COVID-19 Vaccine Neutralization and Cellular Immunity Studies: An Ongoing Systematic Review

Methods

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Methods for an Ongoing Systematic Literature Review of Neutralization Studies Evaluating the Impact of SARS-CoV-2 Variants of Concern on COVID-19 Vaccines

This ongoing systematic review of studies aims to evaluate the impact of SARS-CoV-2 variants of concern on COVID-19 vaccine performance.

Search Strategy

Since March 15, 2021, a search of the preprint and published literature for studies assessing the ability of COVID-19 vaccines to neutralize SARS-CoV-2 variants of concern and variants of interest has been conducted weekly (or daily during times of rapid evolution of the pandemic). PubMed, bioRxiv, and medRxiv are searched using the very broad search terms of “SARS-CoV-2” AND “vaccine” during the pre-Omicron period and the search terms of “Omicron” OR “B.1.1.529” during the Omicron period. This broad search was in response to a rapidly evolving pandemic and was implemented to cast a wide net, particularly over early pre-print studies on emerging variants and to capture other important studies providing new information about the characteristics of new emerging variants. Title and abstract review were conducted to identify relevant studies for full-text review.

Literature searches are generally conducted weekly. During periods of new emerging variants of concern, literature searches are conducted daily.

Eligibility

Pre-Omicron (March 2021 – November 2021)

All studies that report fold reductions in neutralization for any variant of concern or variant of interest relative to the ancestral strain or that report data that enable the calculation of fold reductions in neutralization were eligible for inclusion. During full-text review, studies with the following characteristics were excluded:

- Evaluated partial vaccination
- Collected vaccinee sera < 7 days or > 6 months post final vaccine dose
- Evaluated immunocompromised persons
- Included samples from persons with hybrid immunity
- Used surrogate neutralization assays
- Combined results from multiple vaccines (with the exception of mRNA vaccines for all VOCs other than Omicron)
- Reported ND80 results instead of ND50
- Evaluated unlicensed vaccines

Omicron (November 2022 – present)

All studies that report fold reductions in neutralization for any Omicron sub-variant relative to the ancestral strain or that report data that enable the calculation of fold reductions in neutralization were eligible for inclusion. During full-text review, studies with the following characteristics were excluded:
- Evaluated partial vaccination
- Used a variant of concern (e.g., Alpha, Delta) as the reference strain
- Evaluated unlicensed vaccines

In contrast to the pre-Omicron period, data for all time points post vaccination, for all populations, for persons with hybrid-immunity, and for combined vaccine regimens are abstracted.

Search criteria will be expanded in the event of the emergence of new variants of concern.

**Data fields currently abstracted**

**General study details:**

- First author
- Study title
- Publication date
- Link to publication
- Status of publication (pre-print vs. published)
- Neutralization assay type
- Variants tested

**Cohort specific details:**

- Number of samples
- Median, IQR, minimum, and maximum age
- Vaccine regimen
- Number of doses
- Time of sample collection relative to vaccination (months post vaccination)
- Proportion female
- Dates of infection (if hybrid immunity)
- Location of sampling
- Hybrid immunity (yes/no)
  - If hybrid immunity, order of infection relative to vaccination (breakthrough vs. convalescent)
  - Dates of infection
  - Infecting strain
  - Time of sample collection relative to infection (time post infection)
  - Severity of infection
  - Severity definition
  - Time interval between infection and vaccination or vaccination and infection
- Geometric mean titers (GMT) for prototype strain and all available Omicron sub-variants
- Fold change in GMT for all available Omicron sub-variants relative to prototype
- Fold changes in GMT for earlier variants of concern (Alpha, Beta, Gamma, and Delta) relative to the prototype strain
- Percent of samples above limit of detection for prototype strain and all available Omicron sub-variants
- Reference strain
- Population details
- Comments (other notable information regarding study/cohort).