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

Re: Real-world safety data for the Pfizer BNT162b2 SARS-CoV-2 vaccine, historical cohort study: authors' response

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We thank Dr Scorza et al. for their important comments, and for highlighting the limitations of our study, most of which were already addressed in the discussion of our manuscript [1].

This was an observational study, a design that usually lacks the power to investigate the pathophysiological processes. Consequently, our ability to explain the sensory abnormalities, which were observed more frequently among vaccinees, is limited.

Using visit diagnoses is indeed prone to bias; however, when analysing a cohort of hundreds of thousands of individuals, it is an important tool to track safety signals. Furthermore, this tool does not require the treating clinician to attribute the symptom or diagnosis to the vaccine, and the associations are found using statistical methods. The difficulty in drawing conclusions based on visit diagnoses led us to concentrate on a few robust diagnoses; two of them, Bell's palsy and Guillain–Barré syndrome (GBS), were confirmed by individual medical record review by one of the study investigators with the purpose of providing a reliable conclusion in light of the uncertainty in the literature regarding these two important outcomes.

The single case of GBS found in our study did fulfil the National Institute of Neurological Disorders and Stroke (NINDS) criteria as well as the Brighton criteria [2]. This patient developed progressive and ascending limb weakness as well as bilateral facial nerve palsy 10 days after receiving the first vaccine dose. On physical examination he had bilateral motor weakness as well as proximal hypoesthesia and decreased deep tendon reflexes. Lumbar puncture revealed elevated protein levels and mild (seven cells/μL) pleocytosis. Electromyography and nerve conduction studies demonstrated mild mixed (motor–sensor) demyelinating polyneuropathy.

Regarding the proper terminology for facial nerve palsy, as we found similar incidence rates among vaccinees and unvaccinated controls, our conclusion was that this clinical event could not be attributed to the vaccine; we therefore used the terminology “Bell's palsy”.

Facial sensory symptoms were found more frequently in the vaccinated group. This is a particularly difficult symptom to assess in a retrospective study and may be multifactorial. We do not believe that the symptoms of numbness and tingling were caused by zoster reactivation, as events of zoster were also investigated in this study and found to be of similar incidence among vaccinees and controls.

As correctly noted by Dr Scorza et al., we had to exclude 41% of the vaccinees since we could not match them to unvaccinated individuals. The reason for that was the rapid progression of the vaccination campaign in Israel and the higher priority that was given to the elderly and the sick during the process. Only a few weeks into the campaign, vaccination rates of individuals ≥60 years old reached 80%. The option of comparing adverse events rates between non-matched vaccinees and unvaccinated controls could have led to bias due to the dramatic differences in ages and prevalence of chronic conditions that were higher among the vaccinated.

As suggested, it would be interesting and important to look at a broader array of neurological events and their relation to COVID vaccination. However, in this study, we chose to concentrate on a few adverse events of special concern and those events receiving unusual public attention early on 2021. Real-world data do not necessarily enable investigation of a broader array of clinical outcomes than those examined in registration studies, but such research does allow for the assessment of a larger cohort. Data such as those collected in our study provide important information

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regarding the vaccine's possible adverse effects, especially those with lower incidence rates that cannot be evaluated by registration studies, which are limited in size.

Transparency declaration

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Author contributions

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