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Main expertise: Vaccine immunology, evaluation of immune protection against vaccine-preventable diseases

Immune Surveillance for Vaccine-Preventable Diseases in Adults

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Vaccination is the starting point—but how can we ensure that adult populations remain protected long after the last dose?

What is vaccine-induced immunity based on?

Almost all current vaccines work through antibodies[1]

- Antibodies in serum or on mucosa can block the infection or spread of the pathogens to blood circulation and thus provide a correlate of protection.
- The quantity as well as the functionality (e.g. neutralization) of the antibodies is essential to protective immunity.
- Memory cells are important for long-term immunity, sometimes confer protection even in absence of antibodies.
- The mechanism of protection [from infection] is not necessarily the mechanism of recovery from infection!
- Recovery from infection often based on cellular immunity; T cells recognize infected cells and activate phagocytes.

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[1] Plotkin et al. Correlates of Protection Induced by Vaccination. Clin Vaccine Immunol. 2010 Jul; 17(7): 1055–1065

What is immune surveillance

- Immune surveillance involves monitoring and assessing population immunity against pathogens, whether induced by vaccines or infections, or both.
- Immune surveillance allows for estimating the level of population protection against vaccine-preventable diseases.
- By assessing the level of immunity in a population, and by identifying possible gaps, immune surveillance can inform decisions on booster doses, vaccine updates, and prioritization of at-risk groups.

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Immune surveillance in adults

- Monitoring immunity in adults focuses on maintaining long-term protection, while in children, the emphasis is on finding effective vaccination schedules that induce immunity.
- Unique challenges in adults include waning immunity, aging and comorbidities and other immunocompromised conditions.
- Immunity and vaccine needs can differ for adults based on age, infection history, and overall health status.

Immune surveillance in Finland

- THL has monitored population immunity against vaccine-preventable diseases through its own studies.
- Immunological studies may be used to assess the quantity, quality, and duration of antibody and cell-mediated immune responses across different population groups.

Examples on how serosurveillance data has informed vaccination recommendations

COVID-19 vaccine recommendations

- Throughout the COVID-19 pandemic, THL monitored the progression of the epidemic in the population through antibody studies
- By late 2021, adult immunity was mainly vaccine-derived.
- In early 2022, infection-induced immunity emerged in both vaccinated and unvaccinated groups, showing that booster vaccinations before the infection wave did not prevent transmission.
- THL's findings confirmed that infections boost immune responses, producing hybrid immunity in vaccinated individuals. This knowledge has influenced vaccine recommendations, equating infection to one vaccine dose.
- Antibody studies revealed that a significant proportion of the adult population, especially younger age groups, had hybrid immunity. This information was used to support recommendations focusing vaccinations on older adults and immunocompromised individuals.

