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## Letter to the Editor

### Severe Covid-19 Vaccine Side-Effects are Rare in Older Adults yet are Linked With Depressive Symptoms

COVID-19 vaccine development should have been the “light at the end of the tunnel.” However, antivaccination attitudes and hesitation are common,<sup>1</sup> even among older adults. Such hesitancy has been positively associated with depression, potentially due to concerns about vaccine side-effects.<sup>2</sup> We tested the association between depression and vaccine side-effects in older adults, and hypothesized that, like physical illness,<sup>3</sup> depression should increase with each additional side-effect.

This survey was conducted via iPanel (a probability based panel, see<sup>4</sup> for additional details) to obtain good representation of vaccinated Israeli older adults (N = 939, mean age  $68.9 \pm 3.43$  [range 65–85]; 59.9% females, 46.9% academic education; 75% married). At time of study (January 25th–February 4th, 2021),

respondents were  $28.15 \pm 9.47$  days after the first Pfizer vaccine [BNT162b2mRNA]. Participants completed web-based questionnaires comprising demographics, self-rated health, COVID-19 vaccination side-effects and depressive symptoms. Respondents provided informed consent to procedures approved by the last author’s university institutional review board. The extent of suffering from side-effects (reported by the FDA<sup>1</sup> and the Israeli Ministry of Health<sup>2</sup>) was examined (1-not at all to 5-very severely). We computed the number of side-effects endorsed as severe/very severe. Depressive symptoms were assessed by the PHQ-9 questionnaire ( $\alpha = 0.84$ ), the clinical cut-off score was  $\geq 10$ .<sup>5</sup> A single item indexing self-rated health was used (1-not healthy to 5-very healthy).<sup>6</sup>

Vaccination side-effects were rare (see [Supplementary file](#)). Prevalence of clinical depressive symptom levels was 11%. Clinical depression was logistically regressed on vaccination side-effects. Those with one severe side-effect were twice as likely to report clinical depressive symptom levels (OR = 2.30 [95% CI = 1.26–4.18], Wald = 7.48; df = 1,  $p < 0.0001$ ); those with 2 severe

side-effects, 4.76 times more likely (OR = 4.76 [95% CI = 2.31–9.80]; Wald = 18.195; df = 1,  $p < 0.0001$ ), those with 3+ severe side-effects were 7.34 times more likely to report clinical depressive symptoms (OR = 7.19 [95% CI = 3.58–14.42]; Wald = 30.85; df = 1,  $p < 0.0001$ ). Controlling for relevant variables (demographics, days since vaccination, and self-rated health) yielded similar results (see [Supplementary file](#)).

Although severe vaccination side effects were rare, they positively linked with depressive symptoms. The large scale of global vaccination suggests a potentially important mental health burden for those with side-effects. Depressive symptoms, if untreated, may be detrimental to older adults’ physical and mental health.<sup>3</sup>

Limitations of this study include narrowly focusing on Pfizer’s vaccination and older adults within a narrow age range, potentially mitigating generalizability to other vaccines and ages. Additionally, the directionality of the depression–side-effects link could not be discerned from our cross-sectional data. High depression levels in older adults during COVID-19.<sup>7</sup> may lead to side-effects<sup>8</sup>;

<sup>1</sup> <https://www.fda.gov/media/144414/download>

<sup>2</sup> <https://en.globes.co.il/en/article-covid-vaccine-side-effects-in-israel-match-trials-1001359338>

likewise, side-effects may lead to depression.<sup>8</sup> Future studies measuring these variables across time points may enable discerning causality provided suitable models are applied.<sup>9</sup> Experimental studies may also be revealing, e.g., comparing vaccination side-effects in a group of older adults whose depression rate was experimentally lowered (e.g., via an intervention) to a control group.

The current data suggest that reported side-effects may be useful in identifying depression in older adults. Presenting vaccinated older adults with accurate information regarding depressive symptoms and treatment centers, should be helpful. Psycho-educational interventions emphasizing that vaccination side-effects neither challenge vaccine safety nor efficacy, may aid in reducing potential depressive symptoms.

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## DISCLOSURE

*No disclosures to report.*

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## SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jagp.2021.09.010>.

*Yaakov Hoffman, Ph.D.*<sup>1</sup>

*Yuval Palgi, Ph.D.*<sup>2</sup>

*Robin Goodwin, Ph.D.*<sup>3</sup>

*Menachem Ben-Ezra, Ph.D.*<sup>4</sup>

*Lee Greenblatt-Kimron, Ph.D.*<sup>4</sup>

<sup>1</sup> *Interdisciplinary Department of Social Sciences (YH), Bar-Ilan University, Ramat-Gan, Israel*

<sup>2</sup> *Department of Gerontology (YP), University of Haifa, Haifa, Israel*

<sup>3</sup> *Department of Psychology (RG), Warwick University, Coventry, UK*

<sup>4</sup> *School of Social Work (MBE, LGK), Ariel University, Ariel, Israel*

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