

GUIDANCE ON INTERPRETATION OF THE COVID-19 VACCINE IMPACT ON INFECTIONS IN THE SCIENSANO WEEKLY REPORT

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1.1. INTRODUCTION

Since the 28th of October 2021, we have reported the 14-days incidence rates of COVID-19 infections among persons who have received a primary course of vaccination and those who are unvaccinated. The incidence rate is the number of new infections over this 14-day period, divided by the size of that group (total number of people vaccinated or unvaccinated). By comparing these two rates, we calculate the *relative risk reduction (RRR)* to make a preliminary assessment of the impact of vaccination. The RRR indicates the relative decrease in the risk of a COVID-19 infection for persons having received the primary course of the vaccination as opposed to unvaccinated persons and is calculated as follows :

$$RRR \text{ for infection} = 1 - \frac{\text{Incidence COVID 19 infection in persons with primary course}}{\text{Incidence COVID 19 infection in unvaccinated persons}}$$

Since the 16th of December 2021, we have also reported the RRR for people having received a booster compared to unvaccinated persons as well as people having received a booster to people having received the primary course only.

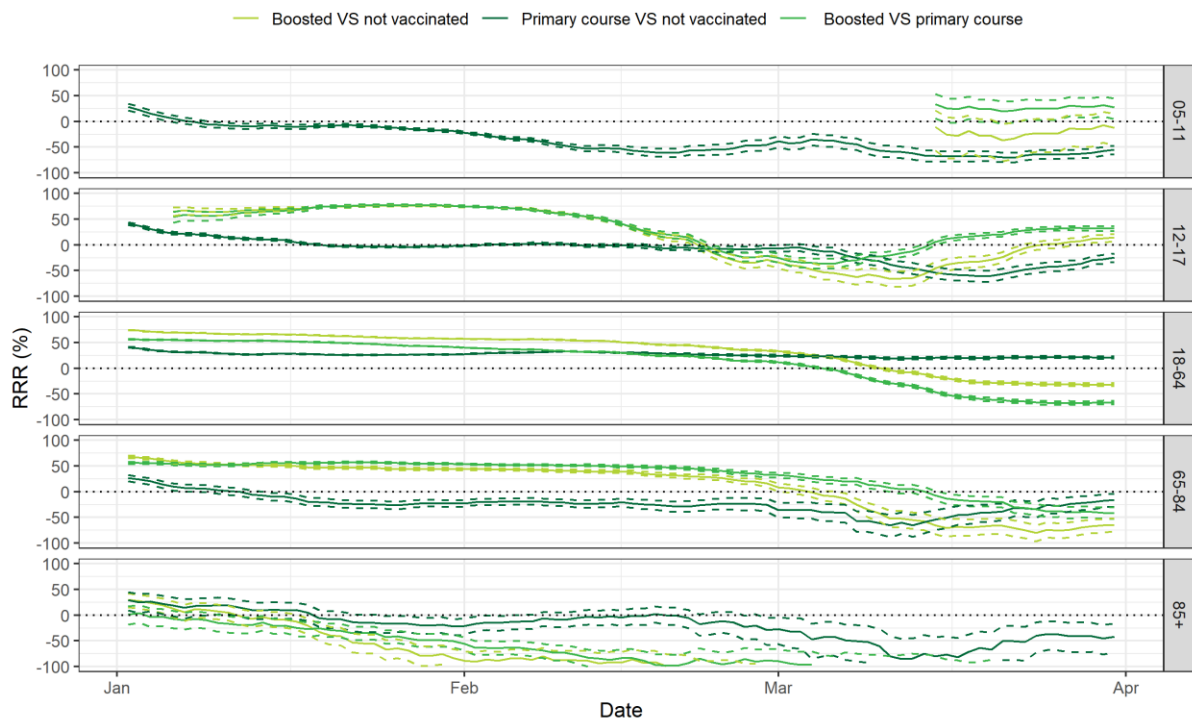
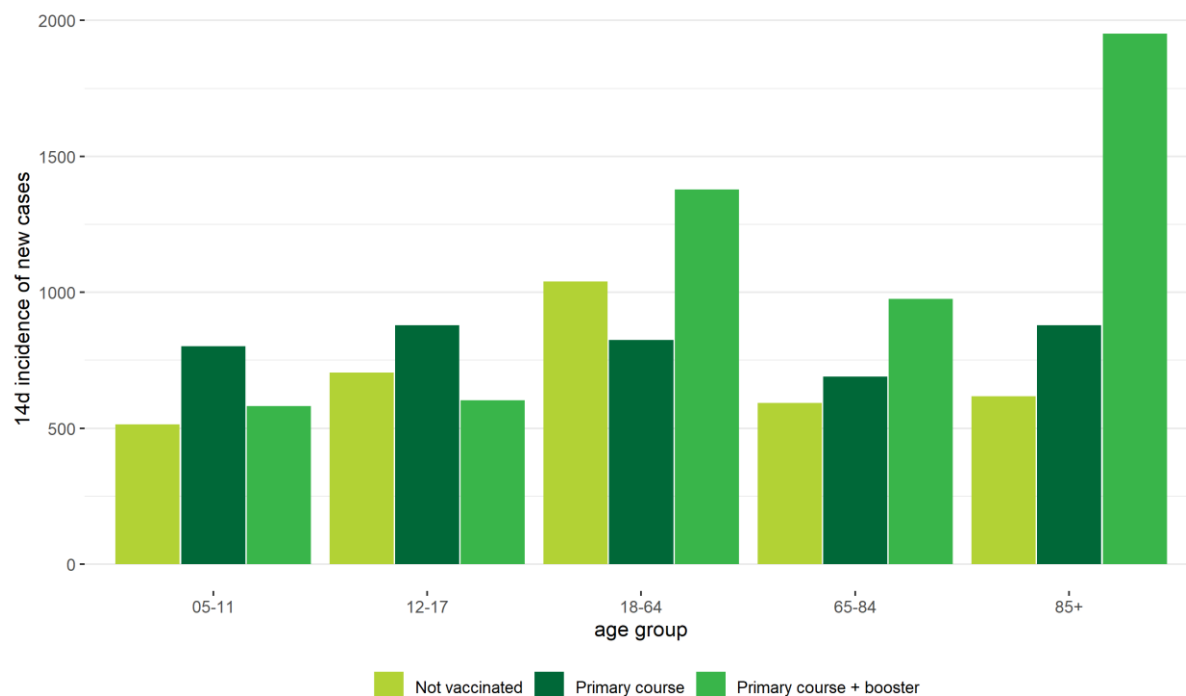


