CORRESPONDENCE

Selection bias: "The unseen enemy is always the most fearsome"

International Journal of Obesity (2022) 46:1247; https://doi.org/10.1038/s41366-021-00981-5

TO THE EDITOR:

The study by Dana et al., "Obesity and mortality in critically ill COVID-19 patients with respiratory failure," [1] reached the conclusion that "COVID-19 patients admitted to the ICU with moderate obesity had a lower risk of death than the other patients, suggesting a possible obesity paradox." We were perplexed by the authors' statement: "By focusing on critically ill COVID-19 patients with ARDS [Acute Respiratory Distress Syndrome], we reduced selection bias by restricting the study population." However, it is well known that restricting the study population to a consequence of obesity is what produces the selection bias responsible for the creation of an apparent obesity paradox [2, 3].

The majority of the manuscript uses terminology suggesting that the study is merely looking at differences in prognosis between those in different BMI categories. Here, we have no concerns. An observational study can reach a valid conclusion for predicting events [4], and the more restrictive the inclusion criteria, the more specific the results for those fitting the criteria [5]. However, the authors proceed to make claims such as "Moderate obesity, although potentially associated with many chronic morbidities, may have a protective effect during critical illness and in particular ARDS." This may seem like a minor point, but it is not. The suggestion of a "protective effect" is the entire premise behind the so-called "paradox." It is not paradoxical to state that obese individuals have a better prognosis than non-obese individuals when studying those with a problem that is caused by obesity. If a participant has the condition that qualifies them to be in the study, then they must have developed this condition as a consequence of either obesity or something else. Participants in these studies who are not obese must therefore over-represent these other causes.

Appropriately, the authors consider obesity as a cause for being in the study by noting "obesity leads to the severe form of COVID-19, and is associated with a greater risk of advanced levels of treatment such as admission to intensive or critical care…" However, when starting to attribute their results to the effects of obesity, the authors fell prey to collider stratification bias, a form of selection bias. When studying only those with severe COVID-19 (a consequence of obesity), the observed effect estimates for the obesity–mortality relationship become distorted, because in this restricted dataset, obesity is inversely correlated with other unmeasured reasons for severe COVID-19. As George R.R. Martin wrote in *A Clash of Kings*, "the unseen enemy is always the most fearsome" [6].

Steven D. Stovitz[1]✉, Hailey R. Banack[2] and Jay S. Kaufman[3]
[1]*Department of Family Medicine and Community Health, University of Minnesota, Minneapolis, MN, USA.* [2]*Department of Epidemiology and Environmental Health, School of Public Health and Health Professions, University at Buffalo, The State University of New York, New York, NY, USA.* [3]*Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada.*
✉*email: stovitz@umn.edu*

REFERENCES

1. Dana R, Bannay A, Bourst P, Ziegler C, Losser M-R, Gibot S, et al. Obesity and mortality in critically ill COVID-19 patients with respiratory failure. Int J Obes. [Internet]. 2021. http://www.ncbi.nlm.nih.gov/pubmed/34112941. Accessed 13 Jun 2021.
2. Hernán MA, Hernández-Díaz S, Robins JM. A structural approach to selection bias. Epidemiology [Internet]. 2004;15:615–25. Available from http://www.ncbi.nlm.nih.gov/pubmed/15308962.
3. Infante-Rivard C, Cusson A. Reflection on modern methods: selection bias—a review of recent developments. Int J Epidemiol [Internet]. 2018;47:1714–22. http://www.ncbi.nlm.nih.gov/pubmed/29982600. Accessed 26 Jan 2020.
4. Huitfeldt A. Is caviar a risk factor for being a millionaire? BMJ [Internet]. 2016. 355. https://pubmed.ncbi.nlm.nih.gov/27940434/. Accessed 8 Dec 2020.
5. Dekkers OM, Mulder JM. When will individuals meet their personalized probabilities? A philosophical note on risk prediction. Eur J Epidemiol [Internet]. 2020; 35:1115–21. http://www.ncbi.nlm.nih.gov/pubmed/33247797. Accessed 17 Jun 2021.
6. Martin GRR. A clash of kings. New York, N.Y: Bantam Books; 1999.

AUTHOR CONTRIBUTIONS

The authors, SDS, HRB and JSK all contributed to the manuscript concept, writing, and editing.

Competing interests

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Steven D. Stovitz.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 23 June 2021 Revised: 19 September 2021 Accepted: 29 September 2021
Published online: 9 February 2022