**Supporting Information**: **Mortality for non-respiratory causes associated with Omicron and influenza infections**

Edward Goldstein, Harvard Medical School, Boston, MA 02114, USA [edmigo3@gmail.com](mailto:edmigo3@gmail.com)

**Section S1:** ***SARS-CoV-2-associated mortality for cardiovascular disease and for mental/behavioral*** ***disorders in the US***

We usedata on US mortality with cardiovascular disease (ICD-10 I00-I99), as well as mortality with mental/behavioral disorders (ICD-10 F01-F99) listed on the death certificate, with each of those data streams further stratified by having COVID-19 (ICD-10 U07.1) listed, or not listed on the death certificate [1]. Figure S1 plots the weekly number of US deaths with a cardiac cause but without COVID-19 listed on death certificate, as well as the number of deaths with both a cardiac cause and COVID-19 listed on the death certificate between Nov. 21, 2020—Nov. 19, 2022. Figure S2 plots the weekly number of US deaths with mental/behavioral disorders but without COVID-19 listed on death certificate, as well as the number of deaths with both mental/behavioral disorders and COVID-19 listed on the death certificate between Nov. 21, 2020—Nov. 19, 2022. Figures S1 and S2 suggest that compared to the SAR-CoV-2 epidemic in the Fall-Winter of 2021-2022, for the first Omicron epidemic wave in 2022 there were significantly higher increases in mortality with cardiovascular disease, as well as in mortality with mental/behavioral disorders listed on the death certificate and COVID-19 NOT listed on the death certificate, and smaller increases (for the first Omicron epidemic wave compared to the 2020-2021 epidemic) in mortality with either cardiovascular disease and COVID-19 listed on the death certificate, or with mental/behavioral disorders and COVID-19 listed on the death certificate.

Figures S1 and S2 suggest that wider detection and treatment of Omicron infections, particularly in persons with underlying health conditions such as cardiac disease and mental/behavioral disorders (see also [2]), should help mitigate the mortality burden of future Omicron epidemic waves.



**Figure S1**: Weekly US deaths with a cardiac cause but without COVID-19 on death certificate and deaths with a cardiac cause and COVID-19 on death certificate, Nov. 21, 2020—Nov. 19, 2022



**Figure S2:** Weekly US deaths with mental/behavioral disorders but without COVID-19 on death certificate and deaths with mental/behavioral disorders and COVID-19 on death certificate, Nov. 21, 2020—Nov. 19, 2022

**Section S2**: ***Influenza-associated mortality for different causes of death***

Studies have shown that only a minority of influenza associated deaths (depending on the circulating influenza strain and practices for coding deaths in different countries) are for respiratory causes. The percent of all influenza-associated deaths that are for respiratory causes ranges from 23% in study [3] to 38% in study [4]. In study [5] we have estimated that in the period prior to the 2008 A/H1N1 pandemic in the US, around 30% of all influenza-associated deaths were for respiratory causes (about half of which were for pneumonia, and another half for chronic lower respiratory disease), around 40% of all influenza-associated deaths were for circulatory causes, with an additional contribution of influenza to mortality for cancer, diabetes, renal disease, Alzheimer disease and other principal causes of death. In France, influenza infections result in a significant hospitalization burden for pneumonia and other respiratory causes [6], with the burden of influenza-associated hospitalization for chronic lower respiratory disease requiring further investigation. All of this, together with evidence about the effectiveness of antiviral use in influenza-associated respiratory hospitalizations [7] suggests the benefit of wider detection of influenza infections, particularly in respiratory hospitalization, as well as the accompanying use of influenza antiviral medications for mitigating the mortality burden associated with influenza infections.

In France, a significant share of influenza-associated mortality belongs to residents of nursing homes for dependent persons (EHPAD), with many influenza-associated deaths in EHPAD residents not taking place in hospitals. Residents of EHPAD made up about a 1/4 of all deaths in the French population in the pre-pandemic period [8,9]. During influenza and Omicron epidemics, the relative contribution of EHPAD residents to mortality in France increases. Data for the 2022-2023 season suggest a sharp rise in EHPAD deaths among all deaths in France around the peak of the Omicron and the influenza epidemics [10]. Further details on the benefit of vaccination of healthcare workers against influenza on mortality in nursing home residents are presented in [11].

**References**

[1] US Centers for Disease Control and Prevention. CDC Wonder mortality data. Available from: <https://wonder.cdc.gov/mcd-icd10-provisional.html>

[2] Australian Bureau of Statistics. COVID-19 Mortality by wave. 2023. Available from: <https://www.abs.gov.au/articles/covid-19-mortality-wave>

[3] Hansen CL, Chaves SS, Demont C, Viboud C. Mortality associated with influenza and respiratory syncytial virus in the US, 1999-2018. JAMA Netw Open. 2022;5(2):e220527

[4] Schmidt SSS, Iuliano AD, Vestergaard LS, Mazagatos‐Ateca IC, Larrauri A, M. Brauner JM, et al. All‐cause versus cause‐specific excess deaths for estimating influenza‐associated mortality in Denmark, Spain, and the United States. Influenza Other Respir Viruses. 2022; 16(4): 707–716

[5] Goldstein E, Viboud C, Charu V, et al. Improving the estimation of influenza-related mortality over a seasonal baseline. Epidemiology. 2012;23(6):829-38.

[6] Bernadou A, Sommen C, Pivette M, Hubert B. Estimating the burden of influenza-attributable severe acute respiratory infections on the hospital system in Metropolitan France, 2012-2018. BMC Infect Dis. 2023;23(1):128

[7] Deshpande A, Klompas M, Yu P-C, Imrey PB, Pallotta AM, Higgins T, et al. Influenza Testing and Treatment Among Patients Hospitalized With Community-Acquired Pneumonia. Chest. 2022;162(3):543-555

[8] Direction de la recherche, des études, de l'évaluation et des statistiques (DREES). L’Ehpad, dernier lieu de vie pour un quart des personnes décédées en France en 2015. 2018. <https://drees.solidarites-sante.gouv.fr/sites/default/files/er1094_toile.pdf>

[9] Botton J, Drouin J, Bertrand M, Jabagi M-J, Weill A, Zureik M, et al. Fréquence des décès et des hospitalisations chez les résidents des établissements d'hébergement pour personnes âgées dépendantes (EHPAD) et des unités de soin longue durée (USLD) en France au cours des années 2018 et 2019. EPI-PHARE - Groupement d’intérêt scientifique (GIS). 2021. <https://www.epi-phare.fr/app/uploads/2021/02/epi-phare_rapport_deces_hospit_hors-ehpad_20210205.pdf>

[10] Institut national de la statistique et des études économiques (INSEE). Daily deaths files broken down by sex, age and place of death. 2023 <https://www.insee.fr/en/statistiques/4493808?sommaire=4493845>

[11] Goldstein E. Benefits of influenza vaccination of healthcare workers. Cochrane Reviews: commentary. 2023. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD005187.pub5/detailed-comment/en?messageId=409503002&fbclid=IwAR0wqLXVy2jn5WjibRcleQsawiQaiQj3xh4ADga-rANY9niwfbCen22JqCY>