Ivermectin is effective for COVID-19: real-time meta analysis of 52 studies

Covid Analysis, Nov 26, 2020 (Version 61, Apr 18, 2021)

https://ivmmeta.com/

- 98% of the 52 studies to date report positive effects (25 statistically significant in isolation). Random effects meta-analysis for early treatment and pooled effects shows an 81% reduction, RR 0.19 [0.09-0.38], and prophylactic use shows 85% improvement, RR 0.15 [0.09-0.25]. Mortality results show 76% lower mortality, RR 0.24 [0.14-0.42] for all treatment delays, and 84% lower, RR 0.16 [0.04-0.63] for early treatment.
- 96% of the 27 Randomized Controlled Trials (RCTs) report positive effects, with an estimated 65% improvement, RR 0.35 [0.24-0.52].
- The probability that an ineffective treatment generated results as positive as the 52 studies to date is estimated to be 1 in 85 trillion (p = 0.000000000000012).
- All data to reproduce this paper and the sources are in the appendix. See *[Bryant, Hill, Kory, Lawrie, Nardelli]* for other meta analyses, all with similar results confirming effectiveness.

	Improvement	Studies	Authors	Patients
Early treatment	**81%** [62-91%]	18	175	1,942
Late treatment	**43%** [27-56%]	20	143	6,831
Prophylaxis	**85%** [75-91%]	14	108	8,789
Mortality	**76%** [58-86%]	18	155	7,267
RCTs only	**65%** [48-76%]	27	246	4,854
All studies	**72%** [64-78%]	**52**	**426**	**17,562**

WHO ivermectin approval status				
Indication	Studies	Patients	Effect size	Status
Scabies	6	613	35% [22-46%]	Approved
COVID-19	52	17,562	72% [64-78%]	Pending

Ivermectin COVID-19 early treatment and prophylaxis studies

ivmmeta.com 4/18/21

		Treatment	Control	Dose (4d)	RR	CI	
Chowdhury (RCT)	hosp.	0/60	2/56	14mg	0.19	[0.01-3.96]	OT[1] CT[2]
Espitia-Hernandez	viral+	0/28	7/7	12mg	0.03	[0.01-0.11]	CT[2]
Carvallo	death	1/33	3/12	36mg	0.12	[0.01-1.06]	CT[2]
Cadegiani	death	0/110	2/137	42mg	0.22	[0.01-4.48]	
Ahmed (DB RCT)	symptoms	0/17	3/19	48mg	0.15	[0.01-2.70]	
Chaccour (DB RCT)	symp. prob.	12	12	28mg	0.47	[0.19-1.16]	
Afsar	symptoms	0/37	7/53	48mg	0.08	[0.00-1.32]	
Babalola (DB RCT)	viral+	40	20	24mg	0.36	[0.10-1.27]	OT[1]
Kirti (DB RCT)	death	0/55	4/57	24mg	0.11	[0.01-2.05]	
Bukhari (RCT)	viral+	4/41	25/45	12mg	0.18	[0.07-0.46]	
Raad (SB RCT)	hosp.	0/50	3/50	14mg	0.14	[0.01-2.70]	MD[3]
Mohan (DB RCT)	no recov.	2/40	6/45	28mg	0.38	[0.08-1.75]	
Schwartz (DB RCT)	hosp.	0/49	2/45	36mg	0.19	[0.01-3.92]	
Elalfy	viral+	7/62	44/51	36mg	0.13	[0.06-0.27]	CT[2]
López-Me.. (DB RCT)	death	0/200	1/198	84mg	0.33	[0.01-8.11]	
Roy	recov. time	14	15	n/a	0.94	[0.52-1.93]	CT[2]
Chahla (CLUS. RCT)	no disch.	2/110	8/62	24mg	0.11	[0.02-0.52]	
Mourya	viral+	5/50	47/50	48mg	0.11	[0.05-0.25]	
Early treatment		21/1,008	164/934		0.19	[0.09-0.38]	**81% improvement**

Tau^2 = 1.52; I^2 = 85.0%

		Treatment	Control	Dose (1m)	RR	CI	
Shouman (RCT)	symp. case	15/203	59/101	36mg	0.09	[0.03-0.23]	
Carvallo	cases	0/131	11/98	14mg	0.04	[0.00-0.63]	CT[2]
Behera	cases	41/117	145/255	42mg	0.46	[0.29-0.71]	
Elgazzar (RCT)	cases	2/100	10/100	112mg	0.20	[0.04-0.89]	
Carvallo	cases	0/788	237/407	48mg	0.00	[0.00-0.02]	CT[2]
Hellwig (ECO.)	cases	ecological		14mg	0.22	[0.05-0.89]	
Bernigaud	death	0/69	150/3,062	84mg	0.01	[0.00-0.10]	
Alam	cases	4/58	44/60	12mg	0.09	[0.04-0.24]	
Vallejos	cases	13/389	61/486	48mg	0.27	[0.15-0.48]	MD[3]
Chahla (RCT)	cases	0/117	10/117	48mg	0.05	[0.00-0.80]	CT[2]
Behera	cases	45/2,199	133/1,147	42mg	0.17	[0.12-0.23]	
Tanioka (ECO.)	death	ecological		14mg	0.12	[0.03-0.51]	
Seet (CLUS. RCT)	severe case	32/617	64/619	12mg	0.50	[0.33-0.76]	OT[1]
Morgenstern (PSM)	hosp.	0/271	2/271	56mg	0.20	[0.01-4.15]	
Prophylaxis		152/5,059	926/6,723		0.15	[0.09-0.25]	**85% improvement**

Tau^2 = 0.58; I^2 = 83.8%

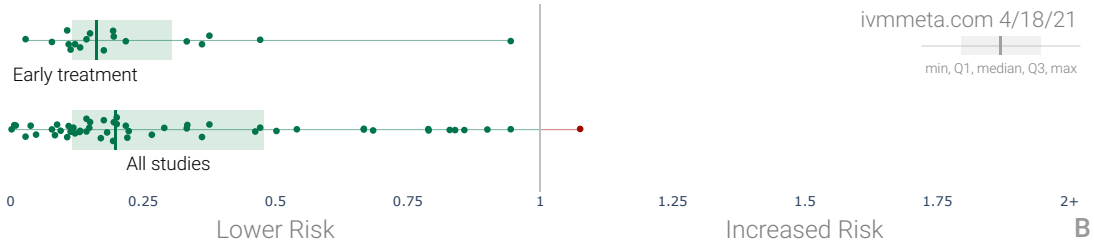
All studies		173/6,067	1,090/7,657		0.16	[0.10-0.25]	**84% improvement**

[1] OT: ivermectin vs. other treatment
[2] CT: study uses combined treatment
[3] MD: minimal detail available currently
Tau^2 = 1.02; I^2 = 90.8%; Z = 7.89 (p < 0.0001)

0 0.25 0.5 0.75 1 1.25 1.5 1.75 2+

Lower Risk Increased Risk

A



B

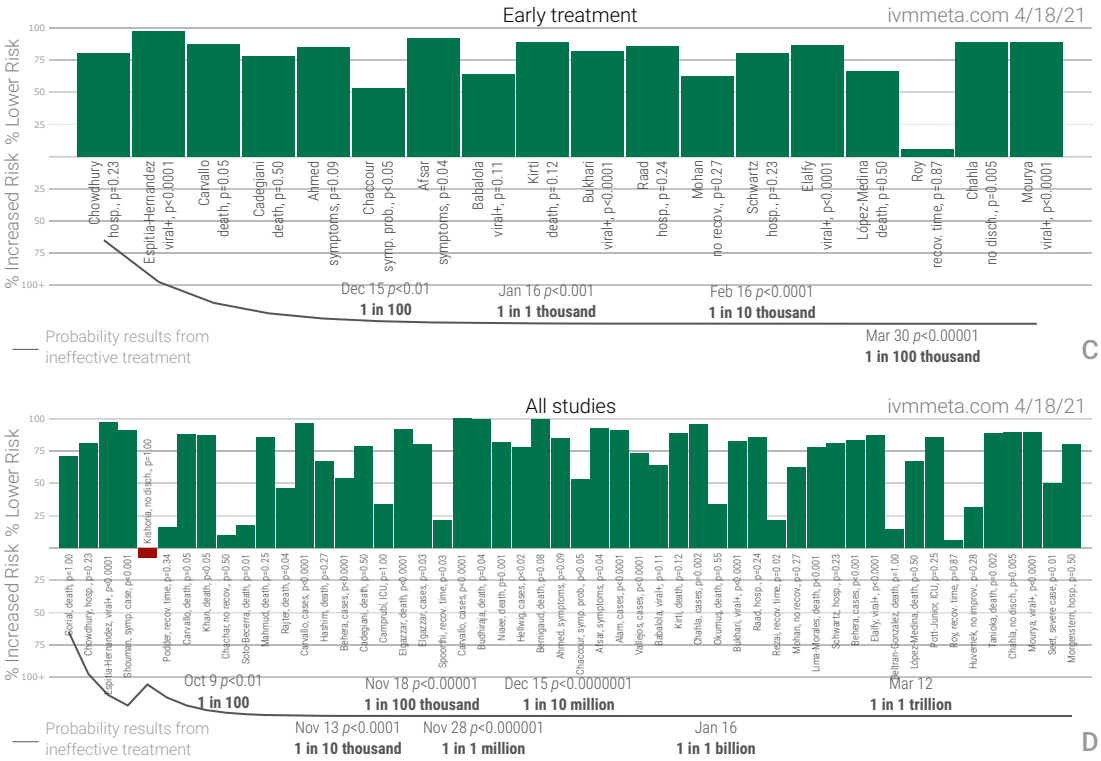


Figure 1. *A. Random effects meta-analysis excluding late treatment. This plot shows pooled effects, analysis for individual outcomes is below, and more details on pooled effects can be found in the discussion section. Simplified dosages are shown for comparison, these are the total dose in the first four days for treatment, and the monthly dose for prophylaxis, for a 70kg person. For full details see the appendix.* ***B.*** *Scatter plot showing the distribution of effects reported in early treatment studies and in all studies.* ***C and D.*** *Chronological history of all reported effects, with the probability that the observed frequency of positive results occurred due to random chance from an ineffective treatment.*

Introduction

We analyze all significant studies concerning the use of ivermectin for COVID-19. Search methods, inclusion criteria, effect extraction criteria (more serious outcomes have priority), all individual study data, PRISMA answers, and statistical methods are detailed in Appendix 1. We present random effects meta-analysis results for all studies, for studies within each treatment stage, for mortality results, for COVID-19 case results, for viral clearance results, for peer-reviewed studies, for Randomized Controlled Trials (RCTs), and after exclusions.

We also perform a simple analysis of the distribution of study effects. If treatment was not effective, the observed effects would be randomly distributed (or more likely to be negative if treatment is harmful). We can compute the probability that the observed percentage of positive results (or higher) could occur due to chance with an ineffective treatment (the probability of >= *k* heads in *n* coin tosses, or the one-sided sign test / binomial test). Analysis of publication bias is important and adjustments may be needed if there is a bias toward publishing positive results.

Figure 2 shows stages of possible treatment for COVID-19. **Prophylaxis** refers to regularly taking medication before becoming sick, in order to prevent or minimize infection. **Early Treatment** refers to treatment immediately or soon after symptoms appear, while **Late Treatment** refers to more delayed treatment.

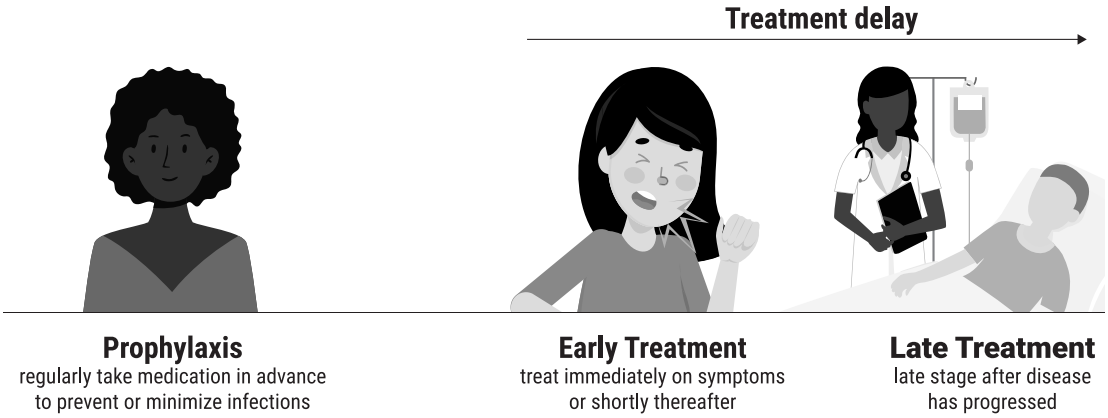


Figure 2. *Treatment stages.*

Results

Figure 3, 4, and 5 show results by treatment stage. Figure 6, 7, 8, and 9 show forest plots for a random effects meta-analysis of all studies with pooled effects, and for studies reporting mortality results, COVID-19 case results, and viral clearance results only. Figure 10 shows results for peer reviewed trials only. Table 1 summarizes the results.

Treatment time	Number of studies reporting positive effects	Total number of studies	Percentage of studies reporting positive effects	Probability of an equal or greater percentage of positive results from an ineffective treatment	Random effects meta-analysis results
Early treatment	18	18	**100%**	**0.0000038** 1 in 262 thousand	**81%** improvement RR 0.19 [0.09-0.38] p < 0.0001
Late treatment	19	20	**95.0%**	**0.00002** 1 in 50 thousand	43% improvement RR 0.57 [0.44-0.73] p < 0.0001
Prophylaxis	14	14	**100%**	**0.000061** 1 in 16 thousand	**85%** improvement RR 0.15 [0.09-0.25] p < 0.0001
All studies	51	52	**98.1%**	**0.000000000000012** 1 in 85 trillion	**72%** improvement RR 0.28 [0.22-0.36] p < 0.0001

