standardized information sheet written in plain language, which shall include, but is not limited to, the indication for the use of the hormonal contraceptive, the importance of follow-up care, and health care referral information.

VI. The board shall adopt rules, pursuant to RSA 541-A, relative to:

(a) Education and training required under paragraph IV.

(b) Content and format of the information sheet required under paragraph V, in consultation with the commissioner of the department of health and human services.

(c) A model statewide protocol, with the consent of the board of medicine, the board of nursing, and the department of health and human services to be used for the purposes of paragraph I.

(d) Other matters necessary to the proper administration of this section.

VII. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of this section and the rules adopted under this section are satisfied. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an APRN based on a pharmacist's failure to follow standing orders provided the provisions of this section and the rules adopted under this section are satisfied. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of this section and the rules adopted under this section are satisfied.

Source. 2018, 205:2, eff. Aug. 7, 2018.

318:47-m Nicotine Cessation Therapy. –

I. In this section, "standing order" means a written and signed protocol authored by a physician licensed under RSA 329:12, a physician assistant licensed under RSA 328-D:2, or an advanced practice registered nurse licensed under RSA 326-B:18. The agreement shall specify a protocol allowing a licensed pharmacist to provide nicotine cessation therapy under the delegated prescriptive authority of the physician, physician assistant, or APRN, a mechanism to document screening performed and the prescription in the patient's medical record, and include a plan for evaluating and treating adverse events. The prescriptions shall be considered a legitimate medical purpose in the usual course of professional practice.

II. Licensed pharmacists following standing orders may provide nicotine cessation therapy to persons in this state without a prior prescription.

III. A pharmacist, pharmacy, physician, physician assistant, or APRN issuing or following standing orders shall be prohibited from seeking personal financial benefit by participating in any incentive-based program or accepting any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

IV. Prior to providing nicotine cessation therapy under this section, a pharmacist shall complete an Accreditation Council for Pharmacy Education (ACPE) accredited educational training program related to nicotine cessation.

V. The pharmacist shall provide each recipient of nicotine cessation therapy with a standardized information sheet written in plain language, which shall include, but is not limited to, the indication for the use of the nicotine cessation therapy, the importance of follow-up care, and health care referral information.

VI. The board shall adopt rules, pursuant to RSA 541-A, relative to:

(a) Education and training required under paragraph IV.

(b) Content and format of the information sheet required under paragraph V, in consultation with the commissioner of the department of health and human services.

(c) A model statewide protocol, with the consent of the board of medicine, the board of nursing, and the department of health and human services to be used for the purposes of paragraph I.

(d) Communication to the patient's primary care provider with the consent of the patient.

VII. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician or physician assistant based on a pharmacist's failure to follow standing orders provided the provisions of this section and the rules adopted under this section are satisfied. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an APRN based on a pharmacist's failure to follow standing orders provided the provisions of this section and the rules adopted under this section are satisfied. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of this section and the rules adopted under this section are satisfied.

Source. 2021, 189:4, eff. Jan. 1, 2022.

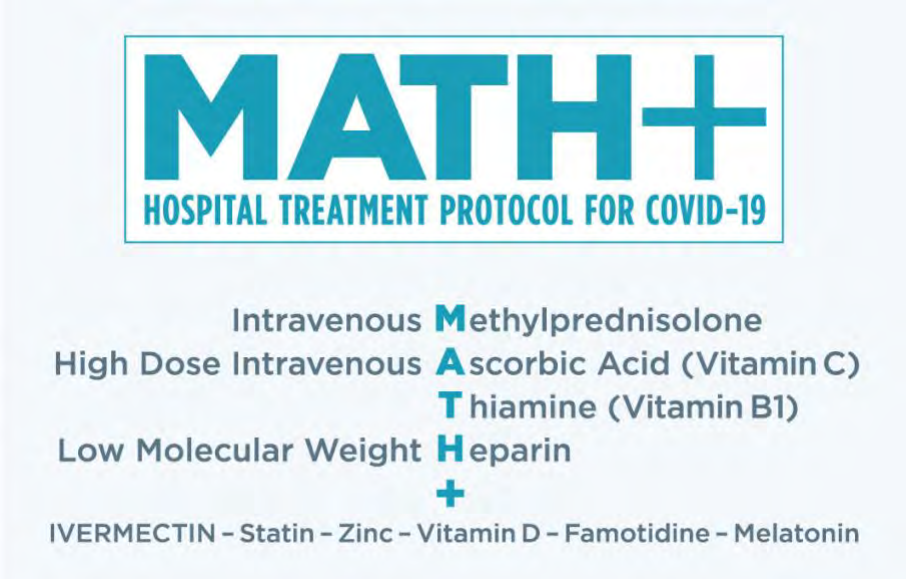
An overview of the MATH+, I-MASK+ and I-RECOVER Protocols

A Guide to the Management of COVID-19

(updated as of 01 January 2022)

Developed and updated by Paul Marik, MD, FCP (SA), FRCP (C), FCCP, FCCM for the COVID-19 Critical Care Alliance (FLCCC Alliance).

This is our recommended approach to COVID-19 based on the best (and most recent) literature. This is a highly dynamic topic; therefore, we will be updating the guideline as new information emerges. Please check on the FLCCC Alliance website for updated versions of this protocol. www.flccc.net



Disclaimer: The information in this document is provided as guidance to physicians worldwide on the prevention and treatment of COVID-19. Our guidance should only be used by medical professionals in formulating their approach to COVID-19. Patients should always consult with their physician before starting any medical treatment.

The FLCCC Alliance™ is registered as a 501(c)(3) non-profit organization.

Index:

1. Introduction

1.1. THE VACCUM OF TRUTH

"The first step is to give up the illusion that the primary purpose of modern medical research is to improve Americans' health most effectively and efficiently. In our opinion, the primary purpose of commercially funded clinical research is to maximize financial return on investment, not health."

—John Abramson, M.D., Harvard Medical School

We are living through a period of time characterized by a ***Vacuum of Truth***, with misinformation, disinformation, blatant lies, censorship, and nefarious intentions being the order of the day. It is difficult to dissect out the actual truth and discern whom to trust. Furthermore, it is no longer controversial to acknowledge that drug makers rigorously control medical publishing and that *The Lancet*, *NEJM*, and *JAMA* are utterly corrupted instruments of Big Pharma. *The Lancet* editor, Richard Horton, confirms, "Journals have devolved into information laundering operations for the pharmaceutical industry."

Dr. Marcia Angell, who served as an *NEJM* editor for 20 years, says journals are "primarily a marketing machine." [1] Pharma, she says, has co-opted "every institution that might stand in its way. Complex scientific and moral problems are not resolved through censorship of dissenting opinions, deleting content from the Internet, or defaming scientists and authors who present information challenging to those in power. Censorship leads instead to greater distrust of both government institutions and large corporations. [2]

1.2 The use of "Off Label Drugs"

Once the FDA approves a prescription medication, federal laws allow any U.S. physician to prescribe the duly approved drug for any reason. [3] Thirty percent of all prescriptions written by American doctors, exercising their medical judgment, are for off-label uses. The Attorney General of Nevada as well as many other states have asserted the right of physicians to prescribe "off-label" drugs such as ivermectin and hydroxychloroquine for the treatment of COVID-19. The office of Nebraska Attorney General Doug Peterson released a legal opinion on October 15 2021 saying it didn't see data to justify legal action against health care professionals who prescribe ivermectin or hydroxychloroquine.

1.3. Overview of the treatment of COVID-19

While there is **no cure or "magic bullet"** for COVID-19, recently, a number of therapeutic agents have shown great promise for both the prevention and treatment of this disease including Ivermectin, Vitamin D, quercetin, melatonin, fluvoxamine, spironolactone, corticosteroids, curcumin (turmeric), *Nigella sativa* and antiandrogen therapy. It is critical to recognize that infection with SARS-CoV-2 progresses through a number of stages/phases and that treatment is highly stage-specific (see Figures 1-4 and Table 1). It is likely that no single drug will be effective in treating this complex disease and that multiple drugs with different mechanisms of action used in specific phases of the disease will be required. A growing body of evidence suggests that many of these agents may act synergistically in various phases of the disease. [4-6] Furthermore, an understanding of the structure of SARS-CoV-2 (see Figure 5) as well as the pathophysiology/pathogenesis of COVID-19 is critical in treating the disease. [7] Finally, the relentless malpractice of deliberately withholding effective early COVID treatments, and of forcing the use of toxic remdesivir in hospitalized patients, may have unnecessarily killed up to 500,000 Americans (see Figures 6a-c). [2]

As the pandemic has played out over the last year, over four million patients have died worldwide, and the pandemic shows no signs of abating. Most countries across the globe have limited resources to manage this humanitarian crisis. We developed the **MATH+ protocol** to provide guidance for the treatment of the pulmonary phase of this disease with the goal of reducing the hospital mortality from this devastating disease. However, it soon became obvious that our emphasis needed to shift to the prevention and early (home) treatment of this catastrophic disease to prevent patients progressing to the pulmonary phase and requiring hospitalization (see Figure 5). Hence, we developed the **I-MASK+ and the Test and Treat protocols.** While we strongly believe that such an approach can mitigate the development and progression of this disease, limit deaths, and allow the economy to re-open, so-called "health care authorities" across the globe have been silent in this regard, including the WHO, CDC, NIH, etc .(see NIH Guidance, Figure 6a and 6b).

While vaccination is part of the solution, it will take many months if not years to vaccinate 70-85% of the world's population of 7.8 billion people required for "herd immunity". We believe that the **I-MASK+** protocol provides a bridge to universal vaccination. Furthermore, we have developed the **I-MASS protocol** for a MASS Distribution campaign to lessen the impact of COVID-19 in resource-poor countries.

Mutant strains of SARS-CoV-2 have recently appeared, demonstrating increased transmissibility.[8,9] [10] Many of these mutations involve the spike protein (which almost all of the vaccines have targeted), raising the real possibility that the vaccines may become less effective against the mutating strains of SARS-CoV-2.[9,11,12] And, finally the Post-COVID syndrome or "long-hauler syndrome" has emerged as a common and disabling disorder, and its pathophysiology is poorly understood. We offer the **I-RECOVER** protocol to help treat this disabling disorder. Recently, the post-vaccination syndrome has emerged as a problematic entity; we believe that the **I-RECOVER** protocol has utility in treating this syndrome.

Figure 1. Treatment phases of COVID-19

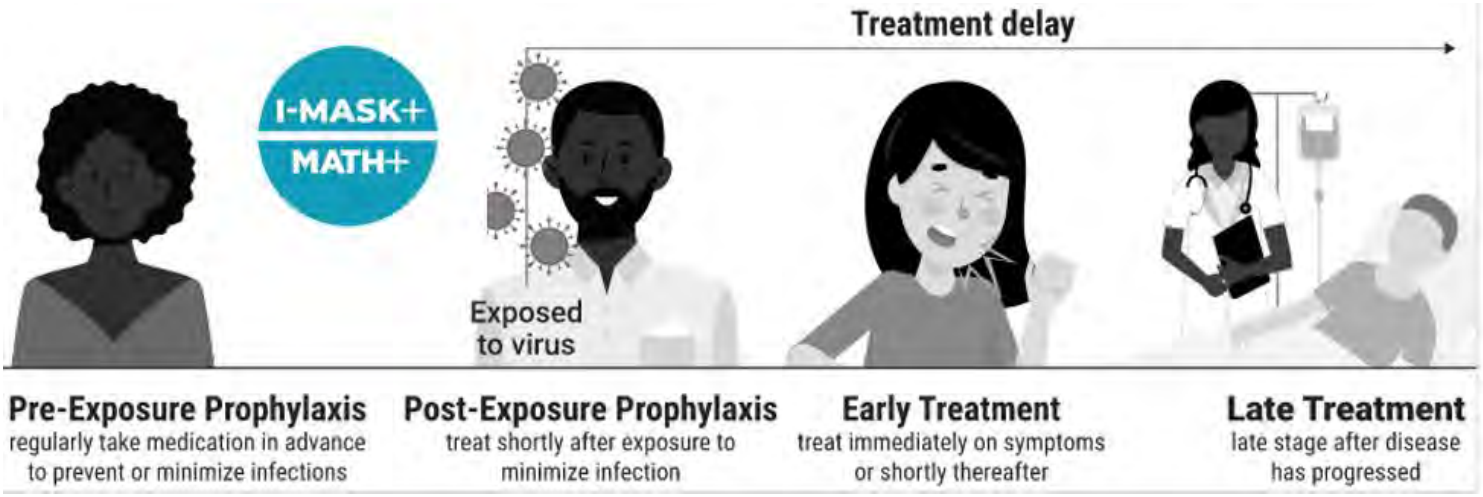
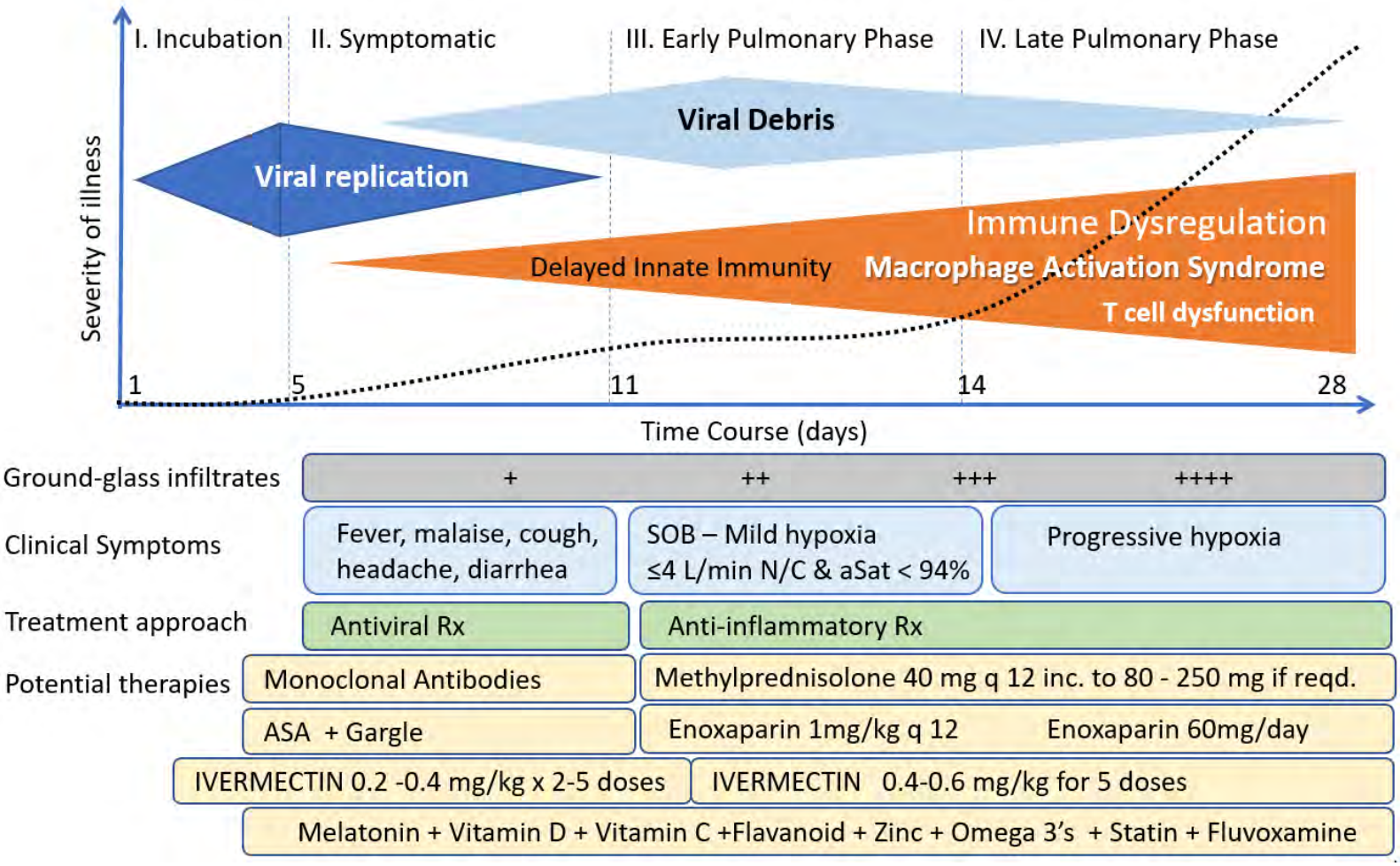


Figure 2. The course of COVID-19 and general approach to treatment

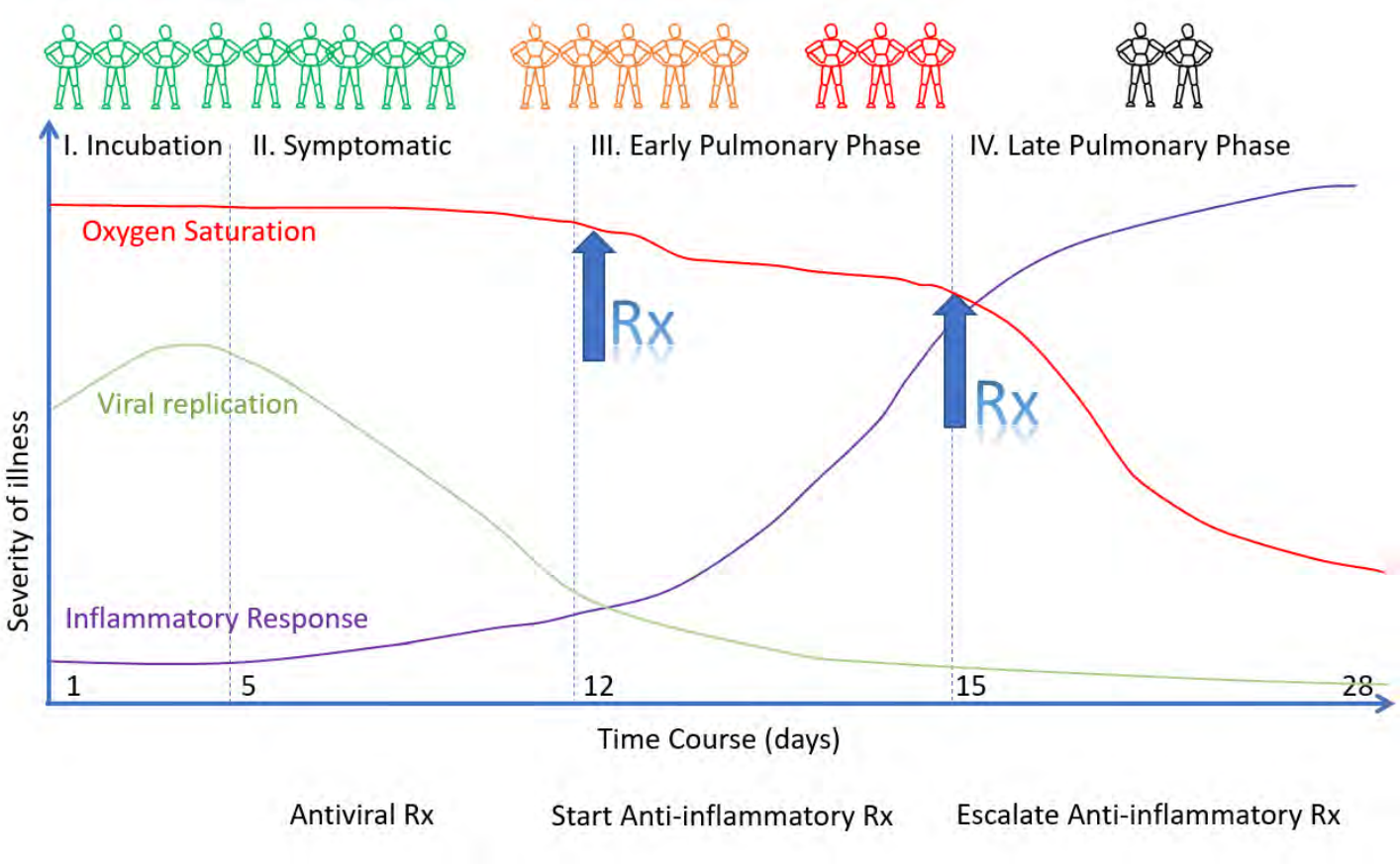


THIS IS A STEROID-RESPONSIVE DISEASE:

HOWEVER, TIMING IS CRITICAL.

Not too early. Not too late.

Figure 3. Timing of the initiation of anti-inflammatory therapy



Note: Viral Replication in Figures 2 and 3 are typical for the original Wuhan SARS-CoV-2 virus (alpha strain). SARS-CoV-2 delta and gamma (P1) variants may present prolonged duration of viral replication. Furthermore, the time course from incubation to symptom onset and to the pulmonary phase may be shortened. The time course of Omicron is unclear at this time.

Figure 4. Time course of laboratory tests for COVID-19

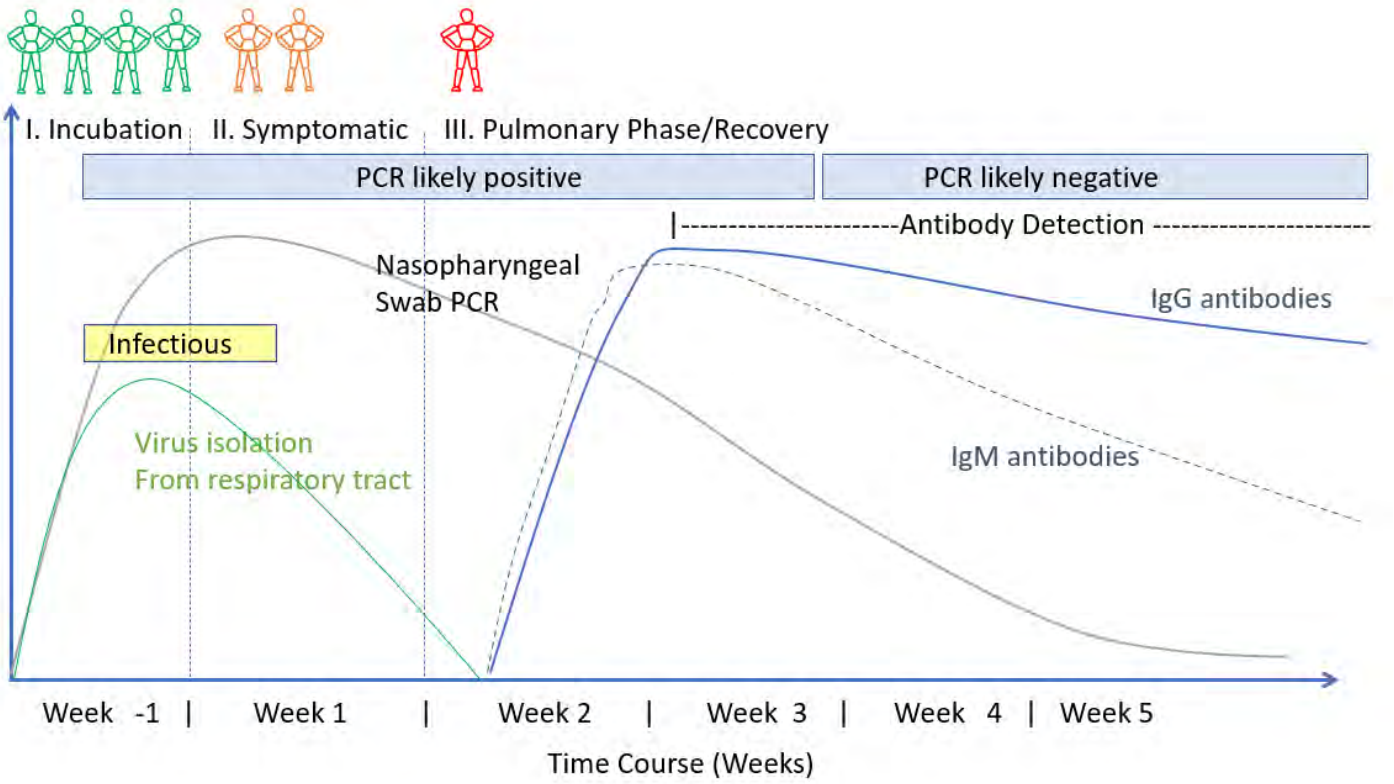


Figure 5. SARS-Co-V-2 structure and RNA genome

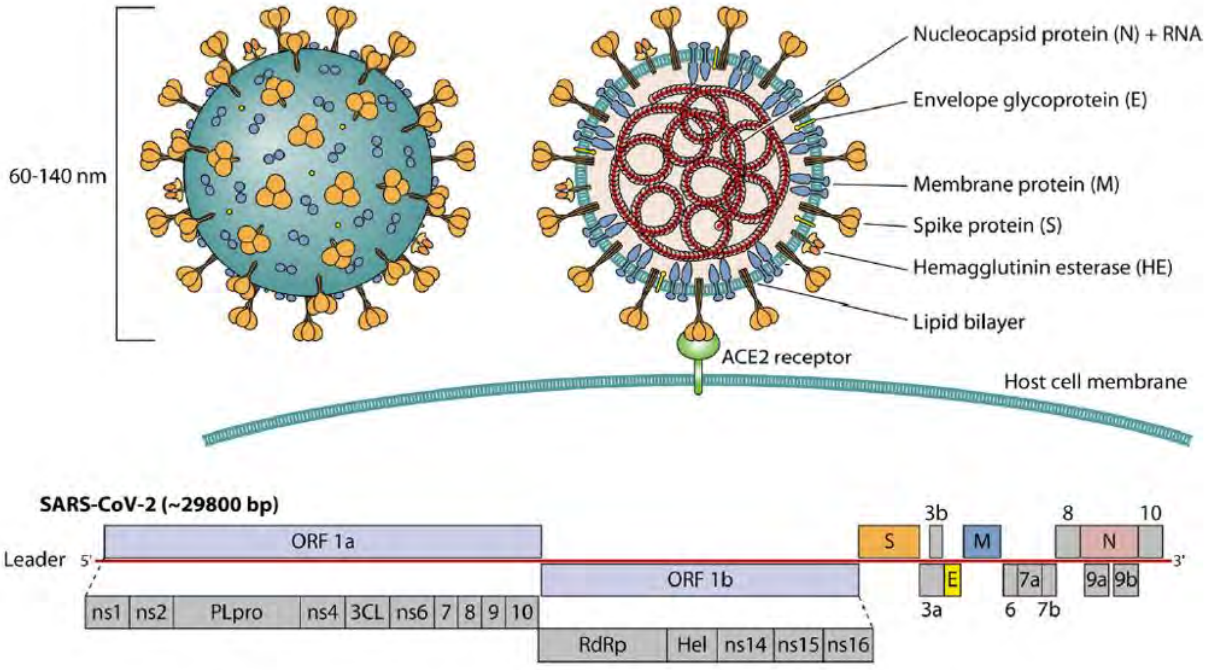


Table 1. Pharmacological therapy for COVID by stage of illness: What has worked and what has failed*

	Pre-exposure/ Post-Exposure/Incubation	Symptomatic Phase	Pulmonary/ inflammatory phase
Anti-androgen Rx	Benefit	BENEFIT	BENEFIT
Ivermectin	BENEFIT	BENEFIT	BENEFIT
Corticosteroids	n/a	Trend to harm	BENEFIT
LMWH	n/a	n/a	BENEFIT
Monoclonal Abs	BENEFIT	BENEFIT (early)	HARM
Hydroxychloroquine	Benefit**	Benefit**	?Trend to harm
Remdesivir	n/a	? Benefit	HARM
Lopivinar-Ritonavir	n/a	No benefit	No benefit
Interferon α/β	Inhaled ? Benefit	No benefit	Harm
Tocilizumab	n/a	n/a	Unclear Benefit
Convalescent Serum	n/a	No benefit	Trend to harm
Colchicine	n/a	Unclear benefit	No Benefit

* Based on randomized controlled trials (see supporting information below)
** Due to extensive fraudulent activity around the design and conduct of RCTs, the benefit of HCQ is supported largely by numerous consistently positive observational trials.

Figure 6a. NIH recommendations for the treatment of COVID-19 across the stages of the disease. (Last Updated: October 19, 2021)

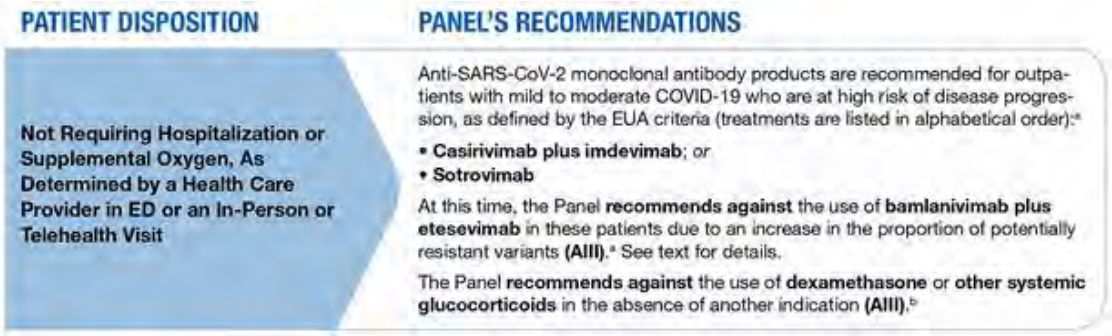


Figure 6b. Therapeutic management of hospitalized adults with COVID-19 based on disease severity. (Last Updated: December 16, 2021)

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use 1 of the following options: • **Remdesivir**[b,c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone plus remdesivir**[b,c] **(BIIb)** • **Dexamethasone (BI)** For patients on dexamethasone with rapidly increasing oxygen needs and systemic inflammation, add a second immunomodulatory drug[d] (e.g., baricitinib[e] or tocilizumab[e]) **(CIIa)**.
Hospitalized and Requires Oxygen Through a High-Flow Device or NIV	Use 1 of the following options: • **Dexamethasone (AI)** • **Dexamethasone plus remdesivir**[b] **(BIII)** For patients with rapidly increasing oxygen needs and systemic inflammation, add either **baricitinib**[e] **(BIIa)** or **IV tocilizumab**[e] **(BIIa)** to 1 of the 2 options above.[d,f]
Hospitalized and Requires MV or ECMO	• **Dexamethasone (AI)**[g] For patients who are within 24 hours of admission to the ICU: • **Dexamethasone plus IV tocilizumab (BIIa)** If IV tocilizumab is not available or not feasible to use, IV **sarilumab** can be used **(BIIa)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

[a] Corticosteroids prescribed for an underlying condition should be continued.
[b] If the patient progresses to requiring high-flow oxygen, NIV, MV, or ECMO, complete the full course of remdesivir (refer to Table A).
[c] Evidence suggests that the benefit of remdesivir is greatest when the drug is given early in the course of COVID-19 (e.g., within 10 days of symptom onset). Clinical trials have not demonstrated a mortality benefit for remdesivir, but a large placebo-controlled trial showed that remdesivir reduced time to clinical recovery in hospitalized patients. See Rationale for the Use of Remdesivir below.
[d] Drugs are listed alphabetically. There are no studies directly comparing baricitinib and tocilizumab, and there is insufficient evidence to recommend 1 drug or 1 class of drug (i.e., JAK inhibitors, anti-IL-6 receptor mAbs) over the other. Treatment decisions should be based on local guidance, drug availability, and patient comorbidities.
[e] If baricitinib and IV tocilizumab are not available or not feasible to use, **tofacitinib** can be used instead of baricitinib **(BIIa)** and **IV sarilumab** can be used instead of IV tocilizumab **(BIIa)**.
[f] The Panel **recommends against** the use of **baricitinib** in combination with **tocilizumab** for the treatment of COVID-19, except in a clinical trial **(AIII)**. Because both baricitinib and tocilizumab are potent immunosuppressants, there is the potential for an additive risk of infection.
[g] The combination of **dexamethasone plus remdesivir** may be considered for patients who have recently been intubated **(CIII)**. The Panel **recommends against** the use of **remdesivir** monotherapy in these patients **(AIIa)**.

Key: ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; IL = interleukin; IV = intravenous; JAK = Janus kinase; mAb = monoclonal antibody; MV = mechanical ventilation; NIV = noninvasive ventilation; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally

Figure 6c. NIH recommendations for prevention of SARS-CoV-2 infection. (Last Updated: December 16, 2021)

Summary Recommendations

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends COVID-19 vaccination for everyone who is eligible according to the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices **(AI)**.
- The Panel recommends using 1 of the following anti-SARS-CoV-2 monoclonal antibodies (listed alphabetically) as post-exposure prophylaxis (PEP) for people who are at high risk of progressing to severe COVID-19 if infected with SARS-CoV-2 **AND** who have the vaccination status **AND** exposure history outlined in the text below:
  - **Bamlanivimab 700 mg plus etesevimab 1,400 mg** administered as an intravenous (IV) infusion **(BIII)**; *or*
  - **Casirivimab 600 mg plus imdevimab 600 mg** administered as subcutaneous injections **(AI)** or an IV infusion **(BIII)**.
- The Panel **recommends against** the use of **hydroxychloroquine** for SARS-CoV-2 PEP **(AI)**.
- The Panel **recommends against** the use of other drugs for SARS-CoV-2 PEP, except in a clinical trial **(AIII)**.
- The Panel **recommends against** the use of any drugs for SARS-CoV-2 pre-exposure prophylaxis (PrEP), except in a clinical trial **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

2. Pre and Postexposure Prophylaxis (The I-MASK+ protocol)

The components of the I-MASK+ Prophylaxis and Early Treatment protocol are illustrated in Figures 7a-c. Recent data suggests that ivermectin, melatonin as well as the combination of quercetin (or mixed flavonoids) and Vitamin C as well as oropharyngeal sanitation may play an important role in both pre-exposure and postexposure prophylaxis. [5,13] The evidence supporting the use of ivermectin for the prophylaxis of COVID-19 is provided by the comprehensive review by Kory et al. [14] It is important to emphasize that ALL of the medications included in our prophylactic regimen are inexpensive, safe, and widely available. The I-MASK+ protocol MUST be part of an overall strategy that includes common sense public health measures, i.e., masks (only for prolonged exposure in confined, poorly ventilated environments), short term quarantine of infected patients, and high risk individuals (advanced aged and comorbidities) avoiding large public and family gatherings. [15] Standard surgical and cloth masks likely only reduce risk of transmission for finite periods in confined environments. For prolonged protection in such settings, N95 type masks would be required.

2.1 Core Components of the I-MASK Prophylactic Protocol

- Ivermectin for post-exposure prophylaxis (see ClinTrials.gov NCT04422561). 0.4 mg/kg immediately then repeat 2nd dose in 48 hours. Ivermectin is best taken with a meal or just following a meal (greater absorption). [16] Oropharyngeal sanitation also suggested (see section on home treatment below).
- Ivermectin for pre-exposure prophylaxis (in healthcare workers) and for prophylaxis in high-risk individuals (> 60 years with co-morbidities, morbid obesity, long term care facilities, etc). 0.2 mg/kg per dose; start treatment with one dose, take 2nd dose 48 hours later, then 1 dose every 7 days (i.e. weekly). [17-22] For those at high risk of contracting COVID-19, we now recommend twice weekly dosing. See Dosing Table below. Ivermectin has a number of potentially serious drug-drug interactions); please check for potential drug interactions at Ivermectin Drug Interactions - Drugs.com (also see Table 4 below). The most important drug-drug interactions occur with *cyclosporin, tacrolimus, anti-retroviral drugs*, and certain antifungal drugs. While ivermectin has a remarkable safety record, [23] fixed drug eruptions (diffuse rash) and Stevens Johnson Syndrome have rarely been reported. [24,25] While hepatitis is commonly quoted as a side effect, we are aware of one published case report of reversible hepatitis. [26] The safety of ivermectin in pregnancy has not been determined. [27] Ivermectin may increase the risk of congenital malformations particularly when used in the first trimester. [27] US Food and Drug Administration (FDA) has classified ivermectin as pregnancy category C—i.e, "Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks." In pregnant patients with symptomatic COVID-19 infections, the risk and benefits of ivermectin should be discussed with the patient, and informed consent obtained from the patient should the drug be prescribed. Additionally, women should be counselled that low concentrations of ivermectin are present in breast milk; the implications of this finding are unclear. [28]
- Melatonin (slow release/extended release): Begin with 0.3 mg and increase as tolerated to 6 mg at night. [4,13,29-35]. Melatonin has anti-inflammatory, antioxidant, immunomodulating and metabolic effects that are likely important in the mitigation of COVID-19 disease. [36-38] Multiple studies have demonstrated the benefit of melatonin at various stages of the disease. [39-41] A recent large retrospective study demonstrated that the use of melatonin in intubated patients with COVID-19 significantly reduced the risk of death (HR 0.1; p=0.0000000715). [37] It is intriguing to recognize that bats, the natural reservoir of coronavirus, have exceptionally high levels of melatonin, which may protect these animals from developing symptomatic disease. [42] Similarly, children have high levels of circulating melatonin approximating those of bats, while elderly people – particularly those over the age of 60 – have very low melatonin levels; this may partly explain the increased

vulnerability of the elderly to COVID-19. The slow release (extended release) formulations of melatonin are preferred as they more closely replicate the normal circadian rhythm. [29] There is marked inter-individual variation in the metabolism of melatonin (first pass metabolism), hence the dose must be individualized. [29] High serum levels are associated with hyper-REM sleep and bad dreams. Rapid release melatonin (usual over-the-counter formulation) results in early high peaks that do not replicate the normal circadian pattern; hence it is important to take the slow release/extended-release formulation.

- Oropharyngeal hygiene with twice daily antiviral mouthwash/gargle (see Figure 7 and below).
- Monoclonal antibodies for post-exposure prophylaxis. A single subcutaneous injection of REG-COV2 (a combination of the monoclonal antibodies casirivimab and imdevimab) has been demonstrated to reduce the risk of symptomatic COVID-19 infection in close contacts by 92.6% (7.8% to 1.5%). [43] Monoclonal antibodies are recommended in high-risk individuals, namely, > 65 years, obesity, pregnancy, chronic kidney disease, diabetes mellitus, immunosuppressed, coronary heart disease, etc. See infusioncenter.org and call 1-877-332-6585 In USA for eligibility and location.
- *Optional:* Famotidine 20–40 mg/day [44-50]. Low level evidence suggests that famotidine may reduce disease severity and mortality. However, the findings of some studies are contradictory. While it was postulated that famotidine inhibits the SARS-CoV-2 papain-like protease (PLpro) as well as the main protease (3CLpro), this mechanism has been disputed. [47] Furthermore, a number of studies have demonstrated an association between the use of proton pump inhibitors (PPIs) with an increased risk of contracting COVID-19 and with worse outcomes. [51,52] This data suggest that famotidine may be the drug of choice when acid suppressive therapy is required.
- *Optional:* Hydroxychloroquine (HCQ) 200 mg BID for 5 days together with ZINC (75-100mg elemental zinc) post COVID-19 exposure. [53-56]

Disclaimer: The safety of ivermectin in pregnancy has not been established. Particularly the use in the 1st trimester should be discussed with your doctor beforehand.

Ivermectin dosing table: 200 ug/kg (0.2 mg/kg) or fixed dose of 12 mg (≤ 80kg) or 18 mg (≥ 80kg). [57] Depending on the manufacturer ivermectin is supplied as 3mg, 6 mg or 12 mg tablets.

Body weight	Dose
50-64.9 kg	12 mg
65-79.9 kg	15 mg
80-94.9 kg	18 mg
95-109.9 kg	21 mg
≥ 110 kg	24 mg

2.2 Nutritional Supplements (in order of priority, not all required)

- Curcumin (Turmeric). Curcumin has antiviral activity against a number of viruses including SARS-CoV-2. In addition, this spice has anti-inflammatory, antioxidant and immune modulating properties. [58-62] Emerging data suggests that curcumin improves the clinical outcome of patients with COVID-19. [63,64]
- *Nigella Sativa* (black cumin) and honey. Both honey and Nigella Sativa have anti-viral, anti-microbial, anti-inflammatory, and immune-modulatory effects with proven safety profiles. [65-72] It should be noted that thymoquinone (the active ingredient of *Nigella Sativa*) decreases the absorption of cyclosporine and phenytoin. [73] Patients taking these drugs should therefore avoid taking *Nigella Sativa*. Furthermore, two cases of serotonin syndrome have been reported in patients taking *Nigella Sativa* who underwent general anaesthesia (probable interaction with fentanyl. [74]

- Vitamin D3 3000- 5000 IU/day (75-125 mcg) (this is the default dosing when the baseline vitamin D level is not available). An alternative strategy is 40 000 IU weekly. Note RDA (Recommended Daily Allowance) is 800–1000 IU/day. The safe upper-dose daily limit is quoted as < 5000 IU/day. It is however **EXTREMELY IMPORTANT** to stress that the optimal regimen for Vitamin D supplementation for both the prophylaxis and treatment of COVID-19 should be based on the baseline vitamin D level (see Tables 2 & 3. The OPTIMAL target vitamin D level is > 50 ng/ml; at this level the risk of acquiring COVID-19 approximates ZERO. [75] It may take many months/years to achieve optimal levels in a patient with a vitamin D level of < 12 ng/ml taking 5000 IU /day. Vitamin D has numerous immunological properties that play a vital role in limiting the acquisition and severity of COVID-19.[76] Vitamin D insufficiency has been associated with an increased risk of acquiring COVID-19 and from dying from the disease. [77-103] Vitamin D supplementation may therefore prove to be an effective and cheap intervention to lessen the impact of this disease, particularly in vulnerable populations, i.e., the elderly, those of color, obese and those living > 45^{o} latitude. [83-98,101] In addition, vitamin D supplementation may be important in pregnant patients.[104] It is likely that the greatest benefit from vitamin D supplementation will occur in vitamin D insufficient individuals who take vitamin D prophylactically; once vitamin D insufficient individuals develop COVID-19 the benefits will likely be significantly less. [105] This concept is supported by a recent study that demonstrated that residents of a long-term care facility who took vitamin D supplementation had a much lower risk of dying from COVID-19. [99]
- Probiotics. There appears to be a bi-directional relationship between the microbiome esp. Bifidobacterium and COVID-19. Low levels of Bifidobacterium may predispose to COVID-19 and increase its severity. [106-109] COVID-19 depletes the microbiome of Bifidobacterium, which may then increase the severity and duration of COVID-19 symptoms. Kefir (a fermented milk drink) is high in Bifidobacterium and other probiotics that have demonstrated health benefits. [110,111] Kefir, probiotic yogurt and/or the addition of Bifidobacterium Probiotics (e.g., Daily Body Restore) together with Prebiotics (e.g. XOS Prebiotic, Bio Nutrition Pre-Biotic) may normalize the microbiome, which may reduce the risk and severity of COVID-19.
- Vitamin C 500 – 1000 mg BID (twice daily) and Quercetin 250 mg daily. [112-124] Due to the possible drug interaction between quercetin and ivermectin (see below) these drugs should not be taken simultaneously (i.e. should be staggered morning and night). Vitamin C has important anti-inflammatory, antioxidant, and immune enhancing properties, including increased synthesis of type I interferons. [115,125,126] Quercetin has direct virucidal properties against a range of viruses, including SARS-CoV-2, and is a potent antioxidant and anti-inflammatory agent. [113,118,123,123,127-135] Quercetin is a potent inhibitor of inflammasome activation, which is believed to play a major role in the pathophysiology of the COVID-19 immune dysfunction. [135] In addition, quercetin acts as a zinc ionophore. [136] It is likely that vitamin C and quercetin have synergistic prophylactic benefit. [5] A mixed flavonoid supplement containing quercetin, green tea catechins and anthrocyanins (from berries) may be preferable to a quercetin supplement alone; [137-141] this may further minimize the risk of quercetin related side effects. It should be noted that *in vitro* studies have demonstrated that quercetin and other flavonoids interfere with thyroid hormone synthesis at multiple steps in the synthetic pathway. [142-145] The use of quercetin has rarely been associated with hypothyroidism. The clinical impact of this association may be limited to those individuals with pre-existent thyroid disease or those with subclinical thyroidism. [146] In women, high consumption of soya was associated with elevated TSH concentrations. [147] The effect on thyroid function may be dose dependent, hence for chronic prophylactic use we suggest that the lowest dose be taken. Quercetin should be used with caution in patients with hypothyroidism and TSH levels should be monitored. It should also be noted quercetin may have important drug-drug interactions; the most important drug-drug interaction is with cyclosporin and tacrolimus. [148] In patients taking these drugs it is best to avoid quercetin; if quercetin is taken cyclosporin and tacrolimus levels must be closely monitored.

- Zinc 30–40 mg/day (elemental zinc). [119,121,122,149-153] Zinc is essential for innate and adaptive immunity. [151] In addition, Zinc inhibits RNA dependent RNA polymerase *in vitro* against SARS-CoV-2 virus. [150] Due to competitive binding with the same gut transporter, prolonged high dose zinc (> 50mg day) should be avoided as this is associated with copper deficiency. [154] Commercial zinc supplements contain 7 to 80 mg of elemental zinc, and are commonly formulated as zinc oxide or salts with acetate, gluconate, and sulfate. 220 mg zin*c* sulfate contains 50 mg elemental zinc.
- B complex vitamins [155-159].

2.3 Prevention Protocol in Children and Adolescents

- Multivitamin with age-appropriate dosages of Vitamin C, D and B complex
- Oropharyngeal sanitization with mouth gargle twice daily (very important)
- Curcumin
- *Nigella sativa* and honey
- Kefir, probiotic yogurt and/or Bifidobacterium probiotics (e.g., Daily Body Restore) together with Prebiotics (e.g. XOS Prebiotic, Bio Nutrition Pre-Biotic).
- Children's Zinc lozenges/chewable 3-5mg/day

Table 2. Guidance on upfront loading dose regimens to replenish Vitamin D stores in the body

Serum vitamin D (ng/mL)	Frequency of administration (per week)	Duration of therapy (weeks)	Total dose for correction * (IU millions)
≤ 5	100,000 IU, one dose; 50,000 twice a week	14	1.3 to 1.5
6–10	50,000 twice a week	12	1.0 to 1.2
11–15	50,000 twice a week	10	0.8 to 1.0
16–20	50,000 twice a week	8	0.6 to 0.8
21–25	50,000 once a week	10	0.4 to 0.5
26–30	50,000 once a week	6	0.2 to 0.3
Maintenance regimens	50,000 IU, or	Monthly	Maintenance
	1,000 to 2,000 IU	Daily	Maintenance
	4,000 or 5,000	Daily	High risk persons

Reproduced with permission from Wimalawansa SJ. [160]

Table 3. Rapid and effective Vitamin D supplementation in patients with COVID-19 infection

COVID-19 VITAMIN D (CHOLECALCIFEROL) SUPPLEMENTATION										
	Patient Definition	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	TOTAL PERIOD	TOTAL DOSE
INPATIENT	Serum 25OHD level < 12 ng/mL	100.000 IU	10.000 IU	10.000 IU	10.000 IU	10.000 IU	10.000 IU	10.000 IU	14 Days	320.000 IU
	Serum 25OHD level 20–12 ng/mL	100.000 IU	5.000 IU	5.000 IU	5.000 IU	5.000 IU	5.000 IU	5.000 IU	14 Days	260.000 IU
	Serum 25OHD level 20–30 ng/mL	100.000 IU	2.000 IU	2.000 IU	2.000 IU	2.000 IU	2.000 IU	2.000 IU	14 Days	224.000 IU
ICU PATIENT	Serum 25OHD level < 12 ng/mL	100.000 IU	100.000 IU	100.000 IU	100.000 IU	100.000 IU			5 Days	500.000 IU
	Serum 25OHD level 20–12 ng/mL	100.000 IU	100.000 IU	100.000 IU	100.000 IU				4 Days	400.000 IU
	Serum 25OHD level 20–30 ng/mL	100.000 IU	100.000 IU	50.000 IU					3 Days	250.000 IU

Reproduced with permission from Gonen et al. [161]

Table 4. Drug interactions with ivermectin (From Medscape).

https://reference.medscape.com/drug/stromectol-ivermectin-342657#3

Patients taking any of these medications should discuss with their treating physicians.

DRUG INTERACTIONS WITH IVERMECTIN			
SERIOUS (4) Use Alternative	MONITOR CLOSELY (possible) (49) Especially those with (*)		
Erdafitinib	Amiodarone	Glecaprevir/Pibrentasvir	Phenytoin
Lasmiditan	Atorvastatin	Indinavir	Ponatinib
Quinidine	Berotralstat	Istradefylline	Quercetin (**)
Tepotinib	Bosutinib	Itraconazole (*)	Ranolazine
	Clarithromycin (*)	Ivacaftor	Rifampin (*)
	Clotrimazole	Ketoconazole (*)	Ritonavir (*)
	Dronedarone	Lapatinib	Sarecycline
	Elagolix	Lomitapide	Simvastatin
	Eliglustat	Lonafarnib	Sirolimus (*)
	Erythromycin base	Loratadine	St John's Wort
	Erythromycin ethylsuccinate (*)	Lovastatin	Stiripentol
	Erythromycin lactobionate (*)	Nefazodone	Tacrolimus (*)
	Erythromycin stearate (*)	Nicardipine	Tolvaptan
	Felodipine	Nifedipine	Trazodone
	Fosphenytoin	Nilotinib	Tucatinib
	Fostamatinib	Phenobarbital	Verapamil (*)
			Warfarin (*)

(**) Not clear. May increase ivermectin levels

3. Symptomatic patients at home (I-MASK+ EARLY Treatment Protocol)

3.1 First Line Treatments (in order of priority, not all required)

- Ivermectin 0.3- 0.6 mg/kg – one dose daily for 5 days or until recovered. [19,23,77-80,162-177]. Higher doses (0.6 mg/kg) are often required: a) in regions with more aggressive variants, b) if treatment started on or after 5 days of symptoms or c) in patients in pulmonary phase, d) extensive CT involvement or e) extensive comorbidities/risk factors (older age, obesity, diabetes). **A dose of 0.3-0.4 mg/kg may be appropriate for the Omicron variant.** Ivermectin is best taken with a meal or just following a meal (greater absorption). See drug-drug interactions above. It should be noted that multiday treatment has been shown to be more clinically effective than single-day dosing.
- Nitazoxanide (NTZ) 600 mg BID for 5 days was shown to reduce disease progression, hospitalization and death when used early in outpatients with mild to moderate disease. [178] The combination of NTZ and ivermectin has been shown to reduce viral clearance and symptom progression in outpatients with COVID-19. [179,180] NTZ is an oral antiparasitic drug having activity against many protozoa and helminths and – similar to ivermectin – has been shown to have antiviral and immune-modulatory effects. [181,182] Like ivermectin, NTZ has broad spectrum antiviral activity that includes SARS-CoV-2. [182-185] Furthermore, as NTZ and ivermectin have differing modes of action, it is likely that these two drugs have synergistic antiviral and anti-inflammatory effects.[180,183,186] NTZ should therefore be considered as an alternative to ivermectin, or as part of a multi-drug combination that includes ivermectin. It should be noted that while NTZ is relatively cheap in most of the world it is very expensive in the USA.
- Oropharyngeal sanitization (see figure 7b and c). [187] Inhaled steam supplemented with antimicrobial essential oils (e.g VapoRub™ inhalations) has been demonstrated to have virucidal activity. [188] Antiseptic-antimicrobial mouthwashes (chlorhexidine, povidone-iodine, cetylpyridinium chloride and the combination of eucalyptus, menthol and thymol [Listerine™]) have been shown to inhibit SARS-CoV-2 replication and to reduce viral load in research studies. [189-196] A mouthwash containing cetylpyridinium chloride (CPC) has broad antimicrobial properties and has been shown to be effective in controlling gingivitis and gingival plaque. [196-198] An *in-vitro* study demonstrated that CPC was highly viricidal against a human coronavirus. [199] In a primary prophylaxis study, a povidone-iodine throat spray administered three times daily proved to be highly effective in reducing the risk of laboratory confirmed SARS-CoV-2 infection. In patients with symptomatic disease treated at home with a 1% povidone iodine mouthwash/gargle, together with nasal and eye drops, resulted in a dramatic reduction in morbidity, hospitalization and death. [200] A nasal spray with 1% povidone-iodine (for example Immune Mist™) administered 2-3 times per day is recommended in post-exposure prophylaxis and in symptomatic patients (early phase of COVID-19 infection). [191] Due to low level systemic absorption, povidone-iodine nasal spray should not be used for longer than 5-7 days in pregnant women. While the use of an iodine-containing mouthwash over a six-month period was demonstrated to increase serum iodine levels, thyroid function tests remained unchanged. [201] Oropharyngeal sanitization will likely reduce the viral load in the upper airways, thereby reducing the risk of symptomatic disease and likely reducing disease severity. This may be particularly important with the Delta variant, which replicates to achieve viral high loads in the nasopharynx/oropharynx.
- ASA 325 mg/day (unless contraindicated). ASA has anti-inflammatory, antithrombotic, immunomodulatory, and antiviral effects. [202-204] Platelet activation plays a major role in propagating the prothrombotic state associated with COVID-19. [205-207]

- Melatonin 10 mg at night. [35-41] The slow release/extended-release preparation is preferred as it minimizes the risk of bad dreams.
- Curcumin (turmeric). Curcumin has antiviral activity against SARS-CoV-2. In addition, this spice has anti-inflammatory and immune modulating properties. [58-62]
- *Nigella Sativa* (black cumin) and honey. A randomized placebo-controlled study demonstrated that the combination of honey and *Nigella sativa* (HNS) hastened recovery, decreased viral shedding and reduced mortality in patients with both moderate and severe COVID-19 infection. [67]
- Kefir and/or Bifidobacterium Probiotics (e.g., Daily Body Restore) together with Prebiotics (e.g. XOS Prebiotic, Bio Nutrition Pre-Biotic) to normalize the microbiome.
- Vitamin D 3000 - 5000 IU daily (125 mcg) if baseline Vitamin D level is unknown. The optimal dose of Vitamin D in the acute setting is controversial. [208,209] However, the dosing schedule as outlined in Table 3 is suggested. [161]
- Vitamin C 500 – 1000 mg BID and Quercetin 250 mg BID (or mixed flavonoid supplement). Due to the possible drug interaction between quercetin and ivermectin (see above) these drugs ***should not be taken simultaneously*** (i.e., should be staggered morning and night).
- Zinc 75–100 mg/day (elemental zinc).
- Hydroxychloroquine (HCQ) 200 mg BID for 5-10 days. [53-56] HCQ may be taken in place of ivermectin or together with ivermectin. While ivermectin should be avoided in pregnancy, the FDA considers HCQ safe in pregnancy. Some 200 peer-reviewed studies (C19Study.com) by government and independent researchers deem HCQ safe and effective against Coronavirus, especially when taken prophylactically or when taken in the initial stages of illness along with zinc and azithromycin. Unfortunately, most of the RCTs that have been conducted to date used toxic doses of HCQ and/or were given very late in the disease and were clearly designed by the "captured" agencies to fail. [2] Instead of using the standard treatment dose of 400 mg/day, the 17 WHO studies administered a borderline lethal *daily* dose starting with 2,400 mg on Day 1 and using 800 mg/day thereafter. Brazilian prosecutors have accused the authors of one study with committing homicide by purposefully poisoning and murdering the elderly subjects of their study. [210]
- In symptomatic patients, monitoring with home pulse oximetry is recommended (due to asymptomatic hypoxia). The limitations of home pulse oximeters should be recognized, and validated devices are preferred. [211] Multiple readings should be taken over the course of the day, and a downward trend should be regarded as ominous. [211] Baseline or ambulatory desaturation < 94% should prompt hospital admission. [212] The following guidance is suggested: [211]
    - Use the index or middle finger
    - Only accept values associated with a strong pulse signal
    - Observe readings for 30–60 seconds to identify the most common value
    - Remove nail polish from the finger on which measurements are made
    - Warm cold extremities prior to measurement

3.2 Second Line Treatments

- B complex vitamins
- Anti-androgen therapy. Androgens augment SARS-CoV-2 infectivity by promoting the expression of transmembrane protease (TMPRSS2) that primes the spike viral entry protein. [213] In addition androgens are pro-inflammatory. [214] Spironolactone is the anti-androgen of choice (in both men and women). Spironolactone has pleiotropic effects in COVID-19 including anti-androgen, anti-inflammatory, anti-fibrotic and restores the RAAS (angiotensin 1-7). [215-218]

The optimal anti-androgenic dose of spironolactone appears to be 100 mg BID. Proxalutamide is the most potent antiandrogen; this agent has been demonstrated to have remarkable efficacy in patients with COVID. [219] The 5-alpha reductase inhibitors dutasteride or finasteride are second line anti-androgen agents (in both men and women). These drugs block the conversion of testosterone to the biologically more active hormone dihydrotestosterone. Finasteride has a very short half-life of 6 hours, compared to 5 weeks for dutasteride. [220,221] Both spironolactone and dutasteride decrease expression of TMPRSS2. [222] Multiple clinical studies support the notion that androgens exacerbate COVID-19 and that anti-androgen therapy improves clinical outcomes. The anti-androgens dutasteride, proxalutamide and spironolactone have been demonstrated to reduce time to viral clearance, improved time to recovery and reduced hospitalization (outpatients) as well as reduced mortality (hospitalized patients) in both men and women. [219,223-228] Dutasteride has been used in women with alopecia and reported to be safe. [229,230] However, this agent **MUST** be avoided in pregnant women. We therefore recommend dutasteride 2 mg day 1, followed by 1.0 mg for 10 days.

- Fluvoxamine 50 – 100 mg BID. [231-238] This selective serotonin reuptake inhibitor (SSRI) is recommended in those patients with more severe symptoms/more advanced disease. Fluvoxamine is a SSRI that activates sigma-1 receptors decreasing cytokine production. [231,232] In addition, fluvoxamine reduces serotonin uptake by platelets, reduces histamine release from mast cells, interferes with lysosomal trafficking of virus and inhibits melatonin degradation.[239,240] Antidepressant medications (SSRI) deplete platelet serotonin content, thereby diminishing the release of serotonin following platelet aggregation. [241-243] The use of antidepressants has be associated with a lower risk of intubation and death in patients hospitalized with COVID-19. [234,235,244,245] Fluoxetine (Prozac; 20-40mg daily), has activity against the sigma-1 receptor and is an alternative should fluvoxamine not be available. [246]
- Monoclonal antibodies for early outpatient treatment (within 7 days of symptom onset). In the REG-COV2 outpatient study, 4057 patients with at least one risk factor for severe COVID were randomized to a single intravenous infusion of REG-COV2 (a combination of the monoclonal antibodies casirivimab and imdevimab) or placebo. [247] In this study the median duration of symptoms prior to enrollment was 3 days. The composite endpoint of hospitalization and death was reduced by 71% (4.6 % to 1.3%). While not reported in the publication, the mortality rate was not significantly different between groups!!! [247] The duration of symptoms was 4 days shorter in the REG-COV2 group. Monoclonal antibodies appear to reduce the risk of hospitalization in patients with mild to moderate disease if administered within 4 days of symptoms.[248,249] The timely administration of monoclonal antibodies are recommended in high-risk individuals, namely, > 65 years, obesity, pregnancy, chronic kidney disease, diabetes mellitus, immunosuppressed, coronary heart disease, etc. See infusioncenter.org and call 1-877-332-6585 In USA for eligibility and location. Sotrovimab is a monoclonal antibody that neutralizes SARS-CoV-2 by targeting an evolutionarily conserved epitope that lies outside the rapidly evolving receptor binding motif. [250] *In vitro*, data suggests that Sotrovimab retained activity against variants of interest and concern (VOC), including the alpha, beta, gamma, delta, and lambda variants. With the rapid emergence of VOC Sotrovimab may be the preferred monoclonal antibody.

3.3 Optional treatments and those of uncertain benefit

- *Optional:* Vascepa (Ethyl eicosapentaenoic acid) 4g daily or Lovaza (EPA/DHA) 4g daily; alternative DHA/EPA 4g daily. Vascepa and Lovaza tablets must be swallowed and cannot be crushed, dissolved, or chewed. Omega-3 fatty acids have anti-inflammatory properties and play an important role in the resolution of inflammation. Omega-3 fatty acids reprogram macrophages/monocytes from a M1 phenotype to a M2 phenotype.[251-253] As discussed later

this is critical in the management of COVID-19. In addition, omega-3 fatty acids may have antiviral properties. [121,254-257]

- *Optional:* Maraviroc 300 mg BID for 10 days. Maraviroc is a C-C-chemokine 5 receptor blocker (CCR5). Genomic and proteomic data have demonstrated that the CCR5 axis plays a major role in the pathophysiology of coronavirus infection, largely by recruiting activated monocytes to the lung. [258-260] Preliminary data demonstrated that disruption of the CCR5 axis with monoclonal antibodies was associated with an improved outcomes in patients with COVID-19. [261-263] Maraviroc is a CCR5 blocker that has been extensively used in patients with HIV, with a good safety record. [264-266] Clinical data suggests that maraviroc may be useful as an adjunctive agent in both acute COVID-19 infection and in the long-haul syndrome. However, at this time there is limited published data on the utility of this drug. Due to the very low risk of hepatotoxicity monitoring LFT's are recommended. Price and availability may however be an issue.
- *Optional:* Famotidine 40 mg BID (reduce dose in patients with renal dysfunction*) [44-50].*
- *Optional*: Interferon-α/β nasal spray, inhalation or s/c injection. [267-271] It should be noted that Zinc potentiates the effects of interferon. [272,273]
- *Unclear benefit.* Losartan 50-100 mg q day (reduce to 25-50 mg with impaired renal function) or telmisartan 40-80 mg BID (reduce to 40 mg q day /BID with impaired renal function). [296-298] SARS -CoV-2 binds the ACE-2 receptor with internalization of the receptor and decreased ACE-2 activity. This results in increased circulating levels of angiotensin II with decreased levels of the vasodilator angiotensin 1-7. Increased angiotensin II levels have been demonstrated to be linearly associated with viral load and lung injury.[299] The role of ARBs in patients with COVID-19 is controversial as clinical studies have produced conflicting results. [274,275] However, it should be noted that ARBs may act synergistically with statins. [302] ARBs are *contraindicated in pregnancy.*
- *Unclear benefit: Inhaled corticosteroids (budesonide).* Two recent RCTs have demonstrated more rapid symptomatic improvement in ambulatory patients with COVID-19 treated with inhaled budesonide, however, with no difference in the rate of hospitalization. [276,277] It should be noted that both these studies were open label (no placebo in the control arm) and that the primary end-point was subjective (time to symptom resolution). Corticosteroids downregulate the expression of interferons (hosts primary antiviral defenses) and downregulate ACE-2 expression (harmful). Furthermore, two population level studies suggest that inhaled corticosteroids may increase the risk of death in patients with COVID-19. [278,279] In a more recent RCT, the inhaled corticosteroid Ciclesonide failed to achieve the primary efficacy end point of reduced time to alleviation of all COVID-19 related symptoms. [280] Based on these data, the role of inhaled corticosteroids in the early phase of COVID-19 is unclear.
- *Unclear benefit (best avoided).* Colchicine 0.6mg BID for 3 days then reduce to 0.6mg daily for a total of 30 days. In the COLCORONA study, colchicine reduced the need for hospitalization (4.5 vs 5.7%) in high risk patients. [281] Colchicine was associated with an increased risk of side effects, most notably diarrhea and pulmonary embolism. It should be noted that in the RECOVERY trial colchicine failed to demonstrate a survival benefit in hospitalized patients. Due to potentially serious drug interactions with ivermectin (and other CYP 3A4 and p-glycoprotein inhibitors) as well as with statins, [282] together with its marginal benefit ,colchicine is best avoided.
- *Not recommended: Systemic corticosteroids.* In the early symptomatic (viral replicative phase), corticosteroids may increase viral replication and disease severity. [283]
- *Not recommended:* Prophylactic azithromycin, as well as doxycycline, or quinolone antibiotics are of little benefit in patients with COVID-19. [284-286]

7a. i-MASK Early treatment protocol

EARLY TREATMENT PROTOCOL[5] (for Delta variant)

1. First line agents (use any or all medicines; listed in order of priority/importance)

ANTI-VIRALS

Ivermectin[2]
0.4–0.6 mg/kg per dose (take with or after a meal) — one dose daily, take for 5 days or until recovered. Use upper dose if: **1)** in regions with aggressive variants (e.g. Delta); **2)** treatment started on or after day 5 of symptoms or in pulmonary phase; or **3)** multiple comorbidities/risk factors.

and/or **Nitazoxanide**
500 mg 2 x daily for 5 days after meals. Combine with ivermectin (preferred) or substitute if ivermectin is not available. (Nitazoxanide is often unavailable or high-priced in the USA.)

ANTI-SEPTIC ANTI-VIRALS

Antiviral mouthwash: Gargle 3 x daily (do not swallow; must contain chlorhexidine, povidone-iodine, or cetylpyridinium chloride). **Iodine nasal spray/drops**: Use 1% povidone-iodine commercial product as per instructions 2–3 x daily. If 1%-product not available, must first dilute the more widely available 10%-solution[6] and apply 4–5 drops to each nostril every 4 hours. (No more than 5 days in pregnancy.)

ANTI-COAGULANTS / IMMUNE FORTIFYING

Aspirin	325 mg daily (unless contraindicated)
Vitamin D	Vitamin D3 5,000 IU daily.
	See dosing Table 3
Melatonin	10 mg before bedtime (causes drowsiness)

SYNERGISTIC THERAPIES

Quercetin	250 mg 2 x daily
Zinc	100 mg/day (elemental zinc)
Vitamin C	500–1,000 mg 2 x daily

NUTRITIONAL THERAPEUTICS (for 14 days)[4]

Curcumin	(turmeric)	500 mg 2 x daily
Nigella Sativa	(black cumin seed)	80 mg/kg daily
Honey		1 gram/kg daily

PULSE OXIMETER

Monitoring of oxygen saturation is recommended
(for instructions see page 3)

Figure 7b. Naso-oropharyngeal sanitization

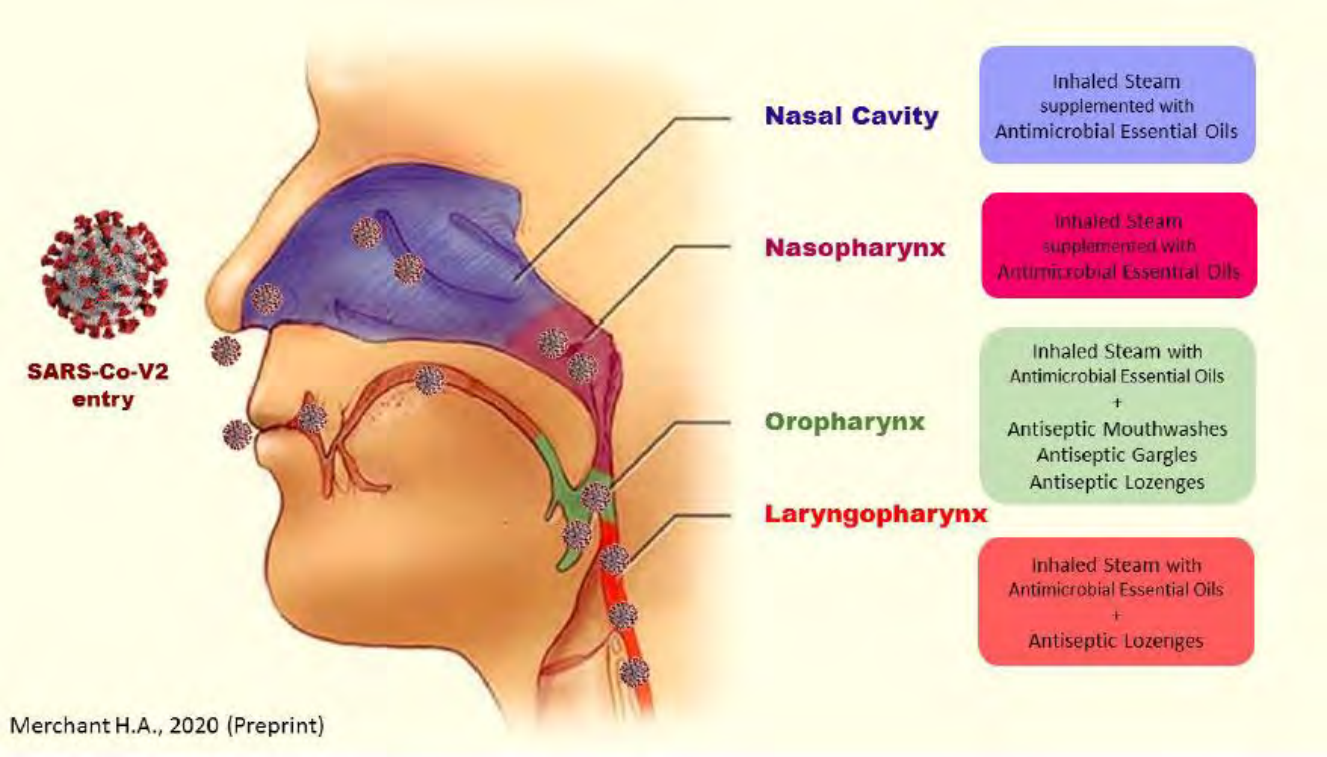


Figure 7c. Commercial products available for Naso-oropharyngeal sanitization

4. Mildly Symptomatic patients (on floor/ward in hospital).

4.1 First Line Therapies (in order of priority)

- It is important to note that ivermectin, LMWH and corticosteroids form the foundation of care for the hospitalized patient. Multiple RCTs have demonstrated that these drugs reduce the mortality of patients hospitalized with COVID-19 (See independent meta-analysis Figure 8).
- Ivermectin 0.4 – 0.6 mg/kg daily for 5 days or until recovered. A higher dose may be required in patients with more severe disease and in those in whom treatment is delayed. [19,23,77-80,162-171,173,175-177]. While ivermectin retains full efficacy against the variants (as best we know), the Delta variant results in very high viral loads and may take longer to eradicate. Ivermectin is best taken with a meal or just following a meal (greater absorption). It should be noted that ivermectin has potent anti-inflammatory properties apart from its antiviral properties.[287-290] Preliminary data suggest that Ivermectin in a dose of 0.3-0.4 mg/kg is highly effective against the Omicron variant; however, in keeping with the general treatment principles, early treatment is preferred. See drug-drug interactions above.
- Nitazoxanide (NTZ) 600 mg BID for 7 days.[291] NTZ should therefore considered as an alternative to ivermectin, or as part of a multi-drug combination that includes ivermectin. It should be noted that while NTZ is relatively cheap in most of the world it is very expensive in the USA.
- Methylprednisolone 80 mg bolus followed by 40 mg q 12 hourly (alternative: 80 mg bolus followed by 80 mg/240 ml normal saline IV infusion at 10 ml/hr); increase to 80 mg and then 125 mg q 12 hourly in patients with progressive symptoms and increasing CRP. There is now overwhelming and irrefutable evidence that corticosteroids reduce the risk of death in patients with the pulmonary phase of COVID-19 i.e., those requiring supplemental oxygen or higher levels of support. [292-304] We believe that the use of low-fixed dose dexamethasone is inappropriate for the treatment of the pulmonary phase of COVID-19. The role of inhaled corticosteroids (budesonide) is unclear and appears to be rather limited (as reviewed above). While 1) methylprednisolone is the corticosteroid of choice (see below) in those regions/counties where it is not available the following (in order of preference) may be substituted for methylprednisolone (dose adjusted according to methylprednisolone dosages), 2) prednisolone, 3) prednisone, 4) hydrocortisone, and 5) LASTLY dexamethasone.
- Enoxaparin 1mg/kg 12 hourly (see dosage adjustments and Xa monitoring below). The ATTACC, ACTIV-4a & REMAP-CAP trials demonstrated a significant reduction of the primary end point (composite of organ support days and hospital mortality) regardless of D-Dimer levels.[305]
- Vitamin C 500–1000 mg q 6 hourly and Quercetin 250–500 mg BID (if available)
- Zinc 75–100 mg/day (elemental zinc)
- Melatonin 10 mg at night . [35-41]
- Anti-androgen therapy (both men and women). Spironolactone 100 mg BID for 10 days. Second line anti-androgen: Dutasteride 2 mg day 1, followed by 1.0 mg for 10 days. **AVOID IN PREGNANCY**. [219,223,224]
- Fluvoxamine 50 -100 mg BID. Fluoxetine 20-40mg daily is an alternative.

4.2 Second Line and optional treatments

- Vitamin D. The optimal dose and vitamin D formulation for the treatment of acute disease is highly controversial. Vitamin D3 takes many days to be converted to 25-OH vitamin D; [306] this may explain the lack of benefit of vitamin D3 in patients hospitalized with severe COVID-19.[105] Vitamin D stores are best repleted in the weeks to months before patients contract

COVID-19. Nevertheless, for patients hospitalized with COVID-19 the dosing scheme as listed in table 3 is suggested.

- ASA 325 mg (if not contraindicated). Moderate-severe COVID infection results in profound platelet activation contributing to the pro-thrombotic state and increasing the inflammatory response. [206,207,307,308]
- B complex vitamins
- Atorvastatin 40-80 mg/day (reduce dose to 40 mg if taken with ivermectin due to possible drug-drug interaction). Statins have pleiotropic anti-inflammatory, immunomodulatory, antibacterial, and antiviral effects. Statins reprogram macrophages/monocytes from a M1 phenotype to a M2 phenotype. [309,310] As discussed later, this is critical in the management of COVID-19. In addition, statins decrease expression of PAI-1. Simvastatin has been demonstrated to reduce mortality in the hyper-inflammatory ARDS phenotype. [311] Preliminary data suggests atorvastatin may improve outcome in patients with COVID-19. [312-316] Due to numerous drug-drug interactions (including ivermectin) simvastatin should be avoided.
- *Optional:* Maraviroc 300 mg BID for 10 days (see above and section on Long-Covid).
- *Optional:* Famotidine 40 mg BID (20–40 mg/day in renal impairment). [44-50] Famotidine may be useful for its protective effect on gastric mucosa, its anti-viral properties and histamine blocking properties.
- *Optional:* JAK inhibitors ruxolitinib or baricitinib. JAK inhibitors target JAK1, JAK2, JAK3, and whose inhibition downregulates the JAK/STAT signaling pathway decreasing cytokine concentrations. [317] These drugs have been shown to decrease the use of mechanical ventilation and the risk of death. [318,319] In these studies low doses of corticosteroids were used. The role of JAK inhibitors with appropriate corticosteroid dosing is unclear
- *Optional:* The anti-serotonin agent, cyproheptadine 4–8 mg PO q 6 hour should be considered in patients with more severe disease. [320,321] Patients with COVID-19 have increased circulating levels of serotonin likely the result of increased platelet activation and decreased removal by the pulmonary circulation due to an extensive microcirculatory vasculopathy. [320,322-324] Increased circulating serotonin is associated with pulmonary, renal and cerebral vasoconstriction, and may partly explain the V/Q mismatch and reduced renal blood flow noted in patients with severe COVID-19 infection. [325-328] Furthermore, serotonin itself enhances platelet aggregation creating a propagating immuno-thrombotic cycle.[329] In addition, serotonin receptor blockade may reduce progression to pulmonary fibrosis. [330]
- *Optional:* Vascepa (Ethyl eicosapentaenoic acid) 4g daily or Lovaza (EPA/DHA) 4g daily; alternative DHA/EPA 4g daily. [331] Vascepa and Lovaza tablets must be swallowed and cannot be crushed, dissolved, or chewed
- *Not recommended:* Remdesivir. The recently published SOLIDARITY trial demonstrated no mortality benefit of this agent in the entire treatment cohort or any subgroup. [332] The VA study showed no mortality benefit with Remdesivir and a longer length of hospital stay. [333] Most recently, the DisCoVeRy trial reported no outcome benefit from remdesivir. [334] A meta-analysis of the six published RCTS demonstrate no mortality reduction with Remdesivir; interestingly enough, the independent studies demonstrate a trend to harm while the two studies conducted by Gilead demonstrate a mortality benefit. (See figure 9).
- Not recommended: Azithromycin, doxycycline, or quinolone antibiotics. [172,173]
- Not recommended: Colchicine. Recruitment to the colchicine arm of the RECOVERY trial has been closed as no mortality benefit was noted with colchicine (Mortality 20% colchicine, 19% standard of care). In addition, potentially serious drug-drug interactions exist with the use of colchicine and CYP 3A4 and p-glycoprotein inhibitors (ivermectin, macrolide antibiotics, cyclosporin, etc) as well as with the use of statins. [282]

N/C 2L/min if required (max 4 L/min; consider early t/f to ICU for escalation of care).
Avoid Nebulization and Respiratory treatments. Use “Spinhaler” or MDI and spacer if required.

T/f EARLY to the ICU for increasing respiratory signs/symptoms, increasing oxygen requirements and arterial desaturation.

Figure 8. Ivermectin real-time meta-analysis of 71 studies (from ivmeta.com).

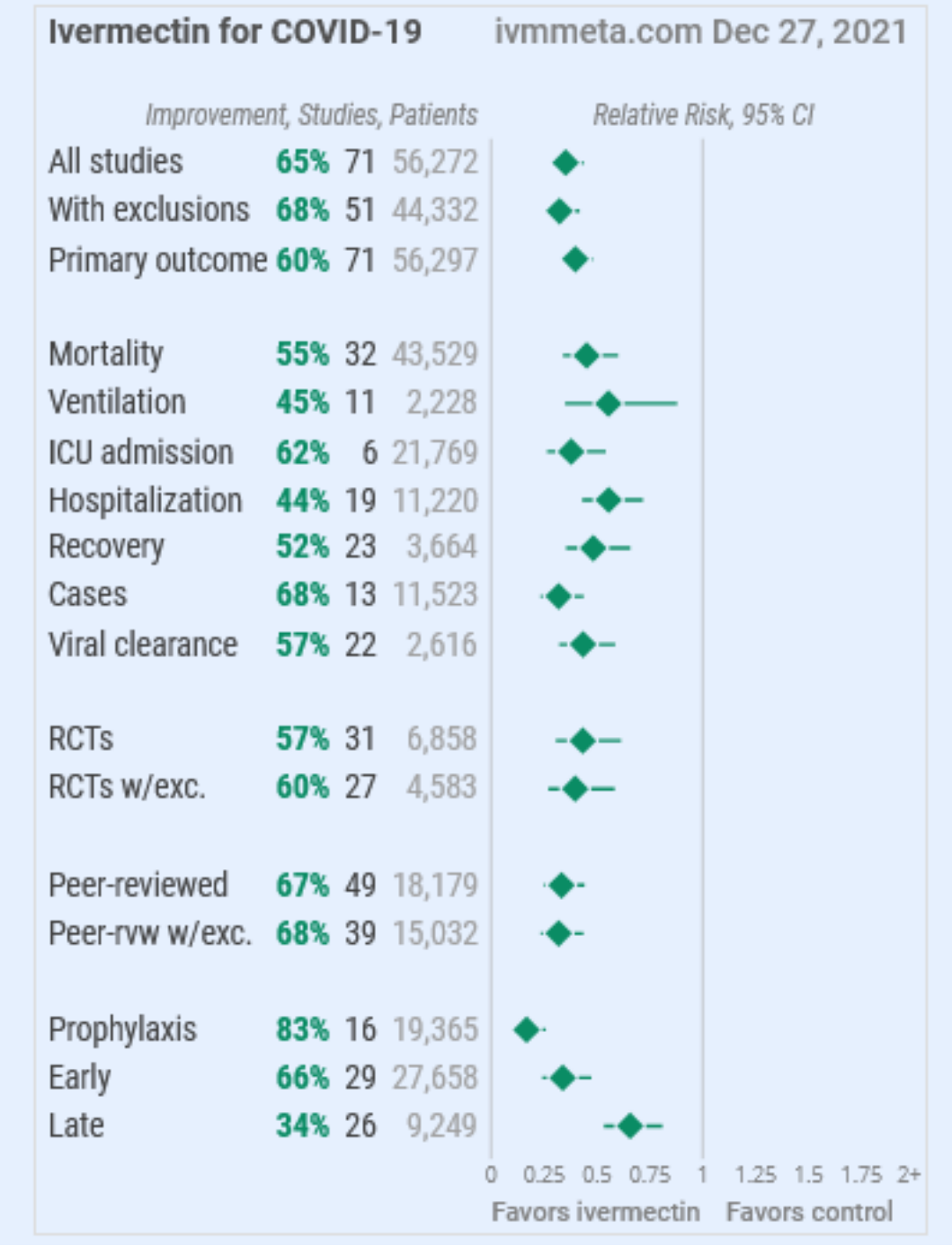
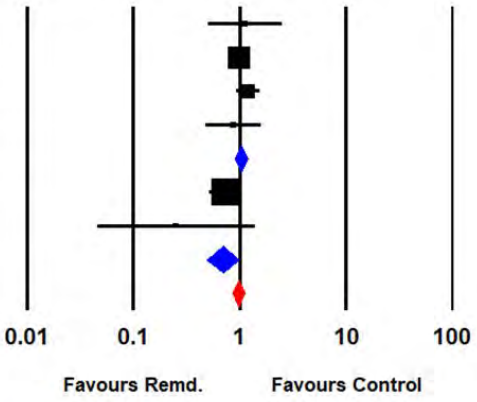


Figure 9. Meta-analysis of the Remdesivir RCTs grouped by independent studies (I) and those done by Gilead™ (P)

Group by Pharma/IND	Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
I	Wang	1.116	0.501	2.488	0.269	0.788
I	SOLIDARITY	0.978	0.826	1.159	-0.254	0.800
I	VA Coperative	1.175	0.910	1.516	1.234	0.217
I	DisCoVery	0.866	0.475	1.581	-0.467	0.640
I		1.027	0.897	1.176	0.391	0.696
P	Beigel	0.724	0.507	1.035	-1.773	0.076
P	Spinner	0.249	0.045	1.370	-1.599	0.110
P		0.692	0.488	0.982	-2.062	0.039
Overall		0.976	0.860	1.107	-0.380	0.704



Meta Analysis

5. MATH+ PROTOCOL (for patients admitted to the ICU) [335,336]

5.1 Core Components

1. ***Methylprednisolone*** 80 mg loading dose followed by 40 mg q 12 hourly for at least 7 days and until transferred out of ICU. In patients with an increasing CRP or worsening clinical status increase the dose to 80 mg q 6 hourly, then titrate down as appropriate. [292-304] Pulse methylprednisolone 500-1000 mg/day for 3 days (followed by taper) may be required. [302] We suggest that all patients admitted to the ICU have a chest CT scan on admission to allow risk stratification based on the extent of the disease; those with extensive disease should be initiated on high dose corticosteroids (see section below on severe COVID). As depicted in Table 2, methylprednisolone is the corticosteroid of choice. Observational and randomized studies have clearly demonstrated the superiority of methylprednisolone over low dose dexamethasone. [337,338] These clinical findings are supported by a genomic study.[204] Methylprednisolone should be weaned slowly over two weeks once oxygen is discontinued to prevent relapse/recurrence (20mg twice daily once of oxygen, then 20 mg/day for 5 days, then 10 mg/day for 5 days). While 1) methylprednisolone is the corticosteroid of choice (see below) in those regions/countries where it is not available the following (in order of preference) may be substituted for methylprednisolone (dose adjusted according to methylprednisolone dosages), 2) prednisolone, 3) prednisone, 4) hydrocortisone, and 5) LASTLY dexamethasone.
2. ***Ascorbic acid (Vitamin C)*** 50 mg/kg (or 3000 mg) IV q 6 hourly for at least 7 days and/or until transferred out of ICU. [116,125,126,339-349]. *Mega-dose vitamin C* should be considered in severely ill patients, those with progressive respiratory failure and as salvage therapy: 25 g vitamin C in 200-500 cc saline over 4-6 hours every 12 hourly for 3-5 days, then 3g IV q 6 hourly for total of 7-10 days of treatment [350] (also see https://www.youtube.com/watch?v=Au-mp6RZjCQ). Mega-dose Vitamin C appears safe in patients with ARF and ESRD. In patients with CRF a dose of 12.5 g q 12 hourly may be an adequate compromise. [351] In the study by Lankadeva et al, mega-dose vitamin C increased renal cortical blood flow and renal cortical pO2; oxalate crystals were not detected.[350] Note caution with POC glucose testing (see below). Oral absorption is limited by saturable transport proteins and it is difficult to achieve adequate levels with PO administration. However, should IV Vitamin C not be available, it would be acceptable to administer PO vitamin C at a dose of 1g every 4–6 hours.
3. ***Anticoagulation***: The ATTACC, ACTIV-4a & REMAP-CAP trials demonstrated a marginally increased mortality in ICU patients treated with full anti-coagulation (35.3% vs. 32.6%).[305] Critically ill COVID-19 patients frequently have impaired renal and it is likely that in the absence of Xa monitoring patients were over-anticoagulated. However, full anti-coagulation should be continued on floor patients transitioned to the ICU who have normal renal function. In all other patients we would suggest intermediate dose enoxaparin i.e 60 mg/day (enhanced thromboprophylaxis) or 0.5 mg/kg q 12 hourly.[352] Full anticoagulation (enoxaparin or heparin) may be required in patients with increasing D-dimer or with thrombotic complications. Due to augmented renal clearance some patients may have reduced anti-Xa activity despite standard dosages of LMWH.[236] We therefore recommend monitoring anti-Xa activity aiming for an anti-Xa activity of 0.5 – 0.9 IU/ml. Heparin is suggested with CrCl < 15 ml/min. It should also be appreciated that vitamin C is a prerequisite for the synthesis of collagen and vitamin C deficiency is classically associated with vascular bleeding.[125,126] This is relevant to COVID-19, as vitamin C levels are undetectable in severely ill COVID-19 patients and this may partly explain the increased risks of anticoagulation in ICU patients (not treated with vitamin C). [353-355] The use of the novel oral anticoagulants (NOAC/DOAC) is not recommended. [356]

Note: A falling SaO2 and the requirement for supplemental oxygen should be a trigger to start anti-inflammatory treatment.

Note: Early termination of ascorbic acid and corticosteroids will likely result in a rebound effect with clinical deterioration.

5.2 Additional Treatment Components

4. Highly recommended: Ivermectin 0.6 – 0.8 mg/kg day orally for 5 days or until recovered [23,77-79,162,165-172,287-289,357-363]. A higher dose (up to 1.0 mg/kg) is suggested in patients with severe disease and/or those with delayed initiation of therapy. Note that ivermectin has potent antiviral and anti-inflammatory effects. As noted above clinical outcomes are superior with multiday as opposed to single day dosing. Furthermore, as indicated above, higher dosages and a longer treatment course are suggested with the Delta variant.
5. Nitazoxanide (NTZ) 600 mg BID for 7 days.[291] NTZ should therefore considered as an alternative to ivermectin, or as part of a multi-drug combination that includes ivermectin. It should be noted that while NTZ is relatively cheap in most of the world it is very expensive in the USA???
6. Melatonin 10 mg at night.[36-38]
7. Thiamine 200 mg IV q 12 hourly for 3-5 days then 200mg daily [364-369] Thiamine may play a role in dampening the cytokine storm. [365,370]
8. ASA 325 mg. COVID infection results in profound platelet activation contributing to the severe pro-thrombotic state and increasing the inflammatory response.[206,207,307,308] As the risk of significant bleeding is increased in patients receiving both ASA and heparin, ASA should therefore not be used in patients at high risk of bleeding. In addition (as noted below) patients should receive famotidine concurrently.
9. The anti-serotonin agent, cyproheptadine. Platelet activation results in the release of serotonin, which may contribute to the immune and vascular dysfunction associated with COVID-19. [215-219] Therefore, the serotonin receptor blocker cyproheptadine 4–8 mg PO q 6 hours should be considered.
10. Anti-androgen therapy (both men and women). Spironolactone 100 mg BID for 10 days. Second line: Dutasteride 2 mg day 1, followed by 1.0 mg for 10 days. Finasteride 10 mg is an alternative (dutasteride cannot be crushed).[221] [371] **AVOID IN PREGNANCY**. [219,224] Bicalutamide 150 mg daily is also an option.
11. Fluvoxamine 50 -100 mg BID. Fluoxetine 20-40 mg daily is an alternative.

5.3 Second line treatments

12. B complex vitamins.
13. Vitamin D3. Dosing as suggested in Table 3.
14. Vascepa (Ethyl eicosapentaenoic acid) 4g daily or Lovaza (EPA/DHA) 4g daily; alternative DHA/EPA 4g daily. Vascepa and Lovaza tablets must be swallowed and cannot be crushed, dissolved, or chewed.
15. Atorvastatin 40- 80 mg/day (reduce dose to 40 mg if taken with ivermectin due to possible drug-drug interaction. Preliminary data suggests atorvastatin may improve outcome in patients with COVID-19.[238-242] *Due to numerous drug-drug interactions simvastatin should be avoided.*
16. Magnesium: 2 g stat IV. Keep Mg between 2.0 and 2.2 mmol/l. [158] Prevent hypomagnesemia (which increases the cytokine storm and prolongs Qtc). [372-374]

5.4 Optional Treatments and those of uncertain benefit

17. *Optional:* Famotidine 40 mg BID (20–40 mg/day in renal impairment). [44-50].
18. *Optional:* JAK inhibitors ruxolitinib or baricitinib.
19. *Unclear benefit. Losartan 50- 100 mg q day (reduce to 25 -50 mg with impaired renal function) or telmisartan 40-80 mg BID (reduce to 40 mg q day /BID with impaired renal function). [275,375,376]*
20. *Unclear benefit.* Maraviroc 300 mg BID for 10 days. Maraviroc is a CCR5 antagonist. [263] CCR5 is a chemokine that activates macrophages/monocytes and whose circulating levels are significantly increased in COVID-19.[260,377] Blocking the CCR5 receptor (CCR5R) repolarizes macrophages/monocytes and decreases the production of proinflammatory cytokines (see section on repolarizing macrophages/monocytes and section on Long-Covid).
21. *Not recommended:* The best information to date suggests that prophylactic azithromycin as well as doxycycline and quinolone antibiotics are of little benefit in patients with COVID-19.[284,378,379] Patients with COVID-19 are at an increased risk of developing bacterial superinfections and prophylactic antibiotics may increase the risk of infection with multi-resistant organisms.
22. *Not recommended:* Remdesivir. This drug has no benefit at this stage of the disease.
23. *Not recommended.* Convalescent serum [380-385] nor monoclonal antibodies. [386] However, convalescent serum/ monoclonal antibodies may have a role in patients with hematologic malignancies.[387]
24. *Not recommended.* Colchicine (see above).
25. *Not recommended.* Tocilizumab. Five RCTS have now failed to demonstrate a clinical benefit from tocilizumab. [388-392] Considering the effect of IL-6 inhibitors on the profile of dysregulated inflammatory mediators this finding is not surprising. [393] Tocilizumab may have of benefit in patients receiving an inadequate dose of corticosteroids.[394] In patients who receive an adequate therapeutic dose of corticosteroid the role of this drug appears limited.
26. Broad-spectrum antibiotics added if complicating bacterial pneumonia is suspected based on procalcitonin levels and respiratory culture (no bronchoscopy). Due to the paradox of hyper-inflammation and immune suppression (a major decrease of HLA-DR on CD14 monocytes, T cell dysfunction and decreased CD4 and CD8 counts) secondary bacterial and fungal infections (Candida and Aspergillus species) and viral reactivation is not uncommon. [395-397] Patients with non-resolving fever, increasing WBC count and progressive pulmonary infiltrates should be screened for COVID-19-associated pulmonary aspergillosis (CAPA). [398] Recommended first-line therapy for CAPA is either voriconazole or isavuconazole (beware drug-drug interactions). While low CD4 counts are typical of severe COVID-19 infection, PJP infections have not been reported; therefore PJP prophylaxis is not required.
27. Maintain *EUVOLEMIA* (this is not non-cardiogenic pulmonary edema). Due to the prolonged "symptomatic phase" with flu-like symptoms (6–8 days) patients may be volume depleted. Cautious rehydration with 500 ml boluses of Lactate Ringers may be warranted, ideally guided by non-invasive hemodynamic monitoring. Diuretics should be avoided unless the patient has obvious intravascular volume overload. Avoid hypovolemia.
28. Early norepinephrine for hypotension. It should however be appreciated that despite the cytokine storm, vasodilatory shock is distinctly uncommon in uncomplicated COVID-19 (when not complicated by bacterial sepsis). This appears to be due to the fact that TNF-α which is "necessary" for vasodilatory shock is only minimally elevated.
29. Escalation of respiratory support (steps); ***Try to avoid intubation if at all possible.*** Intubation is indicated in patients who have failed non-invasive ventilation and in those patients with excessive work of breathing. A subgroup of patients with COVID-19 deteriorates very rapidly. Intubation and mechanical ventilation may be required in these patients.

a. Accept “permissive hypoxemia” (keep O2 Saturation > 84%); follow venous lactate and Central Venous O_2 saturations ($ScvO_2$) in patents with low arterial O_2 saturations
b. N/C 1–6 L/min
c. High Flow Nasal canula (HFNC) up to 60–80 L/min [399]
d. Trial of inhaled Flolan (epoprostenol)
e. Attempt proning (cooperative repositioning-proning) [400-403]
f. Intubation … by Expert intubator; Rapid sequence. No Bagging; Full PPE. Crash/emergency intubations should be avoided.
g. Volume protective ventilation; Lowest driving pressure and lowest PEEP as possible. Keep driving pressures < 15 cm H_2O.
h. Moderate sedation to prevent self-extubation
i. Trial of inhaled Flolan (epoprostenol)
j. Prone positioning.

There is widespread concern that using HFNC could increase the risk of viral transmission. There is however, no evidence to support this fear.[404,405] HFNC is a better option for the patient and the health care system than intubation and mechanical ventilation. HFNC is preferred over conventional oxygen therapy. [399] Intermittent CPAP/BiPAP may be used in select patients, notably those with COPD exacerbation or heart failure.

Figure 10. “Typical” progression of Chest CT findings.

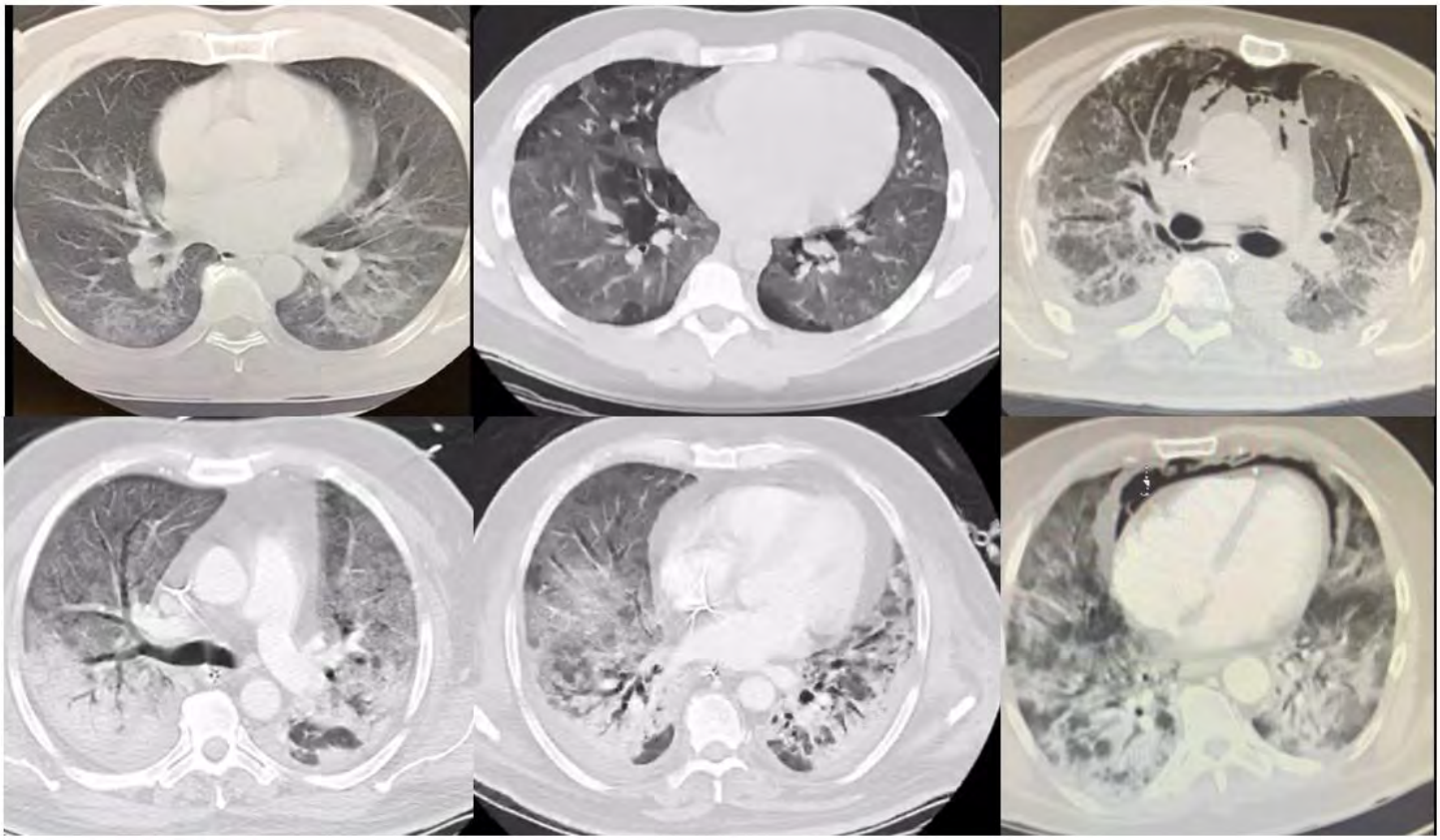


Table 5: Comparison of Methylprednisolone, Dexamethasone and Hydrocortisone - Number Need to Treat (NNT)

PUBLISHED RCT's/OCT's OF CORTICOSTEROID THERAPY IN COVID-19		ABSOLUTE DIFFERENCE IN MORTALITY	NUMBER NEEDED TO TREAT TO SAVE ONE LIFE
METHYLPREDNISONE – HOSPITAL PATIENTS (Edalatifard et al, Italy) 250mg methylprednisone daily x 3 days		5.9% vs. 42.9%	2.7
METHYLPREDNISONE – ICU PATIENTS (Confalonieri et al, Italy) 80mg methylprednisone daily x 8 days		7.2% vs. 23.3%	6.2
METHYLPREDNISONE- ARDS PATIENTS (OCT - Wu C et al- China) 1-2 mg/kg/day for 3-5 days		46.0% vs. 61.8%	6.3
METHLPREDNISONE – HOSPITAL PATIENTS, (OCT - Fadel et al, USA) 0.5-1.0mg/kg/day x 3 days		13.6% vs. 26.3%	7.8
METHYLPREDNISONE - Pts on oxygen – (Fernandez-Cruz at al, Spain) 1mg/kg/day		13.9% vs. 23.9%	10.0
METHYLPREDNISONE VS. DEXAMETHASONE (Ranjbar et al, Iran) 2mg/kg/day MP vs. 6mg/day Dexamethasone		18.6% vs 37.5%	5.3
METHYLPREDNISONE VS. DEXAMETHASONE (OCT - Ko et al, USC) >= 1mg/kg/day MP for min. 3 days vs. 6mg/day Dex for min. 7 days	OVERALL	16.4% vs. 26.5%	10
	PTS ON MV	31% vs. 54%	4.3
HYDROCORTISONE -CAPE-COVID – ICU Patients (Dequin et al France) 200mg/day with taper over 14 days – stopped early		14.7% vs 27.4%	7.9
HYDROCORTISONE –REMAP-CAP – ICU Patients (Angus et al) 200 - 400 mg/day x 7 days – stopped early		28% vs 33% (NS)	20.0
DEXAMETHASONE – CODEX – ICU Patients (Tomazini et al) 20 mg x 5 days, 10 mg x 5 days		56.3% vs 61.5%	19.2
DEXAMATHASONE – RECOVERY (Hornsby et al) 6mg/day x 10 days	PTS ON OXYGEN	23.3% vs. 26.2%	28.6
	PTS ON MV	29.3% vs. 41.4%	8.4

6. An approach to the patient with SEVERE life threatening COVID-19 Organizing Pneumonia

The first task of the clinician is to determine the reversibility of the pulmonary disease. This is a critical assessment. Aggressive anti-inflammatory treatment is futile in patients with advanced fibrotic lung disease. The horse has already bolted and allowing the patient a "peaceful death" is the most compassionate and humane approach. The reversibility of the pulmonary disease is dependent on a number of factors superseded by a good deal of clinical judgement; these include:

a) The length of time that has elapsed since the onset of symptoms. Early aggressive treatment is critical to prevent disease progression. With each day the disease becomes more difficult to reverse. The 'traditional' approach of supportive care alone is simply unacceptable.
b) The level of inflammatory biomarkers particularly the CRP. In general the CRP tracks the level of pulmonary inflammation. [406] A high CRP is indicative of a hyper-inflammatory state and potentially reversible pulmonary inflammation.
c) It is likely that advanced age is a moderating factor making the pulmonary disease less reversible.
d) A chest CT is extremely helpful in determining the reversibility of disease. BEWARE this is not ARDS but organizing pneumonia. [407] The extent of the pulmonary involvement may be determined qualitatively or preferably quantitatively (see Figure 10). [406,408-414] The Ichikado CT Score is a useful quantitative score to evaluate the extent of lung involvement with COVID-19.[415,416] The changes in the CT follow a stereotypic progressive pattern:
    I. Peripheral, patchy, predominantly basal ground glass opacification (GGO). GGO is defined an increase in density of lung with visualization of bronchial and vascular structures through it
    II. Progressive widespread bilateral GGO
    I. Crazy-paving (CGO with interlobular and intralobular septal thickening)
    II. Air space consolidation (air bronchograms)
    III. Dense airspace consolidation
    IV. Coalescent consolidation
    V. Segmental/subsegmental pulmonary vessel dilatation
    VI. Bronchial wall thickening
    VII. Linear opacities
    VIII. Traction bronchiectasis
    IX. Cavitation
    X. Fibrotic changes with bullae and reticulation

GGO pattern is significantly more prevalent in early-phase disease compared with late-phase disease while crazy-paving and consolidation patterns are significantly more common in late-phase. [406] Therefore widespread GGO suggests reversibility while widespread consolidation with other features of more advanced disease suggest irreversible lung disease. However, when in doubt (borderline cases) a time limited therapeutic trial of the aggressive "Full Monty" approach may be warranted.