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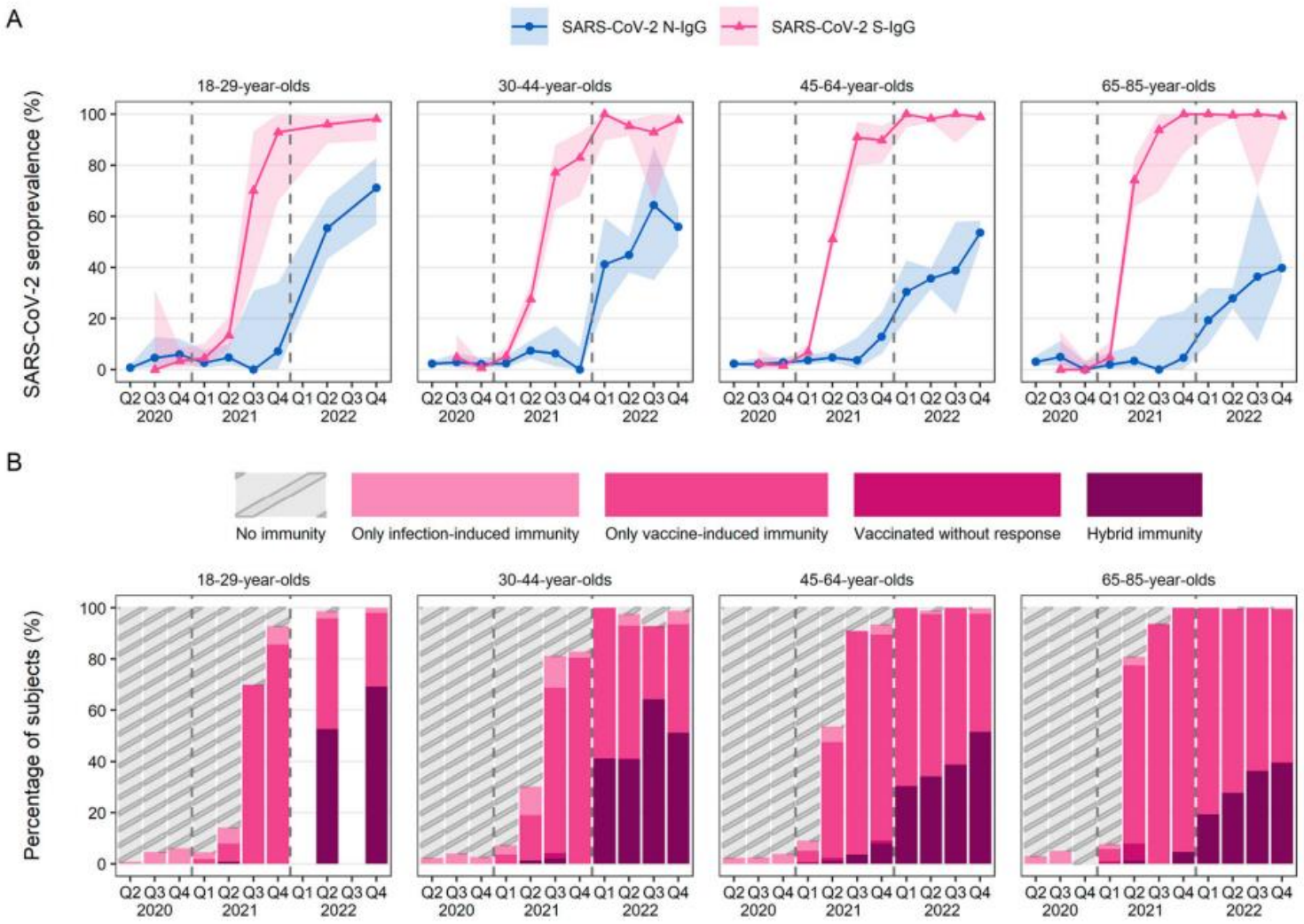
COVID-19
Serosurveillance study

- Seroprevalence of nucleoprotein antibodies remained below 7% until the last quarter of 2021.
- Following the emergence of the Omicron variant, the prevalence of infection-induced antibodies rose rapidly, reaching 31% in Q1/2022 and 54% by Q4/2022.
- We estimated that 51% of the Finnish 18-85-year-old population had antibody-mediated hybrid immunity induced by a combination of vaccinations and infections by the end of 2022.

Solastie A, Nieminen T, Ekström N, Nohynek H, Lehtonen L, Palmu AA, Melin M. Changes in SARS-CoV-2 seroprevalence and population immunity in Finland, 2020-2022. Emerg Microbes Infect. 2023 Dec;12(2):2222849.

