Hybrid immunity against reinfection with SARS-CoV-2 following a previous SARS-CoV-2 infection and vaccination in children and adolescents: a population-based study.

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Introduction Protection against COVID-19 has been mostly studied in vaccinated versus unvaccinated populations and individuals without a previous SARSCoV-2 infection. However, as both infection and vaccination rollout continues to propagate, studies on the effectiveness of hybrid immunity, namely combined protection of naturally acquired and vaccine-induced immunity against reinfection, are needed mostly in the pediatric population. Several adults' cohort found that previous SARS-CoV-2 infection had a protective effect against BA.5 infection, mainly for previous infection with BA.1 and BA.2 [1]. In general, these studies found that previous infection alone, BNT162b2 vaccination alone, and hybrid immunity all showed strong effectiveness (>70%) against omicron infection [2]. A retrospective pediatric cohort study confirms the results, founded a statistically significant protection against BA.1 and BA.2 but not for BA.4 and BA5 making the vaccine campaign under question since BA.4 and BA.5 dominate most of the world [3].

Objective The present study aimed to assess the effectiveness of vaccination in SARS-CoV-2-recovered and SARS-CoV-2-naïve children and adolescents. The protective effect was also evaluated among children with 1 and 2 doses.

Methods A retrospective population-based study in Veneto, Italy, from May/November 2021, respectively for adolescents and children, through May 15, 2023, to evaluate the effectiveness with at least one dose of BNT162b2 (Pfizer-BioNTech), natural immunity due to previous infection (from February 2020 to May/November 2021, respectively for adolescents and children), and hybrid immunity (i.e., previous infection and vaccination) against omicron infection. We included (i) children aged 5-11 years in November 2021 (i.e., date of 5-11 approval vaccination) and adolescents aged 12-15 years in May 2021 (i.e., date of 12-18 approval vaccination), (ii) those with at least a recorded positive swab during the period of interest (i.e., February 2020 to May 2023), (iii) those with the vaccination certificates available, and (iv) those followed from family paediatricians (FP) at least from February 2020. We categorized children/adolescents in November/May 2021 in SARS-CoV-2-recovered and SARS-CoV-2-naïve with respect to the presence or not of at least a positive swab during the wash-out period (from February 2020 to the date of vaccine approval). The exposure of interest was vaccination as at least the 1 dose of Pfizer-BioNTech during the follow-up period (i.e., from May/November 2021 – start follow-up (SF)- to the end of the study – end follow-up (EF)-, respectively for adolescents and children). We excluded children who recorded a SARA-CoV-2 infection between SF and the 1 vaccination dose from the analysis. The outcome of interest was the first SARS-CoV-2 infection recorded after the SF. The end of follow-up was the date of the third dose, the date of omicron infection, and the end of assistance, whichever comes first. The effectiveness (1-hazard ratio (HR)) of vaccination and previous infection was assessed through a Cox model with vaccination as a time-dependent variable. We also evaluated the protection conferred by vaccination, stratifying the analysis for

the previous infection to assess the synergic effect of the hybrid immunity. We also assessed the effectiveness of 2 doses of vaccination. All models were performed separately for children and adolescents and adjusted for gender, age, and deprivation index.

Results We included 15,002 children and 3654 adolescents. Of the 15,002 children, 1513 (10%) were SARS-CoV-2-recovered, and 6052 (40%) were vaccinated. In the adolescents' cohort, 10% had a previous infection, and 71% were vaccinated. The effectiveness of vaccination against omicron infection was 21% (95% CI: 17%-25%) and 40% (32%-47%), and of previous infection was 90% (88%-92%) and 85% (78%-90%), respectively for children and adolescents. The stratified analysis showed the higher protective effect of vaccination among SARS-CoV-2-recovered (44% vs 21% in children; 68% vs 39% in adolescents)(Figure 1). When considering the number of doses performed, results showed higher effectiveness among children double vaccinated than those with only 1 dose compared to unvaccinated children. The higher effect of hybrid immunization persists.

Conclusion We found that vaccination had a protective effect against omicron infection, and this protection was maximal in SARS-CoV-2-recovered children and adolescents.

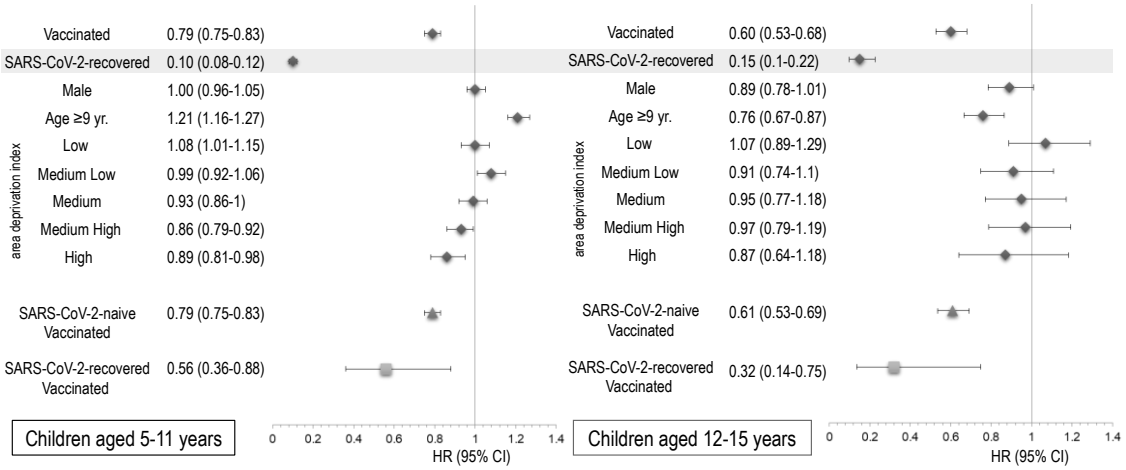

Figure 1. Single dose vaccine effectiveness against reinfection in SARS-CoV-2-recovered and SARS-CoV-2-naïve children and adolescents. Hazard Ratios and 95% Confidence Intervals were estimated through the Cox model considering vaccination as time-dependent variable. All models were adjusted by gender, age, deprivation index

Reference

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