



BIRD

British *Ivermectin* Recommendation Development



Official Statement Regarding Roman et al. 29 June 2021

29 June 2021

OFFICIAL REBUTTAL

Re: Roman et al.

“Ivermectin for the treatment of Covid-19: A systematic review and meta-analysis of randomized controlled trials”. Clinical Infectious Diseases, Accepted for publication ciab591

We have reviewed this recently published analysis. As authors of a recently published [peer-reviewed meta-analysis](#) with a very similar title we note a number of problems which need to be urgently addressed to avoid misleading the public:

Selectively small sample size

We note this recent meta-analysis covering n=1173 patients over 10 studies, asserting a conclusion the opposite of our own covering 3406 patients over 24 studies. This work ignores many of the larger trials, particularly those with mortality as an important endpoint.

Missing studies

Overall, we would recommend that other eligible trials are added in line with other reviews with the same inclusion criteria and data are re-analysed and interpreted correctly to avoid misleading conclusions. Otherwise, this review is of no value as we know the conclusions are incorrect and the results are different when eligible trials are added to the analyses. At present, they are simply underpowered and the assertion that ‘Ivermectin is not a viable option to treat COVID-19 patients’ is incorrect. Even if there were no missing studies from



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the Roman et al review, the results would show no statistically significant difference between the two treatment arms, but with the point estimates all favouring Ivermectin, suggesting if there was power to detect any difference then further trials may change the conclusions. In reality, knowing what the results for these trials are, then this is indeed the case.

Corrections made to article but ignored in the conclusions

This article has an embarrassing history whereby treatment arms in the study of Niaee¹ were reversed, attracting protest from Dr Niaee himself. This egregious error has been corrected in the revised version, but with no change to the Conclusions in spite of dramatic change in the evidence.

Absurd Confidence Levels, errors not corrected

Among other technical errors the study of Chaccour² is assigned a RR of unity with absurd Confidence Intervals [0.02 46.56] when the correct assignment for a study with zero deaths in both arms (mortality outcome) is “not estimable”. Our own paper is particularly careful with analysis of “double-zero” studies. Several further errors are identified by contributors in the Comments section of medRxiv³, apparently uncorrected.

¹ <https://doi.org/10.21203/rs.3.rs-109670/v1>

² <https://doi.org/10.1016/j.eclinm.2020.100720>

³ <https://www.medrxiv.org/content/10.1101/2021.05.21.21257595v2>



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The point mortality reduction estimate of $RR=0.37$ in fact remarkably close to our own findings of $RR=0.38$ though the CIs ([0.12, 1.13] vs [0.19, 0.73]) are not, being based on fewer studies and in part by the absurd values assigned to Chaccour.

The conclusion “ivermectin did not reduce all-cause mortality” does not follow from the evidence, with such selective study inclusion, and mishandling of data.

Bias, statistical questions and ignoring existing evidence

The authors of Roman et al erroneously interpret an absence of evidence of a difference as evidence of no difference. The authors may want to consider approaching a statistician to assist with the data analysis and interpretation of the results when updating their review. The authors could also consider reporting the optimal information size. The authors may want to use the updated review by [Bryant and Lawrie](#) et al as a point of reference. It is also unclear whether the review was guided by a written protocol a priori, this may be something to consider documenting going forward. The ROB-2 tool for assessing risk of bias was used, but the reviewers provide no justification for the judgements made.

Bird Group strongly requests that that the article is withdrawn whilst the mistakes are reviewed, or a warning placed on the journal page to warn others of the incorrect information within.

Bird Team

29 June 2021