



Correction: Cruciani et al. Ivermectin for Prophylaxis and Treatment of COVID-19: A Systematic Review and Meta-Analysis. *Diagnostics* 2021, *11*, 1645

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Affiliation Correction

The correct affiliation 1 should be "Italian National Blood Centre, National Institute of Health, 00162 Rome, Italy".

Missing Citation

In the original article, "Schünemann, H.J.; Oxman, A.D.; Higgins, J.P.; Vist, G.E.; Glasziou, P.; Guyatt, G.H. Chapter 11: Presenting results and 'Summary of findings' tables. In *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (Updated March 2011)*; Higgins, J.P., Green, S., Eds.; The Cochrane Collaboration, 2011. Available online: handbook.cochrane.org (accessed on 1 June 2021)" was not cited. The citation has now been inserted in Section 2.6. Assessment of Risk of Bias in Included Studies, and should read:

Two review authors (I.P., M.C.) independently assessed the risk of bias of each study included following the domain-based evaluation described in the Cochrane Handbook for Systematic Reviews of Interventions (Available from www.handbook.cochrane.org, accessed on 18 August 2021) [33,34].

Text Correction

When submitting in August 2021 our manuscript [1] to *Diagnostics*, we were not aware that one of the trials included in the review, an Egyptian study of ivermectin for COVID-19 by Elgazzar et al. published as preprint in "Research Square" [2], had been retracted over concerns of plagiarism and serious problems with their raw data, as reported in a press release on "The Guardian" and then on "BBC news" [3,4]. Research Square withdrew this preprint on 14 July, when they were presented with "evidence of both plagiarism and anomalies in the dataset associated with the study, neither of which could reasonably be addressed by the author issuing a revised version of the paper".

Subsequently, Open Forum Infectious Diseases, an official journal of the *Infectious Diseases* Society of America published an expression of concern. This has prompted other authors of systematic reviews and meta-analysis of ivermectin for COVID-19 to retract the published paper [3], and to plan the submission of a revised version of the paper, excluding the "Fraudulent" study [5].

In our systematic review [1], we performed a methodological assessment of the included trials using an appropriate check list for risk of bias (ROB for RCTs, and ROBIN-1 for non RCTs) and GRADE assessment, as required by the new Cochrane standards. The certainty of the available evidence was graded as low or very low, considering the risk of bias in the majority of the included studies (including that of Elgazzar et al.), the imprecision (reflecting the inadequate numbers of participants and/or events) and the



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Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). inconsistency (heterogeneity). We concluded that "there is limited evidence for the benefit of ivermectin for COVID-19 treatment and prophylaxis, and most of this evidence is of low quality". Certainly, one of the limitations of our review and other reviews on COVID-19 treatments is related to the fact that many of the data continue to be published in preprints and protocol repositories, which do not follow the recommended processes to ensure high quality standards for publications.

We did not perform sensitivity analyses for the outcomes analysed, also considering that the take home message was about the limited evidence of benefit of ivermectin compared to standard treatment. Considering all of this, we have now performed a sensitivity analysis excluding the study by Elgazzar et al. The take home message of our paper is almost the same, and the only relevant difference after exclusion of this paper is that the difference in the occurrence of mortality in the subgroup of patients with severe baseline conditions is no longer favouring ivermectin compared to controls, as shown below (Table 1 and Figure 1, forest plots of comparisons). As in the previous analyses, the certainty of the available evidence remains low, which means that further research is very likely to have an important impact on the confidence in the estimation of effects and is likely to change the estimate, regardless of the fact that the study by Elgazzar et al. is included or not in the analyses. Therefore, there is no need for a new systematic review and meta-analysis, but just a fine-tuning before and after the exclusion of this study.

In conclusion, the available evidence continues to be not adequate to support the use of ivermectin for the treatment of COVID-19 in clinical practice. However, more studies are underway, and it would be better wait further evidence before concluding that ivermectin has no place in COVID-19 treatment.

The following paragraph is added in the original publication (Section 3.8. Mortality, page 11, after the paragraph "When the analysis was restricted to studies or subsets of patients with baseline severe diseases"):

In sensitivity analysis, after the exclusion of the study by Elgazzar et al. [35] in the subset of studies with baseline severe conditions the difference in the occurrence of mortality is not longer favouring ivermectin compared to controls (MD, -0.14 (95% CIs, -0.30/0.02; p = 0.08). As in the previous analyses, the certainty of the available evidence remains low.

The authors apologize for any inconvenience caused and state that the scientific conclusions are substantially unaffected.

Outcome	All studi	es			Excluding Elgazzar			
Mortality	MD	p value	GRADE	comment	MD (95 %	р	GRADE	comment
in pts with	(95 %		assessment		Cls)	value	assessment	
baseline	Cls)							
severe	-0.17	< 0.00001	$\oplus \oplus \ominus \ominus$	Ivermectin	-0.14 (-	0.08	$\Theta \Theta \Theta \Theta$	On average, it is unclear
conditions	(-		low	decreases	0.30/0.02)		very low	whether or not use of
	0.24/-		Downgraded	mortality in high			Downgraded	Ivermectin compared to
	0.10)		twice for serious	risk population			twice for serious	control decreases
			ROB	1 1			ROB and	mortality in pts with
							imprecision	baseline severe
							*	conditions
Progression of	-0.26	< 0.00001	$\oplus \oplus \ominus \ominus$	Ivermectin	-0.025 (-	0.004	$\Theta \Theta \Theta \Theta$	Ivermectin decreases
disease	(-		low	decreases	0.41/-0.08)		low	progression of disease in
in pts with	0.34/-		Downgraded for	progression of			Downgraded for	high risk population
baseline	0.17)		ROB and	disease in high			ROB and	
severe			inconsistency	risk population			inconsistency	
conditions				r-r-manon				

 Table 1. Sensitivity analysis of some outcomes of the meta-analysis.

