# Dr. B. C. Roy College of Pharmacy and AHS

## REPORT ON PRACTICE SCHOOL ON THE TOPIC

## "Adverse Drug Reporting of Medicines"

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# Study Design

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2) provides natural immunity against reinfection. Recent studies have shown waning of the immunity provided by the Covaxin & Covidshield vaccines. The time course of natural and hybrid immunity is unknown.

Using the google forms, we collected data for August and September 2021, when the B.1.617.2 (delta) variant was predominant, on all persons who had been previously infected with SARS-CoV-2 or who had received coronavirus 2019 vaccine. We used Poisson regression with adjustment for confounding factors to compare the rates of infection as a function of time since the last immunity-conferring event.
In this study, we estimated the incidence of confirmed SARS-CoV-2 infection in the following cohorts:

- previously infected, unvaccinated persons;
- previously infected persons who had also received the vaccine;
- and vaccinated persons who had not been previously infected

For each cohort, we quantified the association between the time that had passed since infection or vaccination and the rate of confirmed infection.

By comparing the rates of infection among these groups, we were able to assess the level of protection afforded by hybrid immunity as compared with that afforded by natural immunity or immunity conferred by vaccination.

# Methods

## Study Population:

Our analysis, which was based on data collected focused on infections that were confirmed during the study period, from August 1 to September 30, 2021. During this period, India was in the midst of a second pandemic wave that was dominated by the B.1.617.2 (delta) variant.
India had already conducted a several campaigns offering two doses of the Covaxin & Covidshield vaccines and had initiated a campaign offering booster doses. In addition, beginning in March 2021, unvaccinated persons who had recovered from coronavirus disease 2020 (Covid-19) at least 3 months previously were eligible to receive a single dose of the vaccine.
In this study, reinfection with SARS-CoV-2 was defined as a positive polymerase-chain-reaction (PCR) test in a person who had a positive test of a sample obtained before the study. The definition of severe Covid-19 was consistent with that of the National Institutes of Health — that is, a resting respiratory rate of more than 30 breaths per minute, an oxygen saturation of less than 94% while the person was breathing ambient air, or a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen of less than 300.
Google form includes, for all residents who have received a Covid-19 vaccine, been tested for Covid-19, or been previously infected with SARS-CoV-2, basic demographic information such as sex, age, place of residence, and population sector, as well as full records of vaccinations and confirmed infections.
Using these data at the individual resident level, we studied confirmed infections among persons 16 years of age or older who had tested positive for SARS-CoV-2 infection before July 1, 2021, or who had received at least two doses of vaccine before the end of the study period.

We excluded from the analysis the following persons: those whose data did not include information on age or sex; those who had tested positive for SARS-CoV-2 between July 1 and July 31, 2021; those who had recovered from a PCR-confirmed SARS-CoV-2 infection and then received more than one dose of vaccine those who had received more than one dose of vaccine and then recovered from a PCR-confirmed SARS-CoV-2 infection; those who had spent the entire study period abroad; and those who had received a vaccine other than these vaccines before August 1, 2021.

**Eligible persons in the study did not have a documented positive polymerase-chain-reaction assay between July 1 and July 30, 2021, had received at most one vaccine dose before recovery or after recovery from coronavirus disease 2019 (Covid-19), and had not received a Covid-19 vaccine other than Covaxin and covid shield before August 1, 2021. Age groups as of November 7, 2022, are shown. SARS-CoV-2 denotes severe acute respiratory syndrome coronavirus 2.**

- Persons ≥16 yr of age who had tested positive for SARS-CoV-2 infection before July 1, 2021, or had received two doses of vaccine before the end of the study period were assessed for eligibility
- Had data regarding sex and age group
- Had not tested positive for SARS-CoV-2 infection during July 2021
- Had not spent the entire study period abroad
- Had not recovered from Covid-19 and then been vaccinated more than once
- Had not been vaccinated more than once and then recovered from Covid-19
- Did not receive a vaccine other than the Covaxin or covid shield vaccine before the study period
- 16–39 yr of age
- 40–59 yr of age
- ≥60 yr of age

