Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

COVID-19 vaccine safety monitoring: Might differential healthcare seeking introduce detection bias into rates of medical events and cause false safety signals?

To the Editors:

In discussing the use of observational studies to evaluate COVID-19 vaccine safety, Black et al. provide an excellent overview of the importance of accurately-determined background rates for adverse events of interest, and highlight the relevant challenges and pitfalls in making those determinations [1]. I would like to bring another important consideration to the attention of the readers: differential detection bias, as a function of vaccination status.

Dramatic declines in healthcare encounters during the pandemic have been well documented [2–4]. Rates of emergency department visits and subsequent hospitalizations have plunged for conditions as dangerous and distressing as strokes, myocardial infarctions, and appendicitis [2–4]. The declines have clearly been mostly artifactual (ie, not reflecting true declines), providing artificially-diminished background rates of medical events. Most observers agree the declines primarily reflected fear of acquiring COVID-19 in the health care settings [2–4] (needless to say, while off topic, the deferral of needed care has had important public health consequences).

Diminished background rates of medical events during the pandemic notwithstanding, once persons became vaccinated, it follows that their healthcare behavior would adjust to their diminished risks and fears. They would increasingly seek care, and detection of medical events would increase to better-approximate true rates. As a result of these considerations, rates of medical event following vaccination would appear to be increased following vaccination as compared to background rates, whether those background rates were derived in self-controlled analyses (ie, from pre-vaccination person-time) or in conventional cohort analyses (from suitable unvaccinated controls). Given the striking decline in healthcare encounters noted above, the magnitude of this detection bias could be considerable, at times falsely-signaling safety concerns.

Of note, since most individuals are aware that COVID-19 provides protection against recurrent SARS-CoV-2 infection for some duration of time, those experiencing COVID-19 might also be expected to adjust their behavior and seek care for subsequent medical events as compared to their pre-COVID-19 disease behavior. In this context, the possible effect might be false evidence of long-term COVID-19 disease complications [5].

Solutions to these vexing problems seem difficult. During the pandemic, healthcare seeking appears to have been deferred for most medical events, although the magnitude of the deferral probably varied by the nature of the event and its perceived seriousness. One partial fix might therefore be to normalize this effect by characterizing the burden of the medical event in question as a proportion of all acute medical events (eg, percentage of total emergency department visits for any acute medical events) rather than to characterize them as rates (incidence) [6].

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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