COVID-19 Serosurveillance study



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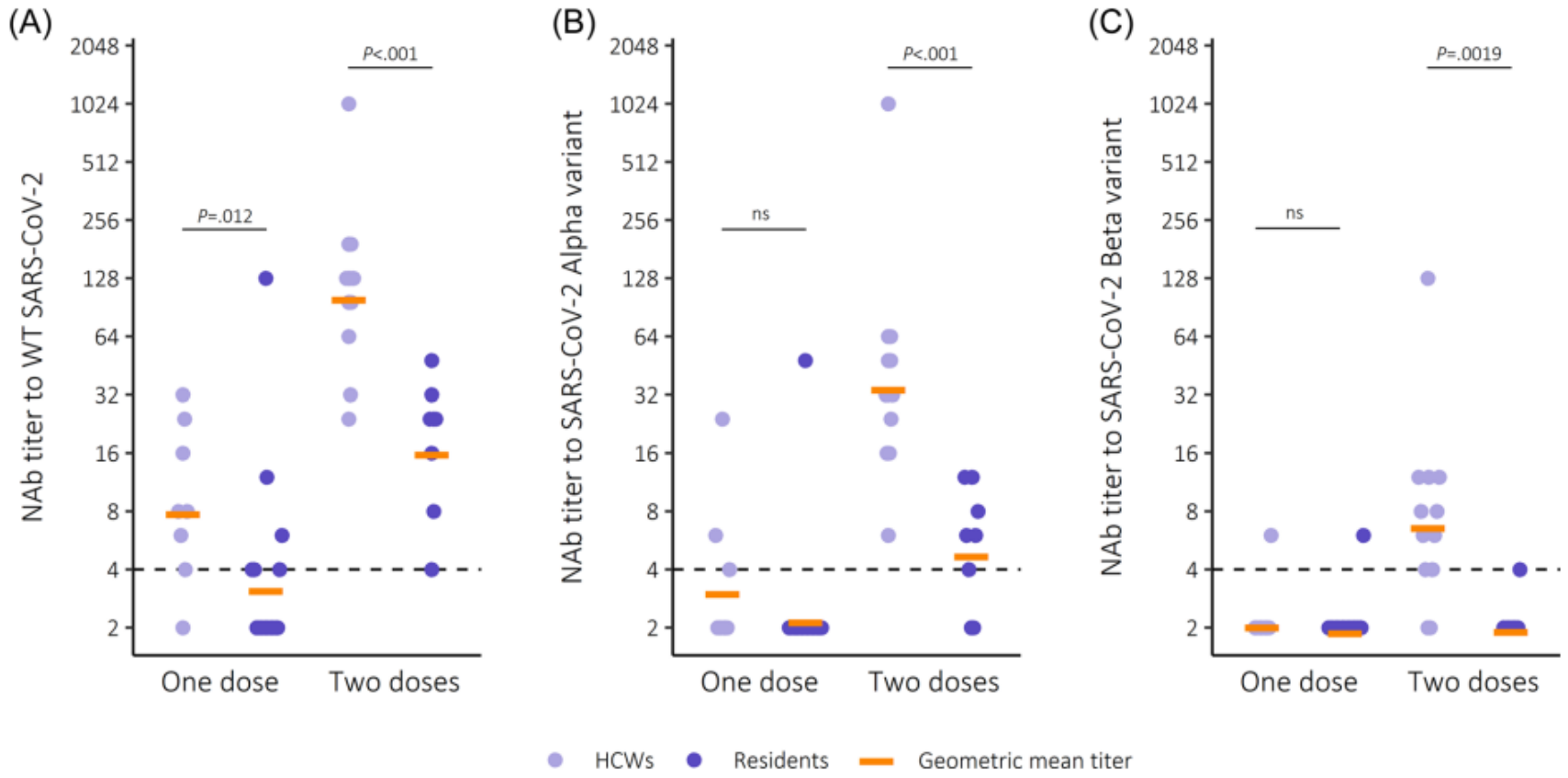
COVID-19
Serosurveillane in outbreaks

- Serosurveillance studies of COVID-19 outbreaks in Finnish long-term care facilities in spring 2021 revealed that recently vaccinated elderly residents had weaker immune responses, particularly to the Alpha and Beta variants which caused the outbreaks, compared to healthcare workers.
- Both antibody responses and T cell responses to vaccination remained inferior, suggesting reduced protection not only against infection but also against severe disease.
- These findings highlighted the need to address the risks posed by emerging variants to vulnerable populations.

Obach D, Solastie A, Liedes O, Vara S, Krzyżewska-Dudek E, Brinkmann L, Haveri A, Hammer CC, Dub T, Meri S, Freitag TL, Lyytikäinen O, Melin M. Impaired immunity and high attack rates caused by SARS-CoV-2 variants among vaccinated long-term care facility residents. Immun Inflamm Dis. 2022 Sep;10(9):e679.