MD, mean difference. CIs. Confidence intervals. ROB, Risk of bias.

	ivermectin		Control		Risk Difference		Risk Difference
Study or Subgroup	Events Total		Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
1.1.1 initially mild/modera	ate						
Ahmed IVM+doxy	0	23	0	22	7.3%	0.00 [-0.08, 0.08]	
Ahmed IVM alone	0	23	0	22	7.3%	0.00 [-0.08, 0.08]	+
Chaccour 2021	0	12	0	12	3.3%	0.00 [-0.15, 0.15]	
Elgazzar-mild/moderate	0	100	0	100	15.1%	0.00 [-0.02, 0.02]	+
Hashim mild/moderate	0	48	0	48	12.6%	0.00 [-0.04, 0.04]	+
LopezMedina 2021	0	200	1	198	15.5%	-0.01 [-0.02, 0.01]	+
Mahmud 2021	0	183	3	180	14.9%	-0.02 [-0.04, 0.00]	-
Ravikirti 2020	0	55	0	57	13.3%	0.00 [-0.03, 0.03]	+
Subtotal (95% CI)		644		639	89.3%	-0.01 [-0.01, 0.00]	
Total events	0		4				
Heterogeneity: Tau² = 0.01 Test for overall effect: Z =			= 7 (P = 0	.98); I²	= 0%		
1.1.2 initially severe							
Elgazzar-severe	2	100	20	100	7.3%	-0.18 [-0.26, -0.10]	
Hashim severe/critical	2	22	6	22	1.7%	-0.18 [-0.40, 0.04]	
Okumus 2020	6	30	9	30	1.7%	-0.10 [-0.32, 0.12]	
Subtotal (95% CI)		152		152	10.7%	-0.17 [-0.24, -0.10]	•
Total events	10		35				
Heterogeneity: Tau ² = 0.01 Test for overall effect: Z =				.78); I²	= 0%		
Total (95% CI)		796		791	100.0%	-0.02 [-0.05, 0.01]	•
Total events	10		39				
Heterogeneity: Tau ² = 0.01 Test for overall effect: Z =	1.37 (P = 1	D.17)					-1 -0.5 0 0.5 Favours ivermectin Favours control
Test for subgroup differen	nces: Chi²	= 19.40), df = 1 (F	° < 0.00	001), I ² = 1	94.8%	
Nortality according	to base	line c	onditio	ons: a	ll studi	es	

ivermectin Control **Risk Difference Risk Difference** Study or Subgroup Events Total Events Total Weight M-H, Random, 95% Cl M-H, Random, 95% CI 1.1.1 initially mild/moderate Ahmed IVM+doxy n n 0.00 [-0.08. 0.08] 23 22 2 2% 22 2.2% 0.00 [-0.08, 0.08] Ahmed IVM alone 23 0 0 Chaccour 2021 0 12 0 12 0.7% 0.00 [-0.15, 0.15] 100 Elgazzar-mild/moderate 100 0.0% 0.00 [-0.02, 0.02] Hashim mild/moderate 0 48 0 48 198 8.9% 0.00 [-0.04, 0.04] Lopez--Medina 2021 0 200 1 47.5% -0.01 [-0.02, 0.01] Mahmud 2021 0 183 180 26.0% -0.02 [-0.04, 0.00] Ravikirti 2020 0 55 0 57 11.8% 0.00 [-0.03, 0.03] Subtotal (95% CI) 544 539 99.4% -0.01 [-0.02, 0.00] n 4 Total events Heterogeneity: Tau² = 0.00; Chi² = 1.21, df = 6 (P = 0.98); I² = 0% Test for overall effect: Z = 1.28 (P = 0.20) 1.1.2 initially severe -0.18 [-0.26, -0.10] Elgazzar-severe 100 20 100 0.0% 2 22 30 52 Hashim severe/critical 2 22 0.3% -0.18 [-0.40, 0.04] 6 9 Okumus 2020 6 30 52 0.3% -0.10 [-0.32, 0.12] -0.14 [-0.30, 0.02] Subtotal (95% CI) Total events 15 Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.60); I² = 0% Test for overall effect: Z = 1.77 (P = 0.08) Total (95% CI) 591 100.0% -0.01 [-0.02, 0.00] 596 Total events 8 19 Heterogeneity: Tau² = 0.00; Chi² = 8.74, df = 8 (P = 0.36); l² = 8% 1 -0.5 0.5 Test for overall effect: Z = 1.21 (P = 0.23) Favours ivermectin Favours control Test for subgroup differences: Chi² = 2.82, df = 1 (P = 0.09), l² = 64.6% Mortality according to baseline condition: sensitivity analysis, excluding Elgazzar

Figure 1. Forest plot of the comparison. Outcome: mortality according to baseline conditions. Top: all studies; bottom: sensitivity analysis excluding Elgazzar et al. [2].

References

- 1. Cruciani, M.; Pati, I.; Masiello, F.; Malena, M.; Pupella, S.; De Angelis, V. Ivermectin for Prophylaxis and Treatment of COVID-19: A Systematic Review and Meta-Analysis. *Diagnostics* **2021**, *11*, 1645. [CrossRef] [PubMed]
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