

# Ivermectin is effective for COVID-19: real-time meta analysis of 36 studies

Covid Analysis, Nov 26, 2020 (Version 25, Feb 2, 2021)

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- 100% of the 36 studies to date report positive effects. Early treatment is more successful, with an estimated reduction of 82% in the effect measured using a random effects meta-analysis, RR 0.18 [0.10-0.34]. Prophylactic use also shows high effectiveness.
- 100% of the 18 Randomized Controlled Trials (RCTs) report positive effects, with an estimated reduction of 71%, RR 0.29 [0.17-0.50].
- The probability that an ineffective treatment generated results as positive as the 36 studies to date is estimated to be 1 in 69 billion ( $p = 0.000000000015$ ).

|                 |                 |                     |
|-----------------|-----------------|---------------------|
| Early treatment | 82% improvement | RR 0.18 [0.10-0.34] |
| Late treatment  | 39% improvement | RR 0.61 [0.47-0.79] |
| Prophylaxis     | 90% improvement | RR 0.10 [0.05-0.23] |

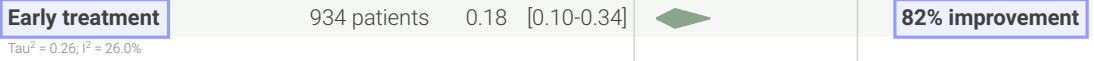
|       |            |             |                 |
|-------|------------|-------------|-----------------|
| Total | 36 studies | 255 authors | 10,423 patients |
| RCT   | 18 studies | 142 authors | 2,613 patients  |

|                       |
|-----------------------|
| Show forest plot for: |
| All studies           |
| Mortality results     |
| With exclusions       |
| RCTs                  |

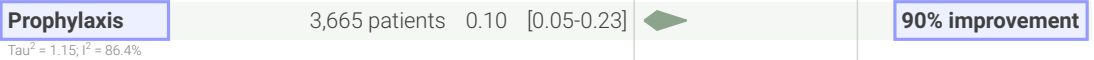
# Ivermectin COVID-19 early treatment and prophylaxis studies

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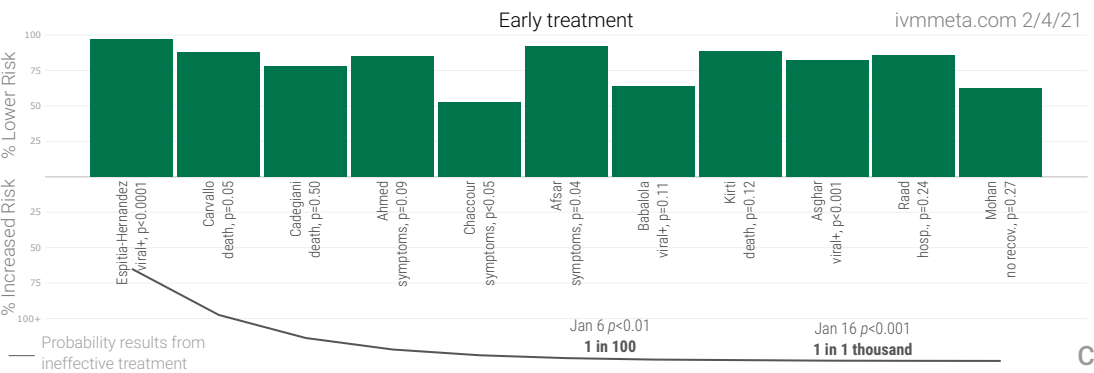
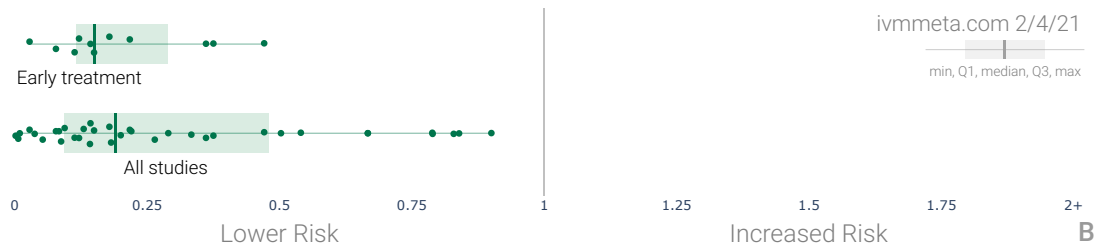
| Study             | Outcome         | N   | Dose | RR   | CI          |
|-------------------|-----------------|-----|------|------|-------------|
| Espitia-Hernandez | viral-          | 35  | 12mg | 0.03 | [0.01-0.11] |
| Carvallo          | death           | 45  | 36mg | 0.12 | [0.01-1.06] |
| Cadegiani         | death           | 247 | 28mg | 0.22 | [0.01-4.48] |
| Ahmed (DB RCT)    | symptoms        | 36  | 24mg | 0.15 | [0.01-2.70] |
| Chaccour (DB RCT) | symptoms        | 24  | 28mg | 0.47 | [0.19-1.16] |
| Afsar             | symptoms        | 90  | 24mg | 0.08 | [0.00-1.32] |
| Babalola (DB RCT) | viral-          | 60  | 12mg | 0.36 | [0.10-1.27] |
| Kirti (DB RCT)    | death           | 112 | 24mg | 0.11 | [0.01-2.05] |
| Asghar (RCT)      | viral-          | 100 | 14mg | 0.18 | [0.06-0.53] |
| Raad (SB RCT)     | hospitalization | 100 | 14mg | 0.14 | [0.01-2.70] |
| Mohan (DB RCT)    | recovery        | 85  | 28mg | 0.38 | [0.08-1.75] |