COVID-19
Serosurveillane in outbreaks



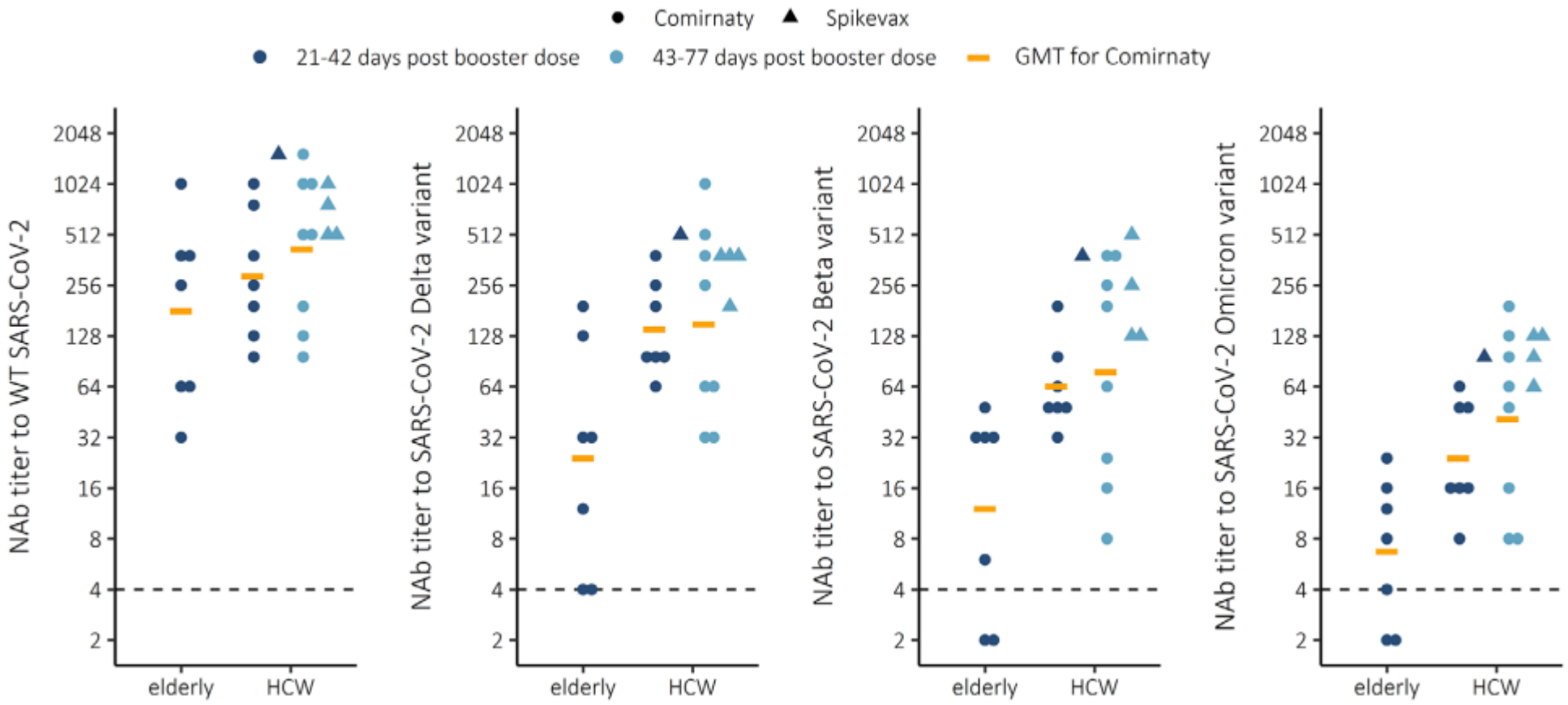
Obach et al. Immun Inflamm Dis. 2022 Sep;10(9):e679.

COVID-19
Responses to booster doses

- We assessed antibody responses to the first COVID-19 mRNA booster doses (third doses) given in December 2021.
- Third vaccine doses induced high antibody levels in healthcare workers (HCWs), but elderly subjects had lower neutralizing antibody titers, especially against Beta and Omicron variants.
- The findings indicated that additional interventions may be required for frail elderly populations.

Haveri A, Solastie A, Ekström N, Österlund P, Nohynek H, Nieminen T, Palmu AA, Melin M. Neutralizing antibodies to SARS-CoV-2 Omicron variant after third mRNA vaccination in health care workers and elderly subjects. Eur J Immunol. 2022 May;52(5):816-824.

COVID-19
Responses to booster doses



Haveri et al. Eur J Immunol. 2022 May;52(5):816-824.

COVID-19
Hybrid immunity

Ekström N, Haveri A, Solastie A, Virta C, Österlund P, Nohynek H, Nieminen T, Ivaska L, Tähtinen PA, Lempainen J, Jalkanen P, Julkunen I, Palmu AA, Melin M. Strong Neutralizing Antibody Responses to SARS-CoV-2 Variants Following a Single Vaccine Dose in Subjects With Previous SARS-CoV-2 Infection. Open Forum Infect Dis. 2022 Nov 19;9(12):ofac625.

