

## BACKGROUND

Children aged <5 years show higher anti-SARS-CoV-2 antibody titers compared to older individuals, suggesting an age-related inverse humoral response to SARS-CoV-2.

## OBJECTIVES

To investigate the **risk of SARS-CoV-2 reinfection in <5-year-old children** post-mild COVID-19, compared to older individuals previously either COVID-19 infected or vaccinated.

## METHODS

- A **cross-sectional web-based survey** to evaluate **SARS-CoV-2 reinfection over 12 months** following primary mild COVID-19 infection or vaccination in **children and adolescents** (aged **0-22 years**) from the COVID-19 household cohort at the University Pediatric Hospital of Padua, **Italy**
- The survey was distributed to 393 families between **December 2022** and **April 2023**
- Data on COVID-19 exposure, reinfections, and vaccination were collected; follow-up ceased upon laboratory-confirmed reinfection or booster vaccination
- Children were grouped by age and immunization status:
  - (a) **0-<5 years, SARS-CoV-2-recovered** (reference group);
  - (b) **≥5-22 years, SARS-CoV-2-recovered**;
  - (c) **≥5-22 years, naïve-vaccinated** with two-dose mRNA COVID-19 vaccination;
  - (d) **≥5-22 years with hybrid immunity**
- Reinfection-free probability was calculated, and Cox proportional hazard regression was used for analysis.

- A total of 156/393 families (40% response rate), including **208 children**, participated in the study
- The median time from the index date to the survey was 741.6 days (IQR=402.1-787.8)
- Among the included children, 168 (81%) experienced SARS-CoV-2 infection in the pre-Omicron era.

The **likelihood of remaining free from SARS-CoV-2 reinfection** was **higher** in children **aged <5 years** compared to older children, regardless of their immunization status (p<0.0001) (Fig.1).

Interestingly, individuals aged 5-22 years with **hybrid immunity** achieved through a single-dose vaccination after previous SARS-CoV-2 infection had a low probability of remaining free from SARS-CoV-2 reinfection.

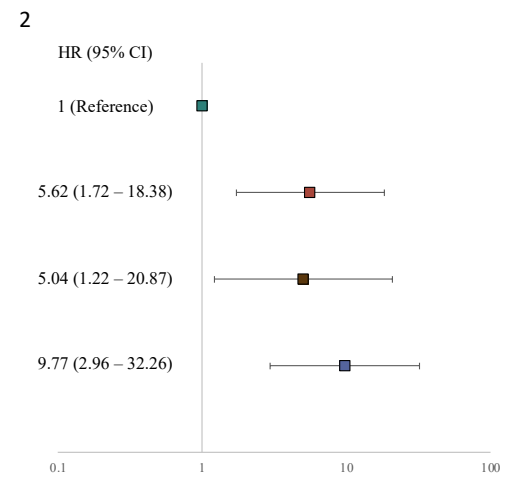
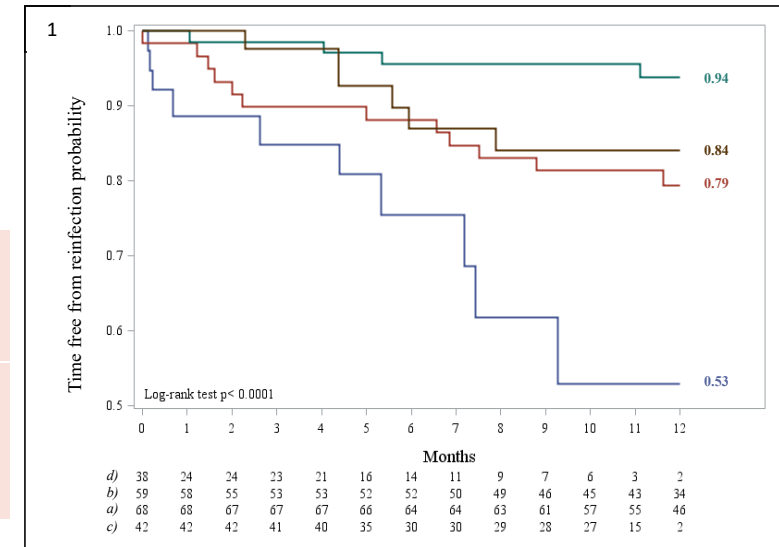


Fig.2 shows adjusted hazard ratio and 95% CI for SARS-CoV-2 reinfection in the 12 months post-immunization, using SARS-CoV-2-recovered participants aged 0-<5 years as reference group.

## RESULTS



Groups definition: — a) — b) — c) — d)

Fig.1 shows Cumulative time free from SARS-CoV-2 reinfection during the 12 months post-immunization among the exposure groups.

Cox model analysis confirmed **increased reinfection risk in older children** (groups b, c, and d) compared to group a, regardless of previous SARS-CoV-2 infection in the pre- or Omicron era (Fig.2).

## CONCLUSIONS

- <5-year-old children experienced a lower risk of reinfection than older infected and/or vaccinated individuals, suggesting potential SARS-CoV-2 humoral correlates of protection in the pediatric population.
- Waning protection was observed in all groups, emphasizing the importance of boosting pre-existing immunity.