

# Review of: "Big Data From TriNetx on the Association of Retinal Vascular Occlusion and COVID-19 Vaccinations"

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**Potential competing interests:** No potential competing interests to declare.

Dear Editor,

I agree with the conclusion that we do not have sufficient data to confirm the correlation. These studies have different comparison groups and possible limitations in study design. Although they do not present directly conflicting results, further meta-analysis or other epidemiologic studies are needed to answer the scientific question on the association of RVaO and COVID-19.

- It is crucial to establish a clear temporal relationship between COVID-19 vaccinations and the onset of RVaO to strengthen the causal inference, but it is not possible in this study.

## **Comparison Groups:**

**Differences in Demographics:** One study may have included a broader age range or a different gender distribution compared to the other. Such differences can affect the generalizability and interpretation of the results. For example, Age: If one study includes a younger population and the other an older population, the incidence of RVaO might vary due to age-related factors. Older individuals are generally at higher risk for vascular events, which could confound the association with the vaccination.

Gender: If one study has a higher proportion of males and the other a higher proportion of females, hormonal and physiological differences could impact the results. For example, certain vascular conditions present differently or with varying frequencies between genders.

**Health Status:** If one study included individuals with pre-existing conditions while the other focused on a generally healthy population, this could lead to differing results regarding the association between RVaO and COVID-19 vaccinations. Individuals with pre-existing vascular conditions might be more susceptible to RVaO, potentially skewing the results.

**Geographic and Temporal Variations:** Variations in the geographic location of participants and the time period during which the data were collected can introduce heterogeneity in the findings. Different regions may have different vaccination rates and healthcare practices, which can influence the outcomes.

Addressing these limitations in future studies will help to provide a more definitive answer to the scientific question of the association between RVaO and COVID-19 vaccinations. For example, prospective cohort studies, following a large cohort of individuals over time, starting before they receive the COVID-19 vaccination, can help establish a temporal relationship and control for potential confounders.



Best regards,

Adriana Gomes Luz