- We found that a single dose of COVID-19 vaccine given a year after an infection strongly enhanced IgG levels and neutralizing antibody potency.
- Neutralizing antibody titers were higher in subjects with previous severe disease than mild disease and higher compared with vaccinated subjects without previous infection.
- The overall lowest neutralizing antibody titers against Omicron BA.1 suggested reduced cross-protection against this variant.
- Our data supported the importance of vaccinating both uninfected and previously infected individuals to elicit cross-variant neutralizing antibodies.

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COVID-19
Hybrid immunity

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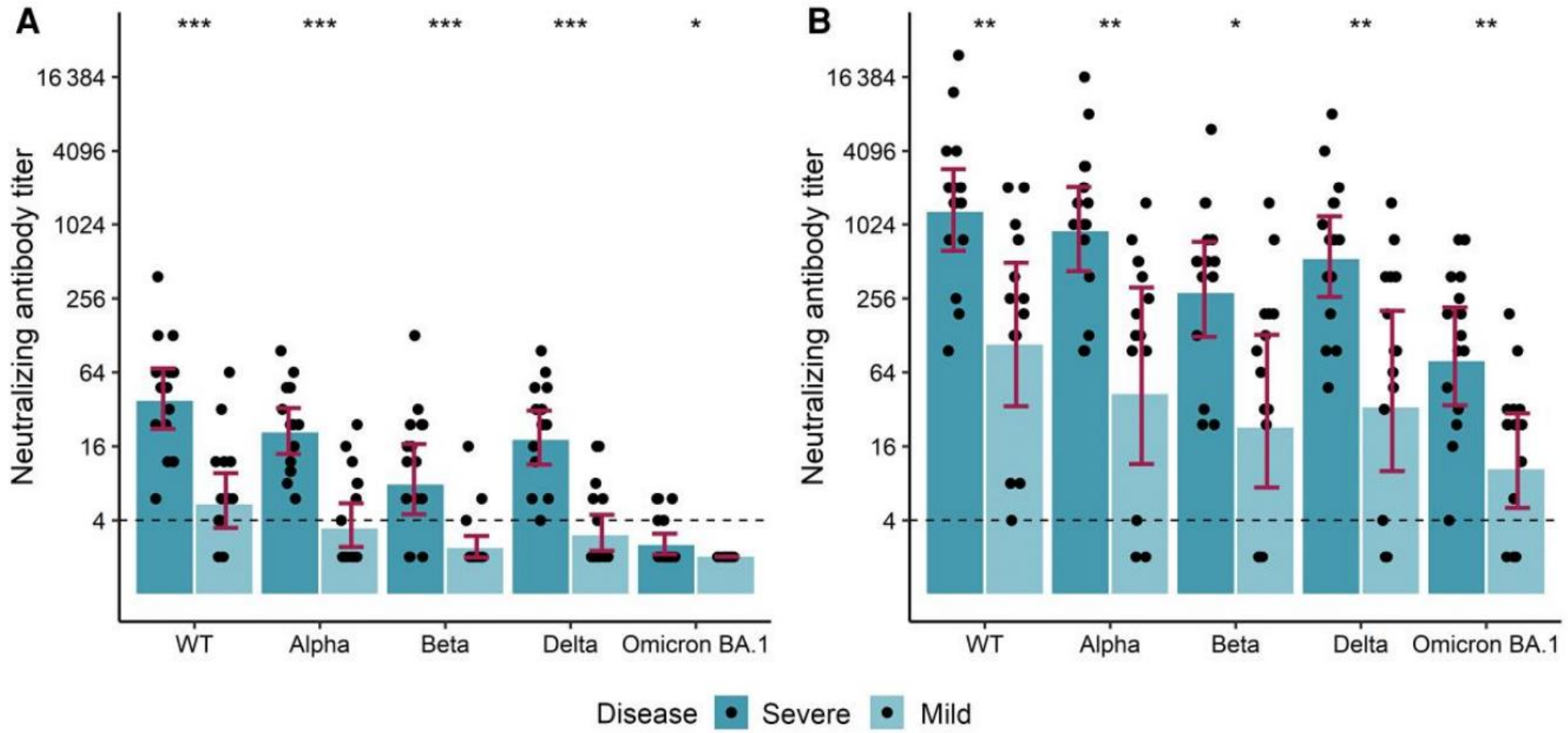

COVID-19
Hybrid immunity in immunocompromised

Ekström N, Leino TM, Juutinen A, Lehtonen T, Haveri A, Liedes O, Vara S, Salo H, Palmu AA, Nohynek H, Martelius T, Melin M. Hybrid Immunity Improves the Immune Response after the Fourth COVID-19 Vaccine Dose in Individuals with Medical Conditions Predisposing to Severe COVID-19. Vaccines (Basel). 2024 Feb 27;12(3):247.