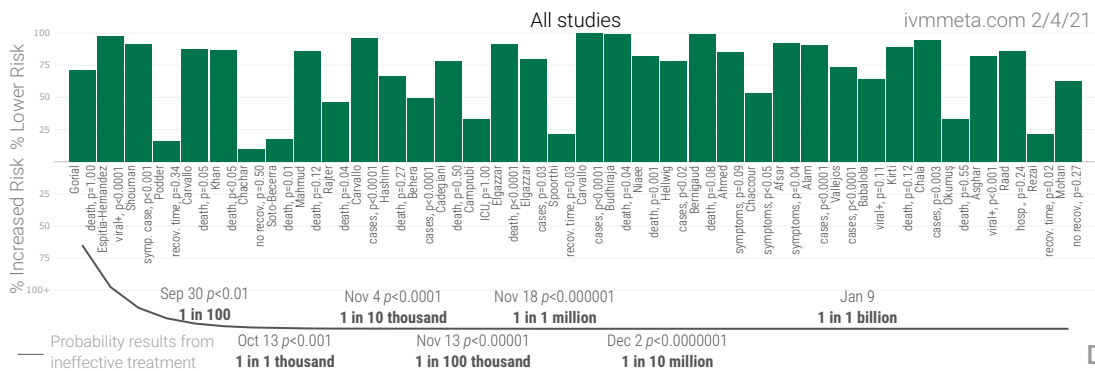


|                |            |       |      |      |             |
|----------------|------------|-------|------|------|-------------|
| Shouman (RCT)  | symp. case | 304   | 18mg | 0.09 | [0.03-0.23] |
| Carvallo       | case       | 229   | 2mg  | 0.04 | [0.00-0.63] |
| Behera         | case       | 372   | 21mg | 0.50 | [0.31-0.73] |
| Elgazzar (RCT) | case       | 200   | 28mg | 0.20 | [0.04-0.89] |
| Carvallo       | case       | 1,195 | 12mg | 0.00 | [0.00-0.02] |
| Hellwig        | case       |       | 14mg | 0.22 | [0.05-0.89] |
| Bernigaud      | death      | 138   | 28mg | 0.01 | [0.00-0.10] |
| Alam           | case       | 118   | 12mg | 0.09 | [0.04-0.24] |
| Vallejos       | case       | 875   | 12mg | 0.26 | [0.14-0.50] |
| Chala (RCT)    | case       | 234   | 12mg | 0.05 | [0.00-0.89] |



Tau<sup>2</sup> = 0.86; I<sup>2</sup> = 75.3%; Z = 7.18 (p < 0.0001)





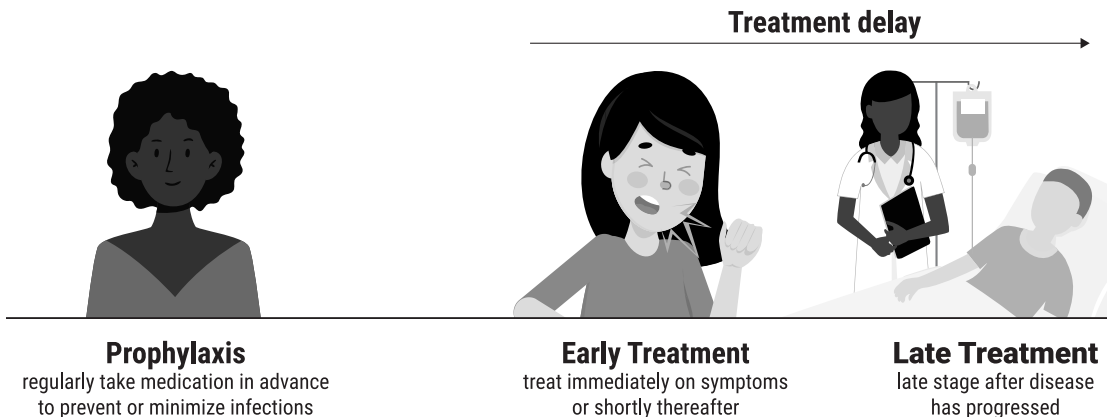
**Figure 1. A.** Random effects meta-analysis excluding late treatment. Simplified dosages are shown for comparison, these are the total dose in the first two days for treatment, and the monthly dose for prophylaxis, for a 70kg person. For full details see the appendix. **B.** Scatter plot showing the 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 only, and for Randomized Controlled Trials (RCTs) only.

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  $\geq k$  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.



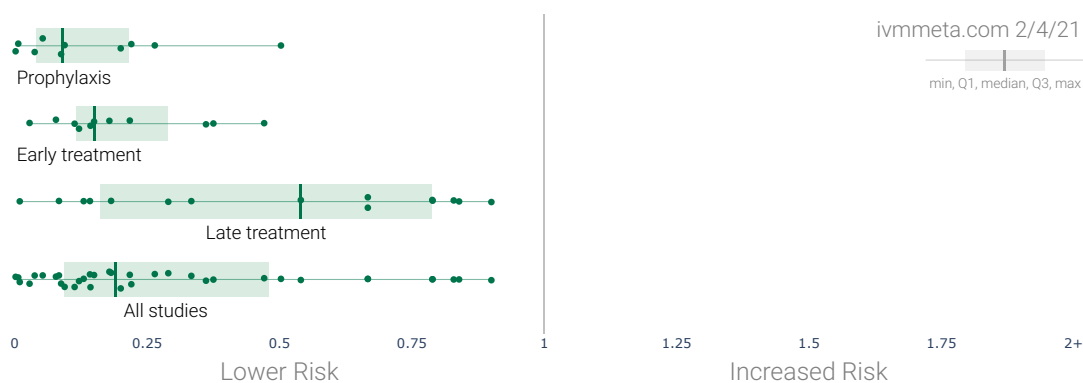
**Figure 2.** Treatment stages.

**Results**

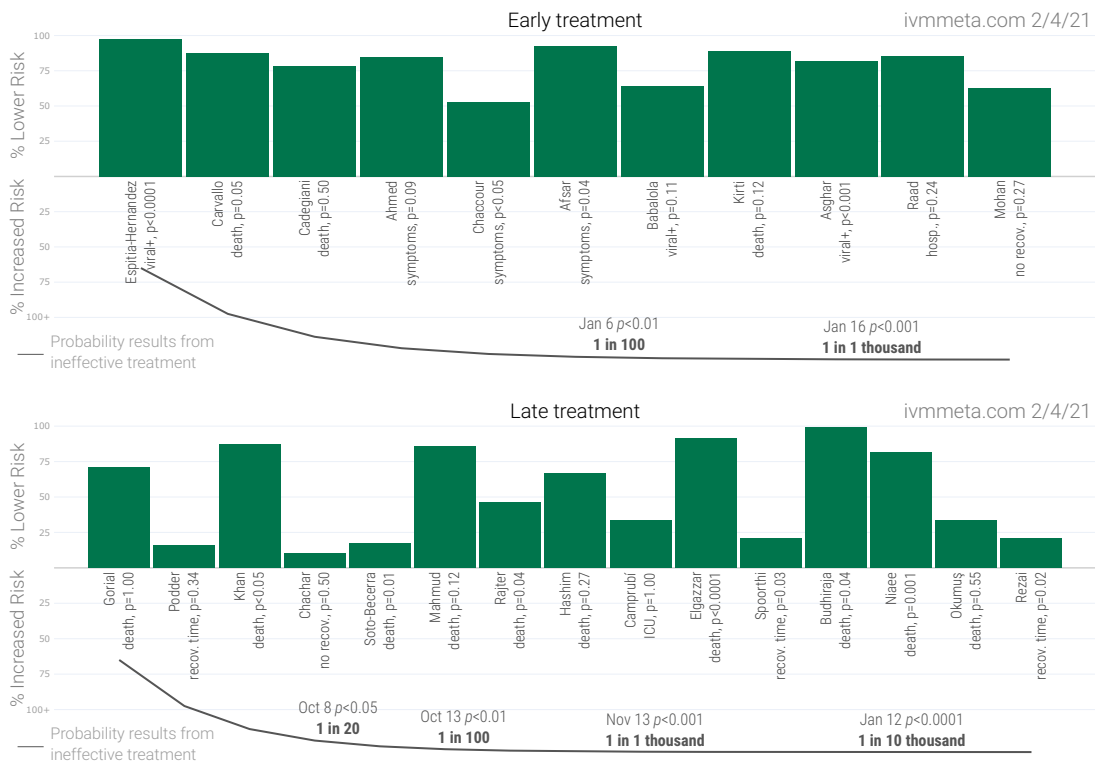
Figure 3, 4, and 5 show results by treatment stage. Figure 6 and 7 show forest plots for a random effects meta-analysis of all studies with pooled effects, and for studies reporting mortality results only. Table 1 summarizes the results.

