# Commentary: Immune imprinting and spike protein toxicity—rethinking COVID-19 vaccines

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This commentary discusses the implications of recent findings regarding excess mortality in Japan, as reported in References 2 and 3. Since 2021, Japan has experienced a notable rise in excess mortality[1]. Ecological and epidemiological evidence from these studies suggests that this trend may be linked to overburdened healthcare infrastructure in rural regions and the repeated administration of booster vaccines targeting SARS-CoV-2 variants[2,3].

The Omicron variants, characterized by numerous spike protein mutations, can evade neutralizing antibodies generated by the original Wuhan-based vaccines. Individuals previously vaccinated with Wuhan-based vaccines experience immune imprinting[4], which weakens their antibody response to the spike proteins produced by Omicron-adapted vaccines—a phenomenon referred to as "original antigenic sin." This may permit the prolonged circulation of free spike proteins unbound by antibodies, which has been associated with serious adverse events such as myocarditis[5].

Epidemiological findings from References 2 and 3 indicate that the fifth and sixth doses of Omicron-adapted mRNA vaccines correlated with increased excess mortality (see Fig. 9 in Refs. 2, 3), while the second and third doses of the original Wuhan vaccines were associated with reduced excess deaths (see Figs. 1a and 3a in Refs. 2, 3). This suggests a significant shift in the impact of

vaccines on mortality.

While early SARS-CoV-2 vaccines helped reduce COVID-19-related deaths[6], continuing with uniform booster policies without accounting for individual immune status and potential vaccine-associated risks may ultimately do more harm than good. Based on the findings presented in References 2 and 3, we argue that it is essential to reconsider vaccine antigen design and adopt a personalized, risk-benefit-based strategy.

## Competing interests

The authors declare no competing interests.

## References


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