- Fourth COVID-19 vaccine doses were, in Finland, first recommended for severely immunocompromised individuals.
- We studied antibody responses after the fourth dose and subsequent infections to define patient groups benefiting most from boosters.
- Fourth doses improved immune responses in immunocompromised individuals but remained suboptimal in those with chronic kidney disease or on immunosuppressive therapy.
- One-third of the participants became infected during the 6-month follow-up, which notably enhanced antibody levels in most immunocompromised participants.
- These findings indicated that tailored vaccination strategies are essential for high-risk groups – and that also the immunocompromised can develop robust immune responses following infection (hybrid immunity).

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COVID-19
Hybrid immunity in immunocompromised

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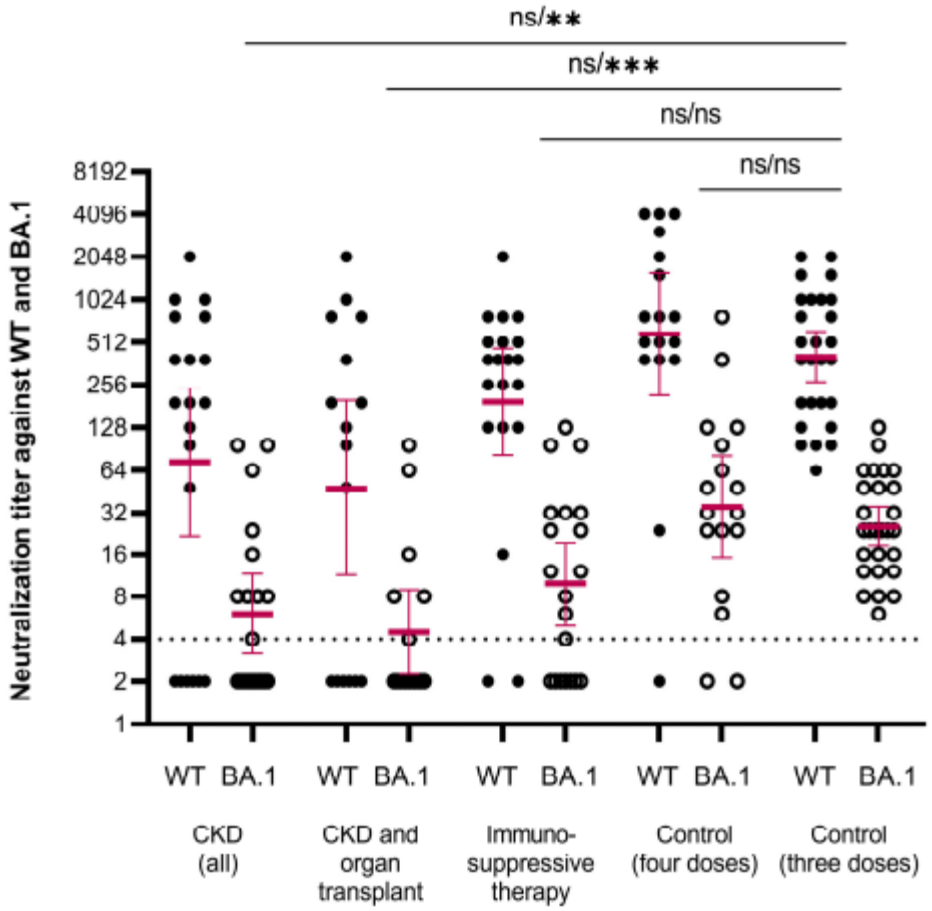

COVID-19
Hybrid immunity

Merit Melin, Maria Heikkilä, Anu Haveri, Oona Liedes, Saimi Vara, Nina Ekström, Anna Solastie, Veli-Jukka Anttila, Anu Kantele, Tea Nieminen, Hanna Välimaa, Ritva Syrjänen, Hanna Nohynek. Development of Hybrid Immunity in Healthcare Personnel Following Infections After Three COVID-19 Vaccine Doses. Poster at Vaccine Congress, Lisbon, Portugal, Sept 2024.