Table 1. *Results by treatment stage.*

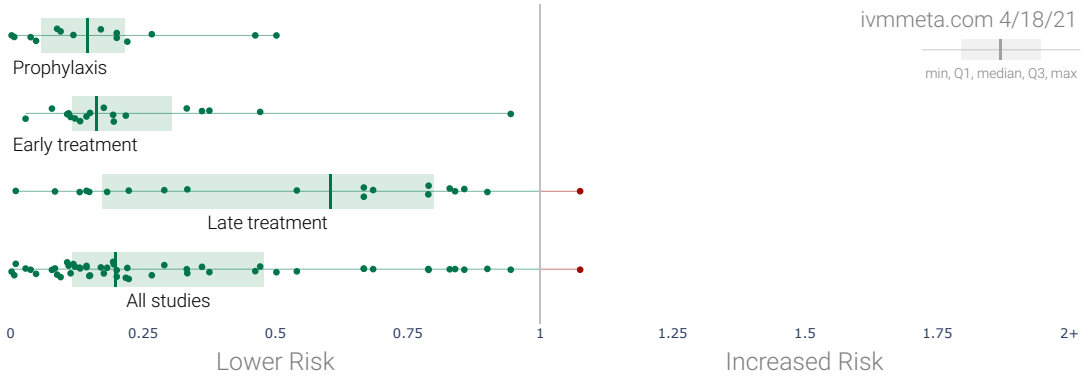


Figure 3. *Results by treatment stage.*

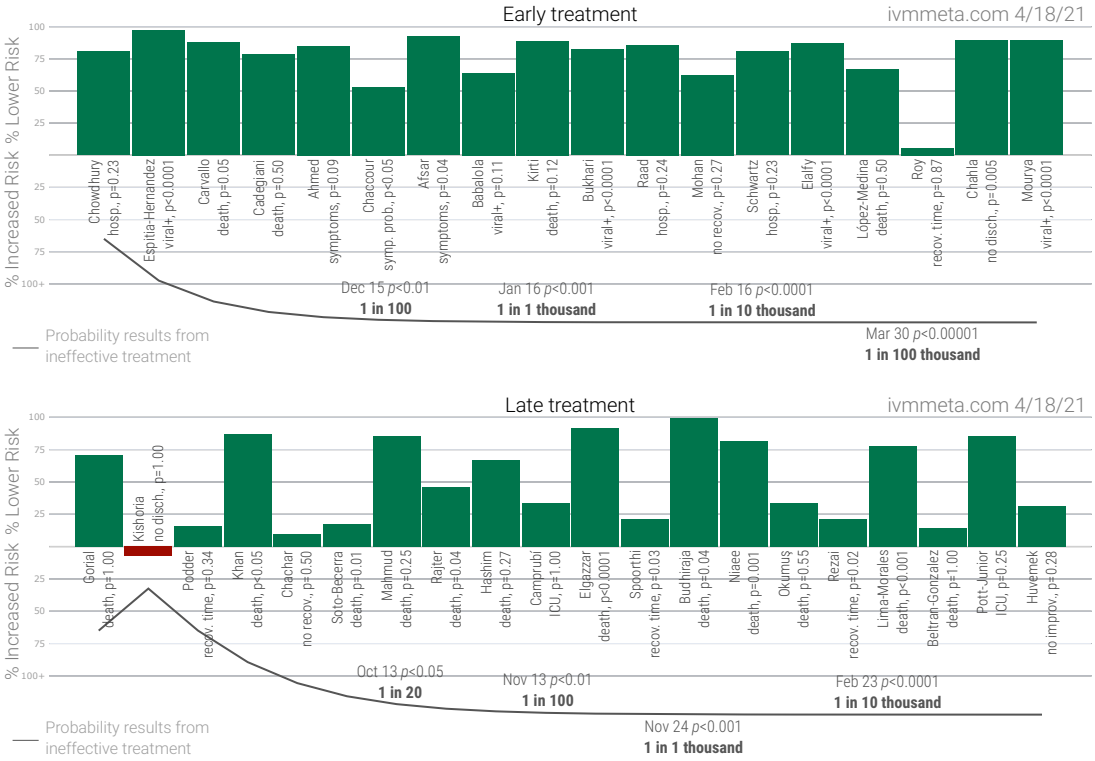


Figure 4. *Chronological history of early and late treatment results, with the probability that the observed frequency of positive results occurred due to random chance from an ineffective treatment.*

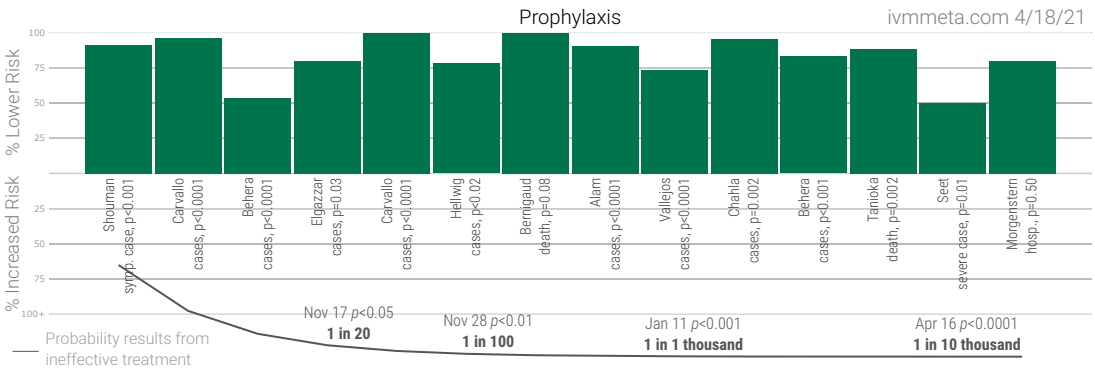


Figure 5. *Chronological history of prophylaxis results.*

All 52 ivermectin COVID-19 studies

ivmmeta.com 4/18/21

		Treatment	Control	Dose (4d)	RR	CI	
Chowdhury (RCT)	hosp.	0/60	2/56	14mg	0.19	[0.01-3.96]	OT[1] CT[2]
Espitia-Hernandez	viral+	0/28	7/7	12mg	0.03	[0.01-0.11]	CT[2]
Carvallo	death	1/33	3/12	36mg	0.12	[0.01-1.06]	CT[2]
Cadegiani	death	0/110	2/137	42mg	0.22	[0.01-4.48]	
Ahmed (DB RCT)	symptoms	0/17	3/19	48mg	0.15	[0.01-2.70]	
Chaccour (DB RCT)	symp. prob.	12	12	28mg	0.47	[0.19-1.16]	
Afsar	symptoms	0/37	7/53	48mg	0.08	[0.00-1.32]	
Babalola (DB RCT)	viral+	40	20	24mg	0.36	[0.10-1.27]	OT[1]
Kirti (DB RCT)	death	0/55	4/57	24mg	0.11	[0.01-2.05]	
Bukhari (RCT)	viral+	4/41	25/45	12mg	0.18	[0.07-0.46]	
Raad (SB RCT)	hosp.	0/50	3/50	14mg	0.14	[0.01-2.70]	MD[3]
Mohan (DB RCT)	no recov.	2/40	6/45	28mg	0.38	[0.08-1.75]	
Schwartz (DB RCT)	hosp.	0/49	2/45	36mg	0.19	[0.01-3.92]	
Elalfy	viral+	7/62	44/51	36mg	0.13	[0.06-0.27]	CT[2]
López-Me.. (DB RCT)	death	0/200	1/198	84mg	0.33	[0.01-8.11]	
Roy	recov. time	14	15	n/a	0.94	[0.52-1.93]	CT[2]
Chahla (CLUS. RCT)	no disch.	2/110	8/62	24mg	0.11	[0.02-0.52]	
Mourya	viral+	5/50	47/50	48mg	0.11	[0.05-0.25]	
Early treatment		21/1,008	164/934		0.19	[0.09-0.38]	**81% improvement**

Tau^2 = 1.52; I^2 = 85.0%

		Treatment	Control	Dose (4d)	RR	CI	
Gorial	death	0/16	2/71	14mg	0.29	[0.01-5.76]	
Kishoria (RCT)	no disch.	11/19	7/13	12mg	1.08	[0.57-2.02]	
Podder (RCT)	recov. time	32	30	14mg	0.84	[0.55-1.12]	
Khan	death	1/115	9/133	12mg	0.13	[0.02-1.01]	
Chachar (RCT)	no recov.	9/25	10/25	36mg	0.90	[0.44-1.83]	
Soto-Becerra	death	92/203	1,438/2,630	14mg	0.83	[0.71-0.97]	
Mahmud (DB RCT)	death	0/183	3/183	12mg	0.14	[0.01-2.75]	CT[2]
Rajter (PSM)	death	13/98	24/98	14mg	0.54	[0.27-0.99]	
Hashim (SB RCT)	death	2/70	6/70	28mg	0.33	[0.07-1.60]	CT[2]
Camprubí	ICU	2/13	3/13	14mg	0.67	[0.13-3.35]	
Elgazzar (RCT)	death	2/200	24/200	112mg	0.08	[0.02-0.35]	OT[1]
Spoorthi	recov. time	50	50	n/a	0.79	[0.62-1.01]	CT[2]
Budhiraja	death	0/34	103/942	n/a	0.01	[0.00-0.15]	
Niaee (DB RCT)	death	4/120	11/60	28mg	0.18	[0.06-0.55]	
Okumuş (DB RCT)	death	6/30	9/30	56mg	0.67	[0.27-1.64]	
Rezai (DB RCT)	recov. time	51	52	14mg	0.79	[0.63-0.98]	MD[3]
Lima-Morales	death	15/481	52/287	12mg	0.22	[0.12-0.41]	CT[2]
Beltran-.. (DB RCT)	death	5/36	6/37	12mg	0.86	[0.29-2.56]	
Pott-Junior (RCT)	ICU	1/27	1/4	14mg	0.15	[0.01-1.93]	
Huvemek (DB RCT)	no improv.	13/50	19/50	84mg	0.68	[0.38-1.23]	
Late treatment		176/1,853	1,727/4,978		0.57	[0.44-0.73]	**43% improvement**

Tau^2 = 0.13; I^2 = 65.6%

		Treatment	Control	Dose (1m)	RR	CI	
Shouman (RCT)	symp. case	15/203	59/101	36mg	0.09	[0.03-0.23]	
Carvallo	cases	0/131	11/98	14mg	0.04	[0.00-0.63]	CT[2]
Behera	cases	41/117	145/255	42mg	0.46	[0.29-0.71]	
Elgazzar (RCT)	cases	2/100	10/100	112mg	0.20	[0.04-0.89]	
Carvallo	cases	0/788	237/407	48mg	0.00	[0.00-0.02]	CT[2]
Hellwig (ECO.)	cases	ecological		14mg	0.22	[0.05-0.89]	
Bernigaud	death	0/69	150/3,062	84mg	0.01	[0.00-0.10]	
Alam	cases	4/58	44/60	12mg	0.09	[0.04-0.24]	
Vallejos	cases	13/389	61/486	48mg	0.27	[0.15-0.48]	MD[3]
Chahla (RCT)	cases	0/117	10/117	48mg	0.05	[0.00-0.80]	CT[2]
Behera	cases	45/2,199	133/1,147	42mg	0.17	[0.12-0.23]	
Tanioka (ECO.)	death	ecological		14mg	0.12	[0.03-0.51]	
Seet (CLUS. RCT)	severe case	32/617	64/619	12mg	0.50	[0.33-0.76]	OT[1]
Morgenstern (PSM)	hosp.	0/271	2/271	56mg	0.20	[0.01-4.15]	
Prophylaxis		152/5,059	926/6,723		0.15	[0.09-0.25]	**85% improvement**

Tau^2 = 0.58; I^2 = 83.8%

All studies		349/7,920	2,817/12,635		0.28	[0.22-0.36]	**72% improvement**

[1] OT: ivermectin vs. other treatment
[2] CT: study uses combined treatment
[3] MD: minimal detail available currently

Tau^2 = 0.47; I^2 = 87.2%; Z = 9.62 (p < 0.0001)