7. The "FULL MONTY" for SEVERE COVID Pulmonary disease

I. Methylprednisolone 250-500 mg q 12 hourly for at least 3 days then titrate guided by clinical status and CRP.
II. Ivermectin 1.0 mg/kg for 5 days
III. Melatonin 10 mg PO at night
IV. Enoxaparin 60 mg daily; critically ill patients usually have some degree of renal impairment and will require a renally adjusted lower dose. Patients with very high D-dimer and or thrombotic complications may require full anticoagulant doses of Lovenox. It may be prudent to monitor Xa levels aiming for 0.4-0.8 IU/ml (a somewhat lower anti-Xa).
V. Vitamin C 3 g 6 hourly to 25g q 12 hourly
VI. Cyproheptadine 4–8 mg PO q 6 hourly
VII. Fluvoxamine 50- 100 mg BID or fluoxetine 20-40mg daily
VIII. Spironolactone 100 mg BID
IX. Atorvastatin 80 mg/day (reduce dose to 40mg if taken with ivermectin due to possible drug-drug interaction)
X. Thiamine 200 mg q 12 hourly
XI. Finasteride 10 mg daily or dutasteride 2mg day 1 then 1mg daily or bicalutamide 150mg daily
XII. Omega-3 fatty acids 4g/day
XIII. Famotidine 40 mg BID
XIV. Consider plasma exchange on admission to the ICU.

While it is unclear which of the above medications included in the "Severe Covid-19" cocktail contributes to improved outcomes, all of these drugs have been shown to be safe and independently to improve the outcome of patients with COVID-19. Ultimately it is irrelevant as to the contribution of each element as long as the patient improves and survives his/her ICU stay. We are in the midst of a pandemic caused by a virus causing devastating lung disease, and there is no place for "ivory tower medicine."

8. Salvage Treatments

- High dose bolus corticosteroids; 500–1000 mg/day methylprednisolone for 3 days then taper. [300,302]
- Plasma exchange [417-423]. Should be considered in patients with progressive oxygenation failure despite corticosteroid therapy as well as in patients with severe MAS. Patients may require up to 5 exchanges. FFP is required for the exchange; giving back "good humors" appears to be more important than taking out "bad humors".
- Mega-dose vitamin C should be considered in severely ill patients and as salvage therapy: 25g vitamin C in 200-500 cc saline over 4-6 hours, 12 hourly for 3-5 days, then 3g IV q 6 hourly for total of 7-10 days of treatment.[350,351] (also see https://www.youtube.com/watch?v=Au-mp6RZjCQ)
- In patients with a large dead-space ventilation i.e. high $PaCO_2$ despite adequate minute ventilation consider "Half-dose rTPA" to improve pulmonary microvascular blood flow; 25mg of tPA over 2 hours followed by a 25mg tPA infusion administered over the subsequent 22 hours, with a dose not to exceed 0.9 mg/kg followed by full anticoagulation.[424,425]
- Combination inhaled nitric oxide (or epoprostenol) and intravenous almitrine (10 – 16 ug/kg/min). The combination of inhaled nitric oxide, a selective pulmonary vasodilator, and almitrine, a specific pulmonary vasoconstrictor, may improve the severe V/Q mismatch in patients with severe COVID-19 "pneumonia". [426-429]
- ECMO [430-432]. Unlike "typical ARDS", COVID-19 patients may not progress into a resolution phase. Rather, patients with COVID-19 with unresolved inflammation may progress to a severe fibro-proliferative phase and ventilator dependency. ECMO in these patients would likely serve little purpose. ECMO however may improve survival in patients with severe single organ failure (lung) if initiated within 7 days of intubation. [433]
- Lung transplantation. [434]

9. Salvage treatments of unproven/no benefit.

- Convalescent serum/monoclonal antibodies: Four RCT's failed to demonstrate a clinical benefit with the use of convalescent serum. [380-382,384,385] Eli Lilly suspended the ACTIV-33 clinical trial as their monoclonal antibody failed to demonstrate a clinical benefit in hospitalized patients.[435] It is noteworthy that the only RCT demonstrating efficacy of convalescent plasma for an infectious disease was conducted more than 40 years ago, for treating Argentine hemorrhagic fever. [211] Furthermore, giving antibodies directed against SARS-CoV-2 appears pointless when the virus is already DEAD (pulmonary phase). In addition, IgG is a large protein which penetrates tissues poorly, and is unlikely to achieve submucosal concentrations required for mucosal immunity.[436] And lastly, COVID-19 pulmonary disease is immune mediated, and it would therefore appear paradoxical to enhance the antibody response with convalescent serum. [437]
- In patients hospitalized with severe COVID-19, Canakinumab, an anti‑interleukin-1 β antibody failed to improve any outcome measure. [438]
- In patients with progressive fibrosis the combination of anti-fibrotic therapy with corticosteroids should be considered. [439-442] It should however be recognized that unlike all the medications in the MATH+ protocol, pirfenidone and nintedanib have complex side-effects and drug interactions and should be prescribed by pulmonary physicians who have experience with these drugs.
- CVVH/D with cytokine absorbing/filtering filters [443,444] This treatment strategy appears to have an extremely limited role.

10. Treatment of Macrophage Activation Syndrome (MAS)

- Severe-COVID pneumonia/organizing pneumonia is in essence caused by the "pulmonary macrophage activation syndrome" and the distinction between severe COVID and MAS is unclear (see below). [7,407,445,446]
- A ferritin > 4400 ng/ml is considered diagnostic of MAS. Other diagnostic features include increasing AST/ALT and CRP and progressive multisystem organ failure.[447]
- "*High dose corticosteroids*." Methylprednisolone 500-1000 mg daily for three days and then wean according to Ferritin, CRP, AST/ALT. Ferritin should decrease by at least 15% before weaning corticosteroids.
- Consider plasma exchange.

11. Approach to the DELTA/P1 Variant

- Both the Delta and P1 variants are highly virulent strains of SARS-COv-2. These variants replicate to achieve very high concentrations in the nasopharynx; hence they are much more transmissible and the time from exposure to symptom onset and to the pulmonary phase is much shorter. It is not uncommon for patients to be symptomatic for as little as 3 days prior to ICU admission.
- Early (day 1) outpatient treatment (MASK +) is critical to prevent progression to the more lethal pulmonary phase.
- ICU patients frequently present with very high levels of inflammatory markers (CRP, Ferritin, D-Dimer)
- The 'Full Monty" should be started on the first ICU Day.
- In those patients with very high inflammatory markers plasma exchange should be considered on admission.

12. Approach to the Omicron Variant

Omicron, the SARS-CoV-2 variant responsible for a cluster of cases in South Africa and that is now spreading around the world, is the most heavily mutated variant to emerge so far and carries mutations similar to changes seen in previous variants of concern associated with enhanced transmissibility and partial resistance to vaccine induced immunity. [448,449] In South Africa, Omicron has completely displaced the Delta variant, with Omicron being the major variant. [449,450] In total, the variant's genome has around 50 mutations, including more than 30 in the spike protein. One of the omicron variant's mutations leads to "S gene target failure" (or "S gene dropout"), meaning that one of several areas of the gene that are targeted by PCR testing gives a false negative. Omicron is highly infectious, spreading rapidly among communities with neutralizing antibodies against SARS-CoV-2 acquired by natural infection or vaccination appearing to have limited protection. [448,451,452] In a case series of 785 cases from Denmark, 76% of patients were fully vaccinated. [453] Despite the apparent lack of efficacy of vaccination and monoclonal antibodies, antivirals directed at SARS-CoV-2 remain effective. [454] A high infectivity rate has been reported in large group gatherings. [453] While Omicron is highly infectious, it appears to cause much milder disease. Anosmia and ageusia are uncommon, which may distinguish Omicron from previous variants. Furthermore, Omicron appears less likely to cause pulmonary disease; this may be related to altered ACE-2 binding to pulmonary alveolar cells. [455] Nevertheless, the elderly and those with significant comorbidities may suffer severe disease.

At this time the prevention and early treatment for Omicron should not differ from that of the previous variants, i.e., the I-MASK+ protocol should be followed. Early treatment is critical to limit spread of the virus, and as this variant is highly infectious prophylaxis of close contacts is important. Those infected

with omicron should be quarantined for up to 5 days. The optimal dose of ivermectin for early treatment is unclear, however, it is likely that a lower dose may suffice i.e. 0.3- 0.4 mg/kg. It is likely that the early treatment of Omicron may limit the progression to Long Covid.

13. Monitoring

- On admission: Procalcitonin (PCT), CRP, BNP, Troponins, Ferritin, Neutrophil-Lymphocyte ratio, D-dimer and Mg. CRP and D-dimer are important prognostic markers.[456] A PCT is essential to rule out coexisting bacterial pneumonia.[457]
- As indicated above (corticosteroid section), a chest CT scan on admission to the ICU is very useful for risk stratification and for the initial corticosteroid dosing strategy. The Ichikado Score is a quantitative method to assess the extent of lung involvement on the CT scan.[415,458] Follow-up CXR, CT scan (if indicated) and chest ultrasound as clinically indicated.
- Daily: *CRP, Ferritin, D-Dimer and PCT*. CRP and Ferritin track disease severity closely (although ferritin tends to lag behind CRP). Early high CRP levels are closely associated with the degree of pulmonary involvement and the CT score. [459]
- In patients receiving IV vitamin C, the Accu-Chek™ POC glucose monitor will result in spuriously high blood glucose values. Therefore, a laboratory glucose is recommended to confirm the blood glucose levels. [460,461]
- ECHO as clinically indicated; Patients may develop a severe "septic" cardiomyopathy and/or COVID-19 myocarditis. [462,463]

14. Post ICU management

- Enoxaparin 40–60 mg s/c daily
- Methylprednisolone 40 mg day, then wean slowly, follow CRP and oxygen requirements – wean off over two weeks once oxygen is discontinued to prevent relapse/recurrence
- Vitamin C 500 mg PO BID
- Melatonin 3–6 mg at night
- Vascepa, Lovaza or DHA/EPA 4g day
- Atorvastatin 40mg daily

15. Post Hospital Discharge management

a. Patients have an increased risk of thromboembolic events post-discharge. [464,465] Extended thromboprophylaxis (? with a DOAC) should be considered in high-risk patients. Risk factors include: [466]
    i. Increased D dimer (> 3 times ULN)
    ii. Increased CRP (> 2 times ULN) [467]
    iii. Age > 60
    iv. Prolonged immobilization
b. Patients with unresolved pulmonary infiltrates and/or those who remain dyspneic and/or oxygen dependent should be discharged on a tapering course of corticosteroids (prednisone).
c. Patients should continue to receive vitamin C, melatonin, omega-3 fatty acids and a statin. These agents may reduce this risk of developing the post-COVID syndrome.
d. Nigella sativa and Kefir.
e. Patients should be followed/monitored for developing the post-COVID/long hauler syndrome.

16. Pathophysiology of COVID-19

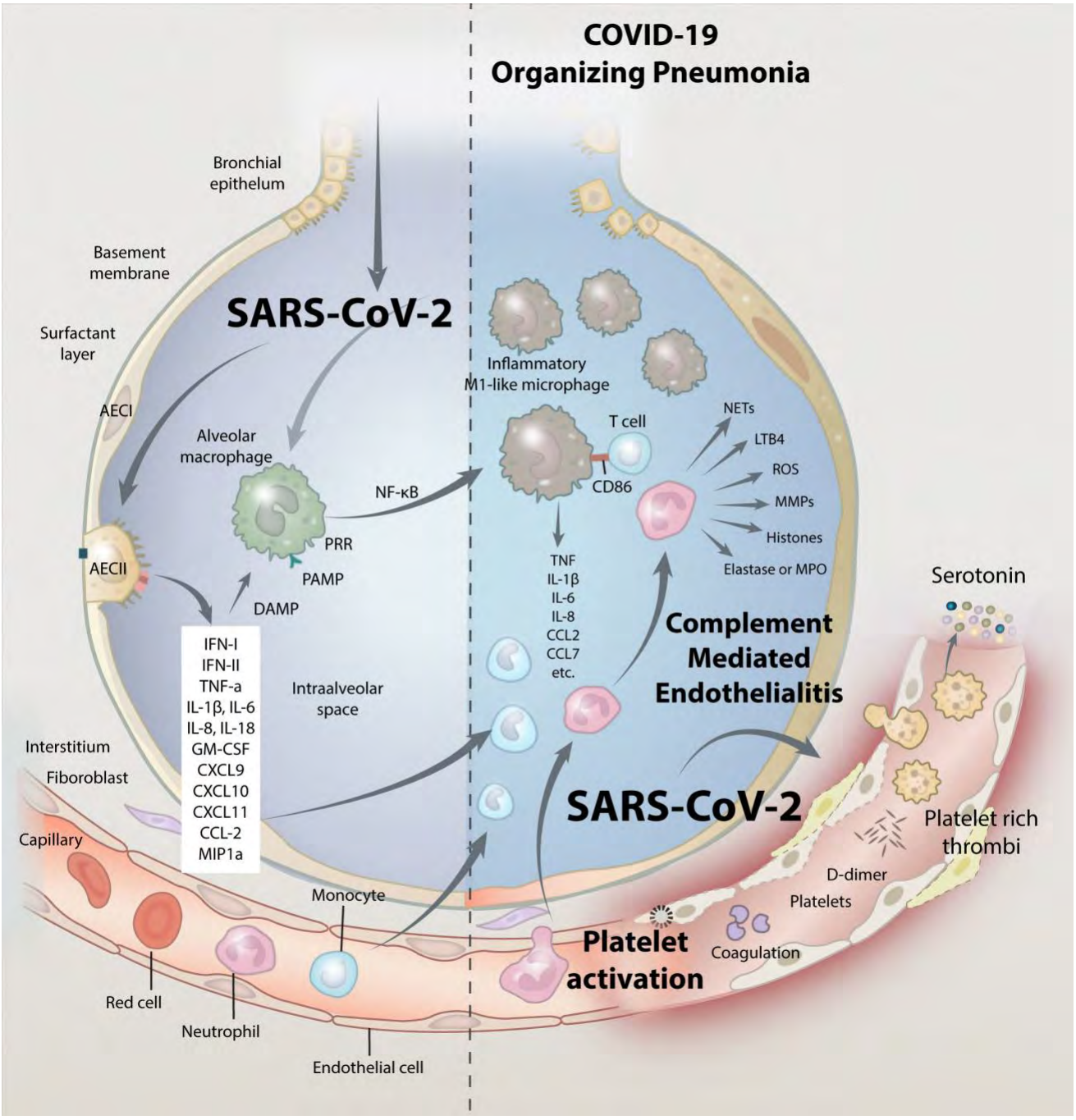
Basic Concept: Need to Understand the Disease to Treat the Disease

The pathophysiology of COVID-19

- Pulmonary Macrophage Activation Syndrome
  - Severe hyperinflammatory status
- Microvascular endothelialitis and thrombosis
  - Activation of clotting esp. platelet thrombi in lung and brain
  - High circulating serotonin
    - Arterial vasoconstriction
    - V/Q mismatch
  - Organ ischemia
- Multiple autoantibodies
- Mast cell activation – histamine release
- ACE-2 deficiency
  - Excess angiotensin II/ angiotensin 1-7
- T cell dysfunction

Based on clinical, proteomic, and genomic studies as well as autopsy data ,severe COVID-19 disease can be considered to be the connection of three basic pathologic processes, namely a pulmonary macrophage activation syndrome with excess production of cytokines and chemokines and uncontrolled inflammation, a complement mediated endothelialitis together with a procoagulant state with a thrombotic microangiopathy (see figure 11). In addition, platelet activation with the release of serotonin and the activation and degranulation of mast cells contributes to the hyper-inflammatory state. Autoantibodies have been demonstrated in a large number of hospitalized patients which adds to the end-organ damage and prothrombotic state. However, activated M1 macrophages appear to be the major driver of severe COVID-19 infection. Similarly, recent data suggests that the Long Haul Covid Syndrome (LHCS) results due to increased circulating levels of activated monocytes with ongoing cytokine production. [377] Interestingly, these monocytes contain high levels of the spike protein. [468] Both activated macrophages and activated monocytes express the same surface activation markers (CD14+, CD16+). This suggests that treatment aimed at repolarizing the macrophage/monocyte should have an important adjunctive role in the treatment of both acute COVID and the LHCS. Those interventions that have been demonstrated to repolarize macrophages/monocytes (from M1 to M2 phenotype) are listed below.

Figure 11. Pathogenetic mechanism of severe COVID-19 disease



17. The Long Haul COVID syndrome (post-COVID syndrome)

The Long Haul COVID Syndrome (LHCS) is characterized by prolonged malaise, headaches, generalized fatigue, sleep difficulties, hair loss, smell disorder, decreased appetite, painful joints, dyspnea, chest pain and cognitive dysfunction.[474-485] Up to 80% of patients experience prolonged illness after Covid-19. LHCS is not only seen after the COVID infection but it is being observed in some people that have received vaccines (likely due to monocyte activation by the spike protein from the vaccine). LHCS may persist for months after the acute infection and almost half of patients report reduced quality of life. Patients may suffer prolonged neuropsychological symptoms, including multiple domains of cognition.[483,486] A puzzling feature of the LHCS syndrome is that it is not predicted by initial disease severity; post-COVID-19 frequently affects mild-to-moderate cases and younger adults that did not require respiratory support or intensive care. [485] The symptom set of LHCS is in majority of the cases very similar to the chronic inflammatory response syndrome (CIRS)/ myalgic encephalomyelitis/chronic fatigue syndrome.[485] An important differentiating factor from CIRS is the observation that LHCS continues to improve on its own albeit slowly in majority of the cases. Another important observation is that LHCS includes more young people compared to severe COVID that affects older people or persons with comorbidities. Furthermore, the similarity between the mast cell activation syndrome and LHCS has been observed, and many consider post-COVID to be a variant of the mast cell activation syndrome.[487]

The LHCS syndrome is highly heterogeneous and likely results from a variety of pathogenetic mechanisms Furthermore, it is likely that delayed treatment (with ivermectin) in the early symptomatic phase will results in a high viral load which increase the risk and severity of LHCS. The following theories have been postulated to explain LHCS: [485]

1. Ongoing respiratory symptoms (SOB, cough, reduced effort tolerance) may be related to unresolved organizing pneumonia (activate pulmonary macrophages).
2. Monocyte activation syndrome. Persistence of viral debris in monocytes results in an ongoing immune response in an attempt by the immune system to clear the offending protein(s) and viral RNA fragments.
3. The neurological symptoms may be related micro- and/or macrovascular thrombotic disease which appears to be common in severe COVID-19 disease.[488] Brain MRIs' 3 months post-infection demonstrated micro-structural changes in 55% of patients. [489] In addition, features of encephalopathy may be related to encephalitis and auto-reactive brain antibodies [490] as well as severe cerebral vasoconstriction. [491] The brain microvasculature expresses ACE-2 receptors and SARS-CoV-2 "pseudovirions" may bind to the microvascular endothelium causing cerebral microvascular inflammation and clotting.[492].
4. An unmasking of mast cell activation syndrome (MCAS), or triggering of mast cell activation syndrome. Mast cells are present in the brain, especially in the median eminence of the hypothalamus, where they are located perivascularly close to nerve endings positive for corticotropin releasing hormone.[493] Following stimulation, mast cells release proinflammatory mediators such as histamine, tryptase, chemokines and cytokines which may result in neurovascular inflammation.[493] The "brain-fog", cognitive impairment and general fatigue reported in long-COVID may be due to mast cell related neurovascular inflammation.

Clinical signs and symptoms can be grouped in the following clusters. The reason for this grouping is to allow organ specific targeted therapy/individualized therapy.

1. Respiratory: shortness of breath, congestion, persistent cough, etc.
2. Neurological/psychiatric: brain fog, malaise, tiredness, headaches, migraines, depression, inability to focus/concentrate, altered cognition, insomnia, vertigo, panic attacks, tinnitus, anosmia, phantom smells, etc.

3. Musculoskeletal: myalgias, fatigue, weakness, joint pains, inability to exercise, post-exertional malaise, inability to perform normal activities of daily life (ADL's).
4. Cardiovascular: Palpitations, arrhythmias, Raynaud like syndrome, hypotension, and tachycardia on exertion.
5. Autonomic: Postural tachycardia syndrome (POTs), abnormal sweating.
6. Gastrointestinal disturbance: Anorexia, diarrhea, bloating, vomiting, nausea, etc.
7. Dermatologic: Itching, rashes, dermatographia
8. Mucus membranes: Running nose, sneezing, Burning and itchy eyes.

17.1 Approach to Treatment:

The treatment approach should be individualized according to the grouping of clinical signs and symptoms. However, in general, it is likely that patients who did not receive adequate antiviral treatment (e.g**.** ivermectin) during the acute symptomatic phase and adequate anti-inflammatory/macrophage repolarization therapy (e.g. corticosteroids, statins, omega-3 fatty acids, fluvoxamine, ivermectin, etc.) during the acute phase of COVID-19 are much more likely to develop the Post-COVID-19 Syndrome. In patients with ongoing respiratory symptoms, chest imaging is suggested (preferably a chest CT scan). Those with unresolved pulmonary inflammation (organizing pneumonia) should be treated with a course of corticosteroids (prednisone) and closely followed. A CRP should be measured, and extended corticosteroids (titrated to the CRP) offered to these patients. Similar to patients who have recovered from septic shock, [494] a prolonged (many months) immune disturbance with elevated pro- and anti-inflammatory cytokines may contribute to the LHCS. This is likely the consequence of monocyte activation syndrome and monocyte repolarization therapy is therefore indicated. In addition, a cytokine panel may allow targeted anti-inflammatory therapy (Maraviroc in patients with high CCR5 levels). It should be noted that much like omega-3 fatty acids, corticosteroids have been demonstrated to increase expression of pro-resolving lipids including Protectin D1 and Resolvin D4. [495] An unknown number of patients who have recovered from COVID-19 organizing pneumonia will develop pulmonary fibrosis with associated limitation of activity. Pulmonary function testing demonstrates a restrictive type pattern with decreased residual volume and DLCO.[480] These patients should be referred to a pulmonologist with expertise in pulmonary fibrosis. Anti-fibrotic therapy may have a role in these patients, [439-442] however additional data is required before this therapy can be more generally recommended. As discussed above, the serotonin receptor blocker cyproheptadine may reduce the risk of pulmonary fibrosis. [330]

17.2 The I-RECOVER Protocol for the treatment of the "Long-haul COVID Syndrome".

Although numerous reports describe the epidemiology and clinical features of LHCS, [474-484] studies evaluating treatment options are glaringly sparse. [312] Indeed, the NICE guideline for managing the long-term effects of COVID-19 provide no specific pharmacologic treatment recommendations. [496] In general, while the treatment of 'Long COVID" should be individualized, the following treatments may have a role in the treatment of this disorder. In addition, the I-RECOVER protocol may have a role in the treatment of post-vaccination syndrome. Patients with Long Covid should be managed by clinicians who have experience treating this troublesome disorder.

- Ivermectin has been reported to have a role in the treatment of post-COVID-19 syndrome. [312] A dose of 0.2-0.4 mg/kg day for 3-5 days, followed by once or twice weekly dosing for ongoing symptoms for up to 4 weeks. A repeat course is recommended in those who respond poorly or relapse once the treatment is stopped. The anti-inflammatory properties of ivermectin may mediate this benefit.
- Prednisone if inadequate response to ivermectin. Prednisone 0.5mg/kg daily for 5 days, 0.25mg/kg for 5 days followed by 0.12 mg/kg for 5 days. Patients with persistent organizing pneumonia may require higher doses for a more prolonged period of time.
- Vitamin C 500 mg BID (vitamin C inhibits histamine and repolarizes monocytes).[125]
- Omega-3 fatty acids: Vascepa, Lovaza or DHA/EPA 4 g day. Omega-3 fatty acids play an important role in the resolution of inflammation by inducing resolvin production. [256,257]
- Melatonin 2- 10 mg at night (slow release/extended release) with attention to sleep hygiene. Increase dose from 2mg as tolerated (may cause severe nightmares at high dosages)
- Curcumin has anti-inflammatory and immunomodulating properties and has been demonstrated to repolarize macrophages. [59]
- Maraviroc (a CCR5 receptor antagonist). C-C chemokine receptor type 5 (CCR5) is a cell surface G protein-coupled receptor expressed on macrophages and dendritic cells. CCR5 interacts with multiple ligands, notably the chemokines CCL3 (macrophage inflammatory protein-1), CCL4 (macrophage inflammatory protein-1), and CCL5 (RANTES). CCR5 and its ligands are overexpressed in COVID-19. [262,263,497] The activated CCR5 pathway may partly explain the persistence of activated monocytes in long-COVID. [377,468] Maraviroc has been extensively used in HIV infected patients, as CCR5 is a co-receptor for HIV. This drug has proven to have a remarkable safety record. [264,498] The approved dose of maraviroc for adults is 300 mg twice daily (BID) in the absence of potent CYP3A inducers or inhibitors. Evolving clinical experience suggests that maraviroc may be particularly effective in the treatment of long-COVID (no published data to date).
- Kefir, probiotic yogurt and/or Bifidobacterium Probiotics (e.g., Daily Body Restore) together with Prebiotics (e.g. XOS Prebiotic, Bio Nutrition Pre-Biotic) to normalize the microbiome. Prolonged dysbiosis has been reported following COVID-19 infection. [499]
- *Nigella sativa* which like curcumin has anti-inflammatory and immunomodulating properties.
- Atorvastatin 40 mg daily (increase resolvin synthesis and repolarizes macrophages) [408]
- Functional rehabilitation with light aerobic exercise paced according to individual capacity. [485]
- Behavioral modification, mindfulness therapy [500] and psychological support may help improve survivors' overall well-being and mental health. [485]
- *Optional:* Luteolin 100-200 mg day or quercetin 250 mg day (or mixed flavonoids). Luteolin and quercetin have broad spectrum anti-inflammatory properties. These natural flavonoids inhibit mast cells,[493,501-504] and have been demonstrated to reduce neuroinflammation. [505]
- *Optional:* Famotidine 20-40 mg day (histamine-2 blocker for Mast Cell Activation syndrome). [487]
- *Optional:* Fluvoxamine, especially in those with neurocognitive issues. Start at 25 mg daily, Increase slowly to 50 -100 mg per day. Monitor response closely as some patients will respond poorly to this medication. Teens and young adults who are prescribed fluvoxamine can experience acute anxiety

which needs to be monitored for and treated by the prescribing clinician to prevent rare escalation to suicidal or violent behavior.

- *Optional:* Antiandrogen therapy which results in macrophage repolarization. [471-473] Spironolactone 50-100 mg BID and dutasteride 1mg daily.
- *Optional:* H1 receptor blockers (for mast cell activation syndrome). Loratadine 10mg daily, Cetirizine 5-10mg daily, Fexofenadine 180mg daily.
- *Optional:* H2 receptor blockers (for mast cell activation syndrome). Famotidine 20 mg, or Nizatidine 150 mg – twice daily as tolerated.
- *Optional:* Montelukast 10 mg/day (for mast cell activation syndrome). Caution as may cause depression is some patients.

Macrophage/monocyte Repolarization Therapy for COVID-19 and Long Haul COVID Syndrome

- Corticosteroids [469]
- Statins [309,310]
- Omega-3 fatty acids [251-253]
- Melatonin [470]
- Vitamin C
- Anti-androgen therapy [471-473]
- Curcumin (turmeric) [59]

I-RECOVER

Management Protocol for Long-haul COVID Syndrome (LHCS)

The approach outlined below is a simplified, consensus protocol based on a collaboration led by Dr. Mobeen Syed ("Dr. Been"), Dr. Ram Yogendra, Dr. Bruce Patterson, Dr. Tina Peers, and the FLCCC Alliance. Given the lack of clinical treatment trials of Long-haul Covid Syndrome, these recommendations are based on the pathophysiologic mechanisms of COVID and post-viral illnesses along with our collective experience observing profound and sustained clinical responses achieved with the treatment approaches below.

This protocol has also been used to treat post-vaccine inflammatory syndromes with similar success. As with all FLCCC Alliance protocols, the components, doses, and durations will evolve as more clinical data accumulates. Several members of this collaboration employ various adjunctive therapies they have found beneficial. Info on these approaches can be found on page 3.

Initial therapy of Long-haul Covid Syndrome:

IVERMECTIN

0.2–0.4 mg/kg dose once daily with meals* for 3–5 days (higher doses are sometimes needed in ansomia).

* Take on empty stomach if presenting with nausea/diarrhea/anorexia.

After 3–5 days, change to once or twice weekly depending on the time to symptom recurrence/persistence.

Discontinue after 2–4 weeks if all symptoms have resolved and do not recur.

Relative Contraindications:
- Patients on Warfarin require close monitoring and dose adjustment.
- Pregnant or lactating women require a more in-depth risk/benefit assessment.

If not all symptoms resolve with ivermectin:

CORTICOSTEROID THERAPY

A tapering dose of prednisone as follows:

1. 0.5 mg/kg daily for 5 days
2. 0.25 mg/kg daily for 5 days
3. 0.12 mg/kg daily for 5 days

Take in morning to lessen impact on sleep.

Side effects may include: Increased appetite, mood changes, insomnia, raised blood glucose, dyspepsia.

Recommended to support the LHCS therapy:

SUPPLEMENTS

- Vitamin C: 500 mg twice daily.
- Vitamin D3: 2,000–4,000 IU daily.
- Melatonin: 2–10 mg nightly – start with low dose, increase as tolerated in absence of sleep disturbance.

If presenting with neurologic symptoms, i.e. poor concentration, forgetfulness, mood distrubance:

FLUVOXAMINE

50 mg – twice daily for 15 days.

Reduce dose or discontinue if side effects develop. Doses as low as 9 mg twice daily have shown efficacy.

If presenting with shortness of breath or low oxygen levels:

PULMONARY EVALUATION

Refer to lung specialist if available, otherwise perform chest imaging (CT preferred) to assess for secondary organizing Pneumonia (OP).

If findings consistent with secondary OP found, initiate **Corticosteroid Therapy** as below. May need to repeat or prolong course of treatment if symptoms or oxygen needs persist.

If symptoms still unresolved or recur after ivermectin and corticosteroid regimens:

TREATMENT OF SUSPECTED MAST CELL ACTIVATION

Choose a Type I and Type II antihistamine along with a mast cell stabilizer – for example, Loratidine, Famotidine, and Rupatadine. Change medicines if poor response. US FDA approved doses of many of the below medicines are daily, but can increase to three times daily with caution and close monitoring if poor response.

First-line Therapy
- Low histamine diet

Type I antihistamines:
- Use up to TDS: Loratadine 10 mg, or Cetirizine 10 mg, or Fexofenadine 180 mg

Type II antihistamines:
- twice daily: Famotidine 20 mg, or Nizatidine 150 mg

Mast cells stabilizers:
- Rupatadine 10 mg, or Ketotifen 1 mg, plus or minus
- Sodium Cromoglycate 200 mg TDS (increase slowly) or Quercetin 500 mg TDS

Second-line Therapy
- Montelukast 10 mg (beware depression in some)
- Low Dose Naltrexone (LDN; avoid if taking opiates), start with 0.5 mg daily increasing by 0.5 mg weekly up to 4.5 mg daily
- Diazepam 0.5-1 mg twice daily
- SSRIs

BID	twice daily	mg/kg	dose in mg per kg body weight
CT	computed tomography scan	OP	organizing pneumonia
GIT	gastrointestinal tract	RDA	recommended dietary allowances
IU	international units	TDS	3 times daily

Please regard our disclaimer on page 3.

For more information on the treatment protocols of the FLCCC Alliance please see: flccc.net

18. Key Concepts of the I-MASK+ and MATH+ Treatment Protocols

This is an extraordinarily complex disease; many of the mysteries are still unravelling. However, a number of concepts are key to the management of this "treatable disease;" they include.

1. It is important to focus on the totality of the evidence and not just on RCTs (see figure 11). We are in the midst of a global pandemic and the use of cheap, effective, and safe repurposed drugs has and will continue to have a major role in the prevention and treatment of this disease.
2. Patients transition through a number of different phases (clinical stages). The treatment of each phase is distinct ... this is critically important (see Figures 1 & 2).
3. Antiviral therapy is likely to be effective only during the viral replicative phase, whereas anti-inflammatory therapy is expected to be effective during the pulmonary phase and possibly the post-COVID-19 phase. While Remdesivir is a non-specific antiviral agent that targets RNA viruses, it is likely that agents specifically designed to target SARS-CoV-2 will be developed.
4. The SARS-CoV-2 PCR remains positive for at least 2 weeks following detection of whole virus (by culture, See figure 3). Patients who progress to the pulmonary phase are usually PCR positive despite cessation of viral replication (and are therefore less likely to be infectious).
5. Due to the imperfect sensitivity of the PCR test, as many as 20% of patients who progress to the pulmonary phase will be PCR negative (even on repeat testing). At symptom onset PCR will be positive in approximately 60% of patients; maximal positivity rate is on day 8 (post infection) when 80% of patients will be positive (see Figure3). [506] COVID-19 is essentially a clinical diagnosis supported by laboratory tests.
6. Symptomatic patients are likely to be infectious during a narrow window starting 2–3 days before the onset of symptoms and to up to 6 days after the onset of symptoms (see Figure 3). [507]
7. It is important to recognize that COVID-19 patients present with a variety of phenotypes, likely dependent on inoculum size and viral load, SARS-CoV-2 variant, genetic heterogeneity mutations and polymorphisms, biotypes, blood type, sex and androgen status, age, race, BMI (obesity), immunological and nutritional status, and co-morbidities.[295,508-518] The phenotype at presentation determines the prognosis and impacts the optimal approach to treatment. It is noteworthy that obesity and increasing BMI are critical prognostic factors. This may be related to the fact that there are more ACE-2 receptors in visceral fat than in the lung. [519]
8. The pulmonary phase is characterized by immune dysregulation, [488,511,520-533] a pulmonary microvascular injury (vasculopathy), [488,533-536] with activation of clotting and a procoagulant state together with the characteristics of an organizing pneumonia. [407,537]
9. Endothelial damage and an imbalance of both innate and adaptive immune responses, with aberrant macrophage activation, plays a central role in the pathogenesis of the severe COVID-19 Disease. [488]
10. As patients, progress down the pulmonary cascade the disease becomes more difficult to reverse. The implications of this are two-fold.
    a. Early treatment (of the pulmonary phase) is ESSENTIAL to a good outcome.
    b. Treatment in the late pulmonary phase may require escalation of the dose of corticosteroids as well as the use of salvage methods (i.e., plasma exchange). However, patients who present in the late pulmonary phase may have progressed to the irreversible pulmonary fibroproliferative phase.
11. The pulmonary phase of COVID-19 is a treatable disease; it is inappropriate to limit therapy to "supportive care" alone. Furthermore, it is unlikely that there will be a single "silver bullet" to treat severe COVID-19 disease. Rather, patients will require treatment with multiple drugs/interventions that have synergistic and overlapping biological effects. Repurposed FDA

approved drugs that are safe, inexpensive, and "readily" available are likely to have a major therapeutic effect on this disease. The impact of COVID-19 on middle- and low-income countries is enormous; these countries are not able to afford expensive propriety "designer" molecules.

12. The radiographic and pathological findings of COVID-19 lung disease are characteristic of a Secondary Organizing Pneumonia (and not ARDS). [407,538,539]
13. THIS is NOT ARDS (at least initially), but rather an organizing pneumonia. The initial pulmonary phase neither looks like, smells like nor is ARDS. [540-542] The ground glass infiltrates are peripheral and patchy, [538] and do not resemble the dependent air space consolidation (sponge/baby lung) seen with "typical ARDS". [543] Extravascular lung water index (EVLWI) is normal or only slightly increased; this by definition excludes non-cardiogenic pulmonary edema (ARDS). Lung compliance is normal (this excludes ARDS). Patients are PEEP unresponsive. Treating patients as if they ARDS is an extremely dangerous approach. The hypoxia is due to an organizing pneumonia with severe ventilation/perfusion mismatch likely due to the microvascular narrowing, thrombosis and vasoplegia.
14. The core principles of the pulmonary phase (MATH+) is the use of anti-inflammatory agents to dampen the "cytokine storms" together with anticoagulation to limit the microvascular and macrovascular clotting and supplemental oxygen to help overcome the hypoxia.
15. Ivermectin has emerged as a highly effective drug for the prophylaxis and treatment of COVID-19. Ivermectin inhibits viral replication and has potent anti-inflammatory properties. Emerging clinical data (including RCTs) suggest that ivermectin may have an important clinical benefit across the spectrum of phases of the disease, i.e pre-exposure prophylaxis, post-exposure prophylaxis, during the symptomatic phase and during the pulmonary phase. [23,77-79,162,165-171,287-289,357-363,544] In the recommended dosages, ivermectin is remarkably safe and effective against SARS-CoV-2. However, as noted above, there is the potential for serious drug-drug interaction.
16. The pulmonary phase of COVID-19 is characterized by PROLONGED immune dysregulation that may last weeks or even months. The early and abrupt termination of anti-inflammatory agents will likely result in rebound inflammation. [545]
17. SARS-CoV-2, as compared to all other respiratory viruses, upregulates cytokines and chemokines while at the same time down regulating the expression of Interferon alpha (the hosts primary antiviral defence mechanism). [131,155] Low innate antiviral defenses and high pro-inflammatory mediators contribute to ongoing and progressive lung injury.
18. An unknown percentage of patients with COVID-19 present with "silent hypoxia" with a blunted respiratory response. This phenomenon may be related to involvement of chemoreceptors of the carotid bodies and/or brain stem dysfunction, [546,547] and necessitates pulse oximetry in symptomatic patients managed at home (as discussed above).
19. It should be recognized that LWMH has non-anticoagulant properties that are likely beneficial in patients with COVID-19, these include anti-inflammatory effects and inhibition of histones. [548] in addition, in vitro studies demonstrate that heparin inhibits SARS-CoV-2 interaction with the ACE-2 receptor and viral entry,[549,550] as well as viral replication [170,551]. Most importantly LWWH inhibits heparanase (HPSE).[552] HSE destroys the endothelial glycocalyx increasing endothelial leakiness, activating clotting and potentiating endothelialitis.[552] HPSE levels have been reported to be increased in patients with severe COVID-19 infection. [553] Due to the ease of administration, greater anti-Xa activity and better safety profile we prefer low molecular weight heparin (LMWH) to unfractionated heparin (UFH).
20. The combination of steroids and ascorbic acid (vitamin C) is essential. Both have powerful synergistic anti-inflammatory actions. [341,346] Vitamin C protects the endothelium from oxidative injury. [125,554-556] Furthermore, vitamin C Increases the expression of interferon-alpha [115] while corticosteroids (alone) decrease expression of this important protein. [557-560] It should be noted that when corticosteroids are used in the pulmonary phase (and not in

the viral replicative phase) they do not appear to increase viral shedding or decrease the production of type specific antibodies. [297,561] It is likely that heparin (LMWH) acts synergistically with corticosteroids and vitamin C to protect the endothelium and treat the endothelialitis of severe COVID-19 disease.

21. Notwithstanding the particularly important and impressive results of the Recovery-Dexamethasone study, methylprednisolone is the corticosteroid of choice for the pulmonary phase of COVID-19. This is based on pharmacokinetic data (better lung penetration),[562] genomic data specific for SARS-CoV-2,[204] and a long track record of successful use in inflammatory lung diseases (see Table 2).
22. It should be noted that animal studies have demonstrated that ivermectin has immunostimulatory effects.[563,564] For this reason patients taking ivermectin do not need to stop taking ivermectin when vaccinated. Indeed, ivermectin may boost the immune response to the vaccine.

And finally: "If what you are doing ain't working, change what you are doing."

Figure 12. Evaluating the totality of evidence.

19. References

1. Angell M. The truth about drug companies: how they deceive us and what to do about it. New York: Random House; 2005.
2. Kennedy RF. The Real Anthony Fauci. Bill Gates, Big Pharma, and the Global War on Democracy and Public Health. New York, NY: Skyhorse Publishing; 2021.
3. Wittich CM, Burkle CM, Lanier WL. Ten common questions (and their answers) about off-label drug use. Mayo Clin Proc 2012; 87:982-90.
4. Fatima S, Zaidi SS, Alsharidah AS et al. Possible prophylactic approach for SARS-CoV-2 infection by combination of melatonin, Vitamin C and Zinc in animals. Fronteirs in Veterinary Science 2020; 7:585789.
5. Arslan B, Ergun NU, Topuz S et al. Synergistic effect of quercetin and vitamin C against COVID-19: Is a possible guard for front liners? ssrn 2020.
6. Ahmed AK, Albalawi YS, Shora HA et al. Effects of quadruple therapy: Zinc, Quercetin, Bromelain and Vitamin C on clinical outcomes of patients infected with COVID-19. Rea Int Jou of End and Dia 2020; 1:1005.
7. Marik P, Iglesias J, Varon J et al. A Scoping Review of the pathophysiology of COVID-19. International Journal of Immunopathology and Pharmacology 2021.
8. Leung K, Shum MMH, Leung GM et al. Early empirical assessment of the N501Y mutant strains of SARS-CoV-2 in the United Kingdom, October to November 2020. medRxiv 2020.
9. Tegally H, Wilkinson E, Giovanetti M et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spke mutations in South Africa. medRxiv 2020.
10. Li B, Deng A, Li K et al. Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 delta variant. medRxiv 2021.
11. Fratev F. The SARS-CoV-2 S1 spike mutation N501Y alters the protein interactions with both hACE2 and human derived antibody: A free energy of perturbation study. bioRxiv 2020.
12. Nonaka CK, Franco MM, Graf T et al. Genomic evidence of a SARS-C0V-2 reinfection case with E484K spike mutation in Brazil. Preprints 2021.
13. Jehi L, Ji X, Milinovich A et al. Individualizing risk prediction for positive COVID-19 testing. Results from 11,672 patients. Chest 2020; 158:1364-75.
14. Kory P, Meduri GU, Iglesias J et al. Review of the emerging evidence demonstrating the efficacy of ivermectin in the propphylaxis and treatment of COVID-19. ssrn 2020.
15. Guy GP, Lee FC, sunshine G et al. Association of State-Issued mask mandates and allowing on premises restaurant dining with County-levels COVID-19 case and death growth rates-United States, March 1 - December 31, 2020. MMWR 2021; 70.
16. Guzzo CA, Furtek CI, Porras AG et al. Safety, tolerability, and pharmacokinetics of escalating high doses of ivermectin in healthy adult subjects. J Clin Pharmacol 2002; 42:1122-33.
17. Behera P, Patro BK, Singh AK et al. Role of ivermectin in the prevention of COVID-19 infection among healthcare workers in India: A matched case-control study. medRxiv 2020.
18. Carvallo H, Hirsch RR, Alkis P et al. Study of the efficacy and safety of topical ivermectin + Iota-carrageenan in the prophylaxis against COVID-19 in health personnel. Journal of Biomedical Research and Clinical Investigation 2020; 2.
19. Kory P, Meduri GU, Iglesias J et al. Review of the emerging evidencce supporting the use of Ivermectin in the prophylaxis and treatment of COVID-19. Front Line Covid-19 Critical Care Alliance. osf io 2020.
20. Hellwig MD, Maia A. A COVID-19 prophylaxis? Lower incidence associated with prophylactic administraion of ivermectin. Int J Antimicrob Agents 2020.
21. Morgenstern J, Redondo JN, Olavarria A et al. Retrospective cohort study of Ivermectin as a SARS-CoV-2 pre-exposure prophylaxis method in Healthcare Workers. medRxiv 2021.
22. Chahla RE, Medina Ruiz L, Mena T et al. Ivermectin reproposing for COVID-19 treatment outpatients in mild stage in primary health centers. medRxiv 2021.
23. Kircik LH, Del Rosso JQ, Layton AM et al. Over 25 years of clinical experience with Ivermectin: An overview of safety for an increasing number of indications. J Drugs Dermatol 2016; 15:325-32.
24. Aroke D, Tchouakam DN, Awungia AT et al. Ivermectin induced Steven-Johnsons syndrome: case report. BMC Research Notes 2017; 10:179.

25. Ngwasiri CA, Abanda MH, Aminde LN. Ivermectin-induced fixed drug eruption in an elderly Cameroonian: a case report. Journal of Medical Case Reports 2018; 12:254.
26. Veit O, Beck B, Steuerwald M et al. First case of ivermectin-induced severe hepatitis. Trans R Soc Trop Med Hyg 2021; 100:795-97.
27. Nicolas P, Maia MF, Bassat Q et al. Safety of oral ivermectin during pregnancy: a systematic review and meta-analysis. Lancet Glob Health 2020; 8:e92-e100.
28. Canga AG, Sahagun Prieto AM, Diez Liebana MJ et al. The pharmacokinetics and interactions of Ivermectin in humans-A mini-review. The AAPS Journal 2007; 10:42-46.
29. Colunga Biancatelli RM, Berrill M, Mohammed YH et al. Melatonin for the treatment of sepsis: the scientific rationale. J Thorac Dis 2020; 12 (Suppl 1):S54-S65.
30. Reiter RJ, Abreu-Gonzalez P, Marik PE et al. Therapeutic algorithm for use of melatonin in patients with COVID-19. Front Med 2020; 7:226.
31. Reiter RJ, Sharma R, Ma Q et al. Melatonin inhibits COVID-19-induced cytokine storm by reversing aerobic glycolysis in immune cells: A mechanistic analysis. Medicine in Drug Discovery 2020; 6:100044.
32. Zhang R, Wang X, Ni L et al. COVID-19: Melatonin as a potential adjuvant treatment. Life Sci 2020; 250:117583.
33. Kleszczynski K, Slominski AT, Steinbrink K et al. Clinical trials for use of melatonin to fight COVID-19 are urgently needed. Nutrients 2020; 12.
34. Coto-Montes A, Boga JA. ER stress and autophagy induced by SARS-CoV-2: The targer for melatonin treatment. Melatonin Res 2020; 3:346-61.
35. Gandolfi JV, Di Bernardo AP, Chanes DA et al. The effects of melatonin supplementation on sleep quality and assessment of the serum melatonin in ICU patients: A randomized controlled trial. Crit Care Med 2020.
36. Castillo RR, Quizon GR, Juco MJ et al. Melatonin as adjuvant treatment for coronavirus disease 2019 pneumonia patients requiring hospitalization (MAC-19 PRO): a case series. Melatonin Res 2021; 3:297-310.
37. Ramiall V, Zucker J, Tatonetti N. Melatonin is significantly associated with survival of intubated COVID-19 patients. medRxiv 2021.
38. Farnoosh G, Akbaariqomi M, Badri T et al. Efficacy of a low dose of melatonin as an adjunctive therapy in hospitalized patients with COVID-19: A randomized, double-blind clinical trial. medRxiv 2021.
39. Farnoosh G, Akbariqomi M, Badri T et al. Efficacy of a low dose of melatonin as an adjunctive therapy in hospitalized patietns with COVID-19: A randomized, double-blind clinical trial. Archives of Medical Research 2021.
40. Darban M, Malek F, Memarian M et al. Efficacy of high dose vitamin C, melatonin and zinc in Iranian patients with acute respiratory sydrome due to Coronavirus infection: A pilot randomized trial. Journal of Cellular & Molecular Anesthesia 2021; 6:164-67.
41. Hasan ZT, AlAtrakji MQ, Mehuaiden AK. The effect of melatonin on thrombosis, sepsis and mortality rate in COVID-19 patients. International Journal of Infectious Diseases 2022; 114:79-84.
42. Shneider A, Kudriavtsev A, Vakhusheva A. Can melatonin reduce the severity of COVID-19 pandemic. medRxiv 2020.
43. O'Brien MP, Forleo-Neto E, Musser BJ et al. Subcutaneous REGEN-COV antibody combination to prevent Covid-19. N Engl J Med 2021.
44. Freedberg DE, Conigliaro J, Sobieszczyk ME et al. Famotidine use is associated with impoved clinical outcomes in hospitalized COVID-19 patients: A propensity score matched retrospective cohort study. medRxiv 2020.
45. Janowitz T, Baglenz E, Pattinson D et al. Famotidine use and quantitative symptom tracking for COVID-19 in non-hospitalized patients: a case series. Gut 2020; 69:1592-97.
46. Mather JF, Seip RL, McKay RG. Impact of famotidine use on clinical outcomes of hospitalized COVID-19 patients. Am J Gastroenterol 2020.
47. Malone RW, Tisdall P, Fremont-Smith P et al. COVID-19: Famotidine, Histamine, Mast Cells, and mechanisms. Research Square 2020.
48. Sethia R, Prasad M, Mahapatra SJ et al. Efficacy of famotidine for COVID-19: A systematic review and meta-analysis. medRxiv 2020.
49. Shoaibi A, Fortin S, Weinstein R et al. Comparative effectiveness of famotidine in hospitalized COVID-19 patients. medRxiv 2020.

50. Yeramaneni S, Doshi P, Sands K et al. Famotidine use is not associated with 30-day mortality: A coarsened exact match study in 7158 hospitalized COVID-19 patients from a large healthcare system. medRxiv 2020.
51. Almario CV, Chey WD, Spiegel BM. Increased risk of COVID-19 among users of proton pump inhibitors. Am J Gastroenterol 2020.
52. Lee SW, Ha EK, Moon SY et al. Severe clinical outcomes of COVID-19 associated with proton pump inhibitors: a nationwide cohort study with propensity score matching. Gut 2021; 70:76-84.
53. McCullough PA, Alexander PE, Armstrong R et al. Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19). Reviews in Cardiovascular Medicine 2020; 21:517-30.
54. Ladapo JA, McKinnon JE, McCullough PA et al. Randomized controlled trials of early ambulatory hydroxychloroquine in the prevention of COVID-19 infection, hospitalization, and death: Meta-analysis. medRxiv 2020.
55. McCullough PA, Kelly RJ, Ruocco G et al. Pathophysiological basis and rationale for Early Outpatient Treatment of SARS-CoV-2 (COVID-19) infection. Am J Med 2021; 134:16-22.
56. Risch HA. Early outpatient treatment of symptomatic, High-Risk Covid-19 patients that should be ramped-up immediately as key to the pandemic crisis. Am J Epidemiol 2020; 189:1218-26.
57. Munoz J, Ballester MR, Antonijoan RM et al. Safety and pharmacokinetic profile of fixed-dose ivermectin with an innovative 18 mg tablet in healthy adult volunteers. PLoS Neglected Tropical Diseases 2018; 12:e0006020.
58. Rattis BA, Ramos SG, Celes MR. Curcumin as a potential treatment for COVID-19. Fronteirs in Pharmacology 2021; 21:675287.
59. Chai YS, Chen YQ, Lin SH et al. Curcumin regulates the differentiation of naive CD4+ T cells and activates IL-10 immune modulation against acute lung injury in mice. Biomedicine and Pharmacotherapy 2020; 125:109946.
60. Thimmulappa RK, Mudnakudu-Nagaraju KK, Shivamallu C et al. Antiviral and immunomodulatory activity of curcumin: A case for prophylactic therapy for COVID-19. Heliyon 2021; 7:e06350.
61. Jena AB, Kanungo N, Nayak V et al. Catechin and curcumin interact with S protein of SARS-CoV2 and ACE2 of human cell membrane: insights from computational studies. Scientific Reports 2021; 11:2043.
62. Somi VK, Mehta A, Ratre YK et al. Curcumin, a traditional spice component, can hold promise against COVID-10? Eur J Pharmacol 2020; 886:173551.
63. Tahmasebi S, El-Esawi MA, Mahmoud ZH et al. Immunomodulatory effects of nanocurcumin on the Th17 cell responses in mild and severe COVID-19 patients. J Cell Physiol 2021; 236:5325-38.
64. Valizadeh H, Danshina S, Gencer MZ et al. Nano-curcumin therapy, a promising method in modulating inflammatory cytokines in COVID-19 patients. International Immunopharmacology 2020; 89:107088.
65. Al-Hatamleh MA, Hatmal MM, Sattat K et al. Antiviral and immnomodulatory effects of phytochemicals from honey against COVID-19: Potential mechanisms of action and future directions. Molecules 2020; 25:5017.
66. Hashem HE. *In Silico* approach of some selected honey constituents as SARS-CoV-2 main protease (COVID-19) inhibitors. medRxiv 2021.
67. Ashraf S, Ashraf S, Ashraf M et al. Honey and *Nigella sativa* against COVID-19 in Pakistan (HNS-COVID-PK): A multi-center placebo-controlled randomized clinical trial. medRxiv 2021.
68. Salim B, Noureddine M. Identification of compounds from Nigella Sativa as new potential inhibitors of 2019 Novel Coronavirus (COVID-10): Molecular docking study. ChemRxiv 2021.
69. Fakhar-e-Alam Kulyar M, Li R, Mehmood K et al. Potential influence of *Nagella sativa (*Black cumin) in reinforcing immune system: A hope to decelerate the COVID-19 pandemic. Phytomedicine 2021; 85:153277.
70. Khazdair MR, Ghafari S, Sadeghi M. Possible therapeutic effects of *Nigella sativa* and its thymoquinone on COVID-19. Pharmaceutical Biology 2021; 59:696-703.
71. Islam MN, Hossain KS, Sarker PP et al. Revisiting pharmacological potentials of *Nigella sativa* seed: A promising option for COVID-19 prevention and cure. Phytotherapy Research 2021; 35:1329-44.
72. Rahman MT. Potential benefits of combination of *Nigella sativa* and Zn supplements to treat COVID-19. J Herbal Med 2020; 23:100382.
73. Hannan MA. Black Cumin (Nigella sativa L.): A Comprehensive Review on Phytochemistry, Health Benefits, Molecular Pharmacology, and Safety. Nutrients 2021; 13.

74. Warner ME, Naranjo J, Pollard EM et al. Serotonergic medications, herbal supplements, and perioperative serotonin syndrome. Can J Anaesth 2017; 64:940-946.
75. Borsche L, Glauner B, von Mendel J. COVID-19 mortality risk correlates inversely with vitamin D3 status, and a mortality rate close to zero could theoretically be achieved at 50ng/ml 25(OH)D3: results of a systematic review and meta-analysis. Nutrients 2021; 13:3596.
76. Kolls JK, Garry RF. Role of the T cell vitamin D receptor in severe COVID-19. Nature Immunology 2022; 23:3-10.
77. Gorial FI, Mashhadani S, Sayaly HM et al. Effectiveness of Ivermectin as add-on therapy in COVID-19 management (Pilot Trial). medRxiv 2020.
78. Khan MS, Khan MS, Debnath Cr et al. Ivermectin treatment may improve the prognosis of patients with COVID-19. Archivos de Bronconeumologia 2020.
79. Rajter JC, Sherman MS, Fatteh N et al. ICON (Ivermectin in COvid Ninteen) study: Use of ivermectin is associated with lower mortality in hospitalized patients with COVID-19. Chest 2020.
80. Niaee MS, Gheibl N, Namdar P et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: A randomized multi-center clinical trial. Research Square 2020.
81. Elgazzar A, Hany B, Youssef SA et al. Efficacy and safety of ivermectin for treatment and prophylaxis of COVID-19 pandemic. Research Square 2020.
82. Hashim HA, Maulood MF, Rasheed AM et al. Controlled randomized clinical trial on using Ivermectin with Doxycycline for treating COVID-19 patients in Bagdad, Iraq. medRxiv 2020.
83. Maghbooli Z, Sahraian MA, Ebrahimi M et al. Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/ml reduced risk for adverse clinical outcomes in patients with COVID-19 infection. PloS ONE 2020; 15:e0239799.
84. Grant WB, Lahore H, McDonnell SL et al. Evidence that Vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients 2020; 12:988.
85. Kaufman HW, Niles JK, Kroll MH et al. SARS-CoV-2 positivity rates associated with circulating 25-hydroxyvitamin D level. PloS ONE 2020; 15:e0239252.
86. Lau FH, Majumder R, Torabi R et al. Vitamin D insufficiency is prevalent in severe COVID-19. medRxiv 2020.
87. Marik PE, Kory P, Varon J. Does vitamin D status impact mortlality from SARS-CoV-2 infection? Medicine in Drug Discovery 2020.
88. Rhodes JM, Subramanian S, Laird E et al. Editorial: Low population mortality from COVID-19 in countries south of 35 degrees North - supports vitamin D as a factor determining severity. Alimentary Pharmacology & Therapeutics 2020; (in press).
89. Dancer RC, Parekh D, Lax S et al. Vitamin D deficiency contributes directly to the acute respiratory distress syndrome (ARDS). Thorax 2015; 70:617-24.
90. LLie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging Clin Exp Res 2020.
91. Daneshkhah A, Eshein A, Subramanian H. The role of vitamin D in suppressing cytokine storm of COVID-19 patients and associated mortality. medRxiv 2020.
92. Bergman P, Lindh AU, Bjorkhem-Bergman L et al. Vitamin D and respiartory tract infections: A systematic review and meta-analysis of randomized controlled trials. PloS ONE 2013; 8:e65835.
93. Carpagnano GE, Lecce V, Quaranta VN et al. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory fialure due to COVID-19. J Endocrinol Invest 2020.
94. Israel A, Cicurel A, Feldhamer I et al. The link between vitamin D deficiency and Covid-19 in a large population. medRxiv 2020.
95. Radujkovic A, Hippchen T, Tiwari-Heckler S et al. Vitamin D deficiency and outcome of COVID-19 patients. Nutrients 2020; 12:2757.
96. Rizzoli R. Vitamin D supplementation: upper limit for safety revisited. Aging Clin Exp Res 2020.
97. Annweiler C, Hanotte B, de L'Eprevier CG et al. Vitamin D and survival in COVID-19 patients: A quasi-experimental study. Journal of Steroid Biochemistry & Molecular Biology 2020.
98. Moozhipurath RK, Kraft L, Skiera B. Evidence of protective role of Ultraviolet-B (UVB) radiation in reducing COVID-19 deaths. Nature Research 2020; 10:17705.
99. Cangiano B, Fatti LM, Danesi L et al. Mortality in an Italian nursing home during COVID-19 pandemic: correlation with gender, age, ADL, vitamin D supplementaion, and limitations of the diagnostic tests. Aging 2020; 12.

100. De Smet D, De Smet K, Herroelen P et al. Serum 25(OH)D level on hospital admission assocaited with COVID-19 stage and mortality. Am J Clin Pathol 2020.
101. Cozier YC, Castro-Webb N, Hochberg NS et al. Lower serum 25(OH) D levles associated with higher risk of COVID-19 infection in U.S. black women. PloS ONE 2021; 16:e0255132.
102. Loucera C, Pena-Chilet M, Esteban-Medina M et al. Real world evidence of calcifediol or vitamin D prescription and mortality rate of COVID-19 in a retrospective cohort of hospitalized Andalusian patients. Scientific Reports 2021; 11:23380.
103. Teshome A, Adane A, Girma B et al. The impact of Vitamin D level on COVID-19 infection: systematic review and meta-analysis. Fronteirs in Public Health 2021; 9:624559.
104. Seven B, Gunduz O, Ozgu-Erdinc AS et al. Correlation between 25-hydroxy vitamin D levels and COVID-19 severity in pregnant women: a cross-sectional study. Journal of Maternal-Fetal & Neonatal Medicine 2021.
105. Murai IH, Fernandes AL, Sales LP et al. Effect of vitamin D3 supplementaion vs placebo on hospital length of stay in patients with severe COVID-19: A multicenter, double-blind, randomized controlled trial. JAMA 2020.
106. Wu Y, Cheng X, Jiang G et al. Altered oral and gut microbiota and its association with SARS-CoV-2 viral load in COVID-19 patients during hospitalization. npj Biofilms and Microbiomes 2021; 7:61.
107. Hazan S, Stollman N, Bozkurt H et al. The missing microbes: Bifidobacterium and Faecalibacterium depletion and loss of microbiome diversity as potential susceptibility markers for SARS-CoV-2 infection and severity. Clinical Gastroenterology & Hepatology 2021.
108. Din AU, Mazhar M, Waseem M et al. SARS-CoV-2 microbiome dysbiosis linked disorders and possible probiotic role. Biomedicine & Pharmacotherapy 2021; 133:110947.
109. Yeoh YK, Zuo T, Lui GC et al. Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. Gut 2021; 70:698-706.
110. Rosa DD, Dias MM, Grzeskowiak LM et al. Milk kefir: nutritional, micobiological and health benefits. Nutrition Research Reviews 2017; 30:82-96.
111. Kim DH, Jeong D, Kim H et al. Modern perspectives on the health benefits of kefir in next generation sequencing era: Improvement of the host gut microbiota. Critical Reviews in Food Science and Nutrition 2019; 59:1782-93.
112. Maggini S, Beveridge S, suter M. A combination of high-dose vitamin C plus zinc for the common cold. Journal of International Medical Research 2012; 40:28-42.
113. Colunga Biancatelli RM, Berrill M, Catravas JD et al. Quercetin and Vitamin C: experimental therapy for the prevention and treatment of SARS-CoV-2 via synergistic action. Front Immunol 2020.
114. Kyung Kim T, Lim HR, Byun JS. Vitamin C supplementaion reduces the odds of developing a common cold in Republic of Korea Army recruits: a randomised controlled trial. BMJ Mil Health 2020.
115. Colunga Biancatelli RM, Berrill M, Marik PE. The antiviral properties of vitamin C. Expert Rev Anti Infect Ther 2020; 18:99-101.
116. Hiedra R, Lo KB, Elbashabsheh M et al. The use of IV vitamin C for patients with COVID-19: a case series. Exp Rev Anti Infect Ther 2020.
117. Khaerunnisa S. Potential inhibitor of COVID-19 main protease (Mpro) from several medicinal plant compuns by molecular docking study. medRxiv 2020.
118. Chen L, Li J, Luo C et al. Binding interaction of quercetin-3-B-galactoside and its synthetic derivatives with SARS-CoV 3CL: structure-activity relationship reveal salient pharmacophore features. Bioorganic & Medicinal Chemistry Letters 2006; 14:8295-306.
119. Nain Z, Rana HK, Lio P et al. Pathogenic profiling of COVID-19 and SARS-like viruses. Briefings in Bioinformatics 2020.
120. Yi L, Li Z, Yuan K et al. Small molecules blocking the entry of severe respiratory syndrome coronavirus into host cells. J Virol 2020; 78:11334-39.
121. Shakoor H, Feehan J, Dhaheri AS et al. Immune-boosting role of vitamins D,C,E, zinc, selenium and omega-3 fatty acids: could they help against COVID-19. Maturitas 2020.
122. Calder PC. Nutrition, immunity and COVID-19. BMJ Nutrition, Prevenion & Health 2020; 3.
123. Abian O, Ortega-Alarcon D, Jimenez-Alesanco A et al. Structural stability of SARS-CoV-2 3CLpro and identification of quercetin as an inhibitor by experimental screening. International Journal of Biological Macromolecules 2020; 164:1693-703.

124. Hemila H, Carr A, Chalker E. Vitamin C may increase the recovery rate of outpatient cases of SARS-CoV-2 infection by 70%: reanalysis of the COVID A to Z randomized clinical trial. Research Square 2021.
125. Marik PE. Hydrocortisone, Ascorbic Acid and Thiamine (HAT therapy) for the treatment of sepsis. Focus on ascorbic acid. Nutrients 2018; 10:1762.
126. Marik PE. Vitamin C for the treatment of sepsis: The scientific rationale. Pharmacol Therapeut 2018; 189:63-70.
127. Chen L, Li J, Luo C et al. Binding interaction of quercetin-3-B-galactoside and its synthetic derivatives with SARS-CoV 3CLpro: Structure-activity relationship studies revela salient pharmacophore features. Bioorganic & Medicinal Chemistry 2020; 14:8295-306.
128. Ono K, Nakane H. Mechanisms of inhibition of various cellular DNA and RNA polymerases by several flavonoids. J Biochem 1990; 108:609-13.
129. Kaul TN, Middleton E, Pgra PL. Antiviral effects of flavonoids on human viruses. J Med Virol 1985; 15:71-79.
130. Shinozka K, Kikuchi Y, Nishino C et al. Inhibitory effect of flavonoids on DNA-dependent DNA and RNA polymerases. Experientia 1988; 44:882-85.
131. Martin JH, Crotty S, Warren P. Does an apple a day keep the doctor away because a phytoestrogen a day keeps the virus at bay? A review of the anti-viral properties of phytoestrogens. Phytochemistry 2007; 68:266-74.
132. Smith M, Smith JC. Repurposing therapeutics for COVID-19: Supercomputer-based docking to the SARS-CoV-2 viral spike protein and viral spike protein-human ACE2 interface. ChemRxiv 2020.
133. Leyva-Lopez N, Gutierrez-Grijalva EP, Ambriz-Perez D. Flavonoids as cytokine modulators: A possible therapy for inflammation-related diseases. Int J Mol Sci 2016; 17:921.
134. Nair MP, Kandaswami C, Mahajan S et al. The flavonoid, quercetin, differentially regulates Th-1 (INF) and Th-2 (IL4) cytokine gene expression by normal peripheral blood mononuclear cells. Biochimica et Biophysica Acta 2020; 1593:29-36.
135. Saeedi-Boroujeni A, Mahmoudian-Sani MR. Anti-inflammatory potential of Quercetin in COVID-19 treatment. J Inflamm 2021; 18:3.
136. Dabbagh-Bazarbachi H, Clergeaud G, Quesada IM et al. Zinc ionophore activity of Quercetin and Epigallocatechin-gallate:From Hepa 1-6 cells to a liposome model. J Agric Food Chem 2014; 62:8085-93.
137. Nieman DC, Simonson A, Sakaguchi CA et al. Acute Ingestion of a Mixed Flavonoid and Caffeine Supplement Increases Energy Expenditure and Fat Oxidation in Adult Women: A Randomized, Crossover Clinical Trial. Nutrients 2019; 11.
138. Nieman DC, Kay CD, Rathore AS et al. Increased Plasma Levels of Gut-Derived Phenolics Linked to Walking and Running Following Two Weeks of Flavonoid Supplementation. Nutrients 2018; 10.
139. Nieman DC, Ramamoorthy S, Kay CD et al. Influence of Ingesting a Flavonoid-Rich Supplement on the Metabolome and Concentration of Urine Phenolics in Overweight/Obese Women. Journal of Proteome Research 2017; 16:2924-35.
140. Cialdella-Kam L, Ghosh S, Meaney MP et al. Quercetin and Green Tea Extract Supplementation Downregulates Genes Related to Tissue Inflammatory Responses to a 12-Week High Fat-Diet in Mice. Nutrients 2017; 9.
141. Ohgitani E, Shin-Ya M, Ichitani M et al. Rapid inactivation in vitro of SARS-CoV-2 in saliva by black tea and green tea. bioRxiv 2021.
142. Giuliani C, Bucci I, Di Santo S et al. The flavonoid quercetin in hibits thyroid-restricted genes expression and thyroid function. Food and Chemical Toxicology 2014; 66:23-29.
143. de Souza dos Santos MC, Goncalves CF, Vaisman M et al. Impact of flavonoids on thyroid function. Food and Chemical Toxicology 2011; 49:2495-502.
144. Chandra AK, De N. Catechin induced modulation in the activities of thyroid hormone synthesizing enzymes leading to hypothyroidism. Mol Cell Biochem 2013; 374:37-48.
145. Pistollato F, Masias M, Agudo P et al. Effects of phytochemicals on thyroid function and their possible role in thyroid disease. Ann N Y Acad Sci 2019; 1433:3-9.
146. Sathyapalan T, Manuchehri AM, Thatcher NJ et al. The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: A randomized, double-blind, crossover study. J Clin Endocrinol Metab 2020; 96:1422-49.
147. Tonstad S, Jaceldo-Siegl K, Messina M et al. The association between soya consumption and serum thyroid-stimulating hormone in the Adventist Health Study-2. Public Health Nutr 2016; 19:1464-70.

148. Colombo D, Lunardon L, Bellia G. Cyclosporine and herbal supplement interactions. Journal of Toxicology 2014; 2014:145325.
149. Vogel-Gonzalez M, Tallo-Parra M, Herrera-Fernandez V et al. Low zinc levels at admission associates with poor clinical outcomes in SARS-CoV-2 infection. Nutrients 2021; 13:562.
150. te Velthuis AJ, van den Worm SH, Sims AC et al. Zn2+ inhibits Coronavirus and Arterivirus RNA polymerase activity In Vitro and Zinc ionophores block the replication of these viruses in cell culture. PLos Pathog 2010; 6:e1001176.
151. Gammoh NZ, Rink L. Zinc in Infection and Inflammation. Nutrients 2017; 9.
152. Hemila H. Zinc lozenges and the common cold: a meta-analysis comparing zinc acetate and zinc gluconate, and the role of zinc dosage. J Royal Soc Med Open 2017; 8:1-7.
153. Hoeger J, Simon TP, Beeker T et al. Persistent low serum zinc is associated with recurrent sepsis in critically ill patients - A pilot study. PloS ONE 2017; 12:e0176069.
154. Willis MS, Monaghan SA, Miller ML et al. Zinc-induced copper deficiency. A report of three cases initially recognized on bone marrow examination. Am J Clin Pathol 2005; 123:125-31.
155. Shakoor H, Freehan J, Mikkelsen K et al. Be well: A potential role for vitamin B in COVID-19. Maturitas 2020.
156. dos Santos LM. Can vitamin B12 be an adjuvant to COVID-19 treatment? GSC Biological and Pharmaceutical Sciences 2020; 11.
157. Kandeel M, Al-Nazawi M. Virtual screening and repurposing of FDA approved drugs against COVID-19 main protease. Life Sci 2020; 251:117627.
158. Tan CW, Ho LP, Kalimuddin S et al. Cohort study to evaluate effect of vitamin D, magnesium, and vitamin b12 in combination on severe outcome progression in older patients with coronavirus (COVID-19). Nutrition 2020; 80:111017.
159. Zhang P, Tsuchiya K, Kinoshita T et al. Vitamin B6 prevents IL-1B protein production by inhibiting NLRP3 inflammasome activation. J Biol Chem 2020; 291:24517-27.
160. Wimalawansa SJ. Effective and practical ways to overcome Vitamin D deficiency. J Family Med Community Health 2021; 8:1-8.
161. Gonen MS, Alaylioglu M, Durcan E et al. Rapid and effective vitamin D supplementation may present better clinical outcomes in COVID-19 (SARS-CoV-2) patients by altering serim INOS1, IL!B, INFg, cathelicidin-LL37 and ICAM1. Nutrients 2021; 13:4047.
162. Hashim HA, Maulood MF, rasheed AM et al. Controlled randomized clinical triaal on using Ivermectin with Doxycycline for treating COVID-19 patients in Bagdad, Iraq. medRxiv 2020.
163. Alam MT, Murshed R, Bhiuyan E et al. A case series of 100 COVID-19 positive patients treated with combination of Ivermectin and Doxycycline. Bangladesh Coll Phys Surg 2020; 38:10-15.
164. Chowdhury AT, Shahabz M, Karim MR et al. A randomized trial of ivermectin-doxycycline and hydrochloroquine-azithromycin therapy on COVID-19 patients. Research Square 2020.
165. Chamie J. Real-World evidence: The case of Peru, casuality between Ivermectin and COVID-19 infection fatality rate. ResearchGate 2020.
166. Caly L, Druce JD, Catton MG et al. The FDA-approved drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res 2020.
167. Lehrer S, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor-binding domain attached to ACE2. In Vivo 2020; 34:3023-26.
168. Maurya DK. A combination of Ivermectin and Doxycycline possibly blocks the viral entry and modulate the innate immune response in COVID-19 patients. ChemRxiv 2020.
169. Yang SN, Atkinson SC, Wang C et al. The broad spectrum antiviral ivermectin targets the host nuclear transport importin alpha/beta1 heterodimer. Antiviral Res 2020; 177:104760.
170. Dayer MR. Coronavirus (2019-nCoV) deactivation via spike glycoprotein shielding by old drugs, bioinformatic study. Preprints 2020.
171. Swargiary A. Ivermectin as a promising RNA-dependent RNA polymerase inhibitor and a therapeutic drug against SARS-CoV2: Evidence from silico studies. Research Square 2020.
172. Kalfas S, Visvanathan K, Chan K et al. The therapeutic potential of ivermectin for COVID-19: A systematic review of mechanisms and evidence. medRxiv 2020.
173. Chamie-Quintero JJ, Hibberd JA, Scheim DE. Ivermectin for COVID-19 in Peru: 14-fold reduction in nationwide excess deaths, p=0.002 for effect by state, then 13-fold increase after ivermectin use restricted. medRxiv 2021.

174. Wehbe Z, Wehbe M, Iratni R et al. Repurposing Ivermectin for COVID-19: Molecular aspects and therapeutic possibilities. Front Immunol 2021; 12:663586.
175. Hazan S, Dave S, Gunaratne AW et al. Effectiveness of ivermectin-based multidrug therrapy in severe hypoxic ambulatory COVID-19 patients. medRxiv 2021.
176. Bryant A, Lawrie TA, Dowswell T et al. Ivermectin for the prevention and treatment of COVID-19 infection: a systematic review and meta-analysis. Lancet 2021.
177. Hill A, Garratt A, Levi J et al. Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection. Open Forum Infectious Diseases 2021.
178. Rossignol JF, Bardin MC, Oaks JB et al. Early treatment with nitazoxanide prevents worsening of mild and moderate COVID-19 and subsequent hospitalization. medRxiv 2021.
179. Cadegiani FA, Goren A, Wambier CG et al. Early COVID-19 therapy with azithromycin plus nitazoxanide, ivermectin or hydroxychloroquine in outpatient settings significantly reduced symptoms compared to known outcomes in untreated patients. New Microbes and New Infections 2021; 43:100915.
180. Elalfy H, Besheer T, El-Mesery A et al. Effect of a combination of nitazoxanide, ribavirin, and ivermectin plus zinc supplement (MANS.NRIZ study) on the clearance of mild COVID-19. J Med Virol 2021; 93:3176-83.
181. Hong SK, Kim HJ, Song CS et al. Nitazoxanide suppresses IL-6 production in LPS-stimulated mouse macrophages and TG-injected mice. International Immunopharmacology 2012; 13:23-27.
182. Rossignol JF. Nitazoxanide: A first-in-class broad-spectrum antiviral agent. Antiviral Res 2014; 110:94-103.
183. Padmanabhan S, Padmanabhan K. The devil is in the dosing- targeting the interferon pathway by repositioning Nitazoxanide against COVID-19. Research Square 2021.
184. Cao J, Forrest CJ, Zhang X. A screen of the NIH clinical collection small molecule library identifies potential anti-coronavirus drugs. Antiviral Res 2015; 114:1-10.
185. Rossignol JF. Nitazoxanide, a new drug candidate for the treatment of Middle East respiratory syndrome coronavirus. Journal of Infection and Public Health 2016; 9:227-30.
186. Piacentini S, La Frazia S, Riccio A et al. Nitazoxanide inhibits paramyxovirus replication by targeting the Fusion protein folding: role of glycoprotein-specific thiol oxireductase ERp57. Scientific Reports 2018; 8:10425.
187. Merchant HA. CoViD-19: An early intervention therapeutic strategy to prevent developing a severe disease as an alternative approach to control the pandemic. medRxiv 2021.
188. da Silva JK, Figueirdo PL, Byler KG et al. Essential oils as antiviral agents, potential of essential oils to treat SARS-CoV-2 infection: an In-Silico investigation. Int J Mol Sci 2020; 21:3426.
189. Seet RC, Quek AM, Ooi DS et al. Positive impact of oral hydroxychloroquine and povidone-iodine throat spray for COVID-19 prophylaxis: an open-label randomized trial. Int J Infect DIs 2021.
190. Vergara-Buenaventura A, Castro-ruiz C. Use of mouthwashes against COVID-19 in dentistry. British Journal of Oral and Maxillofacial Surgery 2020; 58:924-27.
191. Baxter AL, Schwartz KR, Johnson RW et al. Rapid initiation of nasal saline irrigation: hospitalizations in COVID-19 patients randomized to alkalinization or povidone-iodine compared to a national dataset. medRxiv 2021.
192. Seneviratne CJ, Balan P, Ki KK et al. Efficacy of commercial mouth-rinses on SARS-CoV-2 viral load in saliva: Randomized controlled trial in Singapore. Infection 2020; 49:305-11.
193. Frank S, Brown SM, Capriotti JA et al. In vitro efficacy of a providone-iodine nasal antiseptic for rapid inactivation of SARS-CoV-2. JAMA Otolaryngol Head Neck Surg 2020; 146:1054-58.
194. Burton MJ, Clarkson JE, Goulao B et al. Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients withou suspected or conformed COVID-19 infection (Review). Cochrane Database of Syst Rev 2020; 9:CD013628.
195. Meister TL, Briggemann Y, Todt D et al. Virucidal efficacy of different oral rinses against severe acute respiratory syndrome coronavirus 2. J Infect Dis 2020; 222:1289-92.
196. Shiraishi T, Nakagawa Y. Evaluation of the bactericidal activity of povidone-iodine and commercially available gargle preparations. Dermatology 2002; 204 (suppl 1):37-41.
197. Teng F, He T, Huang S et al. Cetylpyridinium chloride mouth rinses alleviate experimental gingivitis by inhibiting dental plaque maturation. Journal of Oral Science 2016; 8:182-90.
198. Rosing CK, Cavagni J, Gaio EJ et al. Efficacy of two mouthwashes with cetylpyridinium chloride: a controlled randomized clinical trial. Braz Oral res 2017; 31:e47.

199. Green A, Roberts G, Tobery T et al. In vitro assessment of the virucidal activity of four mouthwashes containing Cetyylpyridinium Chloride, ethanol, zinc and a mix of enzymes and proteins against human coronavirus. bioRxiv 2021.
200. Choudhury IM, Shabnam N, Ahsan T et al. Effect of 1% povidone iodine mouthwash/gargle, nasal and eye drop in COVID-19 patient. Bioresearch Communications 2021; 7.
201. Ader AW, Paul TL, Reinhardt W et al. Effect of mouth rinsing with two polyvinylpyrrolidine-iodine mixtures on iodine absorption and thyroid function. J Clin Endocrinol Metab 2021; 66:632-35.
202. Bianconi V, Violi F, Fallarino F et al. Is acetylsalicylic acid a safe and potentially useful choice for adult patients with COVID-19? Drugs 2020.
203. Muller C, Karl N, Ziebuhr J et al. D,L-lysine acetylsalicylate + glycine impairs coronavirus replication. J Antivir Antiretovir 2020.
204. Draghici S, Nguyen TM, Sonna LA et al. COVID-19: disease pathways and gene expression chnages predict methylprednisolone can improve outcome in severe cases. Bioinformatics 2020.
205. Varatharajah N. COVID-19 CLOT: What is it? Why in the lungs? Extracellular histone, "auto-activation" of prothrombin, emperipolesis, megakaryocytes, "self-association" of Von Willebrand factor and beyond. Preprints 2020.
206. Cloutier N, Allaeys I, Marcoux G et al. Platelets release pathogenic serotonin and return to circulation after immune complex-mediated sequestration. PNAS 2018;E1550-E1559.
207. Hottz ED, Azevedo-Quintanilha Ig, Palhinha L et al. Platelet activation and platelet-monocyte aggregate formation trigger tissue factor expression in patients with severe COVID-19. Blood 2020; 136:1330-1341.
208. Early high-dose vitamin D3 for critically ill, vitamin D-deficient patients. N Engl J Med 2019; 381:2529-40.
209. Amrein K, Martucci G, McNAlly JD. When not to use meta-analysis: Analysing the meta-analysis on vitamin D in critical care. Clin Nutr 2017; 36:1729-30.
210. Wessel, L. "its a nightmare". How Brazilian scientists became ensnared in chloroquine politics. Researchers accused of killing patients after using a high dose to treat coronavirus infections. https://www.science.org/content/article/it-s-nightmare-how-brazilian-scientists-became-ensnared-chloroquine-politics . 2020. Science. 10-20-0021.
211. Luks AM, Swenson ER. Pulse oximetry for monitoring patients with COVID-19 at home: Potential pitfalls and practical guidance. Ann Thorac Med 2020.
212. Jouffroy R, Jost D, Prunet B. Prehospital pulse oximetry: a red flag for early detection of silent hypoxemia in COVID-19 patients. Crit Care 2020; 24:313.
213. Lucas JM, Heinlein C, Kim T et al. The androgen-regulated protease TMPRSS2 activates a proteolytic cascade involving components of the tumor microenvironment and promotes prostate cancer metastasis. Cancer Discov 2020; 4:1310-1325.
214. Marik PE, DePerrior SE, Ahmad Q et al. Gender-based disparities in COVID-19 patient outcomes. Journal of Investigative Medicine 2021; 69:814-18.
215. Liadet L, Szabo C. Blocking mineralocorticoid receptor with spironolactone may have a wide range of therapeutic actions in severe COVID-19 disease. Crit Care 2020; 24:318.
216. Kotfis K, Lechowicz K, Drozdzal S et al. COVID-19-The potential beneficial therapeutic effects of spironolactone during SARS-CoV-2 infection. Pharmaceuticals 2021; 14:71.
217. Cadegiani FA, Wambier CG, Goren A. Spironolactone: An anti-androgenic and anti-hypertensive drug that may provide protection against the novel Coronavirus (SARS-CoV-2) induced acute respiratory distress syndrome (ARDS) in COVID-19. Fronteirs in Medicine 2020; 7:453.
218. Cadegiani FA, Goren A, Wambier CG. Spironolactone may provide protection from SARA-CoV-2: Targeting androgens, angiotensin converting enzyme 2 (ACE2), and renin-angiotensin-aldosterone system (RAAS). Medical Hypotheses 2020; 143:110112.
219. Cadegiani FA, McCoy J, Zimerman A et al. Efficacy of proxalutamide in hospitalized COVID-19 patients: A randomized, double-blind, placebo-controlled, parallel-design clinical trial. medRxiv 2021.
220. Wambier CG, de Pina Almeida Prado Junior B, Pereira CS et al. Brazilian blood donation eligibility criteria for dermatologic patients. An Bras Dermatol 2021; 87:590-595.
221. Zarehoseinzade E, Allami A, Ahmadi M et al. Finasteride in hospitalized adult males with COVID-19: A risk factor for severity of the disease or an adjunct treatment: A randomized controlled clinical trial. Medical Journal of the Islamic Republic of Iran 2021; 35:30.
222. Samuel RM, Majd H, Richter MN et al. Androgen signaling regulates SARS-CoV-2 receptor levels and is associated with severe COVID-19 symptoms in men. Cell Stem Cell 2020; 27:876-89.

223. Cadegiani FA, McCoy J, Wambier CG et al. Early antiandrogen therapy with dutasteride reduces viral shedding, inflammatory responses, and time-to remission in males with COVID-19: A randomized, double-blind, placebo-controlled interventional trial (EAT-DUTA AndroCoV Trial- Biochemical). Cureus 2021.
224. McCoy J, Goren A, Cadegiani FA et al. Proxalutamide reduces the rates of hospitalization for COVID-19 male outpatients: A randomized double-blinded placebo-controlled trial. Front Med 2021; 8:668698.
225. Wambier CG, Lin EM, Cadegiani FA et al. Accelerated viral clearance and symptom resolution in symptomatic COVID-19 outpatients treated with antiandrogens. medRxiv 2021.
226. Cadegiani FA, Goren A, Wambier CG et al. An open-label prospective observational study of antiandrogen and non-antiandrogen early pharmacological approaches in females with mild-to-moderate COVID-19. The PreAndroCoV Female trial. medRxiv 2021.
227. McCoy J, Cadegiani FA, Wambler CG et al. 5-alpha-reductase inhibitors are associated with reduced frequency of COVID-19 symptoms in males with androgenic alopecia. JEADV 2021; 35:e243-e246.
228. Goren A, Wambler CG, Herrera S et al. Anti-androgens may protect against severe COVID-19 outcomes: results form a prospective cohort of 77 hospitalized men. JEADV 2021; 35:e13-e15.
229. van Zuuren EJ, Fedorowicz Z, Schoones J. Interventions for female pattern hair loss (Review). Cochrane Database of Syst Rev 2016; 5:CD007628.
230. Seale LR, Eglini AN, McMichael AJ. Side effects related to 5 alpha-reductase inhibitor treatment of hair loss in women: A review. J Drugs Dermatol 2016; 15:414-19.
231. Lenze EJ, Mattar C, Zorumski CF et al. Fluvoxamine vs placebo and clinical deterioration in outpatietns with symptomatic COVID-19. A randomized clinical trial. JAMA 2020.
232. Seftel D, Boulware DR. Prospective cohort of fluvoxamine for early treatment of COVID-19. Open Forum Infectious Diseases 2021.
233. Hamed MG, Hagaga RS. The possible immunoreulatory and anti-inflammatory effects of selective serotonin reuptake inhibitors in coronavirus disease patients. Medical Hypotheses 2020; 144:110140.
234. Hoertel N, Sanchez-Rico M, Vernet R et al. Association between antidepressant use and reduced risk of intubation or death in hospitalized patients with COVId-19: results from an observational study. Molecular Psychiatry 2021.
235. Zimering MB, Razzaki T, Tsang T et al. Inverse association between serotonin 2A receptor antagonist medication use and mortality in severe COVID-19 infection. Endocrinol Diabetes Metab J 2020; 4:1-5.
236. Reis G, Moreira-Silva EA, Silva DC et al. Effect of early treatment with fluvoxamine on risk of emergency care and hospitalization among patients with COVID-19: the TOGETHER randomized, platform clinical trial. Lancet Glob Health 2021.
237. Calusic M, Marcec R, Luksa L et al. Safety and efficacy of fluvoxamine in COVID-19 ICU patients: an open label, prospective cohort trial with matched controls. Br J Clin Pharmacol 2021.
238. Lee TC, Vigod S, Hanula R et al. Fluvoxamine for outpatient COVID-19 to prevent hospitalization: A systematic review and meta-analysis. medRxiv 2021.
239. Sukhatme VP, Reiersen AM, Vayttaden SJ et al. Fluvoxamine: A review of its mechanism of action and its role in COVID-19. Fronteirs in Pharmacology 2021; 12:652688.
240. Hartter S, Wang X, Weigmann H et al. Differential effects of fluvoxamine and other antidepressants on the biotransformation of melatonin. J Clin Psychopharmacology 2021; 21:167-74.
241. Maurer-Spurej E, Pittendreigh C, Solomons K. The influence of selective serotonin reuptake inhibitors on human platelet serotonin. Thromb Haemost 2004; 91:119-28.
242. Bismuth-Evenzal Y, Gonopolsky Y, gurwitz D et al. Decreased serotonin content and reduced agonist-induced aggregation in platelets of chronically medicated with SSRI drugs. Journal of Affective Disorders 2012; 136:99-103.
243. Javors MA, Houston JP, Tekell JL et al. Reduction of platelet serotonin content in depressed patients treated with either paroxetine or desipramine. International Journal of Neuropsychopharmacology 2000; 3:229-35.
244. Hoertel N. Do the selective serotonin reuptake inhibitor antidepressants fluoxetine and fluvoxamine reduce mortality among patients with COVID-19? JAMA Network Open 2021; 4:e2136510.
245. Oskotsky T, Maric I, Tang A et al. Mortality risk among patients with COVID-19 prescribed selective serotonin reuptake inhibitor antidepressants. JAMA Network Open 2021; 4:e2133090.
246. Ishima T, Fujita Y, Hashimoto K. Interaction of new antidepressants with sigma-1 receptor chaperones and their potentiation of neurite outgrowth in PC12 cells. Eur J Pharmacol 2014; 727:167-73.

247. Weinreich DM, Sivapalasingam S, Norton T et al. REGEN-CoV antibody cocktail clinical outcomes study in Covid-19 outpatients. N Engl J Med 2021.
248. Verderese JP, Stepanova M, Lam B et al. Neutralizing monoclonal antibody treatment reduces hospitalization for mild and moderate coronavirus disease 2019 (COVID-19): A real-world experience. Clin Infect Dis 2021.
249. Kreuzberger N, Hirsch C, Chai KL et al. SARS-CoV-2-neutralising monoclonal antibodies for treatment of COVID-19. Cochrane Database of Syst Rev 2021;CD013825.
250. Gupta A, Gonzalez-Rojas Y, oya J et al. Early treatment for COVID-19 with SARS-CoV-2 neutralizing antibody Sotrovimab. N Engl J Med 2021; 385:1941-50.
251. Gutierrez S, Svahn SL, Johansson ME. Effects of omega-3 fatty acids on immune cells. Int J Mol Sci 2019; 20:5028.
252. Titos E, Rius B, Gonzalez-Periz A et al. Resolvin D1 and its precursor docosahexaenoic acid promote resolution of adipose tissue inflammation by eliciting macrophage polarization toward an M2-like phenotype. J Immunol 2021; 187:5408-18.
253. Yoshihara T, Shimada K, Fukao K et al. Omega 3 polyunsaturated fatyy acids suppress the development of aortic aneurysms through the inhibition of macrophage-mediated inflammation. Circ J 2015; 79:1470-1478.
254. Hammock BD, Wang W, Gilligan MM et al. Eicosanoids. The overlooked storm in Coronavirus Disease 2019 (COVID-19)? Am J Pathol 2020.
255. Das UN. Can bioactive lipids inactivate coronavirus (COVID-19)? Arch Med Res 2020; 51:282-86.
256. Lee CR, Zeldin DC. Resolvin infectious inflammation by targeting the host response. N Engl J Med 2015; 373:2183-85.
257. Serhan CN. Novel pro-resolving lipid mediators in inflammation are leads for resolution physiology. Nature 2014; 510:92-101.
258. Law HK, Cheng CY, Ng HY et al. Chemokine up-regulation in SARS-coronavirus-infected, monocyte-derived human dendritic cells. Blood 2005; 105:2366-74.
259. Baranova A, Cao H, Zhang F. Unraveling risk genes of COVID-19 by multi-omics integrative analysis. Fronteirs in Medicine 2021.
260. Li S, Jiang L, Li X et al. Clinical and pathological investigation of patients with severe COVID-19. JCI Insight 2020; 5:e138070.
261. Yang B, Fulcher JA, Ahn J et al. Clinical characteristics and outcomes of COVID-19 patients receiving compassionate use Leronlimab. Clin Infect Dis 2021.
262. Patterson BK, seethamraju H, Dhody K et al. Disruption of the CCL5/RANTES-CCR5 pathway restores immune homeostasis and reduces plasma viral load in critical COVID-19. medRxiv 2020.
263. Patterson BK, seethamraju H, Dhody K et al. CCR5 inhibition in critical COVID-19 patients decreases inflammatory cytokines, increases CD8 T-cells, and deceases SARS-CoV2 RNA in plasma by day 14. International Journal of Infectious Diseases 2021; 103:25-32.
264. Gulick RM, Fatkenheuer G, Burnside R et al. Five-year safety evaluation of Maraviroc in HIV-1-infected treatment-experienced patients. J Acquir Immune Defic Syndr 2014; 65:78-81.
265. Ayoub A, Alston S, Goodrich J et al. Hepatic safety and tolerability in the maraviroc clinical development program. AIDS 2010; 24:2743-55.
266. Giaquinto C, Mawela MP, Chokephaibutkit K et al. Pharmacokinetics, safety and efficacy of Maraviroc in treatment-experienced pediatric patients infected with CCR5=tropic HIV-1. Pediatr Infect Dis 2018; 37:459-65.
267. Idelsis Esquivel-Moynelo I, Perez-Escribano J, Duncan-Roberts Y et al. Effect of combination of interferon alpha-2b and interferon-gamma or interferon alpha 2b alone for elimination of SARS-CoV-2 viral RNA. Preliminary results of a randomized controlled clinical trial. medRxiv 2020.
268. Davoudi-Monfarad E, Rahmani H, Khalili H et al. Efficacy and safety of interferon B-1a in treatment of severe COVID-19: A randomized clinical trial. medRxiv 2020.
269. Wang N, Zhan Y, Zhu L et al. Retrospective multicenter cohort study shows early interferon therapy is associated with favorable clinical responses in COVID-19 patients. Cell Host & Microbe 2020;ePub.
270. Meng Z, Wang T, Chen L et al. An experimental trial of recombinant human interferon alpha nasal drops to prevent COVID-19 in medical staff in an epidemic area. medRxiv 2020.
271. Feld JJ, Kandel C, Biondi MJ et al. Peginterferon lamda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial. Lancet Resp Med 2021.

272. Berg K, Bolt G, Andersen H et al. Zinc potentiates the antiviral action of human IFN-alpha tenfold. J Interferon Cytokine Res 2001; 21:471-74.
273. Cakman I, Kirchner H, Rink L. Zinc supplementation reconstitutes the production of interferon-alpha by leukocytes from elderly persons. J Interferon Cytokine Res 1997; 17:469-72.
274. Puskarich MA, Ingraham NE, Merck LH et al. Effect of losartan on hospitalized patients with COVID-19-induced lung injury: A randomized clinical trial. medRxiv 2021.
275. Duarte M, Pelorosso F, Nicolosi L et al. Telmisartan for treatment of COVID-19 patients: an open multicenter randomized clinical trial. EClinicalMedicine 2021; 37:100962.
276. Yu LM, Bafadhel M, Doeward J et al. Inhaled budesonide for COVID-19 in people at higher risk of adverse outcomes in the community: interim analyes from the PRINCIPLE trial. Lancet 2021; 398:843-55.
277. Ramakrishnan S, Nicolau DV, Langford B et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. Lancet Resp Med 2021.
278. Schultze A, Walker AJ, MacKenna B et al. Inhaled corticosteroids use and the risk of COVID-19 related death among 966,461 patients with COPD or asthma: An OpenSAFELY analysis. medRxiv 2020.
279. Aveyard P, Gao M, Lindson N et al. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. Lancet Resp Med 2021.
280. Clemency BM, Varughese R, Morse CG et al. Efficacy of inhaled ciclesonide for outpatient treatment of adolescents and adults with symptomatic COVID-19. A randomized clinical trial. JAMA Intern Med 2021.
281. Tardif JC, Bouabdallaoui N, L'Allier PL et al. Efficacy of colchicine in non-hospitalized patients with COVID-19. Lancet Resp Med 2021.
282. Finkelstein Y, Aks SE, Hutson JR et al. Colchicine poisoning: the dark side of an acient drug. Clinical Toxicology 2010; 48:407-14.
283. Effect of Dexamethasone in hospitalized patients with COVID-19-Preliminary report. N Engl J Med 2020.
284. Azithromycin in hospitalized patients with COVID-19 (RECOVERY) a randomised, controlled, open-label, platform trial. medRxiv 2020.
285. Rosenthal N, Zhun Cao Z, Gundrum J et al. Risk factors associated with in-hospital mortality in a US National Sample of patients with COVID-19. JAMA Network Open 2020; 3:e2029058.
286. Butler CC, Yu LM, Dorward J et al. Doxycycline for community treatment of suspected COVID-19 in people at high risk of adverse outcomes in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. Lancet Resp Med 2021.
287. Zhang X, Song Y, Ci X et al. Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. Inflamm Res 2008; 57:524-29.
288. Ci X, Li H, Yu Q et al. Avermectin exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen activated protein kinase pathway. Fundamental & Clinical Pharmacology 2009; 23:449-55.
289. DiNicolantonio JJ, Barroso-Arranda J, McCarty M. Ivermectin may be a clinically useful anti-inflammatory agent for late-stage COVID-19. Open Heart 2020; 7:e001350.
290. DiNicolantonio JJ, Barroso-Aranda J, McCarty MF. Anti-inflammatory activity of ivermectin in late-stage COVID-19 may reflect activation of systemic glycine receptors. Open Heart 2021; 8:e001655.
291. Blum VF, Cimerman S, Huneter JR et al. Nitazoxanide superioroty to placebo to treat moderate COVID-19 - A pilot prove of concept randomized double-blind clinical trial. EClinicalMedicine 2021; 37:100981.
292. Villar J, Confalonieri M, Pastores SM et al. Rationale for prolonged corticosteroid tratment in the acute respiratory distress syndrome (ARDS) caused by COVID-19. Crit Care Expl 2020; 2:e0111.
293. Fadel R, Morrison AR, Vahia A et al. Early course corticosteroids in hospitalized patients with COVID-19. Clin Infect Dis 2020; 71:2114-20.
294. Chroboczek T, Lacoste M, Wackenheim C et al. Beneficial effect of corticosteroids in severe COVID-19 pneumonia: a propensity score matching analysis. medRxiv 2020.
295. Wu C, Chen X, Cai Y et al. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus disease 2019 pneumonia in Wuhan,China. JAMA Intern Med 2020.
296. Cruz AF, Ruiz-Antoran B, Gomez AM et al. Impact of glucocorticoid treatment in SARS-CoV-2 infection mortality: A retrospective controlled cohort study. medRxiv 2020.
297. Liu J, Zheng X, Huang Y et al. Successful use of methylprednisolone for treating severe COVID-19. J Allergy Clin Immunol 2020.

298. Meduri GU, Bridges L, Shih MC et al. Prolonged glucocorticoid treatment is associated with improved ARDS outomces: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature. Intensive Care Med 2016; 42:829-40.
299. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19. A meta-analysis. JAMA 2020.
300. Ruiz-Irastorza G, Pijoan JI, Bereciatua E et al. Second week methyl-prednisolone pulses improve prognosis in patients with severe coronavirus disease 2019 pneumonia: An observational comparative study using routine care data. medRxiv 2020.
301. Tomazini BM, Maia IS, Cavalcanti AB et al. Effect of dexamethasone on days alive and ventilaor-free in patients with moderate or severe acute respiratory distress syndrome and COVID-19. The CoDEX randomized clinical trial. JAMA 2020; 324:1307-16.
302. Edalatifard M, Akhtari M, Salehi M et al. Intravenous methylprednisolone pulse as a treatment for hospitalized severe COVID-19 patients: results from a randomised controlled clinical trial. Eur Respir J 2020.
303. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19. The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial. JAMA 2020.
304. Dequin PF, Heming N, Meziani F et al. Effect of hydrocortisone on 21-day mortality or respiratory support among critically ill patients with COVID-19. A randomized Clinical trial. JAMA 2020.
305. Therapeutic anticoagulation with heparin in noncritically ill patients with Covid-19. N Engl J Med 2021; 389:790-802.
306. Heaney RP, Armas LA, Shary JR et al. 25-hydroxylation of vitamin D3: relation to circulating vitamin D3 under various input conditions. Am J Clin Nutr 2008; 87:1738-42.
307. Barrett TJ, Lee AH, Xia Y et al. Platelet and vascular biomarkers associate with thrombosis and death in coronavirus disease. Circulation Research 2020; 127:945-47.
308. Zhang S, Liu Y, Wang X et al. SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. Journal of hematology & oncology 2020; 13:120.
309. Kauerova S, Bartuskova H, Muffova B et al. Statins directly influence the polarization of adipose tissue macrophages: A role in chronic inflammation. Biomedicines 2021; 9:211.
310. van der Meij E, Koning GG, Vriens PW et al. A clinical evaluation of statin pleiotrophy: Statins selectively and dose-dependently reduce vascular inflammation. PloS ONE 2013; 8:e53882.
311. Calfee CS, Delucchi KL, Sinha P et al. Acute respiratory distress syndrome subphenotypes and differential response to simvastatin: secondary analysis of a randomised controlled trial. Lancet Resp Med 2018; 6:691-98.
312. Zhang XJ, Qin JJ, Cheng X et al. In-hospital use of statins is associated with a reduced risk of mortality among individuals with COVID-19. Cell Metabolism 2020.
313. Rodriguez-Nava G, Trelles-Garcia DP, Yanez-Bello MA et al. Atorvastatin associated with decreased hazard for death in COVID-19 patients admitted to an ICU: a retrospective cohort study. Crit Care 2020; 24:429.
314. Gupta A, Madhavan MV, Poterucha TJ et al. Association between antecedent statin use and decreased mortality in hospitalized patients with COVID-19. Research Square 2020.
315. Kow CS, Hasan SS. Meta-analysis of effectiveness of statins in patients with severe COVID-19. Am J Cardiol 2020.
316. Tan WY, Young BE, Lye DC et al. Statin use is assocaited with lower disease severity in COVID-19 infection. Nature Research 2020.
317. Spinelli FR, Conti F, Gadina M. HiJAKing SARS-C0V-2? The potential role of JAK inhibitors in the management of COVID-19. Sci Immunol 2020; 5:eabc5367.
318. Chen CX, Wang JJ, Li H et al. JAK-inhibitors for coronavirus disease-2019 (COVID): a meta-analysis. Leukemia 2021.
319. Marconi VC, Ramanan AV, de Bono S et al. Efficacy and safety of baricitinib for the treament of hospitalized adults with COVID-19 (COV-BARRIER): a randomised, double-blind,parallel-group, placebo-controlled phase 3 trial. Lancet Resp Med 2021.
320. Jalali F, Rezaie S, Rola P et al. COVID-19 pathophysiology: Are platelets and serotonin hiding in plain sight? ssrn 2021.
321. Lin OA, Karim ZA, Vemana HP et al. The antidepressant 5-HT2a receptor antagonists Pizotifen and cyproheptadine inhibit serotonin-enhanced platelet function. PloS ONE 2014; 9:e87026.

