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Letter to the Editor

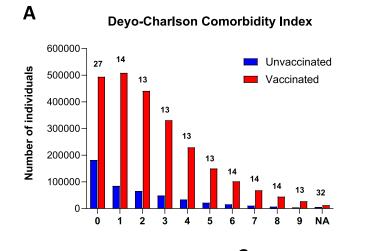
No evidence of a "healthy vaccinee effect" in COVID-19 vaccination data from the Czech Republic

Dear Editor,

With great concern, we read the manuscript "Does the healthy vaccinee bias rule them all?" by Furst et al. [1]. The existence of a potential bias in the characteristics of target populations in observational studies is routinely considered in studies addressing vaccine effectivity. However, the claims by Furst et al. are not substan-

tiated by any valid statistical analysis and are based primarily on speculation. The authors rely on simple descriptive statistics and do not provide any valid statistical quantification of individual contributing factors or comorbidity analysis of target populations. Importantly, the study does not include any information on COVID-19 infections or COVID-19-related deaths in study cohorts. Without this critical information, the conclusions of the presented study are speculative and unsubstantiated.

The study was not performed on 2.2 million individuals, as claimed, but rather on less than 500,000 individuals over 60 years



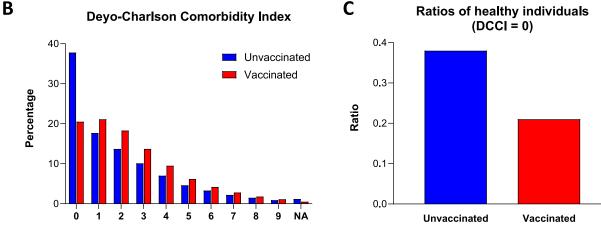


Figure 1. (A) Distribution of fully vaccinated and unvaccinated individuals among the categories of the Deyo-Charlson Comorbidity Index (DCCI). A total of 2889,314 individuals 60 years old or older included in the database of the Institute of Health Information and Statistics (IHIS) of the Czech Republic (data as of January 2022). The numbers above bars denote percentages of unvaccinated individuals within each category. NA; not assigned. (B) Relative distribution normalized to 100% within the unvaccinated and vaccinated populations. (C) Ratios of healthy individuals (DCCI category 0) within the unvaccinated and vaccinated populations. p < .0001 (unvaccinated vs vaccinated individuals in DCCI category 0 vs categories 1-9; analyzed using Chi-square with Yates' correction).

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of age (underrepresented in the utilized health insurance companies). Low numbers of deaths in <4 weeks categories do not allow for robust mortality estimates and should not be included. The presented mathematical model is irrelevant since it is deliberately constructed to show the reported pattern for any nonzero value of the parameter p.

The authors neglect to consider the effect of Post-acute sequelae of SARS-CoV-2 infection (PASC; long COVID). It is estimated that 10-40% of individuals infected with SARS-CoV-2 suffer from long COVID resulting in severe long-term health complications and increased death rates [2-4]. Immunization decreases the chance of developing PASC by up to 50% [5-7]. The protective effect of vaccines against long COVID may explain the observations presented by the authors as putative HVE.

To gain insight into the issue, we conducted an analysis using the IHIS dataset that includes data on all Czech residents insured by officially registered insurance companies [8]. We analyzed individuals aged 60 and above, totaling 2,889,314 persons as of January 2022, when vaccination was fully available. Analysis of the Deyo-Charlson Comorbidity Index, included in 99.3% of the records, clearly demonstrates that a higher percentage of vaccinated individuals was affected by comorbidities (Figure 1). This data provides irrefutable evidence against potential HVE.

Despite the strong claims, the manuscript by Furst et al. neglects COVID-19-related data and does not provide any evidence of the existence of a healthy vaccinee effect. As shown here, the opposite is true—the unvaccinated population was healthier.

References

- [1] Furst T, Bazalova A, Frycak T, Janosek J. Does the healthy vaccinee bias rule them all? Association of COVID-19 vaccination status and all-cause mortality from an analysis of data from 2.2 million individual health records. Int J Infect Dis 2024;142:106976. doi:10.1016/j.ijid.2024.02.019.
- [2] Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol 2023;21(3):133-46. doi:10. 1038/s41579-022-00846-2.
- [3] Li J, Zhou Y, Ma J, Zhang Q, Shao J, Liang S, et al. The long-term health outcomes, pathophysiological mechanisms and multidisciplinary management of long COVID. Signal Transduct Target Ther 2023;8(1):416. doi:10.1038/ s41392-023-01640-z.

[4] Altmann DM, Whettlock EM, Liu S, Arachchillage DJ, Boyton RJ. The immunology of long COVID. Nat Rev Immunol 2023;23(10):618–34. doi:10.1038/ s41577-023-00904-7.

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- [5] Trinh NT, Jodicke AM, Catala M, Mercade-Besora N, Hayati S, Lupattelli A, et al. Effectiveness of COVID-19 vaccines to prevent long COVID: data from Norway. *Lancet Respir Med* 2024;**12**(5):e33–4. doi:10.1016/S2213-2600(24)00082-1.
- [6] Mercade-Besora N, Li X, Kolde R, Trinh NT, Sanchez-Santos MT, Man WY, et al. The role of COVID-19 vaccines in preventing post-COVID-19 thromboembolic and cardiovascular complications. *Heart* 2024;**110**(9):635–43. doi:10.1136/ heartjnl-2023-323483.
- [7] Catala M, Mercade-Besora N, Kolde R, Trinh NTH, Roel E, Burn E, et al. The effectiveness of COVID-19 vaccines to prevent long COVID symptoms: staggered cohort study of data from the UK, Spain, and Estonia. *Lancet Respir Med* 2024;**12**(3):225–36. doi:10.1016/S2213-2600(23)00414-9.
- [8] Institute of Health Information and Statistics of the Czech Republic. ÚZIS ČR. [Retrieved April 25, 2024]. https://www.uzis.cz/index-en.php

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