Figure 1. Evolution of relative risk reduction over time, for persons having received the primary course or the booster dose, by age group.

Until the beginning of 2022, the RRRs clearly showed protection against infection for both those who received a primary course and those who received the booster compared to unvaccinated persons (Fig. 1). However, since mid-January, the 14-day incidence for most age groups is lowest among the unvaccinated population (Fig. 1 & 2), resulting in negative RRRs, which gives the impression that during this period of 14-days, being unvaccinated protects better against infection than being vaccinated.



Data from 2022-03-18 to 2022-03-31

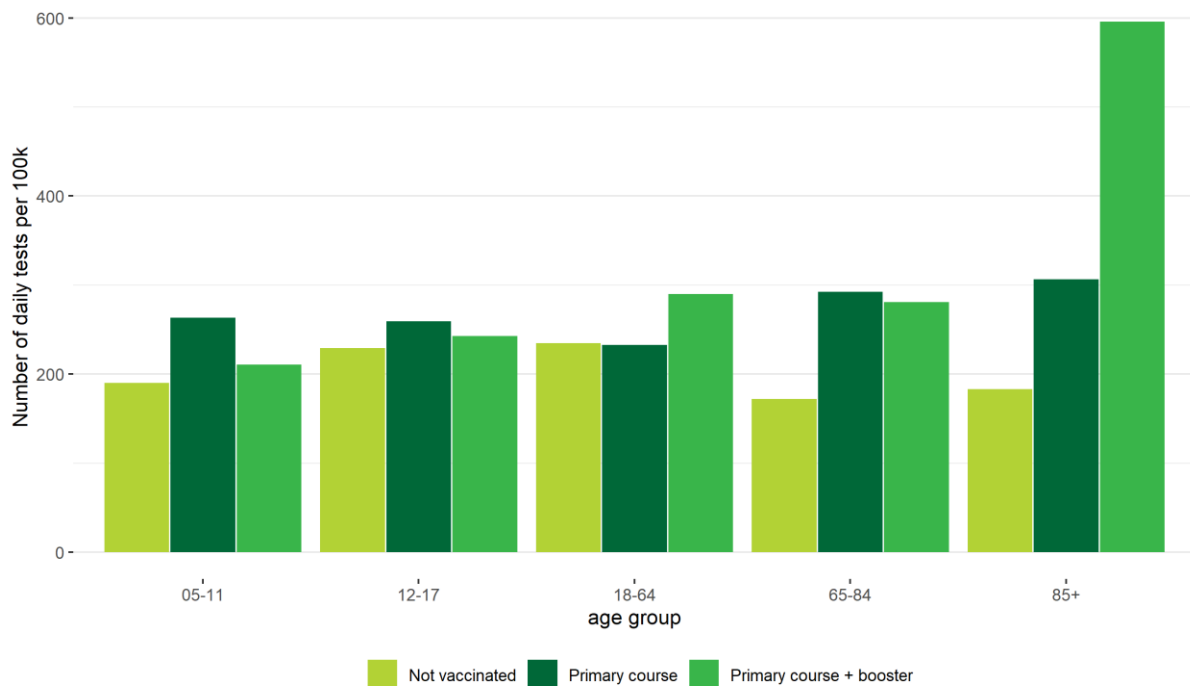
Figure 2. 14-day incidence of cases by vaccination status and age group for the period March 18 to 31, 2022.