322. Zaid Y, Guessous F, Puhm F et al. Platelet reactivity to thrombin differs between patients with COVID-19 and those with ARDS unrelated to COVID-19. Blood Advances 2021; 5:635-39.
323. Zaid Y, Puhm F, Allaeys I et al. Platelets can associate with SARS-CoV-2 RNA and are hyperactivated in COVID-19. Circ Res 2020; 127:1404-18.
324. Dawson C, Christensen CW, Rickaby DA et al. Lung damage and pulmonary uptake of serotonin in intact dogs. J Appl Physiol 1985; 58:1761-66.
325. MacLean MR, Herve P, Eddahibi S et al. 5-hydroxytryptamine and the pulmonary circulation: receptors, transporters and the relevance to pulmonary arterial hypertension. Br J Pharmacol 2000; 131:161-68.
326. Blackshear JL, Orlandi C, Hollenberg NK. Constrictive effect of serotonin on visible renal arteries: a pharmacoangiographic study in anesthetized dogs. J Cardiovasc Pharmacol 1991; 17:68-73.
327. Watchorn J, Hang DY, Joslin J et al. Critically ill COVID-19 patients with acute kidney injury have reduced renal blood flow and perfusion despite preserved cardiac function: A case-control study using contrast enhanced ultrasound. Lancet Resp Med 2021.
328. McGoon MD, Vanhoutte PM. Aggregating platelets contract isolated canine pulmonary arteries by releasing 5-hydroxytryptamine. J Clin Invest 1984; 74:823-33.
329. Almqvist P, Skudder P, Kuenzig M et al. Effect of cyproheptadine on endotoxin-induced pulmonary platelet trapping. Am Surg 1984; 50:503-5.
330. Skurikhin EG, Andreeva TV, Khnelevskaya ES et al. Effect of antiserotonin drug on the development of lung fibrosis and blood system reactions after intratracheal administration of bleomycin. Bull Exp Biol Med 2012; 152:519-23.
331. Doaei S, Gholami S, Rastgoo S et al. The effect of omega-3 fatty acid supplementation on clinical and biochemical parameters of critically ill patients with COVID-19: a randomized clinical trial. J Transl Med 2021; 19:128.
332. Pan H, Peto R, Karim QA et al. Repurposed antiviral drugs for COVID-19 - interim WHO SOLIDARITY trial. medrx 2020.
333. Ohl ME, Miller DR, Lund BC et al. Association of remdesivir treatment with survival and length of hospital stay among US veterans hospitalized with COVID-19. JAMA Network Open 2021; 4:e2114741.
334. Ader F, Hites M, Poissy J et al. Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial. Lancet Infect Dis 2021.
335. Marik PE, Kory P, Varon J et al. MATH+ protocol for the treatment of SARS-CoV-2 infection: the scientific rationale. Exp Rev Anti Infect Ther 2020.
336. Kory P, Meduri GU, Iglesias J et al. Clinical and scientific rationale for the "MATH+" hospital treatment protocol for COVID-19. J Intensive Care Med 2020.
337. Ranjbar K, Shahriarad R, erfani A et al. Methylprednisolone or dexamethasone, which one is the superior corticosteroid in the treatment of hospitalized COVID-19 patients: A triple-blinded randomized controlled trial. BMC Infect Dis 2021; 21:337.
338. Ko JJ, Wu C, Mehta N et al. A comparison of methylprednisolone and dexamethasone in intensive care patients with COVID-19. medRxiv 2021.
339. Fowler AA, Truwit JD, Hite D et al. Vitamin C Infusion for TReatment In Sepsis-Induced Acute Lung Injury-CITRIS-ALI: A Randomized, Placebo Controlled Clinical Trial. JAMA 2018; 322:1261-70.
340. Marik PE, Khangoora V, Rivera R et al. Hydrocortisone, Vitamin C and Thiamine for the treatment of severe sepsis and septic shock: A retrospective before-after study. Chest 2017; 151:1229-38.
341. Barabutis N, Khangoora V, Marik PE et al. Hydrocortisone and Ascorbic Acid synergistically protect and repair lipopolysaccharide-induced pulmonary endothelial barrier dysfunction. Chest 2017; 152:954-62.
342. Cheng RZ. Can early and high-dose vitamin C prevent and treat coronavirus disease 2019 (COVID-19). Medicine in Drug Discovery 2020.
343. Wang Y, Lin H, Lin BW et al. Effects of different ascorbic acid doses on the mortality of critically ill patients: a meta-analysis. Ann Intensive Care 2019; 9:58.
344. Boretti A, Banik BK. Intravenous vitamin C for reduction of cytokines storm in acute respiratory distress syndrome. PharmaNutrition 2020; 12:100190.
345. Iglesias J, Vassallo AV, Patel V et al. Outcomes of metabolic resuscitation using ascorbic acid, thiamine, and glucocorticoids in the early treatment of sepsis. Chest 2020; 158:164-73.
346. de Melo AF, Homem-de-Mello M. High-dose intravenous vitamin C may help in cytokine storm in severe SARS-CoV-2 infection. Crit Care 2020; 24:500.

347. Zhang J, Rao X, Li Y et al. High-dose vitamin C infusion for the treatment of critically ill COVID-19. Research Square 2020.
348. Kumari P, Dembra S, Dembra P et al. The role of vitamin C as adjuvant therapy in COVID-19. Cureus 2020; 12:e11779.
349. Al Sulaiman K, Al Juhani O, Badreldin HA et al. Adjunctive therapy with ascorbic in critically ill patients with COVID-19: A multicenter propensity score matched study. Crit Care 2021.
350. Lankadeva YR, Peiris RM, Okazaki N et al. Reversal of the pathophysiological responses to Gram-negative sepsis by megadose Vitamin C. Crit Care Med 2020.
351. Zhang J, Rao X, Li Y et al. Pilot trial of high-dose vitamin C in critically ill COVID-19 patients. Ann Intenisve Care 2020.
352. Lavinio A, Ercole A, Battaglini D et al. Safety profile of enhanced thromboprophylaxis strategies for critically ill COVID-19 patients during the first wave of the pandemic: observational report from 28 European intensive care units. Crit Care 2021; 25:155.
353. Patterson G, Isales CM, Fulzele S. Low level of vitamin C and dysregulation of vitamin C transporter might be involved in the severity of COVID-19 infection. Aging and Disease 2020; 12.
354. Tomassa-Irriguible TM, Lielsa-Berrocal L. COVID-19: Up to 87% critically ill patients had low vitamin C values. Research Square 2020.
355. Arvinte C, Singh M, Marik PE. Serum levels of vitamin C and vitamin D in a cohort of critically ill COVID-19 patients of a North American Community Hospital Intensive Care Unit in May 2020. A pilot study. Medicine in Drug Discovery 2020; 8:100064.
356. Lopes RD, Furtado RH, Bronhara B et al. Therapeutic versus prophylactic anticoagulation for patients admitted to hospital with COVID-19 and elevated D-dimer concentraion (ACTION): an open-label, multicentre, randomised, controlled trial. Lancet 2021; 397:2253-63.
357. Murshed MR, Bhiuyan E, Saber S et al. A case series of 100 COVID-19 positive patients treated with combination of Ivermectin and Doxycycline. Bangladesh Coll Phys Surg 2020; 38:10-15.
358. Jans DA, Wagstaff KM. Ivermectin as a broad-spectrum host directed anti-viral: The real deal. Cells 2020; 9:2100.
359. Sharun K, Dhama K, Patel SK et al. Ivermectin, a new candidate therapeutic against SARS-CoV-2/COVID-19. Ann Clin Microbiol Antimicrob 2020; 19:23.
360. Peralta EG, Fimia-Duarte R, Cardenas JW et al. Ivermectin, a drug to be considered for the prevention and treatment of SARS-CoV-2. Brief literature review. EC Veterinary Science 2020; 5:25-29.
361. Al-Jassim KB, Jawad AA, Al-Masoudi EA et al. Histopathological and biochemical effects of ivermectin on kidney functions, lung and the ameliorative effects of vitamin C in rabbits. Bas J Vet Res 2016; 14:110-124.
362. Mudatsir M, Yufika A, Nainu F et al. Antiviral activity of ivermectin against SARS-CoV-2: an old-fashioned dog with a new trick- Literature review. Sci Pharm 2020; 88:36.
363. Carvallo H, Hirsch R, Farinella ME. Safety and efficacy of the combined use of Ivermectin, dexamethasone, enoxaparin and aspirin against COVID-19. medRxiv 2020.
364. Menezes RR, Godin AM, Rodrigues FF et al. Thiamine and riboflavin inhibit production of cytokines and increase the anti-inflammatory activity of a corticosteroid in a chronic model of inflammation induced by complete Freund's adjuvant. Pharmacological Reports 2020; 69:1036-43.
365. Vatsalya V, Li F, Frimodig J et al. Therapeutic prospects for Th-17 cell immune storm syndrome and neurological symptoms in COVID-19: Thiamine efficacy and safety, In-vitro evidence and pharmacokinetic profile. medRxiv 2020.
366. Mallat J, Lemyze M, Thevenin D. Do not forget to give thiamine to your septic shock patient! J Thorac Dis 2016; 8:1062-66.
367. Moskowitz A, Donnino MW. Thiamine (vitamin B1) in septic shock: a targeted therapy. J Thorac Dis 2020; 12 (suppl 1):S78-S83.
368. Woolum JA, Abner EL, Kelly A et al. Effect of thiamine administration on lactate clearance and mortality in patients with septic shock. Crit Care Med 2018; 46:1747-52.
369. Marik PE. Thiamine: An essential component of the metabolic resuscitation protocol. Crit Care Med 2018; 46:1869-70.
370. Al Sulaiman K, Aljuhani O, Al Dossari M et al. Evaluation of thiamine as adjunctive therapy in COVID-19 critically ill patients: A multicenter propensity score matched study. Research Square 2021.

371. Chen L, Jiang X, Huang L et al. Bioequivalence of a single 10-mg dose of finasteride 5-mg oral disintegrating tablets and standard tablets in healthy adult male Han Chinese volunteers: A randomized sequence, open-label, two-way crossover study. Clinical Therapeutics 2009; 31:2242-48.
372. Lee CY, Jan WC, Tsai PS et al. Magnesium sulfate mitigates acute lung injury in endotoxemia rats. J Trauma 2011; 70:1177-85.
373. Salem M, Kasinski N, Munoz R et al. Progressive magnesium deficiency inceases mortality from endotoxin challenge:Protective effects of acute magnesium replacement therapy [abstract]. Crit Care Med 1995;A260.
374. Jiang P. Does hypomagnesemia impact on the outcome of patients admitted to the intensive care unit? A systematic review and meta-analysis. Shock 2019; 47:288-95.
375. Rothlin RP, Vetulli HM, Duarte M et al. Telmisartan as tentative angiotensin receptor blocker therapeutic for COVID-19. Drug Dev Res 2020; 81:768-70.
376. Nejat R, Sadr AS, Freitas BT et al. Losartan inhibits SARS-CoV-2 replication in vitro. J Pharm Pharm Sci 2021; 24:390-399.
377. Patterson BK, Guevara-Coto J, Yogendra R et al. Immune-based prediction of COVID-19 severity and chronicity decoded using machine learning. Front Immunol 2021.
378. Oldenburg CE, Doan T. Azithromycin for severe COVID-19. Lancet 2020.
379. Futado RH, Berwanger O, Fonseca HA et al. Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil (COALITION II): a randomised trial. Lancet 2020.
380. Agarwal A, Mukherjee A, Kumar G et al. Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre randomised controlled trial (PLACID Trial). BMJ 2020; 371:m3939.
381. Simonovich VA, Pratx LD, Scibona P et al. A randomized trial of convalescent plasma in COVID-19 severe pneumonia. N Engl J Med 2020.
382. Avendano-Sola C, Ramos-Martinez A, Munez-Rubio E et al. Convalescent plasma for COVID-19: A multicenter, randomized clinical trial. medRxiv 2020.
383. Balcells ME, Rojas L, Le Corre N et al. Early versus deferred anti-SARS-CoV-2 convalescent plasma in patients admitted for COVID-19: A randomized phase II clinical trial. PLOS Med 2021; 18:e1003415.
384. Janiaud P, Axfors C, Schmitt AM et al. Association of convalescent plasma treatment with clinical outcomes in patients with COVID-19. A systematic review and meta-analysis. JAMA 2021.
385. Li L, Zhang W, Hu Y et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19. A randomized clinical trial. JAMA 2020; 324:460-470.
386. Edwards G. Ivermectin: does P-glycoprotein play a role in neurotoxicity? Filaria Jurnal 2003; 3 (Suppl I):S8.
387. Thompson MA, Henderson JP, Shah PK et al. Convalescent plasma and improved survival in patients with hematologic malignancies and COVID-19. medRxiv 2021.
388. Rosas IO, Brau N, Waters M et al. Tocilizumab in hospitalized patients with COVID-19 pneumonia. medRxiv 2020.
389. Hermine O, Mariette X, Tharaux PL et al. Effect of tocilizumab vs usual care in adults hospitalized with COVID-19 and moderate or severe pneumonia.A randomized Clinical Trial. JAMA Intern Med 2020.
390. Stone JH, Frigault MJ, Sterling-Boyd NJ et al. Efficacy of tocilizumab in patients hospitalized with Covid-19. N Engl J Med 2020.
391. Salvarani C, Dolci G, Massari M et al. Effect of tocilizumab vs standard care on clinical worsening in patients hospitalized with COVID-19 pneumonia. A randomized clinical trial. JAMA Intern Med 2020.
392. Salama C, Han J, Yau L et al. Tocilizumab in patients hospitalized with Covid-19 pneumonia. N Engl J Med 2020.
393. Jeffreys L, Pennington SH, Duggan J et al. Remdesivir-Ivermectin combination displays synergistic interactions with improved in vitro antiviral activity against SARS-CoV-2. bioRxiv 2020.
394. Gordon AC, Mouncey PR, Rowan KM et al. Interleukin-6 receptor antagonists in critically ill patients with COVID-19 - Preliminary report. medRxiv 2021.
395. Bassetti M, Kollef MH, Timsit JF. Bacterial and fungal superinfections in critically ill patients with COVID-19. Intensive Care Med 2020.
396. Rawson TM, Wilson RC, Holmes A. Understanding the role of bacterial and fungal infection in COVID-19. Clinical Microbiology & Infection 2021; 27:9-11.

397. Le Balc'h P, Pinceaux K, Pronier C et al. Herpes simplex virus and cytomegalovirus reactivations among severe COVID-19 patients. Crit Care 2020; 24:530.
398. Koehler P, Bassetti M, Chen SC et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. Lancet Infect Dis 2021.
399. Ospina-Tascon GA, Calderon-Tapia LE, Garcia AF et al. Effect of high-flow oxygen therapy vs conventional oxygen therapy on invasive mechanical ventilation and clinical recovery in patients with severe COVID-19. A randomized clinical trial. JAMA 2021; 326:2161-71.
400. Xu Q, Wang T, Quin X et al. Early awake prone position combined with high-flow nasal oxygen therapy in severe COVID-19; a case series. Crit Care 2020; 24:250.
401. Elharrar X, Trigui Y, Dois AM et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. JAMA 2020.
402. Reddy MP, Subramaniam A, Afroz A et al. Prone positioning of nonintubated patients with Coronavirus Disease 2019- A systematic review and meta-analysis. Crit Care Med 2021.
403. Xin Y, Martin K, Morais CC et al. Diminishing efficacy of prone positioning with late application in evolving lung injury. Crit Care Med 2021.
404. Haymet A, Bassi GL, Fraser JF. Airborne spread of SARS-CoV-2 while using high-flow nasal cannula oxygen therapy: myth or reality. Intensive Care Med 2020; 46:2248-51.
405. Winslow RL, Zhou J, Windle EF et al. SARS-CoV-2 environmental contamination from hospitalized patients with COVID-19 receiving erosol-generating procedures. Thorax 2021.
406. Francone M, Lafrate F, Masci GM et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. European Radiology 2020; 30:6808-17.
407. Kory P, Kanne JP. SARS-CoV-2 organizing pneumonia:"Has there been a widespread failure to identify and treat this prevalent condition in COVID-19?'. BMJ Open Resp Res 2020; 7:e000724.
408. Parry AH, Wani AH, Shah NN et al. Chest CT features of coronavirus disease-19 (COVID-19) pnemonia: which findings on initial CT can predict an adverse short-term outcome? BJR Open 2020; 2:20200016.
409. Zhang J, Meng G, Li W et al. Relationship of chest CT score with clinical characteristics of 108 patients hospitalized with COVID-19 in Wuhan, China. Respiratory Research 2020; 21:180.
410. Yang R, Li X, Liu H et al. Chest CT severity score: An imaging tool for assessing severe COVID-19. Radiology: Cardiothoracic Imaging 2020; 2:e2000047.
411. Li K, Wu J, Wu F et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Investigative Radiology 2020; 55:1-5.
412. Pan F, Ye T, Sun P et al. Time course of lung changes at Chest CT during recovery from Coronavirus Disease 2019 (COVID-19). Radiology 2021; 295:715-21.
413. Ding X, Xu J, Zhou J et al. Chest CT findings of COVID-19 pneumonia by duration of symptoms. European Journal of Radiology 2020; 127:109009.
414. Bernheim A, Mei X, Huang M et al. Chest CT findings in Coronavirus disease 2019 (COVID-19): relationship to duration of infection. Radiology 2020; 295:685-91.
415. Ichikado K, Suga M, Muranka H et al. Prediction of prognosis for acute respiratory distress syndrome with thin-section CT: Validation in 44 cases. Radiology 2006; 238:321-29.
416. Ichikado K, Suga M, Muller NL et al. Acute interstitial pneumonia. Comparison of high-resolution computed tomography findings between survivors and nonsurvivors. Am J Respir Crit Care Med 2002; 165:1551-56.
417. Keith P, Day M, Perkins L et al. A novel treatment approach to the novel coronavirus: an argument for the use of therapeutic plasma exchange for fulminant COVID-19. Crit Care 2020.
418. Keith P, Wells AH, Hodges J et al. The therapeutic efficacy of adjunct therapeutic plasma exchange for septic shock with multiple organ failure: A single center experience. Crit Care 2020; 24:518.
419. Busund R, Koukline V, Utrobin U et al. Plasmapheresis in severe sepsis and septic shock: a prospective, randomised, controlled trial. Intensive Care Med 2002; 28:1434-39.
420. Morath C, Weigand MA, Zeier M et al. Plasma exchange in critically ill COVID-19 patients. Crit Care 2020; 24:481.
421. Khamis F, Al-Zakwani I, Al Hashmi S et al. Therapeutic plasma exchange in adults with severe COVID-19 infection. Int J Infect DIs 2020.
422. Fernandez J, Gratacos-Gines J, Olivas P et al. Plasma exchange: An effective rescue therapy in critically ill patients with Coronavirus Disease 2019 infection. Crit Care Med 2020.

423. Gucyetmez B, Atalan HK, Sertdemir I et al. Therapeutic plasma exchange in patients with COVID-19 pneumonia in intensive care unit: a retrospective study. Crit Care 2020; 24:492.
424. Poor HD, Ventetuolo CE, Tolbert T et al. COVID-19 critical illness pathophysiology driven by diffuse pulmonary thrombi and pulmonary endothelial dysfuncion responsive to thrombolysis. medRxiv 2020.
425. Wang J, Najizadeh N, Moore EE et al. Tissue plasminogen activator (tPA) treatment for COVID-19 associated respiratory distress syndrome (ARDS): A case series. J Thromb Haemost 2020.
426. Abou-Arab O, Huette P, Debouvries F et al. Inhaled nitric oxide for critically ill Covid-19 patients: a prospective study. Crit Care 2020; 24:645.
427. Bagate F, Tuffet S, Masi P et al. Rescue thearpy with inhaled nitric oxide and almitrine in COVID-19 patients with severe acute respiratory distress syndrome. Ann Intensive Care 2020.
428. Caplan M, Goutay J, Bignon A et al. Almitrine infusion in severe acute respiratory syndrome coronavirus-2 indued acute respiratory distress syndrome: A single-center observational study. Crit Care Med 2020.
429. Payen D. Coronavirus disease 2019 acute respiratory failure: Almitrine drug resuscitaion or resuscitating patients by almitrine? Crit Care Med 2020.
430. Henry MB, Lippi G. Poor survival with extracorporeal membrane oxygenation in acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19): Pooled analysis of early reports. J Crit Care 2020; 58:27-28.
431. Abrams D, Lorusso R, Vincent JL et al. ECMO during the COVID-19 pandemic: when is it unjustified. Crit Care 2020; 24:507.
432. Supady A, Taccone FS, Lepper PM et al. Survival after extracorporeal membrane oxygenation in severe COVID-19 ARDS: results from an international multicenter registry. Crit Care Med 2021; 25:90.
433. Barbaro RP, MacLaren G, Boonstra PS et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. Lancet 2020.
434. Cypel M, Keshavjee S. When to consider lung transplantation for COVID-19. Lancet Resp Med 2021; 8:944-46.
435. A neutralizing monoclonal antibody for hospitalized patients with Covid-19. N Engl J Med 2020.
436. Cerutti A, Chen K, Chorny A. Immunoglobulin responses at the mucosal interface. Annu Rev Immunol 2011; 29:273-93.
437. Jacobs JJ. Neutralizing antibodies mediate virus-immue pathology of COVID-19. Med Hypotheses 2020; 143:109884.
438. Caricchio R, Abbate A, Gordeev I et al. Effect of canakinumab vs placebo on survival without invasive mechanical ventilation in patients hospitalized with severe COVID-19. A randomized clinical trial. JAMA 2021.
439. Seifirad S. Pirfenidone: A novel hypothetical treatment for COVID-19. Medical Hypotheses 2020; 144:11005.
440. Saba A, Vaidya PJ, Chavhan VB et al. Combined pirfenidone, azithromycin and prednisolone in post-H1N1 ARDS pulmonary firbosis. Sarcoidosis Vasc Diffuse Lung Dis 2018; 35:85-90.
441. Spagnolo P, Balestro E, Aliberti S et al. Pulmonary fibrosis secondary to COVID-19: a call to arms? Lancet Resp Med 2020; 8:750-752.
442. George PM, Wells AU, Jenkins RG. Pulmonary fibrosis and COVID-19: the potential role for antibibrotic therapy. Lancet Resp Med 2020; 8:807-15.
443. Brouwer WP, Duran S, Kuijper M et al. Hemoadsorption with CytoSorb shows a decreased observed versus expected 28-day all-cause mortality in ICU patients with septic shock: a propensity-score-weighted retrospective study. Crit Care 2019; 23:317.
444. Villa G, Romagnoli S, De Rosa S et al. Blood purification therapy with a hemodiafilter featuring enhanced adsorptive properties for cytokine removal in patients presenting COVID-19: a pilot study. Crit Care 2020; 24:605.
445. Otsuka R, Seino KI. Macrophage activation syndrome and COVID-19. Inflammation Regeneration 2020; 40:19.
446. Opoka-Winiarska V, Grywalska E, Rolinski J. Could hemophagocytic lymphohistiocytosis be the core issue of severe COVID-19 cases? BMC Medicine 2020; 18:214.
447. Kyriazopoulou E, Leventogiannis K, Norrby-Teglund A et al. Macrophage activation-like syndrome: an immunological entity associated with rapid progression to death in sepsis. BMC Medicine 2017; 15:172.
448. Torjesen I. COVID-19: Omicron may be more transmissible than other variants and partly resistant to existing vaccines, scientists fear. BMJ 2021; 375:n2943.

449. He X, Hong W, Pan X et al. SARS-CoV-2 Omicron varinat: Characteristics and prevention. MedComm 2021; 2:838-45.
450. Wolter N, Jassat W, Walaza S et al. Early assessment of the clinical severity of the SARS-C0V-2 Omicron variant in South Africa. medRxiv 2021.
451. Cao Y, Wang J, Jian F et al. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. Nature 2021.
452. Jacobsen H, Strengert M, Maa H et al. Diminished neutralization responses towards SARS-CoV-2 Omicron Voc after mRNA or vector-based COVID-19 vaccinations. medRxiv 2021.
453. Espenhain L, Funk T, Overvad M et al. Epidemiological characterisation of the first 785 SARS-CoV-2 Omicron varinat cases in Denmark, December 2021. Euro Surveill 2021; 26:2101146.
454. Dabrowska A, Szczepanski A, Botwina P et al. Efficacy of antiviral drugs against the omicron variant of SARS-CoV-2. bioRxiv 2021.
455. Glocker MO, Opuni KF, Thiesen HJ. Compared with SARS-CoV2 wild type S pike protein, the SARS-CoV-2 omicron's receptor binding motif has adopted a more SARS-CoV1 and or bat/civet-like structure. bioRxiv 2021.
456. Ahmad Q, DePerrior SE, Dodani S et al. Role of inflammatory biomarkers in the prediction of ICU admission and mortality in patients with COVID-19. Medical Research Archives 2020; 8:1-10.
457. Marik PE, Stephenson E. The ability of procalcitonin, lactate, white blood cell count and neutrophil-lymphocyte count ratio to predict blood stream infection. Analysis of a large database. J Crit Care 2020; 60:135-39.
458. Ichikado K, Muranaka H, Gushima Y et al. Fibroproliferative changes on high-resolution CT in the acute respiratory distress syndrome predict mortality and ventilator dependency: a prospective observational cohort study. BMJ Open 2012; 2:e000545.
459. Tan C, Huang Y, Shi F et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol 2020; 92:856-62.
460. Howell AP, Parrett JL, Malcom DR. Impact of high-dose intravenous vitamin C for treatment of sepsis on point-of-care blood glucose readings. J Diabetes Sci Technol 2019.
461. Stephenson E, Hooper MH, Marik PE. Vitamin C and Point of Care glucose measurements: A retrospective, Observational study [Abstract]. Chest 2018; 154 (suppl.):255a.
462. Hekimian G, Kerneis M, Zeitouni M et al. COVID-19 acute myocarditis and multisystem inflanmmatory syndrome in Adult Intensive and cardiac Care Units. Chest 2020.
463. Ma KL, Liu ZH, Cao CF et al. COVID-19 myocarditis and severity factors: An adult cohort study. medRxiv 2020.
464. Brosnahan SB, Bhatt A, Berger JS et al. COVID-19 pneumonia hospitalizations followed by re-presentation for presumed thrombotic event. Chest 2020.
465. Giannis D, allen SL, Tsang J et al. Post-discharge thromboembolic outcomes and mortality of hospitalized COVID-19 patients: The CORE-19 registry. Blood 2021.
466. Spyropoulos AC, Lipardi C, Xu J et al. Modified IMPROVE VTE Risk Score and elevated D-Dimer identify a high venous thromboembolism risk in acutely ill medical population for extended thromboprophylaxis. TH Open 2020; 4:e59-e65.
467. Kunutsor SK, Seidu S, Blom AW et al. Serum C-reactive protein increases the risk of venous thromboembolism: a prospective study and meta-analysis of published prospective evidence. Eur J Epidemiol 2017; 32:657-67.
468. Patterson BK, Francisco EB, Yogendra R et al. Persistence of SARS CoV-2 S1 protein in CD16+ monocytes in post-acute sequelae of COVID-19 (PASC) up to 15 months post-infection. bioRxiv 2021.
469. Luvanda M, Posch W, Vosper J et al. Dexamethasone promotes *Aspergillus fumigatus* growth in macrophages by triggering M2 repolarization via targeting PKM2. J Fungi 2021; 7:70.
470. Reiter RJ, Sharma R, Ma Q et al. Plasticity of glucose metabolism in activated immune cells: advantages for melatonin inhibition of COVID-19 disease. Melatonin Res 2020; 3:362-79.
471. Ma WH, Zhang XG, Guo LL et al. Androgen receptor inhibition alleviated inflammation in experimental autoimmune myocarditis by increasing autophagy in macrophages. European Review for Medical & Pharmacological Sciences 2021; 25:3762-71.
472. Becerra-Diaz M, Strickland AB, Keselman A et al. Androgen and androgen receptor as enhancers of M2 macrophage polarization in allergic lung inflammation. J Immunol 2018; 201:2923-33.

473. Ma W, Zhang J, Guo L et al. Suppressed androgen receptor expression promotes M2 macrophage reprogramming through the STAT3/SOCS3 pathway. EXCLI Journal 2019; 18:21-29.
474. Carfi A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. JAMA 2020.
475. Prescott HC, Girard TD. Recovery from Severe COVID-19. Leveraging the lessons of survival from sepsis. JAMA 2020.
476. Greenhalgh T, Knight M, A'Court C et al. Management of post-acute Covid-19 in primary care. BMJ 2020.
477. Chopra V, Flanders SA, O'Malley M. Sixty-day outcomes among patients hospitalized with COVID-19. Ann Intern Med 2020.
478. Mandal S, Barnett J, Brill SE et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalization for COVID-19. Thorax 2020.
479. Michelen M, Manoharan L, Elkheir N et al. Characterising long-term covid-19: a rapid living systematic review. medRxiv 2020.
480. Huang C, Huang L, Wang Y et al. 6-month consequences of COVID-19 in patients discharged feom hospital: a cohort study. Lancet 2021.
481. Logue JK, Franko NM, McCulloch DJ et al. Sequelae in adults at 6 months after COVID-19 infection. JAMA Network Open 2021; 4:e210830.
482. Janiri D, Carfi A, Kotzalidis GD et al. Posttraumatic stress disorder in patients after severe COVID-19 infection. JAMA Psychiatry 2021.
483. Voruz P, Allali G, Benzakour L et al. Long COVID neuropsychological deficits after severe, moderate or mild infection. medRxiv 2021.
484. Al-Aly Z, Xie Y, Bowe B. High-dimensional characterization of post-acute sequalae of COVID-19. Nature 2021.
485. Yong SJ. Long-haul COVID-19: Putative pathophysiology, risk factors, and treatments. medRxiv 2020.
486. Taquet M, Geddes JR, Husain M et al. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. Lancet Psychiatry 2021.
487. Afrin LB, Weinstock LB, Molderings GJ. COVID-19 hyperinflammation and post-Covid-19 illness may be rooted in mast cell activation syndrome. Int J Infect DIs 2020.
488. Bryce C, Grimes Z, Pujadas E et al. Pathopysiology of SARS-CoV-2: targeting of endothelial cells renders a complex disease with thrombotic microangiopathy and aberrant immune response. The Mount Sinai COVID-19 autopsy experience. medRxiv 2020.
489. Lu Y, Li X, Geng D et al. Cerebral micro-structutal changes in COVID-19 patients - An MRI-based 3-month follow-up study. EClinicalMedicine 2020.
490. Franke C, Ferse C, Kreye J et al. High frequency of cerebrospinal fluid autoantibodies in COVID-19 patients with neurological symptoms. Brain,Behavor, and Immunity 2021.
491. Sirous R, Taghvaei R, Hellinger JC et al. COVID-19-associated encephalopathy with fulminant cerebral vasoconstriction: CT and MRI findings. Radiology Case Reports 2020; 15:2208-12.
492. Magro CM, Mulvey JJ, Laurence J et al. Docked severe acute respiratory syndrome coronavirus 2 proteins within the cutaneous and subcutaneous microvasculature and their role in the pathogenesis of severe coronavirus disease 2019. Human Pathology 2020; 106:106-16.
493. Theoharides TT, Cholevas C, Polyzoidis K et al. Long-COVID syndrome-associated brain fog and chemofog: Luteolin to the rescue. Biofactors 2021; 47:232-41.
494. Riche F. Protracted immune disorders at one year after ICU discharge in patients with septic shock. Crit Care 2018; 22:42.
495. Andreakos E, Papadaki M, Serhan CN. Dexamethasone, pro-resolving lipid mediators and resolution of inflammation in COVID-19. Allergy 2020.
496. COVID-19 rapid guideline: managing the long-term effects of COVID-19. www.nice.org.uk/guidance/ng188 . 2020. National Institute for Health and Care Excellence. 4-26-2021.

Ref Type: Electronic Citation

497. Cuesta-Llavona E, Gomez J, Albaiceta GM et al. Variant-genetic and transcript-expression analysis showed a role for the chemokine-receptor CCR5 in COVID-19 severity. International Immunopharmacology 2021; 98:107825.
498. Giaquinto C, Mawela MP, Chokephaibutkit K et al. Pharmacokinetics, safety and efficacy of Maraviroc in treatment-experienced pediatric patients infected with CCR5-tropic HIV-1. Pediatr Infect Dis 2018; 37:459-65.

499. Chen Y, Gu S, Chen Y et al. Six-month follow-up of gut microbiota richness in patients with COVID-19. Gut 2021.
500. Sanabria-Mazo JP, Montero-Marin J, Feliu-Soler A et al. Mindfulness-based program plus amygdala and inusla retraining (MAIR) for the treatment of women with fibromyalgia: A pilot ramdomized controlled trial. J Clin Med 2020; 9:3246.
501. Theoharides TC. COVID-19, pulmonary mast cells, cytokine storms, and beneficial actions of luteolin. Biofactors 2020; 46:306-8.
502. Bawazeer MA, Theoharides TC. IL-33 stimulates human mast cell release of CCL5 and CCL2 via MAPK and NF-kB, inhibited by methoxyluteolin. Eur J Pharmacol 2019; 865:172760.
503. Weng Z, Patel AB, Panagiotidou S et al. The novel flavone tetramethoxyluteolin is a potent inhibitor of human mast cells. J Allergy Clin Immunol 2015; 135:1044-52.
504. Patel AB, Theoharides TC. Methoxyluteolin inhibits neuropeptide-stimulated proinflammatory mediator release via mTOR activation from human mast cells. J Pharmacol Exp Ther 2017; 361:462-71.
505. Calis Z, Mogulkoc R, Baltaci AK. The roles of flavonols/flavonoids in neurodegeneration and neuroinflammation. Mini Rev Med Chem 2020; 20:1475-88.
506. Kurcicka L, Lauer SA, Laeyendecker O et al. Variation in false-negative rate of reverse transcriptase polmerase chain reacion-based SARS-CoV-2 tests by time since exposure. Ann Intern Med 2020; 173:262-67.
507. Cheng HY, Jian SW, Liu DP et al. Contact tracing assessment of COVI-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. JAMA Intern Med 2020; 180:1156-63.
508. Zhao J, Yang Y, Huang H et al. Relationship between ABO blood group and the COVID-19 susceptibility. medRxiv 2020.
509. Banerjee A, Pasea L, Harris S et al. Estimating excess 1-year mortality associated with the COVID-19 pandemic according to underlying conditions and age: a population-based cohort study. Lancet 2020; 395:1715-25.
510. Goren A, Vamo-Galvan S, Wambier CG et al. A preliminary observation: Male pattern hair loss among hospitalized COVID-19 patients in Spain- A potential clue to the role of androgens in COVID-19 severity. J Cosmetic Dermatol 2020.
511. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan,China. Lancet 2020; 395:497-506.
512. Guan W, Ni Z, Hu Y et al. Clinical characteristics of Coronavirus disease 2019 in China. N Engl J Med 2020.
513. von der Thusen J, van der Eerden M. Histopathology and genetic susceptibility in COVID-19 pneumonia. Eur J Clin Invest 2020.
514. Sweeney TE, Liesenfeld O, Wacker J et al. Validation of inflammopathic, adaptive, and coagulopathic sepsis endotypes in Coronavirus disease 2019. Crit Care Med 2020.
515. Tartof SY, Qian L, Hong V et al. Obesity and mortality among patients diagnosed with COVID-19: Results from an integrated health care organization. Ann Intern Med 2020.
516. Pujadas E, Chaudhry F, McBride R et al. SARS-CoV-2 viral load predictes COVID-19 mortality. Lancet Resp Med 2020.
517. Akbar AN, Gilroy DW. Aging immunity may exacerbate COVID-19. Science 2020; 369.
518. Zhang Q, Bastard P, Liu Z et al. Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. Science 2020.
519. Li MY, Li L, Zhang Y et al. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infectious Diseases of Poverty 2020; 9:45.
520. Zhou Y, Fu B, Zheng X et al. Pathogenic T cellls and inflammatory monocytes incite inflammatory storm in severe COVID-19 patients. Natl Sci Rev 2020; 7:998-1002.
521. Blanco-Melo D, Nilsson-Payant BE, Liu WC et al. Imbalanced host response to SARS-CoV-2 drives development of COVID-19. Cell 2020; 181:1036-45.
522. Giamarellos-Bouboulis EJ, Netea MG, Rovina N et al. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. Cell Host & Microbe 2020.
523. McGonagle D, Sharif K, O'Regan A et al. The role of cytokines including interleukin-6 in COVID-19 induces pneumonia and macrophage activation syndrome-like disease. Autoimmunity Reviews 2020; 19:102537.
524. Zhou F, Yu T, Du R et al. Clinical course and risk factor for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020.

525. Wu D, Yang XO. TH17 responses in cytokine storm of COVID-19: An emerging target of JAK2 inhibitor Febratinib. J Microbiol Immunol Infect 2020.
526. Giamarellos-Bourboulis EJ, Netea MG, Rovina N et al. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. medRxiv 2020.
527. Mehta P, McAuley DF, Brown M et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020; 395:1033-34.
528. Qin C, Zhou L, Hu Z et al. Dysregulation of the immune response in patiens with COID-19 in Wuhan, China. Lancet Infect Dis 2020.
529. Zhang C, Wu Z, Li JW et al. The cytokine release syndrome (CRS) of severe COVID-19 and interleukin-6 receptor (IL-6R) antagonsit Tocilizumab may be the key to reduce the mortality. Int J Antimicrob Agents 2020.
530. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the "Cytokine Storm" in COVID-19. J Infection 2020.
531. Moore JB, June CH. Cytokine release syndrome in severe COVID-19. Science 2020.
532. Tay MZ, Poh CM, Renia L et al. The trinity of COVID-19: immunity, inflammation and intervention. Nature Reviews 2020; 20:363-74.
533. Leisman DE, Deutschman CS, Legrand M. Facing COVID-19 in the ICU: vascular dysfunction, thrombosis, and dysregulated inflammation. Intensive Care Med 2020; 46:1105-8.
534. Teuwen LA, Geldhof V, Pasut A et al. COVID-19: the vasculature unleashed. Nature Reviews 2020.
535. Varga Z, Flammer AJ, Steiger P et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020.
536. Ackermann M, Verleden SE, Kuehnel M et al. Pulmonary vascular endothelialitis, Thrombosis, and Angiogenesis in COVID-19. N Engl J Med 2020; 383:120-128.
537. Torrealba JR, Fisher S, Kanne JP et al. Pathology-radiology correlation of common and uncommon computed tomographic patterns of organizing pneumonia. Human Pathology 2018; 71:30-40.
538. Kanne JP, Little BP, Chung JH et al. Essentials for radiologists on COVID-19: an Update-Radiology Scientific Expert Panel. Radiology 2020.
539. Copin MC, Parmentier E, Duburcq T et al. Time to consider histologic pattern of lung injury to treat critically ill patietns with COVID-19 infection [letter]. Intensive Care Med 2020.
540. Gattinoni L, Chiumello D, Caironi P et al. COVID-19 pneumonia: different respiratory treatment for different phenotypes? Intensive Care Med 2020; 46:1099-102.
541. Chiumello D, Cressoni M, Gattinoni L. Covid-19 does not lead to a "typical" Acute Respiratory Distress syndrome. Lancet 2020.
542. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? Crit Care 2020; 24:154.
543. Gattinoni L, Pesenti A. The concept of "baby lung". Intensive Care Med 2005; 31:776-84.
544. Patel AN, Desai SS, Grainger DW et al. Usefulness of ivermectin in COVID-19 illness. medRxiv 2020.
545. Jeronimo CM, Farias ME, Almeida FF et al. Methylprednisolone as adjunctive therapy for patients hospitalized with COVID-19 (Metcovid): A ramdomised, double-blind, phase IIb, placebo-controlled trial. Clin Infect Dis 2020.
546. Tobin MJ, Laghi F, Jubran A. Why COVID-19 silent hypoxemia is baffling to physicians. Am J Respir Crit Care Med 2020.
547. Schurink B, Roos E, Radonic T et al. Viral presence and immunopathology in patients with lethal COVID-19: a prospective autopsy cohort study. Lancet Microbe 2020.
548. Buijsers B, Yanginlar C, Maciej-Hulme ML et al. Beneficial non-anticoagulant mechanisms underlying heparin treatment of COVID-19 patients. EBioMedicine 2020.
549. Kim SY, Jin W, Sood A et al. Characterization of heparin and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) spike glycoprotein binding interactions. Antiviral Res 2020; 181:104873.
550. Clausen TM, Sandoval DR, Spliid CB et al. SARS-CoV-2 infection depends on cellular heparan sulphate and ACE2. bioRxiv 2020.
551. Kwon PS, Oh H, Kwon SJ et al. Sulphated polysaccharides effectively inhibit SARS-CoV-2 in vitro. Cell Discovery 2020; 6:50.
552. Huang X, Han S, Liu x et al. Both UFH and NAH alleviate shedding of endothelial glycocalyx and coagulopathy in LPS-induced sepsis. Exp Thera Med 2020; 19:913-22.
553. Buijsers B, Yanginlar C, de Nooijer A et al. Increased plasma heparanase activity in COVID-19 patients. medRxiv 2020.

554. May JM, Qu ZC. Ascorbic acid prevents oxidant-induced increases in endothelial permeability. Biofactors 2011; 37:46-50.
555. Utoguchi N, Ikeda K, Saeki K et al. Ascorbic acid stimulates barrier function of cultured endothelial cell monolayer. Journal of Cellular Physiology 1995; 163:393-99.
556. Han M, Pendem S, Teh SL et al. Ascorbate protects endothelial barrier function during septic insult: Role of protein phosphatase type 2A. Free Radic Biol Med 2010; 48:128-35.
557. Elenkov IJ. Glucocorticoids and the Th1/Th2 balance. Ann N Y Acad Sci 2004; 1024:138-46.
558. Shodell M, Siegal FP. Corticosteroids depress INF-alpha-producing plasmacytoid dentritic cells in human blood. J Allergy Clin Immunol 2001; 108:446-48.
559. Thomas BJ, Porritt RA, Hertzog PJ et al. Glucocorticosteroids enhance replication of respiratory viruses: effect of adjuvant interferon. Scientific Reports 2014; 4:7176.
560. Singanayagam A, Glanville N, Girkin JL et al. Corticosteroid suppression of antiviral immunity increases bacterial loads and mucus production in COPD exacerbations. Nature Communications 2018; 9:2229.
561. Salton F, Confalonieri P, Santus P et al. Prolonged low-dose methylprednisolone in patients with severe COVID-19 pneumonia. medRxiv 2020.
562. Braude AC, Rebuck AS. Prednisone and methylprednisolone disposition in the lung. Lancet 1983;995-97.
563. Sajid MS, Iqbal Z, Muhammad G et al. Effects of ivermectin on the cellular and humoral immune responses of rabbits. Life Sci 2007; 80:1966-70.
564. Blakley BR, Rousseaux CG. Effect of ivermectin on the immune response in mice. Am J Vet Res 1991; 52:593-95.

NEW HAMPSHIRE NURSES' ASSOCIATION

25 Hall St. Unit 1E, Concord, NH 03301
PHONE: (603) 225 -3783
EMAIL: office@nhnurses.org
WEBSITE: www.NHNurses.org

1/14/2022

Dear Chairman Pearson and Members of the House Health, Human Services and Elderly Affairs Committee:

I am here today to ask you to oppose HB 1022 relative to permitting pharmacists to dispense Ivermectin by means of a standing order.

The New Hampshire Nurses' Association (NHNA) exists to promote nursing practice and the wellbeing of New Hampshire nurses by providing professional development, fostering nurse innovation and leading in health advocacy to enhance the health of the people in New Hampshire. A core value of NHNA is the promotion of evidence based practice. It is for these reasons that we strongly oppose this bill.

Ivermectin is neither approved nor authorized for the treatment of COVID in humans. While Ivermectin is authorized for use in humans it is only for the treatment of infections caused by some parasitic worms and head lice and skin conditions like rosacea.

The same voices that are opposed to the use of the Covid 19 vaccines citing that they do not have FDA approval and should be considered experimental and used with caution because "there are currently no long term data demonstrating its safety" are advocating for this experimental treatment (ivermectin) to be available on the open market by means of a standing order. The concern is that vaccines, with known preventive benefits will be replaced by the use of Ivermectin as a treatment for the disease, a treatment with no known benefits.

The National Institutes of Health in the United States recently stated that "there are insufficient data to recommend either for or against the use of ivermectin for the treatment of COVID-19," and the World Health Organization recommends against its use outside of clinical trials. While there are a number of emerging clinical trials there are no conclusive results that would warrant making this drug available simply by requesting it from a pharmacist.

In a 2021 study by Lopez-Medina published in the Journal of the American Medical Association results of a double blinded randomized control study showed that among 400 adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19. Larger trials are needed to understand the effects of ivermectin on clinically relevant outcomes. This same author came out in August of the same year to say that the results of the seminal study by Elgazzar which led everyone to believe that ivermectin could reduce death rates by 90% were in fact flawed and the study was subsequently withdrawn from publication. The trickle down effect of withdrawing the results of this study calls into question results of subsequent meta analyses using these data. This continues the call for more and better clinical trials.

Finally, in the most recent evidence disputing the benefits of Ivermectin in the prevention and treatment of Covid 19 are the reports of its toxic effects. In a December issue of the New England Journal of Medicine, in persons who had received prescriptions from either physicians or veterinarians, toxic effects from its

preventative use included gastrointestinal distress, confusion, dizziness, vision symptoms or rash. While none died there are reports of patients being hospitalized in the ICU for seizures, hypotension and ataxia.

In summary, there is no clear evidence that supports to use of the dispensing of ivermectin by standing orders. Standing orders would make the drug widely available and presents a serious health risk to those who are not well informed about the potential side effects. The prevention of Covid 19 highlights the important role of the healthcare community to guide the public vaccinated or unvaccinated to the best choices to improve the health of the people of New Hampshire.

References

National Institute of Health. The Covid-19 Treatment Guidelines Panel's Statement on the Use of Ivermectin for the Treatment of Covid-19. 2021.

World Health Organization. Therapeutics and COVID-19: Living Guideline. Geneva, Switzerland: WHO; 2021. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.1. Accessed April 8, 2021.

Thank you in advance. Feel free to contact me with any questions.

Pamela P DiNapoli, PhD, RN, CNL
Executive Director
25 Hall Street Suite 1E
Concord, NH 03301
(603)225-3783
(603) 566-7407 Cell
nhna.ned@gmail.com

Archived: Thursday, January 20, 2022 3:39:09 PM
From: Kathy K
Sent: Tuesday, January 11, 2022 1:29:52 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Good afternoon, I urge you to SUPPORT this bill. We need to bring control back to the people.

Thank you
Kathy Komar
Merrimack, NH

Archived: Thursday, February 3, 2022 9:32:26 AM
From: Peter Szydlik
Sent: Monday, January 31, 2022 11:41:29 AM
To: ~House Health Human Services and Elderly Affairs
Cc: RomanSus@aol.com
Subject: HB bills in front of committee feedback
Importance: Normal

Hello, as a citizen of New Hampshire and USA, i want to voice my support or opposition to many covid related bills which are disturbing to me, seeing that we are finally seeing that this is a virus that is taking its natural course, getting less lethal and more contagious and should now be classified as endemic.

HB1003--I support
HB1022--I support
HB1126- I oppose
HB1224- I support
HB1099- I support
HB1223- I support
HB1588- I support
HB1131- I support
HB1371--I support
HB1633--I strongly oppose

Best Regards,

Piotr Sz.

Archived: Friday, January 28, 2022 11:14:17 AM
From: Barbara Koehler
Sent: Tuesday, January 25, 2022 8:12:05 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 - Please pass
Importance: Normal

Here is what the Federal Govt. is doing to us....they are in bed with
the pharmaceutical companies:

> https://us-east-2.protection.sophos.com?d=theconservativetreehouse.com&u=aHR0cHM6Ly90aGVjb25zZXJ2YXRpdmV0cmVlaG91c2UuY29tL2Jsb2cvMjAyMi8wMS8yNS93aXRob3V0LW5vdGljZS1mZGEtcmV2b2tlcy1tb25vY2xvbmFsLWFudGlib2R5LXRyZWF0bWVudHMtZm9yLWNvdmlkLXByb21vdGUtZGlmZmljdWx0LXRvLWZpbmQtcGZpemVyLWFuZC1tZXJjay1waWxscy1hcy1yZXBsYWNlbWVudHMv&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=MlRsY3MxTVkrZ24zVVp2M092cVAxWEozYzRyUUdkaDAzQ3J5RTduQmUzQT0=&h=52b658a43661441f9221a72984fe4652
> <https://us-east-2.protection.sophos.com?d=theconservativetreehouse.com&u=aHR0cHM6Ly90aGVjb25zZXJ2YXRpdmV0cmVlaG91c2UuY29tL2Jsb2cvMjAyMi8wMS8yNS93aXRob3V0LW5vdGljZS1mZGEtcmV2b2tlcy1tb25vY2xvbmFsLWFudGlib2R5LXRyZWF0bWVudHMtZm9yLWNvdmlkLXByb21vdGUtZGlmZmljdWx0LXRvLWZpbmQtcGZpemVyLWFuZC1tZXJjay1waWxscy1hcy1yZXBsYWNlbWVudHMv&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=MlRsY3MxTVkrZ24zVVp2M092cVAxWEozYzRyUUdkaDAzQ3J5RTduQmUzQT0=&h=52b658a43661441f9221a72984fe4652>
Barbara Koehler, Moultonborough

Archived: Thursday, January 20, 2022 11:12:21 AM
From: Alfred Lafferty
Sent: Wednesday, January 19, 2022 6:12:18 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB1022
Importance: Normal

From Al Lafferty of Windham NH long time resident and regular voter, Also, thank you for your service to our great Granite State

Sent from Mail for Windows

Archived: Thursday, January 20, 2022 11:12:21 AM
From: monica d
Sent: Wednesday, January 19, 2022 5:48:07 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

I request that you move on the bill allowing freedom to obtain Ivermectin in NH pharmacies. This is a decision that should be left between a doctor and their patients. Do the right thing. Support NH voices for free medical choice.

Thank you,
Monica Dean
Hampstead NH

Archived: Thursday, January 20, 2022 11:12:21 AM
From: Matt Kelley
Sent: Wednesday, January 19, 2022 5:45:22 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Please support this bill

Matt Kelley

Archived: Thursday, January 20, 2022 11:12:21 AM
From: +19787616232@tmomail.net
Sent: Wednesday, January 19, 2022 3:40:06 PM
To: ~House Health Human Services and Elderly Affairs
Importance: Normal
Attachments:
text_1642624671838.txt

Please support the HB1022 Bill. This will save lives and I personally know people who took it with no side effects and their recovery was much faster!

Archived: Thursday, January 20, 2022 11:12:22 AM
From: Sarah C.
Sent: Tuesday, January 18, 2022 7:08:40 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 - OTP
Importance: Normal

Representatives,

I emailed you earlier with testimonies that I had received from individuals in my network, but I realized that I left out *my own experience* with Ivermectin. I will share it with you now.

On Thanksgiving my husband and I were exposed to a family member who was visibly unwell, but convinced they just had "allergies." They were wrong, it wasn't allergies. Subsequently, my husband and I both became ill with COVID-19. I'm an herbalist and have a background in holistic medicine so my usual treatment consists of medicinal herbs, vitamins & supplements, and homeopathic remedies when illness strikes. In other words, I don't use pharmaceuticals. However, based on the potential risks of the illness, the available literature on Ivermectin, along with the overwhelming anecdotal evidence that had been shared with me over the last 18+ months, I decided to make an exception and purchase some. I bought it months earlier in preparation, and it had been sitting in my cupboard for "emergency use." I immediately began giving it to my husband, while I still decided to opt for the non-pharmaceutical approach that I am accustomed to. I did this largely because my symptoms were mild, and I didn't feel it was necessary. I also have a complex medical history and I am cautious about introducing new products that I may react badly to. Over the next several days, I cycled through various symptoms (sinus headache, loss of smell, sore throat, sneezing, chills etc) while my husband was congested, but otherwise unbothered. I eventually grew tired of feeling lousy and having it drag on, and decided to go ahead and try the Ivermectin. Did I have an adverse reaction? No. Was I miraculously healed? No. I can best describe it as *bringing the progression of the illness to a sudden halt.* For the first time, I woke up without any new symptoms. And as I continued taking it daily my symptoms subsided, my sense of smell returned, and I finally began the recovery process. I only wish that I had taken it sooner. Without a doubt in my mind, if/when my parents become ill with this virus *I will not waste any time* giving them this medication and following the full FLCCC protocol. It will be the first thing that I do! I recommend if you're reading this that you be prepared, familiarize yourself with this treatment protocol, and have Ivermectin (among other things) on hand. That being said, it has become more difficult (and expensive) to obtain, so please do anything in your power to make it more accessible.

http://www.flccc.net *http://www.8days.org*

Sarah Courchaine
Sanbornton, NH

Archived: Thursday, January 20, 2022 11:12:22 AM
From: Christine Macpherson
Sent: Tuesday, January 18, 2022 6:20:13 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Save Lives and Medical Integrity, Support HB1022
Importance: Normal

Dear Committee,

Earlier this year, I was prescribed Ivermectin by a licensed MD to treat my COVID symptoms. Imagine my surprise when pulling into the CVS Keene drive-though and being subject to multiple questions from the dispensing pharmacist. She was angry, asked me repeatedly what I needed the Rx for, asked me if I was travelling soon, and clearly was distressed as she attempted to deal with whatever her computer systems was serving up to her.

In the end, she literally threw the prescription through the window at me—then CVS called my phone number for five days straight, no messages. I can only assume they were going to grill me some more. The following week, I was able to get my husband's Rx filled at Walgreens—but later learned that more and more people in NH were having their Ivermectin Rx's rejected at local chain pharmacies.

This situation is beyond unacceptable. I trust my MD, and I am adult who is capable of making decisions based on risk-benefit scenarios as to what products to use when ill or when dealing with a chronic condition. We have since had our MD tell us he cannot provide Rx scripts in the future for Ivermectin. This is criminal.

Around the world, this safe drug has been available over the counter to literally millions of people who use it on a regular basis. It is safer than Tylenol. No one should have to jump through hoops or be afraid or desperate to get an effective medication that is safe and beneficial. I am sure you are likely aware people are attempting to order this drug from other countries or use the animal versions of the drug—a completely ludicrous situation.

Please support this bill.

Thank you,
Christine Macpherson, Chesterfield

Archived: Thursday, January 20, 2022 11:12:22 AM
From: kaycharron@aol.com
Sent: Tuesday, January 18, 2022 4:02:09 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

To all committee members: Please be advised that your vote on HB1022 must be in favor of making Ivermectin available to all citizens of New Hampshire. This drug has been used safely for many decades and has helped earn the Nobel prize for two different researchers of this treatment. I personally have used Ivermectin to successfully treat "long haul" Covid symptoms I experienced with great success. I was only able to get Ivermectin through a very roundabout way and this should not be the case for people wanting to use it. Please vote in favor of the free use of this drug. Regards, Kay Charron

Archived: Thursday, January 20, 2022 11:12:22 AM
From: Melissa Szymansky
Sent: Tuesday, January 18, 2022 2:00:16 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB1022
Importance: Normal

Attention Representatives,

I urge you to support HB1022. My husband had his prescription rejected from Rite Aid pharmacy in Salem, NH. This was prescribed by a MD and denied by the pharmacist. He was told that IVM could not be prescribed “off label” for Covid. This is wrong! We the people have “The Right to Try” medications and are being denied.

Unfortunately many good doctors and pharmacists are being put in a very difficult situation. They are being threatened to have their licenses revoked or put under threat of audit. This is wrong. We must protect not only people in need of the medicine but those that are trying to do the right thing!

Thank you
Melissa Szymansky
Salem NH

Archived: Thursday, January 20, 2022 11:12:22 AM
From: Melissa Morgan
Sent: Tuesday, January 18, 2022 1:12:30 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 testimony
Importance: Normal

To whom it may concern,

I am writing in support of HB1022. Pharmacists should be dispensing Ivermectin as ordered by licensed providers. I fail to understand why this stopped and who is responsible for such a thing.

"The antiviral activity is ivermectin has been shown against a wide range of RNA and DNA viruses…" (https://www.drugs.com/ivermectin.html).
There is plenty of literature available on this.

On a personal note. This medication has been prescribed for my 10 year old for Lyme disease since 2019. The availability of the medicine, the coverage from my insurance, and the cost have changes month to month for almost the year now without satisfactory explanation nor anything supplied to me in writing from the insurance company or pharmacy.

Most recently, my family tested positive for COVID. We were each prescribed Ivermectin as part of our treatment. The pharmacist refused to fill it for fear of "disciplinary action from the board". What purpose is a doctor's medical license and right to prescribe appropriate medications for appropriate illnesses if a pharmacist can just ignore it anyway?

The doctor who prescribed this is a Navy veteran doctor, board certified, integrated medicine specialist, well versed in viruses, autoimmune diseases and I have chosen her for a number of reasons.

This state does not have the authority to tell my doctor how to think and how to practice medicine. I had to travel to another state (with COVID, not very helpful when trying to reduce the spread) to purchase this medicine out of pocket.

My symptoms were resolved in 4 days. My daughter was better in 2 days, and my husband in 5. I did not miss any days from work. We are not the only family with a story like this. COVID is treatable when the focus is on treatment and not following along with the mass media propaganda and money making machine of the pharmaceutical giants.

The countries of Japan and India have Covid med kits available for their citizens for the onset of symptoms containing Ivermectin and Doxycycline.
There is no reason for our country to not follow suit!
Let NH be the leader in restoring the rights of individuals and doctors and let's start healing our community.

Please restore freedom by passing HB1022 and returning the rights of patients to receive what has been appropriately prescribed for them!

I have included resources below for your reference as there is additional science beyond what Dr Fauci and company fraudulently blast on tv on a daily basis.

Thank you for your consideration of my testimony.

Melissa Morgan
Resident of Raymond NH

FLCCC ALLIANCE

FRONT LINE COVID-19 CRITICAL CARE ALLIANCE
PREVENTION & TREATMENT PROTOCOLS FOR COVID-19

I-MASK+

PREVENTION & EARLY OUTPATIENT TREATMENT PROTOCOL FOR COVID-19

EARLY TREATMENT PROTOCOL[5] (for Delta variant)

1. First line agents (use any or all medicines; listed in order of priority/importance)

ANTI-VIRALS

Ivermectin[2]
0.4–0.6 mg/kg per dose (take with or after a meal) — one dose daily, take for 5 days or until recovered. Use upper dose if: **1)** in regions with aggressive variants (e.g. Delta); **2)** treatment started on or after day 5 of symptoms or in pulmonary phase; or **3)** multiple comorbidities/risk factors.

and/or **Nitazoxanide**
500 mg 2 x daily for 5 days after meals. Combine with ivermectin (preferred) or substitute if ivermectin is not available. (Nitazoxanide is often unavailable or high-priced in the USA.)

ANTI-SEPTIC ANTI-VIRALS

Antiviral mouthwash: Gargle 3 x daily (do not swallow; must contain chlorhexidine, povidone-iodine, or cetylpyridinium chloride). **Iodine nasal spray/drops**: Use 1% povidone-iodine commercial product as per instructions 2–3 x daily. If 1%-product not available, must first dilute the more widely available 10%-solution[6] and apply 4–5 drops to each nostril every 4 hours. (No more than 5 days in pregnancy.)

ANTI-COAGULANTS / IMMUNE FORTIFYING

Aspirin	325 mg daily (unless contraindicated)
Vitamin D	Vitamin D3 5,000 IU daily. Preferred form if available: Calcitriol 0.5 mcg on day 1, then 0.25 mcg daily for 7 days
Melatonin	10 mg before bedtime (causes drowsiness)

SYNERGISTIC THERAPIES

Quercetin	250 mg 2 x daily
Zinc	100 mg/day (elemental zinc)
Vitamin C	500–1,000 mg 2 x daily

NUTRITIONAL THERAPEUTICS (for 14 days)[4]

Curcumin	(turmeric)	500 mg 2 x daily
Nigella Sativa	(black cumin seed)	80 mg/kg daily
Honey		1 gram/kg daily

PULSE OXIMETER

Monitoring of oxygen saturation is recommended (for instructions see page 3)

2. Second line agents (listed in order of priority/importance)

Add to first line therapies above if: 1) ≥5 days of symptoms; 2) Poor response to therapies above; 3) Significant comorbidities.

DUAL ANTI-ANDROGEN THERAPY

1. **Spironolactone** 100 mg 2 x daily for ten days.
2. **Dutasteride** 2 mg on day 1, followed by 1 mg daily for 10 days. If dutasteride not available, use **Finasteride** 10 mg daily for 10 days.

FLUVOXAMINE

50 mg 2 x daily for 10 days[7]
Consider **Fluoxetine** 30 mg daily for 10 days as an alternative (it is often better tolerated). Avoid if patient is already on an SSRI.

MONOCLONAL ANTIBODY THERAPY

Casirivimab/Imdevimab[8]
600 mg each in a single subcutaneous injection. Antibody therapy is for patients within 7 days of first symptoms and one or more risk factors as: Age > 65y; BMI > 25; pregnancy; chronic lung, heart, or kidney disease; diabetes; immunosuppressed; developmental disability; chronic tracheostomy; or feeding tube.

3. Third line agent

If below criteria are met, consider

CORTICOSTEROIDS

Prednisone or **Methylprednisolone**
1 mg/kg daily for 5 days followed by slow taper or escalation according to patient response.

Criteria:

After day 7–10 from first symptoms and patient has either: abnormal chest x-ray, shortness of breath, or oxygen saturations of 88–94%.

If oxygen saturation is lower than 88%, emergency room evaluation should be sought.

Notes

1 The I-MASK+ protocol is a bridge to vaccines and a safety net for those who cannot or have not been vaccinated; or are vaccinated and have concerns regarding declining protection against emerging variants. Vaccines have shown efficacy in preventing the most severe outcomes of COVID-19 and are an important part of a multi-modal strategy that must also include early treatment. The decision to get a vaccine should be made in consultation with your health care provider.

2 The dosing may be updated as further scientific studies emerge. The safety of ivermectin in pregnancy has not been definitively established. Use in the 1st trimester should be discussed with your doctor.

3 To use if a household member is COVID-19 positive, or you have prolonged exposure to a COVID-19 positive patient without wearing a mask.

4 For more information on nutritional therapeutics and how they can help with COVID-19 please see: flccc.net/covid-19-protocols/nutritional-therapeutics

5 For late phase – *hospitalized patients* – see the FLCCC's "MATH+ Hospital Treatment Protocol for COVID-19" on www.flccc.net

6 To make 1% povidone/iodine concentrated solution from 10% povidone/iodine solution, *it must be diluted first.*

One dilution method is as follows:

- First pour 1½ tablespoons (25 ml) of 10% povidone/iodine solution into a nasal irrigation bottle of 250 ml.
- Then fill to top with distilled, sterile or previously boiled water.
- Tilt head back, apply 4–5 drops to each nostril. Keep tilted for a few minutes, let drain.

7 Some individuals who are prescribed fluvoxamine experience acute anxiety which needs to be carefully monitored for and treated by the prescribing clinician to prevent rare escalation to suicidal or violent behavior.

8 This medication requires an infusion center. To find the nearest location in the U.S., visit www.infusioncenter.org or call for eligibility and location 1-877-332-6585 for English and 1-877-366-0310 for Spanish.

I-MASK+

PREVENTION & EARLY OUTPATIENT TREATMENT PROTOCOL FOR COVID-19

EARLY TREATMENT PROTOCOL[5] (for Delta variant)

1. First line agents (use any or all medicines; listed in order of priority/importance)

ANTI-VIRALS

Ivermectin[2]
0.4–0.6 mg/kg per dose (take with or after a meal) — one dose daily, take for 5 days or until recovered. Use upper dose if: **1)** in regions with aggressive variants (e.g. Delta); **2)** treatment started on or after day 5 of symptoms or in pulmonary phase; or **3)** multiple comorbidities/risk factors.

and/or **Nitazoxanide**
500 mg 2 x daily for 5 days after meals. Combine with ivermectin (preferred) or substitute if ivermectin is not available. (Nitazoxanide is often unavailable or high-priced in the USA.)

ANTI-SEPTIC ANTI-VIRALS

Antiviral mouthwash: Gargle 3 x daily (do not swallow; must contain chlorhexidine, povidone-iodine, or cetylpyridinium chloride). **Iodine nasal spray/drops**: Use 1% povidone-iodine commercial product as per instructions 2–3 x daily. If 1%-product not available, must first dilute the more widely available 10%-solution[6] and apply 4–5 drops to each nostril every 4 hours. (No more than 5 days in pregnancy.)

ANTI-COAGULANTS / IMMUNE FORTIFYING

Aspirin	325 mg daily (unless contraindicated)
Vitamin D	Vitamin D3 5,000 IU daily. Preferred form if available: Calcitriol 0.5 mcg on day 1, then 0.25 mcg daily for 7 days
Melatonin	10 mg before bedtime (causes drowsiness)

SYNERGISTIC THERAPIES

Quercetin	250 mg 2 x daily
Zinc	100 mg/day (elemental zinc)
Vitamin C	500–1,000 mg 2 x daily

NUTRITIONAL THERAPEUTICS (for 14 days)[4]

Curcumin	(turmeric)	500 mg 2 x daily
Nigella Sativa	(black cumin seed)	80 mg/kg daily
Honey		1 gram/kg daily

PULSE OXIMETER

Monitoring of oxygen saturation is recommended (for instructions see page 3)

2. Second line agents (listed in order of priority/importance)

Add to first line therapies above if: 1) ≥5 days of symptoms; 2) Poor response to therapies above; 3) Significant comorbidities.

DUAL ANTI-ANDROGEN THERAPY

1. **Spironolactone** 100 mg 2 x daily for ten days.
2. **Dutasteride** 2 mg on day 1, followed by 1 mg daily for 10 days. If dutasteride not available, use **Finasteride** 10 mg daily for 10 days.

FLUVOXAMINE

50 mg 2 x daily for 10 days[7]
Consider **Fluoxetine** 30 mg daily for 10 days as an alternative (it is often better tolerated). Avoid if patient is already on an SSRI.

MONOCLONAL ANTIBODY THERAPY

Casirivimab/Imdevimab[8]
600 mg each in a single subcutaneous injection. Antibody therapy is for patients within 7 days of first symptoms and one or more risk factors as: Age > 65y; BMI > 25; pregnancy; chronic lung, heart, or kidney disease; diabetes; immunosuppressed; developmental disability; chronic tracheostomy; or feeding tube.

3. Third line agent

If below criteria are met, consider

CORTICOSTEROIDS

Prednisone or **Methylprednisolone**
1 mg/kg daily for 5 days followed by slow taper or escalation according to patient response.

Criteria:

After day 7–10 from first symptoms and patient has either: abnormal chest x-ray, shortness of breath, or oxygen saturations of 88–94%.

If oxygen saturation is lower than 88%, emergency room evaluation should be sought.

Notes

1 The I-MASK+ protocol is a bridge to vaccines and a safety net for those who cannot or have not been vaccinated; or are vaccinated and have concerns regarding declining protection against emerging variants. Vaccines have shown efficacy in preventing the most severe outcomes of COVID-19 and are an important part of a multi-modal strategy that must also include early treatment. The decision to get a vaccine should be made in consultation with your health care provider.

2 The dosing may be updated as further scientific studies emerge. The safety of ivermectin in pregnancy has not been definitively established. Use in the 1st trimester should be discussed with your doctor.

3 To use if a household member is COVID-19 positive, or you have prolonged exposure to a COVID-19 positive patient without wearing a mask.

4 For more information on nutritional therapeutics and how they can help with COVID-19 please see: flccc.net/covid-19-protocols/nutritional-therapeutics

5 For late phase – *hospitalized patients* – see the FLCCC's "MATH+ Hospital Treatment Protocol for COVID-19" on www.flccc.net

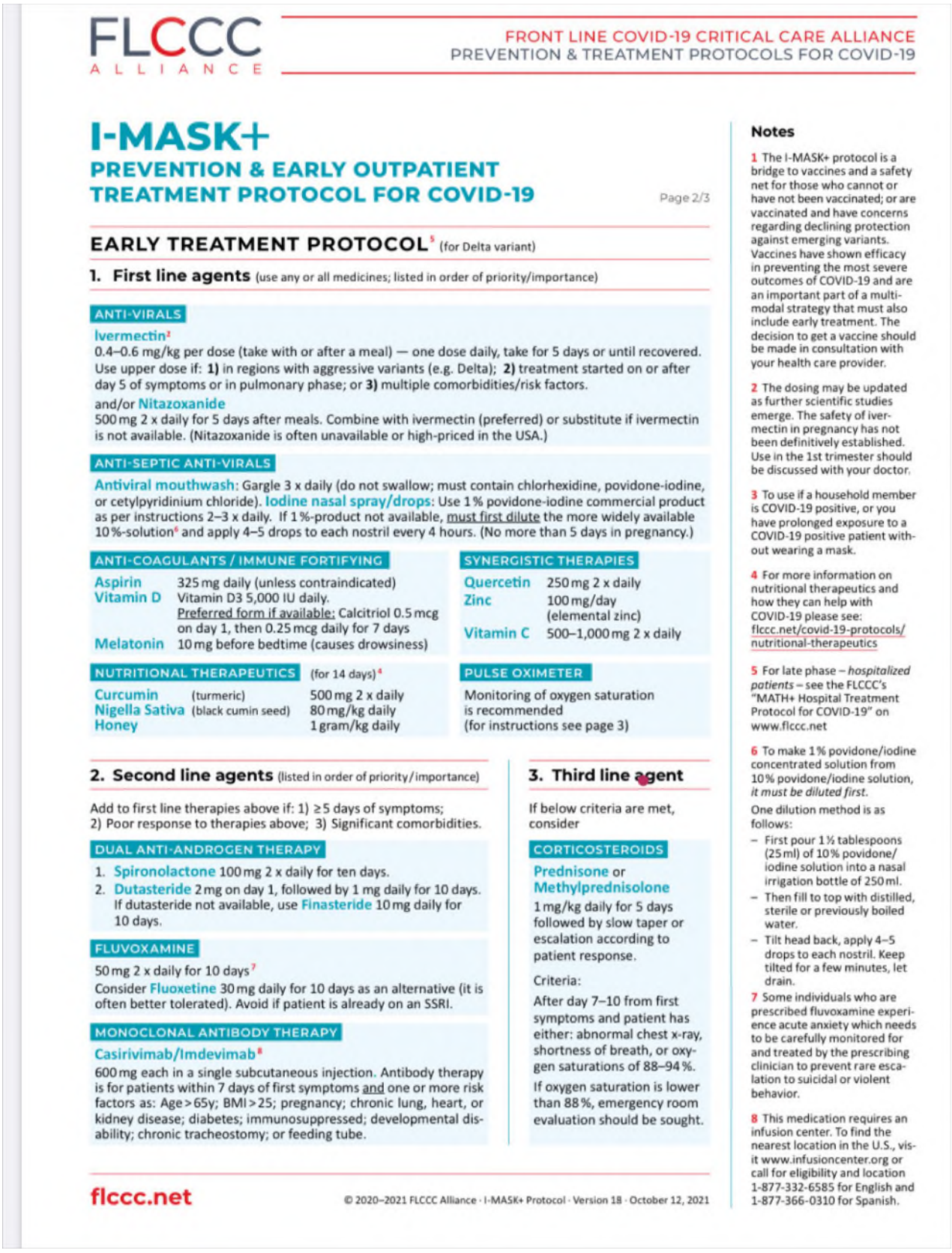
6 To make 1% povidone/iodine concentrated solution from 10% povidone/iodine solution, *it must be diluted first.*

One dilution method is as follows:

- First pour 1½ tablespoons (25 ml) of 10% povidone/iodine solution into a nasal irrigation bottle of 250 ml.
- Then fill to top with distilled, sterile or previously boiled water.
- Tilt head back, apply 4–5 drops to each nostril. Keep tilted for a few minutes, let drain.

7 Some individuals who are prescribed fluvoxamine experience acute anxiety which needs to be carefully monitored for and treated by the prescribing clinician to prevent rare escalation to suicidal or violent behavior.

8 This medication requires an infusion center. To find the nearest location in the U.S., visit www.infusioncenter.org or call for eligibility and location 1-877-332-6585 for English and 1-877-366-0310 for Spanish.



FLCCC ALLIANCE

FRONT LINE COVID-19 CRITICAL CARE ALLIANCE
PREVENTION & TREATMENT PROTOCOLS FOR COVID-19

I-MASK+

PREVENTION & EARLY OUTPATIENT TREATMENT PROTOCOL FOR COVID-19

Page 2/3

EARLY TREATMENT PROTOCOL[5] (for Delta variant)

1. First line agents (use any or all medicines; listed in order of priority/importance)

ANTI-VIRALS

Ivermectin[2]
0.4–0.6 mg/kg per dose (take with or after a meal) — one dose daily, take for 5 days or until recovered. Use upper dose if: **1)** in regions with aggressive variants (e.g. Delta); **2)** treatment started on or after day 5 of symptoms or in pulmonary phase; or **3)** multiple comorbidities/risk factors.

and/or **Nitazoxanide**
500 mg 2 x daily for 5 days after meals. Combine with ivermectin (preferred) or substitute if ivermectin is not available. (Nitazoxanide is often unavailable or high-priced in the USA.)

ANTI-SEPTIC ANTI-VIRALS

Antiviral mouthwash: Gargle 3 x daily (do not swallow; must contain chlorhexidine, povidone-iodine, or cetylpyridinium chloride). **Iodine nasal spray/drops**: Use 1% povidone-iodine commercial product as per instructions 2–3 x daily. If 1%-product not available, must first dilute the more widely available 10%-solution[6] and apply 4–5 drops to each nostril every 4 hours. (No more than 5 days in pregnancy.)

ANTI-COAGULANTS / IMMUNE FORTIFYING

Aspirin	325 mg daily (unless contraindicated)
Vitamin D	Vitamin D3 5,000 IU daily. Preferred form if available: Calcitriol 0.5 mcg on day 1, then 0.25 mcg daily for 7 days
Melatonin	10 mg before bedtime (causes drowsiness)

SYNERGISTIC THERAPIES

Quercetin	250 mg 2 x daily
Zinc	100 mg/day (elemental zinc)
Vitamin C	500–1,000 mg 2 x daily

NUTRITIONAL THERAPEUTICS (for 14 days)[4]

Curcumin	(turmeric)	500 mg 2 x daily
Nigella Sativa	(black cumin seed)	80 mg/kg daily
Honey		1 gram/kg daily

PULSE OXIMETER

Monitoring of oxygen saturation is recommended (for instructions see page 3)

2. Second line agents (listed in order of priority/importance)

Add to first line therapies above if: 1) ≥5 days of symptoms; 2) Poor response to therapies above; 3) Significant comorbidities.

DUAL ANTI-ANDROGEN THERAPY

1. **Spironolactone** 100 mg 2 x daily for ten days.
2. **Dutasteride** 2 mg on day 1, followed by 1 mg daily for 10 days. If dutasteride not available, use **Finasteride** 10 mg daily for 10 days.

FLUVOXAMINE

50 mg 2 x daily for 10 days[7]
Consider **Fluoxetine** 30 mg daily for 10 days as an alternative (it is often better tolerated). Avoid if patient is already on an SSRI.

MONOCLONAL ANTIBODY THERAPY

Casirivimab/Imdevimab[8]
600 mg each in a single subcutaneous injection. Antibody therapy is for patients within 7 days of first symptoms and one or more risk factors as: Age > 65y; BMI > 25; pregnancy; chronic lung, heart, or kidney disease; diabetes; immunosuppressed; developmental disability; chronic tracheostomy; or feeding tube.

3. Third line agent

If below criteria are met, consider

CORTICOSTEROIDS

Prednisone or **Methylprednisolone**
1 mg/kg daily for 5 days followed by slow taper or escalation according to patient response.

Criteria:

After day 7–10 from first symptoms and patient has either: abnormal chest x-ray, shortness of breath, or oxygen saturations of 88–94%.

If oxygen saturation is lower than 88%, emergency room evaluation should be sought.

flccc.net

Notes

1 The I-MASK+ protocol is a bridge to vaccines and a safety net for those who cannot or have not been vaccinated; or are vaccinated and have concerns regarding declining protection against emerging variants. Vaccines have shown efficacy in preventing the most severe outcomes of COVID-19 and are an important part of a multi-modal strategy that must also include early treatment. The decision to get a vaccine should be made in consultation with your health care provider.

2 The dosing may be updated as further scientific studies emerge. The safety of ivermectin in pregnancy has not been definitively established. Use in the 1st trimester should be discussed with your doctor.

3 To use if a household member is COVID-19 positive, or you have prolonged exposure to a COVID-19 positive patient without wearing a mask.

4 For more information on nutritional therapeutics and how they can help with COVID-19 please see: flccc.net/covid-19-protocols/nutritional-therapeutics

5 For late phase – *hospitalized patients* – see the FLCCC's "MATH+ Hospital Treatment Protocol for COVID-19" on www.flccc.net

6 To make 1% povidone/iodine concentrated solution from 10% povidone/iodine solution, *it must be diluted first*.

One dilution method is as follows:

- First pour 1½ tablespoons (25 ml) of 10% povidone/iodine solution into a nasal irrigation bottle of 250 ml.
- Then fill to top with distilled, sterile or previously boiled water.
- Tilt head back, apply 4–5 drops to each nostril. Keep tilted for a few minutes, let drain.

7 Some individuals who are prescribed fluvoxamine experience acute anxiety which needs to be carefully monitored for and treated by the prescribing clinician to prevent rare escalation to suicidal or violent behavior.

8 This medication requires an infusion center. To find the nearest location in the U.S., visit www.infusioncenter.org or call for eligibility and location 1-877-332-6585 for English and 1-877-366-0310 for Spanish.

--
Kindly,

Melissa

Melissa Morgan

Morgan Consulting, LLC "The Beacon of Solutions"
1-877-241-5446

CoachMelissa.Morgan@gmail.com
linkedin.com/in/melissa-morgan-52192241
https://www.facebook.com/BeaconofTransformation

Archived: Thursday, January 20, 2022 11:12:22 AM
From: Christopher Herd
Sent: Tuesday, January 18, 2022 12:23:03 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Regarding HB1022
Importance: Normal

Health, Human Services and Elderly Affairs members:

I am writing today to support HB1022. The concept of having to pass legislation to protect the doctor patient relationship and halt pharmacists from practicing medicine without a license is utterly ridiculous. However this is the situation that we find ourselves in. The demonization of Ivermectin is not based in science and in fact it is a medication with a robust safety profile and long history of safe usage. The re-purposing of drugs is a normal part of the practice of medicine and has been for some time. We are about the enter year 3 of the pandemic and at this point we need to take an all hands on deck approach. Every possible weapon in our arsenal must be used to it's fullest capacity. There is a large amount of evidence showing that Ivermectin has therapeutic activity against COVID 19 and other countries has shown what it can do when widely available. Why pharmacists are blocking access to this medication is a longer conversation for another day however it must end now. They are practicing outside their role and quite frankly I am of the opinion that any pharmacist doing such should face immediate disciplinary action.

I ask you to do the right thing for NH and please support HB1022.

Christopher Herd, PT, DPT, Cert-DN, CSCS
Staff Physical Therapist, Clinical Leader
Concord Hospital Rehabilitation Services-
Concord Hospital Offices North
Family Tree Health Care - Warner
(603)230-5634

Archived: Thursday, January 20, 2022 11:12:22 AM
From: Kathleen Brown
Sent: Tuesday, January 18, 2022 11:53:48 AM
To: ~House Health Human Services and Elderly Affairs
Subject: SUPPORT HB1022
Importance: Normal

Hon. Committee Members:
Please SUPPORT HB1022 because decisions regarding prescriptions should be between a doctor and patient. Currently it is difficult to have a prescription for Ivermectin to be fulfilled almost anywhere in NH. This Bill will eliminate that difficulty.
Thank you.
Kathleen Brown
Newport NH

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Claire Ketteler
Sent: Tuesday, January 18, 2022 10:54:38 AM
To: ~House Health Human Services and Elderly Affairs; Leah Cushman
Subject: Support HB1022
Importance: Normal

Dear Health, Human Services and Elderly Affairs Committee

I support HB1022. Please see the government's very unclear summary of Ivermectin "Ivermectin has been shown to inhibit the replication of SARS-CoV-2 in cell cultures." and "Some observational cohorts and clinical trials have evaluated the use of ivermectin for the prevention and treatment of COVID-19."

Data from these studies can be found in Table 2d at https://us-east-2.protection.sophos.com?d=nih.gov&u=aHR0cHM6Ly93d3cuY292aWQxOXRyZWF0bWVudGd1aWRlbGluZXMubmloLmdvdi90aGVyYXBpZXMvYW50aXZpcmFsLXRoZXJhcHkvaXZlcm1lY3Rpbi8=&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=YTNhT3hZVG9xRHVvTjZjd012S2J2WDNraHYrVUtqQnRzM1U5dmZ1WmxyMD0=&h=0db5c88bbac44ee19fb9a1d3549bef86

If you open the Table 2D on the above website, you will see the results of several Ivermectin studies which were all performed in OTHER countries.

There are no listed studies in the U.S. because the drug was formerly off patent and very cheap, compared with the drug that has been studied in U.S. hospitals, Remdesivir Remdesivir is very expensive, useless against Covid and causes kidney failure in many patients who receive it.

Studies on the effectiveness of ivermectin in the U.S. for Covid have been discouraged and suppressed.

Big pharma companies have a real financial interest to suppress cheap off patent drugs with a proven safety profile that might effectively treat a new disease. Big pharma obviously wants to sell their new drug, like Molnupiravir.

Off label prescription of a drug that might have some good treatment effect on a disease was formerly a standard procedure for MDs, prior to Covid. I had observed this frequently in my 22 years of nursing prior to Covid.

Making ivermectin available by a standing order allows medical freedom to people who want to choose this therapy in the community instead of a Big Pharma pushed, ineffective, new, unproven and expensive therapy.

I would also go a step further in this legislation by REQUIRING all pharmacies in NH to develop a standing order protocol for dispensing ivermectin.

Sincerely,
Claire Ketteler
Newbury NH

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Jim Avallon
Sent: Tuesday, January 18, 2022 10:42:54 AM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

I have several friends who have contracted COVID and have benefited greatly from Ivermectin, particularly when taken early. The problem is acquiring Ivermectin and determining the appropriate dose. That is why I believe in HB1022 so that people like my friends who have had COVID and who have benefited so greatly can take it under a doctor's prescription which will specify details of Ivermectin dose and beneficial accompanying medication dosages and supervision. Ivermectin is a safe medication, has been around for a long time and I think was involved with a Nobel award. There are somewhat like 60-70 sitting studies detailing Ivermectin's benefit as a treatment for COVID.
Thank you
Jim Avallon
North Hampton, NH

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Cat Woman
Sent: Tuesday, January 18, 2022 10:34:18 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 Mandates pharmacists must dispense ivermectin when prescribed
Importance: Normal

Please support this legislation. It's high time that some attention gets paid to therapeutics rather than just to the constant beating of the "vaccine drum."

Thank you very much,

Donna Rae Amato

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 10:28:21 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: hb1022 - opposition - Dr. David Levine
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. David Levine in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: David A. Levine <David.A.Levine@hitchcock.org>
Sent: Tuesday, January 18, 2022 10:11 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: hb1022

Ivermectin is not indicated to treat COVID-19 and prescribing it for such is dangerous and totally out of line with standard of medical care around the world. I would never want this medication prescribed to myself or my family and would take legal action against anyone who recommended this to my loved ones.

David Levine, MD
Assistant Professor of Medicine
Section of General Internal Medicine
Dartmouth-Hitchcock Medical Center
Geisel School of Medicine
One Medical Center Drive
Lebanon, NH 03756
(603) 650-1070

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Laura Piazza
Sent: Tuesday, January 18, 2022 9:47:40 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

Health, Human Services and Elderly Affairs members:

I am writing today to support HB1022. It seems impossible that there needs to be legislation to remind pharmacists that they should not be practicing medicine, but here we are. Health care providers should have the right and ability to use clinical judgement. This is part of being a provider.

Prescribing FDA drugs off label is a part of practicing medicine and happens all the time. The fact that Ivermectin is being singled out and pharmacists have taken it upon themselves to decide whether or not they deem this safe, FDA-approved drug appropriate for patient care is beyond the pale. This needs to be stopped immediately as this is not their role. Decisions regarding prescriptions should be between a doctor and patient alone and the pharmacist needs to know their role.

I ask you to please support HB1022.

Sincerely,
Laura Piazza
Sunapee, NH

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Beth
Sent: Tuesday, January 18, 2022 9:23:34 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

As a concerned citizen I support bill HB1022 to allow ivermectin to be dispensed.
Thank you
Sent from my iPhone

Archived: Thursday, January 20, 2022 11:12:23 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 8:56:47 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fwd: HB1022 video - opposition - Dr. Kate Peters
Importance: Normal
Attachments:
IMG_0709.MOV

Members of the House HHS Committee,

Please see the attached video from Dr. Kate Peters in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Kate Peters <katepetersdo@gmail.com>
Sent: Tuesday, January 18, 2022 7:46 AM
To: Michael Padmore
Subject: HB1022 video

This is insane. I can't believe this even needs to be said. Please see my attached advocacy video.
Thanks,
Kate Peters, D.O.

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Jesse Medeiros
Sent: Tuesday, January 18, 2022 8:43:47 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Hello,

Please consider supporting HB1022. This medicine is safe, effective, FDA approved, with hundreds of minions of doses taken by humans for decades, and is on the World health organization's list of most vital medicines. It also won the Nobel Peace Prize in 2015 for being basically a "wonder drug".

Jesse Medeiros
bgtrck458@gmail.com
603-969-6302
Call, Text, or Email, Thanks!

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Gloria Surber
Sent: Tuesday, January 18, 2022 8:26:15 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

To Whom It May Concern:
I am writing to ask you to pass the above bill to allow physicians to do what they are trained to do! I had covid last year and was able to obtain treatment from America's Frontline Doctors. I am grateful for the successful treatment I received. I would have not been able to receive this treatment from my Primary Care Doctor due to restrictions put on them. I am an RN and work at Cheshire Medical Center in Keene. We are following the CDC guidelines for treatment for covid patients. By email we were informed we would not be using ivermectin because it is not part of the protocol, despite many patients asking their Primary Doctors about it. I personally have ivermectin on hand as well as many others I know. People are treating themselves at home trying to stay out of the hospital and avoid intubation. I personally have many relatives and friends who have successfully been treated with ivermectin in the past couple of months. Many are getting their ivermectin from another country due to our restrictions in America (The land of the free?). As a nurse of 30 years I have never seen anything like this. During the first days of covid, it is critical to get treatment on board. Patients come to the hospital and are sent home to rest and hydrate. No treatment until they return at a later date very sick and require hospitalization. I am pleading with you to let our trained professional doctors do what they do best! Research India. They are pretty much covid free and use ivermectin. Ivermectin has been used successfully by many doctors here in America. But many pharmacies block this prescription from being filled. Anyone involved in blocking this treatment has blood on their hands. This needs to stop. Please vote accordingly to allow doctors to give their patients a chance to live. I thank you for your consideration.
Please see attached article

https://www.thegatewaypundit.com/2022/01/dr-robert-malone-posts-irrefutable-proof-ivermectin-uttar-pradesh-india-success-story/

Gloria Surber

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Kisha Thompson
Sent: Tuesday, January 18, 2022 8:21:27 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 written testimony
Importance: Normal

Dear Committee,

I support HB1022. New Hampshire healthcare providers should have every potentially valuable therapeutic or pharmacological intervention at their disposal. Our providers must continue to have the freedom to personally observe and flexibly treat those under their care, which often includes applying off-label uses to medicines. Any restriction to the stocking, dispensing, and use of ivermectin hinders supporting health. Ivermectin has been used around the globe for several decades, and numerous studies have shown benefit in the prevention and treatment of mild through moderate COVID-19 disease: I've listed six recent studies below attesting to this. Ivermectin is off-patent and reasonably priced with a sufficient safety profile seen in widespread administration. Therefore, pharmacists should be permitted to dispense ivermectin via standing order. The novel COVID-19 pharmacologic therapies and vaccines do not consistently prevent transmission, decrease mortality, or prolong quality of life, and they are expensive. At all times, especially in a crisis, our New Hampshire healthcare providers must be unrestricted in their ability to use every therapy or medication at their disposal. Thank you for doing everything you can to support our health; we appreciate it.

Recent studies supporting the use of Ivermectin:

1. Azeez, T., Lakoh, S., Adeleke, A., Balogun, O., Olanipekun, B., & Olusola, F. (2021). Chemoprophylaxis against COVID-19 among health-care workers using Ivermectin in low- and middle-income countries: A systematic review and meta-analysis. *Indian Journal of Pharmacology, 53*(6), 493-498. https://doi.org/10.4103/ijp.ijp_117_21
2. Cobos-Campos, R., Apiñaniz, A., Parraza, N., Cordero, J., García, S., & Orruño, E. (2021). Potential use of ivermectin for the treatment and prophylaxis of SARS-CoV-2 infection. *Current Research in Translational Medicine, 69*(4), 103309. https://doi.org/10.1016/j.retram.2021.103309
3. Kory, P., Meduri, G. U., Varon, J., Iglesias, J., & Marik, P. E. (2021). Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. *American Journal of Therapeutics, 28*(3), e299-e318. https://doi.org/10.1097/MJT.0000000000001377
4. Kow, C. S., Merchant, H. A., Mustafa, Z. U., & Hasan, S. S. (2021). The association between the use of ivermectin and mortality in patients with COVID-19: a meta-analysis. *Pharmacological Reports, 73*(5), 1473-1479. https://doi.org/10.1007/s43440-021-00245-z
5. Santin, A. D., Scheim, D. E., McCullough, P. A., Yagisawa, M., & Borody, T. J. (2021). Ivermectin: A multifaceted drug of Nobel prize-honoured distinction with indicated efficacy against a new global scourge, COVID-19. *New Microbes & New Infections, 43*, N.PAG-N.PAG. https://doi.org/10.1016/j.nmni.2021.100924
6. Zein, A. F. M. Z., Sulistiyana, C. S., Raffaelo, W. M., & Pranata, R. (2021). Ivermectin and mortality in patients with COVID-19: A systematic review, meta-analysis, and meta-regression of randomized controlled trials. *Diabetes & Metabolic*

Syndrome: Clinical Research & Reviews, *15*(4), 102186. https://doi.org/10.1016/j.dsx.2021.102186

Warmest regards,

Kisha N. Thompson, MS, CRNA |she/her/hers|
Dwelling and working on the unceded ancestral lands of the Abenaki and Pennacook people.
email: kisha.lifgren@gmail.com
phone: 914-260-2218
LinkedIn: https://www.linkedin.com/in/kishathompson
I aim to build stronger relationships. If this email exchange can be handled in a brief phone conversation, I encourage you to call me. I look forward to hearing from you.

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Barbara Koehler
Sent: Tuesday, January 18, 2022 8:02:08 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Dear State Reps.,

Please, please pass HB1022 in NH. We have enough good, credible Doctors across the world who have proven that this drug works for COVID. Beyond that, you need to give our Doctors credit for knowing what they are doing more than some political party.

It has been shown that the most knowledgeable Doctors have stood by the use of Ivermectin, some even at the cost of losing their jobs and threatening their licenses. These Doctors took an oath to "do no harm" and to do all they can to help sick people. Let's not restrict their ability to do so, along with destroying the ability of a person to make their own choice.

Thank you, and please pass this legislation asap.

Barbara Koehler

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:37:17 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: In Opposition to HB1022 (Standing order to dispense Ivermectin) - Dr. Steve Williams
Importance: Normal
Attachments:
2021 10 20 _ Toxic Effects from Ivermectin Use Associated with Prevention and Treatment of Covid-19 _ NEJM Letter.pdf 2021 03 04 _ Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19_ A Randomized Clinical Trial _ JAMA.pdf

---

Members of the House HHS Committee,

Please see the forwarded message from Dr. Steve Williams in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Steven Jones <stevenclarkjones@gmail.com>
Sent: Sunday, January 16, 2022 9:38 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: In Opposition to HB1022 (Standing order to dispense Ivermectin)

Dear Mr. Padmore,

I oppose bill HB1022. Ivermectin is not a benign medication without side effects. (See attached letter to the editor from the New England Journal of Medicine, dated October 20, 2021.) It should not be dispensed without a proper indication. Furthermore, clinical trials have failed to consistently show any no benefit. (See attached JAMA article dated March 4, 2021.)

With no proven benefit in the length of time to improvement of symptoms of COVID-19, and with known toxic side effects, I do not support the dispensing of this drug to treat COVID-19.

Yours,
Steven Jones, MD, MPH
Exeter, NH

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Jennifer Watson
Sent: Tuesday, January 18, 2022 7:36:13 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support the use of Ivermectin
Importance: Normal

Dear Health, Human, and Elderly Services:

There is growing evidence that ivermectin, a very safe drug that has been in use for decades, has anti-viral properties and is being used successfully to help people recover from Covid. In a rather unusual and bizarre way, this inexpensive medicine has been denied to many Covid sufferers even if they have a legitimate prescription for it. This practice needs to stop, and pharmacists must be reassured that they can fill prescriptions for this medication without risking their licenses or in any way suffering repercussions for doing so.

Please support HB1022 which requires pharmacists to dispense this medication to people with Covid who have a prescription for it.

Thank you,
Joe and Jennifer Watson
Stephen and Christa Watson
188 Crockett Rd.
Laconia, NH

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:35:20 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: Ivermectin HB1022 - Opposition - Dr. Gus Emmick
Importance: Normal
Attachments:
Ivermectin_State.docx

Members of the House HHS Committee,

Please see the attached message from Dr. Gus Emmick in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: gge5472@comcast.net <gge5472@comcast.net>
Sent: Sunday, January 16, 2022 3:37 PM
To: Michael Padmore <Michael.Padmore@nhms.org>
Cc: gans71@comcast.net <gans71@comcast.net>
Subject: Ivermectin

Archived: Thursday, January 20, 2022 11:12:24 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:34:43 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: 18 Jan 2 pm - HB1022 Opposition - Dr. Dan Collison
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Dan Collison in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Dan Collison <dan.collison@gmail.com>
Sent: Sunday, January 16, 2022 5:43 PM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: 18 Jan 2 pm

Hi Mike,

I signed in to oppose ivermectin being dispensed by pharmacists. Do I need to attend, or is it enough to express disapproval?

I am a dermatologist, a specialty that deals with patients with diseases due to viruses, parasites and other infectious causes. Ivermectin is a medicine we prescribe.

It is entirely inappropriate for the Legislature to carve out legislation for drugs with systemic effects without the patient being under the care of a physician.

Dan Collison

Archived: Thursday, January 20, 2022 11:12:25 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:33:42 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: HB1022 Opposition - Dr. Mark Szal
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Mark Szal in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Mark Szal <mszal@cecnh.com>
Sent: Monday, January 17, 2022 2:01 PM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: HB1022

This is a dangerous bill and a dangerous precedent. Ivermectin should only be available by a doctor's prescription. Pharmacists should not be granted a standing order for a potentially dangerous prescription medication. There is no need for ivermectin to be more available than it currently is. It will not help with the covid epidemic.
Mark Szal, MD

Archived: Thursday, January 20, 2022 11:12:25 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:33:30 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: HB1022 Opposition - Dr. Ken DolKart
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Ken Dolkart in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Kenneth Dolkart <kenneth.dolkart@gmail.com>
Sent: Monday, January 17, 2022 12:32 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: Greetings and HB1022

Hi Mike - I suspect you will have lots of comments for opposition to HB1022. Enclosed is my reaction to this.

Dear Representatives
Why believe scientists about covid vaccines, ivermectin or any other issue? Perhaps, because scientists are the first to admit that "we are ignorant but curious about that" and are the ones performing the daily research that's led to remarkable medical achievements over the past 200 years. Such research over the past 4 decades prepared the way for the remarkable mRNA vaccines whose track record clearly demonstrates reduced death and hospitalization from this virus, even in the face of changing variants. An overwhelming consensus of vaccine benefit is shared by the people who do this for a living. This includes the medical virologists, infectious disease specialists, the critical care nurses and clinicians in our ICUs who are stressed with the volumes of mostly unvaccinated covid patients, doctors who observe this daily and epidemiologists. These are the same researchers and clinicians who developed the vaccines that eliminated smallpox and reduced parent's anxieties over their children suffering with polio and other serious childhood diseases. It's a fact that these vaccines are remarkably effective. But we now live in a world of "alternative facts."

So, isn't it statistically interesting that the very same non-scientist believers in hydroxychloroquine and invermectin are also the same disbelievers in the benefits of mRNA vaccines to protect the public? Such facebook warriors are rarely the people who actively care for those sick with this novel virus and certainly not the folks who do and study the research. Studies on invermection indeed have been performed by viral biochemists and clinical researchers, and again their consensus is, even at toxic levels conceivably achievable in the bloodstream, that the drug is clinically worthless against covid-19. This misguided bill states:"Nothing on the information sheet shall discourage the recipient from using ivermectin for the treatment of COVID-19" but that is medical malpractice. If House Representatives wish to start practicing bad medicine without a license, then they should be prosecuted for impersonating clinicians. Not that long ago, a political well of support may have demanded that laetrile be provided by standing orders for cancer patients, and the same can apply for various unproven remedies. And if they are not so prosecuted, then they should be held liable for any deaths or hospitalizations resulting from covid among people who were persuaded to avoid genuine prevention and treatment, or any consequences of toxicity from unwarranted "medical treatment by politician."
Respectfully

Ken Dolkart MD FACP

Archived: Thursday, January 20, 2022 11:12:25 AM
From: Renee Broze
Sent: Tuesday, January 18, 2022 6:44:14 AM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

I am writing to oppose this bill. Ivermectin is not an approved or recommended therapy for covid-19. Making it available without a prescription will certainly make the manufacturer a lot of money, as well as encourage people who have active Covid-19 to be out shopping for it, exposing more people to the virus. Ivermectin is a medicine for parasites. Covid-19 is a virus. Some may argue that covid is not the reason why this bill is being considered, but to allow a bill like this to pass at the height of the pandemic is irresponsible and unethical. Furthermore, prior to the pandemic, this was a rarely prescribed medication because we have good sanitation and drinking water. Ivermectin is in my dogs flea and tick medicine. I require at veterinary prescription to purchase it.
Renee Broze MSN, RN, NP-C

Archived: Thursday, January 20, 2022 11:12:25 AM
From: Joseph Mirzoeff
Sent: Tuesday, January 18, 2022 6:34:08 AM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

In Cheshire County, where I live there were 7 COVID deaths in 2020 the year that created an "emergency". In 2021, the year of the inoculations 65 died with COVID. In the first two weeks of 2022 14 died with COVID. Clearly there is more of an emergency now and the governments and medical leadership have failed us. Please facilitate our ability to protect ourselves. Live Free or Die has never been more true.

Archived: Thursday, January 20, 2022 11:12:25 AM
From: D S
Sent: Tuesday, January 18, 2022 5:28:42 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

To Whom it May Concern,

Please support the bill presented which will see that Pharmacists dispense Ivermectin.

Thank you.

Julia Sharpton
Sent from Yahoo Mail on Android

Archived: Thursday, January 20, 2022 11:12:25 AM
From: Donna Kendrick
Sent: Tuesday, January 18, 2022 2:50:26 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Bills
Importance: Normal

Hi please support HB1022 it is obvious therapeutics are being withheld for too long. Please support this bill.
Please oppose HB 1369 No place has the right to impose experimental invasive treatments on their customers. Thankyou.

Sent from my iPhone
Donna Kendrick

Archived: Thursday, January 20, 2022 11:12:25 AM
From: Elizabeth Lidman
Sent: Monday, January 17, 2022 11:01:23 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please Support HB1022
Importance: Normal

Dear Committee Members,

Please support HB1022 allowing pharmacists to dispense ivermectin with a standing order. People should be able to access the drugs that they need especially during a pandemic.

Sincerely,
Elizabeth Sylvia
Nashua, NH

Archived: Thursday, January 20, 2022 11:12:25 AM
From: James Johnson
Sent: Monday, January 17, 2022 10:53:39 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

To the Health, Human Services and Elderly Affairs.
Dear Committee Members,
Please keep the government out of patient - doctor relationship. Please read https://www.scstatehouse.gov/CommitteeInfo/SenateMedicalAffairsCommittee/horse-dewormer-ivermectin-pdf.pdf
I ask this committee to consider the above article in it's entity. The contemplate why the government is encroaching on our personal lives.

Sincerely,
Jim Johnson
Brentwood NH

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Heather
Sent: Monday, January 17, 2022 10:23:45 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

To whom it may concern.

Please support HB1022

Decisions regarding prescriptions should be between a doctor and patient. Currently it is difficult to have a prescription for Ivermectin be fulfilled almost anywhere in NH. This Bill will eliminate that difficulty.

Thank you for your time.

Sincerely,

Mrs. Froumy

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Elizabeth Fleming
Sent: Monday, January 17, 2022 9:56:09 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Please **SUPPORT** this legislation.

Decisions regarding prescriptions should be between a doctor and patient. Currently it is difficult to have a prescription for Ivermectin be filled almost anywhere in NH. This Bill will eliminate that difficulty. There is now overwhelming evidence that Ivermectin is both SAFE and EFFECTIVE and could have saved thousands of lives if it was made available to patients. Pharmacists and doctors must be able to prescribe it to their patients and Pharmacists must make it available- IT COULD SAVE THEIR LIVES.

WHY WOULDN'T YOU SUPPORT THIS BILL??????????????????

E. FLeming

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Zeli B
Sent: Monday, January 17, 2022 9:34:43 PM
To: ~House Health Human Services and Elderly Affairs; ~House Election Law Committee
Subject: legislation
Importance: Normal

HB1022 - MANDATES PHARMACISTS MUST DISPENSE IVERMECTIN WHEN PRESCRIBED

Please **SUPPORT** this legislation.

WHY: Decisions regarding prescriptions should be between a doctor and patient. Currently it is difficult to have a prescription for Ivermectin be fulfilled almost anywhere in NH. This Bill will eliminate that difficulty.

