Sleep Medicine Reviews 63 (2022) 101625

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

LETTER TO THE EDITOR

Reply to Hu et al. Significant association of obstructive sleep apnoea with increased risk for fatal COVID-19

We thank Hu et al. (see Hu M et al. [1]) for referring to our publication, in which we systematically examine the available evidence up until 2nd June 2020 of the relationship between obstructive sleep apnoea (OSA) and adverse COVID-19 outcomes [2]. We examined potential causal mechanisms and what effect COVID-19 has had on OSA diagnosis, treatment, and management. It is clear from our review that the pandemic had a detrimental effect on the treatment, management, and diagnosis of OSA worldwide. There were plausible mechanisms by which OSA may independently increase one's risk of morbidity and mortality associated with COVID-19 but, whilst up to June 2020 there were limited studies available, there was some evidence from the CORONADO study to suggest that individuals with diabetes who were also OSA-treated patients may be at increased risk of death from COVID-19. We concluded that it may be necessary to explore new diagnosis and treatment pathways for these individuals and that further research was required to determine whether COVID-19 presented an increased risk for individuals with OSA.

In this issue, Hu et al. [1] have built on our study and evaluated evidence from several studies that have subsequently been published. It is not clear from the methodology presented as to which time point their review was conducted, but it does include studies published up to and including 2021. They have conducted a systematic review and risk-adjusted meta-analysis with regards to OSA, and COVID-19 morbidity and mortality, in 13 studies that fulfilled their inclusion criteria (of which four studies were prospective and nine were retrospective).

The authors indicate that COVID-19 was statistically significantly associated with a 56% increased risk of fatal COVID-19 based on adjusted effect estimates. The meta-analysis included studies from Europe, US and Asia, and included studies of 'all patients' and those conducted in just 'hospitalised' patients. Their subgroup analysis showed consistent results across age and study design; sensitivity analysis showed that there was no indication of publication bias of COVID outcomes in individuals with OSA.

There are, however, some errors within the manuscript and limitations to the study as published that raise some concerns about the rigour of the methodology used. It would be helpful to include a PRISMA diagram as a supplement with details of studies excluded and for what reason, as well as a list of the adjustments made for the risk estimates in each study.

The study is limited in that it has only considered death as an outcome and most studies only included hospitalised patients. Some patients, with severe disease who were cared for at home or did not make it to hospital may not have been included. The implications for such potential bias are not discussed. Further studies, such as that by Strausz S et al. [3] and Perger et al. [4] are required to examine the effect of OSA as a risk factor for severe COVID-19, examining the effect of OSA on long COVID and to explore the effect of treatment, and immunisation against COVID-19.

These studies highlight that patients with OSA appear to have a higher risk of hospitalisation when affected by COVID-19 (than non-OSA individuals) and have a higher risk of death. We concur with Hu and colleagues in their conclusion that results from well-designed larger prospective populations are required. Furthermore, it would be prudent in the assessment of patients with suspected or confirmed COVID-19 infection, to recognise that OSA may be one of the comorbidity risk factors for developing a severe form of the disease with increased risk of hospitalisation and death. As such, patients with OSA, with suspected or confirmed COVID-19 infection should be monitored closely.

There are a couple of errors as reported in the manuscript by Hu et al. (Yang H corresponding author).

1. Figure A: PMID 326877551 refers to a paper by Atkins et al. as cited in their reference list [ref 5]. But the reported data is from Cade et al. PMID 329462275. The reference list needs to be updated, along with the PMID in Figure A [Cade BE, Dashti HS, Hassan SM, Redline S, Karlson EW. Sleep Apnea and COVID-19 Mortality and Hospitalization. Am J Respir Crit Care Med. 2020 Nov 15; 202 (10):1462–1464. doi: 10.1164/rccm.202006-2252LE. PMID: 32946275; PMCID: PMC7667903].
2. Figure A: PMID 33546658 is mistakenly labelled as Dreher M but this data is from Lohia et al. [ref 3 in their paper]. Cade BE needs to be replaced by Atkins JL and Dreher M needs to be replaced by Lohia P in figures A and B.

References

[1] Hu M, Han X, Ren J, Wang T, Yang H. Significant association of obstructive sleep apnoea with increased risk for fatal COVID-19: a quantitative meta-analysis based on adjusted risk estimates. Sleep Med Rev 2022.
[2] Miller MA, Cappuccio FP. A systematic review of COVID-19 and obstructive sleep apnoea. Sleep Med Rev 2021;55:101382.
[3] Strausz S, Kiiskinen T, Broberg M, Ruotsalainen S, Koskela J, Bachour A, et al. Sleep apnoea is a risk factor for severe COVID-19. BMJ Open Respir Res 2021 Jan;8(1):e000845. https://doi.org/10.1136/bmjresp-2020-000845. PMID: 33436406; PMCID: PMC7804843.

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[4] Perger E, Soranna D, Pengo M, Meriggi P, Lombardi C, Parati G. Sleep-disordered breathing among hospitalized patients with COVID-19. Am J Respir Crit Care Med 2021 Jan 15;203(2):239–41. https://doi.org/10.1164/rccm.202010-3886LE. PMID: 33180549; PMCID: PMC7874403.

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3 March 2022
Available online 15 March 2022