Although it is known that protection offered by vaccines against infection reduces over time as a result of waning immunity, this does not explain a reversal of the initial pattern. In the section 10.8 of our “[Frequently asked questions](#)” document, we mention that these uncorrected estimates cannot be interpreted as vaccine effectiveness indicators as they do not account for certain confounders, such as differences in frailty, behaviour and testing between vaccinated and unvaccinated individuals. In the present document, we further investigate some of these differences in order to explain the trends observed in the impact of vaccination.

1.2. DIFFERENCES BETWEEN VACCINATED AND UNVACCINATED PERSONS

1.2.1. Testing behaviour

Testing behaviour impacts the chance of detecting an infection. For each of the different groups, by vaccination status and by age, we calculated the total number of COVID-19 tests (PCR or rapid antigen test) by 100,000 persons (Fig. 3).



Data from 2022-03-18 to 2022-03-31

Figure 3. Average number of tests per 100,000 population per day, by vaccination status and age group, over the period March 18 to 31, 2022.

For all age groups, the group that currently has the lowest testing frequency is the unvaccinated. Only for 18-64 year olds, the testing frequency is similar for unvaccinated and those who received a primary course. For children (≤ 17 year olds) and elderly (65-84 year olds), people who have received a primary course are those with the highest testing frequency, while for those aged ≥ 85 years the group that received the booster has a much higher testing frequency than the other two groups (the incidence in infections was also very high for this subgroup).

The relatively low testing frequency observed in the unvaccinated population can result in lower chances of being identified as a case. This could lead to an underestimation of the 14-day cumulative incidence of infections detected in the unvaccinated population.