- In Finland, third COVID-19 vaccine doses were given at the end of 2021, starting with the elderly population and healthcare personnel. Booster doses for healthcare personnel have not been recommended since.
- We investigated the surge in infections from 2022 to 2023 within a cohort of healthcare workers that had received three COVID-19 vaccine doses.
- By the end of 2023, most of the cohort had been infected, which substantially enhanced immunity. Re-infections during the Omicron era further enhanced antibody responses, even against newer Omicron variants.
- It was projected that booster vaccines would not yield significant additional benefits for the healthy adult population throughout the fall and winter of 2023/2024.

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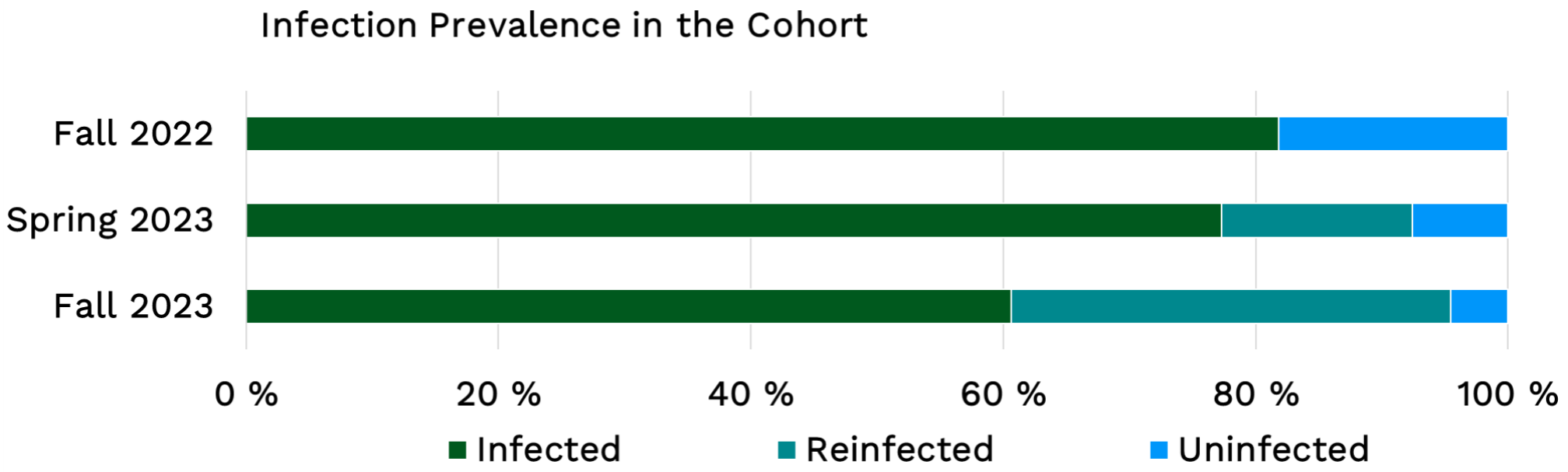

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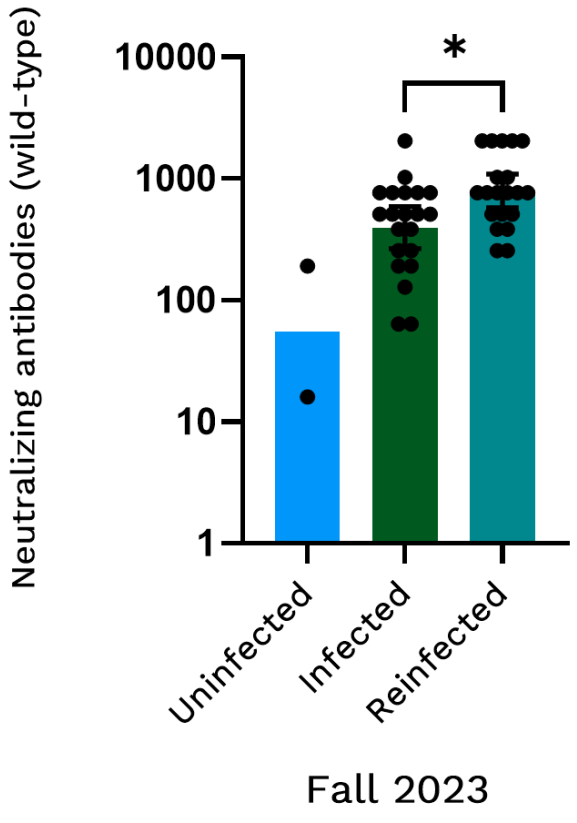