Please add the flowchart of questions in the google form here

## Results and discussion:

Understanding the magnitude of vaccine-induced protection over time and against SARS-CoV2-variants of concern is a public health priority.We evaluated the waning level of protection against confirmed infection with SARS-CoV-2 among persons who had recovered from previous infection and among previously uninfected persons who received the vaccine. We compared protection in these groups with that in persons who had been vaccinated with a single dose and later infected with SARS-CoV-2 and with that in persons who had recovered from SARS-CoV-2 infection and later received a single vaccine dose. Several studies showed higher protection in previously infected persons with or without an additional vaccine dose than in previously uninfected persons who had received two doses of mRNA vaccines.Vaccine effectiveness against the onward transmission of infection during contacts can be separated into two components; infectiousnessand susceptibility. Early analyses showed that vaccines reduced susceptibility of vaccinated persons and, if a variant of concern infection occurred, they reduced infectiousness of the cases.We could however only include data collected from recently vaccinated persons and on infections that were likely caused by the alpha-Variant of Concerns (Alpha). These early studies were also limited by the small number of cases.In addition to the uncertainty around the early Vaccine effectiveness-estimates, two important evolutions required further investigation of Vaccine Effectiveness-estimates: the delta-Variant of concern (Delta) replaced Alpha from late-2021 onwards and early reports on the waning of neutralizing vaccine-induced-antibodies were published.

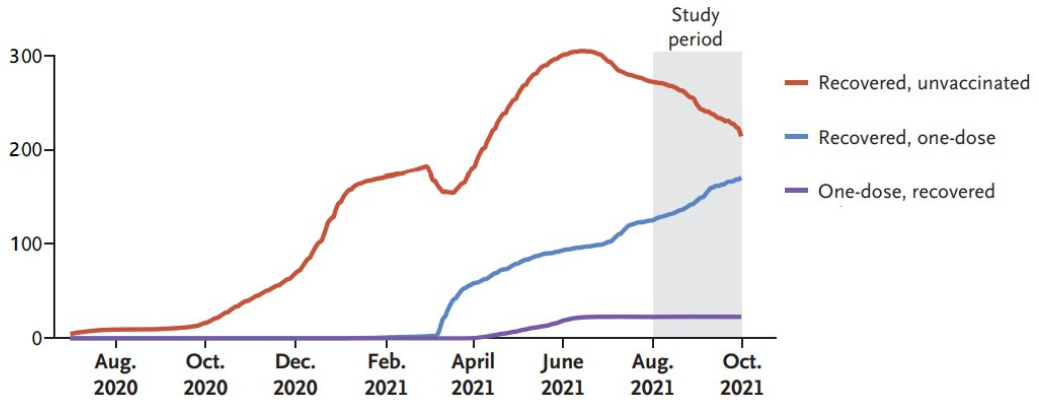


*Figure 1 Vaccine effectiveness in three groups a) recovered unvaccinated b) recovered, one dose c) one dose, recovered*

Vaccine effectiveness against the onward transmission of infection and Vaccine effectiveness reduced susceptibility-estimates, while remaining significant, were reduced by Delta and waned over time. We observed faster waning in the oldest age group.VEs was not estimated for persons younger than 16 years as this age group was not eligible for vaccination during the study period.We should seek to improve vaccineinduced protection in older persons and those vaccinated with viral-vector vaccine.The baseline susceptibility and infectiousness as obtained from the study were lowest for the youngest age group and highest for the oldest age group.