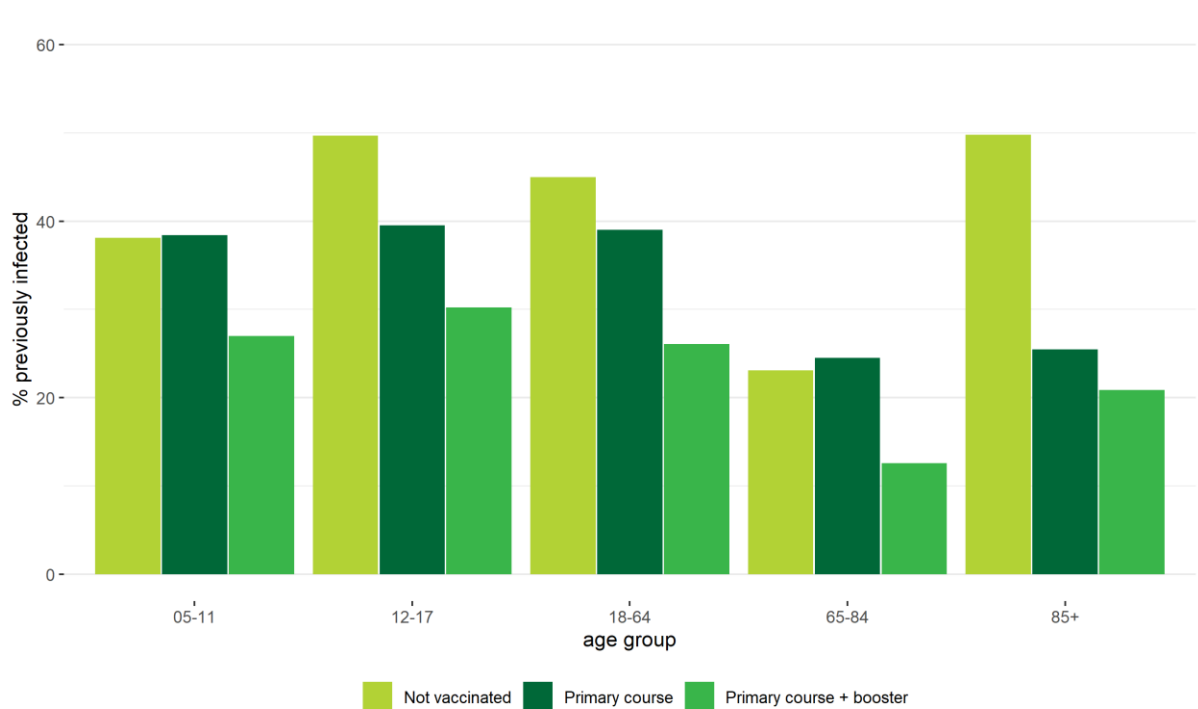
1.2.2. Previous infections

Research has indicated that recovery from viral infectious diseases is followed by a period of infection-induced immunologic protection against reinfection. This phenomenon is observed with many respiratory viral infections, including influenza and COVID-19¹. This may have two consequences :

- Certain level of protection of previously infected people despite being unvaccinated
- A decreased willingness of previously infected unvaccinated persons to get vaccinated.

Here we investigate, for each subgroup according to vaccination status and age, the *proportion of individuals with a previous laboratory-confirmed COVID-19 infection* (Fig. 4).

¹ Braeye T. et al. Vaccine effectiveness against onward transmission of SARS-CoV2-infection by variant of concern and time since vaccination, Belgian contact tracing, 2021. Vaccine, Apr 2022.

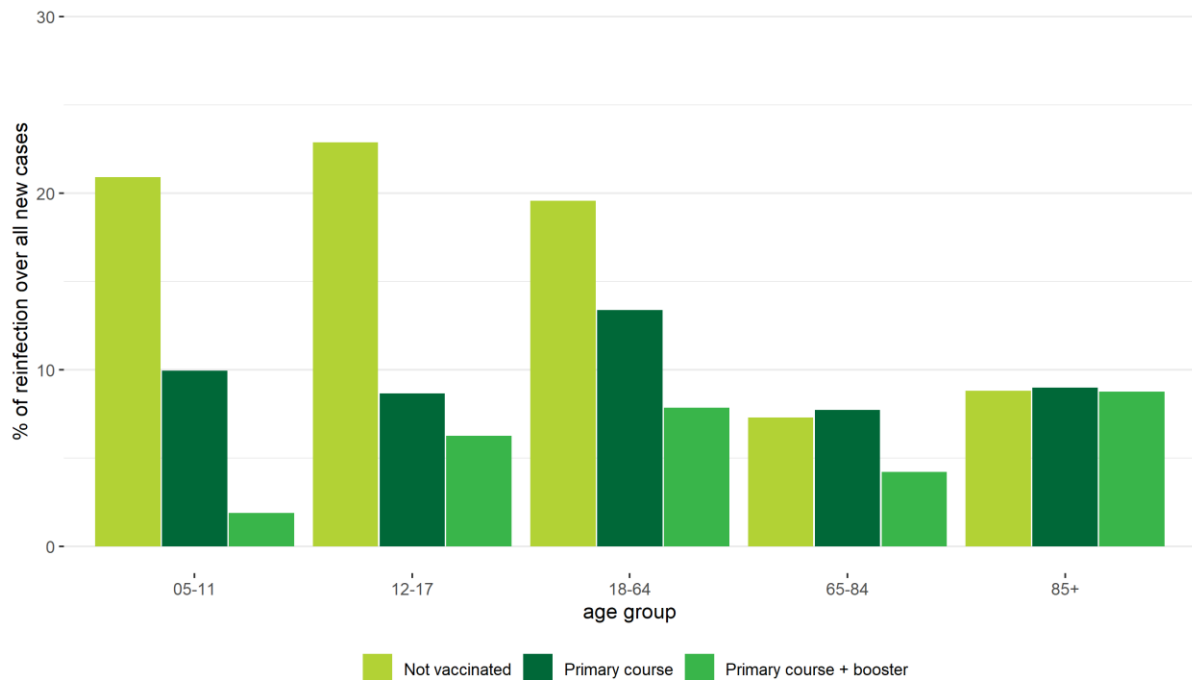


Data until 2022-03-31

Figure 4. Proportion of population that had undergone at least one COVID-19 infection on the 31st of March 2022, by vaccination status and age group.