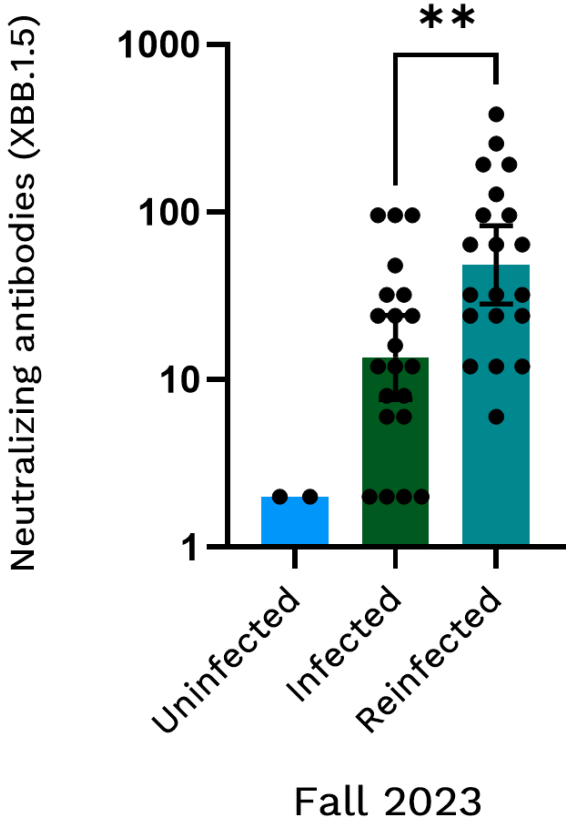

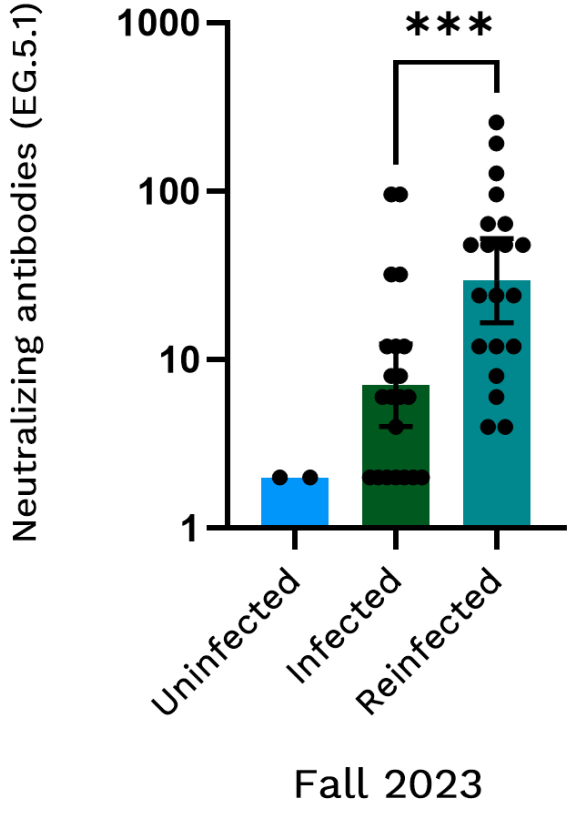

Key insights from COVID-19 serological studies for application to other vaccines and pathogens

- Reduced immune responsiveness can lead to lower immunogenicity and vaccine efficacy in elderly or immunocompromised subjects. Adjuvanted or high-dose vaccines, or more frequent booster doses needed for older adults to boost immune responses.
- Immunity derived from prior infections can combine with vaccine-induced immunity to provide robust protection. This concept is not unique to COVID-19 and has been observed with other diseases like influenza and varicella.
- Hybrid immunity may reduce the frequency of booster doses in adults for diseases where natural infection contributes to lifelong or long-term immunity – lack of natural boosting may increase the need for booster vaccinations.

Future serosurveillance options

- Serosurveillance can be used to evaluate the prevalence of infections in the population for vaccines to be considered for the adult immunisation program (e.g., RSV).
- Disease burden in the adult population can also be assessed for vaccines already included in immunization programs, particularly for evaluating the need for booster doses (e.g., pertussis).
- Immunological studies can assess both antibody- and cell-mediated immunity induced, providing insights into the duration of immunity and enabling predictions of vaccine-induced protection in target populations.
- Extensive serological studies during the COVID-19 pandemic were enabled by additional funding and academic grants. The future of serosurveillance will depend on the availability of resources.