| Treatment time  | Number of studies reporting positive results | Total number of studies | Percentage of studies reporting positive results | Probability of an equal or greater percentage of positive results from an ineffective treatment | Random effects meta-analysis results                 |
|-----------------|--|-------------------------|--|---|--|
| Early treatment | 11   | 11                      | 100%   | 0.00049<br>1 in 2 thousand  | 82% improvement<br>RR 0.18 [0.10-0.34]<br>p < 0.0001 |
| Late treatment  | 15   | 15                      | 100%   | 0.000031<br>1 in 33 thousand  | 39% improvement<br>RR 0.61 [0.47-0.79]<br>p = 0.0002 |
| Prophylaxis     | 10   | 10                      | 100%   | 0.00098<br>1 in 1 thousand  | 90% improvement<br>RR 0.10 [0.05-0.23]<br>p < 0.0001 |
| All studies     | 36   | 36                      | 100%   | 0.000000000015<br>1 in 69 billion   | 74% improvement<br>RR 0.26 [0.19-0.36]<br>p < 0.0001 |

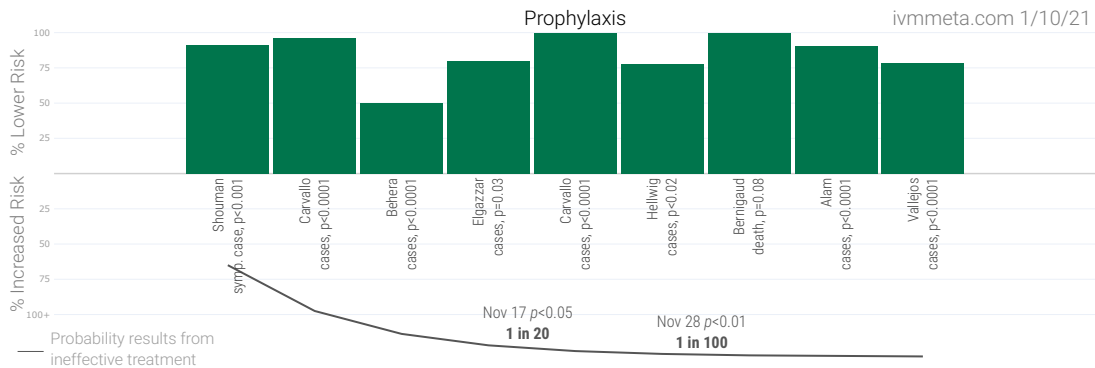
**Table 1.** Results by treatment stage.



**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 ivermectin COVID-19 studies

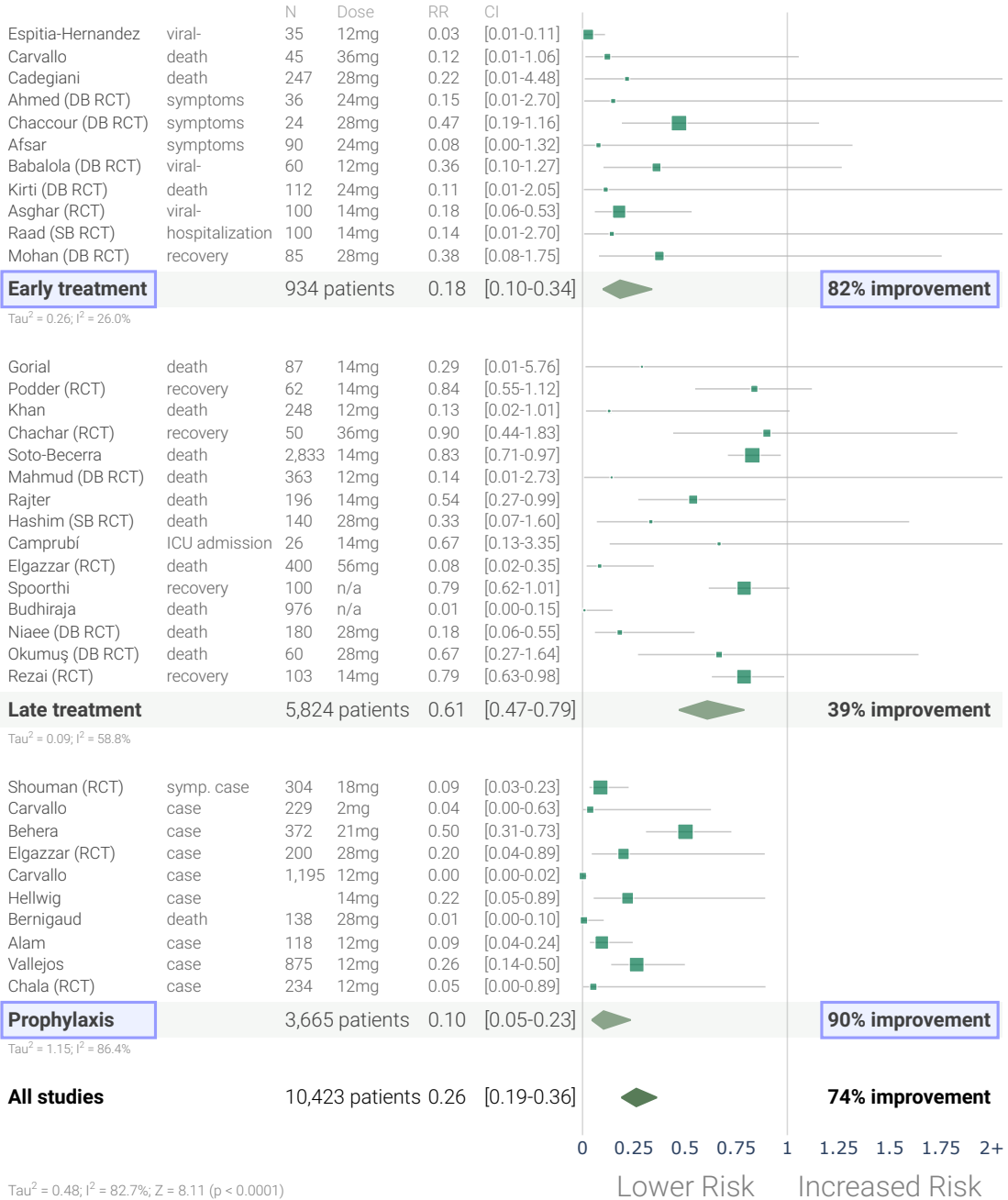


Figure 6. Random effects meta-analysis for all studies.