Figure 6. *Random effects meta-analysis for all studies.*

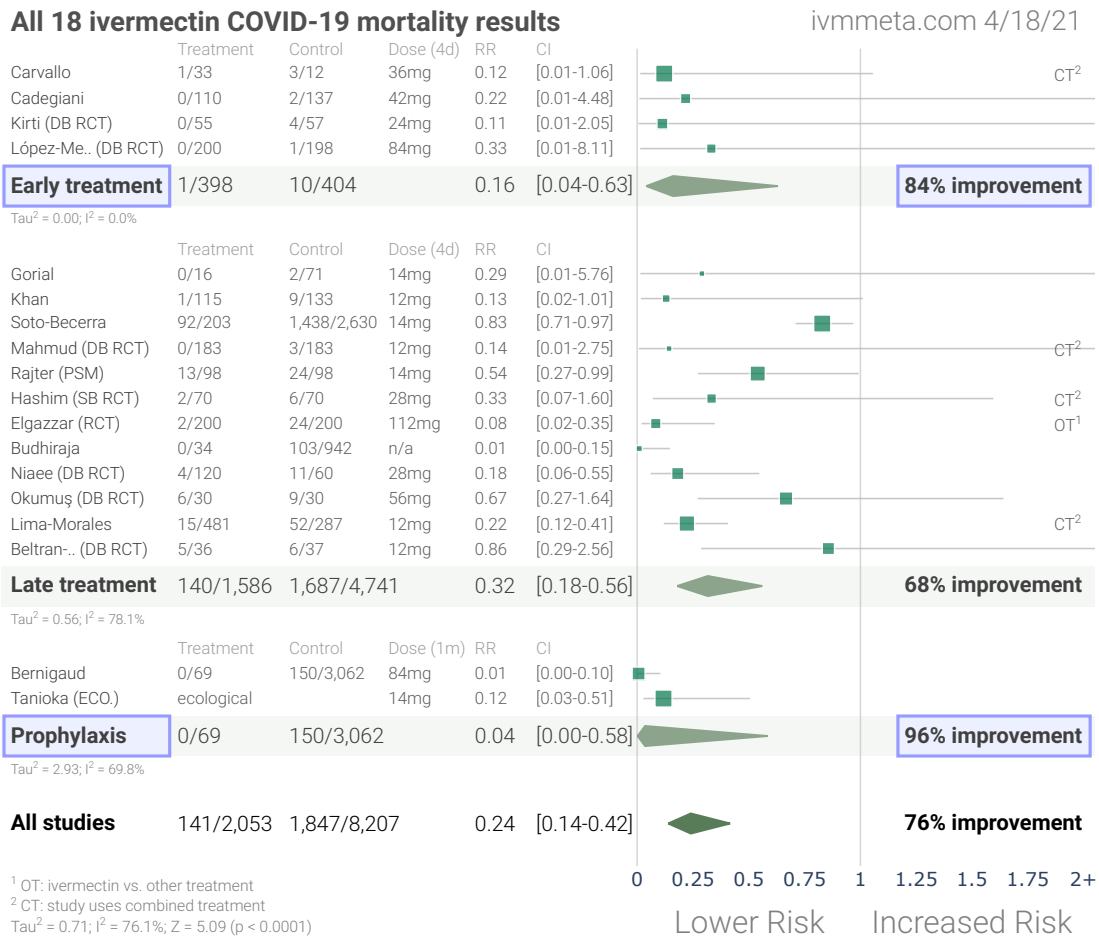


Figure 7. *Random effects meta-analysis for mortality results only.*

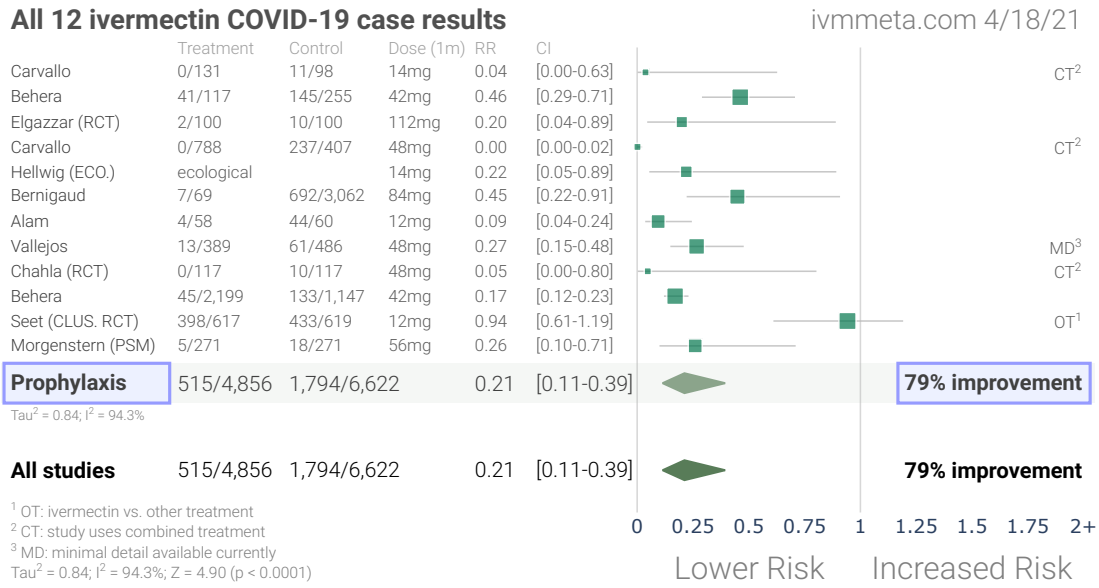


Figure 8. *Random effects meta-analysis for COVID-19 case results only.*

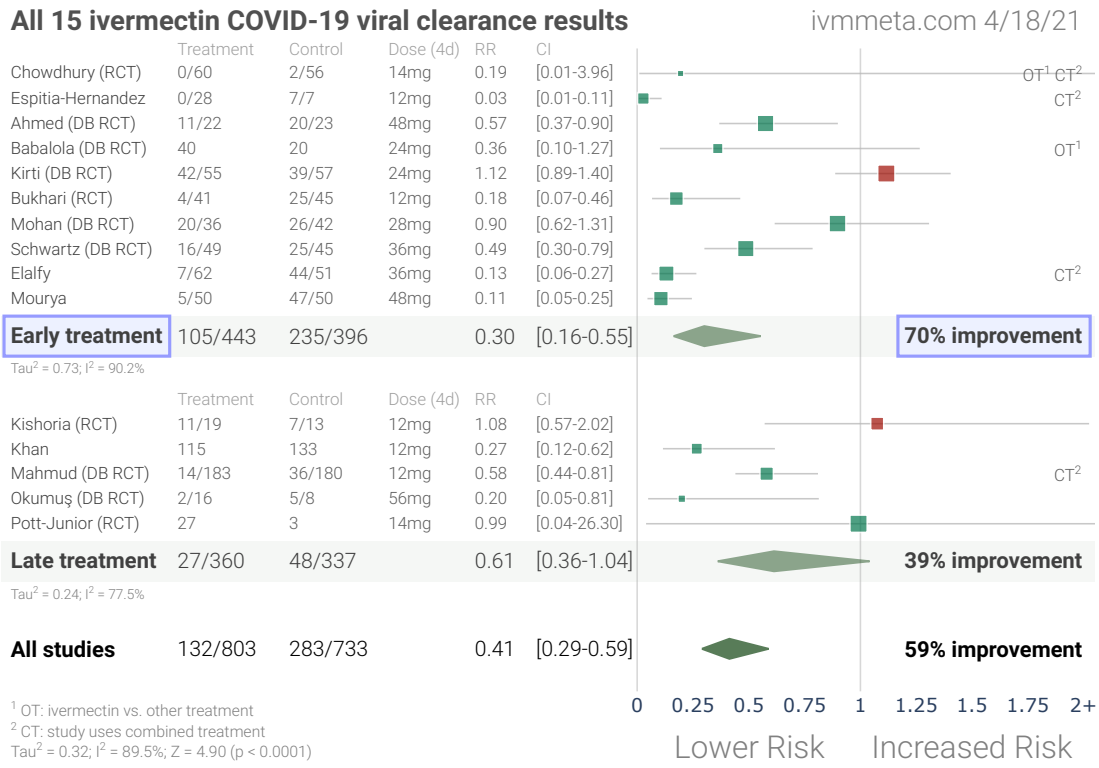


Figure 9. *Random effects meta-analysis for viral clearance results only.*

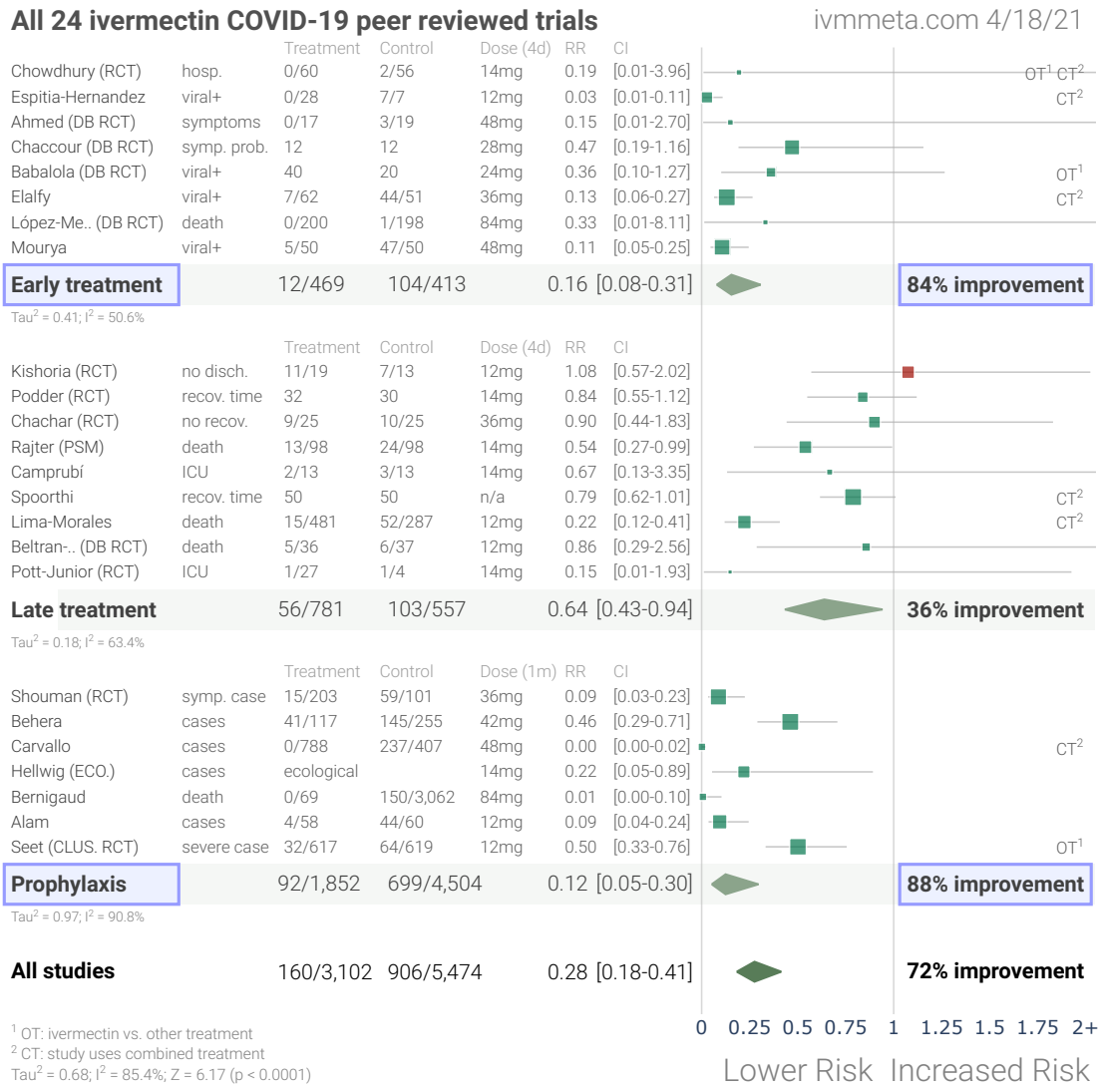


Figure 10. *Random effects meta-analysis for peer reviewed trials only.*

Randomized Controlled Trials (RCTs)

Results restricted to Randomized Controlled Trials (RCTs) are shown in Figure 11, 12, 13, and 14, and Table 2. RCT results are similar to non-RCT results. Evidence shows that non-RCT trials can also provide reliable results. *[**Concato**]* find that well-designed observational studies do not systematically overestimate the magnitude of the effects of treatment compared to RCTs. *[**Anglemyer**]* summarized reviews comparing RCTs to observational studies and found little evidence for significant differences in effect estimates. *[**Lee**]* shows that only 14% of the guidelines of the Infectious Diseases Society of America were based on RCTs. Evaluation of studies relies on an understanding of the study and potential biases. Limitations in an RCT can outweigh the benefits, for example excessive dosages, excessive treatment delays, or Internet survey bias could have a greater effect on results. Ethical issues may also prevent running RCTs for known effective treatments. For more on issues with RCTs see *[**Deaton**, **Nichol**]*.

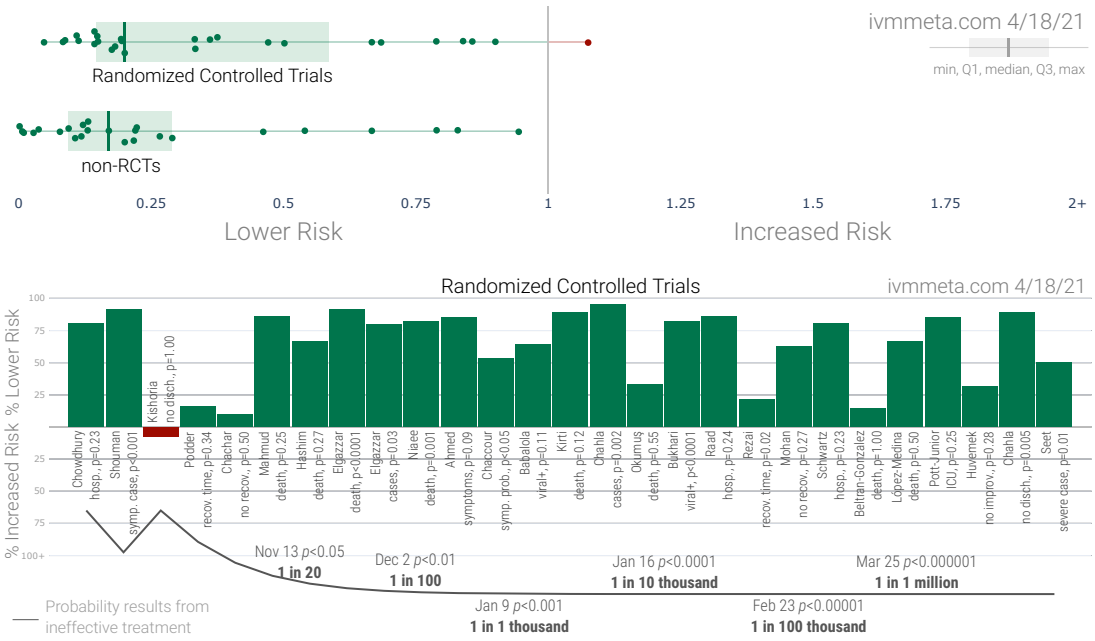


Figure 11. *Randomized Controlled Trials. The distribution of results for RCTs is similar to the distribution for all other studies.*