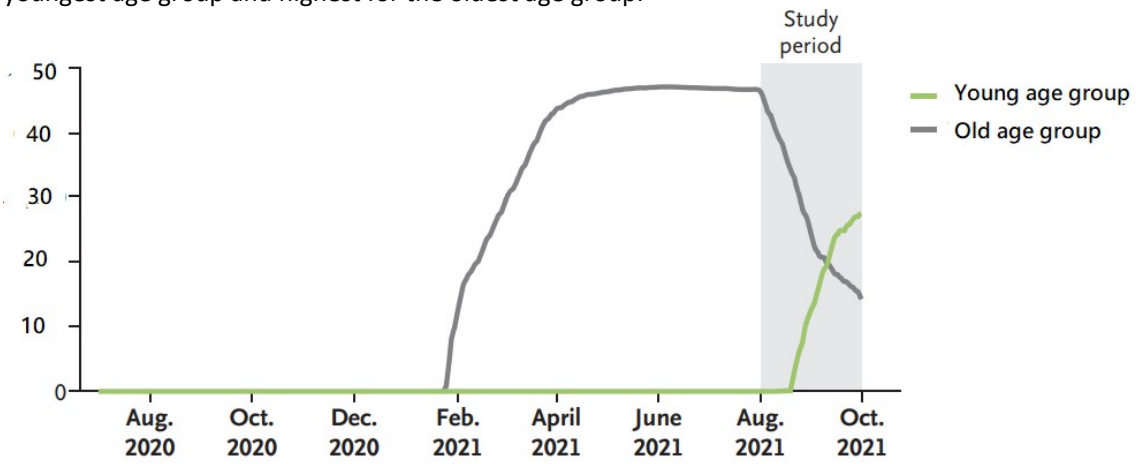


*Figure 2 Susceptibility and infectiousness as obtained from the study were lowest for the youngest age group and highest for the oldest age group.*

Susceptibility was lower in males compared to females; infectiousness was not-significantly different.The odds of transmission during the period when Delta was dominant increased compared to the period when Alpha was dominant.

*Table 1 Demographic data collected at the end of the study divided by group*

| **Demographic data collected at the end of the study period divided by group** | | | |
|---|---|---|---|
| **Age in years** | | **16-60** | **60+** |
| **Total number of persons** | **222** | **186** | **36** |
| **Median age years** | | **44** | **65** |
| **Sex Proportion** | | | |
| **Male** | **170** | **142** | **28** |
| **Female** | **52** | **34** | **18** |

Infection-acquired immunity did not offer significantly different protection compared to vaccination. The estimated reduction in susceptibility for re-infection was high.Hybrid immunity provided the highest protection in previously infected persons.It is evident that previously infected persons with or without one vaccine dose have better protection than uninfected persons who have received two doses of vaccine 3 to less than 8 months after the last infection.

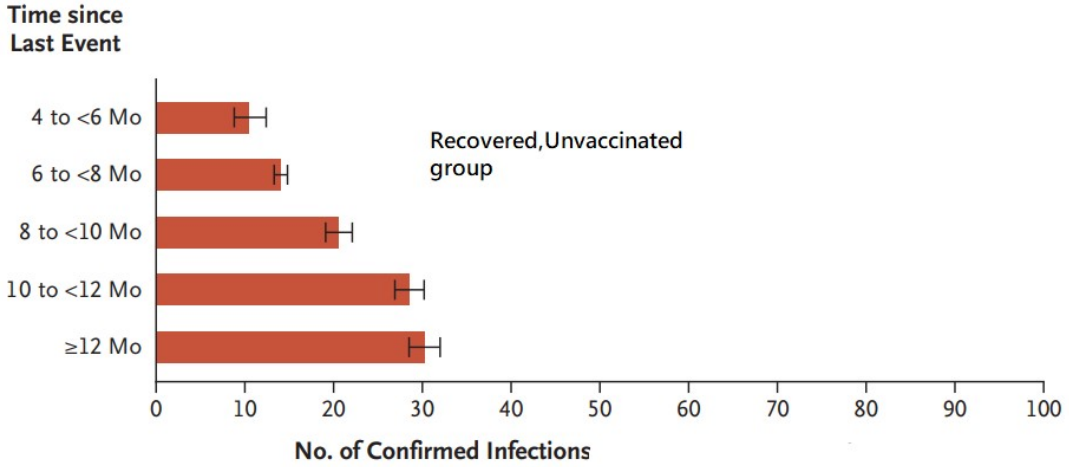


*Figure 3 Vaccine effectiveness in the recovered, unvaccinatedgroup. Data were obtained from the Poisson regression analysis for the study period, separated according to sub groups. Confidence intervals are not adjusted for multiplicity. The error bars denote 95% confidence intervals.*