For age groups 12-17, 18-64 and 85+ years, the highest proportions of persons who have previously been infected with COVID-19 are detected within the unvaccinated. These persons are thus protected against infection to a certain extent, despite the absence of vaccination which may lead to a relative decrease in future incidences. Also, for each age group, those who have received the booster have the lowest proportions of previous COVID-19 infections, ranging around 15-30%. Despite having protection against infection through vaccination, natural immunity for COVID-19 is missing among this population.

We also investigated to what extent those who are infected now have already undergone an infection at an earlier moment in time (considering a delay of at least 90 days between the two episodes), by vaccination status and age group (Fig. 5). For the age groups 5-11, 12-17 and 18-64 years, we see that previous infections are highest among those who are unvaccinated, and lowest among those who have received a booster. For those aged 65-84 years, previous infections are relatively lower among the boosted group but similar among unvaccinated and those with a primary course, while for the group 85 years and older the proportions do not differ by vaccination status.



Data from 2022-03-18 to 2022-03-31

Figure 5. Proportion of reinfections over all new cases, by vaccination status and age group, over the period March 18 to 31, 2022.

1.3. CONCLUSION

In this short report, we identified some factors that could explain the differences in COVID-19 incidence between individuals with different vaccination status (unvaccinated, primary course completed, boosted), apart from waning immunity, leading to a reduction in protection against infection. First, it was shown that people who are unvaccinated undergo on average fewer tests than those who are vaccinated or boosted, which could have an impact on the likelihood of cases being detected. Second, we found that those with a recent infection who are unvaccinated have more often undergone a previous infection than those who have received a primary course or a booster. Since a previous infection provides protection against infection as well (natural immunity), this could be a potential explanation for why the incidence of infection is currently lower among unvaccinated. However, it has been shown that a higher protection is offered by infection in combination with vaccination, the so-called hybrid immunity, compared to infection alone^{2,3}. Nonetheless, a previous infection may give the impression to individuals that they do not need to get vaccinated, as they feel this offers sufficient protection.

In addition to the differences described in this report, there are other potential differences between vaccinated and unvaccinated. This includes differences in behaviour (people that feel more protected might have more contacts), differences in frailty (people with a higher likelihood of developing a (severe) COVID-19 infection might on average get vaccinated more often). Overall, it is important to note that the incidence rates and RRRs that are reported in the weekly report of Sciensano are uncorrected for differences between groups, and provide a snapshot over a relatively short time period. Sciensano also

² Nordström et al. Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden. *The Lancet Infectious Diseases*, March 2022.

³ Pilz et al. SARS-CoV-2 reinfections: Overview of efficacy and duration of natural and hybrid immunity. *Environmental Research*, June 2022 (published ahead of print).

undertakes more elaborate analyses to follow the vaccine effectiveness over time, in which corrections are made for differences between groups in terms of age, sex, circulating variant, and prior infection. These analyses clearly show a protection of vaccination against infection and transmission, during periods in which the Alpha and Delta strains of SARS-CoV-2 were dominant^{4,5}. A vaccine effectiveness study during the Omicron-dominant period is currently available as preprint, and results indicate a protective effect against infection as well, albeit smaller compared to the Delta-dominant period⁶.

⁴ Braeye T. et al. Vaccine effectiveness against infection and onwards transmission of COVID-19: Analysis of Belgian contact tracing data, January-June 2021. *Vaccine*, Sep 2021.

⁵ Braeye T. et al. Vaccine effectiveness against onward transmission of SARS-CoV2-infection by variant of concern and time since vaccination, Belgian contact tracing, 2021. *Vaccine*, Apr 2022.

⁶ Braeye T. et al. COVID-19 Vaccine effectiveness against symptomatic infection and hospitalization in Belgium, July 2021-April 2022. Available as preprint on MedRxiv:
<https://www.medrxiv.org/content/10.1101/2022.05.09.22274623v1>