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## REFERENCES

- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, eds. In: *Cochrane Handbook for Systematic Reviews of Interventions version 6.1 (updated September 2020)*. Cochrane; 2020. Available from: <http://www.training.cochrane.org/handbook>. Accessed 16 Feb 2021.
- Verdoia M, Khedi E, Suryapranata H, De Luca G. Very short dual antiplatelet therapy after PCI and new DES: a meta-analysis of 5 randomized trials. *Rev Esp Cardiol*. 2021;74:140–148.

<https://doi.org/10.1016/j.rec.2021.02.010>

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## The danger of meta-analyses. Response

### El peligro de los metanálisis. Respuesta

#### To the Editor,

We would like to thank Hernández-Vaquero et al. for their interest on our investigation. Indeed, as we acknowledged,<sup>1</sup> the most important limitations of our study concern the synthesis of data from heterogeneous trials, which included patients who differed widely in terms of their ischemic and bleeding risk profiles. Indeed, acute coronary syndrome patients ranged from the total population in the REDUCE trial<sup>2</sup> to far less than 50%, or complete exclusion of ST-segment elevation myocardial infarction patients.

Moreover, the definition of the study endpoints differed among the included trials, leading Verdoia et al.<sup>1</sup> to consider mortality, rather than the composite of “major cardiovascular events” as the primary study endpoint. In contrast, bleeding definition was not consistent across the studies. BARC 2–5 bleeding events were used in 3 studies and BARC 3–5 events were considered in 1 trial, while the STOPDAPT-2 applied the more stringent thrombolysis in myocardial infarction criteria, potentially explaining the greater benefits observed in the present study, which considered only severe bleedings.

Figures 2 and 3 clearly demonstrate that the included studies consistently showed a similar trend for benefit in the reduction of bleeding events with shorter dual antiplatelet therapy, with those events being associated with larger heterogeneity. In contrast, an opposite increase or reduction of deaths was reported in the REDUCE<sup>1</sup> and other trials, although resulting in an  $I^2 = 36\%$ , far lower than the threshold of 50% suggested by the Cochrane guidelines and reported by Hernández-Vaquero et al.

As for publication bias, the same issues could certainly refer to the large number of meta-analyses that have appeared in the literature in the last few years, reaching similar conclusions to our own.



Therefore, while awaiting large scale dedicated randomized controlled trials, the possibility of pooling together the data from different studies, despite some potential limitations, should certainly be considered in order to broaden the spectrum of included patients and increase statistical power for clearly underpowered endpoints.

## FUNDING

None

## AUTHORS' CONTRIBUTION

M. Verdoia and G. De Luca: conception and design, interpretation of the data; drafting of the article; final approval of the manuscript. E. Kedhi: interpretation of the data; critical revision of the article for important intellectual content of the article; final approval of the manuscript.

## CONFLICTS OF INTEREST

None.

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**REFERENCES**

1. Verdoia M, Khedi E, Suryapranata H, De Luca G. Very short dual antiplatelet therapy after PCI and new DES: a meta-analysis of 5 randomized trials. *Rev Esp Cardiol.* 2021;74:140–148.
2. De Luca G, Damen SA, Camaro C, et al. Final results of the Randomised Evaluation of short-term Dual antiplatelet therapy in patients with acute Coronary syndrome E treated with a new generation stent (REDUCE) trial. *Eurointervention.* 2019;15:e990–e998.

<https://doi.org/10.1016/j.rec.2021.05.008>

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