

AB019. Systematic review and meta-analysis of the current coronavirus disease 2019 vaccines for potential dose-optimal vaccine allocation based on reactogenicity and immunogenicity

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Background: With the limited coronavirus disease 2019 vaccine stockpile available, developing an equitable vaccination allocation strategy to maximize the number of people that escape infection is an ongoing global challenge. This study aims to bridge the reactogenicity and immunogenicity effects of coronavirus disease 2019 vaccines to a potential dose-optimal vaccine allocation.

Methods: We included Phase 1 to 3 randomized clinical trials conducted in healthy human subjects 18 years old and older. Data were pooled via random-effects models. Risk ratio (RR) and standardized mean difference (SMD) for reactogenicity and immunogenicity responses were used, respectively. Risk of bias and quality of evidence assessments were performed according to Cochrane's Risk of Bias tool and the Grading of Recommendations, Assessment, Development and Evaluation Approach Handbook.

Results: Fifteen trials comprising 99,102 subjects were included. Local adverse reactions [RR =1.97; 95% CI: 1.61–2.40, P<0.00001] and neutralizing antibody seroconversion rate [SMD =2.84; 95% CI: 1.23–4.45, P=0.0006] were higher using low dosage vaccines on first vaccination. Local

and systemic adverse reactions, neutralizing antibody titer and seroconversion rate were higher using high dosage vaccines on the first and second vaccinations and low dosage vaccines on second vaccination (All RR >1.0, SMD >0 and P<0.05). At 14/21 days dose-timing using low and high dosage vaccines and at 28/56 days dose-timing using low dosage vaccines, neutralizing antibody seroconversion rate was significantly increased [All SMD >0 and P<0.05]. At 28/56 days dose-timing, neutralizing antibody titer [SMD =1.46; 95% CI: 0.26–2.66, P=0.02] using low dosage vaccines and systemic adverse reactions [RR =2.25; 95% CI: 1.21–4.19; P=0.01] using high dosage vaccines were significantly increased.

Conclusions: The current vaccines have uniquely varying magnitudes of reactogenicity and immunogenicity responses per dosage regimen and dose-timing. Vaccinations have shown that the second dose has bigger effects on immunogenicity responses than the first. Therefore, vaccination allocation strategy should be dose-optimal to maximize the immune responses while minimizing reactogenicity responses and achieve equitable use.

Keywords: SARS-CoV-2; coronavirus disease vaccines (COVID-19 vaccines); reactogenicity; immunogenicity; dose-optimal vaccine allocation

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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