Gmail

Avery Orrall <avery@retractionwatch.com>

Media Request: Retraction in PLOS One

Michael Edelstein <[redacted]> Wed, Sep 10, 2025 at 9:45 AM
To: Avery Orrall <avery@retractionwatch.com>
Cc: Amiel Dror <[redacted]>, "Orlyyakir[redacted]" <[redacted]>

Dear Avery

Thank you for the opportunity to expand on the retraction of the paper entitled: **Pre-infection 25-hydroxyvitamin D3 levels and association with severity of COVID-19 illness**

This paper was published in 2022, at the height of the COVID pandemic to determine whether pre-existing Vitamin D deficiency was associated with SARS-CoV-2 infection severity among secondary care patients. There is a wealth of literature, both molecular and clinical, that explores the link between vitamin D metabolism and infection susceptibility and severity, with a range of viruses- providing biological plausibility to our hypothesis of an association. To conduct this study, we recruited patients with PCR evidence of COVID-19 and checked their records for a Vitamin D test in the past, testing possible association using regression analysis. Making use of real-world, observational data, the dataset suffers from limitations, and the possibility of measurement and selection bias is there and acknowledged in the paper.

One of the main reasons for the retraction was the allegation of selection bias based on the fact that not every patient had vit D levels in their records, and only patients with a Vit D level in the records could be included. In our initial response to the editors, we acknowledge this limitation- Vitamin D levels were not checked specifically for the study but rather extracted from existing hospital databases- since there is no systematic testing for Vit D, levels were not available for all. We explain this in the methods.

To completely remove any doubt on how patients were selected: The limitation stemmed from the fact that there is no systematic screening of Vit D levels, and patients without a measurement of the exposure could not be included- however all patients meeting the inclusion criteria and who had Vit D levels in their records were included. There was no selection of patients among those who did have vitD levels available. Because of these limitations we were very cautious regarding claims of causation, and we also explicitly state that our findings should not be interpreted as evidence for using Vitamin D therapeutically for COVID patients.

In addition, we argued in our dialogue with the editor that since vitamin D was measured prior to SARS-COV-2 infection, there is no reason to believe that differential bias occurred , ie that those with more severe COVID disease were more (or less) likely to have their vit D levels measured, since infection had not occurred at the time of the measurement- in other words the missing data is randomly distributed between those with and those without the outcome (severe COVID disease). Since the outcome is not known at the time the exposure is measured It can be argued that those with vit levels are more unwell etc.. And therefore at higher risk of disease. We offered to check the characteristics of those with vit d levels vs. those without to assess indirectly selection bias- but the editors said it was too late (the retraction notice had already been sent).

We also acknowledge the delay between Vit D measurement and the outcome as well as the impossibility to adjust for potential corrective therapy- these are mentioned in the limitations of the first version of the paper. Our delays are relatively short compared to other papers using a similar

approach (also not accounting for potential corrective therapy) and published in the same journal (for example Effects of vitamin D on COVID-19 risk and hospitalisation in the UK biobank | PLOS One, published in 2025.) In our study approximately 2/3 of included patients were tested within a year of their SARS-CoV-2 infection.
While we could not adjust for potential corrective therapy, we did take seasonality into account. Our adjustment for seasonality is an innovative approach that mitigates changes in Vit D levels over time.

We also question the retraction process conducted by the journal. First of all, the retraction notice states that "the analyses performed were inadequate to test the association between 25-hydroxyvitamin D3 levels at the time of infection and severity of COVID-19 illness." the association tested is NOT about levels at the time of infection (since the acute infective process affects vit D levels) but PRE-infection- this is even in the title. We therefore question the diligence of the process on the side of the journal if they incorrectly state the tested hypothesis in the retraction. There is also an error- one author (ML) is listed as not responded, when he responded that he opposes the retraction.

More importantly, the paper was published more than 3 years ago. Following peer-review, we were contacted by the editor a few months after publication (in 2022) to clarify some methodological points- we provided a response. The journal at that point asked for an opinion from their in house statistician, who re-checked and did not highlight any specific issues. No further issues were raised since.

It is not clear why the journal decided to re-open the matter 3 years later, despite previous points having been answered and no new points having been raised. The journal also did not mention that the explanations we gave to their recent questions were unsatisfactory. When we were contacted again (on July 31st 2025), it was to receive a retraction notice (despite retraction not having been previously discussed), with no possibility to appeal but rather 4 days over a weekend in August, to Indicate whether we agree to cancel and ask questions .
As mentioned above, our offer to conduct additional analyses to check for the extent of were rejected as coming too late. Our perception was that the process was not clear and transparent, that the retraction process came without a warning, and that the Journal did not explain to us how a possible appeal process could be carried out. As a result our proposals to provide additional analyses to determine the extent of bias further, for example a comparison of baseline characteristics between patients with and without Vit D levels available, or to check for the association between time since last vit D level test and outcome, which might have satisfied the Journal editors and their concerns, were rejected on the basis that it was too late. We regret the process did not mature into a genuine academic discussion.

Subsequent studies purporting to answer the same questions, and that our results are aligned with the litterature on the topic, further bias Is unlikely to be the main explanation for the direction of the association.

To conclude, while we agree that the study contains some important limitations, mostly inherent to the observational nature of the study and the type of data it uses, these limitations are acknowledged and taken into account when formulating our conclusions. We regret the lack of clarity of the process and of the reasons to re-investigate years after the issues had been raised and answered. We think our results have been a useful addition to the litterature, especially in the context of the acute phase of a pandemic, and that the bias and limitations that we acknowledge do not invalidate the results. We welcome constructive criticism on our research as part of the scientific process and regret that an opportunity to turn the situation into a genuine scientific discussion was not taken.

Regards

Amiel Dror, Michael Edelstein, Orly Yakir on behalf of the authors

Ps please consider this response as the formal response to your enquiry, from the lead author.