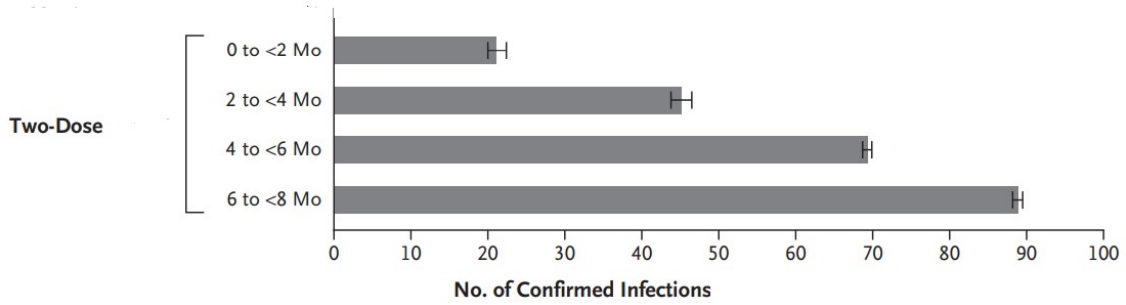


*Figure 4 Vaccine effectiveness in the two-dose group. Data were obtained from the Poisson regression analysis for the study period, separated according to subgroups. Confidence intervals are not adjusted for multiplicity. The error bars denote 95% confidence intervals.*

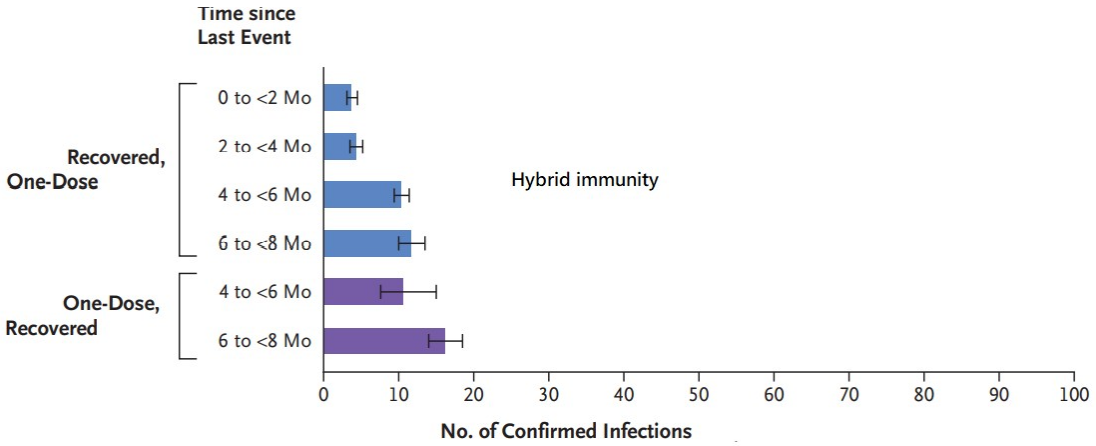


*Figure 5 Vaccine effectiveness in recovered, one dose and one dose, recovered. Data were obtained from the Poisson regression analysis for the study period, separated according to subgroups. Confidence intervals are not adjusted for multiplicity. The error bars denote 95% confidence intervals.*

We did not have enough data to evaluate the level of protection as a function of time between infection and vaccination, while taking the waning effect into account.Moreover, during the study period, most infections were delta variant infections, and our analysis provides no information regarding protection against newer variants.

## Conclusion:

Our pilot study quantifies the waning of natural and hybrid immunity in a real-world setting. Waning immunity was evident across all age groups.An understanding of the rates of waning immunity after immunity-conferring events is important to know the need for and the timing of additional vaccine doses. We found that protection against the delta variant waned over time in both vaccinated and previously infected persons and that an additional vaccine booster dose restored protection.We report significant Vaccine Effectiveness against infection and Vaccine Effectiveness against susceptibility-estimates for both Alpha and Delta. Both increasing time since vaccination and Delta were associated with a decrease in Vaccine Effectiveness-estimates. Infection-acquired immunity was less affected by Delta and, in combination with vaccination, showed slower waning compared to vaccine-induced immunity. Vaccine Effectiveness estimates were highest for hybrid immunity and persons with hybrid immunity were better protected against the infection than uninfected persons who had previously received two doses of vaccine. We observed the fastest waning of Vaccine Effectiveness in persons aged above 60 years, mainly because the effect of vaccination on the infectiousness of cases waned fastest in this age group.

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