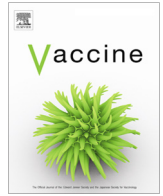




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## Letter to the Editor

### The impact of influenza vaccination on the COVID-19 pandemic? Evidence and lessons for public health policies



#### Letter to the Editor

In recent months, there has been much hype in newspapers and on social media (although less so in the scientific community) regarding an alleged association between influenza vaccination and coronavirus infection, mostly based on the study by GG Wolff that appeared ahead of print in *Vaccine* in October 2019 [1]. In the light of the emergence of the coronavirus Sars-CoV-2, the Wolff article has been artfully manipulated by the anti-vaxxer community as an argument against influenza vaccination. As pointed out by GG Wolff himself in a recent letter [2], the study concerned the 2017–18 winter season, and the reported results have nothing to do with the novel Sars-CoV-2 virus, but represent four endemic coronavirus strains regularly circulating in the US. In addition, Wolff's study was observational (not experimental) in nature, used a crude odds ratio, and, while focusing on influenza, it was also extended to several non-influenza respiratory viruses, some of which were significantly more (coronavirus and human metapneumovirus) or less (parainfluenza and respiratory syncytial virus) often detected among influenza vaccinees. These results remain largely unexplained, could have age confounding effects, and the author could not find any evidence to support the hypothesis of viral interference as a possible explanation. While further research on this topic should be encouraged, it is vital to reiterate that the results of Wolff's paper do not concern the Sars-Cov-2 virus.

There is extensive evidence that influenza vaccination provides both health and economic benefits and it should remain a public health priority unless equally solid evidence emerges that advises against it. We performed a literature review (until 15 June 2020) and found a number of papers that highlight the significant benefits of influenza vaccination in the current COVID-19 pandemic. Skowronski et al. conducted a test-negative design study using historical data (2010–11 to 2016–17) in Canada and found (at odds with Wolff's findings) no effect of influenza vaccination on the risk of coronavirus infection [3]. An inverse correlation between influenza vaccine coverage and COVID-19 mortality emerged in an ecological study analyzing data from thirty-four countries worldwide [4]. Jehi et al. developed and validated a COVID-19 infection prediction model, in which influenza vaccinees had a reduced COVID-19 infection risk [5]. Finally, a modelling paper by Li et al. concluded that “increasing influenza vaccine uptake [...] would facilitate the management of respiratory outbreaks coinciding with the peak flu season”, thus allowing a more efficient use of healthcare resources [6].

In conclusion, we recommend that influenza vaccination continues to be promoted as a central public health measure, as the evidence accrued so far, albeit limited, indicates that it can greatly benefit the management of the coronavirus pandemic, e.g. facilitating differential diagnosis and avoiding an overload of health services and hospitals associated with influenza infections. In addition, influenza vaccination plays an important role in protecting the elderly, which is a group that is particularly vulnerable for COVID-19. In summary, from a public health perspective we think it is important that influenza vaccination programmes are continued during the upcoming winter seasons.

#### Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: [Saverio Caini, Ben Cowling, Susanna Esposito, Angela Gentile, Jan Kyncl, Richard Pitman and Bruno Lina declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. John Paget declares that Nivel has received unrestricted research grants from WHO, Sanofi Pasteur and the Foundation for Influenza Epidemiology. C Raina MacIntyre has received funding from Sanofi and Seqirus for influenza research in the past five years and has been on advisory boards for Sanofi, Seqirus and Pfizer for vaccines. Ann R Falsey has received research funding from Janssen, Pfizer, Merck Sharpe and Dohme and serves on the DSMB for Novavax].

#### References

- [1] Wolff GG. Influenza vaccination and respiratory virus interference among Department of Defense personnel during the 2017–2018 influenza season. *Vaccine*. 2020;38(2):350–4.
- [2] Wolff GG. Letter to the Editor. *Vaccine* 2020;38(30):4651.
- [3] Skowronski DM, Zou M, Clarke Q, Chambers C, Dickinson JA, Sabaiduc S, et al. Influenza vaccine does not increase the risk of coronavirus or other non-influenza respiratory viruses: retrospective analysis from Canada, 2010–11 to 2016–17. *Clin Infect Dis*; 2020 May 22:ciaa626. doi: 10.1093/cid/ciaa626. Epub ahead of print.
- [4] Arokiaraj MC. Correlation of Influenza Vaccination and the COVID-19 Severity (April 10, 2020). Available at SSRN: <https://ssrn.com/abstract=3572814> or <http://dx.doi.org/10.2139/ssrn.3572814>
- [5] Jehi L, Ji X, Milinovich A, Erzurum S, Rubin B, Gordon S, Young J, Kattan MW. Individualizing risk prediction for positive COVID-19 testing: results from 11,672 patients. *Chest*. 2020 Jun 10:S0012-3692(20)31654-8. doi: 10.1016/j.chest.2020.05.580. Epub ahead of print.
- [6] Li Q, Tang B, Bragazzi NL, Xiao Y, Wu J. Modeling the impact of mass influenza vaccination and public health interventions on COVID-19 epidemics with limited detection capability. *Math Biosci*. 2020;325: <https://doi.org/10.1016/j.mbs.2020.108378>. Epub 2020 May 16108378.

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