## All ivermectin COVID-19 mortality results

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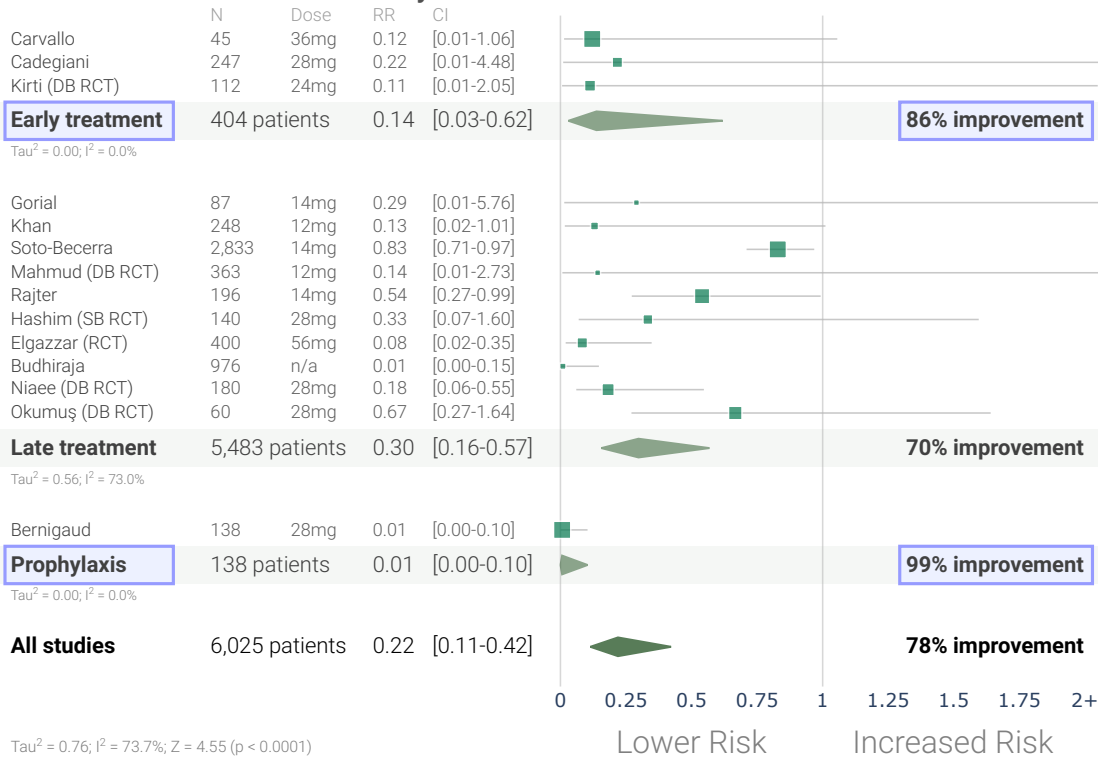
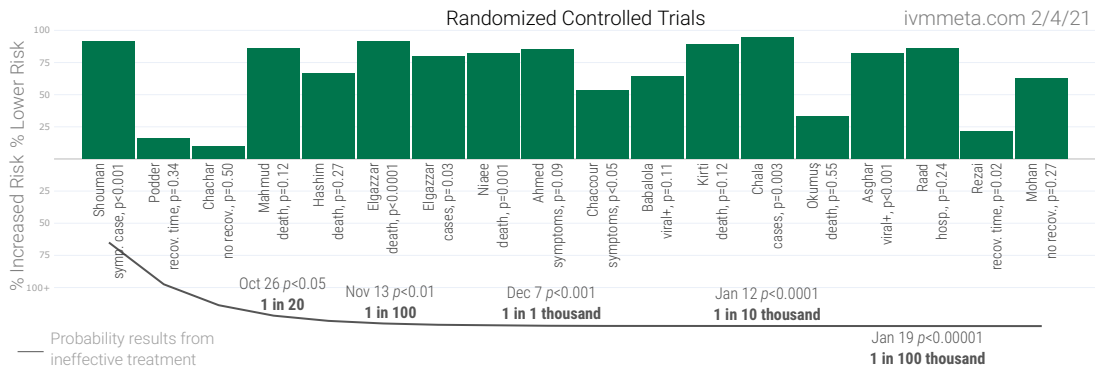
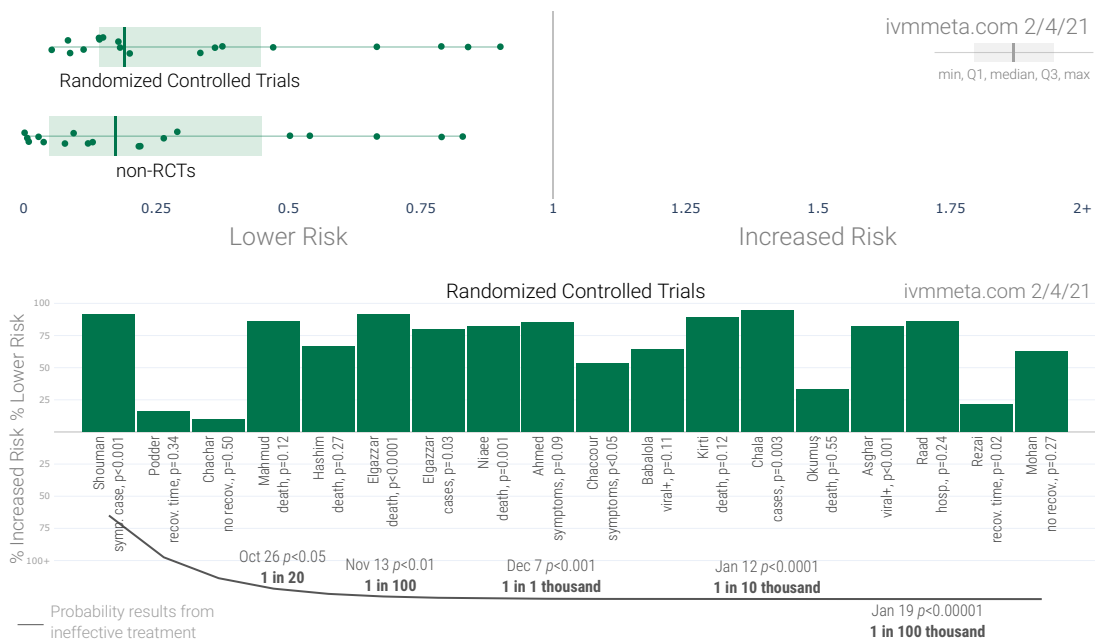


Figure 7. Random effects meta-analysis for mortality results only.