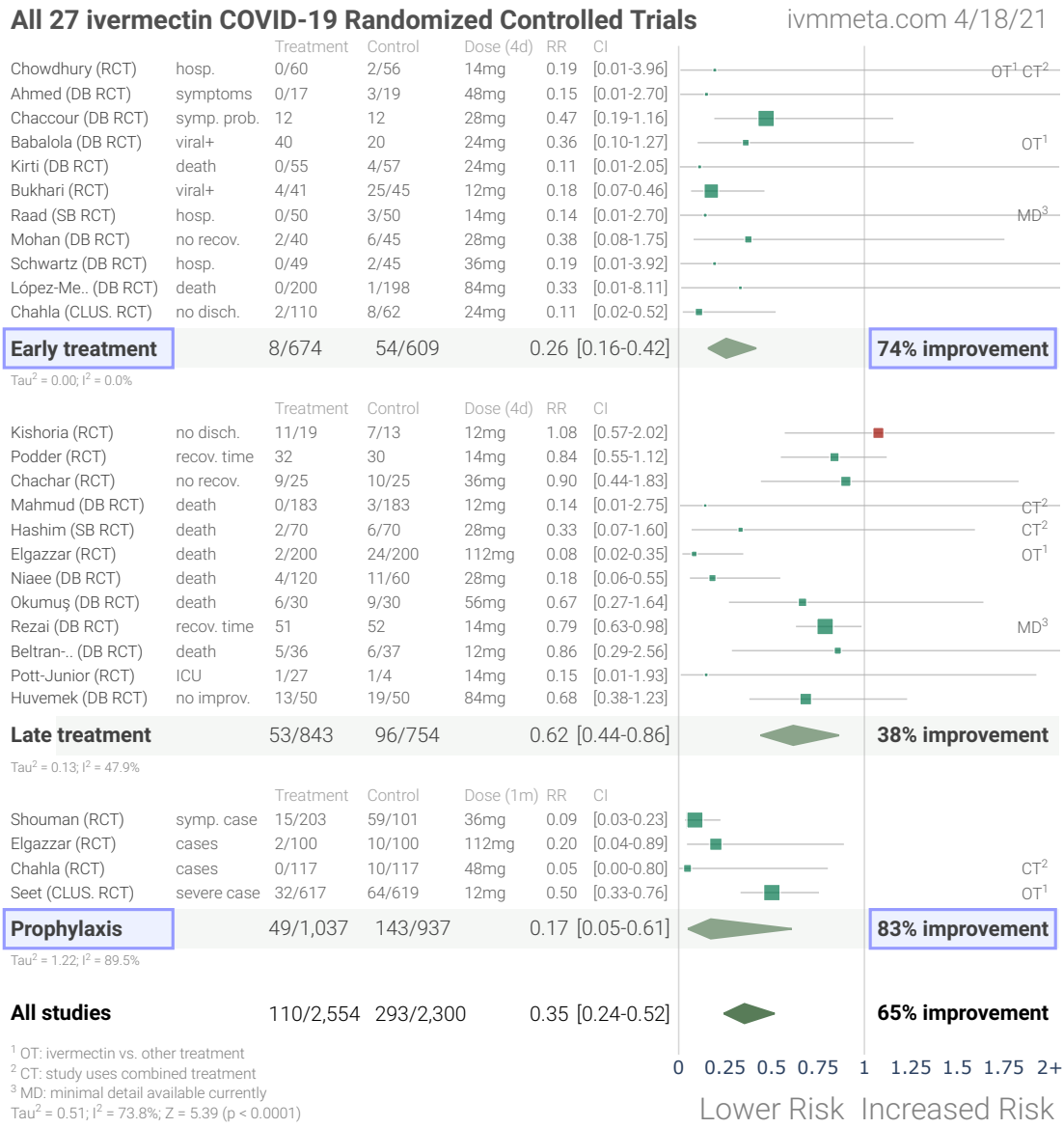


Figure 12. *Random effects meta-analysis for Randomized Controlled Trials only.*

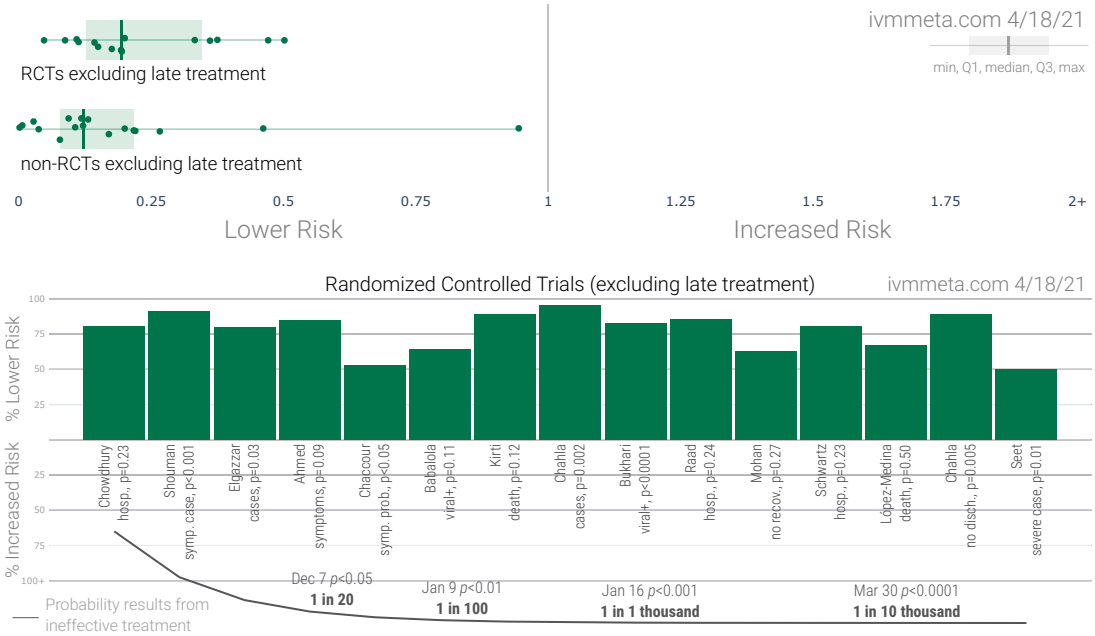


Figure 14. *RCTs excluding late treatment.*

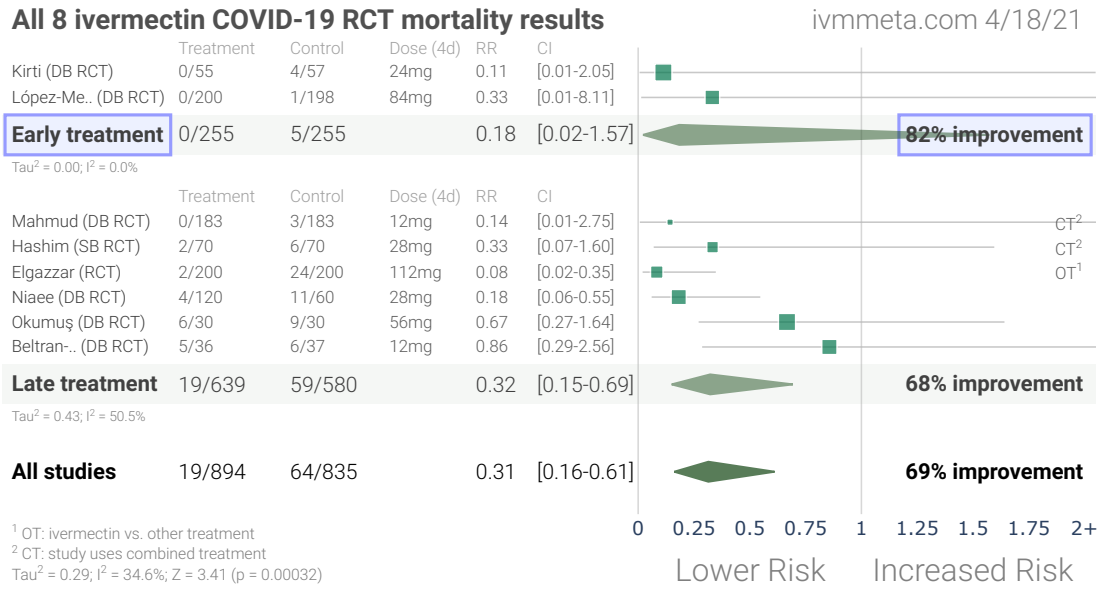


Figure 13. *Random effects meta-analysis for Randomized Controlled Trial mortality results only.*

Treatment time	Number of studies reporting positive effects	Total number of studies	Percentage of studies reporting positive effects	Probability of an equal or greater percentage of positive results from an ineffective treatment	Random effects meta-analysis results
Randomized Controlled Trials	26	27	**96.3%**	**0.00000021** 1 in 5 million	**65%** improvement RR 0.35 [0.24-0.52] p < 0.0001
Randomized Controlled Trials (excluding late treatment)	15	15	**100%**	**0.000031** 1 in 33 thousand	**78%** improvement RR 0.22 [0.13-0.37] p < 0.0001

Table 2. *Summary of RCT results.*

Exclusions

To avoid bias in the selection of studies, we include all studies in the main analysis. Here we show the results after excluding studies with critical issues likely to alter results, non-standard studies, and studies where very minimal detail is currently available.

*[**Soto-Becerra**]* is a database analysis covering anyone with ICD-10 COVID-19 codes, which includes asymptomatic PCR+ patients. Therefore many patients in the control group are likely asymptomatic with regards to SARS-CoV-2, but in the hospital for another reason. For those that had symptomatic COVID-19, there is also likely significant confounding by indication. KM curves show that the treatment groups were in more serious condition, with more than the total excess mortality at 30 days occurring on day 1. All treatments are worse than the control group at 30 days, while at the latest followup all treatments show lower mortality than control. The machine learning system used also appears over-parameterized and likely to result in significant overfitting and inaccurate results. There is also no real control group in this study - patients receiving the treatments after 48 hours were put in the control group. Authors also state that outcomes within 24 hours were excluded, however the KM curves show significant mortality at day 1 (only for the treatment groups). Note that this study provides both 30 day mortality and weighted KM curves up to day 43 for ivermectin, we use the day 43 results as per our protocol. Several protocol violations have also been reported in this study *[**Yim**]*.

*[**Vallejos**]* reports prophylaxis results, however only very minimal details are currently available in a news report. We include these results for additional confirmation of the efficacy observed in other trials, however this study is excluded here. *[**Hellwig**]* analyze African countries and COVID-19 cases in October 2020 as a function of whether widespread prophylactic use of ivermectin is used for parasitic infections. *[**Tanioka**]* perform a similar analysis for COVID-19 mortality in January 2021. These studies are excluded because they are not clinical trials. *[**Krolewiecki**]* show a concentration dependent antiviral activity of ivermectin whereby the viral decay rate for patients with ivermectin >160ng/mL was 0.64 $\log_{10}$ copies/reaction/day versus 0.13 for control. However, they do not provide the results for the entire treatment group vs. control. *[**Galan**]* perform an RCT comparing ivermectin and other treatments with very late stage severe condition hospitalized patients, not showing significant differences between the treatments. Authors were unable to add a control arm due to ethical issues. The closest control comparison we could find is *[**Baqui**]*, which shows 43% hospital mortality in the northern region of Brazil where the study was performed, from which we can estimate the mortality with ivermectin in this study as 47% lower, RR 0.53. Further, the study is

restricted to more severe cases, hence the expected mortality, and therefore the benefit of treatment, may be higher. *[**Kishoria**]* restrict inclusion to patients that did not respond to standard treatment, provide no details on the time of the discharge status, and there are very large unadjusted differences in the groups, with over twice as many patients in the ivermectin group with age >40, and all patients over 60 in the ivermectin group. Results for *[**Raad**, **Rezai**]* are available in *[**Hill**]*, however no paper is currently available.

Summarizing, the studies excluded are as follows, and the resulting forest plot is shown in Figure 15.

*[**Carvallo**]*, control group formed from cases in the same hospital not in the study.

*[**Hellwig**]*, not a typical trial, analysis of African countries that used or did not use ivermectin prophylaxis for parasitic infections.

*[**Kishoria**]*, excessive unadjusted differences between groups.

*[**Raad**]*, detail too minimal.

*[**Rezai**]*, detail too minimal.

*[**Roy**]*, no serious outcomes reported and fast recovery in treatment and control groups, there is little room for a treatment to improve results.

*[**Soto-Becerra**]*, substantial unadjusted confounding by indication likely, includes PCR+ patients that may be asymptomatic for COVID-19 but in hospital for other reasons.

*[**Tanioka**]*, not a typical trial, analysis of African countries that used or did not use ivermectin prophylaxis for parasitic infections.

*[**Vallejos**]*, detail too minimal.

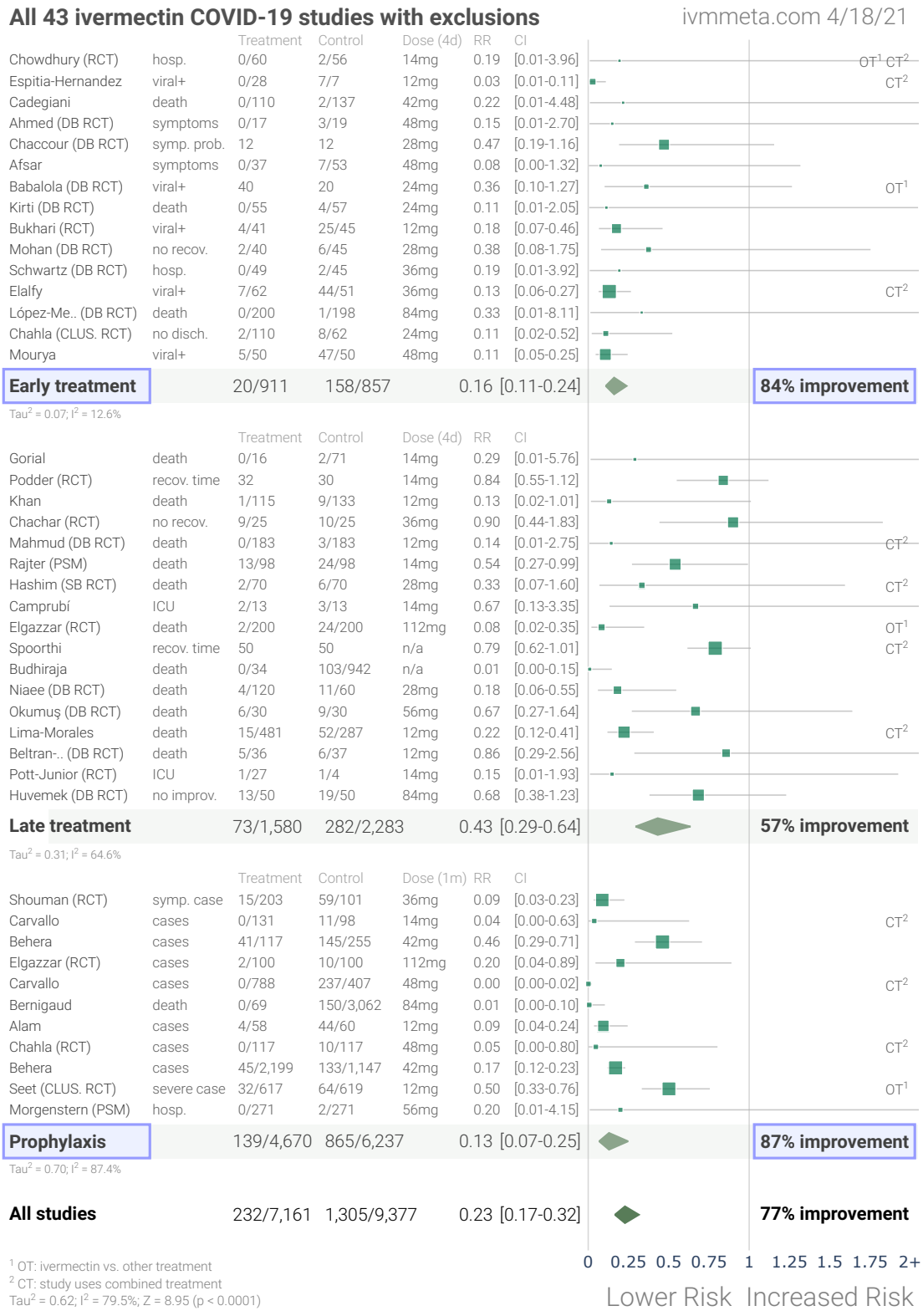


Figure 15. *Random effects meta-analysis excluding studies with significant issues.*

Discussion

We show results with both pooled effects and for individual outcomes. The true effect size may differ for different outcomes, for example the benefit for mortality and hospitalization could be different, or a treatment could be effective at minimizing serious cases while not being very effective for viral clearance. Ivermectin studies show strong benefits for all outcomes, supporting pooled effects which has the advantage of visualizing all studies and providing the most evidence for the question "is ivermectin effective for COVID-19?". For specific estimates regarding mortality etc., the individual outcome analyses are more appropriate.

The expected effect size between studies varies for many other reasons including the patient population, the medication dosage and regimen, and the treatment time, all of which could introduce greater heterogeneity compared to that from different outcomes, or from biases in well done retrospective studies. Patient population could remove the potential benefit of treatment - for example there is less room for improvement with low risk patients that heal quickly without treatment (as in *[López-Medina]*). Treatment time may have the largest effect for many successful COVID-19 treatments. For example an antiviral may be very effective when used early and not effective at a later stage (for comparison, oseltamivir is generally only considered effective for influenza when used within 0-36 or 0-48 hours *[McLean, Treanor]*). We address treatment time by separating early and late treatment, showing a clear difference and advantage for early treatment.

Only one study to date has received significant press coverage in western media *[López-Medina]* although it is neither the largest or the least biased study. This study has many problems. The primary outcome was changed mid-trial from clinical deterioration to complete resolution of symptoms including "not hospitalized and no limitation of activities" as a negative outcome. Critically, temporary side effects of a successful treatment may be considered as a negative outcome, which could result in falsely concluding that the treatment is not effective. Such an outcome is also not very meaningful in terms of assessing how treatment affects the incidence of serious outcomes. With the low risk patient population in this study, there is also little room for improvement - 58% recovered within the first 2 days to "not hospitalized and no limitation of activities" or better. There was only one death (in the control arm), as compared to 17 studies with many more mortality events. This study also gave ivermectin to the control arm for 38 patients and it is unknown if the full extent of the error was identified, or if there were additional undiscovered errors. The side effect data reported in this trial raises major concerns, with more side effects reported in the placebo arm, suggesting that more placebo patients may have received treatment. The study protocol allows other treatments but does not report on usage. The presentation of this study also appears to be significantly biased. While all outcomes show a benefit for ivermectin, the abstract fails to mention that much larger benefits are seen for serious outcomes, including the original primary outcome, and that the reason for not reaching statistical signficance is the low number of events in a low risk population where most recover quickly without treatment.

Publishing is often biased towards positive results, which we would need to adjust for when analyzing the percentage of positive results. For ivermectin, there is currently not enough data to evaluate publication bias with high confidence. One method to evaluate bias is to compare prospective vs. retrospective studies. Prospective studies are likely to be published regardless of the result, while retrospective studies are more likely to exhibit bias. For example, researchers may perform preliminary analysis with minimal effort and the results may influence their decision to continue. Retrospective studies also provide more opportunities for the specifics of data extraction and adjustments to influence results. Figure 16 shows a scatter plot of results for prospective and

retrospective studies. The median effect size for prospective studies is 81% improvement, compared to 80% for retrospective studies, showing no significant difference. *[**Bryant**]* also perform a funnel plot analysis, which they found did not suggest evidence of publication bias.

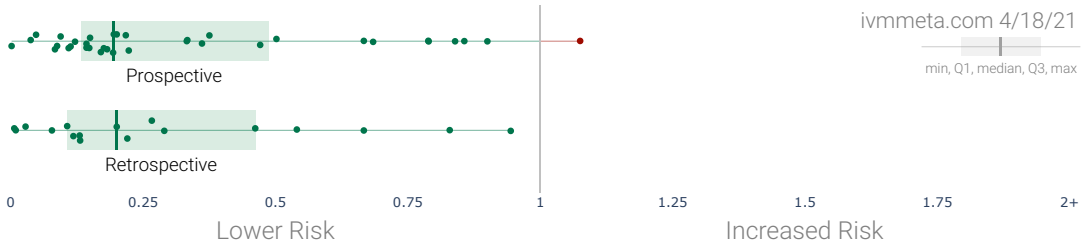


Figure 16. *Prospective vs. retrospective studies.*

4 of the 52 studies compare against other treatments rather than placebo. Currently ivermectin shows better results than these other treatments, however ivermectin may show greater improvement when compared to placebo. 12 of 52 studies combine treatments, for example ivermectin + doxycycline. The results of ivermectin alone may differ. 4 of 27 RCTs use combined treatment, three with doxycycline, and one with iota-carrageenan. 3 of 52 studies currently have minimal published details available.

Typical meta analyses involve subjective selection criteria, effect extraction rules, and study bias evaluation, which can be used to bias results towards a specific outcome. In order to avoid bias we include all studies and use a pre-specified method to extract results from all studies (we also present results after exclusions). The results to date are overwhelmingly positive, very consistent, and very insensitive to potential selection criteria, effect extraction rules, and/or bias evaluation.

