

LETTER TO THE EDITORS

Letter: COVID-19 outcomes and anti-TNF treatments—comprehensive evidence matters. Authors' reply

Editors,

We read with interest the letter by Hung et al.¹ We appreciate their interest in our study and their constructive comments. We acknowledge their remarks on methodological issues regarding our work and provide our perspective. Registration of systematic reviews and meta-analyses is not mandatory and we clearly stated that our study was not registered in our PRISMA checklist upon submission to the journal. While we agree on the merit of pre-registration, it is also a fact that few of the Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) are included in the respective registries.² Additionally, our work was driven by a clearly defined hypothesis, that is to specifically review the effect of anti-TNF treatments on COVID-19 outcomes. For this reason, we do not comment on any other treatments. Regarding reproducibility, we provide a well-stated search strategy and an extensive supplementary appendix. With regards to our search strategy, although not ideal, we believe that our search through PubMed and SCOPUS provides adequate and high-quality peer-reviewed studies, allowing us the safe extraction of our results. As far as the keywords are concerned, we respectfully disagree with the opinion that “tumour necrosis factor inhibitors” would have been a better term than our strategy which included the use of all possible forms of the abbreviation “anti-TNF”, as well as the use of the name of every monoclonal antibody and receptor inhibitor, separately. We recognise the merit of statistical tests evaluating publication bias; nevertheless, we were unable to proceed so in our main analysis, due to the number of studies included being fewer than 10.³ We used graphical demonstrations with funnel plots for our sensitivity (secondary) analyses, where again the number of studies included does not constitute a large enough study sample; thus could probably lead to underpowered analyses.³ Apart from that, it has been shown that statistical tests for this kind of bias often demonstrate moderate to weak agreement among their results, and given the relatively restricted number of studies included we would not make clear inferences.⁴ However, these do not affect our main findings. Further, we discuss this limitation in our paper. Finally, we believe that inability of hospitalisation was not a major factor during the first wave of the pandemic. In fact, during the first wave of the pandemic higher

hospitalisation rates have been reported compared to the second.⁵ This trend was attributed to the experience and evidence that were acquired during the first wave, as vaccines were still not available; thus, the natural history of the infection remained unchanged.⁵ More importantly, an increased risk for hospitalisation due to COVID-19 was observed in IBD patients, without an increased risk of severe disease.⁶ This, probably, relates to higher precaution in patients with immune-mediated diseases, due to treatment-induced immunomodulation. One could argue that the hospitalisation rates for anti-TNF-treated patients are probably overestimated by the meta-analysed studies and the precise association with reduced hospitalisation may be even greater.

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AUTHOR CONTRIBUTIONS

Georgios Kokkotis: Conceptualization (equal); writing – original draft (equal). Konstantina Kitsou: Conceptualization (equal); writing – original draft (equal). Giorgos Bamias: Supervision (lead); writing – review and editing (equal).

LINKED CONTENT

This article is linked to Kokkotis et al papers. To view these articles, visit <https://doi.org/10.1111/apt.16717> and <https://doi.org/10.1111/apt.16872>

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