## Randomized Controlled Trials (RCTs)

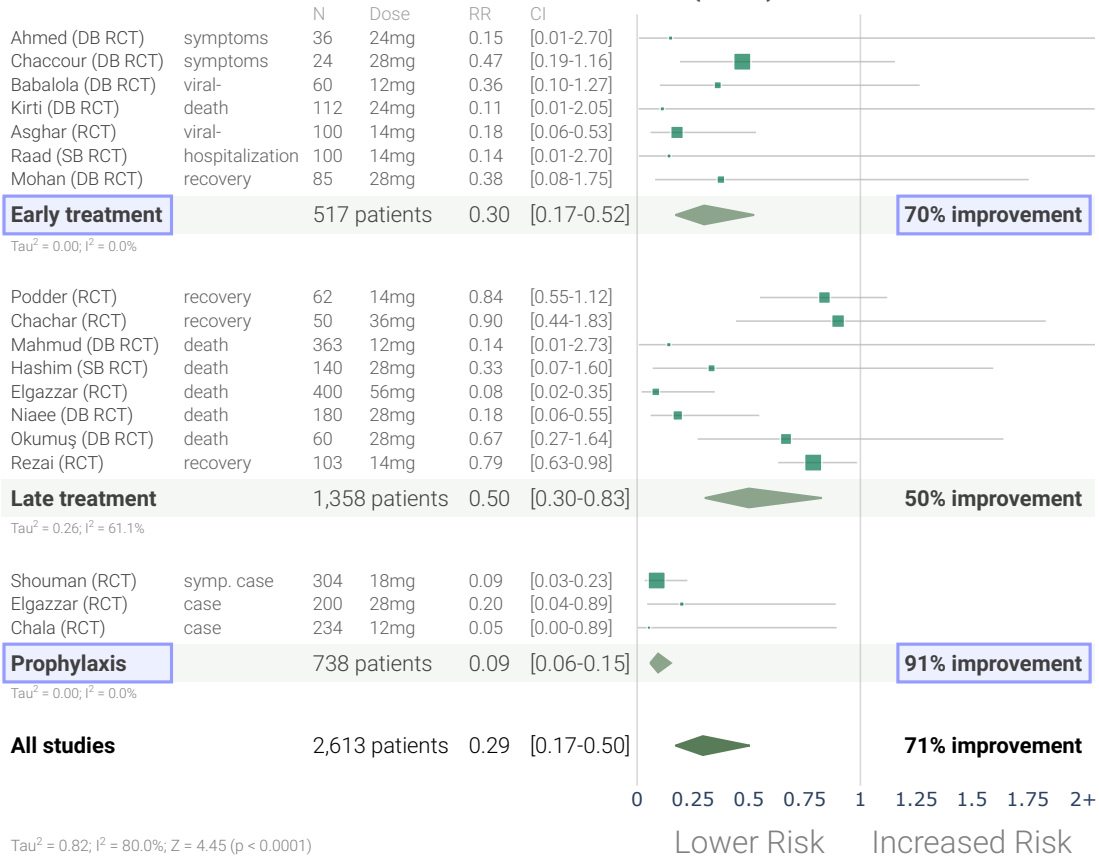
Results restricted to Randomized Controlled Trials (RCTs) are shown in Figure 8, 9, and 10, and Table 2. RCT results are similar to non-RCT results. Evidence shows that non-RCT trials can also provide reliable results. [Concato] find that well-designed observational studies do not systematically overestimate 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 8.** Randomized Controlled Trials. The distribution of results for RCTs is similar to the distribution for all other studies.

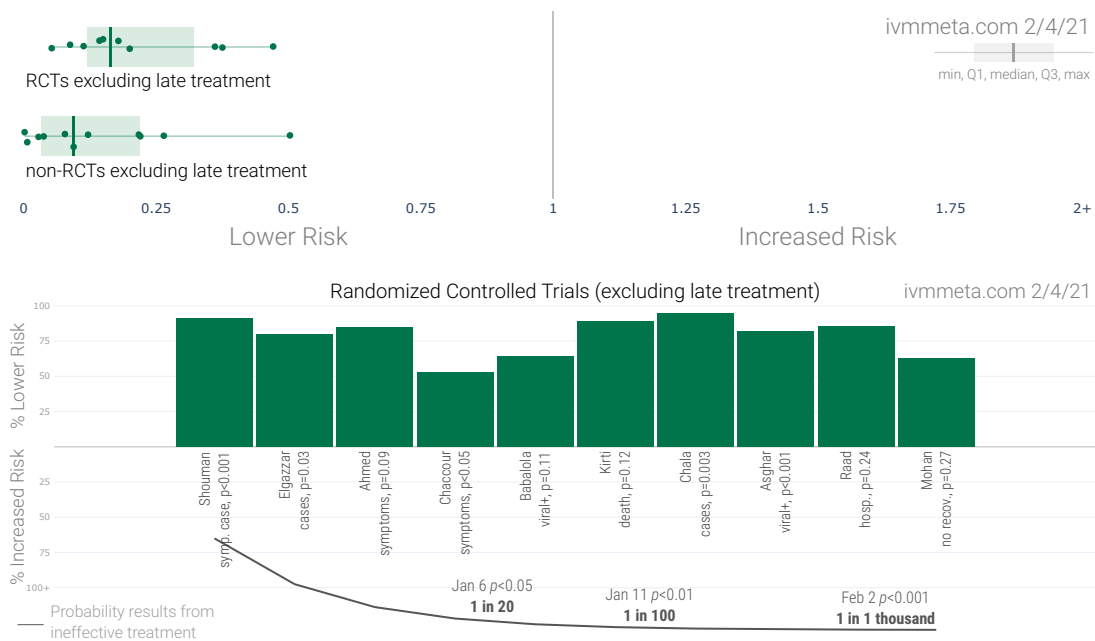
**All ivermectin COVID-19 Randomized Controlled Trials (RCTs)**

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**Figure 9.** Random effects meta-analysis for Randomized Controlled Trials only.





**Figure 10.** RCTs excluding late treatment.

| Treatment time  | Number of studies reporting positive results | Total number of studies | Percentage of studies reporting positive results | Probability of an equal or greater percentage of positive results from an ineffective treatment | Random effects meta-analysis results                 |
|---|--|-------------------------|--|---|--|
| Randomized Controlled Trials                            | 18   | 18                      | 100%   | 0.0000038<br>1 in 262 thousand  | 71% improvement<br>RR 0.29 [0.17-0.50]<br>p < 0.0001 |
| Randomized Controlled Trials (excluding late treatment) | 10   | 10                      | 100%   | 0.00098<br>1 in 1 thousand  | 81% improvement<br>RR 0.19 [0.11-0.33]<br>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. Several factors are consistent with this - all treatments are worse than the control group at 30 days, KM curves show that more than the total excess mortality at 30 days occurred on day 1, and 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. 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. There is no paper currently available for [Asgnar]. [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] provide an analysis of African countries and COVID-19 cases as a function of whether widespread prophylactic use of ivermectin is used for parasitic infections. Since this is a different kind of study to the typical trial, it is excluded here. [Krolewiecki] show a concentration dependent antiviral activity of ivermectin whereby the viral decay rate for patients with ivermectin >160ng/mL was 0.64 log<sub>10</sub> copies/reaction/day versus 0.13 for control. However, they do not provide the results for the entire treatment group vs. control. Results for [Raad, Rezaei] 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 11.