Thankyou,

Hazel Bourassa

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Bonnie Faulkner
Sent: Monday, January 17, 2022 9:02:14 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

Good evening, Congressmen:
I am asking that you please support this legislation. The use of Ivermectin has saved many lives. If a doctor believes that a patient could benefit from this drug, and prevent the patient from being admitted to the hospital, then Ivermectin should be easily accessible. This will help our hospitals from being overwhelmed and save lives.

Thank you for your service and time.

Bonnie St.Onge

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Julie Laughner
Sent: Monday, January 17, 2022 8:54:34 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please vote OTP on HB1022
Importance: Normal

Hello,
Please vote OTP on this bill, to require pharmacists to fill ivermectin prescriptions. Decisions regarding prescriptions should be between a doctor and patient.

Thank you,
Julie Laughner
Raymond NH

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Linda McGrath
Sent: Monday, January 17, 2022 8:51:56 PM
To: ~House Health Human Services and Elderly Affairs
Subject: From a pharmacist for 40 years - HB1022
Importance: Normal

Never in my 40 years as a pharmacist have I been blocked from dispensing an RX for an approved medication…for an "off label use"!
It is unbelievable to me.
The doctor knows that Ivermectin is safe, it is one of the safest medications on the market, safer than Tylenol!
Please support
HB1022 - **MANDATES PHARMACISTS MUST DISPENSE IVERMECTIN WHEN PRESCRIBED**
Pharmacist WANT to dispense this much needed medication but are being blocked, we need your support.

WHAT IS AN OFF LABEL USE?
For instance the blood pressure medication propranolol was found to stop migraines in patients with high blood pressure AND migraines…HENCE doctors started prescribing it for headaches although it was not tested for this condition…off label...doctors knew it was safe.

Thank you for your consideration
Linda McGrath
Hampton, NH

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Nina Mucha
Sent: Monday, January 17, 2022 8:51:40 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

I urge your support for this bill. Ivermectin is a safe, antiviral that works. There is voluminous data that supports this. FLCCC has the data. Most importantly my health care is between me and my physicians. Not a administration. Ivermectin is an approved drug. There is no issue to prescribe this.

Sent from my iPhone
Nina Mucha
518-796-8697

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Janet Aveni
Sent: Monday, January 17, 2022 8:46:12 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

Please support this bill. I had Covid recently, was treated with Ivermectin as well as Quercetin, Vitamins D and C, and Zinc. I recovered quickly and fully. This is an inexpensive, safe medicine that is well documented and researched to be effective in treating viruses including Covid 19. NH hospitals are overwhelmed with Covid patients that are not allowed this treatment. Too many people have died due to lack of access to this life saving medicine. I have many friends that have the same experience with Ivermectin. Please support this bill.
Thank you for your time and attention,
Janet Surman
Spofford, NH
603-313-3158

Sent from Yahoo Mail on Android

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Janet Aveni
Sent: Monday, January 17, 2022 8:24:06 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

Please support this bill. I had Covid recently, was treated with Ivermectin as well as Quercetin, Vitamins D and C, and Zinc. I recovered quickly and fully. This is an inexpensive, safe medicine that is well documented and researched to be effective in treating viruses including Covid 19. NH hospitals are overwhelmed with Covid patients that are not allowed this treatment. Too many people have died due to lack of access to this life saving medicine. I have many friends that have the same experience with Ivermectin. Please support this bill.
Thank you for your time and attention,
Janet Surman
Spofford, NH
603-313-3158

Archived: Thursday, January 20, 2022 11:12:26 AM
From: Donna F.
Sent: Monday, January 17, 2022 7:29:55 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Vote Yes for HB1022
Importance: Normal

Dear Committee :Representative Leaders:

We are concerned with saving lives and Ivermectin has effectively curtailed Covid demise in many people. The results and research show it to be a most desirable treatment for Covid. It is anti-viral and anti-inflammatory. Numerous ethical and responsible physicians have treated patients successfully.
Moreover, citizens should have the right to decide what treatment he/she will take. Doctors should have the right to recommend and/or prescribe Ivermectin to patients who seek treatment that has potentially positive results.

I am shocked at those who would thwart the freedom of this health choice especially when it has proven to prevent demise in patients who have not responded to other treatments. This bill will ensure that pharmacists must dispense Ivermectin when prescribed.

I strongly urge you to protect the rights of doctors and patients to seek Ivermectin treatments that may save their lives and/or decrease the severity of Covid symptoms.

Sincerely Yours,
Donna Ferrantello, Ph.D.
84 Woodland Ave.
Keene, NH 03431

Archived: Thursday, January 20, 2022 11:12:27 AM
From: Peter Geremia
Sent: Monday, January 17, 2022 7:25:58 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 and HB1369
Importance: Normal

Hello,

I am urging you to please **SUPPORT HB1022** which permits pharmacists to dispense Ivermectin. To me it is unbelievable that our PRESS and even many in healthcare paint that drug as dangerous when we see time and time again how many lives it is saving. Do you realize how many stories of people on their death bed and hospitals DENY the use of this drug resulting in someone dying from Covid that did not have to die? And there are other stories of COURT ORDERS being required to FORCE hospitals to allow the use of Ivermectin SAVING these patients lives. Quite honestly I never believed that partisan HEALTHCARE would be a THING here in the USA!!! There should be NO POLITICS HERE. The DRUG WORKS!! Please do not allow more people to die!

I am also urging you to **OPPOSE HB1369** which would allow performing arts Venus to create their OWN COVID protocols including requiring vaccination cards in order to attend. I think at this point in the pandemic it is 100% clear vaccinated or not COVID will be spreading. You cannot stop it and thus this type of bill will basically BAN a group based on a personal health decision for what reason???? That is wrong and against everything NH stands for. Please please please OPPOSE HB1369.

Thank you for your consideration.

Peter P. Geremia
315 Maplewood Ave.
Portsmouth, NH 03801
603-531-3102

Archived: Thursday, January 20, 2022 11:12:27 AM
From: Terry
Sent: Monday, January 17, 2022 7:10:42 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Dear Members,

Please consider the personal relationship for a patient and their doctor when the doctor makes a decision to prescribe any medication. It's imperative that you respect the patient-doctor relationships and allow pharmacies the ability to fulfill their obligations as well.
If there are options for treatment no one should be denied,
Please consider this bill with your own health and family's health in the greatest regard. We should all be allowed to choose our own course in life.

Regards,
Theresa Chabot
New Hampshire

Sent from Yahoo Mail for iPhone

Archived: Thursday, January 20, 2022 11:12:27 AM
From: J
Sent: Monday, January 17, 2022 6:58:01 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please SUPPORT HB1022
Importance: Normal

Dear Committee members,

Please support HB1022 to allow pharmacies to make available Ivermectin to the public. I believe it is the decision of a person and his or her doctor as to what is best for that person. A pharmacy should not have the authority to keep medications/treatments away from people and interfere with that physician/patient relationship.

Thank you for supporting HB1022!

Sincerely,

Janice Hagenow
Warner Resident

Archived: Thursday, January 20, 2022 11:12:27 AM
From: Greg Marshall
Sent: Monday, January 17, 2022 6:29:00 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

My father was not feeling good a couple days before Thanksgiving so he waited a couple days and mom took him to Exeter hospital on Thanksgiving and they told him he had covid!I was wondering why none of us had it and he had just gotten his booster a few weeks before?My dad was sent home after 5hrs so I figured he was ok but a few more days not eating or drinking and mom tried another hospital Portsmouth but after 4 days there his heart couldn't take two weeks of covid!I know the morning he told me he didn't feel right last night and wasn't going deer hunting he could have been easily saved within that week but NH following the rules of the terrible protocol of Dr Death Fauci didn't have ivermectin or hydroxy chloroquine available!!!!!I'm very pissed off with the state of NH and the support of the hospitals making cash off death!You the state of NH have BLOOD on your hands and I want revenge!I pray you read this to everyone there!Greg Marshall. PS I talked to a Dr and he was told that he would be fired if he gave out a prescription for ivermectin,what the hell kinda world are we living in when a Dr can't treat a patient like he thinks he should?I can not bring my dad back and I hate my state now!!!!!!

Archived: Thursday, January 20, 2022 11:12:27 AM
From: mbwadlinger@gmail.com
Sent: Monday, January 17, 2022 11:38:34 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please help your people!
Importance: Normal

Please support HB1022 permitting pharmacists to dispense ivermectin in NH. There is so much good data on this drug being an effective tool against covid19. It is a safe drug that has been used by human beings for decades.

Also please oppose HB1369 - no vax passes in our state!

Sincerely,
Marybeth Wadlinger
Wolfeboro, NH

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:12:27 AM
From: Hershel Nunez
Sent: Monday, January 17, 2022 11:29:08 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Testimony and support documents for HB1022
Importance: Normal
Attachments:
Testimony HB1022 - Ivermectin.odt LCCC-Protocols-–-A-Guide-to-the-Management-of-COVID-19(1).pdf Ivermectin_for_Prevention_and_Treatment_of.7.pdf

---

I plan to give testimony tomorrow at the hearing for HB1022 - permitting pharmacists to dispense the drug Ivermectin by means of standing order.

I do not want to give handouts during the testimony so as not to approach the committee members. But I will be there to testify in person.

Thank you for the opportunity.

Hon. R. Hershel Nunez, Jr.
State Representative
New Hampshire General Court
Hillsborough County District 37
Pelham/Hudson
603-260-9630 (cell)

Archived: Thursday, January 20, 2022 11:12:27 AM
From: paulbabb@protonmail.com
Sent: Monday, January 17, 2022 10:07:59 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Please support HB1022. Both my wife and I contracted covid at the end of December. We used a low dose of Ivermectin as well as zinc and quercetin. We recovered within a couple of days. We know many people who safely and successfully used the same protocol.

Sincerely,

Paul and Julie Babb
Antrim NH

Sent from ProtonMail mobile

Archived: Thursday, January 20, 2022 11:12:27 AM
From: Bikers
Sent: Monday, January 17, 2022 9:47:04 AM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

Please follow the science and uphold our constitution, your oath, and pass this bill. Ivermectin is safer than most medication currently available over the counter, and it has been proven effective in both prevention and treatment of COVID-19.
Thank you for taking this opportunity to show integrity!
Lucy Roy
North Hampton, NH

Sent from my iPad

Archived: Thursday, January 20, 2022 11:12:27 AM
From: danbatten
Sent: Monday, January 17, 2022 9:15:57 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

Dear Legislators,

I urge you to support this bill that protects doctors and pharmacists from disciplinary action by their medical boards and allows doctors to practice long standing tradition in their field to use off label drugs to treat their patients as they see fit in accordance to professional standards.

Yours in liberty,
Dan Batten
Ossipee, NH

Archived: Thursday, January 20, 2022 11:12:28 AM
From: Vanessa Fortini
Sent: Monday, January 17, 2022 9:04:02 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Hearing on Tuesday
Importance: Normal

Good morning
I'm writing you to request that you support HB1022 and to oppose 1369.

Thank you for your help
Vanessa Fortini

Archived: Thursday, January 20, 2022 11:12:28 AM
From: Alan Graustein
Sent: Sunday, January 16, 2022 8:16:55 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

Please support HB1022 and allow NH citizens to make their own medical decisions.

Thank you,

Alan Graustein
Sanbornton, NH

Archived: Thursday, January 20, 2022 11:12:28 AM
From: Jeri Kauffman
Sent: Sunday, January 16, 2022 9:26:19 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Hello,

I'm writing to share my support for this bill. I believe a person should have the availability of ivermectin.

Thank you,
Jeri Kauffman
Laconia NH

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:12:28 AM
From: Aaron Neskey
Sent: Saturday, January 15, 2022 7:52:21 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

I tested positive for Covid on the 24th, December 2021. Promptly got ivermectin through a telehealth appointment, from a Dr in Florida. Started my course of ivermectin on the second day of being positive for covid. The only symptoms I ever endured where a temperature, up to 102°F ar night, and very mild congestion in my chest. Not once was I bed ridden. My O2 never dropped below 94%, my lung capacity never got lower than 2500mL. By my 5th day, my fever was gone. I do believe that having ivermectin available over the counter would help drastically in the reduction of covid deaths.

Archived: Thursday, January 20, 2022 11:12:28 AM
From: Matt Ferreira
Sent: Saturday, January 15, 2022 3:30:21 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Hello,
I am writing in support of HB1022, permitting pharmacists to dispense the drug ivermectin by means of a standing order.

There are over 140 Ivermectin COVID-19 studies, including 90 that have been peer-reviewed. Ivermectin shows significant improvements when used as a prophylactic or as an early or late treatment. I've personally taken it to treat COVID-19 and can attest that it works.

It makes no sense why NH residents have to get Ivermectin prescriptions filled and sent from a pharmacy in the free state of Florida or another state that allows it. Disallowing pharmacists to fill Ivermectin orders here is suppression of a proven treatment for COVID-19. I urge you to support and pass HB1022.

Regards,
Matt Ferreira

Archived: Thursday, January 20, 2022 11:12:28 AM
From: Leane Romano
Sent: Saturday, January 15, 2022 3:20:12 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

I am in support of this bill. There is no reason why pharmacist should not be able to dispense this 2015 Nobel prize winning medication that has been being used successfully off label to treat Covid 19. It is well known that a City in India successfully treated their citizens when a huge surge of cases broke out. The medication treated those that got Covid and they recovered. This medication was also given to healthcare workers as a prophylactic when they worked with positive patients in Brazil it was almost 100% effective in preventing the virus. If this is really about health then why is this medication being stopped from being available? Doctors should not be told what to prescribe and we should be able to use the right to try in our own medical decisions. People have gotten ivermectin in their time of need and have recovered. How are the other protocols working? They are not! Open your eyes vote to allow this medication to be available. If this doesn't pass why? We have worse allowed medications over the counter than this and the FDA approves unsafe things all the time.
Thank you
Leane Romano

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:12:28 AM
From: ashmay723@gmail.com
Sent: Friday, January 14, 2022 8:56:06 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

Yes, I support HB1022.

Ashley Hudson

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:12:28 AM
From: L Patrick
Sent: Friday, January 14, 2022 7:55:44 PM
To: ~House Health Human Services and Elderly Affairs
Subject: In SUPPORT HB1022
Importance: High

Good Evening,

As a longtime resident of Strafford, NH, also as a provider in healthcare, I am requesting All members to Vote YES to support HB1022 on Tuesday, January 18, 2022. Ivermectin is a life saving treatment which should be fully available to all New Hampshire citizens as well as all US citizens.

Respectfully,

Laura Patrick RN, MSN

Archived: Thursday, January 20, 2022 11:12:29 AM
From: Beth
Sent: Friday, January 14, 2022 7:22:24 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

As a concerned citizen in New Hampshire I am requesting that you support Bill HB1022.
Thank you
Sent from my iPhone

Archived: Thursday, January 20, 2022 11:12:29 AM
From: Patti Anastasia
Sent: Friday, January 14, 2022 4:20:17 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Testimony for House Health, Human Services, and Elderly Affairs hearings January 18
Importance: Normal

Dear Committee,

Here is my testimony for bills in your January 18 hearings. Please take this into consideration as you discuss these bills.

HB1609 relative to the scope of the fetal protection act.

I SUPPORT this bill. While I am opposed to legislating a woman's right to choose whether to continue or end a pregnancy, at least the change HB 1609 would make to RSA 329:44 are less repugnant than the law is as it stands. HSA 329:44 needs to be revoked, but in the meantime, this bill addresses some of the horrific clauses in the law.

HB1327 including diabetes in the conditions listed for eligibility for a service animal.

I SUPPORT this bill.

HB1139 relative to ophthalmic prescription requirements.

I SUPPORT this bill. This bill will provide patients with all of the information necessary to fill an ophthalmic prescription at the service provide of their choice.

HB1022 permitting pharmacists to dispense the drug ivermectin by means of a standing order.

I OPPOSE this bill. This bill is a slippery slope. It could easily precipitate an avalanche of similar bills that permit or require pharmacists to dispense drugs that have no scientific studies that support the use of the drug to treat a particular illness.

HB1369 relative to COVID-19 health and safety policies at New Hampshire performing arts venues.

I SUPPORT this bill. All businesses should have the right to set their own health and safety policies.

Regards,
Patricia Anastasia
50 Holstein Avenue
Londonderry, NH

Archived: Thursday, January 20, 2022 11:01:14 AM
From: JaniceBelmont
Sent: Wednesday, January 19, 2022 11:31:33 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Please support this bill!!
Thank you!
Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:14 AM
From: Anthony Amato
Sent: Wednesday, January 19, 2022 7:50:38 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

I want ivermectin available for my family. I want HB 1022 passed.

A. Frank Amato
Hooksett

Archived: Thursday, January 20, 2022 11:01:14 AM
From: Keith
Sent: Wednesday, January 19, 2022 6:47:05 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB 1022 to allow patients to receive Covid-19 medication
Importance: Normal

Dear Committee Members,

With Covid-19 cases on the rise because as multiple studies have shown, the vaccine doesn't protect well against the new Covid-19 variant, something must be done. More than 1000 vaccinated NH health care workers aren't working because they have the virus. Multiple pharmaceutical companies are making pills that mimic the efforts of ivermectin. Like ivermectin, these pills have shown some promise at treating Covid-19. However, the pills are very new, and in shorter supply than ivermectin. Please allow Covid-19 patients to get ivermectin early, when it is shown to be most effective, by supporting HB 1022. If even one death is prevented, you will be a hero!

Respectfully,
Keith Carlsen
Manchester
997-1446

Archived: Thursday, January 20, 2022 11:01:14 AM
From: J
Sent: Wednesday, January 19, 2022 6:03:30 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 Ivermectin
Importance: Normal

Dear Committee Members,

Please support HB 1022 regarding the ability for pharmacies to honor doctor's prescriptions for Ivermectin.

Thank you so much! It's good to have options in medical treatments and keep our freedom to choose.

God bless,

Janice Hagenow
Warner Resident

Archived: Thursday, January 20, 2022 11:01:14 AM
From: Nancy Brennan
Sent: Wednesday, January 19, 2022 5:48:55 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Dear Committee Members:

After listening to yesterday's hearing on HB 1022, a bill that would allow Ivermectin to be dispensed over the counter, I ask the committee to check the background of some of those who spoke as experts. As difficult as it seems to separate fact from fiction these days, I urge the committee to try to do just that as you work towards making a decision on this bill.

Dr. Marik was presented as an expert on the use of ivermectin for covid. I imagine he was invited by the bill's primary sponsor, but he may have come on his own. His testimony should be viewed with some skepticism. Early in the pandemic, he touted chloroquine and hydroxychloroquine as treatments for covid. Trials later showed they were not effective. His current covid protocol added ivermectin to a combination of vitamins he had previously used as a "cure" for sepsis. That sepsis treatment failed a large study and is no longer being used. The statistics and studies he used for support of ivermectin treatment and those the prime sponsor of the bill alluded to should be researched for accuracy before a decision is made on this bill.

Business Insider magazine is considered a factually accurate and non-partisan publication. Its analysis of Dr. Marik may give you pause before you accept his testimony as absolute fact.

https://www.businessinsider.com/why-ivermectin-being-used-treat-covid-2-doctors-leading-charge-2021-9

The problem with conspiracy theories and miracle cures is that they spread on social media and take on a life of their own before they can be disproven. To paraphrase a well-known saying, "A conspiracy theory can travel halfway around the world while the scientific truth is putting on its shoes."

We all hope for a cure or an easy treatment for this current pandemic. How wonderful it would be if it proves to be an inexpensive medicine we already have! But wishing won't make that a reality. Please take the time to study the facts. If you do, I expect you will vote ITL or send it for interim study.

Nancy Brennan, Weare

Archived: Thursday, January 20, 2022 11:01:14 AM
From: bobdutton@aol.com
Sent: Wednesday, January 19, 2022 5:26:50 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB1022, Ivermectin WORKS!!!
Importance: Normal

Dear Committee members, Please support HB 1022 so that NH residents can reap the benefits of Ivermectin. It really does work, it has worked for my family and it would have saved 1,000's of lives if the CDC and FDA hadn't conspired to keep it out of the hands of Americans. Regards, Bob & Bibbs Dutton

Archived: Thursday, January 20, 2022 11:01:14 AM
From: Pam DiNapoli
Sent: Wednesday, January 19, 2022 1:37:00 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Good afternoon Chair Pearson and members of the HHSEA committee
I attended the hearing for HB 1022 yesterday and had signed in to testify and I had submitted a position statement representing the nurses of New Hampshire as executive director of the NH Nurses Association.
Unfortunately because of all of the important work your committee attended to yesterday I had to leave the chamber at 445PM to host an important NHNA Board Meeting.
Listening to the testimony yesterday I wanted to applaud questions and comments by Dr Knirk, Dr Salloway and Dr Woods. The ability to discriminate quality data from invalid data in support of this bill was a key point that I hope was not lost on the committee.
I wanted to highlight some of the key points in my testimony that were supported by the other opponents of this bill including Dr Nick Prevenchovitch who spoke eloquently about the need for further randomized clinical trials before moving this drug to what essentially would be over the counter use. The proponents of this bill are correct that this is a "good drug" but it is not approved for Covid 19 treatment or prevention. As new drugs come to market after robust clinical trials I encourage the committee to oppose this bill so as not to let "experimental drugs" become the norm over the use of prevention and treatments that have undergone efficacy trials such as vaccine use and simple infection control measures such as social distancing masks and hand washing
Thank you for your consideration
Pam D

Pamela P DiNapoli, PhD, RN, CNL
Executive Director
25 Hall Street Suite 1E
Concord, NH 03301
(603)225-3783
(603) 566-7407 Cell
nhna.ned@gmail.com

Archived: Thursday, January 20, 2022 11:01:14 AM
From: David Kiley, CPA
Sent: Wednesday, January 19, 2022 1:13:15 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Ivermectin Access Support HB 1022
Importance: Normal

Dear Honorable Reps,

I have been aware of protease inhibitors for nearly 18 months, having been made aware through the Nobel Prize candidate Vlad Zelenko's work with HCQ and Ivermectin.

As such, I have included in my prevention protocols with Quercetin, as the more powerful preventatives Ivermectin and HCQ have been demonized, censored, and made unavailable to me through influences that likely were designed to reduce vaccine hesitancy and leave patients without prophylactic options.

While potentially noble in it's reasoning, hiding the truth has caused harm and prevented thousands protecting their own lives. I would encourage you to do independent research on the efficacy of these inexpensive treatments that are used globally for decades.

Please support HB 1022 and begin the process of healing our state.

--
Regards,

David Kiley, Atkinson 978-505-5499

Archived: Thursday, January 20, 2022 11:01:14 AM
From: Danielle Snow
Sent: Wednesday, January 19, 2022 9:40:02 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB 1022!
Importance: Normal

Daily we are learning more information about Covid and the vaccines. Drugs that WORK have been kept from the people.. people have died and suffered as a result. I urge you to do the right thing by the people New Hampshire and support HB 1022.
Danielle Snow

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:14 AM
From: Brittany Mahoney
Sent: Tuesday, January 18, 2022 8:12:40 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022 testimony
Importance: Normal

Representatives,

Thank you for your time in considering this important matter.

I will try to be brief. My family contracted COVID-19 in early December of 2021. My son and I showed symptoms first. We managed our illness with vitamins for about 3 days before I decided to test for COVID. Immediately upon getting a positive I started taking the ivermectin I have had set aside in my cabinet. I also put my husband on the prophylactic dose for close contact laid out in the FLCCC guidelines.

At that point I had a fairly mild cough and catch in my larynx. When I woke up the morning after my first dose that catching feeling was gone. The next morning my cough was significantly reduced. I continued to take it and feel that I was benefiting from it throughout my infection. I never felt congestion in my lungs, my O2 stats never fell below 94%. My infection ran a fairly typical course with feeling better for a few days and then feeling worse around day 8, struggling with fever and exhaustion. Thankfully, with the ivermectin, the zpack my doctor prescribed and some iv vitamin therapy I made a full recovery.

My husband, as I said took a preventative low dose every other day during the time I was sick and he wasn't. As soon as he tested positive himself, about a week after I did, we bumped him up to the full dose for infection. His case was, by far, the most mild case of anyone in our family. Our children who were treated with vitamin therapy, myself who began ivermectin on day 3 or 4, and my husband who had it before his active infection. He never had the relapsing symptoms around day 8. The worst part of COVID for him was missing work when he felt perfectly fine the last 7 days of his quarantine. His illness consisted of 3 days of body aches and some fatigue. He never ran a fever, never had a cough, He also took significantly fewer vitamin therapies because he just doesn't think of it.

Neither one of us had any side effects from taking the ivermectin.

Please vote "ought to pass" on this bill so people can easily access this life-saving medication.

Thank you,
Brittany Mahoney
Resident of Manchester, NH

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Linda F. Wade
Sent: Tuesday, January 18, 2022 7:26:58 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please Support House Bill 1022 to Save Lives of New Hampshire Residents
Importance: Normal

Dear Committee of Health, Human Services, and Elderly Affairs:

I am a life-long New Hampshire resident asking you to please save the lives of the residents of New Hampshire by supporting House Bill 1022. HB1022, as you know, will allow pharmacists to dispense Ivermectin, by means of a standing order, and as an over-the-counter medication for Granite Staters. Granite Staters who wish to use Ivermectin, which is FDA approved, are having a very difficult time getting Ivermectin from overseas, if they develop sudden symptoms of COV-19. It can take weeks or even months for them to receive it, and by then their condition can be critical. If the US Postal Service is allowed to confiscate Ivermectin shipments, these people lose the money they paid, but more importantly, their lives.

An unclassified document dated August 13, 2021 by the Defense Advanced Research Projects Agency, written by Commandant of the Marine Corps Fellow, Joseph Murphy is available for your review with a FOIA request. This document states that Ivermectin is "curative" of COVID-19 and "works throughout all phases of the illness because it both inhibits viral replication and modulates the immune response."

On July 8, 2021, the National Institute of Health (NIH) listed Ivermectin as an approved medication for the treatment of COVID-19 in Table 2e. "Characteristics of Antiviral Agents That Are Approved or Under Evaluation for the Treatment of COVID-19". It also listed Ivermectin as safe--"Generally well tolerated." This table was completely removed for political reasons once patients began bringing it to hospitals to request this treatment for their dying relatives. The chart's URL was:
https://www.covid19treatmentguidelines.nih.gov/tables/table-2e/

My cousin recently passed away on December 30, 2021, in the Portsmouth Hospital, Portsmouth, New Hampshire from COVID. I believe his lungs were drowning, because he was on a ventilator for 11 days. I believe he was fighting for his life, because he had a wife, children, and grandchildren whom he wanted to stay alive for. The Portsmouth Hospital did not give Ivermectin to my cousin, as it is not part of hospital protocol anywhere in the State of New Hampshire, as far as I know. I believe my cousin's life was cut short

prematurely, because of the medical staff at Portsmouth Hospital not keeping to the medical oath they took to “Do No Harm”.

People on their death beds who have been given Ivermectin have recovered within a very short time and lived. We all know that COVID patients on Remdesivir and on ventilators in the hospital are dying by the fifth day they are on a ventilator.

Please refer to this link for the Front Line COVID-19 Critical Care Alliance (FLCCC). https://covid19criticalcare.com/ivermectin-in-covid-19/

This life-saving option of Ivermectin should not require New Hampshire residents, in our “Live Free or Die” state, to have to lose their lives because they cannot procure Ivermectin in an emergency situation.

As such, I am imploring your Committee to please support HB1022 and thus protect New Hampshire residents in their Constitutional right to make their own health care choices. God bless you for doing the right thing.

Respectfully Submitted,

Linda F. Wade
North Hampton, NH

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Linda Rea Camarota
Sent: Tuesday, January 18, 2022 2:44:26 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022 testimony - standing order for Ivermectin
Importance: Normal

HHS Committee members,
Please find attached today's testimony for your perusal.
Thank you for your service.
Hon. Linda Rea Camarota, RN

HB 1022 standing order for iv…

HB 1022 standing order for ivermectin

--

Hon. Linda Rea Camarota
State Representative 2018-2020
NH General Court
Hillsborough County - District 7
Bedford

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Crissy Kantor
Sent: Tuesday, January 18, 2022 2:06:42 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support NB1022
Importance: Normal

Please support HB1022, Ivermectin is a life saving drug in the fight against covid!
Americasfrontlinedoctors.org have been prescribing it to patients for a long time. It works.
Currently it is difficult to have a prescription for Ivermectin be fulfilled almost anywhere in NH.
This Bill will eliminate that difficulty. Please support HB 1022
Thank you so much!!!
Grateful American:)
Peace Love & chill

Crissy Kantor
Founder/Creative Director

chill | SPA
complete beauty and well-being

1224 Hanover Street
Manchester, NH 03104
(603) 622-3722 chill
(603) 682-3087 cell
crissy@chillspa.com
http://chillspa.com

http://chillcares.org
http://chilluniverse.com

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Donald Ewing
Sent: Tuesday, January 18, 2022 1:38:38 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: Please support and recommend passage of HB 1022
Importance: Normal

I urge you to vote for and recommend passage of HB 1022. It's time that we provide Covid treatments that people can use early before the virus builds up to drive people to hospitals and become life threatening. Ivermectin has been shown in about 60 tests to help reduce hospitalizations and deaths.

Even if you believe that Ivermectin is not a perfect solution, it is far better than the treatments, or more accurately the lack of treatments, that have been provided for Covid-19 resulting in so many deaths.

One has to wonder with all the money we spend on health why only 18 countries in the world (see www.worldometer.com) have greater death rates than the US. The current approaches identified by our national health authorities are killing hundreds of thousands of Americans needlessly. It is time to change our approach.

The Nobel Prize was given for the creation of Ivermectin. It has been used widely in the world and to some extent in the US, successfully. It was reported as prescribed 800,000 times in the US in 2018.

Ivermectin is as safe as or safer than any drug that people take. The list of side effects of Aspirin is three to four times as long and dangerous as for Ivermectin. The list of side effects of my statin drug is two to three times as long and dangerous.

Ivermectin has been used effectively to treat Covid-19 around the world to greatly cut hospitalizations and death. E.g., here's a link to the results of the use of Ivermectin in Mexico City. Here are two articles about successful use of Ivermectin in India: https://newsrescue.com/the-undeniable-ivermectin-miracle-indias-240m-populated-largest-state-uttar-pradesh-horowitz/ And
https://www.rebelnews.com/doctor_discusses_ivermectin_success_in_india_questions_canadas_covid_approach

It seems only the "first world" is hesitant to use a cheap, safe, and effective drug because it hasn't been through a full study conducted by the American health bureaucracy even though Ivermectin has been used successfully many thousands of times. It seems our health bureaucracy is only interested in expensive and scarce drugs, whether they live up to their promises or not. Remember what we were promised about the vaccines?

Please support passage of HB 1022 and give sick patients a chance for quick recovery.

Thank you,

Don Ewing
Meredith, NH

Archived: Thursday, January 20, 2022 11:01:15 AM
From: cra2
Sent: Tuesday, January 18, 2022 1:00:18 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

I wish to express my support for this Bill. Craig Hadley Thank you

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Deb Roux
Sent: Tuesday, January 18, 2022 12:56:24 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB 1022
Importance: Normal

Hello!

Please support HB 1022 and let our doctors decide what type of treatment we the people need. They have our medical records and know what is best for us, their patients.
Politicians/Government do not.

Thank you!

Deb

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Deb Roux
Sent: Tuesday, January 18, 2022 12:49:24 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB 1022
Importance: Normal

Hello!

Please support HB 1022 and let our doctors decide what type of treatment we the people need.

Politicians are not doctors. Medical treatment should not be politicized like it is right now.

We the people of NH have a strong state motto, live free or die. We want to be free to decide, along with our doctors, how to best treat ourselves when needed. Doctors should not be afraid to treat their patients. My doctor said she could loose her medical license if she prescribed ivermectin. Can you believe this? This is NH and America. How can this be happening?

Please please support HB 1022 and let our doctors decide what treatments we need. They know our medical history and what is best for us.

Thank you!

Deb

Archived: Thursday, January 20, 2022 11:01:15 AM
From: Sarah C.
Sent: Tuesday, January 18, 2022 12:14:39 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 - OTP
Importance: Normal

Representatives,

I'm connected to a large community of individuals ranging from healthcare professionals to chronically ill and medically-complex patients. I recently asked them to share their experiences using Ivermectin to treat symptoms of SARS-CoV-2. The responses were overwhelming positive. I'd like to share some of their responses with you today:

I had all the symptoms except respiratory issues then tested positive for covid. Started ivermectin and 2 days later felt 90% better. Fever broke, no more cold sweats, headache gone, body aches gone, smell and taste returned. Just a residual stuffy/runny nose that lasted about 5 days or so.

My father in law was going downhill quickly, and I started to worry. He had been sick for at least two weeks with a recurring fever, fatigue, weight loss, relentless cough.... then the illness progressed and started affecting his heart. He was diagnosed with AFIB. I only had the (vet) paste on hand at the time because no would prescribe it, but I gave him a tube to take home. Within the first dose or two he began to improve, and by the end of the week he was out on the golf course and renovating the house. He has no lingering symptoms aside from (mild) AFIB and is currently RVing around the country with his wife, living his best life and telling everyone about IVM. I only wish I had given it to him sooner. At minimum, I feel like it saved him from being hospitalized. It may have even saved his life.

My kids worked in the food service industry and needed testing per work. They were positive with loss of sense of smell and taste. I begged their doc for that medication. On day 8, they were given just 6 mg of it. 6 hours later, my son regained smell and taste and my daughter was fine 24 hours later.

Treated hubby with it, high risk category for complications from the virus. Recovered without hospital interventions.

I didn't use it and was in the hospital for 3 days.
My parents did use it and they were able to watch my 7 children while I was in the hospital.
They caught it from me so I was about 2 days ahead of them.
They never missed a beat!
Both have other health conditions. My dad is a smoker.

My 73 year old Gma used it. Even a normal cold makes her very sick, and she is allergic to so many things she is limited in what she can take while sick. Most herbs and supplements she cannot have. The pharmacies here were refusing to fill her prescription so my Gpa drove over an hour to get it for her. All of her labs, and chest X-rays were perfect and she was never hospitalized or anything.

Used it with my daughter in Sept. and she was symptom free in 2 days.

Took it at first symptom. Paste form, though now I have tablets on hand. No respiratory symptoms, and other than fatigue and brain fog I recovered quickly. Mom used the Rx tablets. 62 yrs old with co-morbidities. She was better in about 4 days. Was like a cold for her.

I'm on it right now. I thought I was dying. Ivermectin has been helping me to improve daily!

My son and his gf have covid right now. My son got it first. His gf 4 days later. She was very sick. Took iver at the end

of day 2. Felt so much better the next day. My son thought he could tough it out. Was very sick, started taking iver on day 5 and within hours his body aches, chills and fever were gone.

My MIL (in her 70s) has a blood clotting disorder and gets pneumonia with every cold. She took it and while she still is weaker than her norm, she recovered at home fine, no hospital, and we have monitored her 02 sat and gave her supplemental low flow oxygen as needed. She is definitely very high risk for complication, but she recovered faster and more mild case than my FIL who wouldn't take it.

I feel like it literally saved us. We started it at 10 days in because we were at the point of deciding whether we should go to the hospital or not. Within 48 hours we both could tell that we had made a turn around and were starting to get well.

I have successfully helped out a couple people. One was literally knocking on deaths door!

The day after I tested positive I had no appetite, could barely move, brain fog that made me feel drunk, a severe headache and just felt TERRIBLE. After my 3rd dose that day I felt starving, had energy, less coughing and just better overall. On my second day of schmiverfectin (today) and still feeling good.

My husband took it because he was very sick, fever for 9 days and couldn't get out of bed.
He tried it and a day later he was up and recovering well.

I've used it and have many people in my community who have used it to successfully beat Covid without hospitalization.

I ended up with severe long hauler and I was shocked because I am such a healthy person. I was peeing brown despite drinking at least a gallon of water a day, I had jaundice, I was covered in bruises so badly I looked like a leopard, and I was itching intensely for hours a day, Just climbing my skin off which I read was a sign of liver and kidney failure. I am extraordinarily healthy I never get sick, I am an orthomolecular Homeopath so I have all the right supplements, and this man made bio weapon still nearly killed me.
24 hours after taking my first dose of ivermectin my pee got lighter, the itching stopped, and the jaundice started to clear. About three months later my husband got it, I gave the ivermectin him when he was actively sick. We started it on Monday, by Wednesday his fever had broke and by Thursday he felt good enough to go back to work.

Every person I have talked to recovered within days and no side effects.

A friend whose elderly grandmother was in assisted living, became ill and rapidly deteriorated, was not expected to survive. The doctor tried it because he felt there was nothing to loose, sorta a Hail Mary. She recovered completely in 3 days.

I know someone who pulled his 80 year old dad from the hospital because they wanted to put him on Remdesivir. Treated him with ivermectin himself and father is fully recovered.

We took it. It gave me my taste and smell back and I definitely felt a bit of an improvement. My husband improved more notably than I did. He could barely breathe before he took it. Within a day or two he could breathe with ease and I feel it's what prevented him from going to hospital.

It's the ONLY pharmaceutical in 40 years that hasn't given me any side effects…and same goes for my 13 yr old immune compromised kiddo!

On that note, I would like to end by encouraging you to vote HB 1022 as "ought to pass." Early intervention works, and in many instances can be the difference between life and death. We ought to make effective therapeutics, such as Ivermectin, readily available and more accessible to those who want it. Pharmacists can play an important role in doing that. At a time when our hospitals are understaffed and overburdened, this will offer a welcome reduction in hospitalizations for both patients and healthcare providers.

Sarah Courchaine
Sanbornton, NH

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Joe Torelli
Sent: Tuesday, January 18, 2022 11:56:10 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Opinion on HB1022
Importance: Normal

Committee members:

I fully support HB1022 and urge you to do so as well.

Despite the media's campaign to discredit this medecine, there are numerous areas where results speak for themselves. This includes Africa where the Covid-19 vaccination is unavailable.

Consider Uttar Pradesh in India. It is one of 36 States in India, except this has 3/4 of the US population inhabiting it. 240,000,000 people. Before the "delta" variant was renamed last spring, it was called the India variant and killed a lot of people in March and April of 2021. The politicians and physicians teamed together in April of 2021 to acquire and distribute Ivermectin to all inhabitants of that State.

Results hit the media over here, of course those without the anti-ivermectin narrative… that there were 16 total "cases" out of 240,000,000 people in September 2021. 16 cases, not 16 deaths, not 16,000 cases.

It JUST PLAIN WORKS and shame on the State of NH for allowing not only pharmacies to refuse filling Ivermectin prescriptions, as another bill is working to fix.

This bill (1022) will make it easier to for residents of NH to purchase with ot without a prescription.

My only fear is that hoarders will buy and deplete the amount available at the pharmacies.

Please support HB-1022.

Joe Torelli
(917)209-6074
Hampton NH

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 11:52:19 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: in opposition to HB 1022 - Dr. Peter Degnan
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Peter Degnan in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Peter Degnan <Peter.Degnan@unh.edu>
Sent: Tuesday, January 18, 2022 11:35 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: in opposition to HB 1022

Good day:
As a licensed physician within the state of New Hampshire, I write in opposition to proposed HB 1022, allowing the dispensing of Ivermectin by pharmacists under a standing order.
Physicians are uniquely qualified based on extensive education and training to understand the appropriate prescribing of prescription medication, including the inherent side effects and risks of such medication.
There is no emergency situation that currently exists that requires a circumvention of current prescribing rules and regulations; to do so threatens public health and safety.
Thank you.
Peter Degnan MD

Peter Degnan M.D.
Medical Director
Pronouns: he, him, his

V: 603.862.9355 | F: 603.862.4259

University of New Hampshire
Health & Wellness
4 Pettee Brook Lane
Durham, NH 03824
peter.degnan@unh.edu
www.unh.edu/health

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Matt Severance
Sent: Tuesday, January 18, 2022 11:34:42 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Hello Committee of HHS & Elderly Affairs,

My name is Matt Severance and I live in Dunbarton, NH. I wanted to voice my support for **HB 1022** which would permit Ivermectin to be sold without a prescription.

I learned early on that there are early treatments for Covid-19 that work. I was able to get a prescription for Ivermectin in May 2021 so I had it in the event that I contracted Covid-19. Well, that time came on Dec 19th. I was able to take it immediately and my symptoms quickly went away within 2 days... I tried to order again from that online doctor for my wife and they said that the large pharmacies (CVS/Walgreens/Rite Aid) are no longer fulfilling Ivermectin, In May 2021 the CVS on Hall Street in Concord filled that prescription. I am glad I procured the Ivermectin that I needed and very disappointed that my wife could not get a prescription for a proven safe anti viral medication. She had symptoms for 9 days before recovering. I am convinced had she used Ivermectin her symptoms would have been less and her recovery would have been much faster.

Please support HB 1022.

Thank you,
Matt Severance
Dunbarton, NH 03046

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Jim Avallon
Sent: Tuesday, January 18, 2022 11:34:33 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Dear House Health, Human Services and Elderly Affairs Committee,

I have several friends who have contracted COVID and have benefited greatly from Ivermectin, particularly when taken early. The problem is acquiring Ivermectin and determining the appropriate dose. That is why I believe in HB1022 so that people like my friends who have had COVID and who have benefited so greatly can take it under a doctor's supervision and prescription which will specify details of Ivermectin dose and beneficial accompanying medication dosages. Ivermectin is a safe medication when taken appropriately. It. has been around for a long time and I think was involved with a Nobel Prize award. There are somewhat like 60-70 supporting studies detailing Ivermectin's benefits as a treatment for COVID.

Thank you
Jim Avallon
North Hampton, NH

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 10:26:36 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: HB1022 - oppose this bill - Dr. Martin Black
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Martin Black in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Martin Black <mblack@crhc.org>
Sent: Tuesday, January 18, 2022 10:23 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: HB1022 - oppose this bill

Mr. Padmore,

I am writing on behalf of my opposition to HB 1022. I am a pulmonary/critical care physician at Concord Hospital, writing on my own behalf.

This bill needs to be struck down from legislature. The language below in the bill: "Nothing on the information sheet shall discourage the recipient from using ivermectin for the treatr
19." is contrary to every reputable medical expert, well-
designed clinical trial, and international society guidance (CDC, and WHO). I reviewed all published literature to the best of my ability and do not prescribe ivermectin to patients admi

A standing order could be set-up under this bill by a prescriber in association with the pharmacy to provide on-demand ivermectin to any patient who asks - easily bypassing the primary care provider.

Please add my name to the list of physicians opposing this bill.

Sincerely,

Martin D. Black MD
Concord Hospital Pulmonary and Critical Care Medicine
mblack@crhc.org, mdblackmd@netscape.net
603-770-9446

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Irina Tundel
Sent: Tuesday, January 18, 2022 10:14:49 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

I support this bill

Irina Tundel
Manchester, NH

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Dan G.
Sent: Tuesday, January 18, 2022 10:12:06 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB 1022 and oppose HB 1369
Importance: Normal

Hello,

I hope this is not too late. The committee is having hearings on two bills today (Jan. 18th) that interest me.

Please support HB 1022 which allows pharmacists to dispense ivermectin by means of a standing order. I think there should be fewer barriers to drug access to patients, especially if their doctor approves of use of the drug.

Please oppose HB 1369. I see no reason to enact this law. Private property owners can always impose conditions of entry such as mask requirements. The trespassing law should be enough here.

thanks,
Dan Groves
Merrimack, NH

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Susan Paschell
Sent: Tuesday, January 18, 2022 10:10:23 AM
To: ~House Health Human Services and Elderly Affairs
Cc: Kim Mohan; Siobhan Benham; Christina Dyer; Lindsay Oestreich
Subject: Testimony on HB 1022, ivermectin, from the NH Nurse Practitioner Association
Importance: Normal
Attachments:
1.17.22 Testimony HB 1022 ivermectin.docx ;

Good morning Chairman Pearson and members of the Committee,
Please find attached a letter from the NH Nurse Practitioner Association OPPOSING HB 1022.

Feel free to contact me or Kim Mohan if you have any questions.
Thanks for your kind consideration!
Susan

Susan Paschell, Senior Associate
The Dupont Group
29 School Street, Suite 200
Concord NH 03301
603-228-3322 ext. 107

Archived: Thursday, January 20, 2022 11:01:16 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 10:10:16 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: House Bill 1022 - opposition - Dr. Kenton Powell
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. William Palmer in opposition to HB1022. Kenton is the Governor Elect of the New Hampshire Chapter of the American College of Physicians.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Kenton E. Powell <Kenton.E.Powell@hitchcock.org>
Sent: Tuesday, January 18, 2022 9:14 AM
To: William Palmer <wspalmer56@gmail.com>; Michael Padmore <Michael.Padmore@nhms.org>
Subject: RE: House Bill 1022 **EXTERNAL**

Mike,

I also can not attend the meeting due to patient being scheduled.

I write in opposition to HB1022. Ivermectin is a useful medication for what it is intended for but has not been shown to be effective in treating patients with SARS-COV. Physicians write prescriptions for any number of medications on a daily basis that pharmacists are not allowed to dispense without a prescription due to concerns for toxicity, safety, knowledge of what patient is taking, etc. It is unsafe for patients to obtain this medication for a condition it is not effective for and without the knowledge of their treating clinician.

Kent Powell MD, FACP
Assistant Professor of Medicine and of Medical Education
Associate Program Director, Internal Medicine Residency Program
Program Director, Primary Care Track
Dartmouth-Hitchcock Medical Center
Co-Director Advanced Ambulatory Medicine Clerkship
Geisel School of Medicine at Dartmouth
Medical Director Dartmouth-Hitchcock Medical Center – Lyme
Governor Elect of New Hamphsire Chapter of the American College of Physicians

-----Original Message-----
From: William Palmer <wspalmer56@gmail.com>
Sent: Tuesday, January 18, 2022 8:35 AM
To: Michael Padmore <Michael.Padmore@nhms.org>

Cc: William Palmer <wspalmer56@gmail.com>; Kenton E. Powell <Kenton.E.Powell@hitchcock.org>
Subject: House Bill 1022 **EXTERNAL**

Mike,
I couldn't come to testify but here is what I have to say:

I write in opposition to HB 1022. Ivermectin is not approved by the FDA for use against COVID-19. The CDC, the NIH and the American College of Physicians all specifically recommend against the use of Ivermectin for COVID-19 because there is no good evidence that it is effective and there is potential for harm.
I would also be concerned, given how overwhelmed our New Hampshire healthcare system is, about where patients go and who will cover the care for any ivermectin induced side effects. Please vote this bill down.

Sincerely,
William Palmer MD FACP
Hospitalist
Governor of the New Hampshire Chapter of the American College of Physicians (the group represents more than 560,000 internal medicine physicians nationwide)

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Sarah McClennen
Sent: Tuesday, January 18, 2022 9:45:19 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please SUPPORT HB 1022
Importance: Normal

Dear Committee Members,
I am writing today to ask you to support HB 1022.
The current response to the Covid 19 situation has fallen short. When is it ok to tell sick people to go home and only seek treatment when they are close to death? How did it become ok for Doctors to refuse to treat people and pharmacists refuse to fill prescriptions?
There is ample evidence and now studies which show the incredible benefits of early treatment and prophylaxis with drugs like ivermectin and hydroxycloroquin. As well as prophylactic supplements zinc, Vit D, Vit C and quercitin. The fact that the government is suppressing this information and access to these drugs is criminal. They have tunnel vision for a vaccine which has very serious safety issues. Over 1,000,000 people in the US have had adverse reactions and over 20,000 people have died.
Dr Peter McCullough and 11 million doctors world wide have determined that 85% of deaths from Covid could have been prevented and 100% of hospitalizations prevented.
These drugs have a proven safety record. They have been used for 50 years.
Please google some of his interviews, the best one is with Joe Rogan:

https://open.spotify.com/episode/0aZte37vtFTkYT7b0b04Qz?si=97TBZDXoQSCO-vxCIRDIDQ

With these kinds of results, why are hospitals and the government squelching the information and access. In addition why are we not training doctors how to treat people with Covid. It is increasingly obvious that the vaccine is not the magic bullet it was hoped to be. People who are fully vaccinated are getting sick with Covid.

Please support this bill and begin the process of reversing our path down this treacherous road we are on.

We need to restore the rights of patients and doctors to decide on treatment and medicines, not the government. We need to protect patients privacy and right to make medical decisions with out coercion or fear from the government.
Thank you,
Sarah

Sarah P McClennen Certified Advanced Rolfer, LMT, CST
9 Johnson Lane Suite 102
Andover, NH 03216-3407
603-520-5247
sarah@feelpeaceful.com

feel peaceful

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Laurie A Couture
Sent: Tuesday, January 18, 2022 9:30:25 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please Support HB 1022 and Save NH Lives
Importance: Normal

Dear Committee of Health, Human Services, and Elderly Affairs,

I am writing to ask that you save lives by supporting HB 1022, which allows pharmacists to dispense Ivermectin by means of a standing order, and as an over-the-counter medication for Granite Staters. For Granite Staters who wish to use Ivermectin, which is FDA approved, the laborious process for getting it overseas takes weeks and even months, which wastes precious time when a person develops symptoms of COVID-19. If the US Postal Service confiscates the shipment, people lose money, time, and their chosen option for recovery from COVID.

An unclassified document dated 8/13/2021 by the Defense Advanced Research Projects Agency, written by Commandant of the Marine Corps Fellow, Joseph Murphy--available to you with a FOIA request--identifies that Ivermectin is "curative" of COVID-19 and "works throughout all phases of the illness because it both inhibits viral replication and modulates the immune response."

On July 8, 2021, the National Institute of Health (NIH) listed Ivermectin as an approved medication for the treatment of COVID-19 in Table 2e. "Characteristics of Antiviral Agents That Are Approved or Under Evaluation for the Treatment of COVID-19". It also listed Ivermectin as safe--"Generally well tolerated." This table was completely removed for political reasons once patients began bringing it to hospitals to request this treatment for their dying relatives. The chart's URL was:
https://us-east-2.protection.sophos.com?d=nih.gov&u=aHR0cHM6Ly93d3cuY292aWQxOXRyZWF0bWVudGd1aWRlbGluZXMubmloLmdvdi90YWJsZXMvdGFibGUtMmUv&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=L2dRRHpXcHJwbzV3czJHZ0ZXaVc4dklDaFI4OU5jVnRWaE53K2xreVpnZz0=&h=fb95fac5fc464e5e82b064088f127bb4

On the last day of 2021, my 67-year-old cousin passed away in the hospital on a ventilator because Ivermectin was not made available to him. Had Ivermectin been available to him, I believe he would be alive today and on the road to recovery. Story after story abound of people who recovered rapidly from COVID-19 after starting Ivermectin and even of people who were declining rapidly and dying on the hospital protocol (Remdesivir and ventilator), but once prescribed Ivermectin (usually by court order or after being discharged from the hospital), these patients made a drastic turn around. Many physicians are using Ivermectin to save lives or making recommendations to other doctors and hospitals for doing so, including those of the Front Line COVID-19 Critical Care Alliance (FLCCC). https://us-east-2.protection.sophos.com?d=covid19criticalcare.com&u=aHR0cHM6Ly9jb3ZpZDE5Y3JpdGljYWxjYXJlLmNvbS9pdmVybWVjdGluLWluLWNvdmlkLTE5Lw==&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=MDF6bm92OTNNeVpnUGFlSHVaM3p5aVRnRHAzV3k4QU0vRkNrQ2V5bWJaYz0=&h=fb95fac5fc464e5e82b064088f127bb4

This life-saving option should not require NH residents, in the Live Free or Die state, to have to desperately try to order Ivermectin overseas, risking dying while waiting for it--If it isn't confiscated by

the postal service first.

Please support HB 1022 and support NH residents in their healthcare choice!

Sincerely,

Laurie A. Couture

Newmarket, NH

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 8:59:28 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: House Bill 1022 - opposition - Dr. William Palmer
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. William Palmer in opposition to HB1022. William is the Governor of the New Hampshire Chapter of the American College of Physicians (the group represents more than 560,000 internal medicine physicians nationwide).

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: William Palmer <wspalmer56@gmail.com>
Sent: Tuesday, January 18, 2022 8:34 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Cc: William Palmer <wspalmer56@gmail.com>; Kent Powell <kenton.e.powell@hitchcock.org>
Subject: House Bill 1022

Mike,
I couldn't come to testify but here is what I have to say:

I write in opposition to HB 1022. Ivermectin is not approved by the FDA for use against COVID-19. The CDC, the NIH and the American College of Physicians all specifically recommend against the use of Ivermectin for COVID-19 because there is no good evidence that it is effective and there is potential for harm.
I would also be concerned, given how overwhelmed our New Hampshire healthcare system is, about where patients go and who will cover the care for any ivermectin induced side effects. Please vote this bill down.

Sincerely,
William Palmer MD FACP
Hospitalist
Governor of the New Hampshire Chapter of the American College of Physicians (the group represents more than 560,000 internal medicine physicians nationwide)

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Connie Roberts
Sent: Tuesday, January 18, 2022 8:50:08 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Dear HHSEA Committee Members:
I am a registered voter in NH. I'm asking for your support today of HB 1022> This legislation would mandate that pharmacies must dispense ivermectin when prescribed by a physician. Currently doctors who determine that ivermectin is in their patients' best interest can not get pharmacies to fill the prescriptions they write. This treatment should be between the doctor and the patient. There is a growing body of research to support the effacy of ivermectin in the early treatment of Covid. Supporting this legislation can save lives.
Respectfully,
Connie Roberts

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Nancy Cunning
Sent: Tuesday, January 18, 2022 8:44:58 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Support and Pass Bill HB 1022
Importance: Normal

I am in full support of having decisions being made between Doctor and Patient.
Government needs to have respect for our freedoms and choices.
Pass Bill HB 1022

Thank you,

Nancy Cunning

Archived: Thursday, January 20, 2022 11:01:17 AM
From: sharon@acmswellness.com
Sent: Tuesday, January 18, 2022 8:38:02 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Pending legislation
Importance: Normal

Please support NH Bill 1022 Would Allow “Dispensing Ivermectin to Persons in this State Without a prior Prescription. Mexico is including this valuable, tried and trusted drug in Covid 19 kits.

And oppose **OPPOSE** HB 1369, relative to COVID-19 health and safety policies at New Hampshire performing arts venues. This bill allows performing arts centers to create their own COVID protocols including requiring vaccination for entry.

Trust me. We the people are done being pushed around.

Sharon

Sharon O’Connor
6 Pheasant Run Lane
Stratham, NH 03885

603-738-8054

Archived: Thursday, January 20, 2022 11:01:17 AM
From: hbbarnp@aol.com
Sent: Tuesday, January 18, 2022 7:43:21 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022, 1/18/22
Importance: Normal

To Whom it May Concern;

I am a practicing APRN in the state of NH and **support HB 1022**.
I base my decision on the following facts:

- **IVERMECTIN** (IVM) has been identified by the WHO as an "essential medication" due to its efficacy and safety profile, including use by pregnant women and children. Use and safety findings list **IVM** at the same drug level as Tylenol and aspirin.
- **IVM** is available without a prescription for human use in many countries for decades.
- The FDA approved **IVM** in 1996 as safe and effective for human use.
- Since 2012 in multiple studies, **IVM** demonstrated it stops replication of a variety of viruses.
- In 2020 studies proved **IVM** "demolished" SARS-Covid viral RNA in cells within 48 hours.
- Prevention studies show **IVM** repeatedly demonstrated greater effect against COVID, than COVID vaccines at a fraction of the cost and with few safety concerns.

It is clear from scientific data around the world, **IVM** has been demonstrated to be safe and effective for a variety of parasitic and viral infections to include Covid and Covid variants.

I believe it is our ethical and moral duty to have **IVM** readily available per standing order, for pharmacists to dispense to NH citizens.

Respectfully,

Dr. Holly Buckley, APRN
North Sutton, NH
Hbbarnp@aol.com

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:36:43 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: HB1022 testimony - opposition - Dr. Eric Kropp
Importance: Normal
Attachments:
Addendum; Eric Kropp, MD HB1022.pdf ;Signature.png

Members of the House HHS Committee,

Please see the forwarded message from Dr. Eric Kropp in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Eric Kropp <drkropp@activechoicemd.com>
Sent: Monday, January 17, 2022 11:22 PM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: Fwd: HB1022 testimony.

---------- Forwarded message ---------
From: **Eric Kropp** < drkropp@activechoicemd.com>
Date: Mon, Jan 17, 2022 at 11:21 PM
Subject: HB1022 testimony.
To: Michael Padmore <michael.padmore@gmail.com>

Hi Mike,
Here is my testimony in favor of HB 1022.
Heh, Just kidding. I have struggled with formatting and sharing in google docs, so I just cut and pasted it here.
ADdendum is attached as PDF.
Can you do me a huge favor and give it a quick once over before formatting? Thank you so much.
you can paste in the attached signature, too. :
-Eric

Dear Mr Chairman, and Member of the House Health, Human Services & Elderly Affairs Committee,

Thank you for your kind consideration of my written testimony as my clinical obligations prevent me from being able to attend the hearing in person. I am writing on behalf of the New Hampshire Society in opposition to HB1022. The basis

of this opposition is multifold. Three existing statutes in particular highlight the stark deficiencies in patient protection that are absent from this proposed legislation, and the deviations from the standard of care for these arrangements that have been developed by Boards of Pharmacy, Nursing and Medicine. Specifically, RSA 318:47-l Hormonal Contraceptives; Dispensing , 318:47-m Nicotine Cessation Therapy and RSA 318:16-a Standards for Collaborative Pharmacy Practice, already provides an existing framework for medication management by a Pharmacist under standing orders from a Physician. Please see the attached addendum for highlights.

Ivermectin is a prescription only medication that is FDA approved for the treatment of Strongyloidiasis of the intestinal tract, and Onchocerciasis (River blindness). Use of Ivermectin for prevention or treatment of COVID-19 is off-label. Thus, this Bill cannot be modeled after the standing orders for Hormonal Contraceptives and Nicotine Cessation Therapy, both of which are to be dispensed specifically for widely accepted, longstanding FDA indications. Standing orders amount to the practice of medicine by pharmacists, who are required to complete accredited educational training programs before managing patients. Pharmacists also must follow the most current national guidelines, or a statewide model protocol. The content and format of the standardized information sheets are determined by the Board of Pharmacy and specific to the indication for therapy. These measures, critical to ensure that patients receive safe and effective care are absent from HB1022.
Off-label prescribing is common, but it requires additional considerations from the practitioner and patient. To propose a law in which "Nothing on the information sheet shall discourage the recipient from using ivermectin for the treatment of COVID-19" shows a wanton disregard for patient safety and self-determination. Who determines if information is "discouraging?" Are studies showing lack of efficacy discouraging? Is describing any risk of harm discouraging? No one should be gagged from informing a pregnant patient that Category C in pregnancy means that animal studies DO show risk of adverse developmental outcomes and that there are NO studies in pregnant women. Only a fully informed patient can make a choice free or coercion.

The science and understanding of risks, benefits and application of Ivermectin are constantly evolving as is the target itself, SARS-Cov-2. The legislature is not the place to determine what is an appropriate use of medications during a rapidly evolving pandemic.
State law already allows practitioners and pharmacists to collaborate and develop other protocols based on evidence-based guidelines in RSA 318:16-a. As highlighted in the addendum, not only does this Bill fall woefully short of the established protections and standards of care, it is redundant.
In summary, the NH Medical Society opposes Bill which falls well short of the patient safety afforded by both the existing laws for standing orders for specific FDA approved medications, and RSA 318:16-a, which already establishes the minimum requirements to ensure patient safety in a collaborative model of evidence based medical care between a pharmacist and a practitioner. We ask that you find this Bill Inexpedient to Legislate

Sincerely,

Eric Kropp, MD Family Medicine President, New Hampshire Medical Society

Eric Kropp, MD
Active Choice Healthcare
13 Chenell Dr., Suite 2
Concord, NH
(603) 410-4644

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:35:37 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: 1/18 HHS bill HB1022 - Opposition - Dr. Linda Williams
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Linda Williams in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Williams, Linda <Linda.Williams@snhhs.org>
Sent: Sunday, January 16, 2022 10:38 AM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: 1/18 HHS bill 1022

As a Nashua pediatrician and Bedford resident I am writing in opposition to the bill (1022) allowing pharmacists to dispense ivermectin by standing order. There is no medical evidence that Ivermectin improves covid19, there are significant possible side effects to using ivermectin which patients should be counseled on (for proper diagnoses), and inappropriate use of ivermectin undermines our medical professionals who are counseling against its use in covid.
Thank you for your time,
Linda Williams, MD

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Michael Padmore
Sent: Tuesday, January 18, 2022 7:34:10 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Fw: HB 1022 regarding standing order for ivermectin - Opposition - Dr. Warren Goldblatt
Importance: Normal

Members of the House HHS Committee,

Please see the forwarded message from Dr. Warren Goldblatt in opposition to HB1022.

Thanks,
Mike Padmore
Director of Advocacy
New Hampshire Medical Society
7 North State St, Concord NH
(603) 858-4744 (cell)
michael.padmore@nhms.org

From: Warren Goldblatt <WGoldblatt@EyesightNH.com>
Sent: Sunday, January 16, 2022 7:48 PM
To: Michael Padmore <Michael.Padmore@nhms.org>
Subject: HB 1022 regarding standing order for ivermectin

As a physician, I find it hard to believe that the legislature is considering allowing pharmacists to act as licensed physicians to allow them to prescribe medications, especially something like ivermectin, which has never been proven to be of any benefit in the treatment of COVID.
Please do not allow this travesty to take place

Warren

Archived: Thursday, January 20, 2022 11:01:17 AM
From: Lynn McCarthy
Sent: Tuesday, January 18, 2022 7:27:04 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Health and Human services committee,

I am writing to ask you to support this legislation to give doctors and citizens the right to choose their method of medical treatment. Currently it is difficult to have a prescription for Ivermectin be fulfilled almost anywhere in NH. This Bill will eliminate that difficulty.

Thank you for your integrity.
Lynn McCarthy
New Castle NH

Archived: Thursday, January 20, 2022 11:01:17 AM
From: don.bettencourt@gmail.com
Sent: Tuesday, January 18, 2022 7:06:54 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 permitting pharmacists to dispense the drug ivermectin by means of a standing order.
Importance: Normal

To All NH House Health, Human Services and Elderly Affairs Committee Members

Please support HB 1022. A friend of mine tested positive for Covid just after Thanksgiving. When unable to be treated with Ivermectin by his PCP, he purchased Ivermecton at the local Tractor Supply store. When he told me that, I thought he was kidding but he explained that it is the same drug and just needs to be adjusted for the proper dosage based on the patient's weight. On the day after beginning to take Ivermectin, his symptoms nearly disappeared and he decided to stop taking the drug. The next day, the Covid symptoms returned, although they were milder. He resumed the Ivermectin and again the symptoms nearly disappeared.

I am shocked that NH residents are currently being forced to shop at Tractor Supply in order to obtain Ivermectin. When I asked my PCP if she would be able to get me some if I tested positive for Covid, she indignantly told me that she would lose her license if she did. This is absurd!

Thank you for supporting this bill.

Don Bettencourt,
Sunapee

Archived: Thursday, January 20, 2022 11:01:18 AM
From: Chloe
Sent: Monday, January 17, 2022 11:51:03 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Please support HB 1022 to allow ivermectin to be used to treat corona.

Chloe Sowers
Manchester Ward 11

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:18 AM
From: Den Chapman
Sent: Monday, January 17, 2022 10:28:05 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022 - support
Importance: Normal

The rest of the world can buy ivermectin any time they want to, but the citizens of NH can't. Why not? It is on the top 10 list of treatments by the WHO. It has been used for decades without harming people.

Please support HB 1022

Thank you
kevin chapman
marlborough

Archived: Thursday, January 20, 2022 11:01:18 AM
From: Peter de Bruyn Kops
Sent: Monday, January 17, 2022 10:10:39 PM
To: ~House Health Human Services and Elderly Affairs
Subject: OTP HB 1022
Importance: Normal

Ivermectin is one of the safest drugs sold by pharmacies.

Ivermectin is available without prescription in dozens of countries worldwide.

Our public health infrastructure is captured by Big Pharma and wants to block access to a low cost drug for Covid-19.

We now know that Covid-19 vaccines do not work for preventing catching or transmitting the disease. People need access to early treatments.

Right now, NH residents wanting Ivermectin on hand for treatment or prophylactic use have to mail-order it from out of state. Contrast that with NH policy on tobacco and alcohol, which are more dangerous, where we are happy to have people from other states spend their money in New Hampshire.

Please vote OTP on HB 1022

Peter de Bruyn Kops
Amherst, NH
603-673-3551

Archived: Thursday, January 20, 2022 11:01:18 AM
From: TrackBill
Sent: Monday, January 17, 2022 10:08:28 PM
To: ~House Health Human Services and Elderly Affairs
Subject: New Hampshire HB1022 has been shared with you, Opposition of HB 1022
Importance: Normal

New Hampshire HB1022 has been shared with you, Opposition of HB 1022

New Hampshire HB1022 has been shared with you.

In opposition to HB1022

Dispensing Ivermectin as a Standing Order at first glance, yes it is a cheap drug, yes it has a relatively good safety profile, and yes there is some research on this drug for the treatment of COVID however there are a number of significant issues with this bill.

The first issue is that the FDA, CDC, AMA, APhA have all issued statements that strongly oppose the ordering, prescribing or dispensing of Ivermectin to prevent or treat COVID-19, urging patients against the use of this drug outside of FDA approved indications and outside of clinical trials.

Another issue is, the interpretation of how a "standing order " in the outpatient setting is meant to serve patients. A standing order in the outpatient is setting is typically used for individuals with a chronic or recurring illness that the provider and most importantly the patient has experience with. For example, a patient with asthma can have Prednisone on hand when needed or a patient with recurring urinary tract infections can have an antibiotic on hand at the pharmacy. A provider has to have a degree of confidence that this patient has experience with managing this illness, has comprehended signs and symptoms of when to initiate treatment, recognize worsening symptoms or treatment failure and when to follow up or seek emergency care. This is typically the case for drugs that are recommended and FDA approved for a particular medical condition, less likely an off label drug for a non chronic illness.

Finally, to prescribe an off label drug with low quality evidence for an acute issue at the very least a patient should be evaluated in some capacity either in person or via Telehealth prior to prescribing or dispensing Ivermectin. Omitting an evaluation prior to prescribing under these circumstances is below standard of care in practice. The residents of New Hampshire deserve at the very least to ensure that health care is

delivered at the standard of care and better, it is our job to continue to protect the public health interests of the residents of New Hampshire.

It is for the above reasons that I oppose the HB1022.
Thank you.
S. Nicole Condodemetraky private citizen and APRN (Advanced Practice Registered Nurse)

View

Archived: Thursday, January 20, 2022 11:01:18 AM
From: Valerie
Sent: Monday, January 17, 2022 8:57:51 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB-1022 and oppose HB-1369
Importance: Normal

To the House Committee,

I am emailing to ask you to please support HB-1022. Ivermectin is an extremely safe medication that has been used for decades. It has been highly successful in not only treating, but eliminating devastating diseases globally and has made such a vast impact on global health that it earned its discoverer a Nobel Prize in 2015. Since scientists found that the use of ivermectin as an anti-viral medication was effective in eliminating the virus from tissue that was inoculated with the Covid-19 virus, doctors across the globe have been using ivermectin to treat their Covid positive patients at an outpatient basis with great success. It is vital that this medication be available to the people of New Hampshire so that when individuals test positive they can obtain this medication quickly and reduce their risk of hospitalization. Not only do our people desperately need this, our healthcare workers, and the hospitals and medical facilities desperately need the reduction in Covid admissions. Please ensure that the people you represent have access to this life-saving medication.

I would also ask that you oppose HB-1369. It is highly unconstitutional for any business or organization to have medical requirements for their patrons. If these performing arts venues are given the ability to create whatever Covid protocols that they want, they could very easily overstep their boundaries in demanding things that violate the peoples right to privacy such as vaccination requirements. Please ensure that this does not happen and vote against HB-1369.

Thank you very much for your time and service to this great State.

Sincerely,
Valerie Burkett
Manchester NH

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:19 AM
From: MICHAEL SARACINO
Sent: Monday, January 17, 2022 8:43:00 PM
To: ~House Health Human Services and Elderly Affairs
Cc: Gary Merchant
Subject: HB 1022
Importance: Normal

As a person who worked as a Clinical Pharmacist for decades, I stand seriously opposed to the dispensing of Ivermectin over-the-counter by Pharmacists, or by the recommendation of any health care professional for human use. There is no scientific justification for use of this product in the prevention or treatment of COVID-19.

Honestly, where does the House come up with these things? It is absurd!

If you want to help the people of NH, recommend universal vaccination, the use of effective masking, and social distancing. These have strong scientific justification, safety, and efficacy.

From June 1 to December 31, of 2021, 200,000 unvaccinated Americans died of COVID-19. What a waste of human life. How much love has been lost by the family members and friends of these victims.

Dr. Michael Saracino, Pharm.D
Claremont, New Hampshire

Archived: Thursday, January 20, 2022 11:01:19 AM
From: Sharon Clark
Sent: Monday, January 17, 2022 8:36:01 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB1022
Importance: Normal

Dear Council Members,

Please support HB 1022. People have a natural right to care for their own health as they see fit. The government does not have the right to withhold treatment from those seeking it.

Sincerely,

Archived: Thursday, January 20, 2022 11:01:19 AM
From: Priscilla Maccallum
Sent: Monday, January 17, 2022 7:39:24 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB 1022
Importance: Normal

I urge you to support HB 1022. There are many studies that have shown positive results in treating Covid 19 with ivermectin. In countries where it is used, Covid has not been as deadly.

Ivermectin has been used for years and is safe. There is no reason why it should not be used for Covid… what happened to the “right to try” bill? Making it an OTC medication is the right decision.
I had Covid a few weeks ago. I had ivermectin as well as other recommended supplements on hand. I had 6 hours of fever and chills snd then sniffles and a cough for two days. That was it. I’m 67 years old. I’m convinced ivermectin played a big part in my recovery.

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:19 AM
From: RD BT
Sent: Monday, January 17, 2022 7:26:39 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

Dear Representatives,
I am an independent career scientist. I urge you to SUPPORT HB 1022, which allows Ivermectin to be sold by pharmacies when prescribed by a doctor.

This is such a "no-brainer" I almost don't know where to start. Ivermectin, (the drug for humans) won a Nobel prize. It's considered one of the top 10 most essential drugs to have in your medical toolkit worldwide. It's been proven as safe or safer than aspirin! And it's effective against a variety of ailments - including covid!

My 82-year-old mother is allergic to EVERYTHING. She has been since I was a kid...and now it's worse. Us kids planned to get her vaccinated, but looked into the specifics of the different vaccines to determine which one due to her history of severe allergies, respiratory problems and vascular issues. In the end, we decided NOT to get her vaccinated. Instead, her doctor prescribed ivermectin. She takes it as a preventative before and during travel. We brought her from Florida to Illinois for a large memorial party for my father (who died a year ago), and she enjoyed the company of ~80 family and friends in our family home. No issues. Within the last month, our extended family (mom, my siblings and I, and all the grandkids) traveled together to Egypt and Dubai. Mom, on ivermectin, was actually the only one of us who didn't catch a cold!!

Ignorant people have demonized this award-winning critical medicine for political reasons.

I urge you to ignore the politics and focus on the science. This drug is safe and has been proven safe on humans for many decades. Furthermore, it has been shown to be effective against covid in multiple trials & studies.

This should be your easiest vote today. Vote Yes on HB 1022!

Robin Tyner
Exeter, NH

Archived: Thursday, January 20, 2022 11:01:19 AM
From: Debra Walker
Sent: Monday, January 17, 2022 7:21:46 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Good morning,

Please **SUPPORT** HB 1022.

WHY: Decisions regarding prescriptions should be between a doctor and patient. This bill will eliminate any difficulty that a doctor has prescribing a life saving medicine as well eliminate any difficulty that a patient has in filling a life saving medication.

Sincerely,

Debra Walker

Hooksett, NH

Sent from Yahoo Mail on Android

Archived: Thursday, January 20, 2022 11:01:19 AM
From: Leslie Russell
Sent: Monday, January 17, 2022 7:15:08 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support 1022
Importance: Normal

Dear Committee Members,

Thank you for this Hearing on making Ivermectin available in NH. This is a decision made between me and my doctor. Pharmacies should not be allowed to interfere. Ivermectin saves lives. If I ever need to use it, I want to use it under a doctor's care and not order it in the mail. I want my doctor to tell the pharmacist what I need and not the pharmacist what I need and not the other way around.

Thank you for your service,

Leslie Russell
Salem, NH

Archived: Thursday, January 20, 2022 11:01:19 AM
From: scott barr
Sent: Monday, January 17, 2022 7:00:24 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Dear Committee Members,

HB 1022 is important! Please support HB1022 as Ivermectin is a safe effective treatment yet it is currently difficult to have a prescription fulfilled in New Hampshire!

Thank you,
Lisa Barr

Archived: Thursday, January 20, 2022 11:01:19 AM
From: ajohnston16@comcast.net
Sent: Monday, January 17, 2022 6:23:21 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Regarding HB 1022 (Johnston Family, Bedford New Hampshire)
Importance: Normal

To the distinguished committee members of House Bill 1022:

My family and I support House Bill 1022 which would permit pharmacists to dispense ivermectin via standing order. Health choices should be a private matter and each of us relies on different experiences to guide our current and future decisions. I myself served in Desert Storm and saw what an emergency use authorized drug, pyridostigmine bromide, could do. Young healthy men fell into seizure and many committed suicide years later. My risk assessment is different than someone who lost a loved one to COVID. We each deserve the right to choose our path. No option should be stricken and we should not condemn another person for exercising diversity of thought.

Sincerely,
The Johnston Family
Bedford, New Hampshire

Archived: Thursday, January 20, 2022 11:01:19 AM
From: Myfairpoint
Sent: Monday, January 17, 2022 5:58:52 PM
To: ~House Health Human Services and Elderly Affairs
Subject: NH House Remote Testify: 2:00 pm - HB1022 in House Health, Human Services and Elderly Affairs
Importance: Normal

Support HB 1022

First of all, if you haven't taken the time to research Ivermectin uses over the last 40 years you are not doing your job. The shear number of human prescriptions written, safety of this drug, Nobel Prize for human use...keep looking if you haven't found this evidence.

The last two years brought outright lies and negative innuendos to get the public to think otherwise about Ivermectin. This has been outrageous. Critical Thinking will lead you to the conclusion that this misinformation was only designed to protect the Vaccine EUA by negating a working early treatment for the covid disease.

Secondly, preventing doctors from prescribing Ivermectin or pharmacies from filling by threats of de-licensing or other penalties is absurd. Doctors ordinary prescribe 25% off label FDA approved drugs and Ivermectin should be no different.

Worse are the hospital administrators, corrupted by the incredible flow of Federal dollars designed specifically to prevent early treatment therapeutics, such as Ivermectin. Paying the hospitals to not do any early treatment therapeutics has resulted in hundreds of thousands of needless deaths(or murders). You can call us anything you want, anti-vaxxers, deplorables', whatever, but there a lot of us and we will be heard. And we have lost all faith in government controlled health agencies. We don't trust hospitals and will avoid. Fauci's drug Remdesivir or now commonly known as "Run death is near", the only CDC approved hospital covid drug, is a prime reason.

So the government has forced the "informed" public (people **not** relying on "The Trusted News Initiative"...MSM) to research and seek other means to protect themselves from unconstitutional federal and state oversight and cancel culture. People learn that they can prevent covid with horse paste. Why horse paste? Because the prevention protocol dose for humans is the same that horses use(.2mg/kg). Turns out a weekly dose of horse paste is less than ¼ teaspoon. Easy to measure. If you are aware how much race horses and show horses are worth and the kind of loving care they get, you know horse medicines will have pretty good quality control. Then you weigh or compare the risks of not getting covid and avoiding hospitals that will keep you hostage and feed you "Run death is near" and a ventilator, and then collect thousands from the government. Easy choice – Duvet Ivermectin Paste!

So you can make a difference! Make Ivermectin over the counter! Be brave, take the doctors risk of loosing his/her license out of the equation. Get the people who use horse paste, because of the corrupt government controlled medical agencies, to use over-the-counter Human Ivermectin pills. Live Free or Die, thats all we want. Lead the nation in doing the right think. You are not going to change us. We are willing die on this hill. We are activated and WE WILL VOTE.

Sincerely,
Robert Early
Amherst

Archived: Thursday, January 20, 2022 11:01:19 AM
From: Theriault, Robert Henry
Sent: Monday, January 17, 2022 5:31:08 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB-1022 written testimony
Importance: Normal

House Health and Human Services Committee
HB-1022 Permitting pharmacists to dispense the drug ivermectin by means of a standing order

January 18, 2022

My name is Robert Theriault, I am the Pharmacy Director at Wentworth-Douglass Hospital in Dover and the Legislative Chair of the New Hampshire Society of Health-System Pharmacists (NHSHP). I am submitting written testimony on behalf of NHSHP. The society is **NOT** in favor of HB-1022. NHSHP strongly opposes the ordering, prescribing, or dispensing of ivermectin to prevent or treat COVID-19 outside of a clinical trial. Ivermectin is approved by the U.S. Food and Drug Administration (FDA) for human use to treat infections caused by internal and external parasites. It is not approved to prevent or treat COVID-19. We are alarmed by reports that outpatient prescribing for and dispensing of ivermectin have increased 24-fold since before the pandemic and increased exponentially over the past few months. In addition, we are urging physicians, pharmacists, and other prescribers — trusted healthcare professionals in their communities — to warn patients against the use of ivermectin outside of FDA-approved indications and guidance, as well as purchasing ivermectin from online stores.

The U.S. Centers for Disease Control and Prevention (CDC) and the FDA have issued advisories indicating that ivermectin is not authorized or approved for the prevention or treatment of COVID-19. The National Institutes of Health, World Health Organization, and Merck (the manufacturer of the drug) all state there is insufficient evidence to support the use of ivermectin to treat COVID-19. The Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19 also recommend against the use of ivermectin outside of a clinical trial.
Use of ivermectin for the prevention and treatment of COVID-19 has been demonstrated to be harmful to patients. Calls to poison control centers due to ivermectin ingestion have increased five-fold from their pre-pandemic baseline. A recent CDC Health Alert Network Advisory recommends that healthcare professionals should counsel patients against use of ivermectin as a treatment for COVID-19, including emphasizing the potentially toxic effects of this drug, including "nausea, vomiting, and diarrhea. Overdoses are associated with hypotension and neurologic effects such as decreased consciousness, confusion, hallucinations, seizures, coma, and death."

Thank you for your consideration.

Robert Theriault, Jr., MBA, BSPharm
Chair, Legislative Committee
New Hampshire Society of Health-System Pharmacists
Wentworth-Douglass Hospital
789 Central Avenue
Dover, NH 03820

(603) 609-6177

32 Thatcher Way
Barrington, NH 03825
(603) 252-0771

Archived: Thursday, January 20, 2022 11:01:19 AM
From: mhardt@posteo.net
Sent: Monday, January 17, 2022 12:04:11 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB 1022
Importance: Normal

There's something strange happening in medical circles right now.

When a friend was recently hospitalized with covid-19, I learned that the friend's physician, who wanted to try treating the patient with ivermectin but hadn't done so previously, contacted another doctor whose career had already been ruined by promoting ivermectin. The physician obtained the ivermectin from the second doctor so as not to create a record of having prescribed it himself, and then a third doctor was involved in smuggling the drug in to the patient, while the nursing and support staff were kept unaware. (I find this hard to believe, but I'm told that nurses have been specifically instructed to search for ivermectin among covid patients' personal effects.) The patient's physician said the doctors don't want to involve sympathetic nurses because they don't want them to share the risk of getting caught.

Regardless of where anybody stands on the use of ivermectin to treat covid-19, we now have what amounts to an underground railroad of M.D.s in this state. They may all be quacks, I don't know, but they're of good conscience, citing things like this document on the NIH website on the effectiveness of ivermectin to treat covid-19.

Do we really want to live in a state where medical doctors just treat patients however the government instructs them? Are doctors just boxes in some flowchart cooked up by a combination of pharmaceutical giants, the CDC, and the NIH? I want to live in a state where doctors are free to do the best they can for their patients, knowing they will be liable for malpractice if they do something truly negligent or harmful.

Politicians wonder why there isn't more public trust in the CDC, NIH, and WHO, but whenever a doctor, scientist, or citizen so much as questions their (ever-changing!) guidance, they silence and literally prosecute the non-conformist. Nothing undermines public trust like persecution of dissidents.

I've never taken ivermectin. I don't intend to. I have no idea if it's an effective treatment against covid-19. But I sure as hell want my doctor to have all options on the table when I get sick or injured. Please support HB-1022.

Sincerely,

Michael Hardt
281 River Rd
Canaan, NH 03741
603-523-4583

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Phyllis Burt
Sent: Monday, January 17, 2022 11:39:02 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022 and HB 1369
Importance: Normal

Dear Committee Members,

I am a registered nurse working in long term care for 39 years. I would like to share some brief thoughts about the following bills .

HB 1022 relative to Ivermectin. Throughout my long career, I have witnessed and given many medications that were initially approved for one condition and then discovered to have benefit for other conditions such as: Elavil is an antidepressant but is also used to treat migraines, Gabapentin is an anti-seizure med used also for nerve pain, Depakote is another anti-seizure med now also used for a mood stabilizer, Aspirin for pain but also for blood thinning. These are just a few, there are many more. Ivermectin is a safe med. It has less adverse effects reported according to the WHO than Tylenol and Penicillin. A co worker of mine recently went to St. Martin and talked to a doctor friend over there who regularly prescribed Ivermectin to his patients and he told her the hospitals have very few Covid patients. Please support HB1022.

HB 1369 relative to performing arts venues. Allowing admittance to these venues according to vaccination status is discriminatory. My experience as a nurse has enabled me to witness that vaccination status is no longer preventing the spread of Covid. Last week there were 22 new positive Covid employees in the nursing home where I work. Our staff is over 91% vaccinated. Some had symptoms and some didn't. Very few positive cases in the prior covid group overall but more prominent with this new variant. Education regarding recognizing symptoms and staying home when sick is a better avenue than a discriminatory policy that excludes healthy individuals that may or may not also have natural immunity. Please oppose HB 1369.

Thank you for your consideration in these matters.

Phyllis Burt
Goffstown

Sent from my iPad

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Ufuk
Sent: Monday, January 17, 2022 11:36:38 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Bill hearings on 18/01/2022
Importance: Normal

Dear House Committee of Health, Human Services and Elderly Affairs;

My name is Ufuk Cav from Derry NH. I am writing to respectfully submit my opinion on the three new bills hearings on tuesday.
I oppose HB 1369
I support HB 1022 and SB 347- FN.

Thank you for your public service!

Best Regards,

Ufuk Cav

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Russell Payne
Sent: Monday, January 17, 2022 11:35:41 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

Dear Members of the Health & Human Service and Elderly Affairs Committee:

A basic reason that America has enjoyed 240 plus years of unparalleled liberty is: government has been for the most part prevented from discriminating against one product for the benefit of those who produce a competitive product. This is exactly what disallowing pharmacists to dispense "Ivermectin" is. Government power lust never shrinks in size unless the people demand a stop to their abuse of power. Ivermectin is on the list today, don't be surprised if "penicillin" is on their list tomorrow. This is government operating above the law. Without legal restraint, it up to our state legislatures to put a straight-jacket on this potential tyranny. I urge you to vote OTP to limit bureaucrats and take this straight-jacket off of our liberty in healthcare.

Sincerely & Respectfully

Russ payne

permitting pharmacists to dispense the drug ivermectin by means of a standing order.

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Ufuk
Sent: Monday, January 17, 2022 11:30:31 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Bill hearings on 18/01/2022
Importance: Normal

Dear House Committee of Health, Human Services and Elderly Affairs;

My name is Ufuk Cav from Derry NH. I am writing to respectfully submit my opinion on the three new bills hearings on tuesday.
I oppose HB 1369
I support HB 1022 and SB 347- FN.

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:20 AM
From: enidmack@comcast.net
Sent: Monday, January 17, 2022 11:23:20 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please Support HB 1022 and Oppose HB 1369
Importance: Normal

Hello committee member,
With our freedom continually being eroded, I am asking you to support **HB 1022** which permits pharmacists to dispense ivermectin by means of a standing order. Countless lives could have been saved if the public had access to drugs like Ivermectin. The government in collusion with the pharmaceutical companies and politicians who have a vested interest in profits from the vaccines are guilty of hundreds of thousands of deaths of those who were denied treatment.

I am also asking you to oppose **HB 1369** that would allow performing art centers to create their own covid protocols including requiring vaccination for entry. This is pure discrimination and on this day that we celebrate the life of Martin Luther King, it is shameful that the unvaccinated are being discriminated against and treated like second class citizens…..think Nazi Germany….how quickly we forget the lessons of history!

Thank you for all the work you do on behalf of NH citizens….and don't forget we are not subjects…..I grew up in a country where I was a subject. I never take my citizenship lightly and I'm thankful every day that the Constitution bestows on me the blessings of liberty.

Best regards,
Enid Mackenzie
Goffstown

Archived: Thursday, January 20, 2022 11:01:20 AM
From: ANDREA WARRINER
Sent: Monday, January 17, 2022 9:27:15 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Ivermectin Use - HB1022
Importance: Normal

Dear Representatives,

I am writing to you to ask you to support HB 1022 and to share my experience with Covid 19 and Ivermectin use.

I recently came down with Covid 19. I was very sick, vomiting, fever, weak, achy, the typical flu like symptoms, but they were worse than I had ever experienced. I was also congested and coughing and that concerned me more. I started symptoms on a Sunday but waited until Tuesday morning to test and treat as I wanted to make sure it was Covid 19 and not the flu. I did not want to take Ivermectin if it wasn't Covid and with the tests being inaccurate I wanted to make sure I had enough of a viral load to have as accurate a test as possible.

Tuesday morning I tested positive and started Ivermectin, by Tuesday night I was still symptomatic, but the symptoms were lighter, less intense and fever was less, and by Wednesday night my symptoms were pretty much gone except for some lingering fatigue and loss of taste and smell.

Within 36 hours of taking Ivermectin my symptoms were pretty much gone. This medication possibly saved my life, kept me out of the hospital, reduced the number of days I was sick, therefore lessening the time I had to quarantine.

There is absolutely no reason why this medication should not be available to the general public to treat Covid 19. It would save countless lives and unburden the already burdened healthcare system because of mandates.

If you or your family member were sick, wouldn't you want to treat them as quickly and effectively as possible? Why would you not want the public to have access to this medication?

Thank you for your time and I hope you will do what is right for the people.

Respectfully,

Andrea Warriner

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Pam DiNapoli
Sent: Monday, January 17, 2022 9:23:53 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal
Attachments:
HB 1022 testimony.docx

Good morning Chairman Pearson
I am attaching prepared testimony relative to HB 1022 being heard in committee tomorrow at 2PM. The NH Nurses Association is opposed to this bill. Thank you for your consideration
Pam DiNapoli
Pamela P DiNapoli, PhD, RN, CNL
Executive Director
25 Hall Street Suite 1E
Concord, NH 03301
(603)225-3783
(603) 566-7407 Cell
nhna.ned@gmail.com

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Francine Caroselli
Sent: Monday, January 17, 2022 9:18:29 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

To All HHSEA Committee Members,

I voice my **support for HB 1022,** permitting pharmacists to dispense the drug Ivermectin by means of a standing order, making Ivermectin available without a prescription.

I ask each of you to vote in favor of this bill as well.

Respectfully,

Francine Caroselli
Laconia

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Debbi Schaefer
Sent: Monday, January 17, 2022 8:11:24 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB 1022 & Oppose HB 1369
Importance: Normal

I am writing to ask you to please SUPPORT HB 1022, permitting pharmacists to dispense Ivermectin by means of a standing order. That would make Ivermectin available without a prescription in NH. This should have been made available a long time ago as an optional therapeutic treatment for all people as many have died needlessly over the past 2 years simply because they were not permitted to make their own medical choice. There are many optional therapeutics that were withheld from the public and this in my opinion is a crime.

I also respectfully ask that you OPPOSE HB 1369, which would provide performing arts venues in NH to have the authority to establish their own COVID health and safety policies. In my opinion this is just one more way to divide the people of this state and In My Opinion it is an act of discrimination. Many people would like to live in our state who are just over the boarder because we have allowed the people of this state to live freely. Please do not act like the states who touch our boarders.

I ask this respectfully,
Debbi Schaefer

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Melody Bourgeois
Sent: Monday, January 17, 2022 7:48:41 AM
To: ~House Health Human Services and Elderly Affairs
Subject: SUPPORT HB1022
Importance: Normal

Dear NH Representatives,

I am writing to you today to voice my SUPPORT for HB 1022, permitting pharmacists to dispense the drug ivermectin by means of a standing order. This would make ivermectin available without a prescription in New Hampshire.

As a citizen and Registered Nurse in the State of New Hampshire I believe HB1022 should be supported and passed without delay. The passing of HB1022 would give the citizens of New Hampshire greater access to treatment options beyond the current and limited medications such as Remdesivir, steroids, and monoclonial antibodies.

This Bill is long overdue and NOW is the time to get it passed. Peoples lives are depending on it.
I appreciate your attention and time given to this matter.

Respectfully,
Melody Bourgeois, RN
Weare, NH

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Anthony Amato
Sent: Sunday, January 16, 2022 10:34:37 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

YES! We want HB 1022 passed!
Even El Salvador is passing out ivermectin to its citizens!
It's being used worldwide but not here?????? This is a travesty perpetrated by our government. I personally know several people who have defeated Delta utilizing ivermectin brought in from abroad.

A. Frank Amato
Hooksett

Archived: Thursday, January 20, 2022 11:01:20 AM
From: Linda Howes
Sent: Sunday, January 16, 2022 7:51:16 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022 Please support
Importance: Normal

Dear Representative ~

I'm encouraging your support of HB 1022, permitting pharmacists to dispense Ivermectin.

Ivermectin is a safe, and "powerful, anti-viral, anti-inflammatory wonder drug". Ivermectin won a Nobel prize, has over 63 supportive studies, 30+ randomized trials, and is sold OTC (over-the-counter) in many countries. With the use of Ivermectin India's case counts and deaths rates fell. It's one reason for the low rates of COVID in Africa. This article in Nature shows how Ivermectin is superior to Pfizer's new, expensive, anti-viral drug.

As a health care practitioner I've seen that COVID-19 is highly treatable with early treatment protocols. Fortunately there are many brave front line doctors that take their Hippocratic Oath seriously. They do what they know best to do; research, review data, consult with experts around the world, and treat their patients accordingly using safe and effective, repurposed, inexpensive medications instead of following a "mandated" protocol. Unfortunately, people are having to go "**underground**" to find these brave doctors willing to prescribe early treatment protocols using off-label prescription drugs (40-60% are used off label); anti-virals, steroids, and other appropriately used medications along with recommending targeted nutraceuticals.

Most importantly Ivermectin is being prescribed for early COVID treatment, **keeping people out of hospitals**. These brave doctors then have to find pharmacies willing to fill a prescription for Ivermectin to treat COVID. NH residents are getting their Ivermectin prescription sent from CA, FL, and other states.

Dr Pierre Kory MD, a NY pulmonary and critical care doctor treated patients and saved lives with his early treatment protocol using Ivermectin and steroids while so many were dying. His testimony in the US Senate was excellent. He and his colleagues have formed the FLCCC Alliance providing prevention and treatment protocols.

We can end this pandemic with early treatment protocols!

Thank you for your attention to this important matter,
Linda Howes
Springfield

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Taci Guven
Sent: Sunday, January 16, 2022 7:49:04 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022, HB 1369
Importance: Normal

Dear Committee Members,

I urge you to support HB 1022 and oppose to HB 1369.

Thank you
Taci Guven
Windham, NH

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Maria Therriault
Sent: Sunday, January 16, 2022 7:38:47 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

To Whom It May Concern,
I am writing to express my support for HB 1022 in order to make Ivermectin more widely available without specific prescription. Please consider voting in support of this bill.
Thank you,
Maria Therriault

Sent from Yahoo Mail for iPhone

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Helen Carlson
Sent: Sunday, January 16, 2022 7:02:17 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB 1022; HB1369
Importance: Normal

Please support these bills We do not want government dictating what medications we take or what venues need government control for attendance.

Thanks
Helen carlson
98 exeter River landing
Exeter nh 03833

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Heather Ochieng
Sent: Sunday, January 16, 2022 5:51:26 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Support HB 1022
Importance: Normal

Dear Committee,

Please support HB 1022, permitting pharmacists to dispense the drug ivermectin by means of a standing order and prohibiting them from discouraging patients against using it for COVID-19.

As you know providers can prescribe off-label medications, so long as they obtain informed consent from the patient. It is not the pharmacist's role to interfere with the doctor-patient relationship.

Thanks for your time and attention,

Heather Ochieng

Hollis, NH

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Daniel Richardson
Sent: Saturday, January 15, 2022 1:20:53 PM
To: ~House Health Human Services and Elderly Affairs
Cc: Tom Lanzara; Jim Kofalt; Leah Cushman; Vanessa Sheehan; Michael Yakubovich; Melissa Blasek; Peter Torosian; Tina Harley; Tony Lekas
Subject: In Support of HB 1022 permitting pharmacists to dispense the drug ivermectin by means of a standing,order
Importance: Normal

Ref: Jan 18, 2022 Committee Meeting

HOUSE HEALTH, HUMAN SERVICES AND ELDERLY AFFAIRS COMMITTEE -

I write in support of HB 1022. This bill enables pharmacists to fill and dispense standing orders for ivermectin prescriptions without retaliation from board of medicine. Real life horror stories about about hospital CYA policy standing in the way of life saving ivermectin therapy. Bodily self autonomy and medical choice has been the guiding principle heretofore. Refusal to serve is antithetical to the hippocratic oath and should be subject to legal proceedings. A standing order is an excellent way of allowing the patient to elect their own treatment.

The bill should be amended to include the latest FDA approved therapy Paxlovid. https://us-east-2.protection.sophos.com?d=wikipedia.org&u=aHR0cHM6Ly9lbi53aWtpcGVkaWEub3JnL3dpa2kvTmlybWF0cmVsdmly&i=NWViOWEzNmVkMDA3MzIxNzcxMzJhMTNm&t=cnUrOVMxbEp0U01uK1dwajJJQ05UeElhdVRXMzBRRndHbDdScWpXdm1BVT0=&h=ef0265c4ef2f412dbb5e398144348d01

The bill should be amended to also ban retaliation from the physicians employer and professional association.

Please pass amended HB 1022 as OTP.

Daniel Richardson, Nashua

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Danielle Snow
Sent: Friday, January 14, 2022 7:56:58 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB 1022
Importance: Normal

I ask that you support this bill. We know that medications that work have been withheld from the people. Be bold and support this bill which will make such a difference to the citizens of NH, and this bill could also encourage other states to be brave and show leadership.
Danielle Snow

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:21 AM
From: Maria Mcmanus
Sent: Thursday, January 13, 2022 5:44:08 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Vote
Importance: Normal

HB 1455 oppose, HB 1210 support, HB 1045 support, and HB 1022 support

Thank you,

Maria McManus
Bedford, NH 03110

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:01:21 AM
From: brian trant
Sent: Thursday, January 13, 2022 12:30:41 PM
To: ~House Health Human Services and Elderly Affairs
Subject: HB 1022
Importance: Normal

I support HB 1022 all treatment products should be readily available to everyone.

Brian Trant
Merrimack NH

Archived: Thursday, January 20, 2022 11:20:44 AM
From: sgderoy@gmail.com
Sent: Wednesday, January 19, 2022 9:36:06 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Ivermectin
Importance: Normal

It's time to stop the nonsense. Ivermectin has been an approved drug for many years. Please approve the legislation to allow doctors to treat their patients appropriately!

Regards
Susan DeRoy
New Durham,NH

Archived: Thursday, January 20, 2022 11:20:44 AM
From: TWBridge Associates
Sent: Tuesday, January 18, 2022 7:45:08 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Access to ivermectin
Importance: Normal

I recently had covid that lasted 3 weeks. I believe had I had access to ivermectin, I would not have had to deal with weeks of health challenges.

I would be very happy to discuss this further with you. Ivermectin has a proven efficacy and safety profile that spans decades. Based on large scale success with treatment for covid in India and other countries, why are we limited?

Please, for the sake of humanity, I ask that ivermectin be available in NH for the treatment of covid.

David Francoeur
603-488-1705

Archived: Thursday, January 20, 2022 11:20:44 AM
From: stevethib1@gmail.com
Sent: Tuesday, January 18, 2022 10:49:01 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Invermectin
Importance: Normal

Dear committee members,

Please vote in favor of this legislation to compel pharmacists to fill Ivermectin prescriptions.
I was able to get this treatment & my COVID symptoms started to improve.

No pharmacies as a matter of policy should be able to interfere between patients and doctors unless treatments harm the patient.
There are virtually no harmful effects from taking Ivermectin when taken as prescribed.
There are thousands who've been treated for COVID. When taken immediately, symptoms improve and lives have most certainly been saved.

There is NO REASON to stop patients from taking this drug, and pharmacies have no business getting in the way, even if the director of the NIH – who's been proven to be wrong on just about all things COVID – disapproves!

Decisions regarding prescriptions should be between a doctor and patient.
Currently it is difficult to have a prescription for Ivermectin be fulfilled almost anywhere in NH. This Bill will eliminate that difficulty.

Steve Thiboutot
Hampton, NH
773.490..5080

Archived: Thursday, January 20, 2022 11:20:44 AM
From: Bobbi Slavin
Sent: Tuesday, January 18, 2022 10:44:42 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Ivermectin
Importance: Normal

I am a resident of NH and am requesting that pharmacists should be mandated to fill Ivermection when prescribed. This is potentially a life saving medication - at the very least it is a tested medication and not going to hurt anyone. Those who deny filling prescriptions - may be denying a chance at survival from Covid.
Please do not allow the pharmacists to succumb to the pressure from whoever - to deny that doctor/patient choice.

Bobbi Slavin Cimini

Archived: Thursday, January 20, 2022 11:20:45 AM
From: Timothy Henrick
Sent: Monday, January 17, 2022 10:43:30 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Ivermectin
Importance: Normal

Please support the bill that would allow pharmacist to dispense Ivermectin

Sent from my iPhone

Archived: Thursday, January 20, 2022 11:20:45 AM
From: John Griffin
Sent: Friday, January 14, 2022 8:12:55 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Hb2022
Importance: Normal

I support this bill to make ivermectin an over the counter drug for Early intervention. India used this and vitamin D3 with antibiotic to stop covid cold for, like $2.65 per person.
Jack Griffin Concord

Archived: Thursday, January 20, 2022 11:20:45 AM
From: jpmom39
Sent: Friday, January 14, 2022 5:19:27 PM
To: ~House Health Human Services and Elderly Affairs
Subject: Ivermectin
Importance: Normal

Please support this bill in front of you today Thank you.

Sent from my Galaxy

Archived: Friday, January 28, 2022 11:14:17 AM
From: Tracy Frederick
Sent: Wednesday, January 26, 2022 7:38:46 AM
To: ~House Health Human Services and Elderly Affairs
Subject: HB1022
Importance: Normal

Good morning
I am writing in support of HB1022. There are a great deal of studies showing benefit from ivermectin for the treatment of Covid-19. The studies are more robust than those completed on the vaccines, and there is no reason not to throw every treatment possible at this virus including therapeutics, especially those with demonstrated benefit and little risk. Ivermectin has been used for years all over the world and has an incredibly low risk profile, far lower than Rendesivir. I urge you to make this drug available to the citizens of NH- it will very well save some lives if you do so. Nothing if a fix all here, but the data supports its use and countries all over the world are using it effectively. Thank you.
Sincerely
Tracy Frederick
540 Old East Rd
Whitefield
- under contract in Hollis Nh for full-time residence

Sent from my iPhone

PARTNERS FOR COMMUNITY WELLNESS
Dartmouth-Hitchcock

Dartmouth-Hitchcock
One Medical Center Drive
Lebanon, NH 03756
Phone (603) 650-5000
partnersforcommunitywellness.org

Chairman Mark Pearson
Health, Human Services and Elderly Affairs Committee
Sent Electronically

February 1, 2022

Dear Chairman Pearson and Honorable Members of the Health, Human Services and Elderly Affairs Committee,

I am writing on behalf of Partners for Community Wellness in opposition of HB1455 and HB1022.

Partners for Community Wellness is a network of individuals who work with Dartmouth-Hitchcock Health to improve the health of their communities through education, advocacy and philanthropy. These are neighbors, business leaders, teachers and parents who live throughout the state of New Hampshire and who care about the health of their communities and believe that we all need to work together to make our region the healthiest place it can be.

In support of its mission of building healthier communities, Partners for Community Wellness has established a statement of policy principles that we hope you will consider as you debate HB1455 and HB1022. COVID-19 has undeniably impacted the health of NH in many ways, and we urge you consider the principles and values outlined in the attached letter as you cast your votes. The letter is signed by 22 NH residents and members of Partners for Community Wellness.

Sincerely,

Nicole Coleman
Senior Community Health Partnership Coordinator
Population Health
Dartmouth-Hitchcock

American Journal of Therapeutics 28, e434–e460 (2021)

OPEN

Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines

Andrew Bryant, MSc,[1]* Theresa A. Lawrie, MBBCh, PhD,[2] Therese Dowswell, PhD,[2] Edmund J. Fordham, PhD,[2] Scott Mitchell, MBChB, MRCS,[3] Sarah R. Hill, PhD,[1] and Tony C. Tham, MD, FRCP[4]

Background: Repurposed medicines may have a role against the SARS-CoV-2 virus. The antiparasitic ivermectin, with antiviral and anti-inflammatory properties, has now been tested in numerous clinical trials.