Additional meta analyses confirming the effectiveness of ivermectin can be found in *[**Bryant**, **Hill**, **Kory**, **Lawrie**]*. Figure 17 shows a comparison of mortality results across meta analyses. *[**Kory**]* also review epidemiological data and provide suggested treatment regimens.

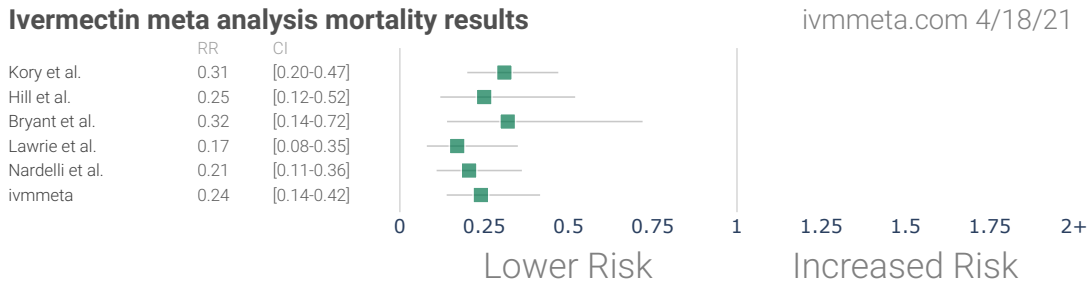


Figure 17. *Comparison of mortality results from different meta analyses. OR converted to RR for [**Kory**, **Nardelli**].*

The evidence supporting ivermectin for COVID-19 far exceeds the typical amount of evidence used for the approval of treatments. *[**Lee**]* shows that only 14% of the guidelines of the Infectious Diseases Society of America were based on RCTs. Table 3 compares the amount of evidence used by the WHO to approve ivermectin for scabies, compared with the current evidence for COVID-19.

WHO ivermectin approval status				
Indication	Studies	Patients	Effect size	Status
Scabies *[Kory (B)]*	6	613	35% [22-46%] (favoring permethrin)	Approved
COVID-19	52	17,562	72% [64-78%]	Pending

Table 3. *Ivermectin approval status.*

Conclusion

Ivermectin is an effective treatment for COVID-19. The probability that an ineffective treatment generated results as positive as the 52 studies to date is estimated to be 1 in 85 trillion (p = 0.000000000000012). As expected for an effective treatment, early treatment is more successful, with an estimated reduction of 81% in the effect measured using a random effects meta-analysis, RR 0.19 [0.09-0.38].

Revisions

This paper is data driven, all graphs and numbers are dynamically generated. We will update the paper as new studies are released or with any corrections. Please submit updates and corrections at https://ivmmeta.com/.

12/2: We added *[Ahmed]*.

12/7: We added *[Chaccour]*.

12/11: We added *[Soto-Becerra]*.

12/16: We added *[Afsar]*.

12/17: We added *[Alam]*.

12/26: We added *[Carvallo (C), Vallejos]*.

12/27: We added the total number of authors and patients.

12/29: We added meta analysis excluding late treatment.

12/31: We added additional details about the studies in the appendix.

1/2: We added dosage information and we added the number of patients to the forest plots.

1/5: We added direct links to the study details in the forest plots.

1/6: We added *[Babalola]*.

1/7: We added direct links to the study details in the chronological plots.

1/9: We added *[**Kirti**]*. Due to the much larger size of the control group in *[**Bernigaud**]*, we limited the size of the control group to be the same as the treatment group for calculation of the number of patients.

1/10: We put all prophylaxis studies in a single group.

1/11: We added *[**Chahla (B)**]*.

1/12: We added *[**Okumuş**]*.

1/15: We added the effect measured for each study in the forest plots.

1/16: We moved the analysis with exclusions to the main text, and added additional commentary.

1/17: We added *[**Bukhari**]*.

1/19: We added *[**Raad**, **Rezai**]*. *[**Chaccour**]* was updated to the journal version of the paper.

1/25: We updated *[**Vallejos**]* with the recently released results.

1/26: We updated *[**Shouman**]* with the journal version of the article.

2/2: We added *[**Mohan**]*.

2/5: We updated *[**Bukhari**]* to the preprint.

2/10: We added *[**Lima-Morales**]*.

2/11: We added more details on the analysis of prospective vs. retrospective studies.

2/12: We added *[**Schwartz**]*.

2/14: We added analysis restricted to COVID-19 case outcomes, and we added additional results in the abstract.

2/15: We added *[**Behera**]*.

2/16: We updated *[**Behera (B)**]* to the journal version of the paper.

2/17: We added *[**Elalfy**]*, and we added analysis restricted to viral clearance outcomes, and mortality results restricted to RCTs.

2/18: We updated *[**Babalola**]* to the journal version of the paper.

2/23: We added *[**Beltran-Gonzalez**]*.

2/24: We added a comparison of the evidence base and WHO approval status for the use of ivermectin with scabies and COVID-19. We updated *[**Okumuş**]* with the Research Square preprint.

2/27: We added analysis restricted to peer reviewed studies.

3/2: We updated *[**Vallejos**]* with the latest results *[**Vallejos (B)**]*.

3/3: We updated the graphs to indicate the time period for the dosage column, now showing the dosage over one month for prophylaxis and over four days for other studies.

3/4: We added *[López-Medina]*, and we added more information in the abstract.

3/5: We added discussion of pooled effects (we show both pooled effects and individual outcome results).

3/6: We added *[Chowdhury]* and we identify studies that compare with another treatment.

3/10: We added *[Pott-Junior]*.

3/12: We added *[Bryant, Roy]*.

3/17: We added *[Nardelli]*.

3/25: We added *[Huvemek]*.

3/26: We added *[Tanioka]*.

3/28: We highlighted and added discussion for studies that use combined treatments.

3/30: We added *[Chahla]*.

3/31: We updated *[Chahla (B)]* to the preprint.

4/4: We added event counts to the forest plots.

4/5: We added *[Mourya]*.

4/7: We identified studies where minimal detail is currently available in the forest plots.

4/9: We corrected a duplicate entry for *[Bukhari]*.

4/10: We added *[Kishoria]*.

4/14: We added *[Seet]*.

4/16: We added *[Morgenstern]*.

4/18: We updated *[Morgenstern]* to the preprint.

Appendix 1. Methods and Study Results

We performed ongoing searches of PubMed, medRxiv, ClinicalTrials.gov, The Cochrane Library, Google Scholar, Collabovid, Research Square, ScienceDirect, Oxford University Press, the reference lists of other studies and meta-analyses, and submissions to the site c19ivermectin.com, which regularly receives submissions of studies upon publication. Search terms were ivermectin and COVID-19 or SARS-CoV-2, or simply ivermectin. Automated searches are performed every hour with

notifications of new matches. All studies regarding the use of ivermectin for COVID-19 that report an effect compared to a control group are included in the main analysis. This is a living analysis and is updated regularly.

We extracted effect sizes and associated data from all studies. If studies report multiple kinds of effects then the most serious outcome is used in calculations for that study. For example, if effects for mortality and cases are both reported, the effect for mortality is used, this may be different to the effect that a study focused on. If symptomatic results are reported at multiple times, we used the latest time, for example if mortality results are provided at 14 days and 28 days, the results at 28 days are used. Mortality alone is preferred over combined outcomes. Outcomes with zero events in both arms were not used. Clinical outcome is considered more important than PCR testing status. When basically all patients recover in both treatment and control groups, preference for viral clearance and recovery is given to results mid-recovery where available (after most or all patients have recovered there is no room for an effective treatment to do better). When results provide an odds ratio, we computed the relative risk when possible, or converted to a relative risk according to *[**Zhang**]*. Reported confidence intervals and *p*-values were used when available, using adjusted values when provided. If multiple types of adjustments are reported including propensity score matching (PSM), the PSM results are used. When needed, conversion between reported *p*-values and confidence intervals followed *[**Altman**, **Altman (B)**]*, and Fisher's exact test was used to calculate *p*-values for event data. If continuity correction for zero values is required, we use the reciprocal of the opposite arm with the sum of the correction factors equal to 1 *[**Sweeting**]*. Results are all expressed with RR < 1.0 suggesting effectiveness. Most results are the relative risk of something negative. If studies report relative times, results are expressed as the ratio of the time for the ivermectin group versus the time for the control group. Calculations are done in Python (3.9.1) with scipy (1.5.4), pythonmeta (1.11), numpy (1.19.4), statsmodels (0.12.1), and plotly (4.14.1).

The forest plots are computed using PythonMeta *[**Deng**]* with the DerSimonian and Laird random effects model (the fixed effect assumption is not plausible in this case). The forest plots show simplified dosages for comparison, these are the total dose in the first four days for treatment, and the monthly dose for prophylaxis, for a 70kg person. For full dosage details see below.

We received no funding, this research is done in our spare time. We have no affiliations with any pharmaceutical companies or political parties.

We have classified studies as early treatment if most patients are not already at a severe stage at the time of treatment, and treatment started within 5 days after the onset of symptoms, although a shorter time may be preferable. Antivirals are typically only considered effective when used within a shorter timeframe, for example 0-36 or 0-48 hours for oseltamivir, with longer delays not being effective *[**McLean**, **Treanor**]*.

Due to the much larger size of the control group in *[**Bernigaud**]*, we limit the size of the control group to be the same as the treatment group for calculation of the number of patients.

A summary of study results is below. Please submit updates and corrections at https://ivmmeta.com/.

Early treatment

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in calculations, which may differ from the effect a paper focuses on.

[Afsar], 12/15/2020, retrospective, Pakistan, South Asia, preprint, 6 authors, dosage 12mg days 1-6.	**risk of fever at day 14, 92.2% lower, RR 0.08, *p* = 0.04**, treatment 0 of 37 (0.0%), control 7 of 53 (13.2%), continuity correction due to zero event (with reciprocal of the contrasting arm).
[Ahmed], 12/2/2020, Double Blind Randomized Controlled Trial, Bangladesh, South Asia, peer-reviewed, mean age 42.0, 15 authors, dosage 12mg days 1-5, ivermectin + doxycycline group took only a single dose of ivermectin.	**risk of unresolved symptoms, 85.0% lower, RR 0.15, *p* = 0.09**, treatment 0 of 17 (0.0%), control 3 of 19 (15.8%), continuity correction due to zero event (with reciprocal of the contrasting arm), day 7 fever ivermectin.
	risk of unresolved symptoms, 62.7% lower, RR 0.37, *p* = 0.35, treatment 1 of 17 (5.9%), control 3 of 19 (15.8%), day 7 fever ivermectin + doxycycline.
	risk of no virological cure, 42.5% lower, RR 0.58, *p* = 0.01, treatment 11 of 22 (50.0%), control 20 of 23 (87.0%), day 7 ivermectin.
	risk of no virological cure, 20.0% lower, RR 0.80, *p* = 0.28, treatment 16 of 23 (69.6%), control 20 of 23 (87.0%), day 7 ivermectin + doxycycline.
	risk of no virological cure, 62.7% lower, RR 0.37, *p* = 0.02, treatment 5 of 22 (22.7%), control 14 of 23 (60.9%), day 14 ivermectin.
	risk of no virological cure, 35.7% lower, RR 0.64, *p* = 0.24, treatment 9 of 23 (39.1%), control 14 of 23 (60.9%), day 14 ivermectin + doxycycline.
	time to viral-, 23.6% lower, relative time 0.76, *p* = 0.02, treatment 22, control 23, ivermectin.
	time to viral-, 9.4% lower, relative time 0.91, *p* = 0.27, treatment 23, control 23, ivermectin + doxycycline.
	hospitalization time, 1.0% lower, relative time 0.99, ivermectin.
	hospitalization time, 4.1% higher, relative time 1.04, ivermectin + doxycycline.
[Babalola], 1/6/2021, Double Blind Randomized Controlled Trial, Nigeria, Africa, peer-reviewed, baseline oxygen requirements 8.3%, 10 authors, dosage 12mg or 6mg q84h for two weeks, this trial compares with another treatment - results may be better when compared to placebo.	**adjusted risk of viral+ at day 5, 63.9% lower, RR 0.36, *p* = 0.11**, treatment 40, control 20, adjusted per study.
	risk of no virological cure, 58.0% lower, RR 0.42, *p* = 0.01, treatment 20, control 20, 12mg - Cox proportional hazard model.
	risk of no virological cure, 40.5% lower, RR 0.60, *p* = 0.12, treatment 20, control 20, 6mg - Cox proportional hazard model.

	time to viral-, 49.2% lower, relative time 0.51, treatment 20, control 20, 12mg.
	time to viral-, 34.4% lower, relative time 0.66, treatment 20, control 20, 6mg.
[Bukhari], 1/16/2021, Randomized Controlled Trial, Pakistan, Middle East, preprint, 10 authors, dosage 12mg single dose.	**risk of no virological cure, 82.4% lower, RR 0.18, $p < 0.001$**, treatment 4 of 41 (9.8%), control 25 of 45 (55.6%), day 7.
	risk of no virological cure, 38.7% lower, RR 0.61, $p < 0.001$, treatment 24 of 41 (58.5%), control 43 of 45 (95.6%), day 3.
[Cadegiani], 11/4/2020, prospective, Brazil, South America, preprint, 4 authors, dosage 200µg/kg days 1-3.	**risk of death, 78.3% lower, RR 0.22, $p = 0.50$**, treatment 0 of 110 (0.0%), control 2 of 137 (1.5%), continuity correction due to zero event (with reciprocal of the contrasting arm), control group 1.
	risk of mechanical ventilation, 94.2% lower, RR 0.06, $p = 0.005$, treatment 0 of 110 (0.0%), control 9 of 137 (6.6%), continuity correction due to zero event (with reciprocal of the contrasting arm), control group 1.
	risk of hospitalization, 98.0% lower, RR 0.02, $p < 0.001$, treatment 0 of 110 (0.0%), control 27 of 137 (19.7%), continuity correction due to zero event (with reciprocal of the contrasting arm), control group 1.
[Carvallo], 9/15/2020, prospective, Argentina, South America, preprint, mean age 55.7, 3 authors, dosage 36mg days 1, 8, dose varied depending on patient condition - mild 24mg, moderate 36mg, severe 48mg, this trial uses multiple treatments in the treatment arm (combined with dexamethasone, enoxaparin, and aspirin) - results of individual treatments may vary.	**risk of death for hospitalized cases in study vs. cases in the same hospital not in the study, 87.9% lower, RR 0.12, $p = 0.05$**, treatment 1 of 33 (3.0%), control 3 of 12 (25.0%), the only treatment death was a patient already in the ICU before treatment.
[Chaccour], 12/7/2020, Double Blind Randomized Controlled Trial, Spain, Europe, peer-reviewed, 23 authors, dosage 400µg/kg single dose.	**symptom probability, 52.9% lower, RR 0.47, $p < 0.05$**, treatment 12, control 12, relative probability of symptoms at day 28, mixed effects logistic regression, data in supplementary appendix.
	viral load, 94.6% lower, relative load 0.05, treatment 12, control 12, day 7 mid-recovery, data in supplementary appendix.
[Chahla], 3/30/2021, Cluster Randomized Controlled Trial, Argentina, South America, preprint, 9 authors, dosage 24mg days 1, 8, 15, 22.	**risk of no medical release, 89.1% lower, RR 0.11, $p = 0.005$**, treatment 2 of 110 (1.8%), control 8 of 62 (12.9%), adjusted per study, odds ratio converted to relative risk.

