

# Active smoking is associated with severity of coronavirus disease 2019 (COVID-19): An update of a meta-analysis

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Dear Editor,

The letter to the Editor of Lippi and Henry<sup>1</sup> published in the European Journal of Internal Medicine and entitled ‘Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19)’ had errors and led to the wrong conclusion.

Lippi and Henry<sup>1</sup> searched PubMed and Web of Science up to 9 March 2020, and identified 5 studies<sup>2-6</sup> with data on smoking and severity of COVID-19. They performed a meta-analysis revealing a pooled OR of 1.69 (95% CI: 0.41–6.92) and concluded that active smoking does not seem to be significantly associated with enhanced risk of progressing towards severe disease in COVID-19. There were several mistakes in their data collection that led to errors in the meta-analysis. In table 1 of their letter, they indicated the outcome of Guan et al. study<sup>2</sup> to be ‘Admission to ICU, mechanical ventilation, death’, however, they used the data of ‘severe disease’ in the study. According to the Guan et al.<sup>2</sup> paper, the number of patients having composite outcome should be 66, and for patients not having a composite outcome should be 1019. However, Lippi and Henry<sup>1</sup> used 172 and 913, respectively, in their paper. This is the most serious mistake because the Guan et al.<sup>1</sup> study contributes to most of the cases in the meta-analysis. Moreover, the non-severe patients in the Huang et al.<sup>3</sup> study should be 28 and not 31. The non-severe patients in the Yang et al.<sup>5</sup> study should be 20 and not 18. The severe patients in the Zhang et al.<sup>6</sup> should be 58 and not 60. The errors led to the wrong sample size of these 3 studies as well. Lippi and Henry<sup>1</sup> were only correct in one<sup>4</sup> out of the 5 studies.

I performed an updated meta-analysis according to the correct data using RevMan Ver. 5.3, and provide the forest plot (Figure 1). The pooled OR was 2.20 (95% CI: 1.31–3.67;  $p=0.003$ ). The heterogeneity was moderate ( $I^2=57\%$ ). There was no obvious publication bias by the funnel plot. Though there are new studies published after the Lippi and Henry<sup>1</sup> paper, the purpose of this letter is to correct their errors, therefore new studies are not included in the updated meta-analysis.

In a systemic review published by Vardavas and Nikitara<sup>7</sup>, 5 studies were included. Though meta-analysis was not performed in that study, the authors

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## KEYWORDS

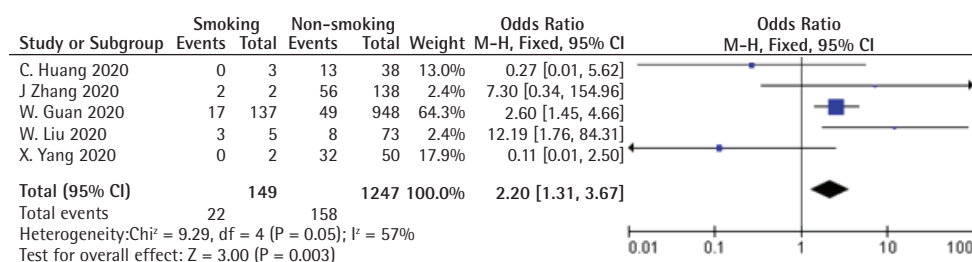
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Figure 1. Forest plot of the updated meta-analysis



concluded that smoking is most likely associated with the negative progression and adverse outcomes of COVID-19. A recent meta-analysis including 7 studies also revealed that smokers have a double risk of severe COVID-19 (pooled OR=1.98; 95% CI: 1.29–3.05)<sup>8</sup>. A meta-analysis published in 2019 including 27 studies and 460592 participants revealed current smokers (pooled OR=2.17; 95% CI: 1.70–2.76) and ex-smokers (pooled OR=1.49; 95% CI: 1.26–1.75) were more likely to develop community-acquired pneumonia compared to never smokers<sup>9</sup>. The evidence suggests that smokers are more vulnerable to lung infection, and COVID-19 is no exception.

In conclusion, the results of this updated meta-analysis suggest that active smoking is significantly associated with the risk of severe COVID-19. Though more data are available now, they are not included in this study. However, the early meta-analysis of the Lippi and Henry<sup>1</sup> paper should have had different results.

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### CONFLICTS OF INTEREST

The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none was reported.

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