[Asgnar], detail too minimal.

[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.

[Raad], detail too minimal.

[Rezaei], detail too minimal.

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

[Vallejos], detail too minimal.

## All ivermectin COVID-19 studies with exclusions

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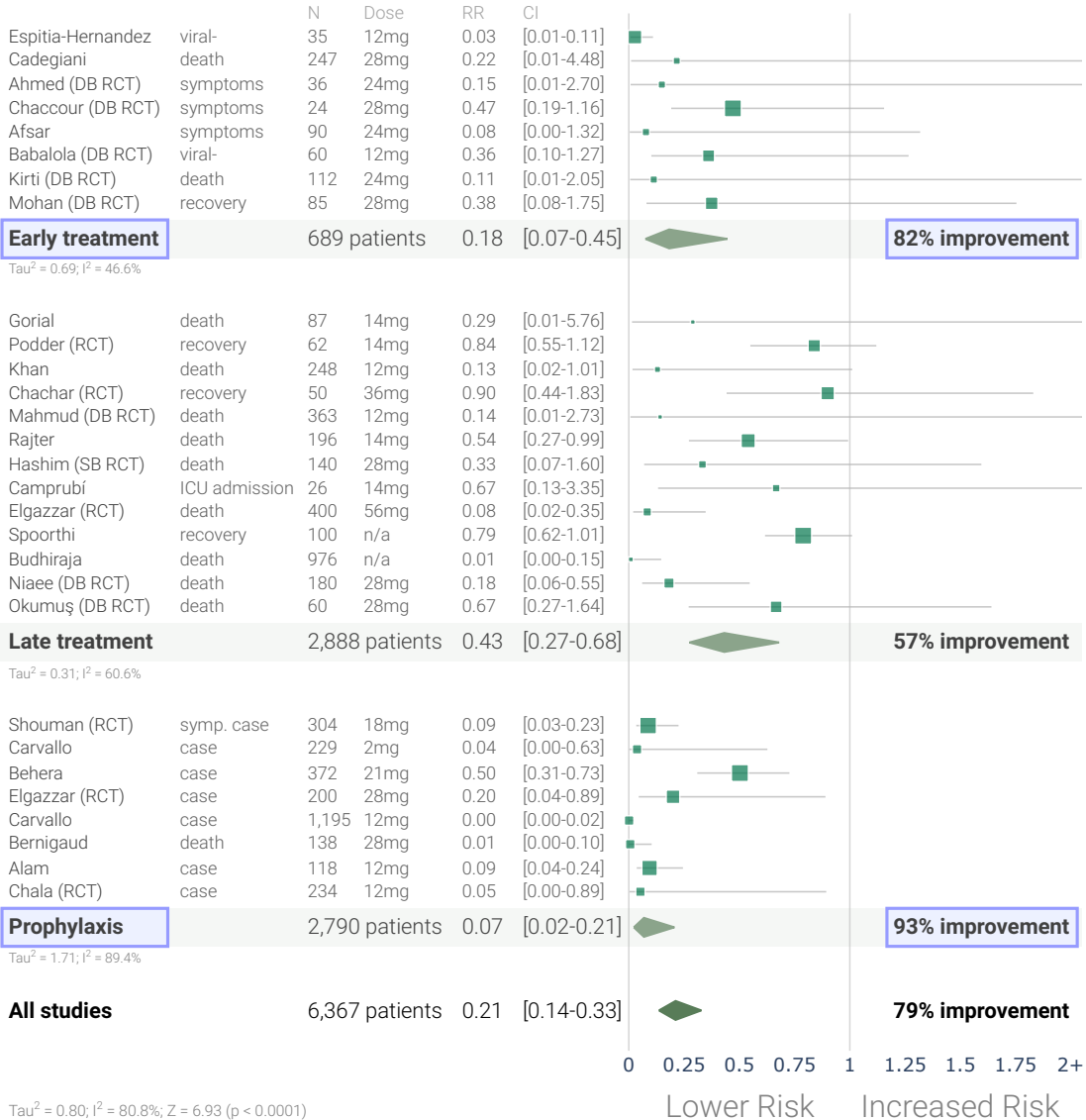


Figure 11. Random effects meta-analysis excluding studies with significant issues.

## Discussion

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. While some effects are not statistically significant when considered alone, currently all ivermectin studies report positive effects. 24 of the 36 studies are prospective studies.

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. Every day that the approval of ivermectin is delayed results in thousands of deaths, so it is important to consider all available data. We note that the positive results to date are very consistent and are relatively insensitive to potential selection criteria, effect extraction rules, and/or bias evaluation.

Studies vary significantly in terms of treatment delay, treatment regimen, patients characteristics, and (for the pooled effects analysis) outcomes, as reflected in the high degree of heterogeneity. However the results consistently show a positive effect of treatment, and with the exception of some late treatment studies, the effect size is large.

Additional meta analyses confirming the effectiveness of ivermectin can be found in [Hill, Kory, Lawrie]. [Kory] also review epidemiological data and provide suggested treatment regimens.

## Conclusion

Ivermectin is an effective treatment for COVID-19. The probability that an ineffective treatment generated results as positive as the 36 studies to date is estimated to be 1 in 69 billion ( $p = 0.000000000015$ ). As expected for an effective treatment, early treatment is more successful, with an estimated reduction of 82% in the effect measured using a random effects meta-analysis, RR 0.18 [0.10-0.34].

## 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 [Carvalho (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 [Chala].

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 [Asghar].

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.

1/17: We added [Mohan].

## 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. For PCR results reported at multiple times, where a majority of patients recover in both groups, preference is given to results mid-recovery (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 two 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. It is easy to propose excluding certain papers for various reasons. To avoid potential bias in evaluation we currently include all studies. Analysis excluding studies with major issues can be found in Appendix 2.

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.

|   |  |
|---|--|
| <p>[Afsar], 12/15/2020, retrospective, Pakistan, South Asia, preprint, 6 authors, dosage 12mg days 1-6.</p>   | <p><b>risk of fever at day 14, 92.2% lower, RR 0.08, <math>p = 0.04</math></b>, treatment 0 of 37 (0.0%), control 7 of 53 (13.2%).</p>                             |
| <p>[Ahmed], 12/2/2020, Double Blind Randomized Controlled Trial, Bangladesh, South Asia, peer-reviewed, 15 authors, dosage 12mg days 1-5, ivermectin + doxycycline group took only a single dose of ivermectin.</p> | <p><b>risk of unresolved symptoms, 85.0% lower, RR 0.15, <math>p = 0.09</math></b>, treatment 0 of 17 (0.0%), control 3 of 19 (15.8%), day 7 fever ivermectin.</p> |
|   | <p>risk of unresolved symptoms, 62.7% lower, RR 0.37, <math>p = 0.35</math>, treatment 1 of 17 (5.9%), control 3 of 19 (15.8%), day 7 fever ivermectin +</p>       |

