Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

'Methodological evaluation of bias in observational COVID-19 studies on drug effectiveness' – Author's reply

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To the Editor

We thank Guaraldi et al. [1] for the opportunity to clarify specific methodological issues that were identified in our review [2]. We agree that the magnitude of immortal bias may be small if the time span between the start of follow up and the treatment initiation is very short. However, this bias has already created many flawed publications in many epidemiological areas, so it cannot be ignored. We also highlight that immortal time is a time-dependent bias that may refer to other non-fatal outcomes under interest, such as discharge alive or initiation of mechanical ventilation [3]. In addition, we would like to remark that the quantification of the magnitude of the biases was beyond the scope of our review.

Competing risk events can occur in both randomized trials and observational studies and competing risk analysis should be performed irrespective of the primary study outcome [4]. In the review we pointed out that there are two main approaches for competing risks and the cause-specific hazard model is considered as an appropriate method for aetiological research [5].

Regarding time-varying confounding, the authors [1] considered glucocorticoids during follow up and therefore potentially later than the initiation of tocilizumab. However, time-varying confounding is evoked by covariates that influence the decision of administrating tocilizumab, so confounders are measured before the potential administration.

Finally, regarding the validity assessment of effect estimates obtained from studies with different design, we fully agree that well-designed observational studies with accurate results might reflect findings from randomized trials and should complement the clinicians' knowledge and support clinical decision-making.

Author contributions

MW, MvC and OM contributed to the conceptualization of the letter, writing of the original draft and reviewing of the letter.

Transparency declaration

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