

SYNOPSIS

Review of “Association Between Risk of COVID-19 Infection in Nonimmune Individuals and COVID-19 Immunity in Their Family Members”

10/14/2021

Article citation: Nordström P, Ballin M, Nordström A. Association between risk of COVID-19 infection in nonimmune individuals and COVID-19 immunity in their family members. *JAMA Intern Med.* 2021 Oct 11. doi: 10.1001/jamainternmed.2021.5814. [Epub ahead of print].

One-minute summary

- This is a retrospective, nationwide cohort study evaluating the association between risk of Coronavirus Disease 2019 (COVID-19) in non-immune individuals and the number of family members with known immunity from previous COVID-19 infection or full vaccination with 2 doses of vaccine (Moderna Spikevax COVID-19 vaccine [mRNA-1273], Pfizer-BioNTech Comirnaty COVID-19 vaccine [BNT162b2], or Oxford/AstraZeneca Vaxzevria vaccine [AZD1222/ChAdOx1-S]) by the index date (April 14, 2021).
- The study included data on **1,789,728 individuals from 814,806 families in Sweden**. The main outcome was incidence of COVID-19 infection in non-immune family members from April 15 to May 26, 2021.
 - During a total follow-up time of 111,454 person-years, 5.7% of non-immune family members were diagnosed with COVID-19 during a mean (range) follow-up time of 26.3 (1-40) days. There was an inverse relationship between the number of immune individuals in each family and the risk of COVID-19 in non-immune family members regardless of family size (2-5 members) with similar results with respect to severe COVID-19 requiring hospitalization. Compared to families with no immune family members:
 - Those with **1 immune family member** had a **45-61% lower risk of COVID-19** (hazard ratio [HR] 0.39-0.55; 95% confidence interval [CI]: 0.37-0.61, $P < .001$)
 - Those with **2 immune family members** had a **75-86% lower risk of COVID-19** (HR 0.14-0.25; 95% CI: 0.11-0.27, $P < .001$)
 - Those with **3 immune family members** had a **91-94% lower risk of COVID-19** (HR 0.06-0.09; 95% CI: 0.04-0.10, $P < .001$).
 - Those with **4 immune family members** had a **97% lower risk of COVID-19** (HR 0.03; 95% CI: 0.02-0.05, $P < .001$).

Additional information

- **Study Participants:** A family was defined as related individuals living at the same address. Each individual with immunity was matched 1:1 to a non-immune individual based on birth year, birth month and municipality resulting in a total cohort of 5,833,003 unique individuals. Families consisted of 2-5 individuals with a mean age at baseline of 51 years.
- **Data Collection:** Demographic data was obtained from Statistics Sweden. Vaccination status and data on COVID-19 infection were obtained from the Swedish National Vaccination Register and SmiNet database which covers 100% of the population. Data on COVID-19-related hospitalizations were obtained from the National Inpatient Register and the National Outpatient Register.
- **Exclusion criteria:**
 - Families were excluded if any family members became infected with COVID-19 between the baseline (April 1, 2021) and index date (April 14, 2021). This meant that any infections that were contracted close to the index date would not alter the risk of infections after the index date.
 - Individuals who died before the index date.
 - Individuals with only a single dose of vaccine before the index date.
- **Analysis:** The main exposure was the number of immune persons within each family and the primary outcome was incident COVID-19 infection in non-immune family members from April 15 to May 26, 2021. Cox proportional hazards regression models for unconditional samples was used to determine the main study outcome. Adjustment for clustering within families was performed. One model adjusted for age; a second model adjusted for sex, educational level, early retirement pension, total income, whether individuals were born in Sweden and underlying health conditions (e.g., myocardial infarction, stroke, diabetes, hypertension, kidney failure, chronic obstructive pulmonary disease, cancer).
 - The difference in risks according to whether immunity was acquired from a previous infection, a single dose of vaccine or full vaccination (2 vaccine doses) was also examined.
 - Immunity was acquired from either a COVID-19 infection before the baseline date or full vaccination, the receipt of 2 doses of an mRNA-1273 (Moderna) or BNT162b2 (Pfizer-BioNTech), or 2 doses of a viral vector ChAdOx1 nCoV-19 (Oxford/AstraZeneca) vaccine before the index date.
 - For non-immune family members, follow-up time was counted from April 15, 2021 until the date of confirmed COVID-19 infection, a first dose of vaccine, death, or May 26, 2021, whichever occurred first.
- **Sensitivity Analysis:** Two sensitivity analyses were performed.
 - The first cohort consisted of individuals with immunity acquired from a previous infection and excluded those with only a first dose of vaccine before April 14, 2021.

- The second cohort included those with immunity acquired from a single dose of vaccine only and excluded individuals with 2 doses of vaccine or a COVID-19 infection before the index date.
- A sensitivity analysis was not done for people who had received 2 doses of vaccine because too few individuals had received both vaccines by the April 1, 2021 baseline date.
- Both sensitivity analyses resulted in similar trends and risk reductions as the main analysis.
- **Variants of Concern (VOC):** greater than 95% of all COVID-19 cases during this study were due to the Alpha variant.

PHO reviewer's comments

- This study provides evidence about the benefits of household immunity in decreasing the risk of COVID-19 infection in non-immune family members.¹ The inverse association between the number of immune members in each family and the risk of infection in non-immune family members is a particularly important consideration for households that include younger children that are not eligible for vaccination.
- Protection of non-immune family members became more pronounced as the number of immune family members increased. Although the absolute risk of infection was associated with the number of non-immune relatives in each family, the relative risk reduction was much higher in larger families. This suggests that the absolute risk of infection is dependent on the number of non-immune members in each family.
- This study found that the decrease in risk of COVID-19 infection was similar irrespective of whether other family members acquired immunity from a previous infection, had a single dose of vaccine, or had 2 doses of vaccine (fully vaccinated). It is important to note that the Alpha variant was dominant during the study timeframe and previous studies have found that single dose vaccine effectiveness is known to be lower for currently circulating VOCs (i.e., Delta).¹
- It is important to note the following limitations of this study: 1) the number of incident cases was rather low in the sensitivity analyses of the largest families, and 2) there were not enough individuals who had received a full (2 dose) vaccination to test the impact of this subgroup alone on household transmission between non-immune and immune family members.

References

1. Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 real-world vaccine effectiveness – what we know so far [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Oct 21]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/covid-wwksf/2021/04/wwksf-vaccine-effectiveness.pdf?sc_lang=en

Citation

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