Areas of uncertainty: We assessed the efficacy of ivermectin treatment in reducing mortality, in secondary outcomes, and in chemoprophylaxis, among people with, or at high risk of, COVID-19 infection.

Data sources: We searched bibliographic databases up to April 25, 2021. Two review authors sifted for studies, extracted data, and assessed risk of bias. Meta-analyses were conducted and certainty of the evidence was assessed using the GRADE approach and additionally in trial sequential analyses for mortality. Twenty-four randomized controlled trials involving 3406 participants met review inclusion.

Therapeutic Advances: Meta-analysis of 15 trials found that ivermectin reduced risk of death compared with no ivermectin (average risk ratio 0.38, 95% confidence interval 0.19–0.73; n = 2438; I^2 = 49%; moderate-certainty evidence). This result was confirmed in a trial sequential analysis using the same DerSimonian–Laird method that underpinned the unadjusted analysis. This was also robust against a trial sequential analysis using the Biggerstaff–Tweedie method. Low-certainty evidence found that ivermectin prophylaxis reduced COVID-19 infection by an average 86% (95% confidence interval 79%–91%). Secondary outcomes provided less certain evidence. Low-certainty evidence suggested that there may be no benefit with ivermectin for "need for mechanical ventilation,"

[1]*Population Health Sciences Institute, Newcastle University, Newcastle Upon Tyne, United Kingdom;* [2]*Evidence-based Medicine Consultancy, Bath, United Kingdom;* [3]*Emergency Department, Princess Elizabeth Hospital, Guernsey, United Kingdom; and* [4]*Division of Gastroenterology, Ulster Hospital, Dundonald, Belfast, Northern Ireland, United Kingdom.*

The preprint of this review received no funding. This updated version was funded by the crowdfunding initiative https://www.gofundme.com/f/help-us-get-lifesaving-drug-approved-for-covid19

The authors have no conflicts of interest to declare.

T. A. Lawrie and A. Bryant cowrote the review; they also sifted the search and classified studies for inclusion and entered and checked the data in RevMan and performed analyses. Data extraction was divided among T. A. Lawrie, A. Bryant, and T. Dowswell. T. Dowswell and A. Bryant graded the evidence. E. J. Fordham prepared the text on ivermectin mechanisms, use in pregnancy, and among the elderly. S. R. Hill prepared the brief economic commentary. Clinicians S. Mitchell and T. C. Tham contributed to the interpretation of the evidence in the discussion and conclusions. All authors reviewed and approved the final version of the manuscript.

This article discusses off-label use of the FDA-approved medication ivermectin against COVID-19.

**Address for correspondence: Population Health Sciences Institute, Newcastle University, Baddiley-Clark Building, Richardson Road, Newcastle Upon Tyne NE2 4AX, United Kingdom. E-mail: andy.bryant@ncl.ac.uk*

whereas effect estimates for "improvement" and "deterioration" clearly favored ivermectin use. Severe adverse events were rare among treatment trials and evidence of no difference was assessed as low certainty. Evidence on other secondary outcomes was very low certainty.

Conclusions: Moderate-certainty evidence finds that large reductions in COVID-19 deaths are possible using ivermectin. Using ivermectin early in the clinical course may reduce numbers progressing to severe disease. The apparent safety and low cost suggest that ivermectin is likely to have a significant impact on the SARS-CoV-2 pandemic globally.

Keywords: ivermectin, prophylaxis, treatment, COVID-19, SARS-CoV-2

INTRODUCTION

To date, very few treatments have been demonstrated to reduce the burden of morbidity and mortality from COVID-19. Although corticosteroids have been proven to reduce mortality in severe disease,[1] there has been little convincing evidence on interventions that may prevent disease, reduce hospitalizations, and reduce the numbers of people progressing to critical disease and death.

Ivermectin is a well-known medicine that is approved as an antiparasitic by the World Health Organization and the US Food and Drug Administration. It is widely used in low- and middle-income countries (LMICs) to treat worm infections.[2,3] Also used for the treatment of scabies and lice, it is one of the World Health Organization's Essential Medicines.[4] With total doses of ivermectin distributed apparently equaling one-third of the present world population,[5] ivermectin at the usual doses (0.2–0.4 mg/kg) is considered extremely safe for use in humans.[6,7] In addition to its antiparasitic activity, it has been noted to have antiviral and anti-inflammatory properties, leading to an increasing list of therapeutic indications.[8]

Since the start of the SARS-CoV-2 pandemic, both observational and randomized studies have evaluated ivermectin as a treatment for, and as prophylaxis against, COVID-19 infection. A review by the Front Line COVID-19 Critical Care Alliance summarized findings from 27 studies on the effects of ivermectin for the prevention and treatment of COVID-19 infection, concluding that ivermectin "demonstrates a strong signal of therapeutic efficacy" against COVID-19.[9] Another recent review found that ivermectin reduced deaths by 75%.[10] Despite these findings, the National Institutes of Health in the United States recently stated that "there are insufficient data to recommend either for or against the use of ivermectin for the treatment of COVID-19,"[11] and the World Health Organization recommends against its use outside of clinical trials.[12]

Ivermectin has exhibited antiviral activity against a wide range of RNA and some DNA viruses, for example, Zika, dengue, yellow fever, and others.[13] Caly et al[14] demonstrated specific action against SARS-CoV-2 in vitro with a suggested host-directed mechanism of action being the blocking of the nuclear import of viral proteins[14,15] that suppress normal immune responses. However, the necessary cell culture EC_{50} may not be achievable in vivo.[16] Other conjectured mechanisms include inhibition of SARS-CoV-2 3CLPro activity[17,18] (a protease essential for viral replication), a variety of anti-inflammatory effects,[19] and competitive *binding* of ivermectin with the viral S protein as shown in multiple *in silico* studies.[20] The latter would inhibit viral binding to ACE-2 receptors suppressing infection. Hemagglutination via viral binding to sialic acid receptors on erythrocytes is a recently proposed pathologic mechanism[21] that would be similarly disrupted. Both host-directed and virus-directed mechanisms have thus been proposed, the clinical mechanism may be multimodal, possibly dependent on disease stage, and a comprehensive review of mechanisms of action is warranted.

Developing new medications can take years; therefore, identifying existing drugs that can be repurposed against COVID-19 that already have an established safety profile through decades of use could play a critical role in suppressing or even ending the SARS-CoV-2 pandemic. Using repurposed medications may be especially important because it could take months, possibly years, for much of the world's population to get vaccinated, particularly among LMIC populations.

Currently, ivermectin is commercially available and affordable in many countries globally.[6] A 2018 application for ivermectin use for scabies gives a direct cost of $2.90 for 100 12-mg tablets.[22] A recent estimate from Bangladesh[23] reports a cost of US$0.60—US$1.80 for a 5-day course of ivermectin. For these reasons, the exploration of ivermectin's potential effectiveness against SARS-CoV-2 may be of particular importance

for settings with limited resources.[24] If demonstrated to be effective as a treatment for COVID-19, the cost-effectiveness of ivermectin should be considered against existing treatments and prophylaxes.

The aim of this review was to assess the efficacy of ivermectin treatment among people with COVID-19 infection and as a prophylaxis among people at higher risk of COVID-19 infection. In addition, we aimed to prepare a brief economic commentary (BEC) of ivermectin as treatment and as prophylaxis for COVID-19.[25]

METHODS

The conduct of this review was guided by a protocol that was initially written using Cochrane's rapid review template and subsequently expanded to a full protocol for a comprehensive review.[26]

Search strategy and selection criteria

Two reviewers independently searched the electronic databases of Medline, Embase, CENTRAL, Cochrane COVID-19 Study Register, and Chinese databases for randomized controlled trials (RCTs) up to April 25, 2021 (see **Appendix 1–3**, **Supplemental digital content 1**, http://links.lww.com/AJT/A95); current guidance[25] for the BEC was followed for a supplementary search of economic evaluations. There were no language restrictions, and translations were planned to be performed when necessary.

We searched the reference list of included studies, and of two other 2021 literature reviews on ivermectin,[9] as well as the recent WHO report, which included analyses of ivermectin.[12] We contacted experts in the field (Drs. Andrew Hill, Pierre Kory, and Paul Marik) for information on new and emerging trial data. In addition, all trials registered on clinical trial registries were checked, and trialists of 39 ongoing trials or unclassified studies were contacted to request information on trial status and data where available. Many preprint publications and unpublished articles were identified from the preprint servers MedRχiv and *Research Square*, and the International Clinical Trials Registry Platform. This is a rapidly expanding evidence base, so the number of trials are increasing quickly. Reasons for exclusion were recorded for all studies excluded after full-text review.

Data analysis

We extracted information or data on study design (including methods, location, sites, funding, study author declaration of interests, and inclusion/exclusion criteria), setting, participant characteristics (disease severity, age, gender, comorbidities, smoking, and occupational risk), and intervention and comparator characteristics (dose and frequency of ivermectin/comparator). The primary outcome for the intervention component of the review included death from any cause and presence of COVID-19 infection (as defined by investigators) for ivermectin prophylaxis. Secondary outcomes included time to polymerase chain reaction (PCR) negativity, clinical recovery, length of hospital stay, admission to hospital (for outpatient treatment), admission to ICU or requiring mechanical ventilation, duration of mechanical ventilation, and severe or serious adverse events, as well as post hoc assessments of improvement and deterioration. All of these data were extracted as measured and reported by investigators. Numerical data for outcomes of interest were extracted according to intention to treat.

If there was a conflict between data reported across multiple sources for a single study (eg, between a published article and a trial registry record), we contacted the authors for clarification. Assessments were conducted by 2 reviewers (T.L., T.D., A.B., or G.G.) using the Cochrane RCT risk-of-bias tool.[27] Discrepancies were resolved by discussion.

Continuous outcomes were measured as the mean difference and 95% confidence intervalss (CI), and dichotomous outcomes as risk ratio (RR) and 95% CI.

We did not impute missing data for any of the outcomes. Authors were contacted for missing outcome data and for clarification on study methods, where possible, and for trial status for ongoing trials.

We assessed heterogeneity between studies by visual inspection of forest plots, by estimation of the I^2 statistic ($I^2 \geq 60\%$ was considered substantial heterogeneity),[28] by a formal statistical test to indicate statistically significant heterogeneity,[29] and, where possible, by subgroup analyses (see below). If there was evidence of substantial heterogeneity, the possible reasons for this were investigated and reported. We assessed reporting biases using funnel plots if more than 10 studies contributed to a meta-analysis.

We meta-analyzed data using the random effects model (DerSimonian and Laird method)[30] using RevMan 5.4.1 software.[27,31] The results used the inverse variance method for weighting.[27] Some sensitivity analyses used other methods that are outlined below and some calculations were performed in *R*[32] through an interface[33] to the *netmeta* package.[34] Where possible, we performed subgroup analyses grouping trials by disease severity, inpatients versus outpatients, and single dose versus multiple doses. We performed sensitivity analyses by excluding studies at high risk of bias. We conducted further post hoc sensitivity analyses using alternative methods to test the robustness of results in the presence of zero events in both arms in a number of trials[35] and estimated odds ratios [and additionally RR for the Mantel–Haenszel

(MH) method] using a fixed effects model. The models incorporate evidence from single-zero studies without having to resort to continuity corrections. However, double-zero studies are excluded from the analysis; so, the risk difference was also assessed using the MH method as this approach can adequately incorporate trials with double-zero events. This method can also use a random-effects component. A "treatment-arm" continuity correction was used, where the values 0.01, 0.1, and 0.25 were added where trials reported zero events in both arms. It has been shown that a nonfixed continuity correction is preferable to the usual 0.5.[35] Other methods are available but were not considered due to difficulty in interpretation, sensitivity of assumptions, or the fact they are rarely used in practice.[36–40]

Trial sequential analysis

When a meta-analysis is subjected to repeated statistical evaluation, there is an exaggerated risk that "naive" point estimates and confidence intervals will yield spurious inferences. In a meta-analysis, it is important to minimize the risk of making a false-positive or false-negative conclusion. There is a trade-off between the risk of observing a false-positive result (type I error) and the risk of observing a false-negative result (type II error). Conventional meta-analysis methods (eg, in RevMan) also do not take into account the amount of available evidence. Therefore, we examined the reliability and conclusiveness of the available evidence using trial sequential analyses (TSA).[41–43] The DerSimonian–Laird (DL) method was used because this is most often used in meta-analytic practice and was also used in the primary meta-analysis.[30]

The TSA was used to calculate the required information size (IS) to demonstrate or reject a relative reduction in the risk (RRR) of death in the ivermectin group, as found in the primary meta-analysis. We assumed the estimated event proportion in the control group from the meta-analysis because this is the best and most representative available estimate. Recommended type I and II error rates of 5% and 10% were used, respectively (power of 90%),[43] powering the result on the effect observed in the primary meta-analyses. We did not identify any large COVID-19 trials powered on all-cause mortality, so powering on some external meaningful difference was not possible. Any small RRR is meaningful in this context, given the scale of the pandemic, but the required IS would be unfeasibly high for this analysis if powered on a small difference. The only reliable data on ivermectin in its repurposed role for treatment against COVID-19 will be from the primary meta-analysis. Therefore, assuming it does not widely deviate from other published systematic reviews, a pragmatic decision was therefore made to power on the pooled meta-analysis effect estimate for all-cause mortality a priori. This is more reflective of a true meaningful difference. We used a model variance-based estimate to correct for heterogeneity. A continuity correction of 0.01 was used in trials that reported zero events in one or both arms. The required IS is the sample size required for a reliable and conclusive meta-analysis and is at least as large as that needed in a single powered RCT. The heterogeneity corrected required IS was used to construct sequential monitoring boundaries based on the O'Brien–Fleming type alpha-spending function for the cumulative z-scores (corresponding to the cumulative meta-analysis),[43] analogous to interim monitoring in an RCT, to determine when sufficient evidence had been accrued. These monitoring boundaries are relatively insensitive to the number of repeated significance tests. They can be used to further contextualize the original meta-analysis and enhance our certainty around its conclusions. We used a two-sided test, so also considered futility boundaries (to test for no statistically significant difference) and the possibility that ivermectin could harm. Sensitivity analyses were performed excluding the trial of Fonseca,[44] which was a cause of substantial heterogeneity (but retained in the core analysis because it was at low risk of bias). Its removal dramatically reduced I^2 and D^2 (diversity) estimates, thus reducing the model variance-based estimate to correct for heterogeneity. Two further sensitivity analyses were performed using 2 alternative random effect models, namely the Biggerstaff–Tweedie (BT) and Sidik–Jonkman (SJ) methods.[43]

All outcomes have been assessed independently by 2 review authors (T.D. and A.B.) using the GRADE approach,[45] which ranks the quality and certainty of the evidence. The results of the TSAs will also form part of the judgment for the primary all-cause mortality outcome. The results are presented in a summary of findings table. Any differences in judgments were resolved by discussion with the wider group. We used Cochrane Effective Practice and Organisation of Care guidance to interpret the evidence.[46]

RESULTS

Search results and risk-of-bias assessment

The combined and preliminary deduplicated total was n = 583. We also identified 11 records from other sources (reference lists, etc). See PRISMA flow diagram for inclusion and exclusion details of these references (Figure 1).

The supplementary search for the BEC identified 17 studies, of which 4 were retrieved in full. No full trial- or model-based economic evaluations (cost–utility analyses, cost–effectiveness analyses, or cost–benefit analyses) were identified.

Twenty-one trials in treatment and 2 trials in prophylaxis of COVID-19 met review inclusion. One further study[47] reported separate treatment and prophylaxis components; we label this study "Elgazzar" under both questions. In effect, there were 22 trials in treatment and 3 in prophylaxis. All of these contributed data to at least one review outcome and meta-analysis. Fifteen trials contributed data for the primary outcome for ivermectin treatment (death); 3 studies reported the primary outcome for prophylaxis (COVID-19 infection). Characteristics of included studies are given in Table 1. Seventeen studies[47–63] were excluded as they were not RCTs and we identified 39 ongoing studies[64–102] and 2 studies[103,104] are awaiting classification.

A risk-of-bias summary graph is given in Figure 2. Eleven studies[23,24,44,47,105,106–111] used satisfactory random sequence generation and allocation concealment. Two trials described satisfactory sequence generation, but it was unclear whether allocation was concealed.[112,113]

Ten trials reported adequate blinding of the participants/personnel and/or the outcome assessors.[23,24,44,105,107,109,110,111,113,114] The others were either unclear or high risk for blinding. We considered blinding to be a less important criterion for evaluation of evidence related to the review's primary outcomes, namely death and laboratory-confirmed COVID-19 infection, which are objective outcomes.

We did not consider publication on preprint web sites to constitute a risk of bias because all studies were scrutinized and peer reviewed by us during the review process and, where additional information was needed, we contacted the authors for clarification.

Main findings

Twenty-four RCTs (including 3 quasi-RCTs) involving 3406 participants were included, with sample sizes ranging from 24 to 476 participants. Twenty-two trials in treatment and 3 trials in prophylaxis met review inclusion, including the trial of Elgazzar et al, which reported both components. For trials of COVID-19 treatment, 16 evaluated ivermectin among participants with mild to moderate COVID-19 only; 6 trials included patients with severe COVID-19. Most compared ivermectin with placebo or no ivermectin; 3 trials included an active comparator (Table 1). Three RCTs involving 738 participants were included in the prophylaxis trials. Most trials were registered, self-funded, and undertaken by clinicians working in the field. There were no obvious conflicts of interest noted, with the exception of two trials.[85,139]

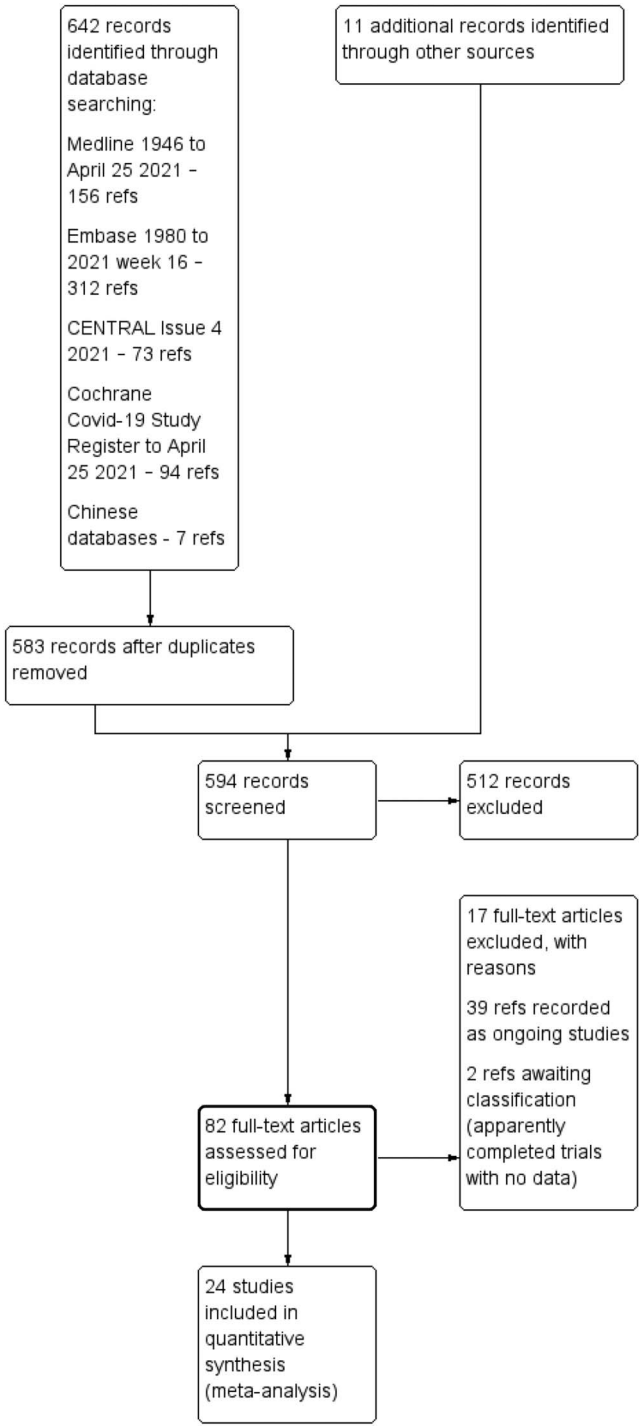


FIGURE 1. Study flow diagram from search on 25 April 2021.

Table 1. Summary of study characteristics.

Study ID	Country	Design	Funding	Participants	Sample size	Ivermectin dose and frequency*	Comparator	Origin of data	Main outcomes reported
COVID-19 treatment studies									
Ahmed 2020[23]	Bangladesh	Double-blind	BPL(Pharma); Bangladesh, Canada, Sweden, and UK govt	Mild to moderate COVID (inpatients)	72	12 mg × 1 day or × 5 days (3 study arms)*	Placebo	Published in PR journal; emailed/ responded with data	Time to viral clearance (PCR –ve), remission of fever and cough within 7 days, duration of hospitalization, mortality, failing to maintain sats >93%, adverse events, PCR –ve at 7 and 14 days
Babalola 2020[105]	Nigeria	Double-blind	Self-funded	Asymptomatic, mild or moderate COVID (45 inpatients and 17 outpatients)	62	6 mg every 84 hrs × 2 wks (arm 1) or 12 mg every 84 hrs × 2 wks (arm 2)	Ritonavir/lopinavir	MedRxiv preprint: emailed/ responded with data. Paper accepted for publication	Time to PCR –ve, laboratory parameters (platelets, lymphocytes, clotting time), clinical symptom parameters
Bukhari 2021[135]	Pakistan	Open-label	None reported	Mild to moderate COVID (inpatients)	100	12 mg × 1 dose	SOC	MedRxiv preprint	Viral clearance, any adverse side effects, mechanical ventilation
Chaccour 2020[24]	Spain	Double-blind	Idapharma, ISGlobal, and the University of Navarra	Mild COVID (outpatients)	24	0.4 mg/kg × 1 dose	Placebo	Published in PR journal	PCR +ve at day 7, proportion symptomatic at day 4,7,14,21, progression, death, adverse events
Chachar 2020[112]	Pakistan	Open-label	Self-funded	Mild COVID (outpatients)	50	12 mg at 0, 12, and 24 hours (3 doses)	SOC	Published in PR journal	Symptomatic at day 7
Chowdhury 2020[136]	Bangladesh	Quasi-RCT	None reported	Outpatients with a +ve PCR (approx. 78% symptomatic)	116	0.2 mg/kg x1 dose*	HCQ 400 mg 1st day then 200 mg BID × 9 days + AZM 500 mg daily × 5 days	Research square preprint	Time to –ve PCR test; period to symptomatic recovery; adverse events
Elgazzar 2020[47]	Egypt	RCT	None reported	Mild to severe COVID (inpatients)	200	0.4 mg/kg daily × 4 days	HCQ 400 mg BID × 1 day then 200 mg BID × 9 days	Research square preprint: emailed/ responded with data	Improved, progressed, died. Also measured CRP, D-dimers, HB, lymphocyte, serum ferritin after one week of treatment
Fonseca 2021[44]	Brazil	Double-blind	Institution-funded	Moderate to severe (inpatients)	167	14 mg daily × 3 days (plus placebos × 2 additional days)	HCQ—400 mg BID on day 0 then daily × 4 days; CQ -450 mg BID day 0 then daily × 4 days	Prepublication data/ manuscript in progress obtained via email	Death, invasive mechanical ventilation
Gonzalez 2021[137]	Mexico	Double-blind	Institution-funded	Moderate to severe (inpatients)	108	12 mg × 1 dose	Placebo	MedRxiv preprint	Length of hospital stay, invasive mechanical ventilation, death, time to negative PCR
Hashim 2020[138]	Iran	Quasi-RCT	None reported	Mild to critical (inpatients)	140	0.2 mg/kg × 2 days* Some had a 3rd dose a week later	SOC	MedRxiv preprint	Death, mean time to recovery, disease progression (deterioration)
Krolewiecki 2020[106]	Argentina	Open-label	None reported	Mild to moderate (inpatients)	45	0.6 mg/kg/d × 5 days	Placebo	Research Gate and SSRN preprints	Viral load reduction in respiratory secretions day 5, IVM concentrations in plasma, severe adverse events
Lopez-Medina 2021[85]	Columbia	Double-blind	Institution-funded	Mild (outpatients)	476	0.3 mg/kg elixir × 5 days	Placebo	Published in a PR journal	Resolution of symptoms within 21 days, deterioration, clinical condition, hospitalization, adverse events
Mahmud 2020[107]	Bangladesh	Double-blind	None reported	Mild to moderate COVID (inpatients)	363	12 mg × 1 dose*	Placebo + SOC	Data published on clinical trial registry and clarification obtained via email	Improvement, deterioration, late clinical recovery, persistent PCR test +ve

(*Continued on next page*)

Table 1. (*Continued*) Summary of study characteristics.

Study ID	Country	Design	Funding	Participants	Sample size	Ivermectin dose and frequency*	Comparator	Origin of data	Main outcomes reported
Mohan 2021[110]	India	Double-blind	Institution-funded	Mild to moderate	152	12 mg or 24 mg elixir × 1 dose	Placebo	MedRxiv preprint research	Conversion of RT-PCR to negative result, decline of viral load at day 5 from enrollment
Niaee 2020[108]	Iran	Double-blind	Institution-funded	Mild to severe COVID	180	0.2 mg/kg × 1 and 3 other dosing options) ~ 14 mg tablet†	Placebo	Research Square preprint	Deaths, length of stay, biochemical parameters
Okumus 2021[115]	Turkey	Quasi-RCT	None reported	Severe COVID	66	0.2 mg/kg × 5 days	SOC	Prepublication data/ manuscript in progress obtained via email	Clinical improvement, deterioration, death, SOFA scores
Petkov 2021[139]	Bulgaria	Double-blind	Pharma-funded	Mild to moderate COVID	100	0.4 mg/kg × 3 days	Placebo	Prepublication data obtained from another source	Rate of conversion to PCR negative
Podder 2020[140]	Bangladesh	Open-label	Self-funded	Mild to moderate (outpatients)	62	0.2 mg/kg × 1 dose	SOC	Published in PR journal	Duration of symptoms, recovery time to symptom free from enrollment, recovery time to symptom free from symptom onset, repeat PCR result on day 10
Raad 2021[113]	Lebanon	Double-blind	Self-funded	Asymptomatic outpatients	100	9 mg PO if 45 kg–64 kg, 12 mg PO if 65 kg–84 kg and 0.15 mg/kg if body weight ≥85 kg	Placebo	Prepublication data/ manuscript in progress obtained via email	Viral load reduction, hospitalization, adverse effects
Ravikirti 2021[109]	India	Double-blind	Self-funded	Mild to moderate COVID (inpatients)	112	12 mg × 2 days + SOC	Placebo + SOC	Published in PR journal	A negative RT-PCR report on day 6, symptomatic on day 6, discharge by day 10, admission to ICU, need for invasive mechanical ventilation, mortality
Rezai 2020[111]	Iran	Double-blind	None reported	Mild to moderate (inpatient)	60	0.2 mg/kg × 1 dose	SOC	Prepublication data obtained from another source	Clinical symptoms, respiratory rate and O2 saturation
Schwartz 2021[114,141]	Israel	Double-blind	None reported	Mild to moderate (outpatients)	94	0.15–0.3 mg/kg × 3 days	Placebo	Prepublication data obtained from another source	Viral clearance at day 4, 6, 8 and 10), hospitalization
COVID-19 prophylaxis studies									
Chahla 2021[142]	Argentina	Open-label	None reported	Health care workers	234	12 mg (in drops) weekly + iota-carrageenan 6 sprays daily × 4 wk	SOC	Prepublication data/ manuscript in progress obtained via email	COVID-19 infection (not clear if measured by PCR or symptoms)
Elgazzar 2020[47]	Egypt	Open-label	Self-funded	Health care and family contacts	200	0.4 mg/kg, weekly × 2 weeks	SOC	Research square preprint: emailed/ responded with data	Positive PCR test
Shouman 2020[143]	Egypt	Open-label	Self-funded	Family contacts	304	2 doses (15–24 mg depending on weight) on day 1 and day 3	SOC	Published in PR journal	Symptoms and/or positive COVID-19 PCR test within 14 days; adverse events

*Also administered doxycycline.
†multiarm trial.
SOC, standard of care; PR, peer review.

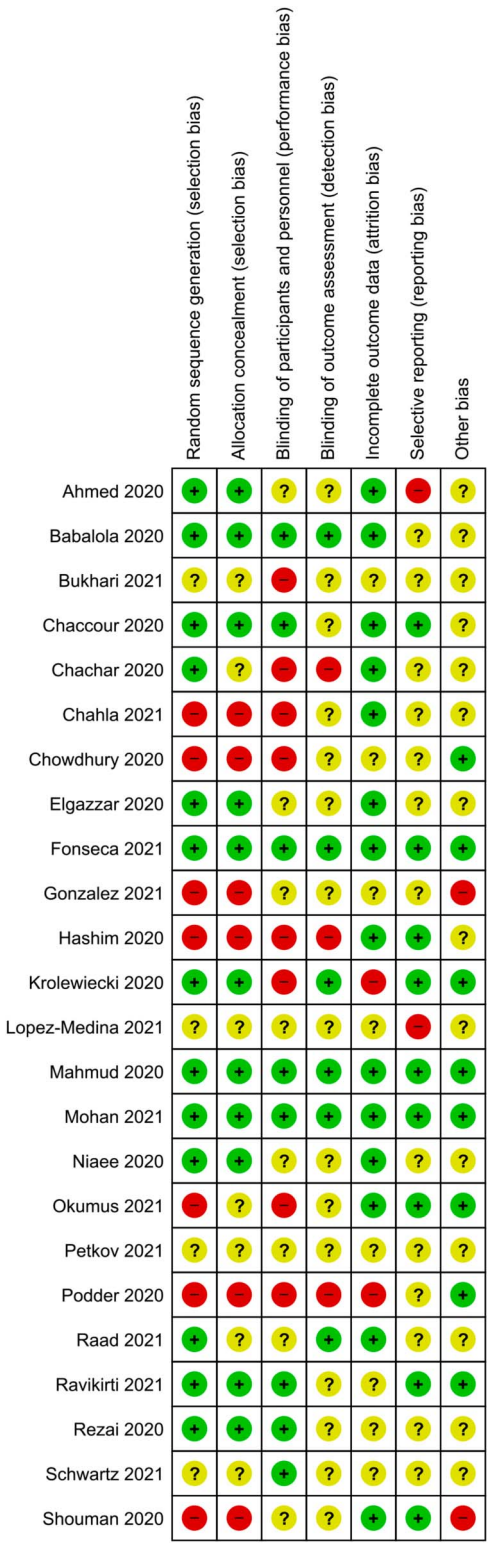


FIGURE 2. Risk-of-bias summary: review authors' judgments about each risk of bias item for each included study.

Ivermectin treatment versus no ivermectin treatment

Twenty-two trials (2668 participants) contributed data to the comparison ivermectin treatment versus no ivermectin treatment for COVID-19 treatment.

All-cause mortality

Meta-analysis of 15 trials, assessing 2438 participants, found that ivermectin reduced the risk of death by an average of 62% (95% CI 27%–81%) compared with no ivermectin treatment [average RR (aRR) 0.38, 95% CI 0.19 to 0.73; $I^2 = 49\%$]; risk of death 2.3% versus 7.8% among hospitalized patients in this analysis, respectively (SoF Table 2 and Figure 3). Much of the heterogeneity was explained by the exclusion of one trial[44] in a sensitivity analysis (average RR 0.31, 95% CI 0.17–0.58, n = 2196, $I^2 = 22\%$), but because this trial was at low risk of bias, it was retained in the main analysis. The source of heterogeneity may be due to the use of active comparators in the trial design. The results were also robust to sensitivity analyses excluding 2 other studies with an active treatment comparator (average RR 0.41, 95% CI 0.23–0.74, n = 1809, $I^2 = 8\%$). The results were also not sensitive to the exclusion of studies that were potentially at higher risk of bias (average RR 0.29, 95% CI 0.10–0.80, 12 studies, n = 2095, $I^2 = 61\%$), but in subgroup analysis, it was unclear as to whether a single dose would be sufficient. The effect on reducing deaths was consistent across mild to moderate and severe disease subgroups. Subgrouping data according to inpatient and outpatient trials was not informative because few outpatient studies reported this serious outcome. The conclusions of the primary outcome were also robust to a series of alternative post hoc analyses that explored the impact of numerous trials that reported no deaths in either arm. Extreme sensitivity analyses using a treatment arm continuity correction of between 0.01 and 0.5 did not change the certainty of the evidence judgments (Table 3).

Trial sequential analysis

TSA, using the DL random-effects method, showed that there may have been sufficient evidence accrued before the end of 2020 to show significant benefit of ivermectin over control for all-cause mortality. The cumulative z-curve in Figure 8 crossed the trial sequential monitoring boundaries after reaching the required IS, implying that there is firm evidence for a beneficial effect of ivermectin use over no ivermectin use in mainly hospitalized participants with mild to moderate COVID-19 infection.

Table 2. Summary of findings table of ivermectin versus no ivermectin for COVID-19 treatment in any setting.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk No ivermectin	Corresponding risk Ivermectin			
Death from any cause	78 per 1000 (all disease severity)	48 fewer deaths per 1000 (21–63)	RR = 0.38 (0.19–0.73)	2438 (15)	Moderate†
Recovery time to negative PCR test, in days	Absolute risks were not computed due to certainty of evidence being low and, in some cases, number of events being sparse		MD = −3.20 (−5.99 to −0.40)	375 (6)	Very low†,‡,§
Time to clinical recovery, in days (outpatients)			MD = −1.06 (−1.63 to −0.49)	176 (2)	Very low†,‡,§
Time to clinical recovery, in days (mild to moderate COVID-19 inpatients)			MD = −7.32 (−9.25 to −5.39)	96 (1)	Very low†,¶
Time to clinical recovery, in days (severe COVID-19 inpatients)			MD = −3.98 (−10.06 to 2.10)	33 (1)	Very low†,¶
Admission to ICU			RR=1.22 (0.75–2.00)	379 (2)	Very low¶,‖
Need for mechanical ventilation			RR=0.66 (0.14–3.00)	431 (3)	Low§,‖
Length of hospital stay, in days			MD= 0.13 (−2.04 to 2.30)	68 (1)	Very low†,¶
Admission to hospital			RR 0.16 (0.02–1.32)	194 (2)	Very low†,¶
Duration of mechanical ventilation	Not reported				
Improvement (mild to moderate COVID-19)*	635 improved per 1000	159 more per 1000 (from 51 more to 286 more)	RR 1.25 (1.08–1.45)	681 (5)	Low†,‡
Deterioration (any disease severity)	143 per 1000	93 fewer per 1000 (from 50 fewer to 116 fewer)	RR 0.35 (0.19–0.65)	1587 (7)	Low†,‡
Serious adverse events	7/867 (0.8%) had an SAE in ivermectin group and 2/666 (0.3%) in control		RR=1.65 (0.44–6.09)	1533 (11)	Low†,‡

*Only one study contributed to the "severe" COVID-19 subgroup and subgroup data were not pooled due to subgroup differences.
†Downgraded −1 for study design limitations.
‡Downgraded −1 for inconsistency.
§Downgraded −1 for imprecision.
¶Downgraded −2 for imprecision/sparse data.
‖Downgraded −1 for indirectness.

The TSA was used to calculate the IS required to demonstrate or reject a 62% RRR of death in the ivermectin group, as observed in the primary meta-analysis. This estimate is similar to effect estimates reported in other reviews.[10] We assumed a 7.8% event proportion in the control group, which was the average control group

Table 3. Sensitivity analyses for death from any cause considering methods for dealing with zero events in trials.

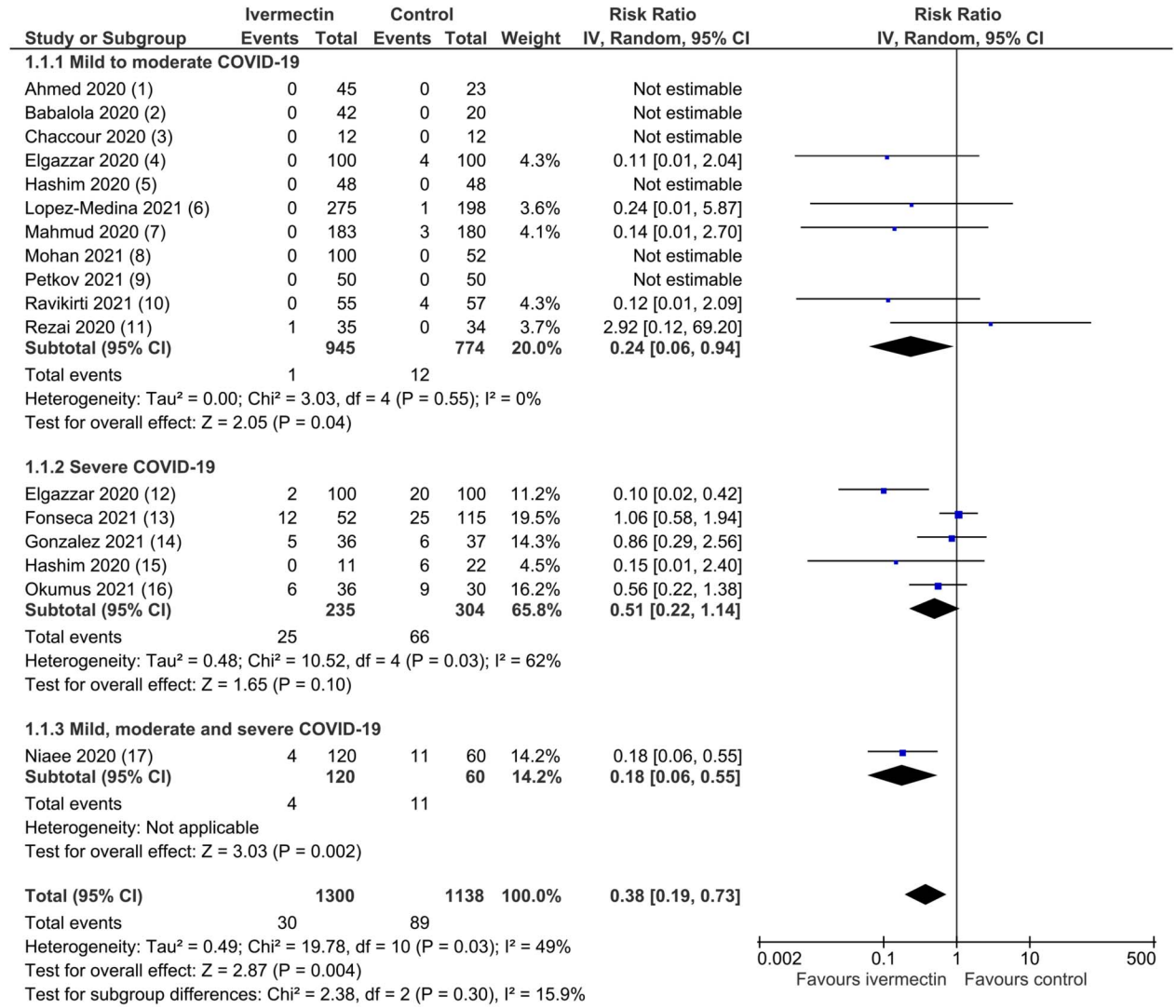
Method	Measure	Model	Effect size (95% CI)	Details
Peto	OR	FE	0.35 (0.24 to 0.53)	Handles single-zero trials
M-H	OR	FE	0.37 (0.24 to 0.56)	Handles single-zero trials
M-H	OR	RE	0.33 (0.16 to 0.68)	Handles single-zero trials
M-H	RR	FE	0.42 (0.29 to 0.60)	Handles single-zero trials
M-H	RR	RE	0.37 (0.19 to 0.74)	Handles single-zero trials
M-H	RD	FE	−0.04 (−0.06 to −0.02)	Handles double-zero trials
M-H	RD	RE	−0.03 (−0.06 to −0.00)	Handles double-zero trials
IV	RD	FE	−0.01 (−0.02 to −0.00)	Handles double-zero trials
IV	RD	RE	−0.02 (−0.04 to −0.00)	Handles double-zero trials
Treatment arm continuity correction methods using IV			Accounting for double zeros	Accounting for all zeros
0.01	RR	FE	0.54 (0.36 to 0.79)	0.58 (0.39–0.88)
0.01	RR	RE	0.43 (0.25 to 0.72)	0.58 (0.39–0.88)
0.1	RR	FE	0.54 (0.37 to 0.79)	0.56 (0.38–0.84)
0.1	RR	RE	0.43 (0.26 to 0.73)	0.46 (0.26–0.80)
0.25	RR	FE	0.54 (0.37 to 0.79)	0.55 (0.37–0.81)
0.25	RR	RE	0.44 (0.26 to 0.73)	0.45 (0.26–0.76)
0.5	RR	FE	0.54 (0.37 to 0.79)	0.55 (0.35–0.78)
0.5	RR	RE	0.45 (0.27 to 0.74)	0.47 (0.29–0.75)

FE, fixed effects; IV, inverse variance; M-H, Mantel-Haenszel; RD, risk difference; RE, random effects; TACC, treatment arm continuity correction.

event rate from the primary meta-analysis. We used a model variance-based estimate of 49.1% (diversity estimate) to correct for heterogeneity. The required IS was 1810 participants (Figure 8), which was exceeded by the total number of observed participants in the meta-analysis (n = 2438). In the TSA plots, the red dashed lines in Figure 8 represent the trial sequential monitoring boundaries using the O'Brien–Fleming alpha-spending function. The solid blue line is the cumulative z-curve and represents the observed trials in the cumulative meta-analysis. The adjusted significance boundaries for the cumulative z-curve were constructed under the assumption that significance testing may have been performed each time a new trial was added to the meta-analysis. In Figure 8, the z-curve crosses the boundary after reaching the required IS, thereby supporting the previous conclusion in RevMan 5.4.1[31] using the DL method that ivermectin is superior to control in reducing the risk of death.

Sensitivity analyses

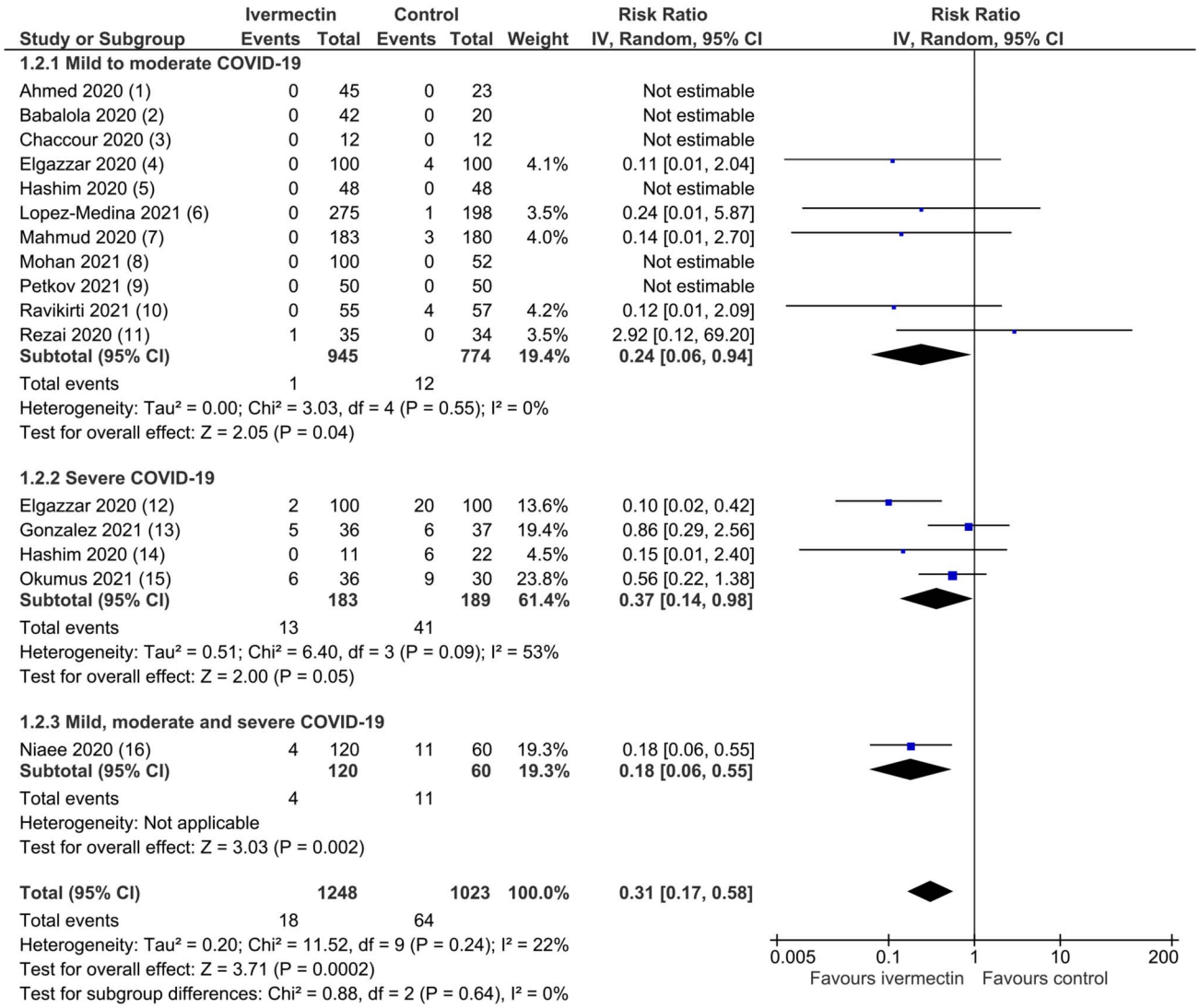
Sensitivity analysis excluding the trial of Fonseca[44] significantly reduced heterogeneity in the meta-analysis and thus the diversity estimate in the TSA using the DL model. This strengthened the suggestion in the primary core analysis that the required IS had been reached (Figure 9). Because the DL estimator could potentially underestimate the between-trials variance,[43] we performed further sensitivity analyses using 2 alternative random-effects model approaches. The results of the primary TSA analysis were robust to sensitivity analysis using the BT method with the same parameters, excluding the Fonseca[44] trial, which was a cause of substantial heterogeneity (Figure 10). The TSA



Footnotes

(1) IVM 12mg x 5 days (24 pts) or IVM 12 mg + doxy x 5 days (24 pts)
(2) IVM 6mg-12mg every 84 hrs for 2 wks; vs lopinavir/ritonavir
(3) IVM 0.4mg/kg single dose
(4) IVM up to 24 mg daily for 4 days vs HCQ
(5) IVM 0.2mg/kg x 2-3 days + Doxy 100 mg BID x 10 days
(6) IVM 0.3mg/kg solution for 5 days vs placebo solution
(7) IVM 6mg once + Doxy 100 mg x 5 days
(8) IVM 12mg or 24 mg single dose
(9) IVM 0.4mg/kg x 3 days
(10) IVM 12 mg x 2 days
(11) IVM 0.2mg/kg single dose
(12) IVM up to 24 mg daily for 4 days vs HCQ
(13) IVM 14 mg x 3 days vs HCQ x 5 days or CQ x 5 days
(14) IVM single dose 12mg or 18mg depending on weight
(15) IVM 0.2mg/kg x 2-3 days + Doxy 100 mg BID x 10 days
(16) IVM 0.2mg/kg x 5 days (both arms received HCQ, favipiravir, azithromycin)
(17) IVM 0.2mg/kg to 400 µgm/kg (1 to 3 doses) vs HCQ

FIGURE 3. Death due to any cause.



Footnotes

(1) IVM 12mg x 5 days (24 pts) or IVM 12 mg + doxy x 5 days (24 pts)
(2) IVM 6mg-12mg every 84 hrs for 2 wks; vs lopinavir/ritonavir
(3) IVM 0.4mg/kg single dose
(4) IVM up to 24 mg daily for 4 days vs HCQ
(5) IVM 0.2mg/kg x 2-3 days + Doxy 100 mg BID x 10 days
(6) IVm 0.3mg/kg for 5 days
(7) IVM 6mg once + Doxy 100 mg x 5 days
(8) IVM 12mg or 24 mg single dose
(9) IVM 0.4mg/kg x 3 days
(10) IVM 12 mg x 2 days
(11) IVM 0.2mg/kg single dose
(12) IVM up to 24 mg daily for 4 days vs HCQ
(13) IVM single dose 12mg or 18mg depending on weight
(14) IVM 0.2mg/kg x 2-3 days + Doxy 100 mg BID x 10 days
(15) IVM 0.2mg/kg x 5 days (both arms received HCQ, favipiravir, azithromycin)
(16) IVM 0.2mg/kg to 400 µgm/kg (1 to 3 doses) vs HCQ

FIGURE 4. Death due to any cause, excluding an outlier study responsible for the heterogeneity.

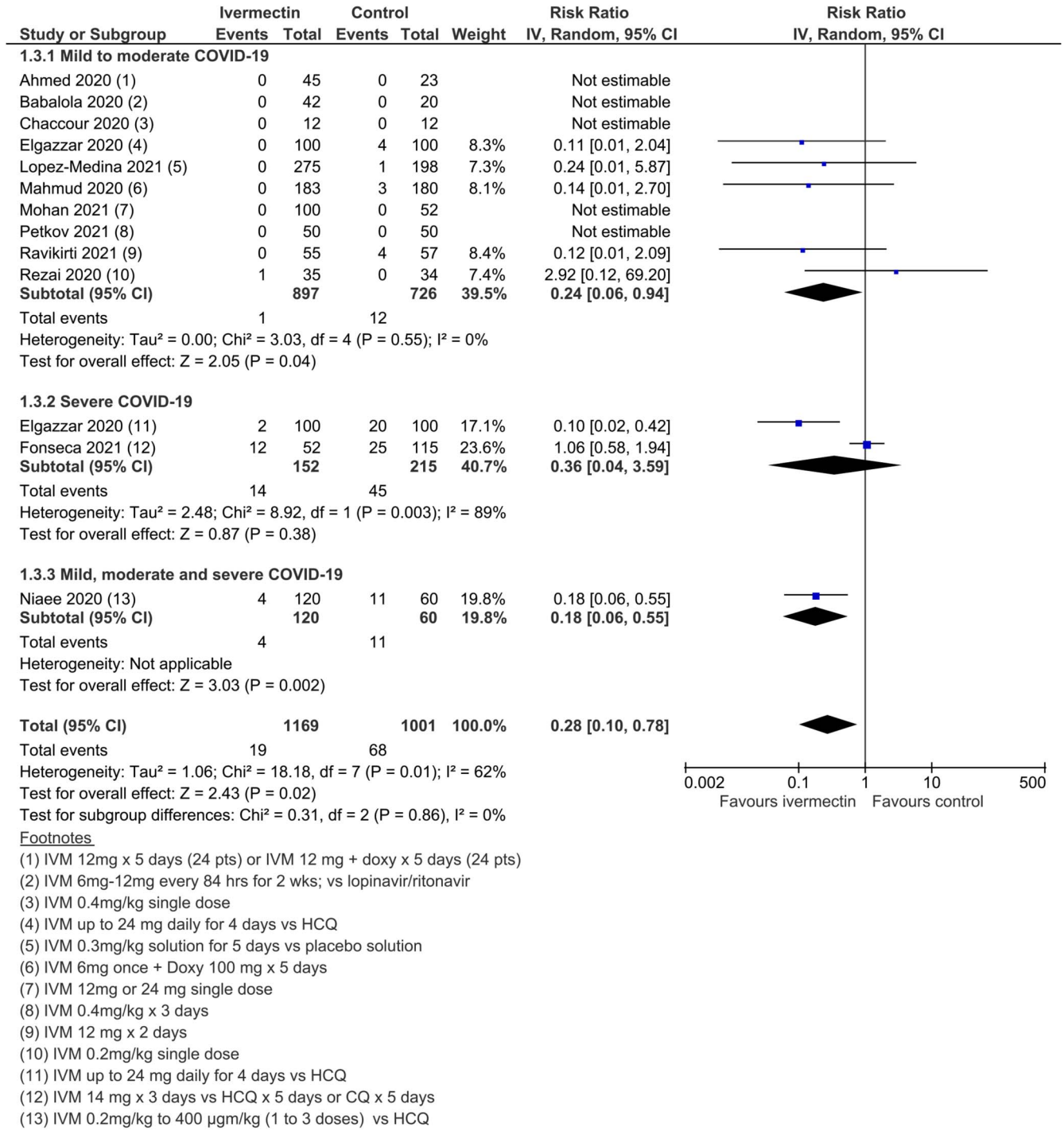


FIGURE 5. Death due to any cause, excluding high risk-of-bias studies.

comprehensively confirms the result of the conventional meta-analysis. The required IS was 1064.

The required IS was not reached in the TSA using the SJ method, largely because diversity from the model was high (Figure 11). The SJ estimator may overestimate the between-trials variance in meta-analyses with mild heterogeneity, thus producing artificially wide confidence intervals.[43] When the diversity estimate was reduced to the same as in the DL model, the required IS was reached in the SJ model (data not shown). There was no evidence of futility using the SJ method in any scenario.

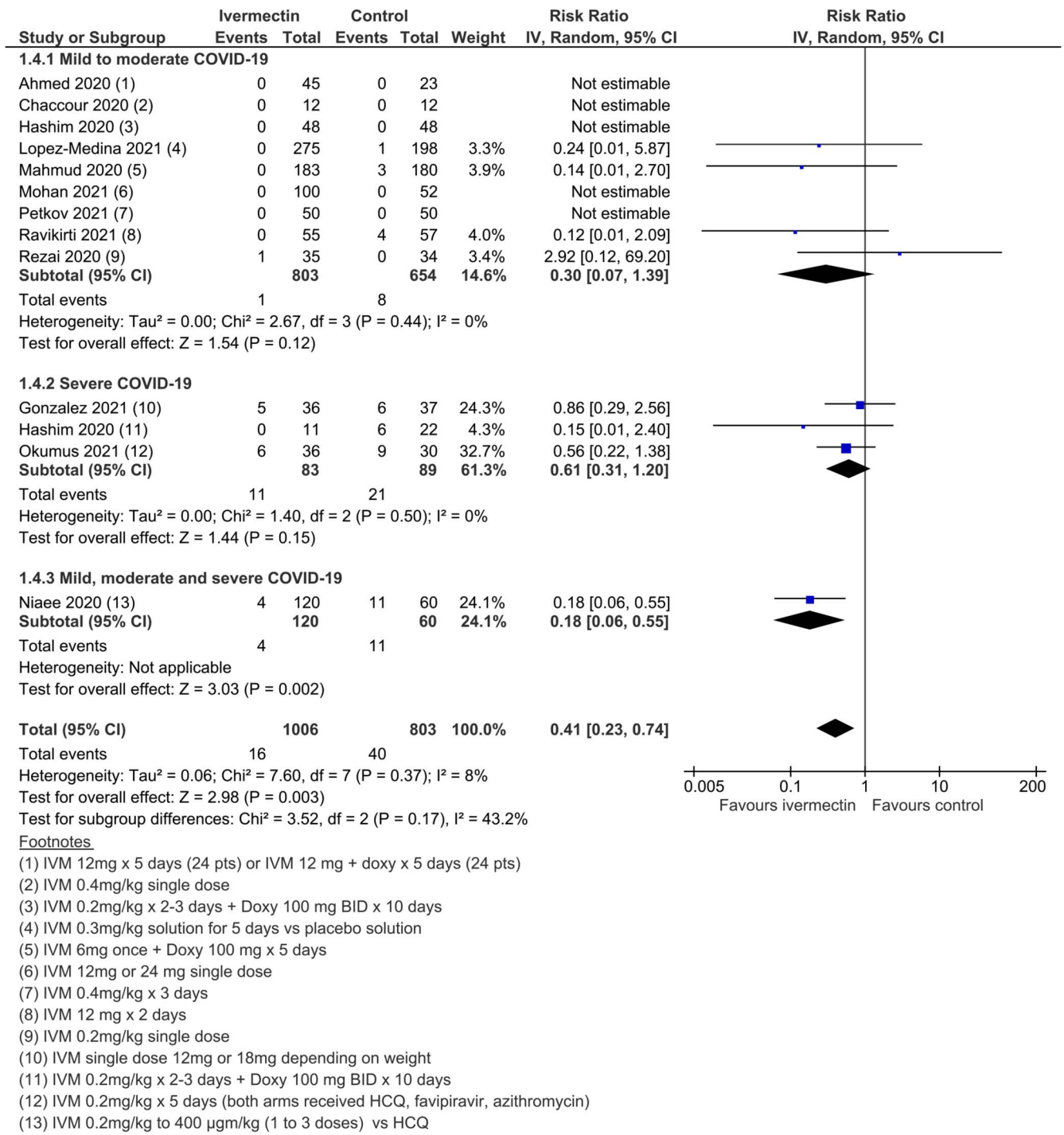


FIGURE 6. Death due to any cause, excluding studies with active controls.

Certainty of the evidence for all-cause mortality

Overall, death from any cause, taking into account all composite analyses, was judged to provide moderate-certainty evidence (SoF Table 2 and Figures 4–11). A funnel plot corresponding to the primary outcome of death from any cause did not seem to suggest any evidence of publication bias (Figure 7). Furthermore, the ease with which trial reports can be uploaded as preprints should reduce this risk.

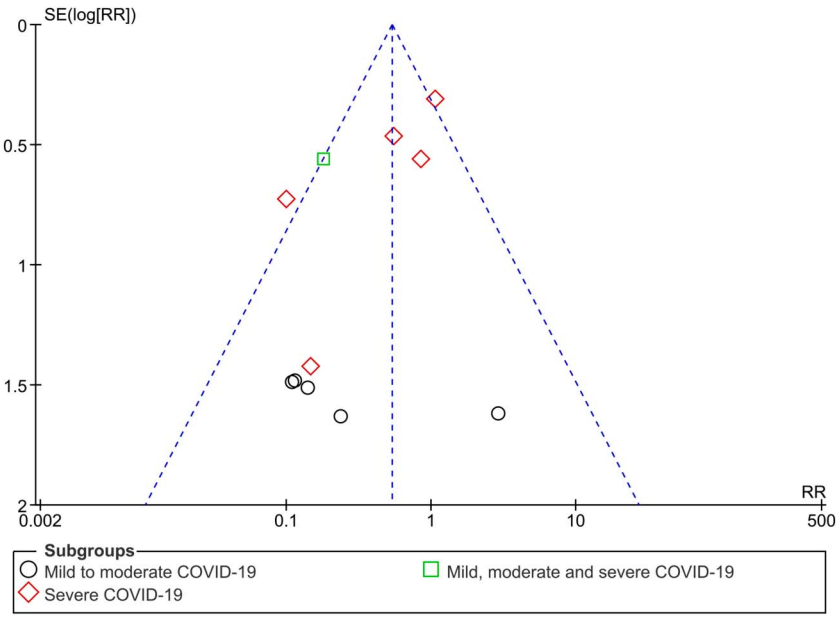


FIGURE 7. Funnel plot of ivermectin versus control for COVID-19 treatment for all-cause death (subgrouped by severity).

Secondary outcomes

Secondary outcomes provided low to very low certainty evidence (SoF Table 2). Low-certainty findings suggested that there may be no benefit with ivermectin for "need for mechanical ventilation," whereas effect estimates for "improvement" and "deterioration" favored ivermectin but were graded as low certainty due to study design limitations and inconsistency (Figures 12–14). All other secondary outcome findings were assessed as very low certainty.

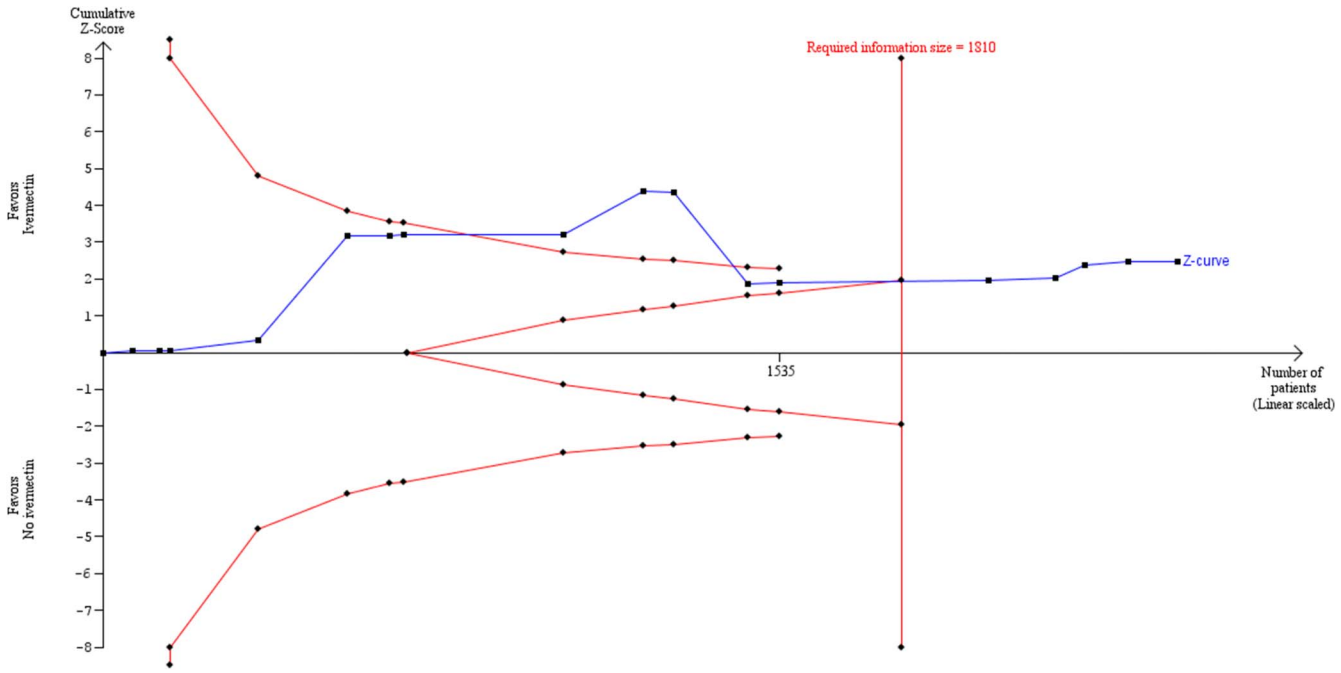


FIGURE 8. Trial sequential analysis using DL random-effects method with parameter estimates of $\alpha = 0.05$, $\beta = 0.1$, control rate = 7.8%, RRR = 62%, and diversity = 49.5%.

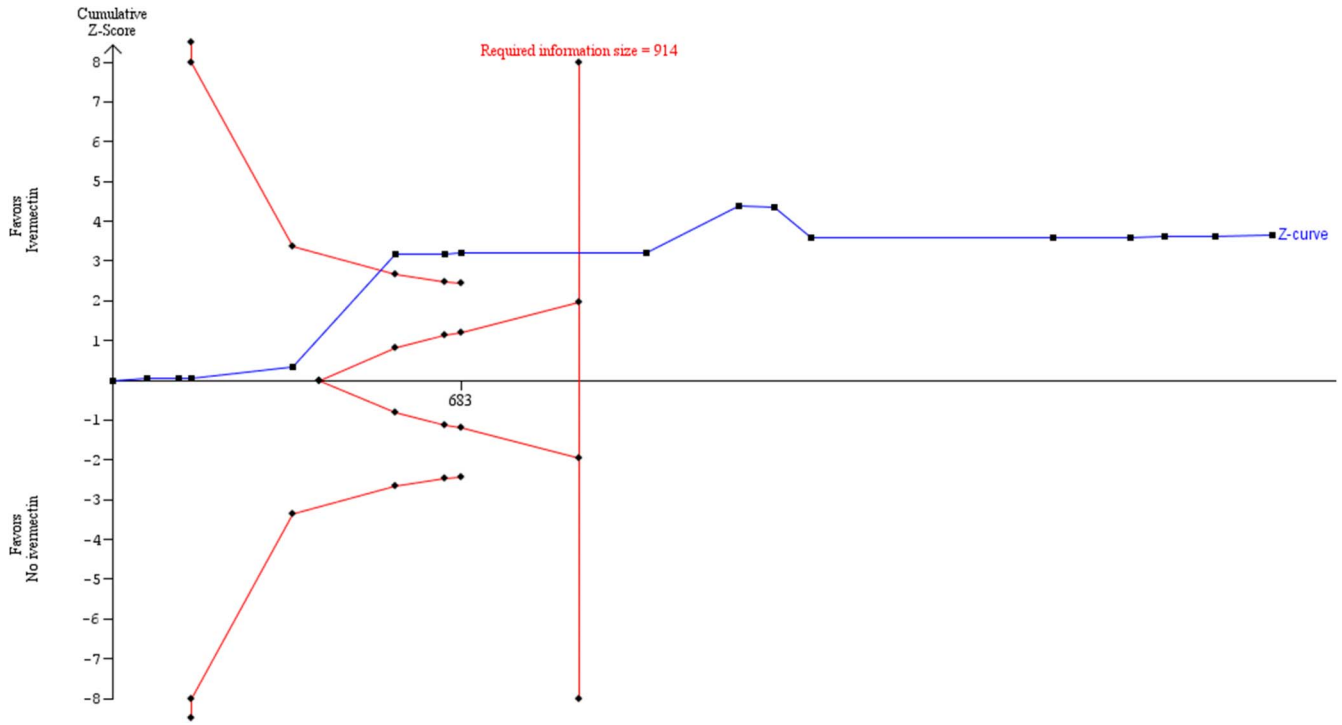


FIGURE 9. Sensitivity analysis excluding an outlier study responsible for the heterogeneity, showing trial sequential analysis using DL random-effects method with parameter estimates of $\alpha = 0.05$, $\beta = 0.1$, control rate = 7.8%, = 62%, and diversity = 0%.

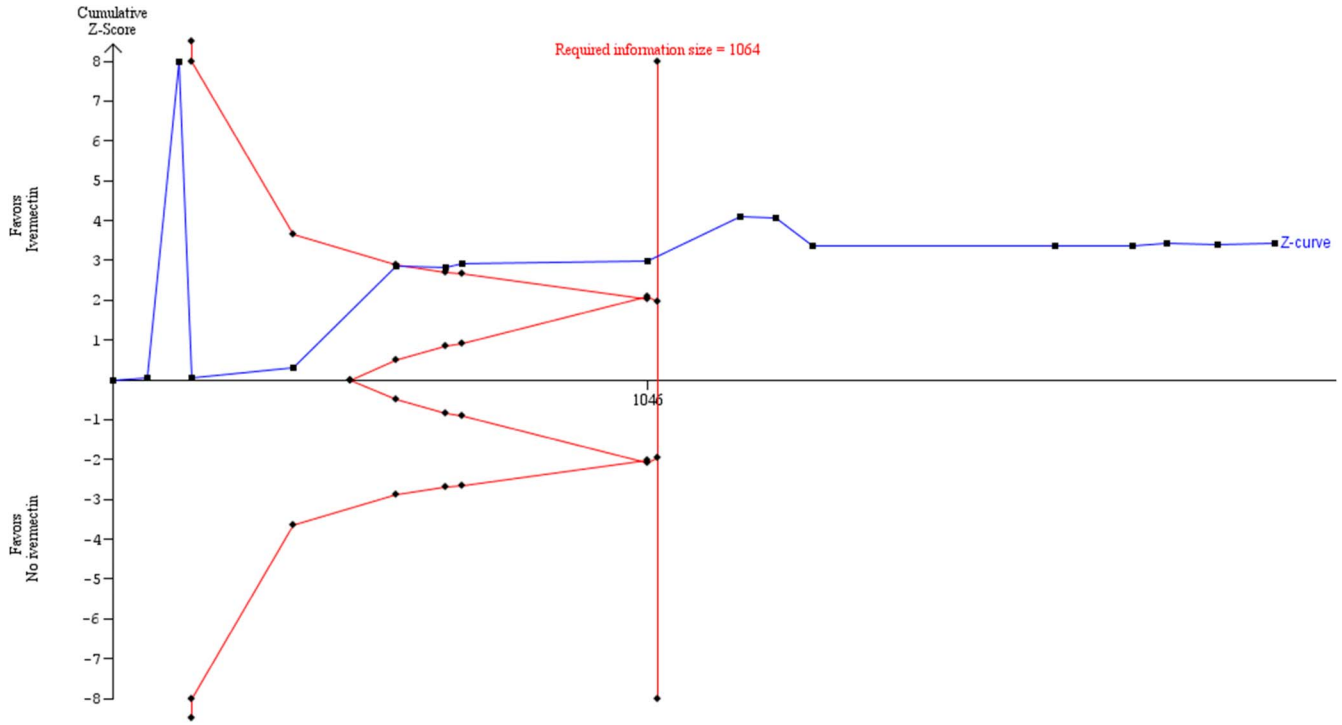


FIGURE 10. Sensitivity analysis excluding an outlier study responsible for the heterogeneity, showing trial sequential analysis using Biggerstaff–Tweedie random-effects method with parameter estimates of $\alpha = 0.05$, $\beta = 0.1$, control rate = 7.8%, RRR = 62%, and diversity = 14.2%.

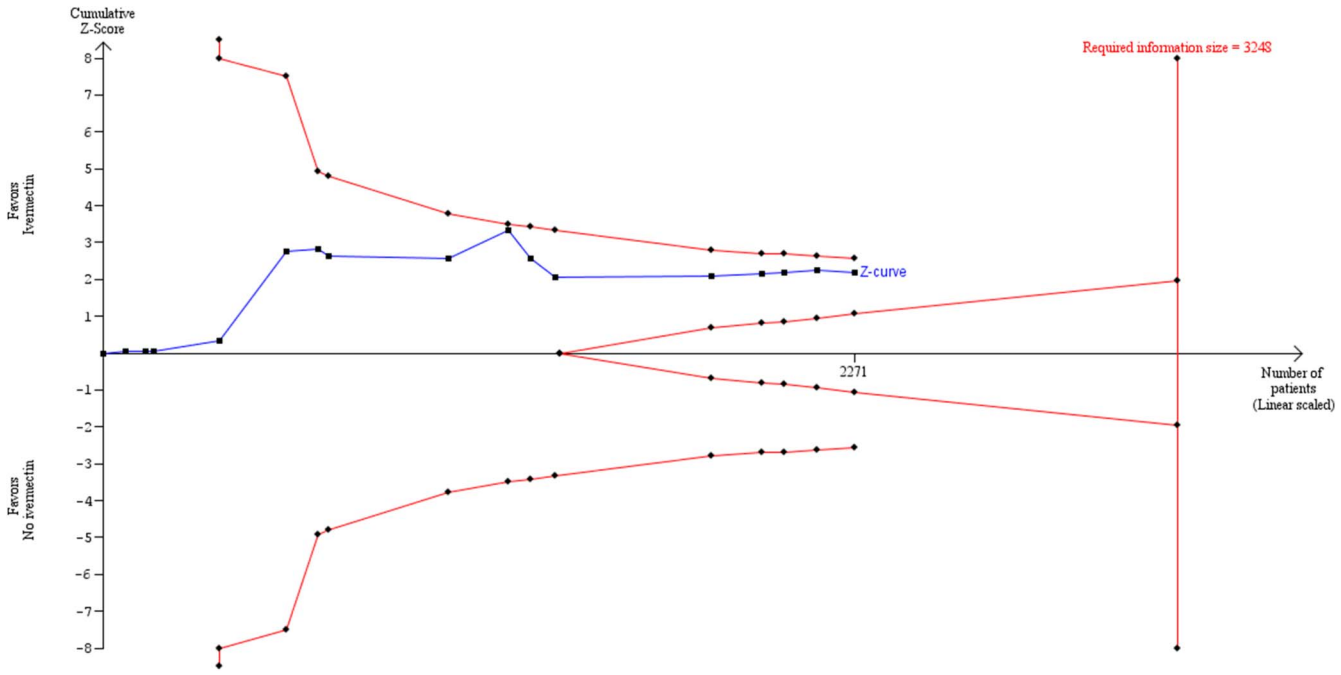


FIGURE 11. Sensitivity analysis excluding an outlier study responsible for the heterogeneity, showing trial sequential analysis using Sidik–Jonkman random-effects method with parameter estimates of $\alpha = 0.05$, $\beta = 0.1$, control rate = 7.8%, RRR = 62%, and diversity = 71.9%.

Meta-analysis of 11 trials, assessing 1533 participants, found that there was no significant difference between ivermectin and control in the risk of severe adverse events (aRR 1.65, 95% CI 0.44–6.09; $I^2 = 0\%$; *low certainty evidence*, downgraded for imprecision and study design limitations). Seven severe adverse events were reported in the ivermectin group and 2 in controls. The SAEs were as follows: 2 patients in the Mahmud trial[107] had esophagitis (this is a known side effect of doxycycline, which was coadministered with ivermectin in this trial); one patient in the study by Krolewiecki et al[106] had hyponatremia (this trial used high-dose ivermectin for 5 days); and 2 patients in a study from Turkey[115] had serious "delirium-like behavior, agitation, aggressive attitude, and altered state of consciousness," which the authors attributed to metabolic insufficiencies in MDR-1/ABCB1 or CYP3A4 genes, screening for which was a study feature. In the Lopez-Medina et al[85] trial, there were 2 SAEs in each arm (SoF Table 2).

Ivermectin prophylaxis versus no ivermectin prophylaxis

Three studies involving 738 participants evaluated ivermectin for COVID-19 prophylaxis among health care workers and COVID-19 contacts. Meta-analysis of these 3 trials, assessing 738 participants, found that ivermectin prophylaxis among health care workers and COVID-19 contacts probably reduces the risk of

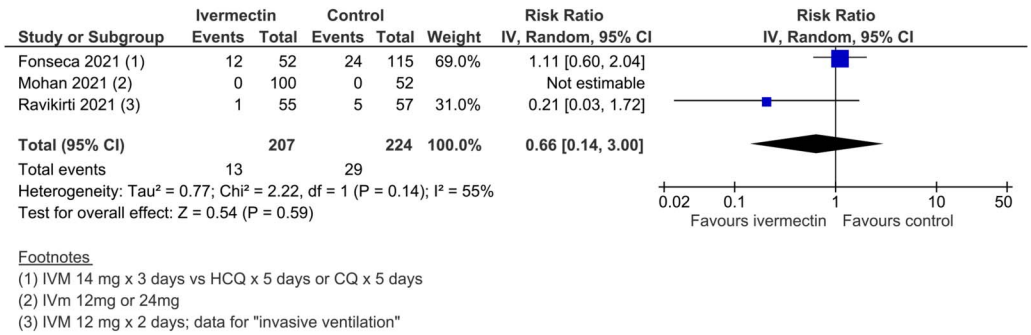
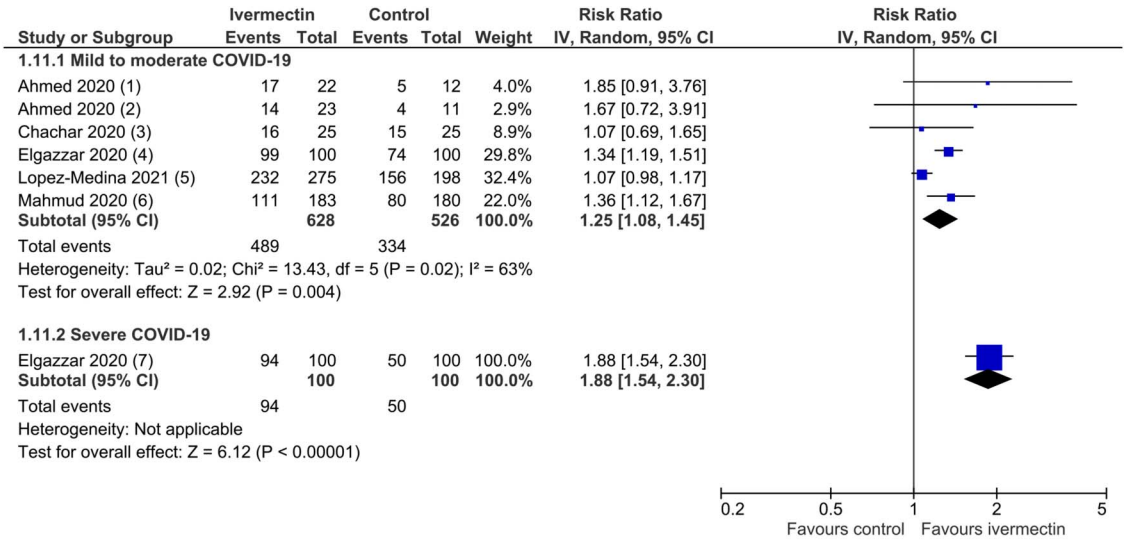


FIGURE 12. Need for mechanical ventilation.



Footnotes
(1) IVM 12mg s+ doxy 200mg stat then 100 mg BD x 4 days
(2) IVM 12mg daily x 5 days
(3) IVM 12 mg at 0, 12, and 24 hours
(4) IVM up to 24 mg daily for 4 days. Control group received hydroxychloroquine
(5) IVM 0.3mg/kg x 5 days
(6) IVM 6mg once + Doxy 100 mg x 5 days
(7) IVM up to 24 mg daily for 4 days. Control group received hydroxychloroquine

FIGURE 13. Improvement.

COVID-19 infection by an average of 86% (79%–91%) (3 trials, 738 participants; aRR 0.14, 95% CI 0.09–0.21; 5.0% vs. 29.6% contracted COVID-19, respectively; *low-certainty evidence*; downgraded due to study design limitations and few included trials) (Figure 15). In 2 trials involving 538 participants, no severe adverse events were recorded (SoF Table 4).

DISCUSSION

The findings indicate with moderate certainty that ivermectin treatment in COVID-19 provides a significant survival benefit. Our certainty of evidence judgment was consolidated by the results of trial sequential analyses, which show that the required IS has probably already been met. Low-certainty evidence on improvement and deterioration also support a likely clinical benefit of ivermectin. Low-certainty evidence suggests a significant effect in prophylaxis. Overall, the evidence also suggests that early use of ivermectin may reduce morbidity and mortality from COVID-19. This is based on (1) reductions in COVID-19 infections when ivermectin was used as prophylaxis, (2) the more favorable effect estimates for mild to moderate disease compared with severe disease for death due to any cause, and (3) on the evidence demonstrating reductions in deterioration.

The evidence on severe adverse events in this review was graded as low certainty, partly because there were too few events to reach statistical significance. Evidence from a recent systematic review of ivermectin use among people with parasitic infections suggests that ivermectin administered at the usual doses (0.2 or 0.4 mg/kg) is safe and could be safe at higher doses.[7,116] A recent World Health Organization document on ivermectin use for scabies found that adverse events with ivermectin were primarily minor and transient.[22]

We restricted the included studies to the highest level of evidence, that is, RCTs, as a policy. This was despite there being numerous observational but nonrandomized trials of ivermectin, which one could argue could also be considered in an emergency. We included preprint and unpublished data from completed but not yet published trials due to the urgency related to evidence synthesis in the context of a global pandemic.[117] Although there is the potential for selective reporting of outcomes and publication bias, we have factored in these considerations in interpreting results and forming conclusions. We adhered to PRISMA guidelines and the WHO statement on developing global norms for sharing data and results during public health emergencies.[117]

There are a number of limitations with this review. Several of the studies contributing data did not

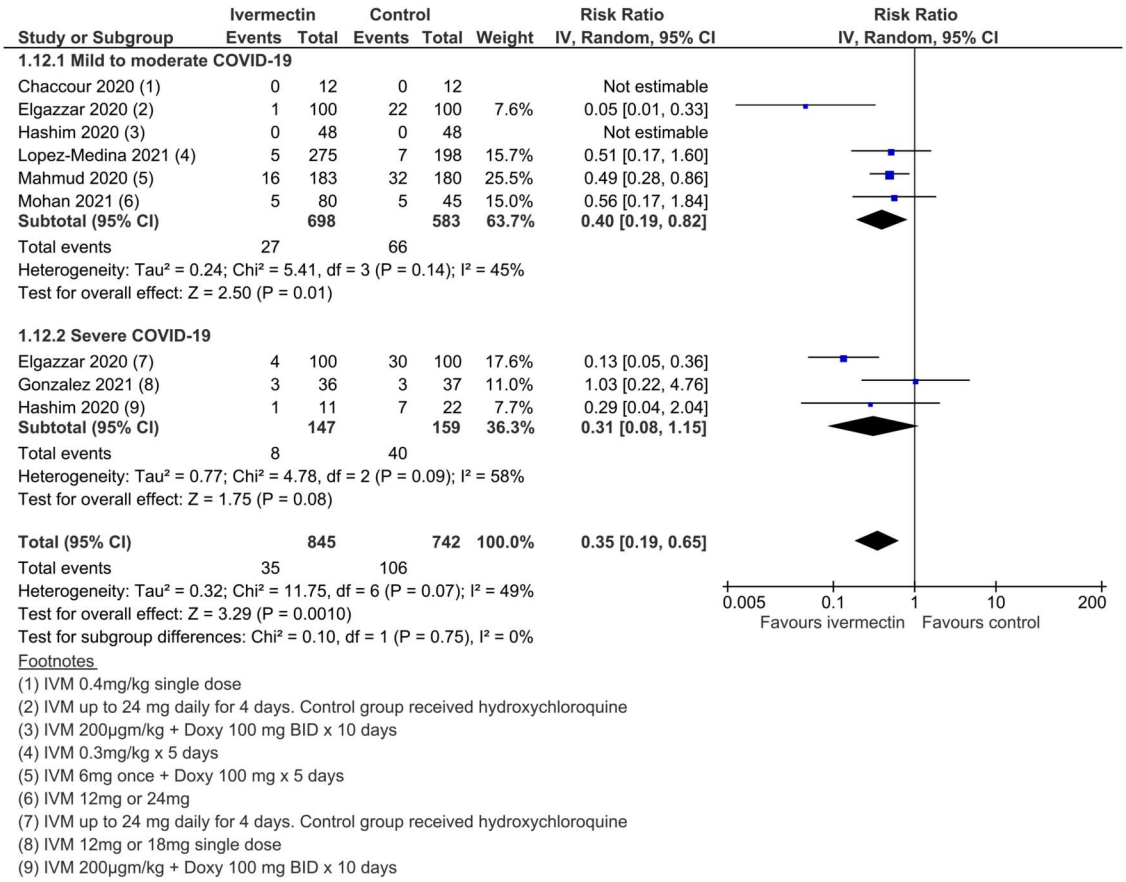


FIGURE 14. Deterioration.

provide full descriptions of methods, so assessing risk of bias was challenging. Where descriptions of study methods were sparse or unclear, we attempted to contact authors to clarify methods, but lack of information led us to downgrade findings in several instances. Overall interpretation of findings was hampered due to variability in the participants recruited, treatment regimen, and the care offered to those in control groups. We have tried to take this variation into account through subgroup and sensitivity analyses. Nevertheless, dosing and treatment regimens and the use of ivermectin with other components of "standard care" require further research. We did not include laboratory outcome measures, such as viral clearance. The latter and other biochemical outcomes have been reported in several studies and reviews and tend to favor ivermectin.[10,47,105,108] Several trials reported continuous data, such as length of hospital stay, as medians and interquartile ranges; therefore, we were unable to include these data in meta-analysis. Because we did not undertake in our protocol to perform narrative evidence synthesis, and because these data tended to favor ivermectin, the certainty of the effects of ivermectin on these continuous outcomes may be underestimated.

At least 5 other reviews of ivermectin use for COVID-19 have been published, including one coauthored with Nobel Laureate Professor Satoshi Ōmura, discoverer of ivermectin,[9,10,118,119,120] but only 3 have been peer-reviewed[9,118,120] and only 2 attempt full systematic review.[10,119] We applied AMSTAR 2,[121] a critical appraisal tool for systematic reviews of health care interventions, to the 2 nonpeered systematic reviews[10,119] and both were judged to be of low quality (Table 5). However, there was also a suggestion that ivermectin reduced the risk of death in treatment of COVID-19 in these reviews.

The recently updated WHO therapeutics guidelines[12] included 7 trials and 1419 people in the analysis of mortality. Reporting a risk reduction of 81% (odds ratio 0.19, 95% CI 0.09–0.36), the effect estimate favoring ivermectin was downgraded by 2 levels for imprecision, although the justification for this is unclear as the reported CI is precise (64%–91%).

In addition to the evidence from systematic reviews, the findings of several controlled observational studies

Table 4. Summary of findings table of ivermectin versus no ivermectin for COVID-19 prophylaxis in healthy population (people without COVID-19 infection).

	Illustrative comparative risks* (95% CI)				
	Assumed risk	Corresponding risk			
Outcomes	No ivermectin	Ivermectin	Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)
COVID-19 infection	296 per 1000	245 fewer infections per 1000 (234–269)	RR = 0.14 (0.09–0.21)	738 (3)	Low†
Admission to hospital	Not reported				
Death from any cause	Not reported				
Serious adverse events	No events occurred in 538 participants (2 studies), therefore the effect could not be estimated.				

GRADE working group grades of evidence; High quality: Further research is very unlikely to change our confidence in the estimate of effect; Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low quality: We are very uncertain about the estimate.
*The basis for the assumed risk (eg, the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
†Downgraded −2 for study design limitations.
NNT, number needed to treat.

are consistent with existing evidence and suggest improved outcomes with ivermectin treatment.[55,57,59] Similarly, with respect to ivermectin prophylaxis of frontline workers and those at risk, controlled observational studies from Bangladesh and Argentina (the latter which involved 1195 health care workers) have shown apparent reductions in COVID-19 transmission with ivermectin prophylaxis, including in some reports total protection (zero infections) where infection rates in the control group exceeded 50%.[122,123] A very large trial of ivermectin prophylaxis in health care workers in India[124] covered 3532 participants and reported risk ratios not significantly different from this meta-analysis (prophylaxis outcome).

Clarifying ivermectin safety in pregnancy is a key question in patient acceptability for pregnant women contracting COVID-19. A recent meta-analysis[5] found little evidence of increased risk of abnormal pregnancies but similarly weak evidence of absence of risk. For (pre-exposure) prophylaxis in pregnancy, where vaccines may be contraindicated, the alternative of hydroxychloroquine has been advocated.[125,126] In addition to safety and relative efficacy, different risk–benefit judgments may be presented for prophylaxis

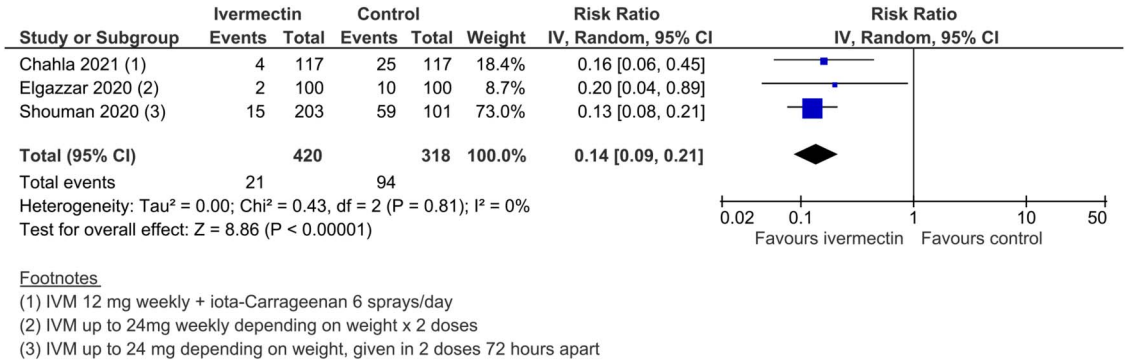


FIGURE 15. COVID-19 infection (prophylaxis studies).

Table 5. Methodological quality of other systematic reviews (AMSTAR 2).

Systematic review	Components of PICO described	A priori study design	Explain selection of study designs	Comprehensive literature search	Duplicate study selection	Duplicate data extraction	List of excluded studies justified	Characteristics of included studies provided
Hill et al, 2021[10]	+	−	+	+	?	?	−*	?†
Castañeda-Sabogal et al 2021[119]	+‖	?	−	?#	+	+	−*	+

Systematic review	Risk of bias adequately assessed and documented	Sources of funding reported	Appropriate methods to combine findings	Appropriate risk-of-bias sensitivity analyses conducted	Risk-of-bias assessment used in conclusions	Satisfactory explanation of observed heterogeneity	Likelihood of publication bias assessed	Conflict of interest stated
Hill et al, 2021[10]	−‡	−	−§	−*	−¶	−*	NA	−
Castañeda-Sabogal et al 2021[119]	−**	−	−††	−‡‡	−*	+	NA	+

Assessed using AMSTAR 2[121]; +, adequately assessed; −, inadequately assessed; ?, unclear assessment; NA, not applicable (less than 10 included studies in meta-analysis).

*Not documented or inadequately reported.

†Participant population, description of comparator interventions, and time frame for follow-up were not described or inadequately reported.

‡No summary of risk-of-bias assessment was given in the main text in the review, other than stating trials were of poor, fair, or high quality. There were some further details about bias in the discussion, but these were largely generic and did not follow the recommended Cochrane tool used to assess risk of bias in RCTs.

§A meta-analysis for all-cause death was presented but authors did not specify why meta-analyses were not conducted for other outcomes, which included at least 2 trials reporting the same comparison and outcome, other than in some parts of the discussion. For example, if viral clearance was reported in most trials, there would have been scope to have performed subgroup analyses and/or split the time point for each comparison to account for the varying duration of follow-up across trials. Instead, they gave a vote count-type narrative of the results, which did not follow synthesis without meta-analysis (SWiM) in systematic review reporting guidelines.[144]

¶There was some further details about bias in the discussion, but this was largely generic and did not follow the recommended Cochrane tool used to assess risk of bias in RCTs. Similarly, in terms of certainty/quality of the evidence, the authors used terms in a summary table that included "good," "fair," and "limited," without offering any explanation or justification.

‖Outcomes were reported but lacked definitions.

#A significant number of pertinent RCTs have not been included in the review. Given the adequate due diligence of review process, the comprehensive nature of the search strategy is questionable.

**No description of risk-of-bias assessment in any domain apart from missing outcome data but attrition rates not documented to justify judgment.

††Authors did not report data from RCTs that we obtained from various sources and some conclusions were not reflective of the observed data. It was reported that in an analysis of 4 preprint retrospective studies at high risk of bias, ivermectin was not associated with reduced mortality (logRR 0.89, 95% CI 0.09–1.70, $P = 0.04$). Although the caveat of studies being at high risk of bias and statistical heterogeneity should be added to any interpretation, it is incorrect to interpret these results as not demonstrating a potential association based on the observed result. Furthermore, the high risk of bias judgment is not adequately justified.

‡‡A sensitivity analysis was performed excluding those studies without adjustment for confounding but no details are provided. Given that there was some evidence of a potential association with ivermectin treatment and survival in 4 retrospective studies (although downplayed as no association due to concerns about attrition), it is highly implausible that any sensitivity analysis would not remove any suggestion of association.

(pre- and post-exposure), and for treatment, with pregnancy a high-risk status for COVID-19.

RCTs in this review did not specifically examine use of ivermectin in the elderly, although this is a known high-risk group for severe COVID-19. In the setting of care homes, it is also notorious for rapid contagion. A standard indication for ivermectin in the elderly is scabies. We identified 2 recent reports suggesting that ivermectin may be efficacious as prevention and treatment of COVID-19 in this age group.[50,127] A letter on positive experience in 7 elder care facilities in Virginia covering 309 patients was sent to NIH[127] and has recently been submitted for publication.

There is also evidence emerging from countries where ivermectin has been implemented. For example, Peru had a very high death toll from COVID-19 early on in the pandemic.[128] Based on observational evidence, the Peruvian government approved ivermectin for use against COVID-19 in May 2020.[128] After implementation, death rates in 8 states were reduced between 64% and 91% over a two-month period.[128] Another analysis of Peruvian data from 24 states with early ivermectin deployment has reported a drop in excess deaths of 59% at 30+ days and of 75% at 45+ days.[129] However, factors such as change in behavior, social distancing, and face-mask use could have played a role in this reduction.

Other considerations related to the use of ivermectin treatment in the COVID-19 pandemic include people's values and preferences, equity implications, acceptability, and feasibility.[130] None of the identified reviews specifically discussed these criteria in relation to ivermectin. However, in health care decision making, evidence on effectiveness is seldom taken in isolation without considering these factors. Ultimately, if ivermectin is to be more widespread in its implementation, then some considerations are needed related to these decision-making criteria specified in the GRADE-DECIDE framework.[130]

There are numerous emerging ongoing clinical trials assessing ivermectin for COVID-19. The trade-off with policy and potential implementation based on evidence synthesis reviews and/or RCTs will vary considerably from country to country. Certain South American countries, Indian states, and, more recently, Slovakia and other countries in Europe have implemented its use for COVID-19.[129,131,132,133,134] A recent survey of global trends[118] documents usage worldwide. Despite ivermectin being a low-cost medication in many countries globally, the apparent shortage of economic evaluations indicates that economic evidence on ivermectin for treatment and prophylaxis of SARS-CoV-2 is currently lacking. This may impact more on LMICs that are potentially waiting for guidance from organizations like the WHO.

Given the evidence of efficacy, safety, low cost, and current death rates, ivermectin is likely to have an impact on health and economic outcomes of the pandemic across many countries. Ivermectin is not a new and experimental drug with an unknown safety profile. It is a WHO "Essential Medicine" already used in several different indications, in colossal cumulative volumes. Corticosteroids have become an accepted standard of care in COVID-19, based on a single RCT of dexamethasone.[1] If a single RCT is sufficient for the adoption of dexamethasone, then a fortiori the evidence of 2 dozen RCTs supports the adoption of ivermectin.

Ivermectin is likely to be an equitable, acceptable, and feasible global intervention against COVID-19. Health professionals should strongly consider its use, in both treatment and prophylaxis.

ACKNOWLEDGMENTS

This work was inspired by the prior literature review of Dr Pierre Kory.

The authors thank Information Specialist, Jo Platt, of the Cochrane Gynaecological, Neuro-oncology, and Orphan Cancer (CGNOC) group for designing the search strategy and running the search, as well as Anna Noel Storr for reviewing the strategy. The authors also thank Isabella Rushforth for her voluntary assistance with the preparation of the reference lists.

The authors thank Gill Gyte for detailed comments, feedback, and involvement in this review, and Michael Grayling and David Tovey for useful peer review comments before submission. The authors also thank the external peer reviewers for their helpful comments and Peter Manu for the opportunity to publish our findings.

REFERENCES

1. Horby P, Lim WS, Emberson J, et al. Dexamethasone in hospitalized patients with covid-19. *NEJM.* 2021;384: 693–704.
2. Barrows NJ, Campos RK, Powell ST, et al. A screen of FDA-approved drugs for inhibitors of zika virus infection. *Cell Host Microbe.* 2016;20:259–270.
3. Conterno LO, Turchi MD, Corrêa I, et al. Anthelmintic drugs for treating ascariasis. *Cochrane Database Syst Rev.* 2020;1. doi: 10.1002/14651858.CD010599.pub2.
4. World Health Organization. *21st Model List of Essential Medicines*. Geneva, Switzerland; 2019. Available at: https://www.who.int/publications/i/item/WHOMVPEMPIAU2019.06. Accessed January 26, 2021.
5. Nicolas P, Maia MF, Bassat Q, et al. Safety of oral ivermectin during pregnancy: a systematic review and meta-analysis. *Lancet Glob Health.* 2020;8:e92–e100.

6. Banerjee K, Nandy M, Dalai CK, et al. The battle against covid 19 pandemic: what we need to know before we "test fire" ivermectin. *Drug Res (Stuttg).* 2020;70:337–340.
7. Navarro M, Camprubí D, Requena-Méndez A, et al. Safety of high-dose ivermectin: a systematic review and meta-analysis. *J Antimicrob Chemother.* 2020;75: 827–834.
8. Kircik LH, Del Rosso JQ, Layton AM, et al. Over 25 Years of clinical experience with ivermectin: an overview of safety for an increasing number of indications. *J Drugs Dermatol.* 2016;15:325–332.
9. Kory P, GU M, Varon J, et al. Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. *Am J Ther.* 2021;28:e299–e318.
10. Hill A, Abdulamir A, Ahmed S, et al. Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection, 19. *Res Square.* 2021. doi: 10.21203/rs.3.rs-148845/v1.Preprint.
11. National Institute of Health. *The Covid-19 Treatment Guidelines Panel's Statement on the Use of Ivermectin for the Treatment of Covid-19*. 2021.
12. World Health Organization. *Therapeutics and COVID-19: Living Guideline*. Geneva, Switzerland: WHO; 2021. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.1. Accessed April 8, 2021.
13. Heidary H, Gharebaghi R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. *J Antibiot.* 2020;73:593–602.
14. Caly L, Druce JD, Catton MG, et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antivir Res.* 2020;178:104787.
15. Jans DA, Wagstaff KM. Ivermectin as a broad-spectrum host-directed anti-viral: the real deal? *Cells.* 2020;9:2100.
16. Schmith VD, Zhou J, Lohmer LRL. The approved dose of ivermectin alone is not the ideal dose for the treatment of Covid-19. *Clin Pharmacol Ther.* 2020;108:762–765.
17. Anand K, Ziebuhr J, Wadhwani P, et al. Coronavirus main proteinase (3CLpro) structure: basis for design of anti-SARS drugs. *Science.* 2003;300:1763–1767.
18. Mody V, Ho J, Wills S, et al. Identification of 3-chymotrypsin like protease (3CLPro) inhibitors as potential anti-SARS-CoV-2 agents. *Nat Commun Biol.* 2021;4:93.
19. DiNicolantonio JJ, Barroso J, McCarty. Ivermectin may be a clinically useful anti-inflammatory agent for late-stage covid-19. *Open Heart.* 2020;7:e001350–e.
20. Lehrer A, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor binding domain attached to ACE2. *vivo*. 2020;34:3023–3026.
21. Scheim D. From cold to killer: how SARS-CoV-2 evolved without hemagglutinin esterase to agglutinate, then clot blood Cells in pulmonary and systemic microvasculature. *SSRN.* 2020. doi: 10.2139/ssrn.3706347. Preprint.
22. *WHO Expert Committee on the Selection and Use of Essential Medicines. Application for Inclusion of Ivermectin on the WHO Model List of Essential Medicines (EML) and Model List of Essential Medicines for Children (EMLc) for the Indication of Scabies*. 2018. Available at: https://www.who.int/selection_medicines/committees/expert/22/applications/s6.6_ivermectin.pdf. Accessed February 21, 2021.
23. Ahmed S, Karim MM, Ross AG, et al. A five day course of ivermectin for the treatment of covid-19 may reduce the duration of illness. *Int J Infect Dis.* 2020;103:214–216.
24. Chaccour C, Casellas A, Blanco-Di Matteo A, et al. The effect of early treatment with ivermectin on viral load, symptoms and humoral response in patients with non-severe COVID-19: a pilot, double-blind, placebo-controlled, randomized clinical trial. *EClinical Med.* 2021;32:100720. doi: 10.1016/j.eclinm.2020.100720
25. Aluko P, Graybill E, Craig D, et al. Chapter 20: economic evidence. In: Higgins J, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions (Version 61). Cochrane*; 2020.
26. Bryant A, Lawrie T, Dowsell T, et al. *Ivermectin for Prevention and Treatment of Covid-19 (Protocol).* The Evidence-Based Medical Consultancy Ltd; 2021. Available at: https://tinyurl.com/cx7pnaxa. Accessed February 27, 2021.
27. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions Version 6. 0 Cochrane*. 2019.
28. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327:557–560.
29. Deeks JJ, Altman DG, Bradburn MJ. Chapter 15: statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: *Systematic Reviews in Health Care: Meta-Analysis in Context*. London, United Kingdom: BMJ Publication Group; 2001.
30. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clin Trials.* 1986;7:177–188.
31. *RevMan. Review Manager 5*. The Cochrane Collaboration; 2020.
32. *R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing V, Austria*. R Foundation for Statistical Computing. Vienna, Austria; 2021.
33. Owen RK, Bradbury N, Xin Y, et al. MetaInsight: an interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. *Res Syn Meth.* 2019;10:569–581.
34. Rücker G, Schwarzer G, Krahn U, et al. *Network Meta-Analysis Using Frequentist Methods*; 2017.
35. Efthimiou O. Practical guide to the meta-analysis of rare events. *Evid Based Ment Health.* 2018;21:72–76.
36. Stijnen T, Hamza TH, Ozdemir P. Random effects meta-analysis of event outcome in the framework of the generalized linear mixed model with applications in sparse data. *Stat Med.* 2010;29:3046–3067.
37. Chen Y, Chu H, Luo S, et al. Bayesian analysis on meta-analysis of casecontrol studies accounting for within-study correlation. *Stat Methods Med Res.* 2015;24:836–855.
38. Rücker G, Schwarzer G, Carpenter J, et al. Why add anything to nothing? The arcsine difference as a

measure of treatment effect in meta-analysis with zero cells. *Stat Med.* 2009;28:721–738.
39. Tian L, Cai T, Pfeffer MA, et al. Exact and efficient inference procedure for meta-analysis and its application to the analysis of independent 2 x 2 tables with all available data but without artificial continuity correction. *Biostatistics.* 2009;10:275–281.
40. Cai T, Parast L, Ryan L. Meta-analysis for rare events. *Stat Med.* 2010;29:2078–2089.
41. Brok J, Thorlund K, Gluud C, et al. Trial sequential analysis reveals insufficient information size and potentially false positive results in many meta-analyses. *J Clin Epidemiol.* 2008;61:763–769.
42. Wetterslev J, Thorlund K, Brok J, et al. Estimating required information size by quantifying diversity in random-effects model meta-analyses. *BMC Med Res Methodol.* 2009;9:86.
43. Thorlund K, Engstrøm J, Wetterslev J, et al. *User Manual for Trial Sequential Analysis (TSA)*. 2011. Available at: www.ctu.dk/tsa. Accessed April 8, 2021.
44. Fonseca AJ. *The Effect of Chloroquine, Hydroxychloroquine OR Ivermectin in Patients with Severe Manifestations of Coronavirus*. 2021. Available at: https://ensaiosclinicos.gov.br/rg/RBR-8h7q82/. Accessed January 20, 2021.
45. Schünemann H, Vist G, Higgins J, et al. Chapter 15: interpreting results and drawing conclusions. In: Higgins J, Thomas J, Chandler J, et al., eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 61. Cochrane*; 2020.updated September 2020.
46. Cochrane Effective Practice and Organisation of Care (EPOC). *EPOC Resources for Review Authors*; 2017. Available at: www.epoc.cochrane.org/epoc-specific-resources-review-authors. Accessed February 1, 2021.
47. Elgazzar A, Eltaweel A, Youssef SA, et al. Efficacy and safety of ivermectin for treatment and prophylaxis of covid-19 pandemic. *Res Square.* 2020. doi: 10.21203/rs.3.rs-100956/v2.Preprint.
48. Alam MT, Murshe R, Bhiuyan E, et al. A case series of 100 covid-19 positive patients treatedwith combination of ivermectin and doxycycline. *J Bangladesh Coll Physicians Surgeons.* 2020;38:10–15.
49. Behera P, Patro BK, Singh AK, et al. Role of ivermectin in the prevention of covid-19 infection among healthcare workers in India: a matched case-control study. *PLoS One.* 2020;16:e0247163.
50. Bernigaud C, Guillemot D, Ahmed-Belkacem A, et al. Oral ivermectin for a scabies outbreak in a long-term–care facility: potential value in preventing COVID-19 and associated mortality? *Br J Dermatol.* 2021. doi: 10.1111/bjd.19821.
51. Budhiraja S, Soni A, Jha V, et al. Clinical Profile of First 1000 Covid-19 Cases Admitted at Tertiary Care Hospitals and the Correlates of Their Mortality: An Indian Experience. *medRxiv.* 2020. doi: 10.1101/2020.11.16.20232223.Preprint.
52. Cadegiani FA, Goren A, Wambier CG, et al. Early covid-19 therapy with azithromycin plus nitazoxanide, ivermectin orHydroxychloroquine in outpatient settings significantly reduced SymptomsCompared to known outcomes in untreated patients. *medRxiv*. 2020. doi: 10.1101/2020.10.31.20223883.Preprint.
53. Camprubí D, Almuedo-Riera A, Martí-Soler H, et al. Lack of efficacy of standard doses of ivermectin in severe covid-19 patients. *PLoS One.* 2020;15:e0242184.
54. Carvallo H, Hirsch R, Farinella M. Safety and efficacy of the combined use of ivermectin, dexamethasone, enoxaparin and aspirin against covid 19. *medRxiv.* 2020. doi: 10.1101/2020.09.10.20191619.Preprint.
55. Rajter JC, Sherman MS, Fatteh N, et al. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019. *CHEST.* 2021;159:85–92.
56. Espitia-Hernandez G, Munguia L, Diaz-Chiguer D, et al. Effects of Ivermectin-azithromycin-cholecalciferol combined therapy on COVID-19 infected patients: a proof of concept study. *Biomed Res.* 2020;31:129–133.
57. Gorial FI, Mashhadani S, Sayaly HM, et al. Effectiveness of ivermectin as add-on therapy in covid-19 management (pilot trial). *medRxiv.* 2020. doi: 10.1101/2020.07.07.20145979.Preprint.
58. Hellwig MD, Maia A. A covid-19 Prophylaxis? Lower incidence associated withprophylactic administration of Ivermectin. *Int J Antimicrob Agent.* 2021;57:106248.
59. Khan M, Khan M, Debnath C, et al. Ivermectin treatment may improve the prognosis of patients with covid-19. *Archivos de Bronconeumología.* 2020;56:832.
60. Morgenstern J, Redondo JN, De León A, et al. The use of compassionate ivermectin in the management of symptomatic outpatients and hospitalized patients with clinical diagnosis of covid-19 at the medical center bournigal and the medical center punta cana, rescue group, Dominican Republic. *medRxiv*. 2020. doi: 10.1101/2020.10.29.20222505.Preprint.
61. Portmann-Baracco A, Bryce-Alberti M, Accinelli RA. Antiviral and anti-inflammatory properties ofivermectin and its potential use in Covid-19. *Arch Bronconeumol.* 2020;56:831.
62. Shokati Z. *A Randomized Clinical Trial Study, Comparison of the Therapeutic Effects of Ivermectin, Kaletra and Chloroquine with Kaletra and Chloroquine in the Treatment of Patients with Coronavirus [Protocol]*. 2019. Available at: https://en.irct.ir/trial/48444. Accessed January 2021.
63. Spoorthi V, Sasank S. Utility of ivermectin and doxycycline combination for the treatment of SARS- CoV-2. *Int Arch Integrated Med.* 2020;7:177–182.
64. Abd-Elsalam S. *The Efficacy of Ivermectin and Nitazoxanide in Covid-19 Treatment*. 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04351347. Accessed January 2021.
65. Abd-Elsalam S. *Ivermectin as a Novel Therapy in Covid-19 Treatment*. 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04403555. Accessed January 2021.
66. Alam MT. *Safety and Efficacy of Ivermectin and Doxycycline in Treatment of Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04551755. Accessed January 2021.