|  |   |
|--|---|
|  | 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, $p = 0.02$ , ivermectin.   |
|  | time to viral-, 9.4% lower, relative time 0.91, $p = 0.27$ , ivermectin + doxycycline.  |
| <b>[Asghar]</b> , 1/16/2021, Randomized Controlled Trial, Pakistan, South Asia, preprint, 1 author, dosage 200 $\mu$ g/kg days 1, 8.   | <b>risk of no virological cure, 82.1% lower, RR 0.18, <math>p &lt; 0.001</math></b> , treatment 50, control 50, day 7.                                |
| <b>[Babalola]</b> , 1/6/2021, Double Blind Randomized Controlled Trial, Nigeria, Africa, preprint, baseline oxygen requirements 8.3%, 10 authors, dosage 12mg or 6mg q84h for two weeks. | <b>adjusted risk of viral+ at day 5, 63.9% lower, RR 0.36, <math>p = 0.11</math></b> , 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.   |
| <b>[Cadejani]</b> , 11/4/2020, prospective, Brazil, South America, preprint, 4 authors, dosage 200 $\mu$ g/kg days 1-3.  | <b>risk of death, 78.3% lower, RR 0.22, <math>p = 0.50</math></b> , treatment 0 of 110 (0.0%), control 2 of 137 (1.5%), control group 1.              |
|  | risk of ventilation, 94.2% lower, RR 0.06, $p = 0.005$ , treatment 0 of 110 (0.0%), control 9 of 137 (6.6%), 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%), control group 1.  |
| <i>[Carvallo]</i> , 9/15/2020, prospective, Argentina, South America, preprint, 3 authors, dosage 36mg days 1, 8, dose varied depending on patient condition - mild 24mg, moderate 36mg, severe 48mg. | <b>risk of death for hospitalized cases in study vs. cases in the same hospital not in the study, 87.9% lower, RR 0.12, <math>p = 0.05</math></b> , 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. |
| <i>[Chaccour]</i> , 12/7/2020, Double Blind Randomized Controlled Trial, Spain, Europe, peer-reviewed, 23 authors, dosage 400µg/kg single dose.   | <b>risk of unresolved symptoms, 52.9% lower, RR 0.47, <math>p &lt; 0.05</math></b> , treatment 12, control 12, relative probability of symptoms at day 28.   |
|   | viral load, 94.6% lower, relative load 0.05, treatment 12, control 12, day 7 mid-recovery.   |
| <i>[Espitia-Hernandez]</i> , 8/15/2020, retrospective, Mexico, North America, peer-reviewed, 5 authors, dosage 6mg days 1-2, 8-9.   | <b>risk of viral+ at day 10, 97.2% lower, RR 0.03, <math>p &lt; 0.001</math></b> , treatment 0 of 28 (0.0%), control 7 of 7 (100.0%).  |
| <i>[Kirti]</i> , 1/9/2021, Double Blind Randomized Controlled Trial, India, South Asia, preprint, 11 authors, dosage 12mg days 1, 2.  | <b>risk of death, 88.7% lower, RR 0.11, <math>p = 0.12</math></b> , treatment 0 of 55 (0.0%), control 4 of 57 (7.0%).  |
|   | risk of 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%).   |
| <i>[Mohan]</i> , 2/2/2021, Double Blind Randomized Controlled Trial, India, South Asia, preprint, 27 authors, dosage 400µg/kg single dose, 200µg/kg also tested.                                      | <b>risk of no discharge at day 14, 62.5% lower, RR 0.38, <math>p = 0.27</math></b> , 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.  |



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|   | 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.          |
| [Raad], 1/16/2021, Single Blind Randomized Controlled Trial, Lebanon, Middle East, preprint, 1 author, dosage 200µg/kg single dose. | <b>risk of hospitalization, 85.7% lower, RR 0.14, <math>p = 0.24</math></b> , treatment 0 of 50 (0.0%), control 3 of 50 (6.0%).                       |
|   | 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. |

### 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.

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| [Budhiraja], 11/18/2020, retrospective, India, South Asia, preprint, 12 authors, dosage not specified.  | <b>risk of death, 99.1% lower, RR 0.009, <math>p = 0.04</math></b> , treatment 0 of 34 (0.0%), control 103 of 942 (10.9%).                    |
| [Camprubi], 11/11/2020, retrospective, Spain, Europe, peer-reviewed, 9 authors, dosage 200µg/kg single dose.  | <b>risk of ICU admission, 33.3% lower, RR 0.67, <math>p = 1.00</math></b> , 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. | <b>risk of no recovery at day 7, 10.0% lower, RR 0.90, <math>p = 0.50</math></b> , 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.  | <b>risk of death, 91.7% lower, RR 0.08, <math>p &lt; 0.001</math></b> , 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%), 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.   | <b>risk of death, 71.0% lower, RR 0.29, <math>p = 1.00</math></b> , treatment 0 of 16 (0.0%), control 2 of 71 (2.8%).                         |
|   | hospitalization time, 42.0% lower, relative time 0.58, $p < 0.001$ , treatment 16, control 71.  |
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| <p>[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.</p>                     | <p><b>risk of death, 66.7% lower, RR 0.33, <math>p = 0.27</math>,</b> treatment 2 of 70 (2.9%), control 6 of 70 (8.6%), all patients.</p>                                |
|  | <p>risk of death, 91.7% lower, RR 0.08, <math>p = 0.03</math>, treatment 0 of 59 (0.0%), control 6 of 70 (8.6%), excluding critical patients.</p>                        |
| <p>[Khan], 9/24/2020, retrospective, Bangladesh, South Asia, preprint, median age 35.0, 8 authors, dosage 12mg single dose.</p>  | <p><b>risk of death, 87.0% lower, RR 0.13, <math>p &lt; 0.05</math>,</b> treatment 1 of 115 (0.9%), control 9 of 133 (6.8%).</p>   |
|  | <p>time to viral-, 73.3% lower, relative time 0.27, <math>p &lt; 0.001</math>.</p>   |
| <p>[Mahmud], 10/9/2020, Double Blind Randomized Controlled Trial, Bangladesh, South Asia, preprint, 1 author, dosage 12mg single dose.</p>   | <p><b>risk of death, 85.8% lower, RR 0.14, <math>p = 0.12</math>,</b> treatment 0 of 183 (0.0%), control 3 of 180 (1.7%).</p>  |
|  | <p>risk of no recovery, 49.0% lower, RR 0.51, <math>p &lt; 0.004</math>, treatment 42 of 183 (23.0%), control 67 of 180 (37.2%), adjusted per study.</p>                 |
|  | <p>risk of disease progression, 55.0% lower, RR 0.45, <math>p &lt; 0.01</math>, treatment 16 of 183 (8.7%), control 32 of 180 (17.8%), adjusted per study.</p>           |
|  | <p>risk of no virological cure, 42.0% lower, RR 0.58, <math>p &lt; 0.001</math>, treatment 14 of 183 (7.7%), control 36 of 180 (20.0%), adjusted per study.</p>          |
| <p>[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.</p>                | <p><b>risk of death, 81.8% lower, RR 0.18, <math>p = 0.001</math>,</b> treatment 4 of 120 (3.3%), control 11 of 60 (18.3%), All IVM vs. all control.</p>                 |
|  | <p>risk of death, 94.3% lower, RR 0.06, <math>p = 0.01</math>, treatment 0 of 30 (0.0%), control 11 of 60 (18.3%), IVM single dose 200mcg/kg vs. all control.</p>        |
|  | <p>risk of death, 45.5% lower, RR 0.55, <math>p = 0.37</math>, treatment 3 of 30 (10.0%), control 11 of 60 (18.3%), IVM three dose 200mcg/kg vs. all control.</p>        |
|  | <p>risk of death, 94.3% lower, RR 0.06, <math>p = 0.01</math>, treatment 0 of 30 (0.0%), control 11 of 60 (18.3%), IVM single dose 400mcg/kg vs. all control.</p>        |
|  | <p>risk of death, 81.8% lower, RR 0.18, <math>p = 0.06</math>, treatment 1 of 30 (3.3%), control 11 of 60 (18.3%), IVM three dose 400/200/200mcg/kg vs. all control.</p> |
| <p>[Okumuş], 1/12/2021, Double Blind Randomized Controlled Trial, Turkey, Middle East, preprint, 1 author, dosage 200µg/kg days 1-5, 36-50kg - 9mg, 51-65kg - 12mg, 66-79kg - 15mg, &gt;80kg 200µg/kg.</p> | <p><b>risk of death, 33.3% lower, RR 0.67, <math>p = 0.55</math>,</b> treatment 6 of 30 (20.0%), control 9 of 30 (30.0%).</p>  |
|  | <p>risk of no improvement at day 5, 15.8% lower, RR 0.84, <math>p = 0.60</math>, treatment 16 of 30 (53.3%), control 19 of 30 (63.3%).</p>                               |