[Chowdhury], 7/14/2020, Randomized Controlled Trial, Bangladesh, South Asia, peer-reviewed, 6 authors, dosage 200µg/kg single dose, this trial compares with another treatment - results may be better when compared to placebo, this trial uses multiple treatments in the treatment arm (combined with doxycycline) - results of individual treatments may vary.	**risk of hospitalization, 80.6% lower, RR 0.19, *p* = 0.23**, treatment 0 of 60 (0.0%), control 2 of 56 (3.6%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of no recovery, 46.4% lower, RR 0.54, *p* < 0.001, treatment 27 of 60 (45.0%), control 47 of 56 (83.9%), mid-recovery day 5.
	recovery time, 15.2% lower, relative time 0.85, *p* = 0.07, treatment 60, control 56.
	risk of no virological cure, 80.6% lower, RR 0.19, *p* = 0.23, treatment 0 of 60 (0.0%), control 2 of 56 (3.6%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	time to viral-, 4.3% lower, relative time 0.96, *p* = 0.23, treatment 60, control 56.
[Elalfy], 2/16/2021, retrospective, Egypt, Middle East, peer-reviewed, 15 authors, dosage 18mg days 1, 4, 7, 10, 13, <90kg 18mg, 90-120kg 24mg, >120kg 30mg, this trial uses multiple treatments in the treatment arm (combined with nitazoxanide, ribavirin, and zinc) - results of individual treatments may vary.	**risk of no virological cure, 86.9% lower, RR 0.13, *p* < 0.001**, treatment 7 of 62 (11.3%), control 44 of 51 (86.3%), day 15.
	risk of no virological cure, 58.1% lower, RR 0.42, *p* < 0.001, treatment 26 of 62 (41.9%), control 51 of 51 (100.0%), day 7.
[Espitia-Hernandez], 8/15/2020, retrospective, Mexico, North America, peer-reviewed, mean age 45.1, 5 authors, dosage 6mg days 1-2, 8-9, this trial uses multiple treatments in the treatment arm (combined with azithromycin and cholecalciferol) - results of individual treatments may vary.	**risk of viral+ at day 10, 97.2% lower, RR 0.03, *p* < 0.001**, treatment 0 of 28 (0.0%), control 7 of 7 (100.0%), continuity correction due to zero event (with reciprocal of the contrasting arm).
[Kirti], 1/9/2021, Double Blind Randomized Controlled Trial, India, South Asia, preprint, 11 authors, dosage 12mg days 1, 2.	**risk of death, 88.7% lower, RR 0.11, *p* = 0.12**, treatment 0 of 55 (0.0%), control 4 of 57 (7.0%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of mechanical ventilation, 79.3% lower, RR 0.21, *p* = 0.09, treatment 1 of 55 (1.8%), control 5 of 57 (8.8%).
	risk of ICU admission, 13.6% lower, RR 0.86, *p* = 0.80, treatment 5 of 55 (9.1%), control 6 of 57 (10.5%).
	risk of no virological cure, 11.6% higher, RR 1.12, *p* = 0.35, treatment 42 of 55 (76.4%), control 39 of 57 (68.4%).
[López-Medina], 3/4/2021, Double Blind Randomized Controlled Trial, Columbia,	**risk of death, 66.8% lower, RR 0.33, *p* = 0.50**, treatment 0 of 200 (0.0%), control 1 of 198 (0.5%),

South America, peer-reviewed, median age 37.0, 19 authors, dosage 300µg/kg days 1-5.	continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of escalation of care, 60.8% lower, RR 0.39, *p* = 0.10, treatment 4 of 200 (2.0%), control 10 of 198 (5.1%), odds ratio converted to relative risk.
	risk of escalation of care with post-hoc <12h exclusion, 34.3% lower, RR 0.66, *p* = 0.51, treatment 4 of 200 (2.0%), control 6 of 198 (3.0%), odds ratio converted to relative risk.
	risk of deterioration by >= 2 points on an 8-point scale, 43.1% lower, RR 0.57, *p* = 0.35, treatment 4 of 200 (2.0%), control 7 of 198 (3.5%), odds ratio converted to relative risk.
	risk of fever post randomization, 24.8% lower, RR 0.75, *p* = 0.33, treatment 16 of 200 (8.0%), control 21 of 198 (10.6%), odds ratio converted to relative risk.
	risk of unresolved symptoms at day 21, 15.3% lower, RR 0.85, *p* = 0.53, treatment 36 of 200 (18.0%), control 42 of 198 (21.2%), odds ratio converted to relative risk, Cox proportional-hazard model.
	hazard ratio for lack of resolution of symptoms, 6.5% lower, RR 0.93, *p* = 0.53, treatment 200, control 198.
	relative median time to resolution of symptoms, 16.7% lower, relative time 0.83, treatment 200, control 198.
[Mohan], 2/2/2021, Double Blind Randomized Controlled Trial, India, South Asia, preprint, 27 authors, dosage 400µg/kg single dose, 200µg/kg also tested.	**risk of no discharge at day 14, 62.5% lower, RR 0.38, *p* = 0.27**, treatment 2 of 40 (5.0%), control 6 of 45 (13.3%), ivermectin 24mg.
	risk of no discharge at day 14, 43.8% lower, RR 0.56, *p* = 0.49, treatment 3 of 40 (7.5%), control 6 of 45 (13.3%), ivermectin 12mg.
	risk of no virological cure, 10.3% lower, RR 0.90, *p* = 0.65, treatment 20 of 36 (55.6%), control 26 of 42 (61.9%), ivermectin 24mg, day 7.
	risk of no virological cure, 3.2% higher, RR 1.03, *p* = 1.00, treatment 23 of 36 (63.9%), control 26 of 42 (61.9%), ivermectin 12mg, day 7.
	risk of no virological cure, 23.8% lower, RR 0.76, *p* = 0.18, treatment 21 of 40 (52.5%), control 31 of 45 (68.9%), ivermectin 24mg, day 5.

	risk of no virological cure, 5.6% lower, RR 0.94, *p* = 0.82, treatment 26 of 40 (65.0%), control 31 of 45 (68.9%), ivermectin 12mg, day 5.
[Mourya], 4/1/2021, retrospective, India, South Asia, peer-reviewed, 5 authors, dosage 12mg days 1-7.	**risk of no virological cure, 89.4% lower, RR 0.11, *p* < 0.001**, treatment 5 of 50 (10.0%), control 47 of 50 (94.0%).
[Raad], 1/16/2021, Single Blind Randomized Controlled Trial, Lebanon, Middle East, preprint, 1 author, dosage 200µg/kg single dose.	**risk of hospitalization, 85.7% lower, RR 0.14, *p* = 0.24**, treatment 0 of 50 (0.0%), control 3 of 50 (6.0%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of viral load, 59.0% lower, RR 0.41, *p* = 0.01, treatment 50, control 50, percentage relative improvement in Ct value with treatment at day 3.
[Roy], 3/12/2021, retrospective, database analysis, India, South Asia, preprint, 5 authors, dosage not specified, this trial uses multiple treatments in the treatment arm (combined with doxycycline) - results of individual treatments may vary.	**relative time to clinical response of wellbeing, 5.6% lower, relative time 0.94, *p* = 0.87**, treatment 14, control 15.
[Schwartz], 2/12/2021, Double Blind Randomized Controlled Trial, Israel, Middle East, preprint, 1 author, dosage 12mg days 1-3, 15mg for patients >= 70kg.	**risk of hospitalization, 80.7% lower, RR 0.19, *p* = 0.23**, treatment 0 of 49 (0.0%), control 2 of 45 (4.4%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of no virological cure, 51.4% lower, RR 0.49, *p* = 0.01, treatment 16 of 49 (32.7%), control 25 of 45 (55.6%), adjusted per study, odds ratio converted to relative risk, multivariable logistic regression, day 6, Ct>30.
	risk of no virological cure, 54.1% lower, RR 0.46, *p* = 0.02, treatment 9 of 49 (18.4%), control 18 of 45 (40.0%), day 10, Ct>30.
	risk of no virological cure, 54.1% lower, RR 0.46, *p* = 0.02, treatment 10 of 49 (20.4%), control 20 of 45 (44.4%), day 8, Ct>30.
	risk of no virological cure, 41.2% lower, RR 0.59, *p* = 0.04, treatment 16 of 49 (32.7%), control 25 of 45 (55.6%), day 6, Ct>30.
	risk of no virological cure, 37.9% lower, RR 0.62, *p* = 0.09, treatment 11 of 26 (42.3%), control 15 of 22 (68.2%), day 4, Ct>30.

Late treatment

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in calculations, which may differ from the effect a paper focuses on.

[Beltran-Gonzalez], 2/23/2021, Double Blind Randomized Controlled Trial, Mexico, North America, peer-reviewed, mean age 53.8, 13 authors, dosage 12mg single dose, 18mg for patients >80kg.	**risk of death, 14.4% lower, RR 0.86, p = 1.00**, treatment 5 of 36 (13.9%), control 6 of 37 (16.2%).
	risk of respiratory deterioration or death, 8.6% lower, RR 0.91, p = 1.00, treatment 8 of 36 (22.2%), control 9 of 37 (24.3%).
	risk of no hospital discharge, 37.0% higher, RR 1.37, p = 0.71, treatment 4 of 36 (11.1%), control 3 of 37 (8.1%).
[Budhiraja], 11/18/2020, retrospective, India, South Asia, preprint, 12 authors, dosage not specified.	**risk of death, 99.1% lower, RR 0.009, p = 0.04**, treatment 0 of 34 (0.0%), control 103 of 942 (10.9%), continuity correction due to zero event (with reciprocal of the contrasting arm).
[Camprubí], 11/11/2020, retrospective, Spain, Europe, peer-reviewed, 9 authors, dosage 200µg/kg single dose.	**risk of ICU admission, 33.3% lower, RR 0.67, p = 1.00**, treatment 2 of 13 (15.4%), control 3 of 13 (23.1%), ICU at day 8.
	risk of no improvement at day 8, 33.3% higher, RR 1.33, p = 1.00, treatment 4 of 13 (30.8%), control 3 of 13 (23.1%).
[Chachar], 9/30/2020, Randomized Controlled Trial, India, South Asia, peer-reviewed, 6 authors, dosage 36mg, 12mg stat, 12mg after 12 hours, 12mg after 24 hours.	**risk of no recovery at day 7, 10.0% lower, RR 0.90, p = 0.50**, treatment 9 of 25 (36.0%), control 10 of 25 (40.0%).
[Elgazzar], 11/13/2020, Randomized Controlled Trial, Egypt, Africa, preprint, 6 authors, dosage 400µg/kg days 1-4, this trial compares with another treatment - results may be better when compared to placebo.	**risk of death, 91.7% lower, RR 0.08, p < 0.001**, treatment 2 of 200 (1.0%), control 24 of 200 (12.0%).
	risk of death, 88.9% lower, RR 0.11, p = 0.12, treatment 0 of 100 (0.0%), control 4 of 100 (4.0%), continuity correction due to zero event (with reciprocal of the contrasting arm), mild/moderate COVID-19.
	risk of death, 90.0% lower, RR 0.10, p < 0.001, treatment 2 of 100 (2.0%), control 20 of 100 (20.0%), severe COVID-19.
[Gorial], 7/8/2020, retrospective, Iraq, Middle East, preprint, 9 authors, dosage 200µg/kg single dose.	**risk of death, 71.0% lower, RR 0.29, p = 1.00**, treatment 0 of 16 (0.0%), control 2 of 71 (2.8%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	hospitalization time, 42.0% lower, relative time 0.58, p < 0.001, treatment 16, control 71.

[Hashim], 10/26/2020, Single Blind Randomized Controlled Trial, Iraq, Middle East, preprint, 6 authors, dosage 200µg/kg days 1-2, some patients received a third dose on day 8, this trial uses multiple treatments in the treatment arm (combined with doxycycline) - results of individual treatments may vary.	**risk of death, 66.7% lower, RR 0.33, p = 0.27**, treatment 2 of 70 (2.9%), control 6 of 70 (8.6%), all patients.
	risk of death, 91.7% lower, RR 0.08, p = 0.03, treatment 0 of 59 (0.0%), control 6 of 70 (8.6%), continuity correction due to zero event (with reciprocal of the contrasting arm), excluding critical patients.
[Huvemek], 3/25/2021, Double Blind Randomized Controlled Trial, Bulgaria, Europe, preprint, 1 author, dosage 400µg/kg days 1-3.	**risk of no improvement, 31.6% lower, RR 0.68, p = 0.28**, treatment 13 of 50 (26.0%), control 19 of 50 (38.0%), day 7, patients with improvement on WHO scale.
	risk of no improvement, 34.5% lower, RR 0.66, p = 0.07, treatment 19 of 50 (38.0%), control 29 of 50 (58.0%), day 4, patients with improvement on WHO scale.
[Khan], 9/24/2020, retrospective, Bangladesh, South Asia, preprint, median age 35.0, 8 authors, dosage 12mg single dose.	**risk of death, 87.0% lower, RR 0.13, p < 0.05**, treatment 1 of 115 (0.9%), control 9 of 133 (6.8%).
	time to viral-, 73.3% lower, relative time 0.27, p < 0.001, treatment 115, control 133.
[Kishoria], 8/31/2020, Randomized Controlled Trial, India, South Asia, peer-reviewed, 7 authors, dosage 12mg single dose.	**risk of no hospital discharge, 7.5% higher, RR 1.08, p = 1.00**, treatment 11 of 19 (57.9%), control 7 of 13 (53.8%).
	risk of no virological cure, 7.5% higher, RR 1.08, p = 1.00, treatment 11 of 19 (57.9%), control 7 of 13 (53.8%), day 3.
	risk of no virological cure, 220.0% higher, RR 3.20, p = 0.45, treatment 1 of 5 (20.0%), control 0 of 6 (0.0%), continuity correction due to zero event (with reciprocal of the contrasting arm), day 5.
[Lima-Morales], 2/10/2021, prospective, Mexico, North America, peer-reviewed, 9 authors, dosage 12mg single dose, this trial uses multiple treatments in the treatment arm (combined with azithromycin, montelukast, and aspirin) - results of individual treatments may vary.	**risk of death, 77.7% lower, RR 0.22, p < 0.001**, treatment 15 of 481 (3.1%), control 52 of 287 (18.1%), adjusted per study, odds ratio converted to relative risk, multivariate.
	risk of hospitalization, 67.4% lower, RR 0.33, p < 0.001, treatment 44 of 481 (9.1%), control 89 of 287 (31.0%), adjusted per study, odds ratio converted to relative risk, multivariate.
	risk of no recovery, 58.6% lower, RR 0.41, p < 0.001, treatment 75 of 481 (15.6%), control 118 of 287 (41.1%), adjusted per study, odds ratio converted to relative risk, recovery at day 14 after symptoms, multivariate.
[Mahmud], 10/9/2020, Double Blind	**risk of death, 85.7% lower, RR 0.14, p = 0.25**,

Randomized Controlled Trial, Bangladesh, South Asia, preprint, 1 author, dosage 12mg single dose, this trial uses multiple treatments in the treatment arm (combined with doxycycline) - results of individual treatments may vary.	treatment 0 of 183 (0.0%), control 3 of 183 (1.6%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of no recovery, 49.0% lower, RR 0.51, p < 0.004, treatment 42 of 183 (23.0%), control 67 of 180 (37.2%), adjusted per study.
	risk of disease progression, 55.0% lower, RR 0.45, p < 0.01, treatment 16 of 183 (8.7%), control 32 of 180 (17.8%), adjusted per study.
	risk of no virological cure, 42.0% lower, RR 0.58, p < 0.001, treatment 14 of 183 (7.7%), control 36 of 180 (20.0%), adjusted per study.
[Niaee], 11/24/2020, Double Blind Randomized Controlled Trial, Iran, Middle East, preprint, mean age 56.0, 14 authors, dosage 400µg/kg single dose, dose varies in different groups.	**risk of death, 81.8% lower, RR 0.18, p = 0.001**, treatment 4 of 120 (3.3%), control 11 of 60 (18.3%), All IVM vs. all control.
	risk of death, 94.3% lower, RR 0.06, p = 0.01, treatment 0 of 30 (0.0%), control 11 of 60 (18.3%), continuity correction due to zero event (with reciprocal of the contrasting arm), IVM single dose 200mcg/kg vs. all control.
	risk of death, 45.5% lower, RR 0.55, p = 0.37, treatment 3 of 30 (10.0%), control 11 of 60 (18.3%), IVM three dose 200mcg/kg vs. all control.
	risk of death, 94.3% lower, RR 0.06, p = 0.01, treatment 0 of 30 (0.0%), control 11 of 60 (18.3%), continuity correction due to zero event (with reciprocal of the contrasting arm), IVM single dose 400mcg/kg vs. all control.
	risk of death, 81.8% lower, RR 0.18, p = 0.06, treatment 1 of 30 (3.3%), control 11 of 60 (18.3%), IVM three dose 400/200/200mcg/kg vs. all control.
[Okumuş], 1/12/2021, Double Blind Randomized Controlled Trial, Turkey, Middle East, preprint, 15 authors, dosage 200µg/kg days 1-5, 36-50kg - 9mg, 51-65kg - 12mg, 66-79kg - 15mg, >80kg 200µg/kg.	**risk of death, 33.3% lower, RR 0.67, p = 0.55**, treatment 6 of 30 (20.0%), control 9 of 30 (30.0%).
	risk of no improvement at day 10, 42.9% lower, RR 0.57, p = 0.18, treatment 8 of 30 (26.7%), control 14 of 30 (46.7%).
	risk of no improvement at day 5, 15.8% lower, RR 0.84, p = 0.60, treatment 16 of 30 (53.3%), control 19 of 30 (63.3%).
	risk of no virological cure, 80.0% lower, RR 0.20, p = 0.02, treatment 2 of 16 (12.5%), control 5 of 8 (62.5%), day 10.