67. Arnold S. *Novel Agents for Treatment of High-Risk Covid-19 Positive Patients*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04374019. Accessed January 2021.
68. Centenario Hospital Miguel Hidalgo. *Hydroxychloroquine and Ivermectin for the Treatment of Covid-19 Infection*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04391127. Accessed January 2021.
69. Ashraf S. *Efficacy of Subcutaneous Ivermectin with or without Zinc and Nigella Sativa in Covid-19 Patients (SINZ-Covid-PK)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04472585. Accessed January 2021.
70. Ataee Z. *Evaluation of the Effect of Ivermectin in Hospitalized Patients with Covid-19 in Imam Reza Hospital in Mashhad*; 2020. Available at: https://en.irct.ir/trial/49180. Accessed January 2021.
71. Bisoffi Z. *COVidIVERmectin: Ivermectin for Treatment of Covid-19 (COVER)*. 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04438850. Accessed January 2021.
72. ProgenaBiom. *Trial of Combination Therapy to Treat Covid-19 Infection*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04482686. Accessed January 2021.
73. Perez A. *Efficacy, Safety and Tolerability of Ivermectin in Subjects Infected with SARS-CoV-2 with or without Symptoms (SILVERBULLET)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04407507. Accessed January 2021.
74. Echeverri E. *Effectiveness and Safety of Ivermectin for the Prevention of Covid-19 Infection in Colombian Health Personnel (IveprofCovid19)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04527211. Accessed January 2021.
75. Elalfy H. *New Antiviral Drugs for Treatment of Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04392427. Accessed January 2021.
76. Exman P. *Early Treatment with Ivermectin and LosarTAN for Cancer Patients with Covid-19 Infection (TITAN)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04447235. Accessed January 2021.
77. Fathalipour M. *The Efficacy and Safety of Ivermectin in Patients with Covid-19: A Randomized Clinical Trial*; 2020. Available at: https://www.irct.ir/trial/49501. Accessed January 2021.
78. George B. *A Phase IIB Open Label Randomized Controlled Trial to Evaluate the Efficacy and Safety of Ivermectin in Reducing Viral Loads in Patients with Hematological Disorders Who Are Admitted with Covid 19 Infection*; 2020. Available at: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=43449. Accessed January 2021.
79. Gheibi N. *Dose-Finding Study of Ivermectin Treatment on Patients Infected with Covid-19:A Clinical Trial*; 2020. Available at: https://en.irct.ir/trial/47012. Accessed January 2021.
80. Gheibi N. *Determination the Therapeutic Effect of Ivermectin and Sovodak on Patients Infected with Covid-19: A Clinical Trial*; 2020. Available at: https://en.irct.ir/trial/51007. Accessed January 2021.
81. Temple University. *Outpatient Use of Ivermectin in Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04530474. Accessed January 2021.
82. Pott Junior H, Bastos Paoliello MM, Miguel AQC, et al. Use of ivermectin in the treatment of Covid-19: a pilot trial. *Toxicol Rep.* 2021;8:505–510.
83. Kamal E. *Ivermectin in Treatment of Covid 19 Patients*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04425707. Accessed January 2021.
84. Saibannavar A. *An Open Label, Prospective Comparative Study to Evaluate the Proposed Therapy in Adults with Mild Symptomatic Covid-19 Patients Receiving the Standard Treatment of Covid Infection*; 2020. Available at: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=46392. Accessed January 2021.
85. López-Medina E, López P, Hurtado IC. Effect of ivermectin on time to resolution of symptoms among adults with mild COVID-19: a randomized clinical trial. *J Am Med Assoc.* 2021;325:1426–1435.
86. García Funegra P. *Randomized Phase IIA Clinical Trial to Evaluate the Efficacy of Ivermectin to Obtain Negative PCR Results in Patients with Early Phase Covid-19 (SAINT-PE-RU)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04635943. Accessed January 2021.
87. Okasha K. *Ivermectin and Nitazoxanide Combination Therapy for Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04360356. Accessed January 2021.
88. Okasha K. *Ivermectin Nasal Spray for Covid19 Patients*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04510233. Accessed January 2021.
89. Rathi S. *Study to Efficacy of Ivermectin in Patients of Covid-19*; 2020. Available at: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=43728. Accessed January 2021.
90. Pathak R. *Effectiveness of Ivermectin in Preventing Development of Symptomatic Covid-19 Among Primary Contacts of Newly Diagnosed Covid-19 Positive Patients at a Tertiary Care Hospital in North India—an Interventional Study*; 2020. Available at: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=46676. Accessed January 2021.
91. Prakash A. *A Clinical Trial to Study the Effects of Hydroxychloroquine, Ciclesonide and Ivermectin in Treatment of Moderate Covid-19 Illness*. 2020. Available at: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=43364. Accessed January 2021.
92. Ochoa-Jaramillo F. *Ivermectin in Adults with Severe Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04602507. Accessed January 2021.
93. Saxena R. *Assessment of Response of Ivermectin on Virological Clearance in Covid 19 Patients*; 2020. Available at: http://www.ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=46873. Accessed January 2021.
94. Hidalgo C. *Pragmatic Study "CORIVER": Ivermectin as Antiviral Treatment for Patients Infected by SARS-COV2 (Covid-19)*; 2020. Available at: https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001971-33/. Accessed January 2021.

95. Shahbazi F. *Evaluation Effects of the Standard Regimen along with Ivermectin on Treatment of Corona Virus Type 2 Pneumonia*; 2020. Available at: https://www.irct.ir/trial/49280. Accessed January 2021.
96. Stein M. *A Randomized Double-Blind Placebo-Controlled Trial of Oral Ivermectin for Outpatient Treatment of Those at High Risk for Hospitalization Due to Covid-19*; 2020. Available at: https://anzctr.org.au/Trial/Registration/TrialReview.aspx?id=380506&isReview=true. Accessed January 2021.
97. Suputtamongkol Y. *Ivermectin vs Combined Hydroxychloroquine and Antiretroviral Drugs (ART) Among Asymptomatic Covid-19 Infection (IDRA-Covid19)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04435587. Accessed January 2021.
98. Fundació Assistencial Mútua Terrassa. *Randomised Clinical Trial of Ivermectin for Treatment and Prophylaxis of Covid-19*; 2020. Available at: https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2020-001994-66. Accessed January 2021.
99. Ghandali M. *Evaluating the Efficacy and Safety of Ivermectin in the Treatment of Covid-19 Patients: A Double-Blind Randomized Controlled Trial, Phase II*; 2020. Available at: https://en.irct.ir/trial/49935. Accessed January 2021.
100. Yamaoka K. *Placebo-controlled Randomized, Double-Blind (Evaluator, Patient) Multicenter, Parallel-Group Comparative Study Investigating the Efficacy and Safety of Ivermectin in Patients with Covid-19*; 2020. Available at: https://jrct.niph.go.jp/en-latest-detail/jRCT2031200120. Accessed January 2021.
101. Zendehdel A. *Evaluation of the Effect of Oral Ivermectin on the Outcome of Patients with Covid-19 and Compare it with the Effect of Conucntional Therapics in Patients Admitted to Ziaeian, Baharloo, Imam Khomeini in the Spring and Summer 2020*; 2020. Available at: https://en.irct.ir/trial/50305. Acessed January 2021.
102. Instituto de Cardiología de Corrientes. *Ivermectin to Prevent Hospitalizations in Covid-19 (IVERCORcovid19)*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04529525. Accessed January 2021.
103. Asghar A. *Efficacy of Ivermectin in COVID-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04392713. Accessed January 2021.
104. National University Hospital Singapore. *A Preventive Treatment for Migrant Workers at High-Risk of Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04446104. Accessed January 2021.
105. Babalola OE, Bode CO, Ajayi AA, et al. Ivermectin shows clinical benefits in mild to moderate COVID19: a randomised controlled double blind dose response study in Lagos. *Int J Med.* 2021. doi: 10.1093/qjmed/hcab035.
106. Krolewiecki A, Lifschitz A, Moragas M, et al. Antiviral effect of high-dose ivermectin in adults with COVID-19: a pilot randomised, controlled, open label, multicentre trial. *SSRN.* 2020. doi: 10.2139/ssrn.3714649.Preprint.
107. Mahmud R. *Clinical Trial of Ivermectin Plus Doxycycline for the Treatment of Confirmed Covid-19 Infection*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04523831. Accessed January 2021).
108. Niaee MS, Gheibi N, Namdar P, et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: a randomized multi-center clinical trial. *Res Square.* 2020. doi: 10.21203/rs.3.rs-109670/v1. Preprint.
109. Ravikirti, Roy R, Pattadar C, et al. Ivermectin as a potential treatment for mild to moderate COVID-19 - a double blind randomized placebo-controlled trial. *medRxiv.* 2021. doi: 10.1101/2021.01.05.21249310. Preprint.
110. Mohan A, Tiwari P, Suri T, et al. Ivermectin in mild and moderate COVID-19 (RIVET-COV): a randomized, placebo-controlled trial. *Res Square.* 2021. doi: 10.21203/rs.3.rs-191648/v1.Preprint.
111. Rezai M. *Effectiveness of Ivermectin in the Treatment of Coronavirus Infection in Patients Admitted to Educational Hospitals of Mazandaran in 2020*. 2020. Available at: https://en.irct.ir/trial/49174. Accessed January 2021.
112. Chachar AZK, Khan KA, Asif M, et al. Effectiveness of ivermectin in SARS-CoV-2/COVID-19 patients. *Int J Sci.* 2020;9:31–35.
113. Raad H. *In Vivo Use of Ivermectin (IVR) for Treatment for Corona Virus Infected Patients (Covid-19): A Randomized Controlled Trial*; 2021. Available at: http://www.chictr.org.cn/showproj.aspx?proj=54707. Accessed January 2021.
114. Schwartz E. *Ivermectin vs. Placebo for the Treatment of Patients with Mild to Moderate Covid-19*; 2020. Available at: https://clinicaltrials.gov/ct2/show/NCT04429711. Accessed January 2021.
115. Okumus N, Demirtürk N, Çetinkaya RA, et al. *Evaluation of the Effectiveness and Safety of Adding Ivermectin to Treatment in Severe COVID-19 Patients*. Research Square; 2021. doi: 10.21203/rs.3.rs-224203/v1.Preprint.
116. Guzzo C, Furtek C, Porras AC, et al. Safety, tolerability, and pharmacokinetics of escalating high doses of ivermectin in healthy adult subjects. *J Clin Pharmacol.* 2002; 42:1122–1133.
117. World Health Organization. *Developing Global Norms for Sharing Data and Results during Public Health Emergencies*; 2015. Available at: https://www.who.int/medicines/ebola-treatment/blueprint_phe_data-share-results/en/. Accessed January 2021.
118. Yagisawa M, Foster PJ, Hanaki H, et al. Global trends in clinical studies of ivermectin in COVID-19. *Jpn J Antibiot.* 2021;74:44–95.
119. Castañeda-Sabogal A, Chambergo-Michilot D, Toro-Huamanchumo CJ, et al. Outcomes of Ivermectin in the treatment of covid-19: a systematic review and meta-analysis. *medRxiv*. 2021. doi: 10.1101/2021.01.26.21250420. Preprint.
120. Nardelli P, Zangrillo A, Sanchini G, et al. Crying wolf in time of Corona: the strange case of ivermectin and hydroxychloroquine. Is the fear of failure withholding

potential life-saving treatment from clinical use? *Signa Vitae.* 2021;17:3–4.
121. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ.* 2017;358:j4008.
122. Alam MT, Murshed R, Gomes PF, et al. Ivermectin as pre-exposure prophylaxis for COVID-19 among healthcare providers in a selected tertiary hospital in dhaka - an observational study. *Eur J Med Health Sci.* 2020;2. doi: 10.24018/ejmed.2020.2.6.599.
123. Carvallo H, Hirsch R, Alkis P, et al. Study of the efficacy and safety of topical ivermectin + iona-Carrageenan in the prophylaxis against COVID-19 in health personnel. *J Biomed Res Clin Invest.* 2020;2:1007.
124. Behera P, Patro BK, Padhy BM, et al. Prophylactic role of ivermectin in SARS-CoV-2 infection among healthcare workers. *Res Square.* 2021. doi: 10.21203/rs.3.rs-208785/v1.Preprint.
125. Fesler ML, Stricker RB. Pre-exposure prophylaxis for covid-19 in pregnant women. *Int J Gen Med.* 2021;14: 279–284.
126. Stricker RB, Fesler ML. Flattening the risk: pre-exposure prophylaxis for COVID-19. *Infect Drug Resist.* 2020;13: 3689–3694.
127. Chesler DL. *Letter to Dr Bray at the National Institutes of Health*. 2021. Available at: https://tinyurl.com/dnemehxn. Accessed March 16, 2021.
128. Chamie J. Real-world evidence: the case of Peru. In: *Causality between Ivermectin and COVID-19 Infection Fatality Rate*. ResearchGate; 2020. Available at: https://www.researchgate.net/publication/344469305. Accessed March 8, 2021.
129. Chamie-Quintero J, Hibberd J, Scheim DE. Sharp reductions in COVID-19 case fatalities and excess deaths in Peru in close time conjunction, state-by-state, with ivermectin treatments. *SSRN.* 2021. doi: 10.2139/ssrn.3765018.Preprint.
130. GRADE-DECIDE. *The DECIDE Project*. 2016. Available at: http://www.decide-collaboration.eu/. Accessed January 2021.
131. Roguski J. *Ivermectin*; 2020. Available at: https://www.thecompleteguidetohealth.com/Ivermectin.html#. Accessed January 2021.
132. Ministerio de Salud y Deportes. *Ministry of Health Authorizes the Use of Ivermectin against COVID-19 under Protocol*; 2020. Available at: https://www.minsalud.gob.bo/4157-ministerio-de-salud-autoriza-uso-de-ivermectina-contra-el-covid-19-bajo-protocolo. Accessed January 2021.
133. Despacho de Comunicaciones y Estrategia Presidencial. *Coronavirus COVID-19 in Honduras*; 2021. Available at: https://covid19honduras.org/. Accessed January 2021.
134. TrialSiteNews. *Slovakia Becomes the First EU Nation to Formally Approve Ivermectin for Both Prophylaxis and Treatment for COVID-19 Patients*. 2021. Available at: https://trialsitenews.com/slovakia-becomes-the-first-eu-nation-to-formally-approve-ivermectin-for-both-prophylaxis-and-treatment-for-covid-19-patients/. Accessed February 2021.
135. Bukhari KHS, Asghar A, Perveen N, et al. Efficacy of Ivermectin in COVID-19 Patients with Mild to Moderate Disease. *medRxiv.* 2021. doi: 10.1101/2021.02.02.21250840.Preprint.
136. Chowdhury ATMM, Shahbaz M, Karim R, et al. A randomized trial of ivermectin-doxycycline and hydroxychloroquine-azithromycin therapy on COVID19 patients. *Res Square.* 2020. doi: 10.21203/rs.3.rs-38896/v1.Preprint.
137. Gonzalez JLB, González Gámez M, Enciso EAM, et al. Efficacy and safety of Ivermectin and Hydroxychloroquine in patients with severe COVID-19. A randomized controlled trial. *medRxiv.* 2021. doi: 10.1101/2021.02.18.21252037.Preprint.
138. Hashim HA, Maulood MF, Rasheed AM, et al. Controlled randomized clinical trial on using Ivermectin with Doxycycline for treating covid-19 patients in Baghdad, Iraq. *medRxiv.* 2020. doi: 10.1101/2020.10.26.20219345.Preprint.
139. Petkov S. *Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Investigating Efficacy, Safety and Tolerability of Ivermectin HUVE-19 in Patients with Proven SARS-CoV-2 Infection (Covid-19) and Manifested Clinical Symptoms*. 2021. Available at: https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-002091-12/BG. Accessed January 2021.
140. Podder CS, Chowdhury N, Mohim IS, et al. Outcome of ivermectin treated mild to moderate covid-19 cases: a single-centre, open-label, randomised controlled study. *IMC J Med Sci.* 2020;14:2.
141. Schwartz E. Viral load and culture viability in mild COVID-19 patients treated with Ivermectin. *New England J Med.* 2021.Submitted.
142. Chahla RE, Ruiz LM, Ortega ES, et al. A randomized trial: intensive treatment based in Ivermectin and iota-Carageenan as pre-exposure prophylaxis for COVID-19 in healthcare agents. *medRxiv*. 2021. doi: 10.1101/2021.03.26.21254398.Preprint.
143. Shouman W, Hegazy AA, Nafae RM, et al. Use of ivermectin as a potential chemoprophylaxis for COVID-19 in Egypt: a randomized clinical trial. *J Clin Diagn Res.* 2021;15:OC27–OC32.
144. Campbell M, McKenzie JE, Sowden A, et al. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. *BMJ*. 2020;16:l6890.

Standing Orders for Ivermectin in the Age of Covid-19

What separates good medicine from poor medicine? What separates 21st century medicine from 16th century medicine? The answer is simple. It is a rigorous adherence to science. Countries like the United States, the United Kingdom, France and Japan and many others have vastly improved the quality of world health through pharmacology and the development of hundreds of medicines used to treat both infectious and chronic disease. Chronic diseases like hypertension and diabetes, and infectious diseases like pneumonia, meningitis and HIV have had massive improvements in treatment due to expanded pharmacology. The common success has relied on evidence-based medicine which includes a rigorous use of double-blind controlled studies. In other words neither the physician (or provider) nor the patient know if the patient is getting a placebo vs. a therapeutic medicine. This helps to limit bias that could result in patients self-reporting effective treatment or providers steering patients into certain treatment arms.

Well what about Ivermectin? Without a doubt this is a super drug that has had dramatic health implications in treating both human and veterinary disease. The medicine has been a tremendous medicine for both human parasitic disease treatment (strongyloidiasis, onchocerciasis) and treatment of veterinary illness (roundworms, lice, mites etc.) Could Ivermectin be used in viral illnesses? Possibly, however, when it comes to treating viral disease the evidence for Ivermectin is tenuous at best. The *in vitro* (i.e. in the lab like cell cultures) level of Ivermectin needed to affect Sars-CoV-2 (the virus that causes COVID-19) is thought to be in the micrograms (i.e. 10^{-6}), whereas the maximum safe blood concentrations that can be obtain in humans is around 20-80 ng/ml (10^{-9}). This is a factor of 1000 different. (F. Heidary, 2020). This creates huge dosing questions and also risks for safety. "Unguarded, off label use of this drug may create increased surge of resistance at previously effective therapeutic dosage, in addition to concerns for prior mentioned toxicities. This situation may aggravate many clinical failures instead of promoting health and well-being of SARS-CoV-2 patients." (Zaheer, 2021)

Are there "good studies" of Ivermectin for treatment of SARS-CoV-2? There are few quality studies, the highest quality being double-blinded placebo controlled. Perhaps the most promising study was in patients who were hospitalized with COVID-19, published in the International Journal of Infectious disease in 2020. The study uses three subgroups Ivermectin, Ivermectin + Doxycycline and a placebo control group. This study did indeed show a reduction improved viral clearance in patients with Ivermectin vs. Placebo (9.7 vs 12.7 days, p=0.02). It also showed no significant adverse effects. Though the improvement in viral clearance was statistically significant, changes in clinical parameters including sore throat, fever, or cough were NOT significantly different between treatment and control groups. Why should this study NOT be extended to permit generalized treatment? There are several concerns regarding this study. First, the study was limited to patients without chronic illnesses including ischemic cardiac disease, CHF, chronic kidney or liver disease, those who were pregnant or lactating; these are all the same diseases and risk factors that place patients at highest risk for complications or death from COVID-19. Second, the study size was small only 24 patients in each study arm (although reportedly randomized baseline table 1 showing characteristics of patients was not available and it is unclear if the patient groups were indeed similar after randomization. Finally, the study was funded by Beximco Pharmaceutical Limited, Bangladesh; a company that produces and markets ivermectin on the world market. (Ahmed, 2021)

Another study, of lower quality due to the nature of it as a "retrospective observational" study did provide some additional support for using Ivermectin, however, again this study was a retrospective study following COVID-19 hospitalized patients at four Broward Health hospitals in Florida from March 15th to May 11th, 2020. It followed 280 patients (173 treated with Ivermectin and 107 without Ivermectin). Most of the patients in both groups also received hydroxychloroquine, azithromycin or both. The data although promising including lower mortality rate, better outcomes for patients with severe pulmonary involvement of COVID are difficult to extrapolate for a variety of reasons. First, the patients who received ivermectin were given this at discretion of treating physicians. There were not clear entry parameters Though the authors attempted to go back and "adjust confounding factors" this is often less than perfect. Furthermore, patients were not just on Ivermectin, but other drugs as well. Assessing the interactions of multiple drugs on outcomes are also less than precise. (Rajter, 2021)

The final, but perhaps most important question to ask is Ivermectin suitable for a standing order for pharmacists? Examining the medicine in context of scientific literature shows that there is limited quality literature that Ivermectin is safe or efficacious for outpatient use in treatment of COVID-19. Furthermore, the medicine is known to have significant neurotoxicity and hepatotoxicity if doses are too high or if patient's have underlying risk factors. You are asking a patient to assess their own risks in context with a drug of limited benefit and asking a pharmacist to dispense such a drug when he or she may not be fully aware of a patient's risks. Why not just allow physicians and providers to stake their own medical reputation on prescribing this drug off label if it is truly beneficial? Why a standing order for Ivermectin and not drugs for other diseases like Amyotrophic Lateral Sclerosis (ALS)- Lou Gehrig's Disease, Muscular Dystrophy, Alzheimer's disease etc. where morbidity and mortality may be even far higher than that of COVID-19? Is New Hampshire going to opt for taking medicine back to the days of placebo and word of mouth? Perhaps we can have snake-oil too by standing dose. The legislature needs to allow health care professionals to continue to practice medicine using the best scientific evidence and not allow for easy access to an abundance of medicines that may produce countless side effects, interactions with other drugs etc. Furthermore, these actions may promote resistance of both viruses and other parasites by prolific use and may deplete stores of ivermectin for proven human and veterinary uses. New Hampshire must not allow politics of the internet and special interest groups to bring the practice of medicine (and pharmacy) to the lowest common denominator. New Hampshire must not become a laughingstock of American medicine with a triumph of ignorance over science.

Gus Emmick, MD, FAAP

>20 years of practice of Medicine

Board Certified Internal Medicine

Board Certified Pediatrics

Licensed for Medicine in NH and MA

Works Cited

Ahmed, S. K. (2021). A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. *International Journal of Infectious Disease, 103*, 214-216.

F. Heidary, R. G. (2020). Ivermectin: a systematic review from antiviral affects to Covid-19 complemntary regimen. *Journal of Antibiotics, 73*, 593-602.

Rajter, J. S. (2021). Use of Ivermectin Is Associated with Lower Mortality in Hospitalized Patients with Coronavirus Disease 2019. *Chest, 159*(1), 85-92.

Zaheer, T. K. (2021). COVID-19 and Ivermectin: potential threats associated with human use. *Journal of Molecular Structure, 1243*(130808).

PARTNERS FOR COMMUNITY WELLNESS
Dartmouth-Hitchcock

Dartmouth-Hitchcock
One Medical Center Drive
Lebanon, NH 03756
Phone (603) 650-5000
partnersforcommunitywellness.org

Partners for Community Wellness is a network of people working with Dartmouth-Hitchcock Health to improve the health of communities through education and outreach. We believe that improving health is not just the responsibility of our doctors and healthcare providers, but of every person who is living and working in the State of New Hampshire. As public service officials, we hope you share this responsibility as well.

As we continue to navigate the pandemic, our health systems are strained and our neighbors are struggling to obtain routine and emergent care. Active cases in New Hampshire are at a record high right now; there are around 2700 active cases each day, compared to 790 this time last year. As you debate legislation this session, we urge you to consider the potential health impacts of any legislation you consider this year.

The undersigned members of Partners for Community Wellness strongly believe in the following principles and encourage you to consider them as you represent the people and communities of New Hampshire during this turbulent and unprecedented time.

We believe the following:

> New Hampshire should respect and listen to its healthcare leaders and scientists when voting on health policy, including legislation that seeks to address COVID-19.
>
> COVID-19 vaccines save lives and prevent hospitalization. COVID-19 vaccines should be easily accessible to everyone in New Hampshire. We need to prioritize continued outreach and education to ensure fair and equitable access for all.
>
> Private entities, including hospitals and private businesses, should have the right to decide what is best for their patients, patrons and/or employees. Private entities should maintain the right to mandate COVID-19 vaccination, testing and/or masking.
>
> Things can change quickly in a pandemic like this one. We should not legislate medicine, because as medicine evolves, our providers need to be able to evolve as well.

Thank you,

Bethany Ames, MD	Hanover	Elizabeth Boucher	Dunbarton
James B. Ames, MD	Hanover	Sanders Burstein, MD	Exeter
Catherine Bardier	Newbury	Polly Campion	Etna
Scott Bardier	Newbury	Ann S. Christiano, APRN	Lyme
Richard D. Baughman, MD	Etna	Sue Conaty	Sunapee
Taralyn Bielaski	Newbury	Jane Difley	Webster

PARTNERS FOR COMMUNITY WELLNESS
Dartmouth-Hitchcock

Dartmouth-Hitchcock
One Medical Center Drive
Lebanon, NH 03756
Phone (603) 650-5000
partnersforcommunitywellness.org

Ken Dolkart	Grantham
Al Griggs	Sunapee
Bill Helm	New London
Karry Lahaye	Lebanon
Jill Lord, RN	Cornish
Jonathan M Ross, MD	Hanover
Nancy Serrell	Hanover
Jane Vance	New London
Jon W. Wahrenberger, MD	Hanover
John E. Xiggoros	Hooksett

From: Deb Roux <sunnydays1729@gmail.com>
Sent: Thursday, January 20, 2022 12:28 AM
To: ~House Health Human Services and Elderly Affairs <HHSEA@leg.state.nh.us>
Subject: Please support HB 1022

Dear Committee Members,

Please allow doctors to prescribe what they feel is best for their patients by supporting HB 1022.

Thank you!

Deb

Archived: Friday, January 28, 2022 11:14:18 AM
From: Rebecca E
Sent: Monday, January 24, 2022 8:33:33 AM
To: ~House Health Human Services and Elderly Affairs
Subject: Please support HB1022 for access to ivermectin
Importance: Normal

Dear Committee Members,

Please vote to pass HB1022. I have been following Dr. Marik and the success ivermectin has had by doctors prescribing it in the US as well as around the world such as the province Uttar Pradesh in India where it was given out to the people with tremendous success.

It is clear that the mass vaccination strategy is not working and the vaccines are not safe nor effective. Ivermectin is safe and affordable and we need this option.

Thank you,
Rebecca Eiler
3 Juniper Lane
Hanover, NH 03755

Archived: Friday, January 28, 2022 11:14:18 AM
From: Whitney, Mark (VP Strategy)
Sent: Monday, January 24, 2022 12:00:31 PM
To: ~House Health Human Services and Elderly Affairs
Cc: 'Paula Minnehan'
Subject: [CAUTION: SUSPECT SENDER] Statement on the Effectiveness of Ivermectin for treating Covid 19
Importance: High

To the honorable members of the House Health, Human Services and Elderly Affairs Committee,

I am forwarding the statement by Dr. Neil Meehan, our Chief Physician Executive on ivermectin that Ms. Paula Minnehan, from NHHA, mentioned during her testimony on HB 1022 at your committee hearing last week. All of us at Exeter Health Resources hope that you will find this statement helpful to your deliberations on this important matter.

Mark

Mark H. Whitney
Vice President, Strategy, Community Relations and Advancement
Exeter Health Resources
(603) 580-7437
mwhitney@ehr.org
Visit Us at:
www.exeterhospital.com
www.facebook.com/ExeterHospital
http://unitedinwellness.org/

To: The Honorable Members of the House Health, Human Services and Elderly Affairs Committee

Date: 1/24/2022

Re: HB 1022 – Permitting Pharmacists to Dispense the Drug Ivermectin by Means of a Standing Order

Ivermectin is a drug that has been approved by the FDA as an anti-parasitic for certain infections including scabies and round worm infections such as Strongyloides (River Blindness). The most recent evidence from several studies has shown Ivermectin to be ineffective for the treatment or prevention of Covid-19. While there were some studies that showed Ivermectin to be effective at killing the Covid 19 virus ***in vitro*** (outside of the body) in a laboratory, there has not been substantial or reliable clinical evidence that Ivermectin is an effective antiviral medication once given to humans.

Unfortunately, in vitro success does not translate to in vivo (in human) success for many medications. Despite this, studies have been done to assess Ivermectin's effectiveness in human subjects. The misperceptions began to emerge early as some of the initial trials, touting extraordinary success, were clearly fraudulent and retracted from publication. Several other flawed studies were also published or began to emerge in pre-print (not peer reviewed) sources. The danger to the public of having unclear, underpowered, and occasionally fraudulent data has been promoted through multimodal channels extolling an ineffective drug to an anxious and under informed public. The latest and most confident meta-analysis in August of 2021 shows Ivermectin has no efficacy in the treatment of Covid 19. The bottom line is that despite the public sharing of information in social media, Ivermectin has not demonstrated any efficacy at all at treating Covid 19 when taken internally. Ivermectin is a medication that is designed to treat nematodes or parasitic worms in horses, by paralyzing their muscles. Covid 19 is a not a parasite, it is a virus and viruses do not have muscles to paralyze.

Given that many sources have "scientific data" of variable reliability, the medical community relies on many trusted resources to discern the most valid evidence sources. These include sources such as the Centers for Disease Control (CDC), Federal Drug Administration (FDA), American Medical Society (AMA), American Pharmacists Association (APhA), and American Society of Health-System Pharmacists (ASHP) to name just a few.

Not only has Ivermectin not demonstrated any efficacy at treating Covid 19, when taken internally without supervision by a physician it can be dangerous.

As recently as last fall multiple organizations, working from reliable data sources, issued strong warnings about Ivermectin's use and increasing popularity among the non-clinical public who have been influenced by misleading information on social media. Particularly:

> "The American Medical Association (AMA), American Pharmacists Association (APhA), and American Society of Health-System Pharmacists (ASHP), **strongly oppose the ordering, prescribing, or dispensing of Ivermectin to prevent or treat COVID-19 outside of a clinical trial**. Ivermectin is approved by the U.S. Food and Drug Administration (FDA) for human use to treat infections caused by internal and external parasites. It is not approved to prevent or treat COVID-19".
>
> "We are calling for an immediate end to the prescribing, dispensing, and use of Ivermectin for the prevention and treatment of COVID-19 outside of a clinical trial. In addition, we are urging physicians, pharmacists, and other prescribers—trusted health care professionals in their communities—to warn patients against the use of Ivermectin outside of FDA-approved indications and guidance, whether intended for use in humans or animals, as well as purchasing Ivermectin from online stores. Veterinary forms of this medication are highly concentrated for large animals and pose a significant toxicity risk for humans." AMA, APhA, ASHP, statement on ending use of Ivermectin to treat COVID-19 | American Medical Association (ama-assn.org).

The CDC also issued a stark warning that US citizens were being misled and put at clinical risk related to the use of Ivermectin.

> "A recent CDC Health Alert Network Advisory (PDF) recommends that health care professionals should counsel patients against use of Ivermectin as a treatment for COVID-19, including emphasizing the potentially toxic effects of this drug, including "nausea, vomiting, and diarrhea. Overdoses are associated with hypotension and neurologic effects such as decreased consciousness, confusion, hallucinations, seizures, coma, and death." CDC_HAN_449.pdf

The National Institute of Health reported that these risks had resulted in a substantial increase in health risks:

> “In 2021, poison control centers across the U.S. received a three-fold increase in the number of calls for human exposures to Ivermectin in January 2021 compared to the pre-pandemic baseline. In July 2021, Ivermectin calls have continued to sharply increase, to a five-fold increase from baseline. These reports are also associated with increased frequency of adverse effects and emergency department/hospital visits.” Ivermectin | COVID-19 Treatment Guidelines (nih.gov)

The bottom line is that the New Hampshire Legislature should join with medical experts across the country in discouraging the use of Ivermectin and other unproven, potentially risky treatments for Covid 19. For complex medical issues it is critical that policy makers trust the immense community of clinical experts who oppose promoting Ivermectin as a treatment and join those clinical experts in promoting vaccinations, masking, social distancing, hand washing and staying home when feeling ill as proven ways of addressing the Covid 19 pandemic. Pushing for greater access to Ivermectin via a standing order at pharmacies is a potentially dangerous distraction that is unjustifiable with science that will encourage patients to spend hard earned money on a treatment that will not help and may put them at risk.

Sincerely,

Dr. Neil Meehan, DO
Chief Physician Executive
Exeter Health Resources

Support for HB 1022

Dear Committee members,

Pleases support HB 1022. There are many people in New Hampshire, a Live FREE or Die state, who want our freedoms back, especially our freedoms around our health. Did you ever think it would be possible for political leaders to have a say in our health care choices? My own husband cannot talk to my doctor without my permission and yet our political leaders want to tell us what medicines we can and cannot take. It doesn't make sense, it is not safe for We the People, and it is not American!

I live with high anxiety and OCD symptoms every single day of my life and I am sure there are many other people out there in our great state that suffer from the same symptoms. The thought of not having Ivermectin available, if needed, only adds to my symptoms. It doesn't have to be this way. It is so crazy. The medication is effective, I heard it is safer than Tylenol and Motrin, cheep, and available. Why wouldn't you let us have access to it? Why?

Please stand up for the people you represent, in New Hampshire, and be a voice for us and vote yes on HB 1022. Thank you!

Please take some time to watch the 15-minute video below and remind yourself of how our Forefathers lead their people.

The Pilgrims Formula To Save America! Kirk Cameron in Monumental

https://www.youtube.com/watch?v=nwrXHUsNC6E

Thank you for your time and please support HB 1022.

God bless you,

Deb

Rep. R. Hershel Nunez, Jr.
HB1022
permitting pharmacists to dispense the drug Ivermectin by means of standing order

Good afternoon. For the record, I am Representative Hershel Nunez, Hillsborough 37, towns of Pelham and Hudson, I live in Pelham. I am not a doctor and in no way want to represent myself as a professional in the health or medical industry. I am however a licensed minister in the state.

I want to tell you a personal story today about my Covid-19 journey, twice, and how I believe Ivermectin actually saved me. In the beginning of November I was notified that I had been exposed to the Sars-Cov-2 virus. I began watching for symptoms and very soon after that I tested positive through a PCR test from my doctor. I was given instruction to go home, quarantine for at least 10 days and that if my symptoms became threatening to go to the emergency room, do not show up at the office. I was not offered any type of prescriptive prophylaxis treatment of any kind nor was I given any instruction of any type of over the counter medicine that could assist with the infection.

That evening I became very ill. After 2 days of being home with me and quarantining, my partner also became very ill. On the night of day 2 I was running a fever of 103.6. I had horrendous body aches and needed assistance just to walk to the facilities. That was a rough night and the next day was no better. Fortunately, there was a knock on my door, from someone I knew who I now consider an Angel. That friend placed an envelope on my doorstep and inside was a note describing where I could do a tele-health appointment to have Ivermectin prescribed. Immediately, with assistance from my partner, I went online and went through the tele-health process and a doctor prescribed Ivermectin to me and then shipped the medicine to me. It arrived the next morning around 11 a.m.

At this point both my partner and I were extremely sick. So sick that we talked about going to the hospital but we decided we'd rather take our chances at home. We literally made our peace with each other and our Creator and asked that He watch over us. We both took the Ivermectin, and amazingly around 3 hours later for both of us the fever broke, the body aches left completely, but we were still very sick. We continued the Ivermectin use as prescribed by our doctor, which was also following the FLCCC guidelines (Front Line COVID-19 Critical Care Alliance Prevention & Treatment Protocols for COVID-19) for Ivermectin use for Covid-19 patients. Each day we got better and better. We still experienced many of the same symptoms that other patients would experience, but I believe the Ivermectin was the saving grace or medication in our illnesses.

Because we were so sick and I knew there could be a chance of contracting the disease again I acquired another prescription of Ivermectin for us to have on hand. A larger one. We both tested negative 12 days after infection. However we still dealt with the residual effects of the disease.

I had researched the FLCCC protocals for post covid infections and continued a reduced dosage as instructed. During the holidays we decided to travel to our vacation home in the US Virgin Islands. We tested negative and traveled. A week prior to travel we increased our dosage for protection, during our stay we took Ivermectin daily. Omicron was beginning to move rampant through the island, there were 127 cases reported when we arrived and there were over 1300 when we left, all in 10 days time. We were fine, we were around hundreds of people, on island, in the airports, on the plane.

When we came home we stopped our Ivermectin protocol. 5 days later I was exposed to the Omicron Variant and became ill and tested positive once again. Why didn't I just keep taking the post covid protocol? I'm happy I had the Ivermectin on hand, I only had 2 1/ 2 days of fever, one tough day, and

Rep. R. Hershel Nunez, Jr.
HB1022
permitting pharmacists to dispense the drug Ivermectin by means of standing order

then the virus presented itself as a nasty cold. I tested negative on day 6, 7, 8 and now I am here testifying before you. This was very recent. I am negative, I tested negative this morning.

I truly believe had I not been following the Ivermectin protocol the illness in both respects would have and could have been much worse.

Our doctors would not prescribe us anything, we were left to our own defenses. We ordered all of the vitamin supplements that our research determined we should use. D3, K2, C, Quercetin, Bromelain, Zinc/Copper. It was like a pill fest every morning along with our dosage of Ivermectin as prescribed following the FLCCC guidelines. I am now using the long haul protocol for post Covid Ivermectin treatment because of contracting the disease more than once. I will be visiting my local doctor regularly for lung checks and blood work. My partner and I both have auto immune diseases that will not allow us to take the vaccine. Therefore we must be allowed to be involved with post covid protocals to keep ourselves safe from the virus during the duration of this pandemic and we both believe that Ivermectin use is the protocal we choose to follow.

I am a firm believer that Ivermectin is a drug that can assist in the weakening of the virus, allowing the patient to be able to work through the disease/infection much easier.

I've included a link to the FLCC guildines for Ivermectin use for Covid-19 and the report
https://covid19criticalcare.com/wp-content/uploads/2020/12/FLCCC-Protocols-%E2%80%93-A-Guide-to-the-Management-of-COVID-19.pdf

I've also included a link to the American Journal of Theraputics where they've listed
"Review of the Emerging Evidence Demonstrating the Efficacy of
Ivermectin in the Prophylaxis and Treatment of COVID-19 and the report
https://covid19criticalcare.com/wp-content/uploads/2020/11/FLCCC-Ivermectin-in-the-prophylaxis-and-treatment-of-COVID-19.pdf

All have been emailed directly to the committee members. I will have no handouts.

I urge you to consider my testimony when it comes time to vote on this bill in Executive session and I would strongly suggest an Ought to Pass outcome.

I can now take any questions.

NEW HAMPSHIRE NURSE PRACTITIONER ASSOCIATION

Empower NPs And Champion Their Practice

Hon. Mark Pearson, Chair
House Health Human Services & Elderly Affairs Committee
Room 205, Legislative Office Building
Concord NH 03301

Via email: HHSEA@leg.state.nh.us

January 18, 2022

RE: HB 1022 - permitting pharmacists to dispense the drug ivermectin by means of a standing order.

Dear Chairman Pearson and members of the Committee:
The NH Nurse Practitioner Association, representing licensed prescribers working in the state of New Hampshire, wishes to register its strong opposition to HB 1022, permitting pharmacists to dispense the drug ivermectin by means of a standing order. We do believe that standing orders, when implemented responsibility, can be a valuable avenue for increasing access to care and health care resources. However, we join with the American Medical Association, American Pharmacists Association (APhA), and American Society of Health-System Pharmacists (ASHP), and other health care advocates and organizations, to strongly oppose the ordering, prescribing, or dispensing of ivermectin to prevent or treat COVID-19 outside of a clinical trial. [1]

In 2021, after the use of ivermectin to treat COVID-19 became a social media-inspired practice, the U.S. Centers for Disease Control and Prevention (CDC) and the FDA issued advisories indicating that the anti-parasitic drug is not authorized or approved for the prevention or treatment of COVID-19. The National Institutes of Health, World Health Organization, and Merck (the manufacturer of the drug) have all stated that there is insufficient evidence to support the use of ivermectin to treat COVID-19. The Infectious Diseases Society of America

[1] https://www.ama-assn.org/press-center/press-releases/ama-apha-ashp-statement-ending-use-ivermectin-treat-covid-19

Guidelines on the Treatment and Management of Patients with COVID-19 also recommended against the use of ivermectin outside of a clinical trial.

Guidelines issued by the National Institutes of Health in 2021 include this statement: "There is insufficient evidence for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of ivermectin for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of ivermectin in the treatment of COVID-19." [2]

In the absence of those trials, legislating the use of ivermectin for COVID-19 would be irresponsible and a threat to public health. As reported by National Public Radio in September 2021, poison control centers around the U.S, have seen a dramatic surge in calls from people who are self-medicating with ivermectin: "According to the National Poison Data System (NPDS), which collects information from the nation's 55 poison control centers, there was a 245% jump in reported exposure cases from July to August — from 133 to 459. Meanwhile, emergency rooms across the country are treating more patients who have taken the drug, after being persuaded by false and misleading information spread on the internet, by talk show hosts and by political leaders. Most patients are overdosing on a version of the drug that is formulated to treat parasites in cows and horses."

We respectfully request that your Committee consider the facts – that ivermectin is not safe or proven to be effective for treating COVID-19, and that more research is needed. We ask that you recommend Inexpedient to Legislate on HB 1022. Thank you for your consideration.

Sincerely,

Kim Mohan, Executive Director

[2] https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ivermectin/

JAMA | Original Investigation

Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19
A Randomized Clinical Trial

Eduardo López-Medina, MD, MSc; Pío López, MD; Isabel C. Hurtado, MD; Diana M Dávalos, MD, MPH, DrPH; Oscar Ramirez, MD, MPhil; Ernesto Martínez, MD; Jesus A. Díazgranados, MD; José M. Oñate, MD; Hector Chavarriaga, MD, MS; Sócrates Herrera, MD; Beatriz Parra, PhD; Gerardo Libreros, PhD; Roberto Jaramillo, MD; Ana C. Avendaño, MD; Dilian F. Toro, MD; Miyerlandi Torres, DrPH; Maria C. Lesmes, MD; Carlos A. Rios, MD; Isabella Caicedo, MD

IMPORTANCE Ivermectin is widely prescribed as a potential treatment for COVID-19 despite uncertainty about its clinical benefit.

OBJECTIVE To determine whether ivermectin is an efficacious treatment for mild COVID-19.

DESIGN, SETTING, AND PARTICIPANTS Double-blind, randomized trial conducted at a single site in Cali, Colombia. Potential study participants were identified by simple random sampling from the state's health department electronic database of patients with symptomatic, laboratory-confirmed COVID-19 during the study period. A total of 476 adult patients with mild disease and symptoms for 7 days or fewer (at home or hospitalized) were enrolled between July 15 and November 30, 2020, and followed up through December 21, 2020.

INTERVENTION Patients were randomized to receive ivermectin, 300 µg/kg of body weight per day for 5 days (n = 200) or placebo (n = 200).

MAIN OUTCOMES AND MEASURES Primary outcome was time to resolution of symptoms within a 21-day follow-up period. Solicited adverse events and serious adverse events were also collected.

RESULTS Among 400 patients who were randomized in the primary analysis population (median age, 37 years [interquartile range {IQR}, 29-48]; 231 women [58%]), 398 (99.5%) completed the trial. The median time to resolution of symptoms was 10 days (IQR, 9-13) in the ivermectin group compared with 12 days (IQR, 9-13) in the placebo group (hazard ratio for resolution of symptoms, 1.07 [95% CI, 0.87 to 1.32]; *P* = .53 by log-rank test). By day 21, 82% in the ivermectin group and 79% in the placebo group had resolved symptoms. The most common solicited adverse event was headache, reported by 104 patients (52%) given ivermectin and 111 (56%) who received placebo. The most common serious adverse event was multiorgan failure, occurring in 4 patients (2 in each group).

CONCLUSION AND RELEVANCE Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand the effects of ivermectin on other clinically relevant outcomes.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT04405843

Visual Abstract

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Eduardo López-Medina, MD, MSc, Centro de Estudios en Infectología Pediátrica, Calle 5 B 5 No. 37 BIS-28, Cali, Colombia (eduardo.lopez@ceiponline.org).

JAMA. doi:10.1001/jama.2021.3071
Published online March 4, 2021.

Therapeutic approaches are needed to improve outcomes in patients with COVID-19. Ivermectin, a widely used drug with a favorable safety profile,[1] is thought to act at different protein-binding sites to reduce viral replication.[2-5] Because of evidence of activity against SARS-CoV-2 in vitro[6] and in animal models,[7,8] ivermectin has attracted interest in the global scientific community[9] and among policy makers.[10] Several countries have included ivermectin in their treatment guidelines,[11-13] leading to a surge in the demand for the medication by the general population and even alleged distribution of veterinary formulations.[14] However, clinical trials are needed to determine the effects of ivermectin on COVID-19 in the clinical setting.

Viral replication may be particularly active early in the course of COVID-19[15] and experimental studies have shown antiviral activity of ivermectin in early stages of other infections.[4] The hypothesis of this randomized trial (EPIC trial [Estudio Para Evaluar la Ivermectina en COVID-19]) was that ivermectin would accelerate recovery in patients with COVID-19 when administered during the first days of infection.

Key Points

Question What is the effect of ivermectin on duration of symptoms in adults with mild COVID-19?

Findings In this randomized clinical trial that included 476 patients, the duration of symptoms was not significantly different for patients who received a 5-day course of ivermectin compared with placebo (median time to resolution of symptoms, 10 vs 12 days; hazard ratio for resolution of symptoms, 1.07).

Meaning The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand effects on other clinically relevant outcomes.

Methods

Study Design and Patients

This study was approved by the Colombian Regulatory Agency (INVIMA No. PI-CEP-1390), the independent ethics committees of Corporación Científica Pediátrica, and collaborating hospitals in Cali, Colombia, and conducted in accordance with Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all patients. Full details of the trial can be found in the protocol (Supplement 1).

This double-blind, randomized trial of ivermectin vs placebo was conducted from July 15 to December 21, 2020, by Centro de Estudios en Infectología Pediátrica in Cali. Study candidates were identified from the state's health department electronic database of all patients with a positive result from a SARS-CoV-2 reverse transcriptase-polymerase chain reaction or antigen test performed in any of the Colombian National Institute of Health-authorized laboratories in the city of Cali.

Potential study participants were identified and selected by simple random sampling from the state's database. Adult men and non-pregnant or breast-feeding women were eligible if their symptoms began within the previous 7 days and they had mild disease, defined as being at home or hospitalized but not receiving high-flow nasal oxygen or mechanical ventilation (invasive or noninvasive). Patients were excluded if they were asymptomatic, had severe pneumonia, had received ivermectin within the previous 5 days, or had hepatic dysfunction or liver function test results more than 1.5 times the normal level. Details of selection criteria can be found in the protocol (Supplement 1). Health disparities by race/ethnicity have been reported in COVID-19 infections.[16,17] Hence, information on this variable was collected by study personnel based on fixed categories as selected by the study participants.

Randomization

Eligible patients were randomly assigned in a 1:1 ratio to receive either oral ivermectin or placebo in solution for 5 days. Patients were randomized in permuted blocks of 4 in a randomization sequence prepared by the unblinded pharmacist in Microsoft Excel version 19.0 who provided masked ivermectin or placebo to a field nurse for home or hospital patient visits. Allocation assignment was concealed from investigators and patients.

Interventions

Study patients received 300 µg/kg of body weight per day of oral ivermectin in solution or the same volume of placebo for 5 days. Ivermectin was provided by Tecnoquímicas SA in bottles of 0.6% solution for oral administration. Patients were asked to take the investigational product on an empty stomach, except on the first study day, when it was administered after screening and randomization procedures took place.

Up to August 26, 2020, the placebo was a mixture of 5% dextrose in saline and 5% dextrose in distilled water, after which placebo was a solution with similar organoleptic properties to ivermectin provided by the manufacturer. Because blinding could be jeopardized due to the different taste and smell of ivermectin and the saline/dextrose placebo, only 1 patient per household was included in the study until the manufacturer's placebo was available. Bottles of ivermectin and placebo were identical throughout the study period to guarantee double-blinding.

Procedures

A study physician contacted potential study participants by telephone to verify selection criteria for eligibility and obtain informed consent. Patients were then visited at home or in hospital by a study nurse who drew blood for liver enzyme evaluations and performed a urine pregnancy test. Eligible patients were revisited by a study nurse for enrollment, documentation of baseline demographic and clinical information, and dispensing of the investigational product. Investigational product was left with the patient for self-administration on days 2 through 5. Subsequently, patients were contacted by telephone by study staff on days 2 through 5, 8, 11, 15, and 21 for a structured interview. A study physician reviewed medical records of hospitalized patients to obtain the information required by the protocol. After study end

(day 21), unused or empty investigational product bottles were collected to certify adherence. Data were entered into an electronic database and validated by the site's quality management department.

Outcome Measures

The primary outcome was the time from randomization to complete resolution of symptoms within the 21-day follow-up period. The 8-category ordinal scale used in this trial has been used in different COVID-19 therapeutic trials[18-20] and is recommended by the World Health Organization's R&D Blueprint.[21] It consists of the following categories: 0 = no clinical evidence of infection; 1 = not hospitalized and no limitation of activities; 2 = not hospitalized, with limitation of activities, home oxygen requirement, or both; 3 = hospitalized, not requiring supplemental oxygen; 4 = hospitalized, requiring supplemental oxygen; 5 = hospitalized, requiring nasal high-flow oxygen, noninvasive mechanical ventilation, or both; 6 = hospitalized, requiring extracorporeal membrane oxygenation, invasive mechanical ventilation, or both; and 7 = death. Time to recovery was defined as the first day during the 21 days of follow-up in which the patient reported a score of 0.

Secondary outcomes included the proportion of patients with clinical deterioration, defined as those with worsening by 2 points (from the baseline score on the 8-category ordinal scale) since randomization. Additional secondary outcomes were the clinical conditions as assessed by the 8-category ordinal scale on days 2, 5, 8, 11, 15, and 21; however, data for days 2 and 15 are not reported here. The proportion of patients who developed fever and the duration of fever since randomization and the proportion of patients who died were also reported. Proportions of patients with new-onset hospitalization in the general ward or intensive care unit or new-onset supplementary oxygen requirement for more than 24 hours were combined into a single outcome called escalation of care. Frequency of incident cases of escalation of care, as well as the duration in both treatment groups, was reported. Evaluation of adverse events (AEs) included solicited AEs, AEs leading to treatment discontinuation, and serious AEs. AEs were classified according to the National Cancer Institute's Common Terminology Criteria for Adverse Events version 5.0.[22]

Post Hoc Analysis

Given that some patients' need for escalation of care was imminent when randomized, the frequency of incident cases of escalation of care occurring 12 or more hours after randomization and the duration up to day 21 in both treatment groups were reported. A comparison of the proportions of patients who required emergency department (ED) or telemedicine consultation was also performed.

Statistical Analysis

The primary outcome was originally defined as the time from randomization until worsening by 2 points on the 8-category ordinal scale. According to the literature, approximately 18% of patients were expected to have such an outcome.[23] However, before the interim analysis, it became apparent that the pooled event rate of worsening by 2 points was substantially lower than the initial 18% expectation, requiring an unattainable sample size. Therefore, on August 31, 2020, the principal investigator proposed to the data and safety monitoring board to modify the primary end point to time from randomization to complete resolution of symptoms within the 21-day follow-up period. This was approved on September 2, 2020. The original sample size of 400 based on the log-rank test for the new primary end point was kept, using an ivermectin to placebo assignment ratio of 1:1. This would allow the detection of 290 events of interest (symptom resolution), assuming that 75% of patients would have the outcome of interest at 21 days,[24] with a 2% dropout rate. This would provide an 80% power under a 2-sided type I error of 5% if the hazard ratio (HR) comparing ivermectin vs placebo is 1.4, corresponding to a 3-day faster resolution of symptoms in patients receiving ivermectin, assuming that time to resolution of symptoms is 12 days with placebo.[24] With an HR of 1.4, 75% and 85% of patients in the placebo and ivermectin groups, respectively, would experience the outcome of interest at 21 days.

On October 20, 2020, the lead pharmacist observed that a labeling error had occurred between September 29 and October 15, 2020, resulting in all patients receiving ivermectin and none receiving placebo during this time frame. The study blind was not unmasked due to this error. The data and safety monitoring board recommended excluding these patients from the primary analysis but retaining them for sensitivity analysis. The protocol was amended to replace these patients to retain the originally calculated study power. The primary analysis population included patients who were analyzed according to their randomization group, but excluded patients recruited between September 29 and October 15, 2020, as well as patients who were randomized but later found to be in violation of selection criteria. Patients were analyzed according to the treatment they received in the as-treated population (sensitivity analysis).

The primary end point of time from randomization to complete resolution of symptoms with ivermectin vs placebo was assessed by a Kaplan-Meier plot and compared with a log-rank test. The HRs and 95% CIs for the cumulative incidence of symptom resolution in both treatment groups were estimated using the Cox proportional hazards model. The proportional hazards assumption was tested graphically using a log-log plot and the test of the nonzero slope. There was no evidence to reject the proportionality assumption.

The time to complete resolution of symptoms was assessed after all patients reached day 21. Data for patients who died or lacked symptom resolution before day 21 were right-censored at death or day 21, respectively. Evaluation of the effect of the treatment in each study visit using the 8-point ordinal scale was estimated using the proportional odds ratio (OR) with its respective 95% CI with an ordinal logistic regression. The proportional odds assumption was met according to the Brant test. The 8-point ordinal scale was inverted in its score, where 0 corresponded to death and 7 to a patient without symptoms.

For sensitivity analysis, primary and secondary end points were compared in the as-treated population.

Clustered standard errors were estimated to adjust for the correlation between multiple patients from the same household. Statistical significance was set at $P < .05$, and all tests were 2-tailed. Because of the potential for type I error due to multiple comparisons, findings for analyses of secondary end points should be interpreted as exploratory. Statistical analyses were done with Stata version 16.0 (StataCorp). Bootstrapping 95% CIs for differences of medians were calculated with R statistical package version 3.6.3 (The R Foundation).

Results

Patients

Of the 476 patients who underwent randomization, 238 were assigned to receive ivermectin and 238 to receive placebo (**Figure 1**). Seventy-five patients were randomized between September 29 and October 15, 2020, and were excluded from the primary analysis population but remained in the as-treated population. Three patients were excluded from all analyses because they were identified as ineligible after randomization (1 asymptomatic patient and 2 who received ivermectin within 5 days prior to enrollment). The primary analysis population included 398 patients (200 allocated to ivermectin and 198 to placebo).

Patients in both groups were balanced in demographic and disease characteristics at baseline (**Table 1**; eTable 1 in Supplement 2). The median age of patients in the primary analysis population was 37 years (interquartile range [IQR], 29-48), 231 (58%) were women, and 316 (79%) did not have any known comorbidities at baseline. At randomization, the median National Early Warning Score 2 was 3 (IQR, 2-4) and most patients (n = 232, 58.3%) were at home and able to perform their routine activities. The most common symptoms were myalgia (310 patients, 77.9%) and headache (305 patients, 76.6%), followed by smell and taste disturbances (223 [56%] and 199 [50%], respectively) and cough (211 patients, 53%), which was most commonly dry (181 patients, 45.5%) (eTable 2 in Supplement 2).

Baseline characteristics of the 75 patients who received ivermectin but were excluded from the primary analysis were not significantly different from the 398 remaining patients in the cohort (eTables 1 and 3 in Supplement 2).

Primary Outcome

Time to resolution of symptoms in patients assigned to ivermectin vs placebo was not significantly different (median, 10 days vs 12 days; difference, −2 days [IQR, −4 to 2]; HR for resolution of symptoms, 1.07 [95% CI, 0.87 to 1.32]; $P = .53$) (**Figure 2** and **Table 2**). In the ivermectin and placebo groups, symptoms resolved in 82% and 79% of patients, respectively, by day 21 (Table 2).

The type of placebo that patients received did not affect the results (HR for ivermectin vs dextrose in saline: 1.14 [95% CI, 0.83-1.55]; HR for ivermectin vs manufacturer's placebo: 1.07 [95% CI, 0.85 to 1.34] (eFigure 1 in Supplement 2).

Similar results were observed in the as-treated population (eFigure 2 and eTable 4 in Supplement 2).

Secondary Outcomes

Few patients had clinical deterioration of 2 or more points in the ordinal 8-point scale, and there was no significant difference between the 2 treatment groups (2% in the ivermectin group and 3.5% in the placebo group; absolute difference, −1.53 [95% CI, −4.75 to 1.69]). The OR for deterioration in ivermectin vs placebo groups was 0.56 (95% CI, 0.16 to 1.93) (Table 2).

The odds of improving the score in the ordinal scale were not significantly different between both treatment groups, as determined by proportional odds models (eFigure 3 and eTable 5 in Supplement 2).

There was no significant difference in the proportion of patients who required escalation of care in the 2 treatment groups (2% with ivermectin, 5% with placebo; absolute difference, −3.05 [95% CI, −6.67 to 0.56]; OR, 0.38 [95% CI, 0.12 to 1.24]). The length of time during which patients required escalation of care in the ivermectin vs placebo groups was not significantly different (median difference, 7 days [IQR, −5.0 to 16.5]). The proportions of patients who developed fever during the study period were not significantly different between the 2 treatment groups (absolute difference of ivermectin vs placebo, −2.61 [95% CI, −8.31 to 3.09]; OR, 0.73 [95% CI, 0.37 to 1.45]), nor was the duration of fever (absolute difference of ivermectin vs placebo, −0.5 days [95% CI, −1.0 to 2.0]) (Table 2). One patient in the placebo group died during the study period. No data were missing for the primary or secondary outcomes. See eTables 4 and 6 in Supplement 2 for the results in the as-treated population.

Post Hoc End Points and Analyses

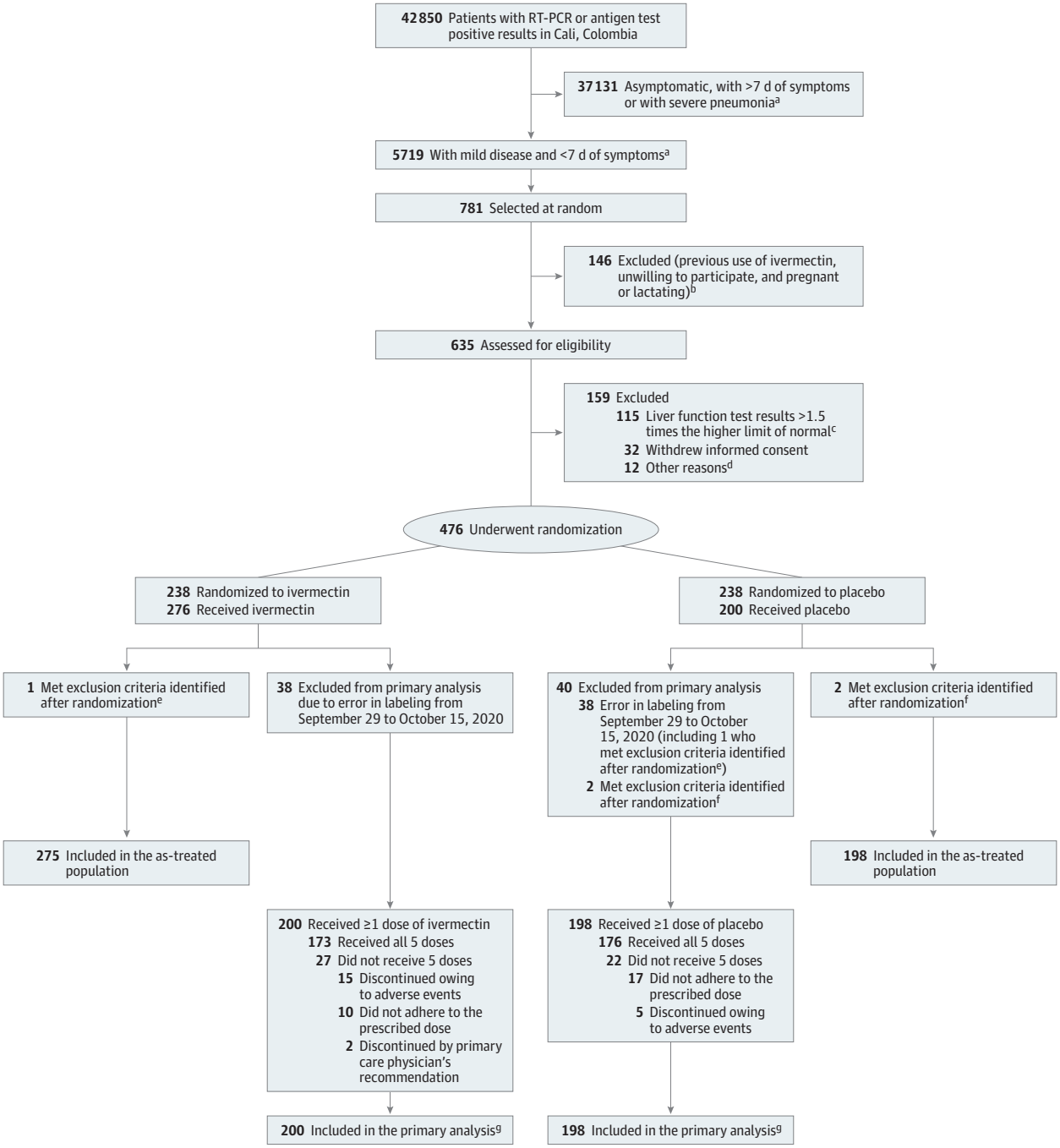
After excluding 4 patients who required hospitalization within 12 hours after randomization (median, 3.25 hours [IQR, 2-6]), there were 4 patients (2%) in the ivermectin group and 6 (3%) in the placebo group who required escalation of care (absolute difference, −1.0 [95% CI, −4.11 to 2.05]; OR, 0.65 [95% CI, 0.18 to 2.36]) (Table 2).

The proportions of patients who sought medical care (ED or telemedicine consultation) were not significantly different between the 2 treatment groups (8.0% in the ivermectin group and 6.6% in the placebo group; absolute difference, 1.43 [95% CI, −3.67 to 6.54]; OR, 1.24 [95% CI, 0.56 to 2.74]) (Table 2). See eTable 4 in Supplement 2 for the results in the as-treated population.

Adverse Events

A total of 154 patients (77%) in the ivermectin group and 161 (81.3%) in the placebo group reported AEs between randomization and day 21. Fifteen patients (7.5%) in the ivermectin group vs 5 patients (2.5%) in the placebo group discontinued treatment due to an AE. Serious AEs developed in 4 patients, 2 in each group, but none were considered by the investigators to be related to the trial medication (**Table 3**; eTable 7 in Supplement 2).

Figure 1. Enrollment, Randomization, and Treatment Assignment



RT-PCR indicates reverse transcriptase–polymerase chain reaction.

[a] Patients with mild disease were at home or hospitalized but not receiving high-flow nasal oxygen or mechanical ventilation (invasive or noninvasive). Patients with severe pneumonia were receiving high-flow nasal oxygen, mechanical ventilation (invasive or noninvasive), or extracorporeal membrane oxygenation.

[b] The numbers of patients with these exclusion criteria were not collected.

[c] Aspartate aminotransferase and alanine aminotransferase.

[d] Eight patients used ivermectin within 5 days prior to randomization, 1 had a positive pregnancy test, 1 was asymptomatic, 1 lived in an inaccessible area, and 1 had onset of symptoms 8 days prior to randomization.

[e] Patient was asymptomatic and was randomized to receive placebo but received ivermectin.

[f] Use of ivermectin before randomization.

[g] Includes deaths and recoveries.

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline and Medications Initiated Since Symptom Onset in the Primary Analysis Population

Characteristic	No. (%)	
	Ivermectin (n = 200)	Placebo (n = 198)
Age, median (IQR), y	37 (29-47.7)	37 (28.7-49.2)
Age groups, y		
<40	119 (59.5)	112 (56.6)
40-64	73 (36.5)	70 (35.3)
≥65	8 (4.0)	16 (8.1)
Sex		
Male	78 (39)	89 (44.9)
Female	122 (61)	109 (55)
Race or ethnic group[a]		
Mixed race	178 (89)	179 (90.4)
Black or African American	16 (8.0)	16 (8.1)
Colombian native	6 (3.0)	3 (1.5)
Health insurance		
Private/semiprivate	177 (88.5)	174 (87.9)
Government subsidized	20 (10.0)	23 (11.6)
Uninsured	3 (1.5)	1 (0.5)
No. of persons in the same household, median (IQR)	4 (3-5)	3 (3-4)
Current smoker	3 (1.5)	8 (4.0)
BMI, median (IQR)	26.1 (23.1-28.8)	26.4 (22.7-29.0)
History of BCG vaccination, No./No. with available information (%)	183/199 (92.0)	184/195 (90.4)
Coexisting conditions[b]		
Obesity (BMI ≥30), No./No. with available information (%)	37/200 (18.5)	38/196 (19.4)
Hypertension	28 (14.0)	25 (12.6)
Diabetes	10 (5.0)	12 (6.1)
Thyroid disease	7 (3.5)	8 (4.0)
Respiratory disease	6 (3.0)	6 (3.0)
Cardiovascular disease	4 (2.0)	3 (1.5)
Any coexisting condition	44 (22.0)	38 (19.2)
Median time (IQR) from symptom onset to randomization, d	5 (4-6)	5 (4-6)
NEWS2 score at randomization, median (IQR)[c]	3 (2-4)	3 (2-4)
Score on ordinal scale at randomization		
1: Not hospitalized and no limitation of activities	123 (61.5)	109 (55.0)
2: Not hospitalized, with limitation of activities, home oxygen requirement, or both	75 (37.5)	87 (43.9)
3: Hospitalized, not requiring supplemental oxygen	1 (0.5)	1 (0.5)
4: Hospitalized, requiring supplemental oxygen[d]	1 (0.5)	1 (0.5)
Medications initiated since symptom onset		
NSAIDs	57 (28.5)	61 (30.8)
Other[e]	41 (20.5)	38 (19.2)
Macrolides	27 (13.5)	22 (11.1)
Other antipyretics	26 (13.0)	23 (11.6)
Nonmacrolide antibiotics	13 (6.5)	11 (5.6)
Glucocorticoids	6 (3.0)	12 (6.1)
Other immunomodulating agents[f]	4 (2.0)	2 (1.0)
Anticoagulants	1 (0.5)	7 (3.5)

Abbreviations: BCG, Bacille Calmette-Guérin; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range; NEWS2, National Early Warning Score 2; NSAIDs, nonsteroidal anti-inflammatory drugs.

[a] Race/ethnic group was collected by study personnel based on fixed categories as selected by the study participants. "Mixed race" refers to an individual of mixed European/Colombian native heritage.

[b] Coexisting conditions were determined by self-report.

[c] NEWS2 includes 6 physiological measures; total scores range from 0 to 20, with higher scores indicating greater clinical risk. Score of 3 indicates low clinical risk.

[d] Not high-flow nasal oxygen nor mechanical ventilation.

[e] Acyclovir, antidiarrheals, antiemetics, antihistamines, antiparasitics, antispasmodics, antitussives, natural or homeopathic medications, proton pump inhibitors, and salbutamol.

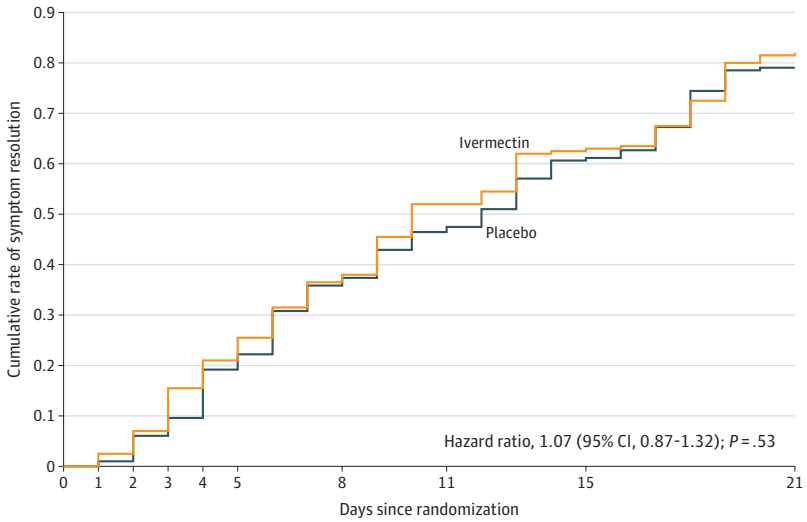
[f] Oral interferon and colchicine.

Discussion

In this double-blind, randomized trial of symptomatic adults with mild COVID-19, a 5-day course of ivermectin vs placebo initiated in the first 7 days after evidence of infection failed to significantly improve the time to resolution of symptoms.

Interest in ivermectin in COVID-19 therapy began from an in vitro study that found that bathing SARS-CoV-2–infected Vero-hSLAM cells with 5-μM ivermectin led to an

Figure 2. Time to Resolution of Symptoms in the Primary Analysis Population



No. at risk

Ivermectin	200	195	186	169	158	127	96	75	37
Placebo	198	196	186	179	160	127	106	77	41

The cumulative rate of symptom resolution is the percentage of patients who experienced their first day free of symptoms. All patients were followed up for 21 days.

Table 2. Outcomes in the Primary Analysis Population

Characteristic	No. (%) Ivermectin (n = 200)	No. (%) Placebo (n = 198)	Absolute difference (95% CI)	Effect estimate (95% CI)	*P* value
Primary outcome: resolution of symptoms[a]					
Time to resolution of symptoms, median No. of days (IQR)	10 (9-13)	12 (9-13)	−2 (−4 to 2)[b]	1.07 (0.87 to 1.32)[c]	.53
Symptoms resolved at 21 d	164 (82.0)	156 (79.0)	3.21 (−4.58 to 11.01)[d]	1.23 (0.75 to 2.01)[e]	
Secondary outcomes					
Deterioration by ≥2 points in an ordinal 8-point scale[f]	4 (2.0)	7 (3.5)	−1.53 (−4.75 to 1.69)[d]	0.56 (0.16 to 1.93)[e]	
Fever since randomization[g]	16 (8.0)	21 (10.6)	−2.61 (−8.31 to 3.09)[d]	0.73 (0.37 to 1.45)[e]	
Duration of febrile episode, median (IQR), d	1.5 (1-3)	2 (1-3)	−0.5 (−1.0 to 2.0)[b]		
Escalation of care since randomization[h]	4 (2.0)	10 (5.0)	−3.05 (−6.67 to 0.56)[d]	0.38 (0.12 to 1.24)[e]	
Duration, median (IQR) d[i]	13 (3.5-21)	6 (3.7-10.7)	7 (−5 to 16.5)[b]		
Deaths	0	1 (0.5)			
Post hoc outcomes					
Escalation of care occurring ≥12 h since randomization[h]	4 (2.0)	6 (3.0)	−1.0 (−4.11 to 2.05)[d]	0.65 (0.18 to 2.36)[e]	
Duration, median (IQR), d[i]	6.5 (4.5-21)	8 (4.2-13.2)	−1.5 (−7.5 to 15.5)[b]		
Emergency department visits or telemedicine consultations, No. of patients	16 (8.0)	13 (6.6)	1.43 (−3.67 to 6.54)[d]	1.24 (0.56 to 2.74)[e]	

Abbreviation: IQR, interquartile range.

[a] Resolution of symptoms was defined as the first day free of symptoms.

[b] Absolute difference is the median difference with 95% CIs estimated by bootstrap sampling.

[c] Hazard ratio for resolution of symptoms was estimated by the Cox proportional-hazard model. The *P* value for this ratio was calculated with the log-rank test.

[d] Absolute difference is the difference in proportions.

[e] Effect estimate is odds ratio (2-sided 95% CI) from a logistic model.

[f] Ordinal scale: 0 = no clinical evidence of infection; 1 = not hospitalized and no limitation of activities; 2 = not hospitalized, with limitation of activities, home oxygen requirement, or both; 3 = hospitalized, not requiring supplemental oxygen; 4 = hospitalized, requiring supplemental oxygen; 5 = hospitalized, requiring nasal high-flow oxygen, noninvasive mechanical ventilation, or both; 6 = hospitalized, requiring extracorporeal membrane oxygenation, invasive mechanical ventilation, or both; and 7 = death.

[g] Fever defined as an axillary temperature ≥38 °C. Patients took their own temperatures while at home.

[h] Escalation of care defined as new-onset hospitalization in the general ward or intensive care unit or new-onset supplementary oxygen requirement for more than 24 hours.

[i] Number of days that patients required hospitalization or supplementary oxygen. If both were required, the longer duration was recorded.

Table 3. Summary of Adverse Events During the 21-Day Follow-up Period in the Primary Analysis Population

Event	Any grade, No. (%)[a]	
	Ivermectin (n = 200)	Placebo (n = 198)
Solicited adverse events[b]		
Headache	104 (52.0)	111 (56.1)
Duration, median (IQR), d	2 (1-5)	2 (1-5)
Dizziness	68 (34.0)	68 (34.3)
Duration, median (IQR), d	1.5 (1-3)	2 (1-3.7)
Diarrhea	52 (26.0)	65 (32.8)
Duration, median (IQR), d	2 (1-4)	2 (1-3)
Nausea	46 (23)	47 (23.7)
Duration, median (IQR), d	1 (1-3.5)	2 (1-4)
Abdominal pain	36 (18.0)	49 (24.7)
Duration, median (IQR), d	2 (1-4)	2 (1-3)
Disturbances of vision	33 (16.5)	28 (14.4)
Duration, median (IQR), d	2 (1-3)	2 (1-4.7)
Photophobia	7 (3.5)	4 (2.0)
Blurry vision	23 (11.5)	23 (11.6)
Reduction in visual acuity	4 (2.0)	2 (1.0)
Tremor	13 (6.5)	6 (3.0)
Duration, median (IQR), d	1 (1-6.5)	3.5 (1-6.5)
Skin discoloration	13 (6.5)	4 (2.0)
Duration, median (IQR), d	3 (1.2-5.2)	4 (2.5-13)
Skin rash	12 (6.0)	19 (9.6)
Duration, median (IQR), d	4.5 (3-7)	4 (1-8)
Swelling	4 (2.0)	3 (1.5)
Duration, median (IQR), d	3 (1.2-4.7)	1 (1-1)
Vomiting	3 (1.5)	6 (3.0)
Duration, median (IQR), d	1 (1-3)	1 (1-1.5)
No. of patients with ≥1 solicited adverse events	154 (77.0)	161 (81.3)
Adverse events leading to treatment discontinuation	15 (7.5)	5 (2.5)
Serious adverse events[c]		
Respiratory failure	2 (1.0)	1 (0.5)
Acute kidney injury	2 (1.0)	1 (0.5)
Multiorgan failure	2 (1.0)	2 (1.0)
Gastrointestinal hemorrhage	2 (1.0)	0
Sepsis	1 (0.5)	1 (0.5)
No. of patients with ≥1 serious adverse events	2 (1.0)	2 (1.0)

Abbreviation: IQR, interquartile range.

[a] Grade refers to the severity of the adverse event, determined according to the following: Grade 1, mild: asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2, moderate: minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL). Grade 3, severe or medically significant but not immediately life-threatening: hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL. Grade 4, life-threatening consequences: urgent intervention indicated. Grade 5, death related to adverse events. Grade 3 solicited adverse events: headache, n = 1 in the placebo group, duration of 6 days; dizziness, n = 1 in the ivermectin group, duration of 6 days and n = 3 in the placebo group (median duration of 2 days [IQR, 1-8]); and skin rash, n = 2 in the ivermectin group (median duration of 8 days [IQR, 7-9]). No grade 4 events occurred.

[b] Adverse events were solicited by telephone at each follow-up call.

[c] Serious adverse events were severe, medically significant, or life-threatening conditions occurring in study patients documented from revision of patients' electronic medical records. All were grade 3 or 4, except 1 patient in the placebo group who had grade 5 respiratory failure, acute kidney injury, multiorgan failure, and sepsis.

approximately 5000-fold reduction in viral RNA.[8] However, pharmacokinetic models indicated that the concentrations used in the in vitro study are difficult to achieve in human lungs or plasma,[25] and inhibitory concentrations of ivermectin are unlikely to be achieved in humans at clinically safe doses.[26] Despite this, a retrospective study using logistic regression and propensity score matching found an association between 200 µg/kg of ivermectin in a single dose (8% of patients received a second dose) and improved survival for patients admitted with severe COVID-19.[27] The contrast with the findings in this trial may be related to differences in patient characteristics, exposures and outcomes that were measured, or unmeasured confounders in the observational study. To our knowledge, preliminary reports of other randomized trials of ivermectin as treatment for COVID-19 with positive results have not yet been published in peer-reviewed journals.[28-31]

Daily doses were used in this trial because pharmacokinetic models have shown higher lung concentrations with daily rather than intermittent dosing,[32] and have proven to be well tolerated.[33,34] In addition, the US Food and Drug Administration–approved dose for the treatment of helminthic diseases (200 µg/kg) showed clinical benefit in an observational study,[27] supporting a hypothesis that higher doses could be clinically relevant.

This study did not find any significant effect of ivermectin on other evaluated measures of clinical benefit for the treatment of COVID-19. Although a numerically smaller proportion of ivermectin-treated patients required escalation of care (2.0% with ivermectin vs 5.0% with placebo), the difference was not statistically significant and was further attenuated in a post hoc analysis after excluding 4 patients who were hospitalized at a median time of 3.25 hours after randomization. In addition, ivermectin did not reduce ED or

telephone consultations, further supporting the lack of efficacy for these outcomes. However, the relatively young and healthy study population rarely developed complications, rendering the study underpowered to detect such effects. Therefore, the ability of ivermectin to prevent the progression of mild COVID-19 to more severe stages would need to be assessed in larger trials.

The study was sufficiently powered to detect faster resolution of symptoms in patients soon after they became apparent, and no significant difference was identified. However, the study population was relatively young, with few comorbidities and with liver enzyme levels less than 1.5 times the normal level, so the findings may be generalizable only to such populations.

Cumulatively, the findings suggest that ivermectin does not significantly affect the course of early COVID-19, consistent with pharmacokinetic models showing that plasma total and unbound ivermectin levels do not reach the concentration resulting in 50% of viral inhibition even for a dose level 10-times higher than the approved dose.[32]

Limitations

This study has several limitations. First, the study was not conducted or completed according to the original design, and the original primary outcome to detect the ability of ivermectin to prevent clinical deterioration was changed 6 weeks into the trial. In the study population, the incidence of clinical deterioration was below 3%, making the original planned analysis futile. Ultimately, findings for primary and secondary end points were not significantly different between the ivermectin and placebo groups.

Second, the study was well-powered to detect an HR for resolution of symptoms of 1.4 in the ivermectin vs placebo groups, but may have been underpowered to detect a smaller but still clinically meaningful reduction in the primary end point.

Third, virological assessments were not included, but the clinical characteristics that were measured indirectly reflect viral activity and are of interest during the pandemic.

Fourth, the placebo used in the first 65 patients differed in taste and smell from ivermectin. However, patients from the same household were not included until the placebo with the same organoleptic properties was available, and the lack of effect of ivermectin on the primary outcome was similar when compared with either formulation of placebo.

Fifth, 2 secondary outcomes used an 8-category ordinal scale that in initial stages requires patient self-reporting and thus allows subjectivity to be introduced. Sixth, data on the ivermectin plasma levels were not collected. Seventh, as already noted, the study population was relatively young and results may differ in an older population.

Conclusions

Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand the effects of ivermectin on other clinically relevant outcomes.

ARTICLE INFORMATION

Accepted for Publication: February 18, 2021.

Published Online: March 4, 2021. doi:10.1001/jama.2021.3071

Author Affiliations: Centro de Estudios en Infectología Pediátrica, Cali, Colombia (López-Medina, López); Department of Pediatrics, Universidad del Valle, Cali, Colombia (López-Medina, López, Hurtado); Clínica Imbanaco, Cali, Colombia (López-Medina, Ramirez, Oñate, Caicedo); State Health Department, Valle del Cauca, Colombia (Hurtado, Lesmes); Department of Public Health, Universidad Icesi, Cali, Colombia (Dávalos); POHEMA (Pediatric Oncologist and Hematologist) Foundation, Cali, Colombia (Ramirez); Cali's Cancer Population-based Registry, Cali, Colombia (Ramirez); Department of Internal Medicine, Universidad del Valle, Cali, Colombia (Martínez, Oñate); Christus Sinergia Salud, Cali, Colombia (Martínez); Neurólogos de Occidente, Cali, Colombia (Díazgranados); Clínica de Occidente, Cali, Colombia (Oñate); Municipal Health Department, Cali, Colombia (Chavarriaga, Torres); Caucaseco Scientific Research Center, Malaria Vaccine and Drug Development Center, Cali, Colombia (Herrera); Department of Microbiology, Universidad del Valle, Cali, Colombia (Parra, Libreros); Hemato Oncólogos, Cali, Colombia (Jaramillo, Avendaño); Health Experts Committee, Valle del Cauca, Colombia (Toro); Centro Médico Santuario, Cali, Colombia (Rios).

Author Contributions: Drs López-Medina and Ramirez had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: López-Medina, López, Hurtado, Dávalos, Ramirez, Martínez, Díazgranados, Oñate, Chavarriaga.
Acquisition, analysis, or interpretation of data: López-Medina, Hurtado, Ramirez, Martínez, Oñate, Chavarriaga, Herrera, Parra, Libreros, Jaramillo, Avendaño, Toro, Torres, Lesmes, Rios, Caicedo.
Drafting of the manuscript: López-Medina, Hurtado, Dávalos, Chavarriaga, Caicedo.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: López-Medina, Ramirez.
Obtained funding: López-Medina, López.
Administrative, technical, or material support: Hurtado, Dávalos, Martínez, Díazgranados, Chavarriaga, Herrera, Parra, Libreros, Jaramillo, Avendaño, Toro, Torres, Lesmes, Rios, Caicedo.
Supervision: López-Medina, López, Oñate, Rios, Caicedo.

Conflict of Interest Disclosures: Dr López-Medina reported receiving grants from Sanofi Pasteur, GlaxoSmithKline, and Janssen and personal fees from Sanofi Pasteur during the conduct of the study. Dr López reported receiving grants from Sanofi Pasteur, GlaxoSmithKline, and Janssen and personal fees from Sanofi Pasteur during the conduct of the study. Dr Oñate reported receiving grants from Janssen and personal fees from Merck Sharp & Dohme and Gilead outside the submitted work. Dr Torres reported receiving nonfinancial support from Tecnoquímicas unrelated to this project during the conduct of the study. No other disclosures were reported.

Funding/Support: This study received an unrestricted grant from Centro de Estudios en Infectología Pediátrica (grant ScDi823).

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: In addition to the authors, the following collaborators from Centro de Estudios en Infectología Pediátrica participated in the Estudio Para Evaluar la Ivermectina en COVID-19 (EPIC) trial: Catalina De La Cruz, MD; Camilo Andrade; Iñigo Prieto, MD, MSc; Viviana Márquez, MD; Mary Luz Hernandez; Carlos Gonzalez, MD; Victoria Aguirre, RN; Gloria Tamayo; Leidy Gomez; Aracelly Romero; Socorro Mutis; Nidia Guaza; Eliana Valencia; James Riascos; Ovidio Maldonado; Laura Victoria, RN; Hilda Giraldo; Lina Solano, RN; Maria F. Collazos, RN; Elizabeth Toro, MD; Carlos Cortés, MD; Alexandra Sierra, MD; Carolina Ospina, MD; Diana P. Mazo, PharmD; Jhon J. Calderón; Jenny Yela, RN; Diego Rivera, RN; and Diana Suárez, PharmD.

Data Sharing Statement: See Supplement 3.

Additional Contributions: We are grateful to the patients who participated in this trial; Erika Cantor, MSc, from the Institute of Statistics, Universidad de

Valparaíso, Valparaíso, Chile, for her contribution during data analysis; Keith Veitch for his writing assistance; and Neal Alexander, PhD, from CIDEIM in Cali, Colombia, and Rodrigo DeAntonio, DrPH, from Cevaxin in Panamá City, Panamá, for their contribution during study planning. Ms Cantor and Mr Veitch received compensation for their roles in the study. Drs Alexander and DeAntonio did not receive compensation for their roles in the study. We thank Tecnoquímicas for its donation of the investigational product and placebo from August 26, 2020, until the end of the trial.

REFERENCES

1. Omura S. Ivermectin: 25 years and still going strong. *Int J Antimicrob Agents*. 2008;31(2):91-98. doi:10.1016/j.ijantimicag.2007.08.023

2. Yang SNY, Atkinson SC, Wang C, et al. The broad spectrum antiviral ivermectin targets the host nuclear transport importin α/β1 heterodimer. *Antiviral Res*. 2020;177:104760. doi:10.1016/j.antiviral.2020.104760

3. Wagstaff KM, Sivakumaran H, Heaton SM, Harrich D, Jans DA. Ivermectin is a specific inhibitor of importin α/β-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. *Biochem J*. 2012;443(3):851-856. doi:10.1042/BJ20120150

4. Mastrangelo E, Pezzullo M, De Burghgraeve T, et al. Ivermectin is a potent inhibitor of flavivirus replication specifically targeting NS3 helicase activity: new prospects for an old drug. *J Antimicrob Chemother*. 2012;67(8):1884-1894. doi:10.1093/jac/dks147

5. Tay MY, Fraser JE, Chan WK, et al. Nuclear localization of dengue virus (DENV) 1-4 non-structural protein 5: protection against all 4 DENV serotypes by the inhibitor Ivermectin. *Antiviral Res*. 2013;99(3):301-306. doi:10.1016/j.antiviral.2013.06.002

6. Frontline Covid-19 Critical Care Alliance. Accessed December 19, 2020. https://covid19criticalcare.com/

7. US Senate Committee on Homeland Security & Governmental Affairs. Early outpatient treatment: an essential part of a COVID-19 solution, part II. Accessed December 19, 2020. https://www.hsgac.senate.gov/early-outpatient-treatment-an-essential-part-of-a-covid-19-solution-part-ii

8. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Res*. 2020;178:104787. doi:10.1016/j.antiviral.2020.104787

9. de Melo GD, Lazarini F, Larrous F, et al. Anti-COVID-19 efficacy of ivermectin in the golden hamster. *bioRxiv*. Preprint posted November 22, 2020. doi:10.1101/2020.11.21.392639

10. Arévalo A, Pagotto R, Pórfido J, et al. Ivermectin reduces coronavirus infection in vivo: a mouse experimental model. *bioRxiv*. Preprint posted November 2, 2020. doi:10.1101/2020.11.02.363242

11. Ministerio de Salud, República del Perú. Resolución ministerial No. 270-2020-MINSA. Accessed December 19, 2020. https://cdn.www.gob.pe/uploads/document/file/694719/RM_270-2020-MINSA.PDF

12. Rodriguez Mega E. Latin America's embrace of an unproven COVID treatment is hindering drug trials. *Nature*. Accessed December 19, 2020. https://www.nature.com/articles/d41586-020-02958-2

13. Ministerio de Salud, Gobierno del Estado de Bolivia. Resolución ministerial No. 0259. Accessed December 19, 2020. https://www.minsalud.gob.bo/component/jdownloads/?task=download.send&id=425&catid=27&m=0&Itemid=646

14. Molento MB. COVID-19 and the rush for self-medication and self-dosing with ivermectin: a word of caution. *One Health*. 2020;10:100148. doi:10.1016/j.onehlt.2020.100148

15. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. *J Heart Lung Transplant*. 2020;39(5):405-407. doi:10.1016/j.healun.2020.03.012

16. Mahajan UV, Larkins-Pettigrew M. Racial demographics and COVID-19 confirmed cases and deaths: a correlational analysis of 2886 US counties. *J Public Health (Oxf)*. 2020;42(3):445-447. doi:10.1093/pubmed/fdaa070

17. Karaca-Mandic P, Georgiou A, Sen S. Assessment of COVID-19 hospitalizations by race/ethnicity in 12 states. *JAMA Intern Med*. 2021;181(1):131-134. doi:10.1001/jamainternmed.2020.3857

18. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe COVID-19. *N Engl J Med*. 2020;382(19):1787-1799. doi:10.1056/NEJMoa2001282

19. Beigel JH, Tomashek KM, Dodd LE, et al; ACTT-1 Study Group Members. Remdesivir for the treatment of COVID-19: final report. *N Engl J Med*. 2020;383(19):1813-1826. doi:10.1056/NEJMoa2007764

20. Spinner CD, Gottlieb RL, Criner GJ, et al; GS-US-540-5774 Investigators. Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. *JAMA*. 2020;324(11):1048-1057. doi:10.1001/jama.2020.16349

21. World Health Organization. WHO R&D blueprint: novel coronavirus: COVID-19 therapeutic trial synopsis. Accessed December 20, 2020. https://www.who.int/blueprint/priority-diseases/key-action/COVID-19_Treatment_Trial_Design_Master_Protocol_synopsis_Final_18022020.pdf

22. US Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Published November 27, 2017. Accessed December 20, 2020. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf

23. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323(13):1239-1242. doi:10.1001/jama.2020.2648

24. Mitjà O, Corbacho-Monné M, Ubals M, et al; BCN PEP-CoV-2 RESEARCH GROUP. Hydroxychloroquine for early treatment of adults with mild COVID-19: a randomized-controlled trial. *Clin Infect Dis*. 2020;ciaa1009.

25. Bray M, Rayner C, Noël F, Jans D, Wagstaff K. Ivermectin and COVID-19: a report in antiviral research, widespread interest, an FDA warning, two letters to the editor and the authors' responses. *Antiviral Res*. 2020;178:104805. doi:10.1016/j.antiviral.2020.104805

26. Momekov G, Momekova D. Ivermectin as a potential COVID-19 treatment from the pharmacokinetic point of view: antiviral levels are not likely attainable with known dosing regimens. *Biotechnol Biotechnol Equipment*. 2020;34:469-74. doi:10.1080/13102818.2020.1775118

27. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter JJ. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019: the ICON Study. *Chest*. Published online October 12, 2020. doi:10.1016/j.chest.2020.10.009

28. Ahmed E, Hany B, Abo Youssef S, et al Efficacy and safety of ivermectin for treatment and prophylaxis of COVID-19 pandemic. *Research Square*. Preprint posted November 17, 2020. doi:10.21203/rs.3.rs-100956/v1

29. Hashim HA, Maulood MF, Rasheed AM, Fatak DF, Kabah KK, Abdulamir AS. Controlled randomized clinical trial on using ivermectin with doxycycline for treating COVID-19 patients in Baghdad, Iraq. *medRxiv*. Preprint posted October 27, 2020. doi:10.1101/2020.10.26.20219345

30. Niaee MS, Gheibi N, Namdar P, et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: a randomized multi-center clinical trial. *Research Square*. Preprint posted November 24, 2020. doi:10.21203/rs.3.rs-109670/v1

31. Clinical Trial of Ivermectin Plus Doxycycline for the Treatment of Confirmed Covid-19 Infection. Accessed December 21, 2020. https://clinicaltrials.gov/ct2/show/results/NCT04523831

32. Schmith VD, Zhou JJ, Lohmer LRL. The approved dose of ivermectin alone is not the ideal dose for the treatment of COVID-19. *Clin Pharmacol Ther*. 2020;108(4):762-765. doi:10.1002/cpt.1889

33. Diazgranados-Sanchez JA, Mejia-Fernandez JL, Chan-Guevara LS, Valencia-Artunduaga MH, Costa JL. Ivermectin as an adjunct in the treatment of refractory epilepsy [article in Spanish]. *Rev Neurol*. 2017;65(7):303-310.