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| <i>[Podder]</i> , 9/3/2020, Randomized Controlled Trial, Bangladesh, South Asia, peer-reviewed, 4 authors, dosage 200µg/kg single dose.                      | <b>recovery time from enrollment, 16.1% lower, relative time 0.84, <math>p = 0.34</math></b> , treatment 32, control 30.   |
| <i>[Rajter]</i> , 10/13/2020, retrospective, USA, North America, peer-reviewed, 6 authors, dosage 200µg/kg single dose.                                      | <b>risk of death, 46.0% lower, RR 0.54, <math>p = 0.04</math></b> , 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.   |
| <i>[Rezai]</i> , 1/19/2021, Randomized Controlled Trial, Iran, Middle East, preprint, 1 author, dosage 200µg/kg single dose.                                 | <b>recovery time, 21.2% lower, relative time 0.79, <math>p = 0.02</math></b> , treatment 51, control 52.   |
|  | hospitalization time, 17.9% lower, relative time 0.82, $p = 0.01$ , treatment 51, control 52.  |
| <i>[Soto-Becerra]</i> , 10/8/2020, retrospective, database analysis, Peru, South America, preprint, median age 59.4, 4 authors, dosage 200µg/kg single dose. | <b>risk of death, 17.1% lower, RR 0.83, <math>p = 0.01</math></b> , 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.   |
| <i>[Spoorthi]</i> , 11/14/2020, prospective, India, South Asia, peer-reviewed, 2 authors, dosage not specified.  | <b>recovery time, 21.1% lower, relative time 0.79, <math>p = 0.03</math></b> , 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.

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| <i>[Alam]</i> , 12/15/2020, prospective, Bangladesh, South Asia, peer-reviewed, 13 authors, dosage 12mg monthly. | <b>risk of COVID-19 case, 90.6% lower, RR 0.09, <math>p &lt; 0.001</math></b> , treatment 4 of 58 (6.9%), control 44 of 60 (73.3%).  |
| <i>[Behera]</i> , 11/3/2020, retrospective, India, South Asia, preprint, 12 authors, dosage 300µg/kg days 1, 4.  | <b>risk of COVID-19 case, 49.7% lower, RR 0.50, <math>p &lt; 0.001</math></b> , treatment 38 of 115 (33.0%), control 148 of 257 (57.6%), adjusted per study, odds ratio converted to relative risk, matched pair analysis. |
|  | risk of COVID-19 case, 53.4% lower, RR 0.47, $p <$   |

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|   | 0.001, treatment 38 of 115 (33.0%), control 148 of 257 (57.6%), adjusted per study, odds ratio converted to relative risk, model 2 2+ doses aOR.               |
| [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.                                | <b>risk of death, 99.4% lower, RR 0.006, p = 0.08</b> , treatment 0 of 69 (0.0%), control 150 of 3062 (4.9%).  |
|   | 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%).   |
| [Carvalho (B)], 11/17/2020, prospective, Argentina, South America, peer-reviewed, 4 authors, dosage 12mg weekly.  | <b>risk of COVID-19 case, 99.9% lower, RR 0.001, p &lt; 0.001</b> , treatment 0 of 788 (0.0%), control 237 of 407 (58.2%).                                     |
| [Carvalho (C)], 10/19/2020, prospective, Argentina, South America, preprint, 1 author, dosage 1mg days 1-14.  | <b>risk of COVID-19 case, 96.3% lower, RR 0.04, p &lt; 0.001</b> , treatment 0 of 131 (0.0%), control 11 of 98 (11.2%).  |
| [Chala], 1/11/2021, Randomized Controlled Trial, Argentina, South America, preprint, 1 author, dosage 12mg weekly.  | <b>risk of COVID-19 case, 94.7% lower, RR 0.05, p = 0.003</b> , treatment 0 of 117 (0.0%), control 9 of 117 (7.7%), 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%), all cases.                                       |
| [Elgazzar (B)], 11/13/2020, Randomized Controlled Trial, Egypt, Africa, preprint, 6 authors, dosage 400µg/kg weekly.  | <b>risk of COVID-19 case, 80.0% lower, RR 0.20, p = 0.03</b> , treatment 2 of 100 (2.0%), control 10 of 100 (10.0%).   |
| [Hellwig], 11/28/2020, retrospective, multiple countries, Africa, peer-reviewed, 2 authors, dosage 200µg/kg, dose varied, typically 150-200µg/kg.   | <b>risk of COVID-19 case, 78.0% lower, RR 0.22, p &lt; 0.02</b> , African countries.   |
|   | risk of COVID-19 case, 80.0% lower, RR 0.20, p < 0.001, worldwide.   |
| [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. | <b>risk of symptomatic case, 91.3% lower, RR 0.09, p &lt; 0.001</b> , 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.                                 |
| [Vallejos], 12/20/2020, retrospective, Argentina, South America, preprint, 1 author, dosage 12mg weekly.  | <b>risk of COVID-19 case, 73.6% lower, RR 0.26, p &lt; 0.001</b> , treatment 11 of 389 (2.8%), control 52 of 486 (10.7%).                                      |

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