[Podder], 9/3/2020, Randomized Controlled Trial, Bangladesh, South Asia, peer-reviewed, 4 authors, dosage 200µg/kg single dose.	**recovery time from enrollment, 16.1% lower, relative time 0.84, p = 0.34**, treatment 32, control 30.
[Pott-Junior], 3/9/2021, Randomized Controlled Trial, Brazil, South America, peer-reviewed, 10 authors, dosage 200µg/kg single dose, dose varies in three arms 100, 200, 400µg/kg.	**risk of ICU admission, 85.2% lower, RR 0.15, p = 0.25**, treatment 1 of 27 (3.7%), control 1 of 4 (25.0%).
	relative improvement in Ct value, 0.8% lower, RR 0.99, p = 1.00, treatment 27, control 3.
	risk of no virological cure, 11.1% higher, RR 1.11, p = 1.00, treatment 10 of 27 (37.0%), control 1 of 3 (33.3%).
	time to viral-, 16.7% lower, relative time 0.83, treatment 27, control 3.
[Rajter], 10/13/2020, retrospective, USA, North America, peer-reviewed, 6 authors, dosage 200µg/kg single dose.	**risk of death, 46.0% lower, RR 0.54, p = 0.04**, treatment 13 of 98 (13.3%), control 24 of 98 (24.5%), adjusted per study, odds ratio converted to relative risk, PSM.
	risk of death, 66.9% lower, RR 0.33, p = 0.03, treatment 26 of 173 (15.0%), control 27 of 107 (25.2%), adjusted per study, odds ratio converted to relative risk, multivariate.
[Rezai], 1/19/2021, Double Blind Randomized Controlled Trial, Iran, Middle East, preprint, 1 author, dosage 200µg/kg single dose.	**recovery time, 21.2% lower, relative time 0.79, p = 0.02**, treatment 51, control 52.
	hospitalization time, 17.9% lower, relative time 0.82, p = 0.01, treatment 51, control 52.
[Soto-Becerra], 10/8/2020, retrospective, database analysis, Peru, South America, preprint, median age 59.4, 4 authors, dosage 200µg/kg single dose.	**risk of death, 17.1% lower, RR 0.83, p = 0.01**, treatment 92 of 203 (45.3%), control 1438 of 2630 (54.7%), IVM vs. control day 43 (last day available) weighted KM from figure 3, per the pre-specified rules, the last available day mortality results have priority.
	risk of death, 39.0% higher, RR 1.39, p = 0.16, treatment 47 of 203 (23.2%), control 401 of 2630 (15.2%), adjusted per study, day 30, Table 2, IVM wHR.
[Spoorthi], 11/14/2020, prospective, India, South Asia, peer-reviewed, 2 authors, dosage not specified, this trial uses multiple treatments in the treatment arm (combined with doxycycline) - results of individual treatments may vary.	**recovery time, 21.1% lower, relative time 0.79, p = 0.03**, treatment 50, control 50.
	hospitalization time, 15.5% lower, relative time 0.84, p = 0.01, treatment 50, control 50.

Prophylaxis

Effect extraction follows pre-specified rules as detailed above and gives priority to more serious outcomes. Only the first (most serious) outcome is used in calculations, which may differ from the effect a paper focuses on.

[Alam], 12/15/2020, prospective, Bangladesh, South Asia, peer-reviewed, 13 authors, dosage 12mg monthly.	**risk of COVID-19 case, 90.6% lower, RR 0.09, $p < 0.001$**, treatment 4 of 58 (6.9%), control 44 of 60 (73.3%).
[Behera], 2/15/2021, prospective, India, South Asia, preprint, 13 authors, dosage 300µg/kg days 1, 4.	**risk of COVID-19 case, 83.0% lower, RR 0.17, $p < 0.001$**, treatment 45 of 2199 (2.0%), control 133 of 1147 (11.6%), two doses.
	risk of COVID-19 case, 4.0% higher, RR 1.04, $p = 0.85$, treatment 23 of 186 (12.4%), control 133 of 1147 (11.6%), patients only receiving the first dose.
[Behera (B)], 11/3/2020, retrospective, India, South Asia, peer-reviewed, 13 authors, dosage 300µg/kg days 1, 4.	**risk of COVID-19 case, 53.8% lower, RR 0.46, $p < 0.001$**, treatment 41 of 117 (35.0%), control 145 of 255 (56.9%), adjusted per study, odds ratio converted to relative risk, model 2 2+ doses conditional logistic regression.
	risk of COVID-19 case, 44.5% lower, RR 0.56, $p < 0.001$, treatment 41 of 117 (35.0%), control 145 of 255 (56.9%), odds ratio converted to relative risk, matched pair analysis.
[Bernigaud], 11/28/2020, retrospective, France, Europe, peer-reviewed, 12 authors, dosage 200µg/kg days 1, 8, 15, 400µg/kg days 1, 8, 15, two different dosages.	**risk of death, 99.4% lower, RR 0.006, $p = 0.08$**, treatment 0 of 69 (0.0%), control 150 of 3062 (4.9%), continuity correction due to zero event (with reciprocal of the contrasting arm).
	risk of COVID-19 case, 55.1% lower, RR 0.45, $p = 0.01$, treatment 7 of 69 (10.1%), control 692 of 3062 (22.6%).
[Carvallo (B)], 11/17/2020, prospective, Argentina, South America, peer-reviewed, 4 authors, dosage 12mg weekly, this trial uses multiple treatments in the treatment arm (combined with iota-carrageenan) - results of individual treatments may vary.	**risk of COVID-19 case, 99.9% lower, RR 0.001, $p < 0.001$**, treatment 0 of 788 (0.0%), control 237 of 407 (58.2%), continuity correction due to zero event (with reciprocal of the contrasting arm).
[Carvallo (C)], 10/19/2020, prospective, Argentina, South America, preprint, 1 author, dosage 1mg days 1-14, this trial uses multiple treatments in the treatment arm (combined with iota-carrageenan) - results of individual treatments may vary.	**risk of COVID-19 case, 96.3% lower, RR 0.04, $p < 0.001$**, treatment 0 of 131 (0.0%), control 11 of 98 (11.2%), continuity correction due to zero event (with reciprocal of the contrasting arm).
[Chahla (B)], 1/11/2021, Randomized Controlled Trial, Argentina, South America, preprint, 1 author, dosage 12mg weekly, this trial uses multiple	**risk of COVID-19 case, 95.2% lower, RR 0.05, $p = 0.002$**, treatment 0 of 117 (0.0%), control 10 of 117 (8.5%), continuity correction due to zero event

treatments in the treatment arm (combined with iota-carrageenan) - results of individual treatments may vary.	(with reciprocal of the contrasting arm), moderate/severe COVID-19.
	risk of COVID-19 case, 84.0% lower, RR 0.16, $p < 0.001$, treatment 4 of 117 (3.4%), control 25 of 117 (21.4%), adjusted per study, odds ratio converted to relative risk, all cases.
	risk of COVID-19 case, 84.0% lower, RR 0.16, $p < 0.001$, treatment 4 of 117 (3.4%), control 25 of 117 (21.4%), all cases.
[Elgazzar (B)], 11/13/2020, Randomized Controlled Trial, Egypt, Africa, preprint, 6 authors, dosage 400µg/kg weekly.	**risk of COVID-19 case, 80.0% lower, RR 0.20, $p = 0.03$**, treatment 2 of 100 (2.0%), control 10 of 100 (10.0%).
[Hellwig], 11/28/2020, retrospective, ecological study, multiple countries, Africa, peer-reviewed, 2 authors, dosage 200µg/kg, dose varied, typically 150-200µg/kg.	**risk of COVID-19 case, 78.0% lower, RR 0.22, $p < 0.02$**, African countries, PCTI vs. no PCT, relative cases per capita.
	risk of COVID-19 case, 80.0% lower, RR 0.20, $p < 0.001$, worldwide, PCTI vs. no PCT, relative cases per capita.
[Morgenstern], 4/16/2021, retrospective, Dominican Republic, Caribbean, preprint, 16 authors, dosage 200µg/kg weekly.	**risk of hospitalization, 80.0% lower, RR 0.20, $p = 0.50$**, treatment 0 of 271 (0.0%), control 2 of 271 (0.7%), continuity correction due to zero event (with reciprocal of the contrasting arm), PSM.
	risk of COVID-19 case, 74.0% lower, RR 0.26, $p = 0.008$, treatment 5 of 271 (1.8%), control 18 of 271 (6.6%), adjusted per study, PSM, multivariate Cox regression.
[Seet], 4/14/2021, Cluster Randomized Controlled Trial, Singapore, Asia, peer-reviewed, 15 authors, dosage 12mg single dose, 200µg/kg, maximum 12mg, this trial compares with another treatment - results may be better when compared to placebo.	**risk of COVID-19 severe case, 49.8% lower, RR 0.50, $p = 0.01$**, treatment 32 of 617 (5.2%), control 64 of 619 (10.3%).
	risk of COVID-19 case, 5.8% lower, RR 0.94, $p = 0.61$, treatment 398 of 617 (64.5%), control 433 of 619 (70.0%), adjusted per study, odds ratio converted to relative risk, model 6.
[Shouman], 8/28/2020, Randomized Controlled Trial, Egypt, Africa, peer-reviewed, 8 authors, dosage 18mg days 1, 3, dose varies depending on weight - 40-60kg: 15mg, 60-80kg: 18mg, >80kg: 24mg.	**risk of symptomatic case, 91.3% lower, RR 0.09, $p < 0.001$**, treatment 15 of 203 (7.4%), control 59 of 101 (58.4%), adjusted per study, multivariate.
	risk of COVID-19 severe case, 92.9% lower, RR 0.07, $p = 0.002$, treatment 1 of 203 (0.5%), control 7 of 101 (6.9%), unadjusted.
[Tanioka], 3/26/2021, retrospective, ecological study, multiple countries, Africa, preprint, 3 authors, dosage 200µg/kg, dose varied, typically 150-200µg/kg.	**risk of death, 88.2% lower, RR 0.12, $p = 0.002$**, relative mean mortality per million.

[Vallejos], 12/20/2020, retrospective, Argentina, South America, preprint, 1 author, dosage 12mg weekly.	risk of COVID-19 case, 73.4% lower, RR 0.27, $p < 0.001$, treatment 13 of 389 (3.3%), control 61 of 486 (12.6%).

References

1. **Afsar** et al., SSRN, *Ivermectin Use Associated with Reduced Duration of COVID-19 Febrile Illness in a Community Setting*, https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3734478.

2. **Ahmed** et al., International Journal of Infectious Diseases, doi:10.1016/j.ijid.2020.11.191, *A five day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness*, https://www.sciencedirect.com/science/article/pii/S1201971220325066.

3. **Alam** et al., European Journal ofMedical and Health Sciences, doi:10.24018/ejmed.2020.2.6.599, *Ivermectin as Pre-exposure Prophylaxis for COVID-19 among Healthcare Providers in a Selected Tertiary Hospital in Dhaka – An Observational Study*, https://ejmed.org/index.php/ejmed/article/view/599.

4. **Altman**, D., BMJ, doi:10.1136/bmj.d2304, *How to obtain the P value from a confidence interval*, https://www.bmj.com/content/343/bmj.d2304.

5. **Altman (B)** et al., BMJ, doi:10.1136/bmj.d2090, *How to obtain the confidence interval from a P value*, https://www.bmj.com/content/343/bmj.d2090.

6. **Anglemyer** et al., Cochrane Database of Systematic Reviews 2014, Issue 4, doi:10.1002/14651858.MR000034.pub2, *Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials*, https://www.cochranelibrary.com/cd..0.1002/14651858.MR000034.pub2/full.

7. **Babalola** et al., QJM: An International Journal of Medicine, doi:10.1093/qjmed/hcab035 (preprint 1/6), *Ivermectin shows clinical benefits in mild to moderate COVID19: A randomised controlled double-blind, dose-response study in Lagos*, https://academic.oup.com/qjmed/adv../doi/10.1093/qjmed/hcab035/6143037.

8. **Baqui** et al., The Lancet Global Health, doi:10.1016/S2214-109X(20)30285-0, *Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: a cross-sectional observational study*, https://www.sciencedirect.com/science/article/pii/S2214109X20302850.

9. **Behera** et al., Research Square, doi:10.21203/rs.3.rs-208785/v1, *Prophylactic role of ivermectin in SARS-CoV-2 infection among healthcare workers*, https://www.researchsquare.com/article/rs-208785/v1.

10. **Behera (B)** et al., PLoS ONE, doi:10.1371/journal.pone.0247163 (preprint 11/3), *Role of ivermectin in the prevention of SARS-CoV-2 infection among healthcare workers in India: A matched case-control study*, https://journals.plos.org/plosone/..le?id=10.1371/journal.pone.0247163.

11. **Beltran-Gonzalez** et al., medRxiv, doi:10.1101/2021.02.18.21252037, *Efficacy and safety of Ivermectin and Hydroxychloroquine in patients with severe COVID-19. A randomized controlled trial*, https://www.medrxiv.org/content/10.1101/2021.02.18.21252037v1.

12. **Bernigaud** et al., Annals of Dermatology and Venereology, doi:10.1016/j.annder.2020.09.231, *Ivermectin benefit: from scabies to COVID-19, an example of serendipity*, https://www.sciencedirect.com/science/article/pii/S015196382030627X.

13. **Bryant** et al., Research Square, doi:10.21203/rs.3.rs-317485/v1 (OSF preprints 3/11), *Ivermectin for prevention and treatment of COVID-19 infection: a systematic review and meta-analysis*, https://www.researchsquare.com/article/rs-317485/v1.

14. **Budhiraja** et al., medRxiv, doi:10.1101/2020.11.16.20232223, *Clinical Profile of First 1000 COVID-19 Cases Admitted at Tertiary Care Hospitals and the Correlates of their Mortality: An Indian Experience*, https://www.medrxiv.org/content/10.1101/2020.11.16.20232223v1.

15. **Bukhari** et al., medRxiv, doi:10.1101/2021.02.02.21250840 (results 1/16), *Efficacy of Ivermectin in COVID-19 Patients with Mild to Moderate Disease*, https://www.medrxiv.org/content/10.1101/2021.02.02.21250840v1.