34. Smit MR, Ochomo EO, Aljayyoussi G, et al. Safety and mosquitocidal efficacy of high-dose ivermectin when co-administered with dihydroartemisinin-piperaquine in Kenyan adults with uncomplicated malaria (IVERMAL): a randomised, double-blind, placebo-controlled trial. *Lancet Infect Dis*. 2018;18(6):615-626. doi:10.1016/S1473-3099(18)30163-4

HB1022

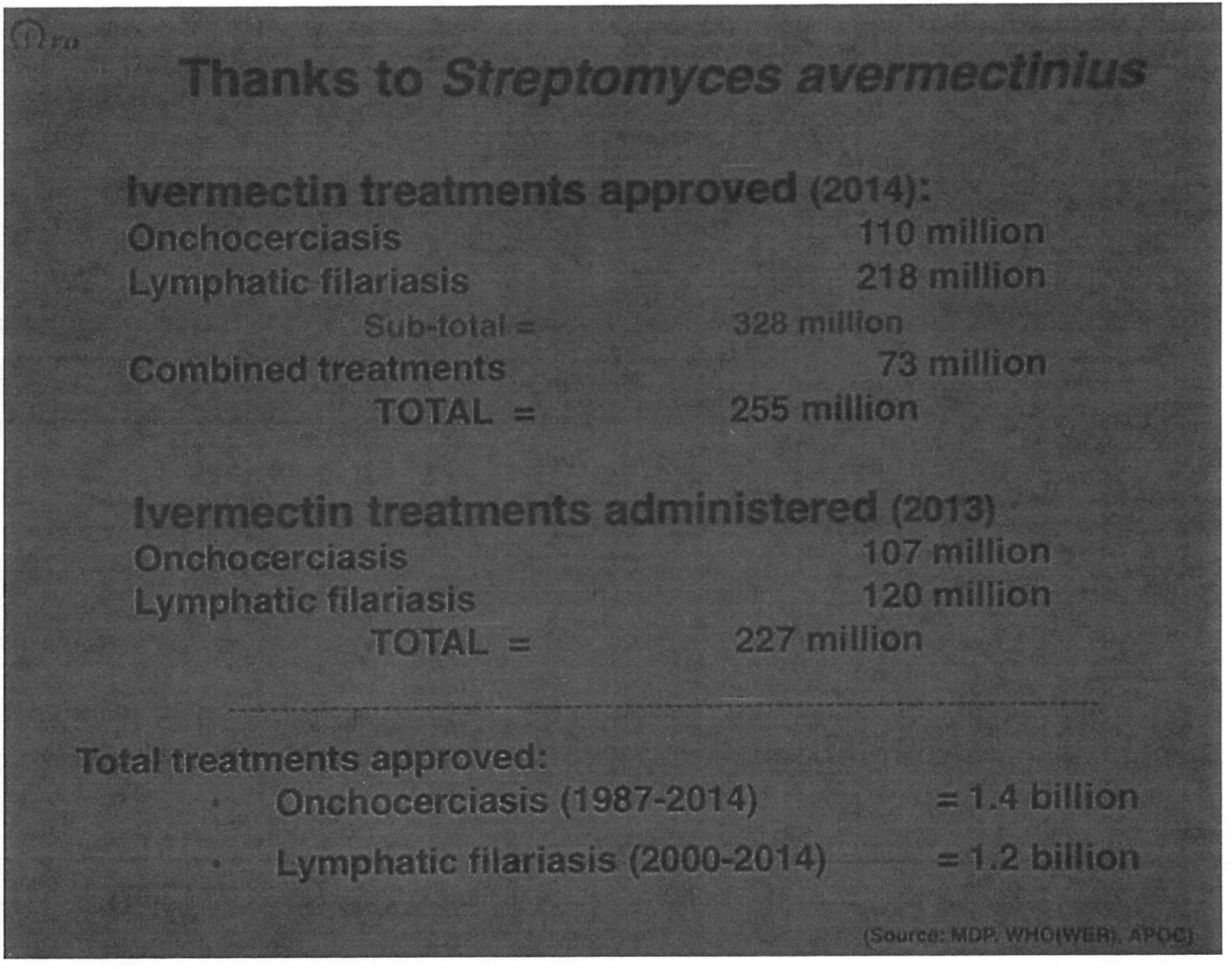
COVID-19:
The Safety of Ivermectin

Paul Marik MD, FCCM,FCCP

Treatment: Focus on IVERMECTIN

- William Campbell and Satoshi Omura awarded Nobel Prize in 2015 for their 1975 discovery of Ivermectin
- Ivermectin was first used in humans in 1987
- On World Health Organization's (WHO) list of essential medicines
- Over the past three decades, approximately 3.7 billion doses of ivermectin have been distributed
- Broad spectrum anti-parasitic and anti-viral activity
- Potent anti-inflammatory and immune modulating effects
- Safe and well tolerated in humans up to 2000 ug/kg. Minor side effects include pruritis, fever, rash, arthralgia

Nobel Lecture of Prof. Satoshi Omura



JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS
https://doi.org/10.1080/07391102.2021.1911857

Taylor & Francis
Taylor & Francis Group

Elucidation of the inhibitory activity of ivermectin with host nuclear importin α and several SARS-CoV-2 targets

Martiniano Bello

Laboratorio de Diseño y Desarrollo de Nuevos Fármacos e Innovación Biotecnológica de la Escuela Superior de Medicina, Instituto Politécnico Nacional, Ciudad de Mexico, Mexico

System	ΔE_{vdw}
Importin-α-IVM	−40.54 (5.3)
Nsp9-IVM	−41.03 (4.2)
RdRp-IVM	−37.89 (4.9)
RBD-spike-IVM	−36.59 (3.4)
$3CL^{pro}$-sub1-IVM	−57.74 (7.6)
$3CL^{pro}$-sub2-IVM	−50.75 (3.6)

IVERMECTIN FOR COVID-19

71 TRIALS, 675 SCIENTISTS, 50,180 PATIENTS

31 RANDOMIZED CONTROLLED TRIALS

83% IMPROVEMENT IN 16 PROPHYLAXIS TRIALS RR 0.17 [0.11-0.27]

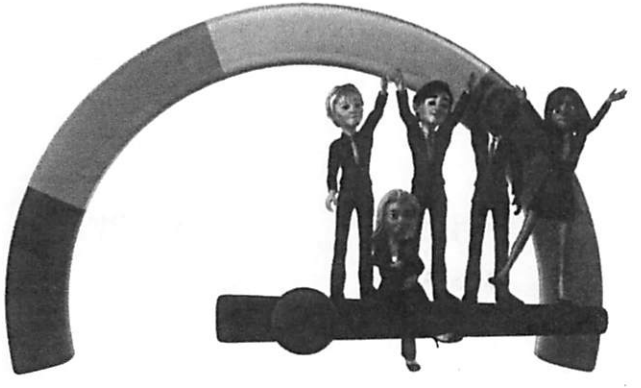
66% IMPROVEMENT IN 29 EARLY TREATMENT TRIALS RR 0.34 [0.24-0.47]

34% IMPROVEMENT IN 26 LATE TREATMENT TRIALS RR 0.66 [0.53-0.81]

52% IMPROVEMENT IN 32 MORTALITY RESULTS RR 0.48 [0.37-0.63]

57% IMPROVEMENT IN 31 RANDOMIZED CONTROLLED TRIALS RR 0.43 [0.31-0.61]

SUMMARY OF RESULTS REPORTED IN IVERMECTIN TRIALS FOR COVID-19. 12/24/21. IVMMETA.COM

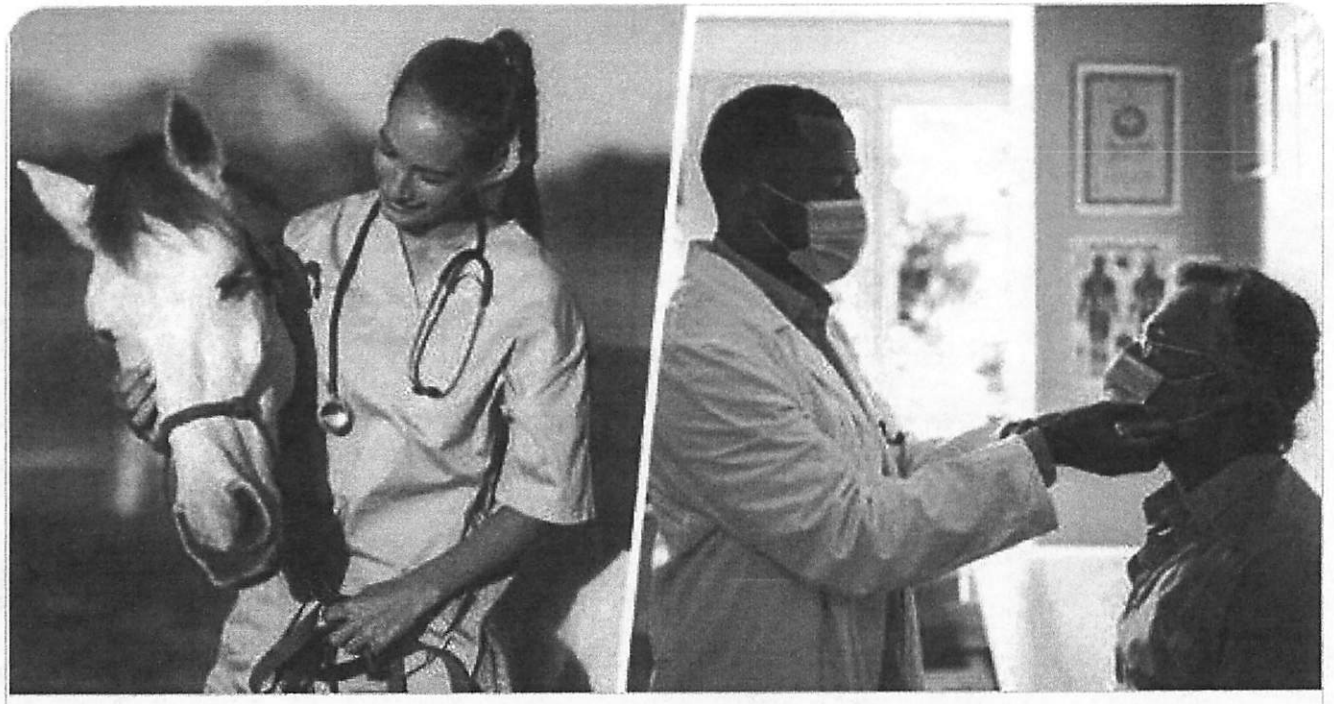


Tweets | Tweets & replies | Media | Likes

Pinned Tweet

U.S. FDA @US_FDA · 9h

You are not a horse. You are not a cow. Seriously, y'all. Stop it.



Why You Should Not Use Ivermectin to Treat or Prevent COVID-19

Using the Drug ivermectin to treat COVID-19 can be dangerous and even lethal. The FDA has not approved the drug for that purpose.

fda.gov

A Myth is Born: How CDC, FDA, and Media Wove a Web of Ivermectin Lies That Outlives The Truth

New Mexico officials admit they were wrong: Two people died from covid. NOT from ivermectin. Yet the CDC generated the nation's highest health alert and a thousand fake headlines on false cases.

Linda Bonvie and Mary Beth Pfeiffer
Dec 23, 2021

Mississippi health alert on reports to the state's poison control center: "At least 70% of the recent calls have been related to ingestion of livestock or animal formulations of ivermectin purchased at livestock supply centers."

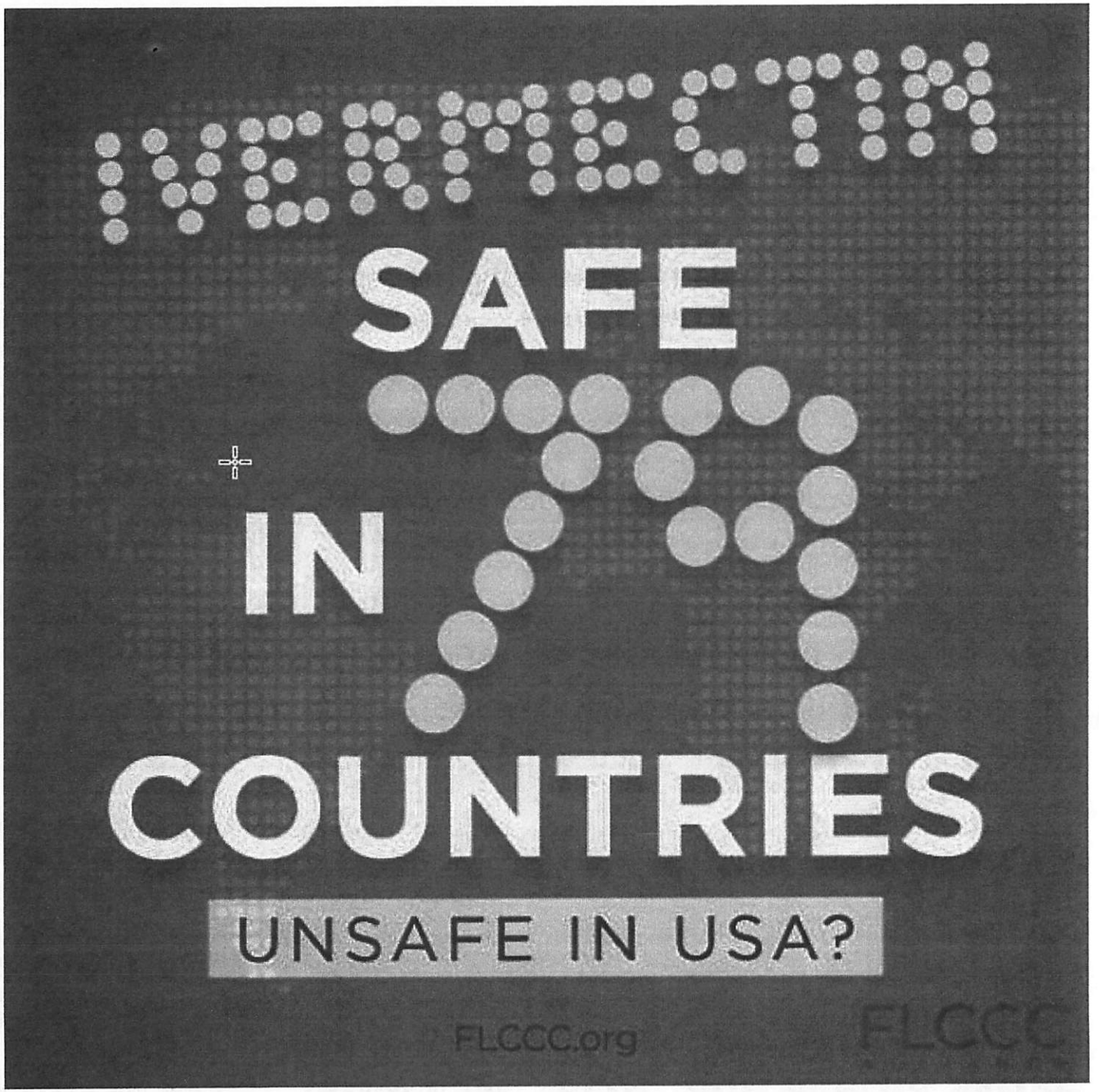
This is an official

CDC HEALTH ADVISORY

Distributed via the CDC Health Alert Network
August 26, 2021, 11:40 AM ET
CDCHAN-00449

Rapid Increase in Ivermectin Prescriptions and Reports of Severe Illness Associated with Use of Products Containing Ivermectin to Prevent or Treat COVID-19

Three cases of alleged ivermectin side effects, two involving animal formulations. All uneventful recovery.


IVERMECTIN
SAFE
IN
COUNTRIES
UNSAFE IN USA?
FLCCC.org
FLCCC

VigiAccess™

Uppsala Monitoring Centre

WHO Collaborating Centre for International Drug Monitoring

Medicine	Year started reporting	Deaths	Adverse events
Ivermectin	1992	20	5 840
Remdesivir	2020	579	7 798
Tocilizumab	2005	786	47 345
COVID-19 vaccines	2021	**14 774**	**2 878 362**
Tetanus vaccine	1968	32	14 697
Measles vaccine	1992	35	3 696
Acetaminophen (Tylenol)	1968	3 865	> 146 000

World Health Organization

FDA

MERCK

VigiAccess™

FAQ

ivermectin

Search

ivermectin contains the active ingredient(s): **Ivermectin**.
Result is presented for the active ingredient(s).
Total number of records retrieved: **5840**.

Pyrexia (142)
Asthenia (141)
Fatigue (113)
Application site erythema (97)
Condition aggravated (97)
Pain (84)
Swelling face (82)
Application site pain (72)
Application site pruritus (70)
Malaise (66)
No adverse event (59)
Chest pain (48)
Gait disturbance (45)
Oedema (42)
Oedema peripheral (38)
Drug ineffective for unapproved indication (37)
Application site rash (35)
Face oedema (35)
Chills (34)
Swelling (34)

Over 25 Years of Clinical Experience With Ivermectin: An Overview of Safety for an Increasing Number of Indications

- Cannot be used in collie dogs due to increased BB permeability to Ivermectin
- Negligible adverse reaction in humans
- Not a single death directly related to IVERMECTIN
- Robust safety profile, can be used in children and neonates
- Allergic reaction due to the death of microfilaria (itching, rash)
- Encephalopathy, rarely in patients with Loa Loa
- Not recommended in pregnancy or lactation
- Drug-drug interactions, caution with calcineurin inhibitors

A systematic review and an individual patient data meta-analysis of ivermectin use in children weighing less than fifteen kilograms

Findings

Overall, a total of 1.4% (15/1,088) of children experienced 18 adverse events all of which were mild and self-limiting. No serious adverse events were reported.

Conclusions

Existing limited data suggest that oral ivermectin in children weighing less than 15 kilograms is safe.

Jittamala P, et al. Plos Neg Trop Dis 2021;15:e000914-

FLCCC ALLIANCE

REMDESIVIR VS IVERMECTIN

COMPARISONS	REMDESIVIR	IVERMECTIN
COST	$ 3,000.00	PENNIES
LOWER DEATH RATE IN STUDIES	NO	YES 50% +
SIMPLE ACCESS AT HOME	NO	YES
CAUSES ORGAN DAMAGE	YES	NO
STUDIES NEEDED FOR APPROVAL	1 and approved	60 + and not considered
MAJOR CONFLICTS OF INTEREST	YES	NO
SUPPORT OF FDA AND FAUCI	YES	NO

- **Ivermectin** 1tab 6 mg

2 : 200 µg/kg/day

2 : 2 tab /day (BW ~ 60 kg)

2 : 2 Day

2 : 2 cents a tab
(WHO Pricing)


Thank you

Cureus

Open Access Original Article

DOI: 10.7759/cureus.21272

Ivermectin Prophylaxis Used for COVID-19: A Citywide, Prospective, Observational Study of 223,128 Subjects Using Propensity Score Matching

Review began 01/04/2022
Review ended 01/13/2022
Published 01/15/2022

Lucy Kerr [1], Flavio A. Cadegiani [2,3], Fernando Baldi [4], Raysildo B. Lobo [5], Washington Luiz O. Assagra [6], Fernando Carlos Proença [7], Pierre Kory [8], Jennifer A. Hibberd [9], Juan J. Chamie-Quintero [10]

1. Medicine, Instituto Kerr, São Paulo, BRA 2. Clinical Endocrinology, Corpometria Institute, Brasilia, BRA 3. Clinical Endocrinology, Applied Biology Inc, Irvine, USA 4. Animal Sciences, Universidade Estadual de São Paulo (UNESP), São Paulo, BRA 5. Genetics, Universidade de São Paulo, Ribeirão Preto, BRA 6. Genetics, Centro Técnico de Avaliação Genômica - C.T.A.G., Ribeirão Preto, BRA 7. Bioinformatics, Itajaí City Hall, Itajaí, BRA 8. Internal Medicine, Front Line COVID-19 Critical Care Alliance (FLCCC), Madison, USA 9. Dentistry, University of Toronto, Toronto, CAN 10. Data Analysis, Universidad EAFIT, Medellín, COL

Corresponding author: Flavio A. Cadegiani, flavio.cadegiani@unifesp.br

Abstract

Background: Ivermectin has demonstrated different mechanisms of action that potentially protect from both coronavirus disease 2019 (COVID-19) infection and COVID-19-related comorbidities. Based on the studies suggesting efficacy in prophylaxis combined with the known safety profile of ivermectin, a citywide prevention program using ivermectin for COVID-19 was implemented in Itajaí, a southern city in Brazil in the state of Santa Catarina. The objective of this study was to evaluate the impact of regular ivermectin use on subsequent COVID-19 infection and mortality rates.

Materials and methods: We analyzed data from a prospective, observational study of the citywide COVID-19 prevention with ivermectin program, which was conducted between July 2020 and December 2020 in Itajaí, Brazil. Study design, institutional review board approval, and analysis of registry data occurred after completion of the program. The program consisted of inviting the entire population of Itajaí to a medical visit to enroll in the program and to compile baseline, personal, demographic, and medical information. In the absence of contraindications, ivermectin was offered as an optional treatment to be taken for two consecutive days every 15 days at a dose of 0.2 mg/kg/day. In cases where a participating citizen of Itajaí became ill with COVID-19, they were recommended not to use ivermectin or any other medication in early outpatient treatment. Clinical outcomes of infection, hospitalization, and death were automatically reported and entered into the registry in real time. Study analysis consisted of comparing ivermectin users with non-users using cohorts of infected patients propensity score-matched by age, sex, and comorbidities. COVID-19 infection and mortality rates were analyzed with and without the use of propensity score matching (PSM).

Results: Of the 223,128 citizens of Itajaí considered for the study, a total of 159,561 subjects were included in the analysis: 113,845 (71.3%) regular ivermectin users and 45,716 (23.3%) non-users. Of these, 4,311 ivermectin users were infected, among which 4,197 were from the city of Itajaí (3.7% infection rate), and 3,034 non-users (from Itajaí) were infected (6.6% infection rate), with a 44% reduction in COVID-19 infection rate (risk ratio [RR], 0.56; 95% confidence interval (95% CI), 0.53-0.58; $p < 0.0001$). Using PSM, two cohorts of 3,034 subjects suffering from COVID-19 infection were compared. The regular use of ivermectin led to a 68% reduction in COVID-19 mortality (25 [0.8%] versus 79 [2.6%] among ivermectin non-users; RR, 0.32; 95% CI, 0.20-0.49; $p < 0.0001$). When adjusted for residual variables, reduction in mortality rate was 70% (RR, 0.30; 95% CI, 0.19-0.46; $p < 0.0001$). There was a 56% reduction in hospitalization rate (44 versus 99 hospitalizations among ivermectin users and non-users, respectively; RR, 0.44; 95% CI, 0.31-0.63; $p < 0.0001$). After adjustment for residual variables, reduction in hospitalization rate was 67% (RR, 0.33; 95% CI, 023-0.66; $p < 0.0001$).

Conclusion: In this large PSM study, regular use of ivermectin as a prophylactic agent was associated with significantly reduced COVID-19 infection, hospitalization, and mortality rates.

Categories: Infectious Disease
Keywords: coronavirus, prevention, prophylaxis, ivermectin, sars-cov-2, covid-19

Introduction

Ivermectin has been demonstrated to have not only extensive anti-parasitic actions [1,2], but also anti-viral, anti-bacterial, and anti-protozoan properties. Ivermectin has been long proposed for use as a repurposed antiviral agent [3-6]. Indeed, antiviral effects of ivermectin have been reported against both RNA and DNA

types of viruses, including HIV-1, yellow fever, Japanese encephalitis, tick-borne encephalitis, West Nile, Zika, dengue fever, chikungunya, Venezuelan equine encephalitis, and the pseudorabies virus [3,5,7,8], as well as functioning in regulation of proteins involved in antiviral responses [8].

Additional actions of ivermectin described include agonism activity to the liver X receptor (LXR) and farnesoid X receptor (FXR), with multiple potential metabolic benefits [9,10]; neuronal regeneration [11,12], prevention of muscle hypoxia [13], and actions on specific sites, including interferon (INF) [14], nuclear factor-κB (NF-κB), lipopolysaccharide (LPS) [15], and Janus kinase/signal transducer and activator of transcription (JAK-STAT) and PAI-1 pathway [16,17]; generation of P21 activated kinase 1 (PAK-1) [18,19]; reduction of interleukin-6 (IL-6) levels [15]; allosteric modulation of P2X4 receptor [20]; inhibition of high mobility group box 1 (HMGB1) [21,22]; and suppression of mucus hypersecretion, diminished recruitment of immune cells, and production of cytokines in the lung [23]. Ivermectin is also described to induce T helper 1 cell (Th1)-type immune response against protozoan infections [24], and anti-coagulant action through binding to the S protein of some viruses [25].

The hypothesis that ivermectin could be protective against coronavirus disease 2019 (COVID-19) is substantiated by its multi-pathway, anti-inflammatory effects [15,26], and multi-antiviral mechanisms. COVID-19 pathogenesis is largely understood as an inflammation-mediated hemagglutinating infection disrupting pulmonary, vascular, and endothelial systems, leading to a multi-systemic disease. In vitro and in silico, ivermectin has demonstrated anti-severe acute respiratory syndrome coronavirus 2 activity through more than 20 direct and indirect mechanisms [2,27,28].

Ivermectin has demonstrated preliminary protective effects against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in terms of reducing times to clinical recovery and rates of disease progression and mortality [2,29,30]. However, more robust studies with larger sample sizes are still recommended to confirm the possible beneficial effects of ivermectin in COVID-19.

Since the onset of the COVID-19 pandemic, the use of inexpensive options based on a consistently beneficial signal of efficacy, a well-established safety profile, and favorable cost-effectiveness, ivermectin is a highly attractive intervention for the patient-centered medicine practiced by frontline clinicians, with use aligning strongly with the bioethical principles for medical practice outlined in Article 36 of the Declaration of Helsinki [31].

However, despite this favorable risk/benefit profile and absence of therapeutic alternatives, ivermectin is yet to be approved for prophylaxis and treatment of COVID-19 by agencies throughout the world, including FDA (USA), European Medicines Agency (EMA; Europe), and ANVISA (Agência Nacional de Vigilância Sanitária - Brazilian Health Regulatory Agency; Brazil).

The ability to prescribe ivermectin or any other off-label drug for COVID-19 has long been at the discretion of frontline physicians once all risks, uncertainties, potential benefits, and patients' rights are exposed, and informed consent has been obtained. Of particular note, in Brazil, this follows the medical autonomy to determine the best therapeutic strategies for individuals, as per the Medical Code of Ethics of the Brazilian Board of Medical Doctors, the Federal Council of Medicine - Conselho Federal de Medicina (CFM), that determines the obligations and rights of medical doctors in Brazil [32].

Since vaccines for COVID-19 were not available in Brazil until 2021, and because of the lack of prophylactic alternatives in the absence of vaccines, Itajaí, a city in the southern Brazilian state of Santa Catarina, initiated a population-wide government program for COVID-19 prophylaxis. The medical-focused decision parameters established are based on the distribution of ivermectin to whole populations in different countries. To ensure the safety of the population, a well-controlled computer program was developed to compile and maintain all relevant demographic and clinical data (detailed in the Materials & Methods section). The use of ivermectin was optional and based on patients' preferences, given its benefits as a preventative agent was unproven.

This study's objective is to assess the impact on important clinical outcomes when ivermectin is used as prophylaxis for COVID-19. The prophylaxis program occurred in addition to the standard non-pharmacological strategies of masking and social distancing, as part of a citywide program conducted in outpatient settings.

Materials And Methods

Study population

This was a prospective, observational study. Although study design, institutional review board (IRB) approval, and data analysis occurred after completion of the voluntary prophylaxis program, all data were collected prospectively in real time with mandated reporting to the registry of all events as they occurred during the citywide governmental COVID-19 prevention with ivermectin program, from July 2020 to December 2020, developed in the city of Itajaí, in the state of Santa Catarina, Brazil. Demographic and clinical data were reported from medical records of patients followed in a large outpatient setting (a

provisional outpatient clinic set in the Convention Center of Itajaí) and several secondary outpatient settings, as part of the universal health system (Sistema Único de Saúde [SUS]).

The objective was to determine the number of patients affected by COVID-19 (positivity rate of reverse transcription-polymerase chain reaction [RT-PCR] for SARS-CoV-2), risk of death due to COVID-19 (whether infected or not), and COVID-19 mortality rate (risk of death from COVID-19) of those who used and did not use ivermectin prophylactically for COVID-19. These data were stratified by age, sex, presence of comorbidities, and correlated demographic characteristics.

The present retrospective analysis of the prospectively collected data was approved by the National Research Ethics Council (CONEP) under the number 4.821.082 with the project number CAAE: 47124221.2.0000.5485. Although study design, IRB approval, and data analysis occurred after completion of the voluntary prophylaxis program, all data were collected prospectively in real-time with mandated reporting to the registry of all events as they occurred during the citywide governmental COVID-19 prevention with ivermectin program, from July 7, 2020, to December 2, 2020, developed in the city of Itajaí, in the state of Santa Catarina, Brazil.

Study procedures and data collection

Optional, voluntary prophylactic use of ivermectin was offered to patients during regular medical visits between July 7, 2020, and December 2, 2020, in 35 different sites, including 34 local SUS health centers and a large temporary patient setting 24/7. Doctors working in these sites were free to prescribe ivermectin prophylactically. Subjects that did not use ivermectin either refused or their primary care physicians opted not to offer ivermectin.

To avoid underreported data, strict procedure sequencing was followed: (1) registration and recording of patient data, documented by assistants; (2) weighing subjects (subject's weight was essential to calculate the appropriate dose of ivermectin); (3) brief medical evaluation of past medical history, comorbidities, use of medications, and contraindications to drugs; and (4) medical prescription with prophylactic doses of ivermectin (within recommended usual, safe doses of ivermectin), according to medical judgment and following a subject's informed consent related to potential benefits, risks, and side effects. All details of this citywide program and campaign had been previously agreed upon between the city local department of the National Healthcare System (SUS), city mayor, and local public prosecutors.

Regarding drug interactions with ivermectin, the use of warfarin was a contraindication for prophylaxis with ivermectin due to drug interactions. Subjects under chronic use of glucocorticoids, protease inhibitors, and anti-epileptics were recommended to schedule regular medical visits every six to eight weeks. Subjects were recommended to inform medical doctors about the use of ivermectin, in case one or more of the following medications were prescribed: warfarin, azithromycin, dexamethasone, prednisone, or prednisolone (hydrocortisone or cortisone are not commercially available in regular pharmacies in Brazil).

The following variables were analyzed: (1) age, (2) sex, (3) previous diseases (myocardial infarction [MI] and stroke), (4) pre-existing comorbidities (type 2 diabetes [T2D], asthma, chronic obstructive pulmonary disease [COPD], hypertension, dyslipidemia, cardiovascular diseases [CVD], cancer [any type], and other pulmonary diseases), and (5) smoking. Variables were adjusted as confounding factors and used as variables for balancing and matching groups for propensity score matching (PSM).

Patients who presented signs or the diagnosis of COVID-19 before July 7, 2020, were excluded from the sample. Other exclusion criteria were contraindications to ivermectin and subjects below 18 years of age. The dose and frequency of ivermectin treatment was 0.2 mg/kg/day; i.e., giving one 6 mg tablet for every 30 kg for two consecutive days every 15 days.

During the study, subjects who were diagnosed with COVID-19 underwent a specific medical visit to assess COVID-19 clinical manifestations and severity. All subjects were recommended not to use ivermectin, nitazoxanide, hydroxychloroquine, spironolactone, or any other drug claimed to be effective against COVID-19. The city did not provide or support any specific pharmacological outpatient treatment for subjects infected with COVID-19.

They were questioned for the presence of common COVID-19 symptoms. These included chills, high-grade fever, cough, myalgia, fatigue, anosmia, ageusia, sore throat, headache, nasal congestion, sneeze, runny nose, hemoptysis, nausea, vomiting, abdominal pain, diarrhea, cutaneous rash, arthralgia, chest pain, eye pain and pinkeye, and presence of alert signs, including shortness of breath, signs of hypoxia, signs of coagulation abnormalities, and an altered level of consciousness. Systolic and diastolic blood pressure, heart rate, respiratory rate, oxygen saturation, and axillary temperature were measured. The same signs and symptoms and vital signs were collected at each following medical visit during COVID-19. Individual data were compiled and reviewed by the researchers.

Registry data of all patient records from the city of Itajaí between July 7, 2020, and December 2, 2020,

including those who used ivermectin and did not use ivermectin were reviewed. All subjects who tested positive for COVID-19 in the city of Itajaí during the study were considered for this analysis. Of the infected subjects, two groups were considered: subjects who used ivermectin prophylactically (treated group) and subjects who did not use ivermectin prophylactically (untreated group). Missing data from patients were clarified with patients or relatives directly, via phone or in person, by the investigators. Since this is a citywide program, all recorded data must have matched the exact number of COVID-19 cases and deaths of the city. This strict interval avoids differences in terms of periods of exposure.

Due to the uncertainty of reinfection with COVID-19, subjects with a history of previous COVID-19 did not participate in the program although they were still permitted to use ivermectin prophylactically. Limiting parameters of the government system allowed the recording of a first episode of COVID-19 infection only. Subjects below 18 years old and subjects with a diagnosis of COVID-19 before July 7, 2020, were excluded from all datasets and analyses.

From the registry of the city population (223,128 inhabitants), subjects below 18 years old (61,583 subjects) were removed. Of the 161,545 subjects above 18 years old from the city of Itajaí, we removed the 1,984 COVID-19 cases that occurred before July 7, 2020, and 159,561 subjects remained. Subjects above 18 years old were considered those who were born before June 30, 2002.

A total of 147,223 subjects participated in the program of ivermectin prophylaxis used for COVID-19. Of these, 24,304 subjects were below 18 years old. Of the 122,919 ivermectin users above 18 years old, 8,346 were from other cities, and 728 had COVID-19 before July 7, 2020, although they used ivermectin afterward. In total, 113,845 subjects that participated in the program remained in the dataset. The 45,716 non-participants, remaining subjects among the 159,561 subjects, were considered as the ivermectin non-users.

Finally, citywide COVID-19 hospitalization and mortality rates of Itajaí were compared between the period before the program (before July 7, 2020) and during the program (between July 7, 2020, and December 2, 2020) aiming to evaluate whether a program of prophylaxis with ivermectin for COVID-19 would cause a positive impact in the overall numbers of the city, despite only partial adoption. Chances of dying of COVID-19 in the overall population, according to use or non-use of ivermectin (irrespective of COVID-19 infection) were only calculated prior to matching. Conversely, the mortality rate among those who were infected by the SARS-CoV-2 was calculated for both pre and post-matched cohorts.

Hospitalization and mortality rates before matching groups, the mortality rate in subpopulations before and after PSM, and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist are presented in the Appendix.

Statistical analysis

The full underlying data for the present analysis were analyzed by two independent statisticians, and discrepancies were evaluated by a third statistics expert. In this outpatient study of those who tested positive for SARS-CoV-2, the mortality rate was evaluated according to each parameter that was adjusted against other variables (for multivariate regression analysis) and used for balancing and matching groups, including age intervals, sex, history of smoking, prophylactic ivermectin use, T2D, asthma, COPD, cardiovascular diseases and other pulmonary diseases, hypertension, current cancer (any type), and history of stroke and/or MI.

Before matching, a generalized linear mixed model was employed, assuming the binomial distribution for the residues and including the fixed classificatory effects of each of these parameters. Age intervals were adjusted for the evaluation of ivermectin prophylactic use as an independent predictor of death from COVID-19. Unadjusted and multivariate Poisson-adjusted probabilities to survive from COVID-19 (p-value), according to each parameter, were provided.

PSM was performed for mortality risk between ivermectin and non-ivermectin users. COVID-19 infection rate and risk of dying were also calculated for variables. After PSM, a second adjustment ("double adjustment") with multivariate linear regression was performed for residual variables [33,34].

There were no missing data since the registry system design mandated that all data variables be filled to be formally included in the registry. Only erroneously entered (illogical) data were found. In such instances, a medical record review was performed to obtain accurate data. The program used for the analysis was the Statistical Analysis Software (SAS/STAT) (SAS Institute Inc., Cary, NC). For transparency reasons, two datasets of the 7,345 COVID-19 cases and the 113,845 participating subjects considered for the present analysis will be made public upon peer-reviewed publication.

Results

A detailed description of the data considered for the present analysis is illustrated in Figure *1*. Of the 220,517 citizens of Itajaí without COVID-19 until July 7, 2020, 159,561 were above 18 years old. Of the

159,561 citizens above 18 years old without COVID-19 until July 7, 2020, 113,845 (71.3% of the population above 18 years old) received ivermectin before being infected by COVID-19. A total of 45,716 citizens (28.7%) did not receive or did not want to receive ivermectin during the program, including as a prophylactic or as a treatment after having COVID-19.

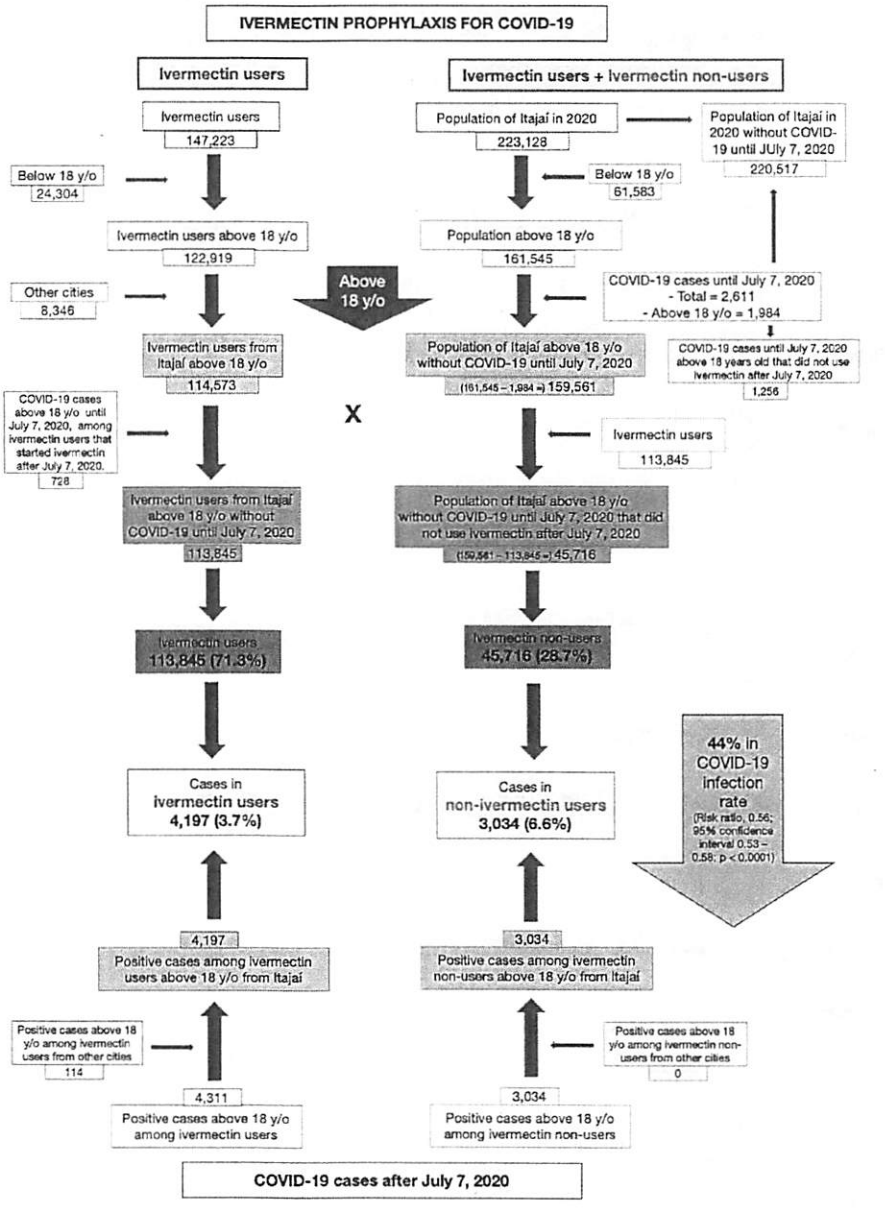


FIGURE 1: Underlying data for the study on ivermectin prophylaxis used for COVID-19.

Of the 113,845 prophylaxed subjects from the city of Itajaí, 4,197 had a positive RT-PCR SARS-CoV-2 (3.7% infection rate), while 3,034 of the 37,027 untreated subjects had positive RT-PCR SARS-CoV-2 (6.6% infection rate), a 44% reduction in COVID-19 infection rate (risk ratio [RR], 0.56; 95% confidence interval (95% CI), 0.53-0.58; $p < 0.0001$). An addition of 114 subjects who used ivermectin and were infected were originally from other cities but were registered as part of the program, in a total of 4,311 positive cases among ivermectin users. For the present analysis, the 4,311 positive cases among subjects that used ivermectin and 3,034 cases among subjects that did not use ivermectin were considered. After PSM, two cohorts of 3,034 subjects were created.

Baseline characteristics of the 7,345 subjects included prior to PSM and the baseline characteristics of the

6,068 subjects in the matched groups are shown in Table *1*. Prior to PSM, ivermectin users had a higher percentage of subjects over 50 years old ($p < 0.0001$), higher prevalence of T2D ($p = 0.0004$), hypertension ($p < 0.0001$), and CVD ($p = 0.03$), and a higher percentage of Caucasians ($p = 0.004$), than non-users. After PSM, all baseline parameters were similar between groups. Figure *2* summarizes the main findings of this study.

	Pre-matching				Propensity score-matched		
	Overall (n = 7,345)	Ivermectin users (n = 4,311)	Non-ivermectin users (n = 3,034)	p-value	Overall (n = 6,068)	Ivermectin users (n = 3,034)	Non-ivermectin users (n = 3,034)
Age							
Mean ± SD	42.0 ± 14.7	43.5 ± 14.9	39.8 ± 14.2	<0.0001	39.7 ± 14.0	3967 ± 13.8	39.8 ± 14.2
<30 years old	1,730 (23.6%)	886 (20.5%)	844 (27.8%)		1,691 (27.9%)	844 (27.9%)	847 (27.8%)
30-50 years old	3,703 (50.4%)	2,121 (49.2%)	1,582 (52.2%)		3,155 (52.0%)	1,573 (51.9%)	1,582 (52.1%)
>50 years old	1,912 (26.0%)	1,304 (30.3%)	608 (20.0%)		1,222 (20,1%)	614 (20.2%)	608 (20.1%)
Sex				0.31			
Female	3,983 (54.2%)	2,359 (54.7%)	1,624 (53.5%)		3,231 (53.2%)	1,607 (53.0%)	1,624 (53.5%)
Male	3,362 (45.8%)	1,952 (45.3%)	1,410 (46.5%)		2,837 (46.8%)	1,427 (47.0%)	1,410 (46.5%)
Race							
Caucasians	5,437 (74.0%)	3,245 (75.3%)	2,192 (72.2%)	0.004	4,398 (72.5%)	2,206 (72.7%)	2,192 (72.3%)
Afro-Brazilians	209 (2.8%)	109 (2.5%)	100 (3.3%)	0.052	193 (3.2%)	93 (3.1%)	100 (3.3%)
Mixed	1,583 (22.6%)	901 (20.9%)	682 (22.5%)	0.10	1,364 (22.5%)	93 (3.1%)	100 (3.3%)
Asian-Brazilians	116 (1.6%)	56 (1.3%)	60 (2.0%)	0.023	113 (1.9%)	53 (1.8%)	60 (2.0%)
Type 2 diabetes				0.0004			
Yes	214 (2.9%)	151 (3.5%)	63 (2.1%)		141 (2.3%)	78 (2.6%)	63 (2.1%)
No	7,131 (97.1%)	4,160 (96.5%)	2,971 (97.9%)		5,927 (97.7%)	2,956 (97.4%)	2,971 (97.9%)
Asthma				0.067			
Yes	26 (0.3%)	20 (0.5%)	6 (0.2%)		21 (0.3%)	15 (0.5%)	6 (0.2%)
No	7,319 (99.7%)	4,291 (99.5%)	3,028 (99.8%)		6,047 (99.7%)	3,019 (99.5%)	3,028 (99.8%)
COPD				0.72			
Yes	13 (0.2%)	7 (0.2%)	6 (0.2%)		12 (0.2%)	6 (0.2%)	6 (0.2%)
No	7,332 (99.8%)	4,304 (99.8%)	3,028 (99.8%)		6,056 (99.8%)	3,028 (99.8%)	3,028 (99.8%)
Hypertension				<0.0001			
Yes	528 (7.2%)	362 (8.4%)	166 (5.5%)		343 (5.6%)	177 (5.8%)	166 (5.5%)
	6,817				5,725		

No	(92.8%)	3,949 (91.6%)	2,868 (94.5%)		(94.4%)	2,857 (94.2%)	2,868 (94.5%)
CVD				0.03			
Yes	56 (0.8%)	41 (1.0%)	15 (0.5%)		32 (0.5%)	17 (0.6%)	15 (0.5%)
No	7,289 (99.2%)	4,270 (99.0%)	3,019 (99.5%)		6,036 (99.5%)	3,017 (99.4%)	3,019 (99.5%)
Other pulmonary diseases				0.53			
Yes	15 (0.2%)	10 (0.2%)	5 (0.2%)		9 (0.1%)	4 (0.1%)	5 (0.1%)
No	7,330 (99.8%)	4,301 (99.8%)	3,029 (99.8%)		6,059 (99.9%)	3,030 (99.9%)	3,029 (99.9%)
Cancer (any type)				0.66			
Yes	32 (0.4%)	20 (0.5%)	12 (0.4%)		22 (0.4%)	10 (0.3%)	12 (0.4%)
No	7,313 (99.6%)	4,291 (99.5%)	3,023 (99.6%)		6,046 (99.6%)	3,024 (99.7%)	3,022 (99.6%)
Current smoking				0.76			
Yes	110 (1.5%)	63 (1.5%)	47 (1.5%)		95 (1.6%)	48 (1.6%)	47 (1.6%)
No	7,235 (98.5%)	4,248 (98.5%)	2,987 (98.5%)		5,973 (98.4%)	2,986 (98.4%)	2,987 (98.4%)
History of MI				0.26			
Yes	15 (0.2%)	11 (0.3%)	4 (0.1%)		8 (0.1%)	4 (0.1%)	4 (0.1%)
No	7,330 (99.8%)	4,300 (99.7%)	3,030 (99.9%)		6,060 (99.9%)	3,030 (99.9%)	3,030 (99.9%)
History of stroke				0.56			
Yes	21 (0.3%)	11 (0.3%)	10 (0.3%)		21 (0.4%)	11 (0.4%)	10 (0.3%)
No	7,324 (99.7%)	4,300 (99.7%)	3,024 (99.7%)		6,047 (99.6%)	3,023 (99.6%)	3,024 (99.7%)

TABLE 1: Baseline characteristics of subjects enrolled in the study before matching and after propensity score matching.

COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MI = myocardial infarction; SD = standard deviation.

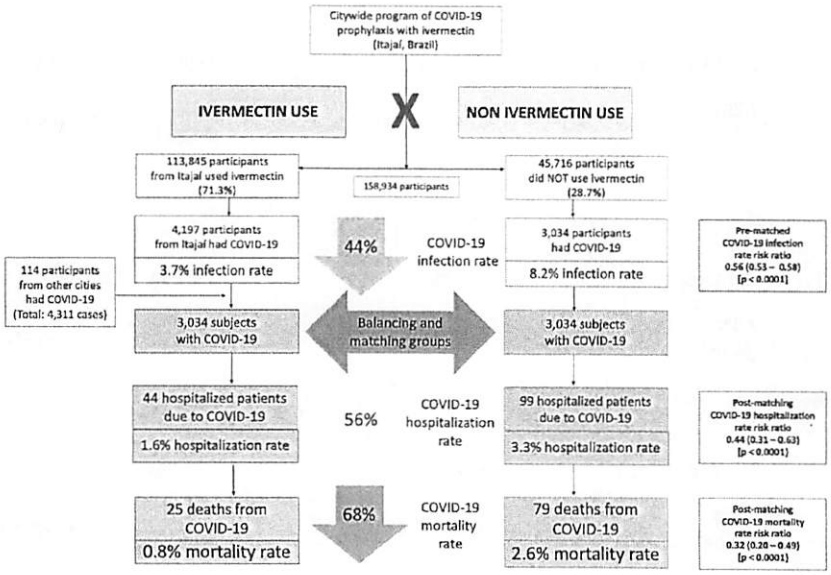


FIGURE 2: Summary of the findings.

Hospitalization and mortality rates in ivermectin users and non-users in propensity score-matched analysis

As described in Table 2, after employing PSM, of the 6,068 subjects (3,034 in each group), there were 44 hospitalizations among ivermectin users (1.6% hospitalization rate) and 99 hospitalizations (3.3% hospitalization rate) among ivermectin non-users, a 56% reduction in hospitalization rate (RR, 0.44; 95% CI, 0.31-0.63). When adjustment for variables was employed, the reduction in hospitalization rate was 67% (RR, 0.33; 95% CI, 023-0.66; p < 0.0001).

		Overall	IVM users	Non-IVM users	PSM mortality risk ratio (95% CI) and p-value [p]	Adjusted PSM mortality risk ratio (95% CI) and p-value [p]
COVID-19 infection	Infected population (n)	6,068	3,034	3,034	-	-
COVID-19 hospitalization	Hospitalization due to COVID-19	143	44	99	-	-
	Hospitalization rate* (in case of COVID-19) (%)	2.3%	1.6%	3.3%	0.44 (0.31-0.63) [<0.0001]	0.33 (0.23-0.46) [<0.0001]
COVID-19 death	COVID-19 deaths (n)**	104	25	79	-	-
	Mortality rate (among infected subjects) (%)	1.7%	0.8%	2.6%	0.32 (0.20-0.49) [<0.0001]	0.30 (0.19-0.46) [<0.0001]

TABLE 2: Propensity score-matched hospitalization and mortality rate among ivermectin users and non-users.

IVM = ivermectin; PSM = propensity score matching. * Only subjects hospitalized in public hospitals. ** All deaths, including from public and private hospitals, and in-home.

There were 25 deaths among ivermectin users (0.8% mortality rate) and 79 deaths among non-ivermectin users (2.6% mortality rate), a 68% reduction in mortality rate (RR, 0.32; 95% CI, 0.20-0.49). When PSM was

adjusted, reduction in mortality rate was 70% (RR, 0.30; 95% CI, 0.19-0.46; p < 0.0001).

Determinants of COVID-19 mortality through propensity score-matched analysis

Table *3* describes the resulting risk factors for COVID-19 death amongst the overall population through PSM analysis. Risk factors for mortality in COVID-19 included aging (p < 0.0001), male sex (p = 0.015), T2D (p < 0.0001), hypertension (p < 0.0001), asthma (p = 0.011), COPD (p < 0.0001), other pulmonary diseases (p = 0.048), history of MI (p = 0.034), and history of stroke (p < 0.0001). To detect independent risk factors, post-PSM adjustment for variables showed that ivermectin (p < 0.0001; 70% reduction in mortality risk) and female sex (p = 0.022; 38% reduction in mortality risk) were protectors, whereas T2D (p = 0.041; 79% increase in mortality risk), hypertension (p = 0.008; 98% increase in mortality risk), and, marginally, other pulmonary diseases (p = 0.061; 468% increase in mortality risk) and history of stroke (p = 0.054; 97% increase in mortality risk) were identified as independent risk factors.

	Propensity score-matched groups			
Variable	Overall (n = 6,068)	Death (%)	Unadjusted COVID-19 mortality risk ratio and p-value [p]	Multivariate adjusted COVID-19 mortality risk ratio and p-value [p]
Ivermectin use - n (%)			0.32 (0.20-0.49) [<0.0001]	0.30 (0.19-0.46) [<0.0001]
Yes	3,034	25 (0.8%)		
No	3,034	79 (2.6%)		
Age - n (%)			[<0.0001]	[<0.0001]
<30 years old	1,691	1 (0.1%)		
30-50 years old	3,155	12 (0.4%)		
>50 years old	1,222	91 (7.4%)		
Sex - n (%)			0.62 (0.42-0.91) [0.015]	0.64 (0.44-0.93) [0.022]
Female	3,231	43 (1.3%)		
Male	2,837	61 (2.2%)		
Race - n (%)			[0.24]	[0.44]
Caucasians	4,398	79 (1.8%)		
Afro-Brazilians	193	6 (3.1%)		
Mixed	1.364	17 (1.3%)		
Asian-Brazilians	113	2 (1.9%)		
Type 2 diabetes - n (%)			10.0 (6.32-15.8) [<0.0001]	1.79 (1.03-3.12) [0.041]
Yes	141	20 (14.2%)		
No	5,927	84 (1.4%)		
Hypertension - n (%)			8.83 (5.99-13.0) [< 0.0001]	1.98 (1.19-3.30) [0.008]
		36		

Yes	343	(10.5%)		
No	5,725	68 (1.2%)		
Asthma - n (%)			5.64 (1.49-21.4) [0.011]	1.74 (0.52-5.81) [0.36]
Yes	21	2 (9.5%)		
No	6,047	102 (1.7%)		
COPD - n (%)			15.0 (5.52-40.7) [<0.0001]	1.71 (0.68-4.31) [0.25]
Yes	12	3 (25.0%)		
No	6,056	101 (1.7%)		
Cardiovascular diseases - n (%)			7.54 (2.96-19.3) [<0.0001]	1.22 (0.44-3.37) [0.70]
Yes	32	4 (12.5%)		
No	6,036	100 (1.7%)		
Other pulmonary diseases - n (%)			6.54 (1.02-41.9) [0.048]	5.68 (0.92-35.0) [0.061]
Yes	9	1 (11.1%)		
No	6,059	103 (1.7%)		
Cancer (any type) - n (%)			2.67 (0.39-18.3) [0.32]	1.97 (0.30-12.9) [0.48]
Yes	22	1 (4.6%)		
No	6,046	103 (1.7%)		
Current smoking - n (%)			1.23 (0.31-4.92) [0.77]	0.36 (0.08-1.70) [0.20]
Yes	95	2 (2.1%)		
No	5,973	102 (1.7%)		
History of MI - n (%)			7.35 (1.16-46.5) [0.034]	1.91 (0.17-21.6) [0.60]
Yes	8	1 (12.5%)		
No	6,060	103 (1.7%)		
History of stroke - n (%)			17.6 (8.72-35.7) [< 0.0001]	1.97 (0.99-3.92) [0.054]
Yes	21	6 (28.6%)		
No	6,047	98 (1.6%)		

TABLE 3: Propensity score-matched COVID-19 mortality rate according to each characteristic in the overall population, ivermectin users, and non-users.

COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; MI = myocardial infarction.

In a comparison of citywide COVID-19 hospitalization rates prior to and during the program, COVID-19 mortality decreased from 6.8% before the program with prophylactic use of ivermectin, to 1.8% after its beginning (RR, 0.27; 95% CI, 0.21-0.33; p < 0.0001), and in COVID-19 mortality rate, from 3.4% to 1.4% (RR, 0.41; 95% CI, 0.31-0.55; p < 0.0001) (Table *4*).

	Overall	Until July 30th	After July 30th	Relative risk ratio (95% CI)	p-value
Infected COVID-19 population (n)	9,956	2,663	7,293	-	-
Infected non-hospitalized COVID-19 population (n)	9,641	2,481	7,160	-	-
Hospitalized COVID-19 population (n)	315	182	133	-	-
COVID-19 hospitalization rate COVID-19 (%)	3.2%	6.8%	1.8%	0.27 (0.21-0.33)	<0.0001
Overall number of COVID-19 deaths	192	90	102	-	-
Overall mortality rate (%)	1.9%	3.4%	1.4%	0.41 (0.31-0.55)	<0.0001

TABLE 4: Hospitalization and mortality rates registered in the city of Itajaí, Brazil, before versus after the beginning of the citywide program with ivermectin use as prophylaxis for COVID-19, independent of the ivermectin use status.

Discussion

This prospective, citywide COVID-19 ivermectin prophylaxis program resulted in significant reductions in COVID-19 infections, hospitalizations, and deaths. The ivermectin non-users were two times more likely to die of COVID-19 than ivermectin users in the overall population analysis. Since groups were compared for the exposure during the same period, in a parallel manner, changes in transmission rates would affect ivermectin users and non-users equally.

The city of Itajaí, in the state of Santa Catarina, Brazil, started a citywide program of prophylaxis with ivermectin in July 2020 as part of several initiatives to reduce the burden of COVID-19. The use of ivermectin was based on the existing literature at that time and on the virtual absence of risks. The National Health System (SUS) functions as full healthcare support to the entire population allowed the city to establish a non-restricted population program. This program included a support structure consisting of a large outpatient clinic located at the Convention Center of Itajaí. This outpatient clinic became the main locale of assistance for COVID-19 patients, supported by multiple public facilities where general practitioners regularly saw patients.

The use of ivermectin was optional unless contraindicated and given upon medical discretion. A structured medical-based program with a medical visit and evaluation of basic demographic characteristics and comorbidities offered ivermectin as optional prophylaxis to those who agreed to participate in this preventive treatment program. Health status was assessed and data were entered prospectively throughout the period of the program, in a fully digitized system provided by the National Health System (SUS). Since the system existed prior to the pandemic, a significant number of the population were already registered with their health information, including past and current diseases, use of medications, and other characteristics. The adaptations made to the SUS for the pandemic preparedness, prior to the initiation of this ivermectin outpatient program, allowed a structured, well-organized collection of the data that monitored any missing values, reinforcing the reliability of the results.

An important conservative bias was present. Major risk factors for severe COVID-19 and mortality due to COVID-19, including aging, diabetes, and hypertension, were more present among ivermectin users, which may have underestimated the benefits of ivermectin as it was demonstrated to be particularly effective in subjects above 49 years old in terms of reduction of absolute risk, which corresponds to the group at the highest risk for COVID-19. This allows the understanding that prophylactic use of ivermectin can be particularly impactful in older subjects. In addition, ivermectin seemed to reduce the exceeding risk of hypertension, T2D, and other diseases.

In accordance with the literature, subjects with higher age, diabetes, and males were less likely to survive ($p < 0.05$ for all), and only aging remained as an independent risk factor after PSM ($p < 0.0001$). However, prophylactic ivermectin use appears to mitigate the additional risk of COVID-19 death due to T2D, hypertension, and cardiovascular diseases.

The narrative that using preventive and early treatment therapies will have people relax their caution of remaining socially and physically distanced to allow more COVID-19-related infections is not supported here. These study data demonstrate that the use of preventive ivermectin significantly lowers the infection rate and that benefits outweigh the speculated increased risk of changes in social behaviors. Hence, we can speculate that the prophylactic use of ivermectin could play an important role in the reduction of the pandemic burden.

Even after adjustments to measure the most relevant variables that could influence COVID-19-related outcomes, including age, sex, comorbidities, and habits, aiming to avoid overestimation of the effects of ivermectin and to resemble a randomized clinical trial, prophylactic ivermectin proved to be protective for the overall population, with a reduction of 68% in mortality rate and $p < 0.0001$ after employment of PSM.

The protection provided by ivermectin when used prophylactically for COVID-19 may have reflected in the reduction in COVID-19 hospitalization and mortality rates observed at a population level. Compared to before the beginning of the program, COVID-19 hospitalization and mortality rates were reduced by 73% and 59%, respectively ($p < 0.0001$ for both). These reductions were obtained when the overall population and the number of COVID-19 cases, hospitalizations, and deaths in the city of Itajaí were considered, irrespective of the percentage of patients using ivermectin prophylactically. There were no changes in SARS-CoV-2 variants, infectivity, and pathogenicity before and during the program.

When compared to all other major cities in the state of Santa Catarina, differences in COVID-19 mortality rate before July 7, 2020, and between July 7, 2020, and December 21, 2020, Itajaí was ranked number one [35]. These results indicate that medical-based optional prescription and citywide covered ivermectin can have a positive impact on the healthcare system. However, the present results do not provide sufficient support for the hypothesis that ivermectin could be an alternative to COVID-19 vaccines.

Due to a large number of participants, this citywide program was unable to supervise whether ivermectin users were using ivermectin regularly, although the accumulated number of ivermectin tablets was strictly controlled. This occurred to be a potential conservative bias since the effects of ivermectin on prophylaxis could be underestimated due to adherence to the recommended frequency of ivermectin use.

While ivermectin is a multi-target drug [36], its maximum benefits occur when it is present at a minimum concentration in a wide range of sites to inhibit multiple metabolic and inflammatory pathways. However, although the dose of ivermectin employed in the program was smaller than the minimum to reach the concentration required to act in these multiple sites, the reduction in infection, mortality, and death rates in the infected group that used ivermectin prophylactically was surprisingly lower. Long-term or accumulated ivermectin could also play a critical role in its long-term protection against COVID-19.

Limitations

Being a prospective observational study that allowed subjects to self-select between treatment vs. non-treatment instead of relying on randomization, important confounders may have been differentially present, which could otherwise explain the differences observed. Given that the benefits measured occurred despite negative risk factors being more present in the treatment group, this suggests the benefits are likely accurate and unbiased. Further, studies relying on PSM techniques have been shown to consistently agree with those employing randomization [37,38], again supporting the likelihood that the benefits measured are accurate. The prevailing type of SARS-CoV-2 in the city was unknown due to the lack of genotyping surveillance during the period of the program. Whether the prophylaxis proposed in this program would be as effective in other SARS-CoV-2 variants is unclear. Also, there was no strict control on whether infected subjects used any specific drug in case of COVID-19 infection, and this allows the possibility that the differences may be explained by differences in the use of ivermectin or other medications as treatment.

Final discussion

In this citywide ivermectin prophylaxis program, a large, statistically significant decrease in mortality rate was observed after the program began among the entire population of city residents. When comparing subjects that used ivermectin regularly, non-users were two times more likely to die from COVID-19 while ivermectin users were 7% less likely to be infected with SARS-CoV-2 ($p = 0.003$).

Although this study is not a randomized, double-blind, placebo-controlled clinical trial, the data were prospectively collected and resulted in a massive study sample that allowed adjustment for numerous confounding factors, thus strengthening the findings of the present study.

Due to the well-established, long-term safety profile of ivermectin, with rare adverse effects, the absence of proven therapeutic options to prevent death caused by COVID-19, and lack of effectiveness of vaccines in real-life all-cause mortality analyses to date, we recommend that ivermectin be considered as a preventive strategy, in particular for those at a higher risk of complications from COVID-19 or at higher risk of contracting the illness, not as a substitute for COVID-19 vaccines, but as an additional tool, particularly during periods of high transmission rates.

Conclusions

In a citywide ivermectin program with prophylactic, optional ivermectin use for COVID-19, ivermectin was associated with significantly reduced COVID-19 infection, hospitalization, and death rates from COVID-19.

Appendices

Table of contents

STROBE checklist

Table *5* describes the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist of this study.

Section	Item No.	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract - PRESENT IN BOTH TITLE (lines 2-3) AND ABSTRACT (lines 50-52) (b) Provide in the abstract an informative and balanced summary of what was done and what was found - BALANCED SUMMARY OF METHODS (lines 52-64) AND FINDINGS (lines 65-78)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported - SCIENTIFIC BACKGROUND (lines 111-165) AND RATIONALE (lines 167-173)
Objectives	3	State-specific objectives, including any prespecified hypotheses (lines 175-178)
Methods		
Study design	4	Present key elements of study design early in the paper (lines 185-190)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (lines 190-235)
Participants	6	(a) Cohort study: Give the eligibility criteria and the sources and methods of selection of participants. Describe methods of follow-up (lines 237-275) (b) Cohort study: For matched studies, give matching criteria and number of exposed and unexposed (lines 177-288)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (lines 228-235; 277-281)
Data sources/measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (lines 277-311)

Bias	9	Describe any efforts to address potential sources of bias (lines 266-270; 313-317)
Study size	10	Explain how the study size was arrived at (lines 261-264)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (lines 293-311)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (lines 293-320)
		(b) Describe any methods used to examine subgroups and interactions (lines 301-311)
		(c) Explain how missing data were addressed 313-317
		(d) Cohort study: If applicable, explain how the loss to follow-up was addressed - NO LOSS OF FOLLOW-UP
		(e) Describe any sensitivity analyses (lines 301-303; 310-311)
Results		
Participants	13	(a) Report numbers of individuals at each stage of the study, e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed (lines 331-338)
		(b) Give reasons for non-participation at each stage - NOT APPLICABLE
		(c) Consider the use of a flow diagram - NOT APPLICABLE
Descriptive data	14	(a) Give characteristics of study participants (e.g., demographic, clinical, and social) and information on exposures and potential confounders (lines 342-347 and Table 1)
		(b) Indicate the number of participants with missing data for each variable of interest - NO MISSING DATA
		(c) Cohort study: Summarize follow-up time (e.g., average and total amount) (lines 266-267)
Outcome data	15	Cohort study: Report numbers of outcome events or summary measures over time (lines 336-338; 357-359; 364-365; 390-395; Tables 2-3 and Figure 1)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (lines 338-340; 359-362; 365-367; 379-389; 394-398, Tables 2-4 and Figure 1)
		(b) Report category boundaries when continuous variables were categorized - NOT APPLICABLE
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period - NOT APPLICABLE
Other analyses	17	Report other analyses done, e.g., analyses of subgroups and interactions, and sensitivity analyses (APPENDIX – pages 3- 8)
Discussion		
Key results	18	Summarize key results with reference to study objectives (lines 435-438)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (lines 522-535)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, the multiplicity of analyses, results from similar studies, and other relevant evidence (lines 440-518)
Generalizability	21	Discuss the generalizability (external validity) of the study results (lines 564-569)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (lines 600-602)

TABLE 5: STROBE checklist.

STROBE = Strengthening the Reporting of Observational Studies in Epidemiology.

Unmatched analysis of infected patients

Table 6 compares the hospitalization and mortality rates from COVID-19 infected patients between ivermectin users and non-users. Of the 7,345 subjects with COVID-19, there were 185 hospitalizations (2.52% hospitalization rate) among the non-users. Of the 4,311 ivermectin users, there were 86 hospitalizations (2.0% hospitalization rate), while among the 3,034 ivermectin non-users, there were 99 hospitalizations (3.3% hospitalization rate), with a reduction in hospitalization rate due to COVID-19 of 39% (RR, 0.61; 95% CI, 0.46-0.81; p = 0.0007). After adjustment for variables, reduction in hospitalization rate was 59% (RR < 0.41; 95% CI, 0.31-0.55; p < 0.0001).

		Overall	Ivermectin users	Non-IVM users	Risk ratio (95% CI) and p-value [p]	Adjusted risk ratio (95% CI) and p-value [p]
COVID-19 infection	Overall population (n)	159,561	113,845 (71.3%)	45,716 (28.7%)	-	-
	Infected population in the city of Itajaí (n)	7,345	4,197	3,034	-	-
	Infection rate (%)	4.6%	3.7%	6.6%	0.56 (0.53-0.58) [<0.0001]	-
COVID-19 hospitalization	Infected population considered for the analysis (n)	7,345	4,311	3,034		
	Hospitalization due to COVID-19*	185	86	99	-	-
	Hospitalization rate (in case of COVID-19) (%)	2.5%	2.0%	3.3%	0.61 (0.46-0.81) [0.0007]	0.41 (0.31-0.55) [<0.0001]
COVID-19 death	COVID-19 deaths (n)	141	62	79	-	-
	Risk of dying from COVID-19 in Itajaí (%)	0.09%	0.054%	0.173%	0.31 (0.23-0.44) [<0.0001]	-
	Mortality rate (among infected subjects) (%)	1.9%	1.4%	2.6%	0.55 (0.40-0.77) [0.0004]	0.43 (0.32-0.59) [<0.0001]

TABLE 6: Pre-matching infection, hospitalization, death, and mortality rate among ivermectin users and non-users.

IVM = ivermectin; CI = confidence interval. * Only subjects hospitalized in public hospitals. ** All deaths, including from public and private hospitals, and in-home.

Among the 7,345 subjects from both groups with COVID-19, there were 141 deaths (1.9% mortality rate). Among the 4,311 ivermectin users, there were 62 deaths (1.4% mortality rate), while among the 3,034 subjects who did not use ivermectin prophylactically, there were 79 deaths (2.6% mortality rate), with a reduction in mortality rate of 45% (RR, 0.55; 95% CI, 0.40-0.77; p = 0.0004). When adjusted for residual variables, reduction in COVID-19 mortality rate was 57% (RR, 0.43; 95% CI, 0.32-0.59; p < 0.0001).

Determinants of COVID-19 mortality before matching

Table 7 describes the risk factors associated with death amongst the overall population before PSM. In unmatched analysis, unadjusted risk factors for COVID-19 among all participants included ivermectin non-users (p = 0.0004), age (p < 0.0001), sex (p = 0.014), T2D (p < 0.0001), hypertension (p < 0.0001), asthma (p = 0.041), COPD (p < 0.0001), cancer (overall) (p = 0.004), CVD (p < 0.0001), pulmonary diseases other than asthma and COPD (p = 0.003), and history of stroke (p < 0.0001). After adjustment for variables, ivermectin non-users (p < 0.0001), age (p < 0.0001), sex (p = 0.002), race (p = 0.052), T2D (p = 0.008), and pulmonary diseases other than asthma and COPD (p = 0.024) were demonstrated to be risk factors.

	Pre-matching			
Variable	Overall (n = 7,345)	Death (%)	Unadjusted COVID-19 mortality risk ratio and p-value [p]	Multivariate adjusted p-value

Ivermectin use - n (%)			0.55 (0.40-0.77) [0.0004]	<0.0001
Yes	4,311	62 (1.4%)		
No	3,034	79 (2.6%)		
Age - n (%)			[<0.0001]	<0.0001
<30 years old	2,336	0 (0.0%)		
30-50 years old	4,915	22 (0.45%)		
>50 years old	2,705	170 (6.28%)		
Sex - n (%)			0.66 (0.48-0.92) [0.014]	0.002
Female	3,983	62 (1.6%)		
Male	3,362	79 (2.4%)		
Race - n (%)			[0.20]	0.052
Caucasians	5,437	110 (2.0%)		
Afro-Brazilians	209	7 (3.3%)		
Mixed	1;583	22 (1.4%)		
Asian-Brazilians	114	2 (1.7%)		
Type 2 diabetes - n (%)			5.38 (3.59-8.06) [<0.0001]	0.008
Yes	214	27 (12.6%)		
No	7131	114 (1.6%)		
Hypertension - n (%)			6.57 (4.91-8.81) [<0.0001]	0.79
Yes	528	47 (8.9%)		
No	6,817	94 (1.4%)		
Asthma - n (%)			4.05 (1.06-15.5) [0.041]	0.27
Yes	26	2 (7.7%)		
No	7,319	139 (1.9%)		
COPD - n (%)			12.3 (4.48-33.5) [<0.0001]	0.11
Yes	13	3 (23.1%)		
No	7,332	138 (1.9%)		
Cardiovascular diseases - n (%)			6.46 (4.60-9.06) [<0.0001]	0.52
Yes	56	5 (8.9%)		
No	7,289	136 (1.9%)		
Other pulmonary diseases - n (%)			7.03 (1.91-25.8) [0.003]	0.024
Yes	15	2 (13.3%)		
No	7,330	139 (1.9%)		

Cancer (any type) - n (%)			4.97 (1.67-14.8) [0.004]	0.65
Yes	32	3 (9.4%)		
No	7,313	138 (1.9%)		
Current smoking - n (%)			1.43 (0.46-4.42) [0.53]	0.74
Yes	110	3 (2.7%)		
No	7,235	138 (1.9%)		
History of MI - n (%)			3.49 (0.52-23.4) [0.20]	0.91
Yes	15	1 (6.7%)		
No	7,330	140 (1.9%)		
History of stroke - n (%)			15.5 (6.58-27.1) [<0.0001]	0.13
Yes	21	6 (28.6%)		
No	7,324	135 (1.8%)		

TABLE 7: Pre-matching COVID-19 mortality rate according to each characteristic in the overall population, ivermectin users, and non-users.

COPD = chronic obstructive pulmonary disease; MI = myocardial infarction.

Ivermectin versus non-ivermectin users in subpopulations

Tables *8*, *9* depict the differences in mortality rate in different subpopulations of ivermectin users and ivermectin non-users, and compare mortality rates in each subpopulation between ivermectin users and non-users, before and after matching, respectively.

	Ivermectin users				Non-ivermectin users				Users versus non-users
Variable	N (n = 4,311)	Mortality rate among ivermectin users (%)	Unadjusted COVID-19 mortality risk ratio (95% CI) and p-value [p]	Multivariate adjusted p-value	N (n = 3,034)	Mortality rate among non-ivermectin users (%)	Unadjusted COVID-19 mortality risk ratio (95% CI) and p-value [p]	Multivariate adjusted p-value	COVID-19 mortality risk ratio comparing ivermectin users versus non-users (95% CI) [p-value]
Age			[<0.0001]	<0.0001			[<0.0001]	<0.0001	
<30 years old	886	0 (0.0%)			844	1 (0.1%)			0.32 (0.01-7.78) [0.48]
31-49 years old	2,119	2 (0.1%)			1,572	10 (0.6%)			0.15 (0.03-0.68) [0.014]
>50 years old	1,304	60 (4.6%)			608	68 (11.2%)			0.41 (0.30-0.57) [<0.0001]
Sex			[0.044]	0.14			[0.15]	0.012	
Female	2,359	26 (1.1%)			1,624	36 (2.2%)			0.50 (0.30-0.82) [0.006]
Male	1,952	36 (1.8%)			1,410	43 (3.1%)			0.60 (0.39-0.94) [0.024]
Race			0.55	0.079			-	0.74	
Caucasians	3,245	48 (1.5%)			2,192	62 (2.8%)			0.52 (0.36-0.76) [0.0007]
Afro-Brazilians	109	3 (2.7%)			100	4 (4.0%)			0.69 (0.16-3.00) [0.62]

Mixed	901	10 (1.1%)			682	12 (1.8%)			0.63 (0.27-1.45) [0.28]
Asian-Brazilians	56	1 (1.8%)			60	1 (1.7%)			1.07 (0.07-16.7) [0.96]
Type 2 diabetes			5.94 (3.16-11.2) [<0.0001]	0.089			12.0 (7.35-19.5) [<0.0001]	0.024	
Yes	151	11 (7.3%)			63	16 (25.4%)			0.29 (0.14-0.58) [0.0006]
No	4,160	51 (1.2%)			2,971	63 (2.0%)			0.58 (0.40-0.83) [0.003]
Hypertension			4.82 (2.84-8.18) [<0.0001]	0.97			8.95 (5.79-13.8) [<0.0001]	0.29	
Yes	362	19 (5.2%)			166	28 (16.9%)			0.33 (0.19-0.57) [0.0001]
No	3,949	43 (1.1%)			2,868	51 (1.8%)			0.61 (0.40-0.91) [0.017]
Cardiovascular diseases			5.30 (1.73-16.2) [0.003]	0.40			5.40 (1.46-20.0) [0.012]	0.87	
Yes	41	3 (7.3%)			15	2 (13.3%)			0.55 (0.10-2.97) [0.49]
No	4,270	59 (1.4%)			3,019	77 (2.6%)			0.56 (0.40-0.78) [0.0007]
Asthma			3.52 (0.51-24.1) [0.20]	0.34			6.47 (1.07-39.2) [0.042]	0.59	
Yes	20	1 (5.0%)			6	1 (16.7%)			0.30 (0.02-4.11) [0.90]
No	4,291	61 (1.4%)			3,028	78 (2.6%)			0.55 (0.40-0.77) [0.0004]
COPD			20.5 (6.19-67.9) [<0.0001]	0.068			6.47 (1.07-39.2) [0.042]	0.69	
Yes	7	2 (28.6%)			6	1 (16.7%)			1.71 (0.20-14.5) [0.62]
No	4,304	60 (1.4%)			3,028	78 (2.6%)			0.54 (0.39-0.75) [0.0003]
Other pulmonary diseases			7.05 (1.08-46.0) [0.041]	0.26			9.70 (1.75-53.7) [0.009]	0.16	
Yes	10	1 (10.0%)			4	1 (20.0%)			0.40 (0.03-4.96) [0.48]
No	4,301	61 (1.4%)			3,029	78 (2.6%)			0.55 (0.39-0.77) [0.0004]
Cancer (any type)			7.20 (1.89-27.5) [0.004]	0.62			3.23 (0.49-21.4) [0.22]	0.96	
Yes	20	2 (10.0%)			12	1 (8.3%)			1.20 (0.12-11.9) [0.88]
No	4,291	60 (1.4%)			3,022	78 (2.6%)			0.54 (0.39-0.76) [0.0003]
Current smoking			2.25 (0.56-8.99) [0.25]	0.51			0.81 (0.12-5.73) [0.84]	0.58	
Yes	63	2 (3.2%)			47	1 (2.1%)			1.49 (0.14-16.0) [0.74]
No	4,248	60 (1.4%)			2,987	78 (2.6%)			0.54 (0.39-0.75) [0.0003]
History of MI			2.87 (0.19-43.8) [0.44]	-			9.71 (1.75-53.8) [0.009]	0.49	
Yes	11	0 (0.0%)			4	1 (25.0%)			0.14 (0.01-2.87) [0.20]

No	4,300	62 (1.4%)			3,030	78 (2.6%)			0.56 (0.40-0.78) [0.0006]
History of stroke			13.0 (3.63-46.8) [0.0001]	0.72			16.1 (7.31-35.6) [<0.0001]	0.15	
Yes	11	2 (18.2%)			10	4 (40.0%)			0.45 (0.11-1.97) [0.29]
No	4,300	60 (1.4%)			3,024	75 (2.5%)			0.56 (0.40-0.79) [0.0008]

TABLE 8: Pre-matching COVID-19 mortality rate according to each characteristic in ivermectin users and ivermectin non-users, and mortality rate between ivermectin users versus non-users in each group.

CI = confidence interval; n/a = not applicable; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction.

	Ivermectin users				Non-ivermectin users				Users versus non-users
Variable	N (n = 3,034)	Death (%)	Unadjusted COVID-19 mortality risk ratio (95% CI) and p-value [p]	Multivariate adjusted p-value	N (n = 3,034)	Death (%)	Unadjusted COVID-19 mortality risk ratio (95% CI) and p-value [p]	Multivariate adjusted p-value	COVID-19 mortality risk ratio comparing ivermectin users versus non-users [p-value]
Age			[<0.0001]	<0.0001			[<0.0001]	<0.0001	
<30 years old	847	0 (0.0%)			844	1 (0.1%)			n/a
30-50 years old	1,573	2 (0.1%)			1,572	10 (0.6%)			0.20 (0.04-0.91) [0.037]
>50 years old	614	23 (3.7%)			608	68 (11.2%)			0.33 (0.21-0.53) [<0.0001]
Sex			0.35 (0.14-0.82) [0.017]	0.014			0.73 (0.47-1.12) [0.15]	0.012	
Female	1,607	7 (0.4%)			1,624	36 (2.2%)			0.29 (0.18-0.46) [<0.0001]
Male	1,427	18 (1.3%)			1,410	43 (3.1%)			0.41 (0.24-0.71) [0.001]
Race			[0.33]	0.077			[0.74]	0.74	
Caucasians	2,206	17 (0.8%)			2,192	62 (2.8%)			0.28 (0.16-0.46) [<0.0001]
Afro-Brazilians	93	2 (2.1%)			100	4 (4.0%)			0.54 (0.10-2.87) [0.47]
Mixed	682	5 (0.7%)			682	12 (1.8%)			0.42 (0.15-1.18) [0.098]
Asian-Brazilians	53	1 (1.9%)			60	1 (1.7%)			1.13 (0.07-17.7) [0.93]
Type 2 diabetes	-		7.22 (2.54-20.5) [0.0002]	0.64			12.0 (7.35-19.5) [<0.0001]	0.24	
Yes	78	4 (5.1%)			63	16 (25.4%)			0.21 (0.07-0.59) [0.003]
No	2,956	21 (0.7%)			2,971	63 (2.1%)			0.33 (0.20-0.55) [0.098]
Hypertension			7.60 (3.32-17.4) [<0.0001]	0.99			8.95 (5.79-13.8) [<0.0001]	0.29	

Yes	177	8 (4.5%)			166	28 (16.9%)			0.28 (0.13-0.61) [0.001]
No	2,857	17 (0.6%)			2,868	51 (1.8%)			0.33 (0.19-0.58) [0.0001]
Cardiovascular diseases			15.4 (3.94-60.4) [0.0001]	0.90			5.40 (1.46-20.0) [0.012]	0.87	-
Yes	17	2 (11.8%)	-		15	2 (13.3%)			0.88 (0.14-5.52) [0.89]
No	3,017	23 (0.8%)			3,019	77 (2.6%)			0.30 (0.19-0.47) [<0.0001]
Asthma			8.99 (1.30-61.9) [0.026]	0.029			6.47 (1.07-39.2) [0.042]	0.59	
Yes	14	1 (6.7%)			6	1 (16.7%)			0.43 (0.03-5.78) [0.64]
No	3,019	24 (0.8%)			3,028	78 (2.6%)			0.31 (0.20-0.49) [<0.0001]
COPD	-		43.9 (13.2-146.1) [0.0001]	0.042			6.47 (1.07-39.2) [0.042]	0.70	
Yes	6	2 (33.3%)			6	1 (16.7%)			2.00 (0.24-16.6) [0.52]
No	3,028	23 (0.8%)			3,028	78 (2.6%)			0.30 (0.19-0.47) [<0.0001]
Other pulmonary diseases			n/a	0.89			9.70 (1.75-53.7) [0.009]	0.16	
Yes	4	0 (0.0%)			4	1 (20.0%)			n/a
No	3,030	25 (0.8%)			3,029	78 (2.6%)			0.30 (0.19-0.47) [<0.0001]
Cancer (any type)			n/a	0.85			3.23 (0.49-21.4) [0.22]	0.96	
Yes	10	0 (0.0%)			12	1 (8.3%)			n/a
No	3,240	25 (0.8%)			3,022	78 (2.6%)			0.32 (0.20-0.50) [<0.0001]
Current smoking			2.59 (0.36-18.8) [0.35]	0.68			0.81 (0.12-5.73) [0.84]	0.57	
Yes	48	1 (2.1%)			47	1 (2.1%)			0.97 (0.06-15.2) [0.99]
No	2,986	24 (0.8%)			2,987	78 (2.6%)			0.31 (0.20-0.48) [<0.0001]
History of MI			n/a	0.91			9.71 (1.75-53.8) [0.009]	0.49	
Yes	4	0 (0.0%)			4	1 (25.0%)			n/a
No	3,030	25 (0.8%)			3,030	78 (2.6%)			0.32 (0.20-0.50) [<0.0001]
History of stroke			23.9 (6.40-89.3) [<0.0001]	0.90			16.1 (7.31-35.6) [<0.0001]	0.15	
		2				4			

Yes	11	(18.2%)	10	(40.0%)	0.45 (0.10-1.97) [0.29]
No	3,023	23 (0.8%)	3,024	75 (2.5%)	0.32 (0.20-0.50) [<0.0001]

TABLE 9: Propensity score-matched COVID-19 mortality rate according to each characteristic in ivermectin users and ivermectin non-users, and mortality rate between ivermectin users versus non-users in each group.

PSM = propensity score matching; CI = confidence interval; n/a = not applicable; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction.

Unmatched analysis

Before matching (Table *5*), unadjusted values showed that risk factors for both ivermectin users and non-users were aging ($p < 0.0001$ for both), T2D ($p < 0.0001$ for both), hypertension ($p < 0.0001$ for both), CVD ($p = 0.003$ and $p = 0.012$, respectively), COPD ($p < 0.0001$ and $p = 0.042$, respectively), other pulmonary diseases ($p = 0.041$ and $p = 0.009$, respectively), and history of stroke ($p = 0.0001$ and $p < 0.0001$, respectively). Male sex and cancer were risk factors for ivermectin users ($p = 0.044$ and $p = 0.22$, respectively). History of MI was a risk factor for ivermectin non-users ($p = 0.009$).

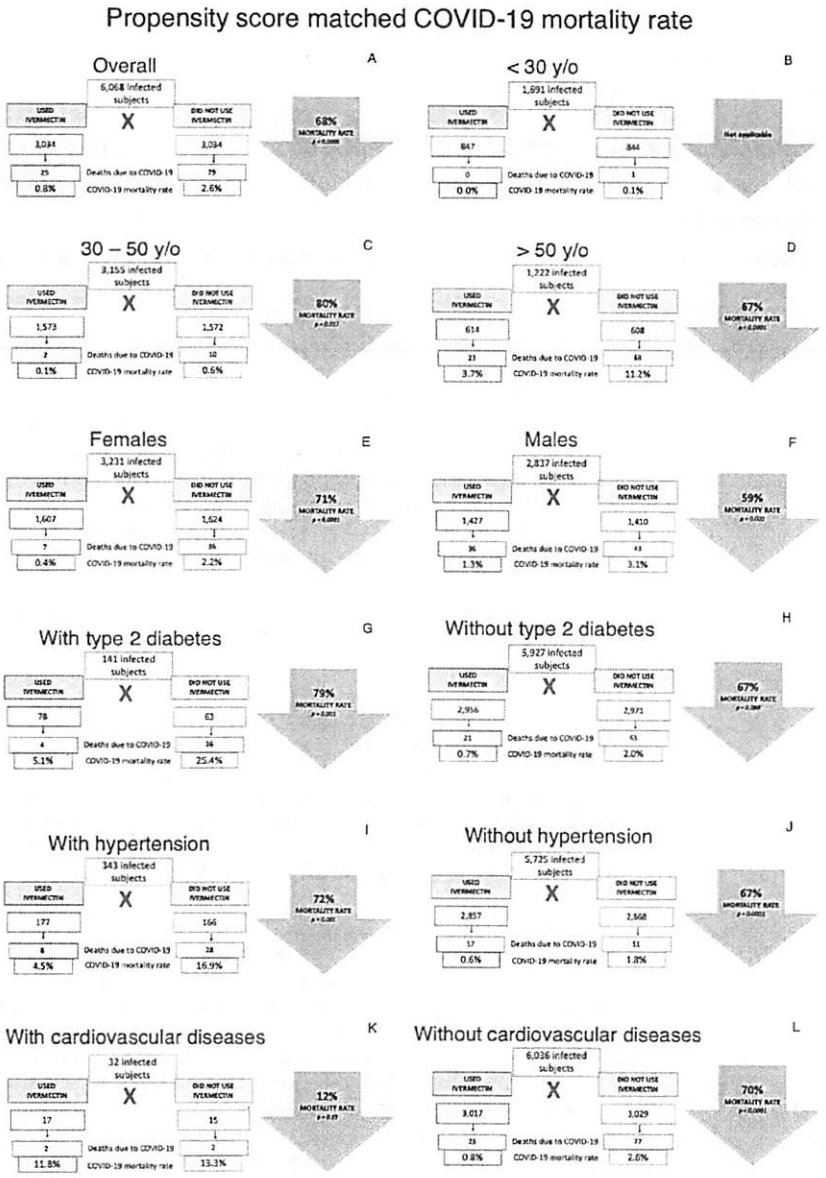
After adjustment for variables, remaining independent risk factors include aging for both ivermectin users ($p < 0.0001$) and non-users ($p < 0.0001$), male sex for non-users ($p = 0.012$), and T2D for ivermectin non-users ($p = 0.024$).

Mortality rates between ivermectin users were statistically lower than non-users among the following groups: between 31 and 49 years old (RR, 0.15; 95% CI, 0.03-0.68; $p = 0.014$), above 50 years old (RR, 0.41; 95% CI, 0.30-0.57; $p < 0.0001$), male sex (RR, 0.60; 95% CI, 0.39-0.94; $p = 0.024$), female sex (RR, 0.50; 95% CI, 0.30-0.82; $p = 0.006$), Caucasians (RR, 0.52; 95% CI, 0.36-0.76; $p = 0.0007$), subjects with T2D (RR, 0.29; 95% CI, 0.14-0.58; $p = 0.0006$), with hypertension (RR, 0.33; 95% CI, 0.19-0.57; $p = 0.0001$), and subjects without hypertension, T2D, COPD, asthma, other pulmonary diseases, CVD, history of MI, history of stroke, and non-smokers (RR, 0.54-0.61; 95% CI, 0.19-0.91; $p = 0.0003$ to 0.017).

Relative reduction of mortality risk rate with ivermectin use was more substantial in those with major common comorbidities, including T2D (71% reduction among subjects with T2D versus 42% reduction among subjects without T2D), hypertension (67% reduction in the COVID-19 death rate among subjects with hypertension versus 39% reduction among subjects without hypertension), asthma (70% reduction in the COVID-19 death rate among subjects with asthma versus 45% among subjects without asthma), and history of MI (86% reduction in the COVID-19 death rate among subjects with a history of MI versus 44% among subjects without a history of MI). Reduction of death risk was higher in females (50%) than in males (40%), in Caucasians (48%) than in mixed-race subjects (37%) and afro-Brazilians (31%), and between 30 and 50 years old (85%) than above 50 years old (59%). However, the absolute risk reduction was higher among those above 50 years old (6.6 points percent [p.p.]) than those between 30 and 50 years old (0.5 p.p.) and below 30 years old (0.1 p.p.).

Propensity score-matched analysis

Table *9* describes propensity score-matched mortality rates in subpopulations of ivermectin users and ivermectin non-users and then compares ivermectin users and non-users for each characteristic. Figure *3* illustrates COVID-19 mortality rates in subpopulations after matching. Post-matching mortality rates, risk ratios, and p-values among ivermectin non-users remained the same as before matching. Among ivermectin users, the values were as follows: aging ($p < 0.0001$), male sex ($p = 0.017$), T2D ($p = 0.0002$), hypertension ($p < 0.0001$), CVD ($p = 0.0001$), asthma ($p = 0.026$), COPD ($p = 0.0001$), and history of stroke ($p < 0.0001$). There were no deaths in ivermectin users with other pulmonary diseases, cancer, and a history of MI.



A = Overall population; B = Below 30 years old (y/o); C = Between 30 and 50 y/o; D = Above 50 y/o; E = Females; F = Males; G = With type 2 diabetes; H = Without type 2 diabetes; I = With hypertension; J = Without hypertension; K = With cardiovascular diseases; L = Without cardiovascular diseases

FIGURE 3: Propensity score-matched COVID-19 mortality rates in subpopulations.

After PSM, the ratio between mortality rates of ivermectin users and ivermectin non-users showed statistical reduction in mortality rate with ivermectin use in subjects above 30 years old (30-50 years old; RR, 0.20; 95% CI, 0.04-0.91; p = 0.037; >50 years old; RR, 0.33; 95% CI, 0.21-0.53; p < 0.0001), in both sexes (male sex; RR, 0.41; 95% CI, 0.24-0.71; p = 0.001; female sex; RR, 0.29; 95% CI, 0.18-0.46; p < 0.0001), Caucasians (RR, 0.28; 95% CI, 0.16-0.46; p < 0.0001), subjects with T2D (RR, 0.21; 95% CI, 0.07-0.59; p = 0.003), with hypertension (RR, 0.28; 95% CI, 0.13-0.61; p = 0.001), and subjects without hypertension, T2D, COPD, asthma, other pulmonary diseases, CVD, history of MI, history of stroke, and non-smokers (RR, 0.30-0.32; 95% CI, 0.19-0.58; p < 0.0001 for all, except for no diabetes, p = 0.098).

After matching, relative reductions in mortality risk with the use of ivermectin was slightly higher in subjects with T2D (79% and 67% reduction among subjects with T2D and without T2D, respectively) and hypertension (72% and 67% reduction in COVID-19 mortality rate in subjects with and without hypertension, respectively), but not with other comorbidities. The absolute risk reduction was higher among those above 50 years old, of 75 subjects saved for every 1,000 subjects infected with COVID-19 (7.5 p.p.) than those between 30 and 50 years old (0.5 p.p.; five subjects saved for every 1,000 COVID-19 cases) and below

30 years old (0.1 p.p.; one subject saved for every 1,000 COVID-19 cases).

Protocol modification for the calculation of infection rates

Previously, we had considered the full population of Itajaí as the source for the calculation of ivermectin non-users, which falsely raised the number of non-users and, consequently, falsely reduced the infection rate among ivermectin non-users. We also excluded subjects below 18 years old and participating subjects from other cities, since their outcomes would not be accounted for in the statistics of the city of Itajaí. Figure *4* summarizes the modifications.

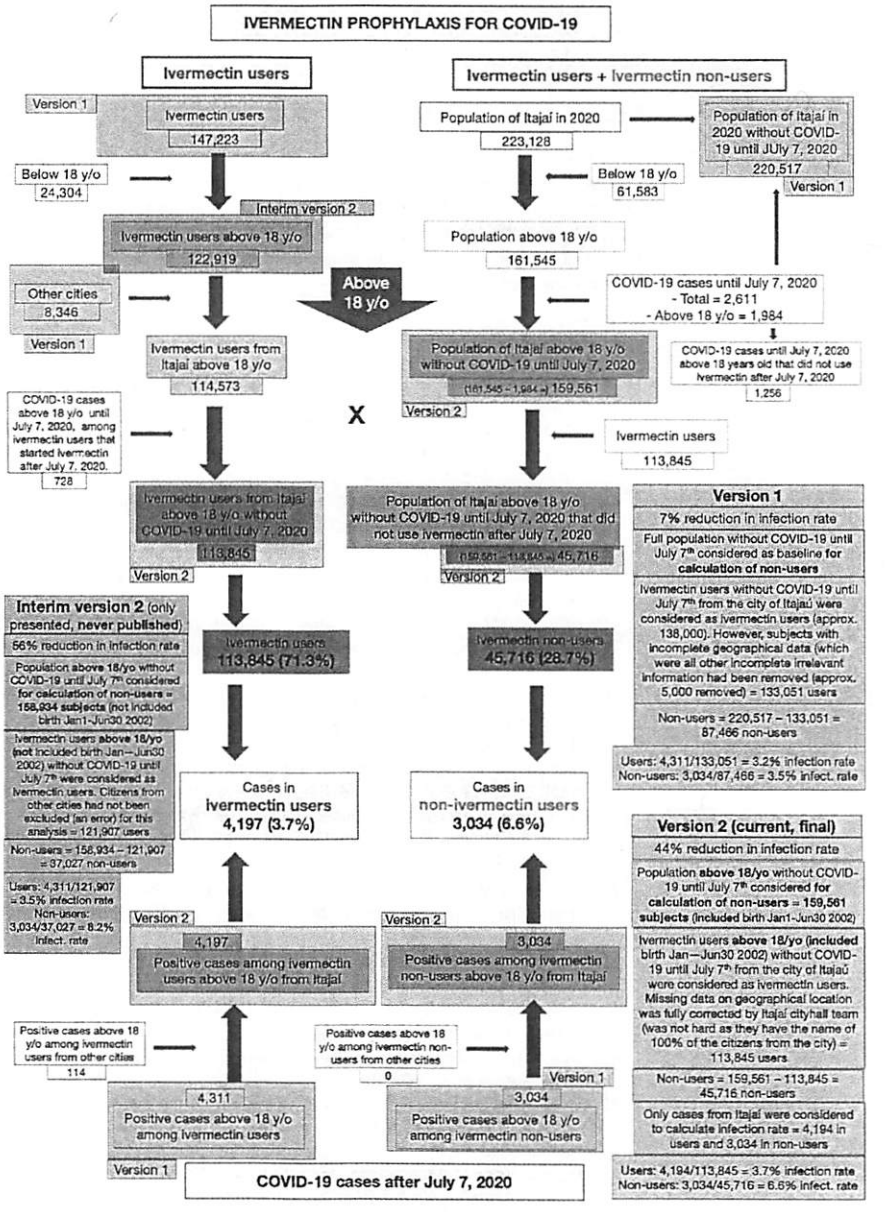


FIGURE 4: Modifications in the reported reduction in infection rate with ivermectin prophylaxis for COVID-19.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. National Research Ethics Council (CONEP) issued approval 4.821.082. The present retrospective analysis of the prospectively

collected data was approved by the National Research Ethics Council (CONEP) under the number 4.821.082 with the project number CAAE: 47124221.2.0000.5485. Although study design, IRB approval, and data analysis occurred after completion of the voluntary prophylaxis program, all data were collected prospectively in real time with mandated reporting to the registry of all events as they occurred during the citywide governmental COVID-19 prevention with ivermectin program, from July 2020 to December 2020, developed in the city of Itajaí, in the state of Santa Catarina, Brazil. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

We acknowledge Dr. Volnei José Morastoni, the city mayor of Itajaí, state of Santa Catarina, Brazil, for developing and enabling the citywide program of ivermectin for COVID-19 prophylaxis. We also acknowledge all the staff that worked at the citywide program for COVID-19 prevention with ivermectin in Itajaí, state of Santa Catarina, Brazil, and also, those who directly or indirectly offered pro bono support for the subjects that participated in the program, compilation of data, or were involved in any other step that led to the present analysis.

References

1. Chen IS, Kubo Y: Ivermectin and its target molecules: shared and unique modulation mechanisms of ion channels and receptors by ivermectin. J Physiol. 2018, 596:1833-45. 10.1113/JP275236
2. Kaur H, Shekhar N, Sharma S, Sarma P, Prakash A, Medhi B: Ivermectin as a potential drug for treatment of COVID-19: an in-sync review with clinical and computational attributes. Pharmacol Rep. 2021, 73:736-49. 10.1007/s43440-020-00195-y
3. Martin RJ, Robertson AP, Choudhary S: Ivermectin: an anthelmintic, an insecticide, and much more. Trends Parasitol. 2021, 37:48-64. 10.1016/j.pt.2020.10.005
4. Mastrangelo E, Pezzullo M, De Burghgraeve T, et al.: Ivermectin is a potent inhibitor of flavivirus replication specifically targeting NS3 helicase activity: new prospects for an old drug. J Antimicrob Chemother. 2012, 67:1884-94. 10.1093/jac/dks147
5. Wagstaff KM, Sivakumaran H, Heaton SM, Harrich D, Jans DA: Ivermectin is a specific inhibitor of importin α/β-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. Biochem J. 2012, 443:851-6. 10.1042/BJ20120150
6. Crump A: Ivermectin: enigmatic multifaceted 'wonder' drug continues to surprise and exceed expectations. J Antibiot (Tokyo). 2017, 70:495-505. 10.1038/ja.2017.11
7. Heidary F, Gharebaghi R: Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. J Antibiot (Tokyo). 2020, 73:593-602. 10.1038/s41429-020-0336-z
8. Li N, Zhao L, Zhan X: Quantitative proteomics reveals a broad-spectrum antiviral property of ivermectin, benefiting for COVID-19 treatment. J Cell Physiol. 2021, 236:2959-75. 10.1002/jcp.30055
9. Jin L, Feng X, Rong H, et al.: The antiparasitic drug ivermectin is a novel FXR ligand that regulates metabolism. Nat Commun. 2013, 4:1937. 10.1038/ncomms2924
10. Yang JS, Qi W, Farias-Pereira R, Choi S, Clark JM, Kim D, Park Y: Permethrin and ivermectin modulate lipid metabolism in steatosis-induced HepG2 hepatocyte. Food Chem Toxicol. 2019, 125:595-604. 10.1016/j.fct.2019.02.005
11. Cairns DM, Giordano JE, Conte S, Levin M, Kaplan DL: Ivermectin promotes peripheral nerve regeneration during wound healing. ACS Omega. 2018, 3:12392-402. 10.1021/acsomega.8b01451
12. Zheng YY, Ma YT, Zhang JY, Xie X: COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020, 17:259-60. 10.1038/s41569-020-0360-5
13. Nagai H, Satomi T, Abiru A, et al.: Antihypertrophic effects of small molecules that maintain mitochondrial ATP levels under hypoxia. EBioMedicine. 2017, 24:147-58. 10.1016/j.ebiom.2017.09.022
14. Park A, Iwasaki A: Type I and type III interferons - induction, signaling, evasion, and application to combat COVID-19. Cell Host Microbe. 2020, 27:870-8. 10.1016/j.chom.2020.05.008
15. Zhang X, Song Y, Ci X, et al.: Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. Inflamm Res. 2008, 57:524-9. 10.1007/s00011-008-8007-8
16. Okeahialam BN: Serine protease inhibitors could be of benefit in the treatment of COVID-19 disease . Ther Adv Infect Dis. 2021, 8:10.1177/20499361211032048
17. Matsuyama T, Kubli SP, Yoshinaga SK, Pfeffer K, Mak TW: An aberrant STAT pathway is central to COVID-19. Cell Death Differ. 2020, 27:3209-25. 10.1038/s41418-020-00633-7
18. Wang K, Gao W, Dou Q, Chen H, Li Q, Nice EC, Huang C: Ivermectin Induces PAK1-mediated cytostatic autophagy in breast cancer. Autophagy. 2016, 12:2498-9. 10.1080/15548627.2016.1231494
19. Dou Q, Chen HN, Wang K, et al.: Ivermectin induces cytostatic autophagy by blocking the PAK1/Akt axis in breast cancer. Cancer Res. 2016, 76:4457-69. 10.1158/0008-5472.CAN-15-2887
20. Layhadi JA, Turner J, Crossman D, Fountain SJ: ATP evokes Ca2+ responses and CXCL5 secretion via P2X4 receptor activation in human monocyte-derived macrophages. J Immunol. 2018, 200:1159-68. 10.4049/jimmunol.1700965
21. Juarez M, Schcolnik-Cabrera A, Dueñas-Gonzalez A: The multitargeted drug ivermectin: from an antiparasitic agent to a repositioned cancer drug. Am J Cancer Res. 2018, 8:317-31.
22. Andersson U, Ottestad W, Tracey KJ: Extracellular HMGB1: a therapeutic target in severe pulmonary

inflammation including COVID-19?. Mol Med. 2020, 26:42. 10.1186/s10020-020-00172-4
23. Yan S, Ci X, Chen N, et al.: Anti-inflammatory effects of ivermectin in mouse model of allergic asthma . Inflamm Res. 2011, 60:589-96. 10.1007/s00011-011-0307-8
24. Reis TA, Oliveira-da-Silva JA, Tavares GS, et al.: Ivermectin presents effective and selective antileishmanial activity in vitro and in vivo against Leishmania infantum and is therapeutic against visceral leishmaniasis. Exp Parasitol. 2021, 221:108059. 10.1016/j.exppara.2020.108059
25. Scheim D: Ivermectin for COVID-19 treatment: clinical response at quasi-threshold doses via hypothesized alleviation of CD147-mediated vascular occlusion. [PREPRINT]. SSRN J. 2020, 10.2139/ssrn.3636557
26. Ci X, Li H, Yu Q, et al.: Avermectin exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen-activated protein kinase activation pathway. Fundam Clin Pharmacol. 2009, 23:449-55. 10.1111/j.1472-8206.2009.00684.x
27. Zaidi AK, Dehgani-Mobaraki P: The mechanisms of action of Ivermectin against SARS-CoV-2: an evidence-based clinical review article. [PREPRINT]. J Antibiot (Tokyo). 2021, 10.1038/s41429-021-00430-5
28. Kalfas S, Visvanathan K, Chan K, Drago J: The therapeutic potential of ivermectin for COVID- 19: a systematic review of mechanisms and evidence. [PREPRINT]. medRxiv. 2020, 10.1101/2020.11.30.20236570
29. Behera P, Patro BK, Singh AK, et al.: Role of ivermectin in the prevention of SARS-CoV-2 infection among healthcare workers in India: a matched case-control study. PLoS One. 2021, 16:e0247163. 10.1371/journal.pone.0247163
30. Hellwig MD, Maia A: A COVID-19 prophylaxis? Lower incidence associated with prophylactic administration of ivermectin. Int J Antimicrob Agents. 2021, 57:106248. 10.1016/j.ijantimicag.2020.106248
31. World Medical Association. Declaration of Helsinki. (2020). Accessed: December 24, 2021: https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/doh-oct2000/.
32. Conselho Federal de Medicina (CFM). Código de Ética Médica . (2010). Accessed: December 24, 2021: https://portal.cfm.org.br/images/stories/biblioteca/codigo%20de%20etica%20medica.pdf.
33. Nguyen TL, Collins GS, Spence J, Daurès JP, Devereaux PJ, Landais P, Le Manach Y: Double-adjustment in propensity score matching analysis: choosing a threshold for considering residual imbalance. BMC Med Res Methodol. 2017, 17:78. 10.1186/s12874-017-0338-0
34. Zhang Z, Kim HJ, Lonjon G, Zhu Y: Balance diagnostics after propensity score matching. Ann Transl Med. 2019, 7:16. 10.21037/atm.2018.12.10
35. Boletim epidemiológico do estado de Santa Catarina, Brasil . (2020). Accessed: December 24, 2021: http://www.dive.sc.gov.br.
36. Choudhury A, Das NC, Patra R, Bhattacharya M, Ghosh P, Patra BC, Mukherjee S: Exploring the binding efficacy of ivermectin against the key proteins of SARS-CoV-2 pathogenesis: an in silico approach. Future Virol. 2021, 16:277-91. 10.2217/fvl-2020-0342
37. Austin PC: An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res. 2011, 46:399-424. 10.1080/00273171.2011.568786
38. Propensity score matching in the absence of randomized controlled trials: a case study on the effects of breastfeeding on childhood obesity. (2020). Accessed: December 24, 2021: https://methods.sagepub.com/case/propensity-score-matching-trials-effects-breastfeeding-childhood-obesity.

Queen Mary University of London
London, United Kingdom

The authors have no conflicts of interest to declare.

REFERENCES

1. Bryant A, Lawrie TA, Dowswell T, et al. Ivermectin for prevention and treatment of COVID-19 infection: a systematic review, meta-analysis, and trial sequential analysis to inform clinical guidelines. *Am J Ther.* 2021;28:e434–e460.
2. Roman YM, Burela PA, Pasupuleti V, et al. Ivermectin for the treatment of COVID-19: a systematic review and meta-analysis of randomized controlled trials.,*Clin Infect Dis.* 2021; ciab591. doi: 10.1093/cid/ciab591.
3. Crawford M. *The Meta-Analytical Fixers: An Ivermectin Tale;* 2021. Available at: https://roundingtheearth.substack.com/p/the-meta-analytical-fixers-an-ivermectin. Accessed July 7, 2021.
4. Neil M, Fenton NE, *Bayesian Hypothesis Testing and Hierarchical Modelling of Ivermectin Effectiveness in Treating Covid-19, 2021.* Available at: http://dx.doi.org/10.13140/RG.2.2.19703.75680.
5. Niaee MS, Gheibi N, Namdar P, et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: a randomized multi-center clinical trial. *Asian Pac J Trop Med.* 2021;14:266.
6. Elgazzar A, Hany B, Youssef SA, et al. *Efficacy and Safety of Ivermectin for Treatment and Prophylaxis of COVID-19 Pandemic;* 2020. Available at: https://www.researchsquare.com/article/rs-100956/v2.