16. **Cadegiani** et al., medRxiv, doi:10.1101/2020.10.31.20223883, *Early COVID-19 Therapy with Azithromycin Plus Nitazoxanide, Ivermectin or Hydroxychloroquine in Outpatient Settings Significantly Reduced Symptoms Compared to Known Outcomes in Untreated Patients*, https://www.medrxiv.org/content/10.1101/2020.10.31.20223883v1.

17. **Camprubí** et al., PLoS ONE, 15:11, doi:10.1371/journal.pone.0242184, *Lack of efficacy of standard doses of ivermectin in severe COVID-19 patients*, https://journals.plos.org/plosone/..le?id=10.1371/journal.pone.0242184.

18. **Carvallo** et al., medRxiv, doi:10.1101/2020.09.10.20191619, *Safety and Efficacy of the combined use of ivermectin, dexamethasone, enoxaparin and aspirin against COVID-19*, https://www.medrxiv.org/content/10.1101/2020.09.10.20191619v1.

19. **Carvallo (B)** et al., Journal of Biomedical Research and Clinical Investigation, doi:10.31546/2633-8653.1007, *Study of the Efficacy and Safety of Topical Ivermectin + Iota-Carrageenan in the Prophylaxis against COVID-19 in Health Personnel*, https://medicalpressopenaccess.com/upload/1605709669_1007.pdf.

20. **Carvallo (C)** et al., NCT04425850, *Usefulness of Topic Ivermectin and Carrageenan to Prevent Contagion of Covid 19 (IVERCAR)*, https://clinicaltrials.gov/ct2/show/results/NCT04425850.

21. **Chaccour** et al., EClinicalMedicine, doi:10.1016/j.eclinm.2020.100720 (preprint 12/7), *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*, https://www.thelancet.com/journals../PIIS2589-5370(20)30464-8/fulltext.

22. **Chachar** et al., International Journal of Sciences, 9:31-35, doi:10.18483/ijSci.2378, *Effectiveness of Ivermectin in SARS-CoV-2/COVID-19 Patients*, https://www.ijsciences.com/pub/article/2378.

23. **Chahla** et al., medRxiv, doi:10.1101/2021.03.29.21254554, *Ivermectin reproposing for COVID-19 treatment outpatients in mild stage in primary health care centers*, https://www.medrxiv.org/content/10.1101/2021.03.29.21254554v1.

24. **Chahla (B)** et al., medRxiv, doi:10.1101/2021.03.26.21254398, *A randomized trial - intensive treatment based in ivermectin and iota-carrageenan as pre-exposure prophylaxis for COVID-19 in healthcare agents*, https://www.medrxiv.org/content/10.1101/2021.03.26.21254398v1.

25. **Chowdhury** et al., Eurasian Journal of Medicine and Oncology, doi:10.14744/ejmo.2021.16263, *A Comparative Study on Ivermectin-Doxycycline and Hydroxychloroquine-Azithromycin Therapy on COVID-19 Patients*, https://ejmo.org/10.14744/ejmo.2021.16263/.

26. **Concato** et al., NEJM, 342:1887-1892, doi:10.1056/NEJM200006223422507, https://www.nejm.org/doi/full/10.1056/nejm200006223422507.

27. **Deaton** et al., Social Science & Medicine, 210, doi:10.1016/j.socscimed.2017.12.005, *Understanding and misunderstanding randomized controlled trials*, https://www.sciencedirect.com/science/article/pii/S0277953617307359.

28. **Deng**, H., *PyMeta, Python module for meta-analysis*, http://www.pymeta.com/.

29. **Elalfy** et al., J. Med. Virol., doi:10.1002/jmv.26880, *Effect of a combination of Nitazoxanide, Ribavirin and Ivermectin plus zinc supplement (MANS.NRIZ study) on the clearance of mild COVID-1*, https://onlinelibrary.wiley.com/doi/10.1002/jmv.26880.

30. **Elgazzar** et al., Research Square, doi:10.21203/rs.3.rs-100956/v2, *Efficacy and Safety of Ivermectin for Treatment and prophylaxis of COVID-19 Pandemic*, https://www.researchsquare.com/article/rs-100956/v3.

31. **Elgazzar (B)** et al., Research Square, doi:10.21203/rs.3.rs-100956/v2, *Efficacy and Safety of Ivermectin for Treatment and prophylaxis of COVID-19 Pandemic*, https://www.researchsquare.com/article/rs-100956/v3.

32. **Espitia-Hernandez** et al., Biomedical Research, 31:5, *Effects of Ivermectin-azithromycin-cholecalciferol combined therapy on COVID-19 infected patients: A proof of concept study*, https://www.biomedres.info/biomedi..-proof-of-concept-study-14435.html.

33. **Galan** et al., Pathogens and Global Health, doi:10.1080/20477724.2021.1890887, *Phase 2 randomized study on chloroquine, hydroxychloroquine or ivermectin in hospitalized patients with severe manifestations of SARS-CoV-2 infection*, https://www.tandfonline.com/doi/full/10.1080/20477724.2021.1890887.

34. **Gorial** et al., medRxiv, doi:10.1101/2020.07.07.20145979, *Effectiveness of Ivermectin as add-on Therapy in COVID-19 Management (Pilot Trial)*, https://www.medrxiv.org/content/10.1101/2020.07.07.20145979v1.

35. **Hashim** et al., medRxiv, doi:10.1101/2020.10.26.20219345, *Controlled randomized clinical trial on using Ivermectin with Doxycycline for treating COVID-19 patients in Baghdad, Iraq*, https://www.medrxiv.org/content/10.1101/2020.10.26.20219345v1.

36. **Hellwig** et al., International Journal of Antimicrobial Agents, doi:10.1016/j.ijantimicag.2020.106248, *A COVID-19 Prophylaxis? Lower incidence associated with prophylactic administration of Ivermectin*, https://www.sciencedirect.com/science/article/pii/S0924857920304684.

37. **Hill** et al., Research Square, doi:10.21203/rs.3.rs-148845/v1, *Meta-analysis of randomized trials of ivermectin to treat SARS-CoV-2 infection*, https://www.researchsquare.com/article/rs-148845/v1.

38. **Huvemek** Press Release, *Kovid-19 - Huvemek® Phase 2 clinical trial*, https://huvemec.bg/covid-19-huveme..linichno-izpitanie/za-isledvaneto/.

39. **Khan** et al., Archivos de Bronconeumología, doi:10.1016/j.arbres.2020.08.007, *Ivermectin treatment may improve the prognosis of patients with COVID-19*, https://www.archbronconeumol.org/e..ognosis-articulo-S030028962030288X.

40. **Kirti** et al., medRxiv, doi:10.1101/2021.01.05.21249310, *Ivermectin as a potential treatment for mild to moderate COVID-19: A double blind randomized placebo-controlled trial*, https://www.medrxiv.org/content/10.1101/2021.01.05.21249310v1.

41. **Kishoria** et al., Paripex - Indian Journal of Research, doi:10.36106/paripex, *Ivermectin as adjuvant to hydroxychloroquine in patients resistant to standard treatment for SARS-CoV-2: results of an open-label randomized clinical study*, https://www.worldwidejournals.com/..August_2020_1597492974_4801859.pdf.

42. **Kory** et al., FLCCC Alliance, *Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19*, https://covid19criticalcare.com/wp..axis-and-treatment-of-COVID-19.pdf.

43. **Kory (B)** et al., Feb 11, 2021, *FLCCC Weekly Update - I-MASK+ and MATH+ Protocols*, https://www.youtube.com/watch?v=xy85K1hENn4&t=1829s.

44. **Krolewiecki** et al., SSRN, *Antiviral Effect of High-Dose Ivermectin in Adults with COVID-19: A Pilot Randomised, Controlled, Open Label, Multicentre Trial*, https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3714649.

45. **Lawrie** et al., Preprint, *Ivermectin reduces the risk of death from COVID-19 – a rapid review and meta-analysis in support of the recommendation of the Front Line COVID-19 Critical Care Alliance*, https://b3d2650e-e929-4448-a527-4e..b655bd21b1448ba6cf1f4c59f0d73d.pdf.

46. **Lee** et al., Arch Intern Med., 2011, 171:1, 18-22, doi:10.1001/archinternmed.2010.482, *Analysis of Overall Level of Evidence Behind Infectious Diseases Society of America Practice Guidelines*, https://jamanetwork.com/journals/j..nternalmedicine/fullarticle/226373.

47. **Lima-Morales**, *Effectiveness of a multidrug therapy consisting of ivermectin, azithromycin, montelukast and acetylsalicylic acid to prevent hospitalization and death among ambulatory COVID-19 cases in Tlaxcala, Mexico*, https://www.sciencedirect.com/science/article/pii/S1201971221001004.

48. **López-Medina** et al., JAMA, doi:10.1001/jama.2021.3071, *Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial*, https://jamanetwork.com/journals/jama/fullarticle/2777389.

49. **Mahmud** et al., Clinical Trial Results, NCT04523831, *Clinical Trial of Ivermectin Plus Doxycycline for the Treatment of Confirmed Covid-19 Infection*, https://clinicaltrials.gov/ct2/show/results/NCT04523831?view=results.

50. **McLean** et al., Open Forum Infect. Dis. September 2015, 2:3, doi:10.1093/ofid/ofv100, *Impact of Late Oseltamivir Treatment on Influenza Symptoms in the Outpatient Setting: Results of a Randomized Trial*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4525010/.

51. **Mohan** et al., Research Square, doi:10.21203/rs.3.rs-191648/v1, *Ivermectin in mild and moderate COVID-19 (RIVET-COV): a randomized, placebo-controlled trial*, https://www.researchsquare.com/article/rs-191648/v1.

52. **Morgenstern** et al., medRxiv, doi:10.1101/2021.04.10.21255248, *Retrospective cohort study of Ivermectin as a SARS-CoV-2 pre-exposure prophylactic method in Healthcare Workers*, https://www.medrxiv.org/content/10.1101/2021.04.10.21255248v1.

53. **Mourya** et al., Int. J. Health and Clinical Research, *Comparative Analytical Study of Two Different Drug Regimens in Treatment of Covid 19 Positive Patients in Index Medical College Hospital and Research Center, Indore, India*, https://ijhcr.com/index.php/ijhcr/article/view/1263.

54. **Nardelli** et al., Signa Vitae, doi:10.22514/sv.2021.043, *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?*, https://www.signavitae.com/articles/10.22514/sv.2021.043.

55. **Niaee** et al., Research Square, doi:10.21203/rs.3.rs-109670/v1, *Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: A randomized multi-center clinical trial*, https://www.researchsquare.com/article/rs-109670/v1.

56. **Nichol** et al., Injury, 2010, doi: 10.1016/j.injury.2010.03.033, *Challenging issues in randomised controlled trials*, https://www.injuryjournal.com/article/S0020-1383(10)00233-0/fulltext.

57. **Okumuş** et al., NCT04646109, *Evaluation of the Effectiveness and Safety of Adding Ivermectin to Treatment in Severe COVID-19 Patients*, https://www.researchsquare.com/article/rs-224203/v1.

58. **Podder** et al., IMC J. Med. Science, 14:2, July 2020, *Outcome of ivermectin treated mild to moderate COVID-19 cases: a single-centre, open-label, randomised controlled study*, http://imcjms.com/registration/journal_abstract/353.

59. **Pott-Junior** et al., Toxicology Reports, doi:10.1016/j.toxrep.2021.03.003, *Use of ivermectin in the treatment of Covid-19: a pilot trial*, https://www.sciencedirect.com/science/article/pii/S2214750021000445.

60. **Raad** et al., ChiCTR2000033627, *In vivo use of ivermectin (IVR) for treatment for corona virus infected patients (COVID-19): a randomized controlled trial*, http://www.chictr.org.cn/showprojen.aspx?proj=54707.

61. **Rajter** et al., Chest, doi:10.1016/j.chest.2020.10.009, *Use of Ivermectin is Associated with Lower Mortality in Hospitalized Patients with COVID-19 (ICON study)*, https://www.sciencedirect.com/science/article/pii/S0012369220348984.

62. **Rezai** et al., IRCT20111224008507N3, *Effectiveness of Ivermectin in the Treatment of Coronavirus Infection in Patients admitted to Educational Hospitals of Mazandaran in 2020*, https://en.irct.ir/trial/49174.

63. **Roy** et al., medRxiv, doi:10.1101/2021.03.08.21252883, *Outcome of Different Therapeutic Interventions in Mild COVID-19 Patients in a Single OPD Clinic of West Bengal: A Retrospective study*, https://www.medrxiv.org/content/10.1101/2021.03.08.21252883v1.

64. **Schwartz**, E., Sheba Ivermectin Project, *Ivermectin vs. placebo treatment in non-hospitalized patients with COVID-19 - A double blind, randomized controlled trial*, https://vimeo.com/511687719.

65. **Seet** et al., International Journal of Infectious Diseases, doi:10.1016/j.ijid.2021.04.035, *Positive impact of oral hydroxychloroquine and povidone-iodine throat spray for COVID-19 prophylaxis: an open-label randomized trial*, https://www.ijidonline.com/article/S1201-9712(21)00345-3/fulltext.

66. **Shouman** et al., Journal of Clinical and Diagnostic Research, doi:10.7860/JCDR/2020/46795.0000, *Use of Ivermectin as a Potential Chemoprophylaxis for COVID-19 in Egypt: A Randomised Clinical Trial*, https://www.jcdr.net/articles/PDF/..Sh)_PF1(SY_OM)_PFA_(OM)_PN(KM).pdf.

67. **Soto-Becerra** et al., medRxiv, doi:10.1101/2020.10.06.20208066, *Real-World Effectiveness of hydroxychloroquine, azithromycin, and ivermectin among hospitalized COVID-19 patients: Results of a target trial emulation using observational data from a nationwide Healthcare System in Peru*, https://www.medrxiv.org/content/10.1101/2020.10.06.20208066v1.

68. **Spoorthi** et al., IAIM, 2020, 7:10, 177-182, *Utility of Ivermectin and Doxycycline combination for the treatment of SARSCoV-2*, http://iaimjournal.com/wp-content/..oads/2020/10/iaim_2020_0710_23.pdf.

69. **Sweeting** et al., Statistics in Medicine, doi:10.1002/sim.1761, *What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data*, https://onlinelibrary.wiley.com/doi/10.1002/sim.1761.

70. **Tanioka** et al., medRxiv, doi:10.1101/2021.03.26.21254377, *Why COVID-19 is not so spread in Africa: How does Ivermectin affect it?*, https://www.medrxiv.org/content/10.1101/2021.03.26.21254377v1.

71. **Treanor** et al., JAMA, 2000, 283:8, 1016-1024, doi:10.1001/jama.283.8.1016, *Efficacy and Safety of the Oral Neuraminidase Inhibitor Oseltamivir in Treating Acute Influenza: A Randomized Controlled Trial*, https://jamanetwork.com/journals/jama/fullarticle/192425.

72. **Vallejos** et al., Trials, doi:10.1186/s13063-020-04813-1, *Ivermectin to prevent hospitalizations in patients with COVID-19 (IVERCOR-COVID19): a structured summary of a study protocol for a randomized controlled trial*, https://trialsjournal.biomedcentra..rticles/10.1186/s13063-020-04813-1.

73. **Vallejos (B)** et al., *Ivermectina en agentes de salud e ivercor COVID-19: resultados al 18 de feb 2021*, https://twitter.com/Covid19Crusher/status/1365420061859717124.

74. **Yim**, P., TrialSiteNews, *Systemic unreported protocol violations in key ivermectin study*, https://trialsitenews.com/systemic..iolations-in-key-ivermectin-study/.

75. **Zhang** et al., JAMA, 80:19, 1690, doi:10.1001/jama.280.19.1690, *What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes*, https://jamanetwork.com/journals/jama/fullarticle/188182.