Ivermectin, A Reanalysis of the Data

To the Editor:

Our article entitled "Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19" was recently published in the *American Journal of Therapeutics.*[1] Our article included randomized and observational trial meta-analyses on the efficacy of ivermectin for the prophylaxis and treatment of COVID-19. Recently, the study conducted by Elgazzar et al[2] has come under scrutiny with accusations of scientific misconduct. His paper was apparently retracted without his knowledge and without giving him the opportunity to defend these serious claims. This situation is most unfortunate. While this issue is being resolved, we decided to redo the original meta-analyses excluding this study. The summary point estimates were largely unaffected when the study by Elgazzar et al was removed. The revised forest plots are provided below (Figures 1–3).

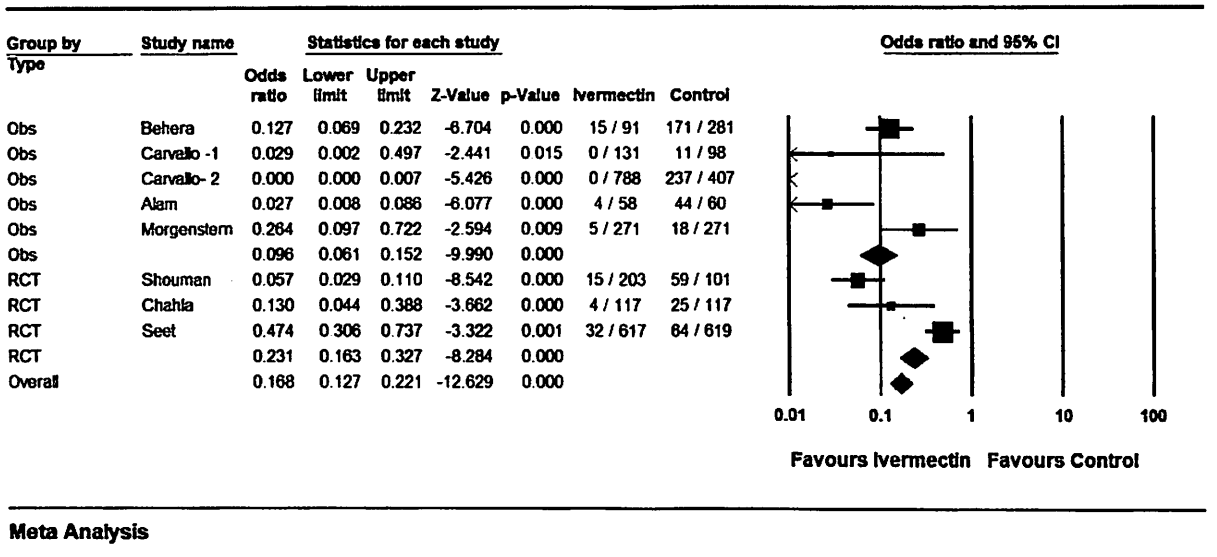


FIGURE 1. Meta-analysis of ivermectin prophylaxis trials in COVID-19. Symbols: Squares indicate treatment effect of an individual study. Large diamond reflects summary of study design immediately above. Size of each symbol correlates with the size of the CI around the point estimate of treatment effect with larger sizes indicating a more precise CI. CI, confidence interval; OBS, observational study; RCT, randomized controlled trial.

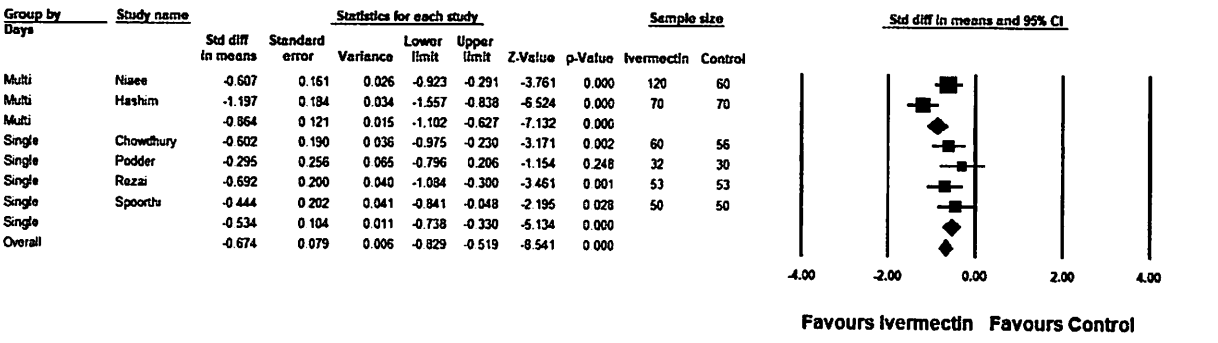


FIGURE 2. Meta-analysis of the outcome of time to clinical recovery from controlled trials of ivermectin treatment in COVID-19. Symbols: Squares indicate treatment effect of an individual study. Large diamond reflects summary of study design immediately above. Small diamond indicates sum effect of all trial designs. Size of each symbol correlates with the size of the CI around the point estimate of treatment effect with larger sizes indicating a more precise CI. CI, confidence interval.

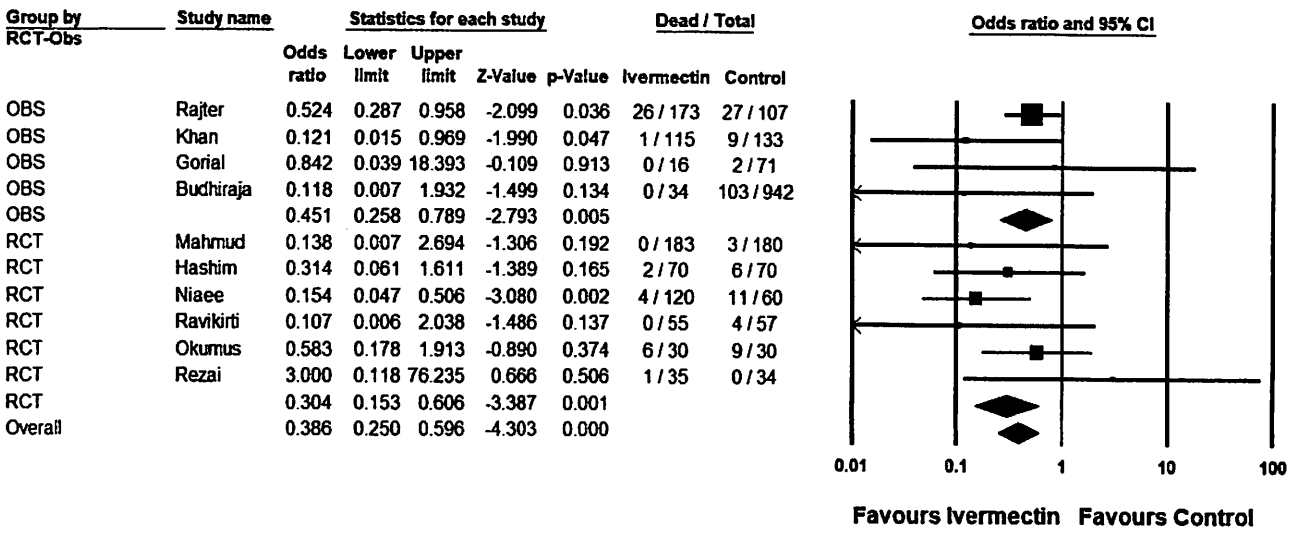


FIGURE 3. Meta-analysis of the outcome of mortality from controlled trials of ivermectin treatment in COVID-19. Symbols: Squares indicate treatment effect of an individual study. Large diamond reflects summary of study design immediately above. Small diamond indicates sum effect of all trial designs. Size of each symbol correlates with the size of the CI around the point estimate of treatment effect with larger sizes indicating a more precise CI. CI, confidence interval; OBS, observational study; RCT, randomized controlled trial.

Paul E. Marik, MD, FCCM, FCCP[1]
Pierre Kory, MD[2]
[1]Eastern Virginia Medical School
Norfolk, VA
[2]Front Line Covid 19 Critical Care Alliance
Madison, WI

The authors have no conflicts of interest to declare.

REFERENCES

1. Kory P, Meduri GU, Iglesias J, et al. Review of the emerging evidence demonstrating the efficacy of ivermectin in the prophylaxis and treatment of COVID-19. *Am J Ther.* 2020;28:e299–e318.
2. Elgazzar A, Hany B, Youssef SA, et al. Efficacy and safety of ivermectin for treatment and prophylaxis of COVID-19 pandemic. *Research Square.* 2020.

The Journal of Antibiotics
https://doi.org/10.1038/s41429-021-00430-5

JARA Japan Antibiotics Research Association
The Society for Actinomycetes Japan

REVIEW ARTICLE

The mechanisms of action of Ivermectin against SARS-CoV-2: An evidence-based clinical review article

Asiya Kamber Zaidi[1,2] · Puya Dehgani-Mobaraki[3]

Received: 11 May 2021 / Revised: 17 May 2021 / Accepted: 20 May 2021

Abstract

Considering the urgency of the ongoing COVID-19 pandemic, detection of various new mutant strains and future potential re-emergence of novel coronaviruses, repurposing of approved drugs such as Ivermectin could be worthy of attention. This evidence-based review article aims to discuss the mechanism of action of ivermectin against SARS-CoV-2 and summarizing the available literature over the years. A schematic of the key cellular and biomolecular interactions between Ivermectin, host cell, and SARS-CoV-2 in COVID-19 pathogenesis and prevention of complications have been proposed.

Introduction

A relatively recent surge in zoonotic diseases has been noted over the past few decades. Several reasons could be responsible for this "spill-over" of disease-causing agents from animals to humans. These include an exponential rise in the global population causing man to encroach new ecological habitats in search of space, food, and resources as well as improved opportunities for rampant wildlife trade causing inter-species pathogen jumps. The 1980s was known for HIV/AIDS crisis that originated from the great apes, while the Avian flu pandemic in 2004-07 came from the birds. The pigs lead to the Swine flu pandemic in 2009 and bats were the original hosts of Ebola, Severe Acute Respiratory Syndrome (SARS), Middle Eastern respiratory syndrome (MERS), and probably Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) outbreak as well.

COVID-19 has already caused millions of deaths worldwide and has paralyzed not only the world's health-care system but also the political and economic relations between countries [1]. The fact that the SARS-CoV-2 virus has been thought to have originated from wildlife and may have "jumped" into humans, not only highlights future risks from animal-borne diseases but also provides an important clue to its resolution. In such a scenario, where this "jump" has been made from animal to human, it seems only logical to review a drug that has worked efficiently against a disease-causing agent and is available in a form that is safe for human consumption since the early 1980 s.

Ivermectin belongs to a group of avermectins (AVM), which is a group of 16 membered macrocyclic lactone compounds discovered at the Japanese Kitasato institute in 1967 during actinomycetes cultures with the fungus *Streptomyces avermitilis* [2]. This drug radically lowered the incidence of river blindness and lymphatic filariasis and was discovered and developed by William C. Campbell and Satoshi Ōmura for which they received the Nobel Prize in Physiology or Medicine in 2015 [3, 4]. Ivermectin is enlisted in the World Health Organization's Model List of Essential Medicines [5].

Drug repurposing, drug redirecting, or drug reprofiling is defined as the identification of novel usages for existing drugs. The development risks, costs as well as safety-related failure, are reduced with this approach since these drugs have a well-established formulation development, in vitro and in vivo screening, as well as pharmacokinetic and pharmacodynamic profiles. Moreover, the first clinical trial phases of many such drugs have been completed and can be bypassed to reduce several years of development. Therefore, drug repurposing has the potential to reduce the time frame for the whole process by up to 3–12 years and carries great potential [6].

✉ Asiya Kamber Zaidi
asiyazaidia@gmail.com

1 Member, Association "Naso Sano" Onlus, Umbria Regional Registry of volunteer activities, Corciano, Italy

2 Mahatma Gandhi Memorial Medical College, Indore, India

3 President, Association "Naso Sano" Onlus, Umbria Regional Registry of volunteer activities, Corciano, Italy

Published online: 15 June 2021

Table 1 All 55 ivermectin COVID-19 trials (As per data available on 16 May 2021) divided based on stage of treatment (Early Vs Late) and the type of study

Study	Study Type
EARLY TREATMENT	
Random effects meta-analysis with pooled effects showed 79% improvement for early treatment RR 0.21 and CI [0.11-0.37]	
Double-Blind Randomized controlled trial	Mahmud et al.*, Ahmed et al.*, Chaccour et al.*, Babalola et al.*, Kirti et al., Mohan et al., Schwartz et al., Lopez- Medina et al.*, Chahla et al.
Single-blind Randomized controlled trial	Raad et al.
Randomized controlled trial	Bukhari et al., Chowdhury et al.*, Faisal et al.*
Retrospective quasi-randomized study	Loue et al*, Merino et al
Other studies	Espitia-Hernandez et al.*, Carvallo et al., Cadegiani et al., Afsar et al., Elalfy et al.*, Roy et al., Mourya et al.*
LATE TREATMENT	
Random effects meta-analysis with pooled effects showed 46% improvement for late treatment RR 0.54 and CI [0.40-0.72]	
Randomized controlled trial	Kishoria et al.*, Podder et al.*, Chachar et al.*, Elgazzar et al.. Pott-Junior et al.*
Double-Blind Randomized controlled trial	Niaee et al.,Okumus et al.*, Shahbazn et al.*, Gonzalez et al.*. Huvemek et al.
Single-Blind Randomized controlled trial	Hashim et al.
Other studies	Gorial et al., Khan et al., Soto-Becerra et al, Rajter et al.*, Camprubi et al.*, Spoorthi et al*, Budhiraja et al., Lima Morales et al.*

The 29 peer-reviewed trials have been marked with an asterisk as a superscript. (*) (source: https://ivmmeta.com/)

Although several drugs received Emergency Use Authorization for COVID-19 treatment with unsatisfactory supportive data, Ivermectin, on the other hand, has been sidelined irrespective of sufficient convincing data supporting its use. Nevertheless, many countries adopted ivermectin as one of the first-line treatment options for COVID-19.

With the ongoing vaccine roll-out programs in full swing across the globe, the longevity of the immunity offered by these vaccines or their role in offering protection against new mutant strains is still a matter of debate. The adoption of Ivermectin as a "safety bridge" by some sections of the population that are still waiting for their turn for vaccination could be considered as a "logical" option.

Several doctor-initiated clinical trial protocols that aimed to evaluate outcomes, such as reduction in mortality figures, shortened length of intensive care unit stay and/or hospital stay and elimination of the virus with ivermectin use have been registered at the US ClinicalTrials.gov [7]. Real-time data is also available with a meta-analysis of 55 studies to date. As per data available on 16 May 2021, 100% of 36 early treatment and prophylaxis studies report positive effects (96% of all 55 studies). Of these, 26 studies show statistically significant improvements in isolation. Random effects meta-analysis with pooled effects using the most serious outcome reported 79% and 85% improvement for early treatment and prophylaxis respectively (RR 0.21 [0.11–0.37] and 0.15 [0.09–0.25]). The results were similar after exclusion based sensitivity analysis: 81% and 87% (RR 0.19 [0.14–0.26] and 0.13 [0.07–0.25]), and after restriction to 29 peer-reviewed studies: 82% and 88% (RR 0.18 [0.11–0.31] and 0.12 [0.05–0.30]). Statistically significant improvements were seen for mortality, ventilation, hospitalization, cases, and viral clearance. 100% of the 17 Randomized Controlled Trials (RCTs) for early treatment and prophylaxis report positive effects, with an estimated improvement of 73% and 83% respectively (RR 0.27 [0.18–0.41] and 0.17 [0.05–0.61]), and 93% of all 28 RCTs. These studies are tabulated in Table 1. The probability that an ineffective treatment generated results as positive for the 55 studies to date is estimated to be 1 in 23 trillion ($p = 0.000000000000043$). The consistency of positive results across a wide variety of cases has been remarkable. It is extremely unlikely that the observed results could have occurred by chance [8].

However, a controlled outpatient trial by López-Medina et al. demonstrated that, in mild COVID-19, Ivermectin showed no improvement [9]. Misinterpretation of results were noted due to possible gaps in regards to the study quality (study design, the methodology adopted, statistical analysis, and hence the conclusion).

Ivermectin has rapid oral absorption, high liposolubility, is widely distributed in the body, metabolized in the liver (cytochrome P450 system) and excreted almost exclusively in feces [4]. Following a standard oral dose in healthy humans, it reaches peak plasma levels at 3.4 to 5 h; and plasma half-life has been reported to be 12 to 66 h [10]. Despite its widespread use, there are relatively few studies

Table 2 A list of studies demonstrating the role of Ivermectin (IVM) on SARS-CoV-2

MAIN ROLE OF IVERMECTIN AGAINST SARS-COV-2	STUDY AUTHORS	STUDY YEAR	REFERENCES
A. DIRECT ACTION ON SARS-COV-2			
Level 1: Action on SARS-CoV-2 cell entry			
IVM docks in the region of leucine 91 of the spike protein and histidine 378 of the ACE2 receptor	Leher et al.	2020	[22]
IVM has the highest binding affinity to the predicted active site of the S glycoprotein; Considerable binding affinity to the predicted active site of the SARS-CoV-2 RdRp protein; Highest binding affinity to the predicted active site of nsp14; highest binding affinity to the active site of the TMPRSS2 protein	Eweas et al.	2021	[23]
IVM utilizes viral spike protein, main protease, replicase, and human TMPRSS2 receptors as the most possible targets for executing its antiviral efficiency by disrupting binding	Choudhury et al.	2021	[24]
Level 2: Action on Importin (IMP) superfamily			
in presence of a viral infection, IVM targets the IMPα component of the IMP α/β1 heterodimer and binds to it, preventing interaction with IMP β1, subsequently blocking the nuclear transport of viral proteins.	Yang, S.N.Y et al.	2020	[26]
Level 3: Action as an Ionophore			
Two ivermectin molecules, reacting with each other in a "head-tail" mode, can create a complex suitable to be considered as ionophore. These ionophores allow neutralizing the virus at an early stage of the infection before it can adhere to the host cells and enter it.	Rizzo E et al.	2020	[28]
B. ACTION ON HOST TARGETS FOR VIRAL REPLICATION			
Level 4: Action as an antiviral			
IVM has antiviral properties against other viruses including the RNA viruses such as Zika Virus (ZKV), Dengue virus, yellow fever virus (YFV), and West Nile virus (WNV), Hendra virus (HEV), Newcastle virus, Venezuelan equine encephalitis virus (VEEV), Chikungunya virus (CHIKV), Semliki Forest virus (SFV), and Sindbis virus (SINV), Avian influenza A virus, Porcine Reproductive and Respiratory Syndrome virus (PRRSV), Human immunodeficiency virus type 1 as well as DNA viruses such as Equine herpesvirus type 1 (EHV-1) and Pseudorabies virus (PRV).	Heidary, F et al.	2020	[29]
Level 5: Action on viral replication and assembly			
In Vero/hSLAM cells infected with the SARS-CoV-2 virus when "exposed" to 5 μM IVM showed a 5000-fold reduction in viral RNA at 48 h when compared to the control group	Caly L et al.	2020	[30]
utilizing modeling approach, predicted lung accumulation of Ivermectin over 10 times higher than EC 50	Arshad et al	2020	[31]
best binding interaction between IVM and RNA-dependent RNA polymerase (RdRp)	Swargiary et al.*	2020	[33]
highly efficient binding of IVM to nsp14	Ma et al.	2015	[35]
highly efficient binding of IVM to the viral N phosphoprotein and M protein	Eweas et al.	2021	[23]
Level 6: Action on post-translational processing of viral polyproteins			
IVM binds to both proteins, Mpro, and to a lesser extent to PLpro of SARS-CoV-2	Eweas et al.	2021	[23]
Level 7: Action on Karyopherin (KPNA/KPNB) receptors			
IVM inhibits the KPNA/KPNB1- mediated nuclear import of viral proteins	Caly L et al.	2020	[30]
C. ACTION ON HOST TARGETS FOR INFLAMMATION			
Level 8: Action on Interferon (INF) levels			
IVM promotes the expression of several IFN-related genes, such as IFIT1, IFIT2, IF144, ISG20, IRF9, and OASL	Seth C	2016	[40]
Level 9: Action on Toll- like-Receptors (TLRs)			
IVM blocks activation of NF-kappa B pathway and inhibition of toll-like receptor 4 (TLR4) signaling	Zhang X et al.	2008	[42]
Level 10: Action on Nuclear Factor-κB (NF-κB) pathway			
IVM at its very low dose, which did not induce cytotoxicity, drastically reversed the resistance of tumor cells to the chemotherapeutic drugs both in vitro and in vivo by inhibition of the transcriptional factor NF-κB.	Jiang L et al.	2019	[44]

Table 2 (continued)

MAIN ROLE OF IVERMECTIN AGAINST SARS-COV-2	STUDY AUTHORS	STUDY YEAR	REFERENCES
IVM inhibits lipopolysaccharide (LPS)-induced production of inflammatory cytokines by blocking the NF-κB pathway and improving LPS-induced survival in mice.	Zhang X et al.	2008	[42]
Level 11: Action on the JAK-STAT pathway, PAI-1 and COVID-19 sequalae			
IVM inhibits STAT-3, SARS-CoV-2-mediated inhibition of IFN and STAT 1, with the subsequent shift to a STAT 3- dominant signaling network that could result in almost all of the clinical features of COVID-19; STAT-3 acts as a "central hub" that mediates the detrimental COVID-19 cascade	Matsuyama, T.,	2020	[39]
STAT-3 induces a C-reactive protein that upregulates PAI-1 levels. Ivermectin inhibits STAT-3.	Matsuyama, T.,	2020	[39]
The PD-L1 receptors present on the endothelial cells are activated by STAT-3 causing T cell lymphopenia. IVM inhibits STAT-3 through direct inhibition	Matsuyama, T.,	2020	[39]
Level 12: Action on P21 activated Kinase 1 (PAK-1)			
IVM suppresses the Akt/mTOR signaling and promotes ubiquitin-mediated degradation of PAK-1 hence compromising STAT-3 activity and decreasing IL-6 production.	Dou Q et al.	2016	[54]
Level 13: Action on Interleukin-6 (IL-6) levels			
IVM suppressed IL-6 and TNFα production	Zhang X et al.	2008	[42]
IVM "dramatically reduced" IL-6/IL-10 ratio modulating infection outcomes.	G D de Melo et al. *	2020	[55]
Level 14: Action on allosteric modulation of P2X4 receptor			
Positive allosteric modulation of $P2X_4$ by IVM enhances ATP-mediated secretion of CXCL5	Layhadi JA et al.	2018	[58]
Level 15: Action on high mobility group box 1 (HMGB1)			
Ivermectin inhibits HMGB1	Juarez M et al.	2018	[60]
Level 16: Action as an immunomodulator on Lung tissue and olfaction			
No olfactory deficit was observed in IVM-treated females; IVM dramatically reduced the IL-6/IL-10 ratio in lung	G D de Melo et al. *	2020	[55]
Level 17: Action as an anti-inflammatory			
anti-inflammatory action of IVM was explained as inhibition of cytokine production by lipopolysaccharide challenged macrophages, blockade of activation of NF-kB, and the stress-activated MAP kinases JNK and p38, and inhibition of TLR4 signaling.	Zhang X et al., Ci X et al., Yan S et al.	2008 2009 2011	[42, 62, 63]
Immune cell recruitment, cytokine production in bronchoalveolar lavage fluid, IgE, and IgG1 secretion in serum as well as hyper-secretion of mucus by goblet cells was reduced significantly by IVM	Yan S et al.	2011	[63]
D. ACTION ON OTHER HOST TARGETS			
Level 18: Action on Plasmin and Annexin A2			
Annexin acts as a co-receptor for the conversion of plasminogen to plasmin in the presence of t-PA. increased levels of plasmin leads to direct activation of STAT-3.	Kamber Zaidi et al.	2020	[64]
IVM directly inhibits STAT-3 and could play a role in the inhibition of COVID-19 complications.	Matsuyama et al.	2020	[39]
Level 19: Action on CD147 on the RBC			
The SARS-CoV-2 does not internalize into the red blood cells but such attachments can lead to clumping. IVM binds to the S protein of the SARS-CoV-2 virus making it unavailable to bind with CD147.	David E.Scheim et al.	2020	[65]
Level 20: Action on mitochondrial ATP under hypoxia on cardiac function			
IVM increased mitochondrial ATP production by inducing Cox6a2 expression and maintains mitochondrial ATP under hypoxic conditions. This prevents pathological hypertrophy and improves cardiac function.	Nagai H et al.	2017	[67]

*available as preprint; Clinical trials of IVM on COVID-19 available on https://clinicaltrials.gov[7]; Ivermectin for COVID-19: real-time meta-analysis available on https://ivmmeta.com [8]

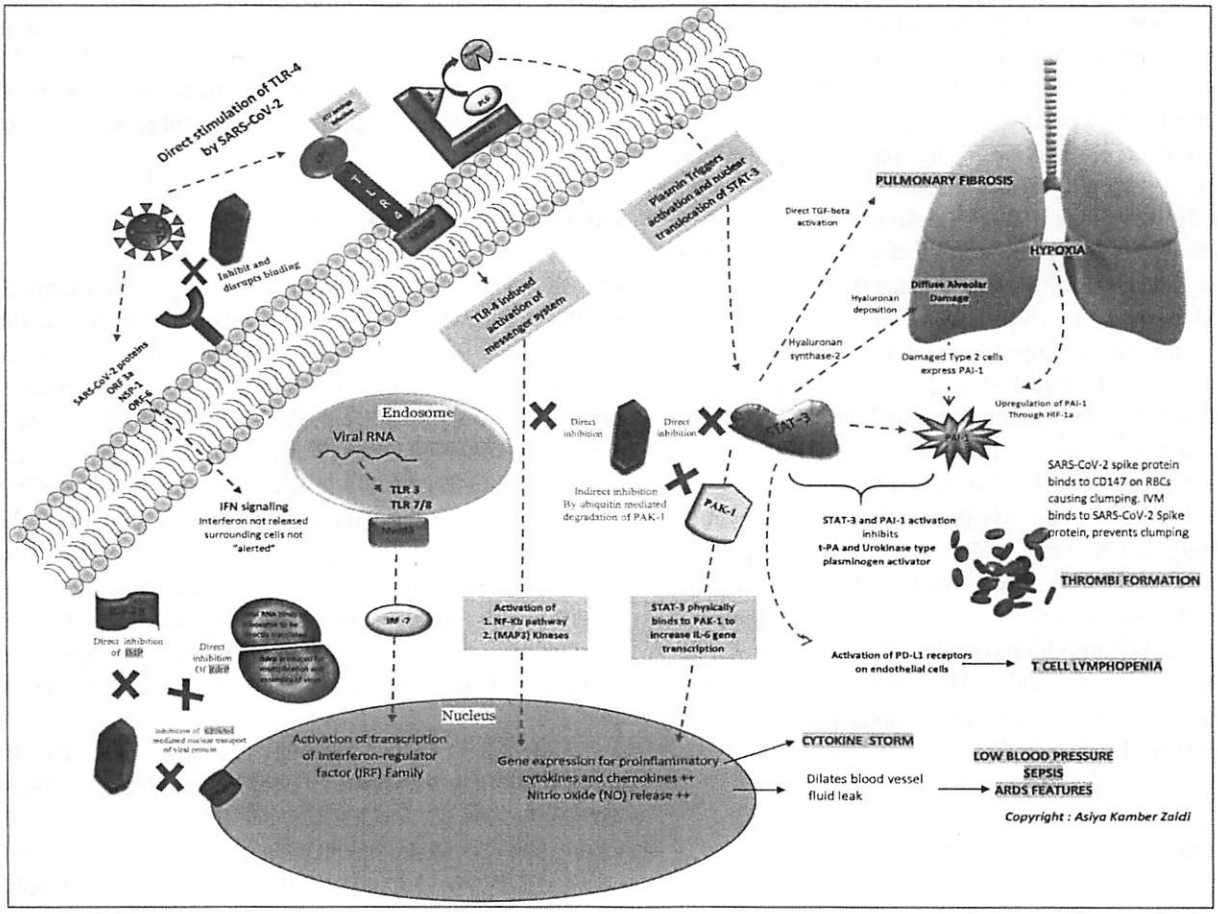


Fig. 1 A schematic of the key cellular and biomolecular interactions between Ivermectin, host cell, and SARS-CoV-2 in COVID-19 pathogenesis and prevention of complications. Ivermectin; IVM (red block) inhibits and disrupts binding of the SARS-CoV-2 S protein at the ACE-2 receptors (green). The green dotted lines depict activation pathways and the red dotted lines depict the inhibition pathways. The TLR-4 receptors are directly activated by SARS-CoV-2 and also by LPS mediated activation (seen during ICU settings) causing activation of NF-Kb pathway and MAP3 Kinases leading to increased intranuclear gene expression for proinflammatory cytokines and chemokines (responsible for cytokine storm) and NO release (responsible for blood vessel dilatation, fluid leak, low blood pressure, ARDS and sepsis). The NF-Kb and STAT-3 pathway activation is central to the pathogenesis and sequelae of COVID-19. STAT-3 physically binds to PAK-1 and increases IL-6 transcription. The annexin A2 at the cell surface converts plasminogen; PLG to plasmin under the presence of t-PA. Plasmin triggers activation and nuclear translocation of STAT-3. An upregulation of STAT-3 stimulates hyaluronan synthase-2 in the lung cells causing hyaluronan deposition leading to diffuse alveolar damage and hypoxia. STAT-3 also directly activates TGF-beta initiating pulmonary fibrosis; a typical characteristic of SARS-COV-2 lung pathology. The damaged type 2 cells express PAI-1 and an already hypoxic state also causes an upregulation of PAI (through Hypoxic inducible factor-1) along with direct stimulation by STAT-3. Simultaneous STAT-3 and PAI-1 activation inhibits t-PA and urokinase-type plasminogen activator leading to thrombi formation. Also, the SARS-CoV-2 spike protein binds to the CD147 on red blood cells and causes clumping. *IVM in turn, binds to SARS-CoV-2 Spike protein and hence prevents clumping*. T cell lymphopenia in COVID-19 can also be attributed to the direct activation of PD-L1 receptors on endothelial cells by STAT-3. *IVM directly inhibits the NF-kb pathway, STAT-3, and indirectly inhibits PAK-1 by increasing its ubiquitin-mediated degradation*. The natural antiviral response of a cell is through interferon regulatory genes and viral RNA mediated activation of TLR-3 and TLR7/8- Myd88 activation of transcription of interferon-regulator (IRF) family. For a virus to establish an infection, this antiviral response needs to be inhibited by blocking interferon production. The proteins such as importin and KPNA mediate nuclear transport of viral protein and subsequent IFN signaling. The SARS-CoV-2 proteins (ORF-3a, NSP-1, and ORF-6) directly block IFN signaling causing the surrounding cells to become unsuspecting victims of the infection. *IVM inhibits both importin a-b (green) as well as the KPNA-1 receptors (brown) causing natural antiviral IFN release. IVM also inhibits viral RdrP, responsible for viral replication. IVM* Ivermectin, *ACE-2* angiotensin-converting-enzyme 2, *LPS* Lipopolysaccharide, *TLR* Toll-like receptor, *t-PA* tissue-like plasminogen activator, *PLG* Plasminogen, *IMPab* Importin alpha-beta, *Rdrp* RNA dependant RNA polymerase, *KPNA-1* Karyopherin Subunit Alpha 1, *NF-kB* nuclear factor kappa-light-chain-enhancer of activated B cells, *Map3Kinases* Mitogen-activated Kinases, *PAK-1* P21 Activated Kinase 1, *STAT-3* Signal transducer and activator of transcription 3, *PAI-1* Plasminogen activator inhibitor-1, *HIF-1* Hypoxia-Inducible Factor

on the pharmacokinetics of Ivermectin in humans [11]. Ivermectin binds strongly to plasma proteins in healthy subjects (93.2%) [12]. Such an "avid binding" can be beneficial when administered in countries where malnutrition and hypoalbuminemia are common, leading to an increased availability of "free fraction" of ivermectin [4].

Hypoalbuminemia is a frequent finding in patients with COVID-19 and it also appears to be linked to the severity of lung injury [13]. Therefore, Ivermectin might be useful when used in such a setting.

There is evidence supporting the use of Ivermectin in decreasing mortality figures in patients with SARS-CoV-2 infection. However, the use of ivermectin orally in an outpatient setting also requires strict and well defined guidelines to avoid any form of overdosing that could lead to toxicity. A study by Baudou, E et. al described two human ABCB1 nonsense mutations associated with a loss of function in a patient who had an adverse reaction to ivermectin after the administration of a usual dose. This finding warrants caution regarding medical prescriptions of ivermectin and other ABCB1 substrates [14].

This article aims to discuss the mechanism of action by summarizing the in vitro and in vivo evidence demonstrating the role of Ivermectin in COVID-19 as per the available literature over the years. [Table 2] A schematic of the key cellular and biomolecular interactions between Ivermectin, host cell, and SARS-CoV-2 in COVID-19 pathogenesis and prevention of complications has been proposed. [Fig. 1]

Methods

A comprehensive search of the PubMed database was conducted from January 1, 2008 up to January 30, 2021 using syntax constructed using MeSH Database as follows: (stromectol OR Ivermectin OR "dihydroavermectin") OR (22 AND 23-dihydroavermectin B) AND (antiviral OR virus OR COVID-19 OR SARS-CoV-2). All the results obtained were manually reviewed for content, relevance and included when considered appropriate. The papers cited in the references were also reviewed and included when considered appropriate. The articles were retrieved manually to exclude any duplicates.

Results

Ivermectin as an anti-helminth

Ivermectin has been approved as an anti-helminthic [15]. It is a selective positive allosteric modulator at the glutamate-gated chloride channels found in nematodes and insects and acts by binding to these channels leading to chloride ion influx causing hyperpolarization of the cell and hence, dysfunction [16]. However, at higher concentrations, Ivermectin can also bind to host GABA receptors only when the blood-brain barrier (BBB) is "leaky". This is not the case in healthy human beings with an intact BBB as the drug is "excluded" by a *p*-glycoprotein drug pump (MDR-1). Chandler et al. considered Ivermectin to be free of potential neurological adverse drug reactions, except in situations of overdose [17].

SARS-CoV-2 virus structure

SARS-CoV-2 is a sarbecovirus with structural similarity to SARS-CoV-1. Out of the four structural proteins of the SARS-CoV-2 beta coronavirus, namely: Spike (S) protein, membrane (M) protein, envelope (E) protein, and nucleocapsid (N) protein, the S protein is responsible for eliciting potent neutralizing antibody responses. The entry of SARS-CoV-2 into the host cell is mediated by the binding of the S1 subunit of its S protein (receptor binding domain) to the Angiotensin-converting enzyme 2 (ACE-2) receptors present on the host cell surface [18]. The S2 subunit is associated with a fusion protein that binds with the cell membrane after priming with Transmembrane protease, serine 2 (TMPRSS-2) and is responsible for fusion with the host cell.

The SARS-CoV-2 genome consists of ~29.8 kb nucleotides; it possesses 14 open reading frames (ORFs) encoding 27 proteins [19]. The 5′ two-thirds of the viral genome encodes the replicase gene. It contains two ORFs: ORF1a and ORF1b. ORF1a/b encodes two polyproteins by polymerase frameshifting; these are then post-translationally cleaved into 15 non-structural proteins (nsps): nsp1–10 and nsp12–16. The rest of the genome encodes for the four structural proteins [(S protein, E protein, M protein, N protein], in addition to eight accessory proteins (3a/3b, p6, 7a/7b, 8b, 9b, and ORF14) [19]. The replicase also encodes the papain-like protease (PLpro) and the serine-type protease or main protease (Mpro) [20].

In principle, a molecule can act as an anti-viral drug if it "inhibits some stage of the virus replication cycle, without being too toxic to the body's cells [21]."

The possible modes of action of anti-viral agents would include the following:

1. Inactivate extracellular virus particles.
2. Prevent viral attachment and/or entry.
3. Prevent replication of the viral genome.
4. Prevent synthesis of specific viral protein(s).
5. Prevent assembly or release of new infectious virions

The role of Ivermectin against the SARS-CoV-2 virus

The targets of activity of Ivermectin can be divided into the following four groups:

A. *Direct action on SARS-CoV-2*
   Level 1: Action on SARS-CoV-2 cell entry
   Level 2: Action on Importin (IMP) superfamily
   Level 3: Action as an Ionophore
B. *Action on host targets important for viral replication*
   Level 4: Action as an antiviral
   Level 5: Action on viral replication and assembly
   Level 6: Action on post-translational processing of viral polyproteins
   Level 7: Action on Karyopherin (KPNA/KPNB) receptors
C. *Action on host targets important for inflammation*
   Level 8: Action on Interferon (INF) levels
   Level 9: Action on Toll- like-Receptors (TLRs)
   Level 10: Action on Nuclear Factor-κB (NF-κB) pathway
   Level 11: Action on the JAK-STAT pathway, PAI-1 and COVID-19 sequalae
   Level 12: Action on P21 activated Kinase 1 (PAK-1)
   Level 13: Action on Interleukin-6 (IL-6) levels
   Level 14: Action on allosteric modulation of P2X4 receptor
   Level 15: Action on high mobility group box 1 (HMGB1),
   Level 16: Action as an immunomodulator on Lung tissue and olfaction
   Level 17: Action as an anti-inflammatory
D. *Action on other host targets*
   Level 18: Action on Plasmin and Annexin A2
   Level 19: Action on CD147 on the RBC
   Level 20: Action on mitochondrial ATP under hypoxia on cardiac function

The direct "antiviral targets" may be useful in the early stages while the anti-inflammatory targets might be addressed in the later stages of the disease.

Direct action of Ivermectin on SARS-CoV-2

Level 1: Action on SARS-CoV-2 cell entry

A study by Lehrer S et al observed that Ivermectin docked in the region of leucine 91 of the SARS-CoV-2 spike protein and histidine 378 of the host cell ACE-2 receptor blocking its entry into the host cell [22]. In yet another study by Eweas et al., potential repurposed drugs such as Ivermectin, chloroquine, hydroxychloroquine, remdesivir, and favipiravir were screened and molecular docking with different SARS-CoV-2 target proteins including S and M proteins, RNA-dependent RNA polymerase (RdRp), nucleoproteins, viral proteases, and nsp14, was performed. Ivermectin showed the following 5 important docking properties [23]:

1. Highest binding affinity to the predicted active site of the S glycoprotein (Mol Dock score −140.584) and protein–ligand interactions (MolDock score−139.371).
2. Considerable binding affinity to the predicted active site of the SARS-CoV-2 RdRp protein (MolDock score −149.9900) and protein–ligand interactions (MolDock score −147.608), it formed H-bonds with only two amino acids: Cys622 and Asp760.
3. Highest binding affinity (MolDock score −212.265) to the predicted active site of nsp14.
4. The highest binding affinity to the active site of the TMPRSS2 protein (MolDock score −174.971) and protein–ligand interactions (MolDock score −180.548). Moreover, it formed five H-bonds with Cys297, Glu299, Gln438, Gly462, and Gly464 amino acid residues present at the predicted active site of the TMPRSS protein
5. The free binding energy of the spike protein (open) was higher in Ivermectin (−398.536 kJ/mol) than remdesivir (−232.973 kJ/mol).

An In-silico data analysis conducted by Choudhury et al. demonstrated that Ivermectin efficiently utilizes viral spike protein, main protease, replicase, and human TMPRSS2 receptors as the most possible targets for executing its "antiviral efficiency" by disrupting binding. Since Ivermectin exploits protein targets from both, the virus and human, this could be the behind its excellent in vitro efficacy against SARS-CoV-2 [24].

The development of vaccines for SARS-CoV-2 is centered around spike protein biology (virus targeted) and the recently documented "vaccine escape strains" have been a cause of worry. In such a situation, Ivermectin, is both, virus as well as host targeted and hence could act as a potential therapeutic against these new strains that could "escape" immunity offered by the vaccine.

Level 2: Action on Importin (IMP) superfamily

Inside the cell, the nuclear transport of proteins into and out of the nucleus is signal-dependent and mediated by the Importin (IMP) superfamily of proteins that exist in α and β forms. This IMPα/β1 exists as a heterodimer with a "IBB" (IMP β-binding) site present over IMP α that binds to IMP β1 on "cargo recognition" by IMPα. The SARS-CoV-2 virus upon host cell entry tends to "load" its proteins over the host protein IMP α/β1 heterodimer (importin) to enter the nucleus through the nuclear pore complex. Once inside, the importin molecule detaches while the viral protein from the SARS-CoV-2 virus hijacks the host cell machinery and inhibits the natural cell "anti-viral" response by blocking the release of

interferon (an antiviral substance released by an infected cell to alert the surrounding cells of an ongoing viral attack). As a result, the surrounding cells become "unsuspecting victims" of the virus and the infection continues with the virus escaping recognition by the immune cells [25]. Ivermectin, in presence of a viral infection, targets the IMPα component of the IMP α/β1 heterodimer and binds to it, preventing interaction with IMP β1, subsequently blocking the nuclear transport of viral proteins. This allows the cell to carry out its normal antiviral response [26]. In such a case, it should be noted that the activity of Ivermectin here is viro-static, that is, it neutralizes the virus by competing for the same receptor.

Level 3: Action as an Ionophore

Ionophores are molecules that typically have a hydrophilic pocket which constitutes a specific binding site for one or more ions (usually cations), while its external surface is hydrophobic, allowing the complex thus formed to cross the cell membranes, affecting the hydro-electrolyte balance [27]. It can be hypothesized that two ivermectin molecules, reacting with each other in a "head-tail" mode, can create a complex suitable to be considered such [28]. These ionophores allow neutralizing the virus at an early stage of the infection before it can adhere to the host cells and enter it to exploit their biochemical machinery for the production of other viral particles.

Action on host targets for viral replication

Level 4: Action as an antiviral

A systematic review article by Heidary, F. discussed the "anti-viral" properties of Ivermectin against other viruses including the RNA viruses such as Zika Virus (ZKV), Dengue virus, yellow fever virus (YFV), and West Nile virus (WNV), Hendra virus (HEV), Newcastle virus, Venezuelan equine encephalitis virus (VEEV), Chikungunya virus (CHIKV), Semliki Forest virus (SFV), and Sindbis virus (SINV), Avian influenza A virus, Porcine Reproductive and Respiratory Syndrome virus (PRRSV), Human immunodeficiency virus type 1 as well as DNA viruses such as Equine herpesvirus type 1 (EHV-1) and Pseudorabies virus (PRV) [29].

Level 5: Action on viral replication and assembly

An in-vitro study by Caly L et al. demonstrated that the Vero/hSLAM cells infected with the SARS-CoV-2 virus when "exposed" to 5 μM Ivermectin showed a 5000-fold reduction in viral RNA at 48 h when compared to the control group [30]. This study attracted opinions regarding the inability of Ivermectin to achieve the therapeutic effect of COVID-19 through routine dosage. Contrary to this, Arshad et al, by utilizing modeling approach, predicted lung accumulation of Ivermectin over 10 times higher than EC_{50}. This likelihood of attainment of higher lung tissue concentrations of Ivermectin leaves the door open for further research especially for respiratory infections [31].

An explanation for the study by Caly et al was provided in a review article: Global trends in clinical studies of ivermectin in COVID-19 by Yagisawa et al., co-authored by Prof. Satoshi Ōmura, regarding the "setting of the sensitivity for experimental systems in vitro". As per the authors, using Vero/hSLAM cells, the antiviral activity of the test drug was reliably measured and the sensitivity of the $IC_{50} = 2$ μM set by them was appropriate as neither false positives nor false negatives occurred. Therefore, the study by Caly et al. merely indicated that ivermectin was found to have anti-SARS-CoV-2 activity in vitro—no more, no less. Also, the fact that there are in vivo infection experiments that could be used to connect in vitro experiments to clinical studies [32].

Another in-silico study by Swargiary et al. demonstrated the best binding interaction of −9.7 kcal/mol between Ivermectin and RdRp suggesting inhibition of viral replication [33]. The RdRP residing in nsp12 is the centerpiece of the coronavirus replication and transcription complex and has been suggested as a promising drug target as it is a crucial enzyme in the virus life cycle both for replication of the viral genome but also for transcription of subgenomic mRNAs (sgRNAs) [34]. Ivermectin binds to the viral rdrp and disrupts it. The highly efficient binding of ivermectin to nsp14 confirms its role in inhibiting viral replication and assembly. It is well known that nsp14 is essential in transcription and replication. It acts as a proofreading exoribonuclease and plays a role in viral RNA capping by its methyltransferase activity [35]. Moreover, highly efficient binding of ivermectin to the viral N phosphoprotein and M protein is suggestive of its role in inhibiting viral replication and assembly [23].

Level 6: Action on post-translational processing of viral polyproteins

Once gaining entry into the host cell, the viral RNA is translated by the host ribosome into a large "polyprotein". Some enzymes break away through autoproteolysis from this polyprotein and further help other proteins to break off and carry out their function for replication. One such enzyme, 3 chymotrypsin-like proteases (3'cl pro/ Mpro) is responsible for working on this polyprotein causing other proteins to "librate" and carry out viral replication. Ivermectin binds to this enzyme and disrupts it. It also efficiently binds to both proteins, Mpro, and to a lesser extent to PLpro of SARS-CoV-2; therefore, it has a role in preventing the post-translational processing of viral polyproteins [23].

Level 7: Action on Karyopherin (KPNA/KPNB) receptors

Karyopherin-α1 (KPNA1) is essential for the nuclear transport of signal transducers and activators of transcription 1 (STAT1) [36], and the interaction between STAT1 and KPNA1 (STAT1/KPNA1) involves a nonclassical nuclear

localization signal (NLS). Ivermectin inhibits the KPNA/KPNB1- mediated nuclear import of viral proteins allowing the cell to carry out its normal antiviral response [30].

Action on host targets for inflammation

Level 8: Action on Interferon (INF) levels

These virus-infected cells release interferons that bind to the IFN receptors present on neighboring cells alerting them of a viral attack. The IFN-I and IFN-III receptors then further activate members of the JAK-STAT family. The virus after gaining entry into the host cell hijacks the host cell machinery and works towards antagonizing the normal interferon-mediated host cell antiviral response. SARS-CoV-2 proteins such as ORF3a, NSP1, and ORF6 inhibit IFN-I signaling [37, 38]. As a result, the cells surrounding the SARS-CoV-2 virus-infected cell "fail" to receive "critical and protective IFN signals" causing this SARS-CoV-2 virus to replicate and spread without any hindrance. This is one of the main reasons that, at this stage, COVID-19 infection is "hard to detect" clinically [39].

Ivermectin has been shown to promote the expression of several IFN-related genes, such as IFIT1, IFIT2, IF144, ISG20, IRF9, and OASL [40].

Level 9: Action on Toll- like-Receptors (TLRs)

Upon virus entry, the intracellular pattern recognition receptors (PRRs) present on the host cells are responsible for detecting the viral attack. The virus activates one such PRR named the Toll-like receptors (TLRs). These receptors are present on various immune system cells that help them locate and bind with the pathogen. The activation of TLRs, causes oligomerization, further activating downstream interferon regulatory factors (IRFs) and nuclear factor-kappa B (NF-kB) transcription factors inducing INF production [41]. Ivermectin plays a role in the blockade of activation of NF-kB pathway and inhibition of TLR4 signaling [42].

Level 10: Action on Nuclear Factor-κB (NF-κB) pathway

Activation of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway induces the expression of various pro-inflammatory genes, including those encoding cytokines and chemokines [43]. Jiang et al. demonstrated that Ivermectin at its very low dose, which did not induce cytotoxicity, drastically reversed the resistance of tumor cells to the chemotherapeutic drugs both in vitro and in vivo by inhibition of the transcriptional factor NF-κB [44]. Also, Zhang et al., suggested that Ivermectin inhibits lipopolysaccharide (LPS)-induced production of inflammatory cytokines by blocking the NF-κB pathway and improving LPS-induced survival in mice [42]. Therefore, using Ivermectin would be helpful in ICU settings where there are increased chances of bacterial infections (LPS mediated).

Level 11: Action on the JAK-STAT pathway, PAI-1 and COVID-19 sequalae

A strong correlation exists between SARS-CoV-2 viral load, disease severity, and progression [45]. COVID-19 not only causes flu-like symptoms such as fever, dry cough but could also lead to widespread thrombosis with micro-angiopathy in pulmonary vessels [46], raise D-dimer levels [47], cause lymphopenia [48], raise proinflammatory cytokine and chemokine production [49] as well as lead to a significant elevation of CRP levels [50]. SARS-CoV-2 has structural similarity with SARS-CoV-1. Several SARS-CoV-1 proteins antagonize the antiviral activities of IFNs and the downstream JAK (Janus kinase)-STAT signaling pathways they activate. JAK family kinases display a wide range of functions in ontogeny, immunity, chronic inflammation, fibrosis, and cancer [51].

The host proteins, such as the members of the signal transducers and activators of transcription (STATs) and NF-κB, enter the nucleus through nuclear envelope-embedded nuclear pores mediated by the IMPα/β1 heterodimer and play a role in COVID-19 pathogenesis. Frieman et al. demonstrated that accessory SARS ORF6 antagonizes STAT1 function by sequestering nuclear import factors on the rough endoplasmic reticulum/Golgi membrane [52]. A review article by Matsuyama et al, hinted at SARS-CoV-2-mediated inhibition of IFN and STAT 1, with the subsequent shift to a STAT 3 dominant signaling network that could result in almost all of the clinical features of COVID-19 [39].

Before discussing further, it is important to understand the link between STAT-3 upregulation and COVID-19 sequelae and the role of Ivermectin in inhibiting STAT-3. STAT-3 acts as a "central hub" that mediates the detrimental COVID-19 cascade. In the lungs, STAT-3 activates Hyaluronan synthase-2 leading to deposition of hyaluronan causing diffuse alveolar damage. The damaged type 2 alveolar cells express PAI-1 (plasminogen activator inhibitor-1). Additionally, hypoxia due to diffuse alveolar damage causes an upregulation of PAI-1 through HIF-1a. STAT-3 also directly activates PAI-1. The simultaneous activation of PAI-1 and STAT-3 inhibits t-PA and urokinase-type plasminogen activator leading to thrombi formation in the capillaries. PAI-1 also binds to TLR-4 receptors on macrophages further activating the NF-kB pathway.

The "cytokine storm" typical of severe COVID-19 involves STAT-3 mediated upregulation of proinflammatory cytokines, TNFα, and IL-6 in macrophages. Additionally, STAT-3 induces a C-reactive protein that upregulates PAI-1 levels. STAT-3 is directly responsible for activating IL-6 gene transcription which further leads to an increase in TGF-β causing pulmonary fibrosis. The PD-L1 receptors present on the endothelial cells are activated by

STAT-3 causing T cell lymphopenia. Ivermectin inhibits STAT-3 through direct inhibition preventing COVID-19 sequalae [39].

Level 12: Action on P21 activated Kinase 1 (PAK-1)

The p21 activated kinase 1 (PAK1) physically binds to both JAK1 and STAT3, and the resultant PAK1/STAT3 complex activates IL-6 gene transcription responsible for cytokine storm in COVID-19 [53]. Ivermectin suppresses the Akt/mTOR signaling and promotes ubiquitin-mediated degradation of PAK-1 hence compromising STAT-3 activity and decreasing IL-6 production [54].

Level 13: Action on Interleukin-6 (IL-6) levels

A study by Zhang et al. demonstrated that Ivermectin suppressed IL-6 and TNFα production, two major components of the detrimental cytokine storm induced by SARS-CoV-2 and "dramatically reduced" IL-6/IL-10 ratio modulating infection outcomes [42, 55].

Level 14: Action on allosteric modulation of P2X4 receptor

P2X receptors are the channels selective to cation, are gated by extracellular ATP [56] and mediate several functions in health and disease [57]. From the seven subunits of P2X receptors, $P2X_4$ is most sensitive to Ivermectin. Positive allosteric modulation of $P2X_4$ by Ivermectin enhances ATP-mediated secretion of CXCL5 (pro-inflammatory chemokine). CXCL5 is a chemo-attractant molecule expressed in inflammatory cells in different tissues and modulates neutrophil chemotaxis and chemokine scavenging [58].

Level 15: Action on high mobility group box 1 (HMGB1)

The damage-associated molecular pattern high mobility group box 1 (HMGB1), is released by damaged cells acting as an agonist for the TLR4 receptor and hence mediating lung inflammation associated with COVID-19 [59]. Ivermectin inhibits HMGB1 [60].

Level 16: Action as an immunomodulator on Lung tissue and olfaction

In a study by DeMelo et al., the effects of Ivermectin were investigated on SARS-CoV-2 infection using the golden Syrian hamster as a model for COVID-19. Both, male and female adult golden Syrian hamsters were intranasally inoculated with 6×10^4 PFU of SARS-CoV-2. At the time of infection, animals received a single subcutaneous injection of Ivermectin (antiparasitic dose of 400 μg/kg) classically used in a clinical setting and were monitored over four days. Mock-infected animals received the physiological solution only. Interestingly, Ivermectin had a sex-dependent and compartmentalized immunomodulatory effect, preventing clinical deterioration and reducing the olfactory deficit in infected animals. This effect was sex-dependent: infected males presented a reduction in the clinical score whereas a complete absence of signs was noticed in the infected females. Regarding the olfactory performance, 83.3% (10/12) of the saline-treated males presented with hyposmia/anosmia, in contrast to only 33.3% (4/12) of IVM-treated males (Fisher's exact test $p = 0.036$). No olfactory deficit was observed in IVM-treated females (0/6), while 33.3% (2/6) of saline-treated females presented with hyposmia/anosmia (Fisher's exact test $p = 0.455$). Ivermectin dramatically reduced the IL-6/IL-10 ratio in lung tissue, which likely accounts for the more favorable clinical presentation in treated animals [55]. Loss of smell has been reported as one of the common symptoms in COVID-19 [61]. Interestingly, majority of patients in India regained their sense of smell after a brief anosmic period during their clinical course. Ivermectin is being used in India as one of the first-line drugs for COVID-19 treatment. It could be hypothesized that Ivermectin might have a role to play in reducing SARS-CoV-2 induced olfactory deficit.

Level 17: Action as an anti-inflammatory

The mechanism for anti-inflammatory action of Ivermectin was explained as inhibition of cytokine production by lipopolysaccharide challenged macrophages, blockade of activation of NF-kB, and the stress-activated MAP kinases JNK and p38, and inhibition of TLR4 signaling [42, 61, 62]. Moreover, Immune cell recruitment, cytokine production in bronchoalveolar lavage fluid, IgE, and IgG1 secretion in serum as well as hyper-secretion of mucus by goblet cells was reduced significantly by Ivermectin [63].

Action on other host targets

Level 18: Action on Plasmin and Annexin A2

As per study by Kamber Zaidi et al, annexin A2 may be linked to COVID-19 pathophysiology. Annexin A2 acts as a co-receptor for the conversion of plasminogen to plasmin in the presence of t-PA. Increased plasmin levels are found in co-morbid states and is also responsible for early stages of viral infection. Plasmin leads to direct activation of STAT-3 inducing detrimental COVID-19 sequelae. Ivermectin directly inhibits STAT-3 and could play a role in the inhibition of COVID-19 complications.

Level 19: Action on CD147 on the RBC

The transmembrane receptor CD147, present on the red blood cell (RBC) along with ACE-2 has been recognized as a key binding site for SARS-CoV-2 spike protein. The SARS-CoV-2 does not internalize into the RBC but such attachments can lead to clumping [65]. Ivermectin binds to the S protein of the virus making it unavailable to bind with CD147. This action might also be beneficial in advanced stages of COVID-19 presenting with clotting/thrombotic phenomena.

Level 20: Action on mitochondrial ATP under hypoxia on cardiac function

SARS-CoV-2 has been a well-known cause for acute myocardial injury and chronic damage to the cardiovascular

system in active infection as well as in long haulers [66]. Nagai et al. demonstrated that Ivermectin increased mitochondrial ATP production by inducing Cox6a2 expression and maintains mitochondrial ATP under hypoxic conditions preventing pathological hypertrophy and improving cardiac function [67].

Conclusion

Considering the urgency of the ongoing COVID-19 pandemic, simultaneous detection of various new mutant strains and future potential re-emergence of novel coronaviruses, repurposing of approved drugs such as Ivermectin could be worthy of attention.

Acknowledgements We would like to thank all the academicians, physicians, and scientists dedicating their efforts and time to COVID-19 research. A special thank you to children who bring positivity and hope in these difficult times, especially Ginevra Dehgani.

Compliance with ethical standards

Conflict of interest The authors declare no competing interest.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

1. Gharebaghi R, Heidary F. COVID-19 and Iran: swimming with hands tied! Swiss Med Wkly. 2020;150:w20242. https://doi.org/10.4414/smw.2020.20242
2. Crump A, Ōmura S. Ivermectin, 'wonder drug' from Japan: the human use perspective. Proc Jpn Acad Ser B Phys Biol Sci. 2011;87:13–28. https://doi.org/10.2183/pjab.87.13
3. Kircik LH, Del Rosso JQ, Layton AM, Schauber J. Over 25 years of clinical experience with ivermectin: an overview of safety for an increasing number of indications. J Drugs Dermatol. 2016;15:325–32.
4. Gonzalez Canga A, et al. The pharmacokinetics and interactions of ivermectin in humans–a mini-review. AAPS J. 2008;10:42–6. https://doi.org/10.1208/s12248-007-9000-9
5. Kumar BS, Jeyaraman M, Jain R, Anudeep TC. A Wonder Drug in the Arsenal against COVID—19: Medication Evidence from Ivermectin. J Adv Med Med Res 2020;32:30–37. [CrossRef]
6. Novac N. Challenges and opportunities of drug repositioning. Trends Pharm Sci. 2013;34:267–72.
7. ClinicalTrials.gov [Internet]. Clinicaltrials.gov. 2021 [cited 2 May 2021]. Available from: https://clinicaltrials.gov/ct2/home Home - ClinicalTrials.gov.
8. Ivermectin for COVID-19: real-time meta analysis of 52 studies [Internet]. Ivmmeta.com. 2021 [cited 2 May 2021]. Available from: https://ivmmeta.com/.
9. López-Medina E, et al. Effect of Ivermectin on time to resolution of symptoms among adults with mild COVID-19: a randomized clinical trial. JAMA 2021;325:1426–35. https://doi.org/10.1001/jama.2021.3071
10. Edwards G, Dingsdale A, Helsby N, Orme ML, Breckenridge AM. The relative systemic availability of ivermectin after administration as capsule, tablet, and oral solution. Eur J Clin Pharm. 1988;35:681–4.
11. Verrest L, Dorlo TPC. Lack of clinical pharmacokinetic studies to optimize the treatment of neglected tropical diseases: a systematic review. Clin Pharmacokinet. 2017;56:583–606.
12. Klotz U, Ogbuokiri JE, Okonkwo PO. Ivermectin binds avidly to plasma proteins. Eur J Clin Pharmacol 1990;39:607–8. https://doi.org/10.1007/BF00316107
13. Wu MA, Fossali T, et al. Hypoalbuminemia in COVID-19: assessing the hypothesis for underlying pulmonary capillary leakage. J Intern Med. 2021 Jan. https://doi.org/10.1111/joim.13208.
14. Baudou E, et al. Serious Ivermectin toxicity and human ABCB1 nonsense mutations. N. Engl J Med. 2020;383:787–9. https://doi.org/10.1056/NEJMc1917344.
15. World Health Organization. Application for Inclusion of Ivermectin on the WHO Model List of Essential Medicines (EML) and Model List of Essential Medicines for Children (EMLc) 2016.
16. Martin RJ, Robertson AP, Choudhary S. Ivermectin: an anthelmintic, an insecticide, and much more. Trends Parasitol. 2021;37:48–64. https://doi.org/10.1016/j.pt.2020.10.005. Epub 2020 Nov 11. PMID: 33189582; PMCID: PMC7853155
17. Chandler RE. Serious neurological adverse events after ivermectin-do they occur beyond the indication of onchocerciasis? Am J Trop Med Hyg. 2018;98:382–8. https://doi.org/10.4269/ajtmh.17-0042
18. Wang Q, Zhang Y, Wu L, Niu S, Song C, Zhang Z et al. Structural and functional basis of SARS-CoV-2 entry by using human ACE2. Cell. 2020. https://doi.org/10.1016/j.cell.2020.03.045.
19. Wu A, Peng Y, Huang B et al. (2020) Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe. https://doi.org/10.1016/j.chom.2020.02.001
20. Mielech AM, Kilianski A, Baez-Santos YM, Mesecar AD, Baker SC. MERS-CoV papain-like protease has deISGylating and deubiquitinating activities. Virology 2014;450–451:64–70.
21. BioS 353 [Internet]. Lehigh.edu. 2021 [cited 2 May 2021]. Available from: https://www.lehigh.edu/~jas0/V14.html
22. Lehrer S, Rheinstein PH. Ivermectin Docks to the SARS-CoV-2 Spike Receptor-binding Domain Attached to ACE2. Vivo 2020;34:3023–6. https://doi.org/10.21873/invivo.12134. PMID: 32871846; PMCID: PMC7652439
23. Eweas AF, Alhossary AA, Abdel-Moneim AS. Molecular docking reveals Ivermectin and Remdesivir as potential repurposed drugs against SARS-CoV-2. Front Microbiol 2021;11:592908 https://doi.org/10.3389/fmicb.2020.592908. Published 2021 Jan 25
24. Choudhury A, Das NC, Patra R, Bhattacharya M, Ghosh P, Patra BC, et al. Exploring the binding efficacy of ivermectin against the key proteins of SARS-CoV-2 pathogenesis: an in silico approach. Future Virol. 2021;10.2217/fvl-2020-0342. https://doi.org/10.2217/fvl-2020-0342.
25. Fulcher A, Jans DA. Regulation of nucleocytoplasmic trafficking of viral proteins; an integral role in pathogenesis?. Biochem. Biophys. 2011;1813:2176–90.
26. Yang SNY, Atkinson SC, Wang C, Lee A, Bogoyevitch MA, Borg NA, et al. The broad spectrum antiviral ivermectin targets the host nuclear transport importin α/β1 heterodimer. Antivir Res. 2020;177:104760.
27. Freedman JC (2012) Chapter 4 - Ionophores in planar lipid bilayers. In: Sperelakis N (ed) Cell Physiology Source Book, 4th edn. Academic Press, pp 61–66 ISBN 9780123877383.
28. Rizzo E. Ivermectin, antiviral properties and COVID-19: a possible new mechanism of action. Naunyn Schmiedebergs Arch Pharm. 2020;393:1153–6. https://doi.org/10.1007/s00210-020-01902-5

29. Heidary F, Gharebaghi R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. J Antibiot. 2020;73:593–602. https://doi.org/10.1038/s41429-020-0336-z
30. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. Antiviral Res. 2020:104787. https://doi.org/10.1016/j.antiviral.2020.104787.
31. U Arshad, H Pertinez, H Box, et al. Prioritization of Anti-SARS-Cov-2 drug repurposing opportunities based on plasma and target site concentrations derived from their established human pharmacokinetics. Clin Pharmacol Ther (2020), https://doi.org/10.1002/cpt.1909
32. Yagisawa M, Foster PJ, Hanaki H, Ōmura S Global trends in clinical studies of ivermectin in COVID-19. The japanese journal of antibiotics. 44. 74-1
33. Ananta Swargiary. Ivermectin as a promising RNA-dependent RNA polymerase inhibitor and a therapeutic drug against SARS-CoV2: evidence from in silico studies, 09 September 2020, PREPRINT (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-73308/v1]
34. V'kovski P, Kratzel A, Steiner S, et al. Coronavirus biology and replication: implications for SARS-CoV-2. Nat Rev Microbiol. 2021;19:155–70. https://doi.org/10.1038/s41579-020-00468-6
35. Ma Y, Wu L, Shaw N, Gao Y, Wang J, Sun Y, et al. Structural basis and functional analysis of the SARS coronavirus nsp14-nsp10 complex. Proc Natl Acad Sci USA. 2015;112:9436–41.
36. Sekimoto T, Imamoto N, Nakajima K, Hirano T, Yoneda Y. Extracellular signal-dependent nuclear import of Stat1 is mediated by nuclear pore-targeting complex formation with NPI-1, but not Rch1. EMBO J. 1997;16:7067–77.
37. Konno Y, Kimura I, Uriu K, Fukushi M, Irie T, Koyanagi Y et al. SARS-CoV-2 ORF3b is a potent interferon antagonist whose activity is further increased by a naturally occurring elongation variant. bioRxiv. 2020. https://doi.org/10.1016/j. celrep.2020.108185.
38. Yang D, Chu H, Hou Y, Chai Y, Shuai H, Lee AC-Y et al. Attenuated interferon and pro-inflammatory response in SARSCoV-2-infected human dendritic cells is associated with viral antagonism of STAT1 phosphorylation. J Infect Dis. 2020. https://doi.org/10.1093/infdis/jiaa356.
39. Matsuyama T, Kubli SP, Yoshinaga SK, et al. An aberrant STAT pathway is central to COVID-19. Cell Death Differ. 2020;27:3209–25. https://doi.org/10.1038/s41418-020-00633-7
40. Seth C, Mas C, Conod A, Mueller J, Siems K, Kuciak M, et al. LongLasting WNT-TCF response blocking and epigenetic modifying activities of withanolide f in human cancer cells. PLoS One. 2016;11:e0168170.
41. Park A, Iwasaki A, Type I. and type III interferons—induction, signaling, evasion, and application to combat COVID-19. Cell Host Microbe. 2020;27:870–8.
42. Zhang X, Song Y, Ci X, et al. Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. Inflamm Res. 2008;57:524–9. https://doi.org/10.1007/s00011-008-8007-8. [PMID: 19109745]
43. Liu T, Zhang L, Joo D, Sun S-C. NF-κB signaling in inflammation. Signal Transduct Target Ther. 2017;2:17023 https://doi.org/10.1038/sigtrans.2017.23. [PMID: 29158945]
44. Jiang L, Wang P, Sun YJ, Wu YJ. Ivermectin reverses the drug resistance in cancer cells through EGFR/ERK/Akt/NF-κB pathway. J Exp Clin Cancer Res. 2019;38:265 https://doi.org/10.1186/s13046-019-1251-7. [PMID: 31215501]
45. Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load dynamics and disease severity in patients infected with SARSCoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ 2020;369:m1443.
46. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2015432.
47. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. *J Infect.* 2020. https://doi.org/10.1016/j.jinf.2020.04.021
48. Diao B, Wang C, Tan Y, Chen X, Liu Y, Ning L, et al. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). Front Immunol. 2020;11:827.
49. Hadjadj J, Yatim N, Barnabei L, Corneau A, Boussier J, Smith N, et al. Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. Science 2020;369:718–24.
50. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z, et al. Level is positively associated with the severity of COVID-19. Ann Clin Microbiol Antimicrob. 2020;19:18.
51. Bharadwaj U, Kasembeli MM, Robinson P, Tweardy DJ. Targeting janus kinases and signal transducer and activator of transcription 3 to treat inflammation, fibrosis, and cancer: rationale, progress, and caution. Pharm Rev. 2020;72:486–526.
52. Frieman M, Yount B, Heise M, Kopecky-Bromberg SA, Palese P. BaricRS. Severe acute respiratory syndrome coronavirus ORF6 antagonizes STAT1 function by sequestering nuclear import factors on the rough endoplasmic reticulum/golgi membrane. J Virol. 2007;81:9812–24.
53. Kim J-H, Choi HS, Kim S-L, Lee D-S. The PAK1-Stat3 signaling pathway activates IL-6 gene transcription and human breast cancer stem cell formation. Cancers 2019;11:1527.
54. Dou Q, Chen H-N, Wang K, Yuan K, Lei Y, Li K, et al. Ivermectin induces cytostatic autophagy by blocking the PAK1/Akt axis in breast cancer. Cancer Res. 2016;76:4457–69.
55. de Melo GuilhermeDias, et al. Anti-COVID-19 efficacy of ivermectin in the golden hamster. bioRxiv. 2020. https://doi.org/10.1101/2020.11.21.392639. 11.21.392639..
56. Priel A, Silberberg SD. Mechanism of ivermectin facilitation of human P2X4 receptor channels. J Gen Physiol. 2004;123:281–93. https://doi.org/10.1085/jgp.200308986.
57. Stokes L, Layhadi JA, Bibic L, Dhuna K, Fountain SJ. P2X4 receptor function in the nervous system and current breakthroughs in pharmacology. Front Pharm. 2017;8:291 https://doi.org/10.3389/fphar.2017.00291
58. Layhadi JA, Turner J, Crossman D, Fountain SJ. ATP evokes Ca2 + responses and CXCL5 secretion via P2X4 receptor activation in human monocyte-derived macrophages. J Immunol Balt Md 1950 2018;200:1159 https://doi.org/10.4049/jimmunol.1700965
59. Andersson U, Ottestad W, Tracey KJ. Extracellular HMGB1: a therapeutic target in severe pulmonary inflammation including COVID-19? Mol Med. 2020;26:42.
60. Juarez M, Schcolnik-Cabrera A, Dueñas-Gonzalez A. The multitargeted drug ivermectin: from an antiparasitic agent to a repositioned cancer drug. Am J Cancer Res. 2018;8:317–31. Published 2018 Feb 1
61. Xydakis MS, Dehgani-Mobaraki P, Holbrook EH, et al. Smell and taste dysfunction in patients with COVID-19. Lancet Infect Dis. 2020;20:1015–6. https://doi.org/10.1016/S1473-3099(20)30293-0. Epub 2020 Apr 15. PMID: 32304629; PMCID: PMC7159875
62. Ci X, Li H, Yu Q. Avermectin exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen-activated protein kinase activation pathway. Fundam Clin Pharm. 2009;23:449–55.
63. Yan S, Ci X, Chen N. Anti-Inflammatory effects of ivermectin in mouse model of allergic asthma. Inflamm Res. 2011;60:589–96.
64. Kamber Zaidi A, Dawoodi S, Pirro M, Monti M, Dehgani Mobaraki P. Key role of Annexin A2 and Plasmin in COVID-19 pathophysiology, clinical presentation and outcomes – A Review.

Italian Journal of Prevention, Diagnostic and Therapeutic Medicine [Online] 2020;3: Available from: https://doi.org/10.30459/2020-24.

65. David E Scheim.Ivermectina for COVID 19 treatment Clinical response at quasi-threshold doses via hypothesized alleviation of CD147 mediated vascular occlusive (June, 2020) SS RN:https://SSRN.com/abstract=3636557.
66. Zheng YY, Ma YT, Zhang JY, et al. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17:259–60. https://doi.org/10.1038/s41569-020-0360-5
67. Nagai H, Satomi T, Abiru A, Miyamoto K, Nagasawa K, Maruyama M, et al. Antihypertrophic effects of small molecules that maintain mitochondrial ATP levels under hypoxia. EBioMedicine 2017;24:147–58. https://doi.org/10.1016/j.ebiom.2017.09.022.

I-MASK+

PREVENTION & EARLY OUTPATIENT TREATMENT PROTOCOL FOR COVID-19

PREVENTION PROTOCOL (for Delta variant)

ANTI-VIRALS & ANTISEPTICS

Ivermectin[2]

Chronic Prevention

0.2 mg/kg per dose (take with or after a meal) — twice a week for as long as disease risk is elevated in your community.

Post COVID-19 Exposure Prevention[3]

0.4 mg/kg per dose (take with or after a meal) — one dose today, repeat after 48 hours.

Gargle mouthwash

2 x daily – gargle (do not swallow) antiseptic mouthwash with cetylpyridinium chloride (e.g. Scope™, Act™, Crest™), 1% povidone/iodine solution or Listerine™ with essential oils.

IMMUNE FORTIFYING / SUPPORTIVE THERAPY

Vitamin D3	1,000–3,000 IU/day
Vitamin C	500–1,000 mg 2 x daily
Quercetin	250 mg/day
Zinc	30–40 mg/day (elemental zinc)
Melatonin	6 mg before bedtime (causes drowsiness)

IVERMECTIN ALTERNATIVE

Nigella Sativa 40 mg/kg daily [4]
(black cumin seed)

To be used if ivermectin not available or added to ivermectin for optimal prevention.

EARLY TREATMENT PROTOCOL → see page 2

Supporting information

Questions regarding the multiple additions to the I-MASK+ protocol for the Delta variant can be found in our Frequently Asked Questions page flccc.net/new-i-mask-faqs. Here you will find answers to the the critical role of anti-androgen therapy, the safety and need for higher dosing of ivermectin, and guidance on the number of components of the protocol that should be used in the treatment of an individual patient.

Efficacy of Ivermectin

Ivermectin is a medication uniquely suited to treat COVID-19 given its now well-described, potent anti-viral and anti-inflammatory properties.

The efficacy of ivermectin is supported by results from 64 controlled trials, 32 of them randomized, and 16 of those were double-blinded, the gold standard of research design. A summary (meta-analysis) of these trials find statistically significant reductions in transmission, time to recovery, hospitalization, and death.

The most up-to-date summary of the totality of the supportive evidence for ivermectin in COVID-19 can be found here: flccc.net/flccc-summary-of-the-evidence-of-ivermectin-in-covid-19

Finally, in a historic achievement of public health, as of September 16, 2021, the North Indian state of Uttar Pradesh has effectively eradicated COVID from its population of 241 million people after widely distributing ivermectin in their treatment and prevention protocols for COVID-19. Please see also The Latest Results of Ivermectin's Success in Treating Outbreaks of COVID-19.

For an overview of the developments in prevention and treatment of COVID-19, please visit flccc.net/covid-19-protocols.

Please check our homepage regularly for updates of our COVID-19 Protocols! — New medications may be added and/or dose changes to existing medications may be made as further scientific studies emerge.

CONSULT HEALTH CARE PROVIDER

Discuss all protocol elements as well as the role of vaccination.[1]

WEAR MASKS

Wear a cloth, surgical, or N95 mask when in confined, poorly ventilated, crowded indoor spaces with non-household members.

KEEP DISTANCE

Until the end of the COVID-19 crisis, we recommend keeping a minimum distance of approx. 2 m / 6 feet in public from people who are not from your own household.

WASH HANDS

We recommend, after a stay during and after outings from home (shopping, subway etc.), a thorough hand cleaning (20–30 sec. with soap), or also to use a hand disinfectant in between.

I-MASK+

PREVENTION & EARLY OUTPATIENT TREATMENT PROTOCOL FOR COVID-19

EARLY TREATMENT PROTOCOL[5] (for Delta variant)

1. First line agents (use any or all medicines; listed in order of priority/importance)

ANTI-VIRALS

Ivermectin[2]
0.4–0.6 mg/kg per dose (take with or after a meal) — one dose daily, take for 5 days or until recovered. Use upper dose if: **1)** in regions with aggressive variants (e.g. Delta); **2)** treatment started on or after day 5 of symptoms or in pulmonary phase; or **3)** multiple comorbidities/risk factors.

and/or Nitazoxanide
500 mg 2 x daily for 5 days after meals. Combine with ivermectin (preferred) or substitute if ivermectin is not available. (Nitazoxanide is often unavailable or high-priced in the USA.)

ANTI-SEPTIC ANTI-VIRALS

Antiviral mouthwash: Gargle 3 x daily (do not swallow; must contain chlorhexidine, povidone-iodine, or cetylpyridinium chloride). **Iodine nasal spray/drops:** Use 1% povidone-iodine commercial product as per instructions 2–3 x daily. If 1%-product not available, must first dilute the more widely available 10%-solution[6] and apply 4–5 drops to each nostril every 4 hours. (No more than 5 days in pregnancy.)

ANTI-COAGULANTS / IMMUNE FORTIFYING

Aspirin	325 mg daily (unless contraindicated)
Vitamin D	Vitamin D3 5,000 IU daily. Preferred form if available: Calcitriol 0.5 mcg on day 1, then 0.25 mcg daily for 7 days
Melatonin	10 mg before bedtime (causes drowsiness)

SYNERGISTIC THERAPIES

Quercetin	250 mg 2 x daily
Zinc	100 mg/day (elemental zinc)
Vitamin C	500–1,000 mg 2 x daily

NUTRITIONAL THERAPEUTICS (for 14 days)[4]

Curcumin	(turmeric)	500 mg 2 x daily
Nigella Sativa	(black cumin seed)	80 mg/kg daily
Honey		1 gram/kg daily

PULSE OXIMETER

Monitoring of oxygen saturation is recommended (for instructions see page 3)

2. Second line agents (listed in order of priority/importance)

Add to first line therapies above if: 1) ≥5 days of symptoms; 2) Poor response to therapies above; 3) Significant comorbidities.

DUAL ANTI-ANDROGEN THERAPY

1. **Spironolactone** 100 mg 2 x daily for ten days.
2. **Dutasteride** 2 mg on day 1, followed by 1 mg daily for 10 days. If dutasteride not available, use **Finasteride** 10 mg daily for 10 days.

FLUVOXAMINE

50 mg 2 x daily for 10 days[7]
Consider **Fluoxetine** 30 mg daily for 10 days as an alternative (it is often better tolerated). Avoid if patient is already on an SSRI.

MONOCLONAL ANTIBODY THERAPY

Casirivimab/Imdevimab[8]
600 mg each in a single subcutaneous injection. Antibody therapy is for patients within 7 days of first symptoms and one or more risk factors as: Age>65y; BMI>25; pregnancy; chronic lung, heart, or kidney disease; diabetes; immunosuppressed; developmental disability; chronic tracheostomy; or feeding tube.

3. Third line agent

If below criteria are met, consider

CORTICOSTEROIDS

Prednisone or Methylprednisolone
1 mg/kg daily for 5 days followed by slow taper or escalation according to patient response.

Criteria:

After day 7–10 from first symptoms and patient has either: abnormal chest x-ray, shortness of breath, or oxygen saturations of 88–94%.

If oxygen saturation is lower than 88%, emergency room evaluation should be sought.

Notes

1 The I-MASK+ protocol is a bridge to vaccines and a safety net for those who cannot or have not been vaccinated; or are vaccinated and have concerns regarding declining protection against emerging variants. Vaccines have shown efficacy in preventing the most severe outcomes of COVID-19 and are an important part of a multi-modal strategy that must also include early treatment. The decision to get a vaccine should be made in consultation with your health care provider.

2 The dosing may be updated as further scientific studies emerge. The safety of ivermectin in pregnancy has not been definitively established. Use in the 1st trimester should be discussed with your doctor.

3 To use if a household member is COVID-19 positive, or you have prolonged exposure to a COVID-19 positive patient without wearing a mask.

4 For more information on nutritional therapeutics and how they can help with COVID-19 please see: flccc.net/covid-19-protocols/nutritional-therapeutics

5 For late phase – *hospitalized patients* – see the FLCCC's "MATH+ Hospital Treatment Protocol for COVID-19" on www.flccc.net

6 To make 1% povidone/iodine concentrated solution from 10% povidone/iodine solution, *it must be diluted first.*

One dilution method is as follows:

- First pour 1½ tablespoons (25 ml) of 10% povidone/iodine solution into a nasal irrigation bottle of 250 ml.
- Then fill to top with distilled, sterile or previously boiled water.
- Tilt head back, apply 4–5 drops to each nostril. Keep tilted for a few minutes, let drain.

7 Some individuals who are prescribed fluvoxamine experience acute anxiety which needs to be carefully monitored for and treated by the prescribing clinician to prevent rare escalation to suicidal or violent behavior.

8 This medication requires an infusion center. To find the nearest location in the U.S., visit www.infusioncenter.org or call for eligibility and location 1-877-332-6585 for English and 1-877-366-0310 for Spanish.

I-MASK+

PREVENTION & EARLY OUTPATIENT TREATMENT PROTOCOL FOR COVID-19

Additional information

Pulse Oximeter (usage instructions)

In symptomatic patients, monitoring with home pulse oximetry is recommended (due to asymptomatic hypoxia). The limitations of home pulse oximeters should be recognized, and validated devices are preferred. Multiple readings should be taken over the course of the day, and a downward trend should be regarded as ominous. Baseline or ambulatory desaturation < 94% should prompt hospital admission. The following guidance is suggested:

- Use the index or middle finger; avoid the toes or ear lobe.
- Only accept values associated with a strong pulse signal.
- Observe readings for 30–60 seconds to identify the most common value.
- Remove nail polish from the finger on which measurements are made.
- Warm cold extremities prior to measurement.

Calculation for ivermectin dose (0.2 mg per kg)

Body weight Conversion: 1 kg ≈ 2.2 lbs (doses calculated per upper end of weight range)		Dose 0.2 mg/kg ≈ 0.09 mg/lb (Each tablet = 3 mg; doses rounded to nearest half tablet above)	
70–90 lb	32–40 kg	8 mg	(3 tablets = 9 mg)
91–110 lb	41–50 kg	10 mg	(3.5 tablets)
111–130 lb	51–59 kg	12 mg	(4 tablets)
131–150 lb	60–68 kg	13.5 mg	(4.5 tablets)
151–170 lb	69–77 kg	15 mg	(5 tablets)
171–190 lb	78–86 kg	16 mg	(5.5 tablets)
191–210 lb	87–95 kg	18 mg	(6 tablets)
211–230 lb	96–104 kg	20 mg	(7 tablets = 21 mg)
231–250 lb	105–113 kg	22 mg	(7.5 tablets=22.5 mg)
251–270 lb	114–122 kg	24 mg	(8 tablets)
271–290 lb	123–131 kg	26 mg	(9 tablets = 27 mg)
291–310 lb	132–140 kg	28 mg	(9.5 tablets=28.5 mg)

For higher doses used in our I-MASK+ Protocol please multiply the value found in the table for 0.2 mg/kg, e.g.:

- **0.4 mg/kg:** double the 0.2 mg/kg dose
- **0.6 mg/kg:** triple the 0.2 mg/kg dose

Tablets can be halved for more accurate dosing. Then round to nearest half tablet above.

Note that Ivermectin is available in different tablet strengths (e.g. with 3, 5 or 6 mg) and administration forms (tablets, drops) depending on the country (please refer to the package information).

In our table we calculate doses using 3 mg tablets (the most common dose per tablet in the U.S.).

If your tablets contain a different amount of ivermectin than 3 mg, you must calculate the number of tablets to equal the dose of ivermectin required.

Disclaimer

The "I-MASK+ Prevention & Early Outpatient Treatment Protocol for COVID-19" is solely for educational purposes regarding potentially beneficial therapies for COVID-19. Never disregard professional medical advice because of something you have read on our website and releases. This protocol is not intended to be a substitute for professional medical advice, diagnosis, or treatment in regards to any patient. Treatment for an individual patient should rely on the judgement of your physician or other qualified health provider. Always seek their advice with any questions you may have regarding your health or medical condition. Please note our full disclaimer at: www.flccc.net/disclaimer

Please check our homepage regularly for updates of our COVID-19 Protocols!
New medications may be added and/or dose changes to existing medications may be made as further scientific studies emerge.

TESTIMONY HB 1022
Rep. Jerry Knirk, Carroll-3 Jan 18, 2022
Retired orthopedic surgeon

The decision to use a medication or surgical intervention is based upon an analysis of the risks and benefits of the proposed intervention to treat a specific clinical diagnosis, using the best currently available evidence. If there is clear benefit with a low risk profile, then using the intervention may be a good choice. It may even be a good choice if risk is moderate but the benefit is substantial.

We have received numerous emails from people claiming the ivermectin worked because they took it and recovered. But those anecdotes are not data. They mean nothing since most people who develop COVID recover.

Determining the benefits and risks require well designed studies, analyzed by investigators free of conflict of interest. Analyzing studies requires a high level of knowledge of study design, randomization protocols, comparison of the intervention and control groups to ensure they are comparable, analysis of the statistical power, and an understanding of the limitations of the studies. Many studies which look compelling, upon further analysis either have design flaws, do not apply to the clinical situation, have study groups which are too small, do not reach statistical significance or are not reproducible by other investigators.

Ivermectin has clear benefit for certain indications such as treating parasitic worms and even some external parasites. The risk profile in appropriate doses is small, but include headache, dizziness, muscle pain, nausea and diarrhea, birth defects, potential neurologic effects, and interaction with other medications..

The rational for using ivermectin for COVID is based upon the ability of ivermectin to inhibit SARS-CoV-2 in cell cultures, but this does not necessarily predict success in the clinical setting as massive doses are necessary. Numerous clinical studies have been published with conflicting results. Most ivermectin studies published so far are limited by too small sample sizes, non-blinding, the use of concomitant medications which confound the assessment, and poorly defined study groups and outcome measures. Even the well designed studies still have significant limitations

such that definitive conclusions regarding the clinical efficacy of ivermectin in the treatment of COVID can not yet be reached.

As an example, the sponsor distributed to us by email a meta-analysis by Bryant. The table on page e442 demonstrated that the quality of evidence for various endpoints was very low for 7, low for 4, and moderate for 1. That is not very compelling. The one outcome which was graded as moderate quality of evidence was based substantially on the paper from Egypt by Elgazzar which was later retracted when it was found to be fraudulent.

The Cochrane organization has decades of experience in meta-analyses and their analysis has found that most studies are very low- to low-certainty evidence. Only a few are high quality and do not support the use of ivermectin for treatment or prevention of COVID outside of well-designed clinical trials.

Currently, best available evidence does not show ivermectin is effective against COVID-19. There are numerous ongoing clinical trials on its effectiveness. The Infectious Disease Society of America recommends the use of ivermectin only in the context of clinical trials until we have better data.

Standing orders with pharmacists should never be used for medications being used for indications which are not clearly supported by the best available medical evidence. Ivermectin does not reach this level of evidence. As a result, this bill should be voted ITL.

References:

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

https://www.fda.gov/consumers/consumer-updates/why-you-should-not-use-ivermectin-treat-or-prevent-covid-19

https://www.covid19treatmentguidelines.nih.gov/tables/ivermectin-data/

Safety of Ivermectin

Standard doses of ivermectin (0.2 mg/kg x 1–2 days) have a nearly unparalleled safety profile historically among medicines as evidenced by the following findings:

- **WHO Guidelines for Scabies**: "the majority of side effects are minor and transient"
- **Prof Jacques Descotes, Toxicologist, Expert on Safety of Ivermectin:** "severe adverse events are unequivocally and exceedingly rare"
- **LiverTox Database**: Not considered toxic to the liver
- **Nephrotox Database-** Not considered toxic to the kidney
- **PneumoTox:** Not considered toxic to the lungs

Safety of High Dose Ivermectin

In COVID-19, particularly in regard to the emerging variants of concern, viral loads are higher and viral replication is thought to be prolonged. Given that ivermectin has demonstrated a strong dose-response relationship in terms of viral clearance, higher doses have not only been required, but have demonstrated clinical efficacy. Below are hyperlinked references to numerous studies demonstrating the wide safety profile of high dose ivermectin in COVID and other diseases

COVID-19 Studies

1) Randomized controlled trial of ivermectin in COVID using 0.6mg/kg x 5 days reported no differences in side effects.
2) Randomized controlled trial, with 3 arms; one arm treated with 1.2 mg/kg for 5 days, and another treated with 0.6mg/kg for 5 days with no differences in side effects
3) A report by the State Health Minister on 3,000 patients in La Pampa, Argentina who were part of a "test and treat" program were given 0.6 mg/kg daily for 5 days. Liver function tests and significant side effects were closely monitored and none were reported.
4) A report by the Health Minister in Misiones, Argentina, also using 0.6 mg/kg for 5 days with no significant adverse events reported.

Malaria Studies

1) Safety trial of patients with malaria given 0.3, 0.6, and 1.2 mg/kg daily of ivermectin for 7 days was well tolerated with no adverse events
2) Study of "Efficacy and Safety of High dose ivermectin for Reducing Malaria Transmission" compared 0, 0.3 and 0.6 mg/kg for 3 days and found no differences in side effects.

Healthy Volunteers

1) Report of a group of healthy adult subjects given up to 10x standard dose, either 2-4x the standard dose three times a week or 6–10x standard dose once and found the doses generally well tolerated

Systematic Reviews

1) A systematic review and meta-analysis of high dose ivermectin found no difference in side effects between dose of up to 0.4 mg/kg and higher doses (up to 0.8 mg/kg doses every 3 months.
2) A comprehensive review of 350 articles by the famous French toxicologist Jacques Descotes was presented in early 2021. In this document, he states,

    a. "Based on all the data presented above, the author of this report believes it is fair to say that ivermectin did not directly induce an excess of deaths in treated groups of human subjects. Statements, past or present, that ivermectin can kill patients, are therefore considered to be misleading as they do not take into account all the medical information that has been accumulated over the last decades."
    b. "Only very few cases of accidental human overdose have been reported despite the wide availability of ivermectin as a veterinary and human medicine [Hall et al., 1985;Graeme et al., 2000; Deraemecker et al., 2014; Goossens et al., 2014]. Usually, moderate neurotoxic manifestations with rapid recovery after unspecific supportive measures were the predominating course of events. No accidental overdose including in infants and young children had a lethal outcome."

Case Series

1) A case series of 3 children with relapsed leukemia treated with high dose (1.0 mg/kg) ivermectin daily for between 2 weeks and 6 months reported no significant adverse events.

FLCCC Alliance
September 21, 2021

Dartmouth-Hitchcock

Dartmouth-Hitchcock Medical Center
One Medical Center Drive
Lebanon, NH 03756-0001
Phone (603) 650-5000
Dartmouth-Hitchcock.org

January 18, 2022
Members of the House Health, Human Services and Elderly Affairs Committee

HB 1022, permitting pharmacists to dispense the drug Ivermectin by means of a standing order

Thank you for the opportunity to comment on HB 1022. We are *opposed* to this bill for several reasons.

First and foremost, Ivermectin is not recommended by the CDC, FDA, NIH or IDSA to treat COVID-19 outside of clinical trials. Please see attached for risks involved in treating COVID-19 with Ivermectin. Fortunately, effective therapeutics exist: In addition to monoclonal antibody therapeutics, the FDA has granted emergency use authorization for Pfizer's Paxlovid and Merck's Molnupiravir antiviral medications.

There are also logistical concerns with the bill: It is not clear who would be responsible for writing a standing order - the state of New Hampshire's Chief Medical Officer or the chief medical officer at a hospital or other health care facility? Nor is it clear that a standing order would be necessary at all as any provider can write for Ivermectin or any other medication if they so choose.

The purpose of standing orders is to increase access to care where there are demonstrated benefits to the general public by getting prescriptions/vaccines into the hands of patients as quickly as possible. If the general public isn't getting Ivermectin, it is because it doesn't work – and no provider should be compelled to issue a standing order for, nor should a pharmacist feel obligated to dispense, a product that has not demonstrated safety and efficacy.

Thank you for your time and consideration. We are happy to answer any questions.

Michael S. Calderwood, MD, MPH, FIDSA
Chief Quality Officer, Dartmouth Hitchcock Medical Center
Associate Professor of Medicine, Geisel School of Medicine at Dartmouth
Staff Physician, Infectious Disease & International Health

Staci A. Hermann, PharmD, MS, Chief Pharmacy Officer
Dartmouth-Hitchcock Health

GET THE FACTS

Ivermectin and COVID-19

What is ivermectin?

Ivermectin is a medication used for parasitic infections (primarily worms) and is safe when used at recommended doses.

Should ivermectin be used to treat COVID-19?

No. The doses needed to possibly work against COVID-19 in a test tube are

50-100x HIGHER

than current recommended doses. These doses would not be safe in humans.

What are the risks of using ivermectin to treat COVID-19?

If you use veterinary ivermectin, or very high doses of ivermectin, you could have significant nervous system toxicity. This includes severe side effects such as **confusion**, **coma**, **seizures**, and **death**.

The bottom line

Ivermectin has not been proven to treat COVID-19, and it can cause harm.

For information on effective COVID-19 treatments visit: **COVID19LearningNetwork.org**

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

New Hampshire Hospital Association

HOUSE HEALTH, HUMAN SERVICES AND ELDERLY AFFAIRS COMMITTEE

Tuesday, January 18, 2022

HB 1022 – Permitting Pharmacists to Dispense the Drug Ivermectin by Means of a Standing Order

Testimony

Good afternoon, Mr. Chairman and members of the committee. My name is Paula Minnehan, Senior Vice President with the New Hampshire Hospital Association (NHHA), representing all 26 of the state's community hospitals as well as all specialty hospitals.

The NHHA is opposed to HB 1022. The bill before you would allow pharmacists to dispense Ivermectin pursuant to a standing order entered into by licensed health care providers. We consulted with our hospitals' pharmacy directors, and all expressed strong opposition to allowing this drug to be used in this manner. The chief medical officers (CMOs) and other clinical leaders have expressed similar concerns.

It is important to understand that the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) and the National Institutes of Health (NIH) as well as other federal agencies charged with protecting public safety, all have indicated that Ivermectin is not recommended to treat COVID-19. The FDA has not authorized or approved ivermectin for use in preventing or treating COVID-19 in humans or animals. Currently available data do not show that ivermectin is effective against COVID-19. Clinical trials assessing ivermectin tablets for the prevention or treatment of COVID-19 in people are ongoing. I have attached a document from the FDA to this testimony that explains their position in more detail.

There are many problems with this bill and health care professionals are here today to share those concerns with you and hopefully answer any questions you may have. And, if there are other clinical questions that arise that cannot be answered today, I'm happy to connect the members of this committee with other clinicians that could assist.

Besides the very real clinical concerns about the efficacy of ivermectin, we also are unclear about how the standing order could actually be issued and managed.

For these reasons, NHHA is strongly opposed to this bill. On behalf of our hospitals, we urge you to find HB 1022 inexpedient to legislate.

Thank you for the opportunity to provide our comments in opposition to HB 1022.

Why You Should Not Use Ivermectin to Treat or Prevent COVID-19

Español (/consumers/articulos-en-espanol/por-que-no-debe-utilizar-ivermectina-para-tratar-o-prevenir-el-covid-19)

Português (/consumers/consumer-updates/por-que-voce-nao-deve-usar-ivermectina-para-tratar-ou-prevenir-covid-19)

中文 (/consumers/consumer-updates/weishenmebuyinggaishiyongyiweijunsuzhiliaohuoyufang2019xinguanfeiyan)

Tagalog (/consumers/consumer-updates/bakit-hindi-ka-dapat-gumamit-ng-ivermectin-upang-gamutin-o-maiwasan-ang-covid-19)

Tiếng Việt (/consumers/consumer-updates/tai-sao-ban-khong-nen-su-dung-ivermectin-de-dieu-tri-hoac-ngan-ngua-covid-19)

한국어 (/consumers/consumer-updates/kobideu-19-covid-19leul-chilyohago-yebanghagi-wihayeo-ibeomegtineul-sayonghaji-malaya-haneun-iyu)

COVID-19. We've been living with it for what sometimes seems like forever. Given the number of deaths that have occurred from the disease, it's perhaps not surprising that some consumers are turning to drugs not approved or authorized by the Food and Drug Administration (FDA).

One of the FDA's jobs is to carefully evaluate the scientific data on a drug to be sure that it is both safe and effective for a particular use. In some instances, it can be highly dangerous to use a medicine for the prevention or treatment of COVID-19 that has not been approved by or has not received emergency use authorization from the FDA.

There seems to be a growing interest in a drug called ivermectin for the prevention or treatment of COVID-19 in humans. Certain animal formulations of ivermectin such as pour-on, injectable, paste, and "drench," are approved in the U.S. to treat or prevent parasites in animals. For humans, ivermectin tablets are approved at very specific doses to treat some parasitic worms, and there are topical (on the skin) formulations for head lice and skin conditions like rosacea.

However, the FDA has received multiple reports of patients who have required medical attention, including hospitalization, after self-medicating with ivermectin intended for livestock.

Here's What You Need to Know about Ivermectin

- The FDA has not authorized or approved ivermectin for use in preventing or treating COVID-19 in humans or animals. Ivermectin is approved for human use to treat infections caused by some parasitic worms and head lice and skin conditions like rosacea.
- Currently available data do not show ivermectin is effective against COVID-19. Clinical trials (https://www.clinicaltrials.gov/ct2/results?cond=COVID-19&term=ivermectin&cntry=&state=&city=&dist=&Search=Search) assessing ivermectin tablets for the prevention or treatment of COVID-19 in people are ongoing.
- Taking large doses of ivermectin is dangerous.
- If your health care provider writes you an ivermectin prescription, fill it through a legitimate source such as a pharmacy, and take it *exactly* as prescribed.
- Never use medications intended for animals on yourself or other people. Animal ivermectin products are very different from those approved for humans. Use of animal ivermectin for the prevention or treatment of COVID-19 in humans is dangerous.

What is Ivermectin and How is it Used?

Ivermectin tablets are approved by the FDA to treat people with intestinal strongyloidiasis and onchocerciasis, two conditions caused by parasitic worms. In addition, some topical forms of ivermectin are approved to treat external parasites like head lice and for skin conditions such as rosacea.

Some forms of animal ivermectin are approved to prevent heartworm disease and treat certain internal and external parasites. It's important to note that these products are different from the ones for people, and safe only when used in animals as prescribed.

When Can Taking Ivermectin Be Unsafe?

The FDA has not authorized or approved ivermectin for the treatment or prevention of COVID-19 in people or animals. Ivermectin has not been shown to be safe or effective for these indications.

There's a lot of misinformation around, and you may have heard that it's okay to take large doses of ivermectin. It is not okay.

Even the levels of ivermectin for approved human uses can interact with other medications, like blood-thinners. You can also overdose on ivermectin, which can cause nausea, vomiting, diarrhea, hypotension (low blood pressure), allergic reactions (itching and hives), dizziness, ataxia (problems with balance), seizures, coma and even death.

Ivermectin Products for Animals Are Different from Ivermectin Products for People

For one thing, animal drugs are often highly concentrated because they are used for large animals like horses and cows, which weigh a lot more than we do— up to a ton or more. Such high doses can be highly toxic in humans. Moreover, the FDA reviews drugs not just for safety and effectiveness of the active ingredients, but also for the inactive ingredients. Many inactive ingredients found in products for animals aren't evaluated for use in people. Or they are included in much greater quantity than those used in people. In some cases, we don't know how those inactive ingredients will affect how ivermectin is absorbed in the human body.

Options for Preventing and Treating COVID-19

The most effective ways to limit the spread of COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html) include getting a COVID-19 vaccine when it is available to you and following current CDC guidance.

Talk to your health care provider about available COVID-19 vaccines and treatment options. Your provider can help determine the best option for you, based on your health history.

HB 1022 - AS INTRODUCED

2022 SESSION

22-2137
05/08

HOUSE BILL ***1022***

AN ACT permitting pharmacists to dispense the drug ivermectin by means of a standing order.

SPONSORS: Rep. Cushman, Hills. 2; Rep. Kofalt, Hills. 4; Rep. Sheehan, Hills. 23; Rep. Yakubovich, Merr. 24; Rep. Blasek, Hills. 21; Rep. Torosian, Rock. 14; Rep. Harley, Rock. 20; Rep. T. Lekas, Hills. 37

COMMITTEE: Health, Human Services and Elderly Affairs

ANALYSIS

This bill allows pharmacists to dispense invermectin pursuant to a standing order entered into by licensed health care providers.

- -

Explanation: Matter added to current law appears in ***bold italics.***
Matter removed from current law appears [~~in brackets and struckthrough.~~]
Matter which is either (a) all new or (b) repealed and reenacted appears in regular type.

HB 1022 - AS INTRODUCED

22-2137
05/08

STATE OF NEW HAMPSHIRE

In the Year of Our Lord Two Thousand Twenty Two

AN ACT permitting pharmacists to dispense the drug ivermectin by means of a standing order.

Be it Enacted by the Senate and House of Representatives in General Court convened:

1 New Section; Invermectin; Dispensing. Amend RSA 318 by inserting after section 47-l the following new section:

318:47-m Ivermectin; Dispensing.

I. In this section, "standing order" means a written and signed protocol authored by one or more physicians licensed under RSA 329:12 or one or more advanced practice registered nurses licensed under RSA 326-B:18. Such agreement shall specify a protocol allowing the pharmacist licensed under RSA 318:18 to dispense ivermectin under the delegated prescriptive authority of the physician or APRN, specify a mechanism to document screening performed and the prescription in the patient's medical record, and include a plan for evaluating and treating adverse events. Any such prescription shall be regarded as being issued for a legitimate medical purpose in the usual course of professional practice.

II. Licensed pharmacists following standing orders may dispense ivermectin to persons in this state without a prior prescription.

III. A pharmacist, pharmacy, physician, or APRN issuing or following standing orders shall be prohibited from seeking personal financial benefit by participating in any incentive-based program or accepting any inducement that influences or encourages therapeutic or product changes or the ordering of tests or services.

IV. The pharmacist shall provide each recipient of ivermectin pursuant to this section with a standardized information sheet written in plain language, which shall include, but is not limited to, the importance of follow-up care, and health care referral information. Nothing on the information sheet shall discourage the recipient from using ivermectin for the treatment of COVID-19.

V. The board of medicine shall not deny, revoke, suspend, or otherwise take disciplinary action against a physician based on a pharmacist's failure to follow standing orders provided the provisions of this section and the rules adopted under this section are satisfied. The board of nursing shall not deny, revoke, suspend, or otherwise take disciplinary action against an APRN based on a pharmacist's failure to follow standing orders provided the provisions of this section and the rules adopted under this section are satisfied. The board of pharmacy shall not deny, revoke, suspend, or otherwise take disciplinary action against a pharmacist who follows standing orders based on a defect in those standing orders provided the provisions of this section and the rules adopted under this section are satisfied.

2 Effective Date. This act shall take effect 60 days after its passage.