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Main expertise (1-2 lines): Vaccine effectiveness and safety, register-based analysis





COVID-19 Vaccine Effectiveness in Risk Groups

Eero Poukka

Content

- COVID-19 vaccine effectiveness (VE) monitoring during pandemic in Finland
- Risk Groups: Why Identification Matters
- COVID-19 outcomes
- Absolute and relative risk differences



03/12/2024



COVID-19 VE monitoring – How it began

- Monitoring began in February 2021
 - First VE estimates for the elderly and risk groups
- Real-time nationwide register-based analyses



03/12/2024

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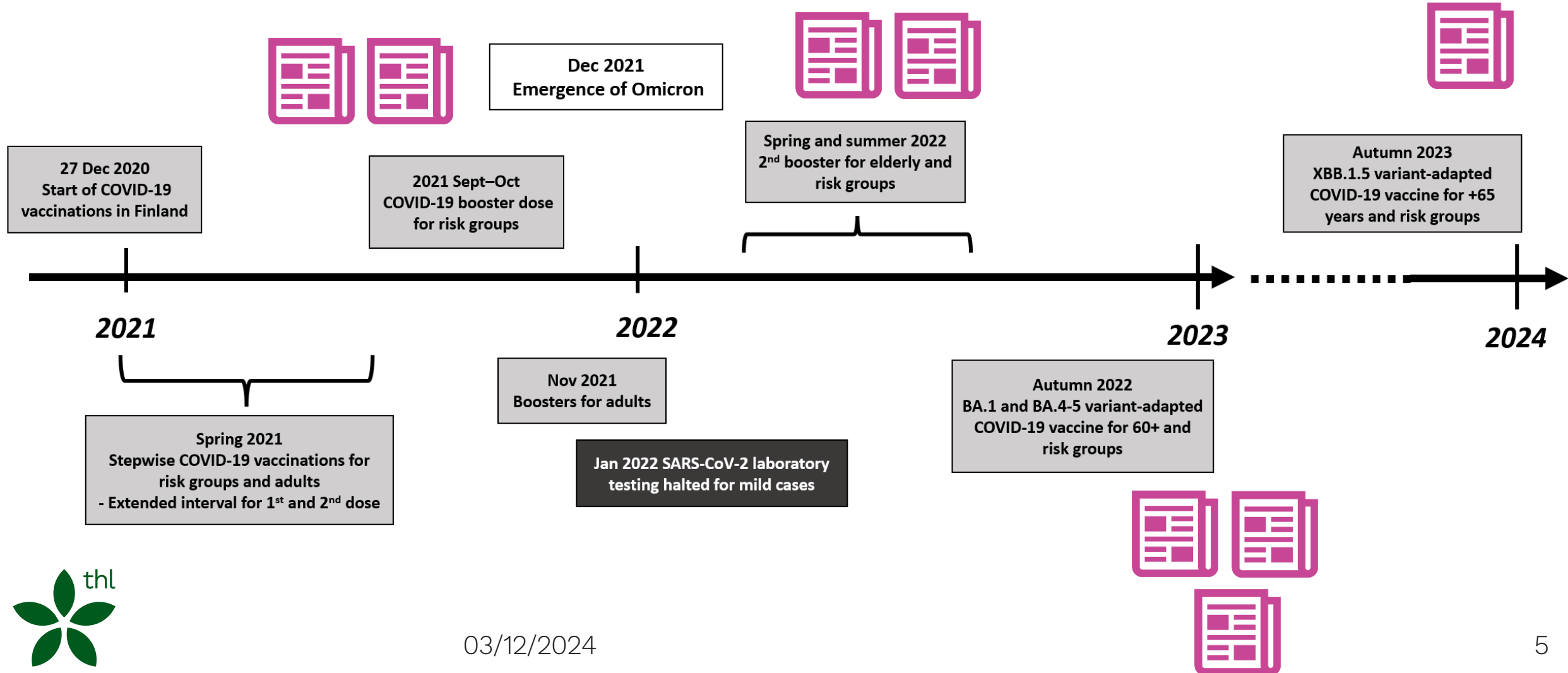
RESEARCH ARTICLE

Effectiveness of vaccination against SARS-CoV-2 infection and Covid-19 hospitalisation among Finnish elderly and chronically ill—An interim analysis of a nationwide cohort study

Ulrike Baum  , Eero Poukka  , Arto A. Palmu, Heini Salo, Toni O. Lehtonen, Tuija Leino



COVID-19 vaccination campaign for adults in Finland



Register-based COVID-19 VE studies in Finland

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RESEARCH ARTICLE

Effectiveness of vaccination against SARS-CoV-2 infection and Covid-19 hospitalisation among Finnish elderly and chronically ill—An interim analysis of a nationwide cohort study

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Short communication

Cohort study of Covid-19 vaccine effectiveness among healthcare workers in Finland, December 2020 - October 2021

Eero Poukka, Ulrike Baum, Arto A. Palmu, Toni O. Lehtonen, Heini Salo, Hanna Nohynek, Tuija Leino

High vaccine effectiveness against severe COVID-19 in the elderly in Finland before and after the emergence of Omicron

Ulrike Baum, Eero Poukka, Tuija Leino, Terhi Kilpi, Hanna Nohynek & Arto A. Palmu

BMC Infectious Diseases 22, Article number: 816 (2022) | Cite this article

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Research

Relative effectiveness of bivalent boosters against severe COVID-19 outcomes among people aged ≥ 65 years in Finland, September 2022 to August 2023

Eero Poukka, Jori Perälä, Hanna Nohynek, Sirikka Goebeler, Kari Auranen, Tuija Leino, Ulrike Baum

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Comparative effectiveness of bivalent BA.4-5 and BA.1 mRNA booster vaccines among adults aged ≥50 years in Nordic countries: nationwide cohort study

Niklas Worm Andersson, Emilia Myrup Thiesson, Ulrike Baum, Nicklas Pihlström, Jostein Starrfelt, Kristýna Faksová, Eero Poukka, Hinta Meijerink, Rickard Ljung, Anders Hviid

Comparative effectiveness of bivalent BA.4–5 or BA.1 mRNA booster vaccines among immunocompromised individuals across three Nordic countries: A nationwide cohort study

Mie Agermose Gram, Emilia Myrup Thiesson, Nicklas Pihlström, Jori Perälä, Eero Poukka, Tuija Leino, Rickard Ljung, Niklas Worm Andersson, Anders Hviid

Affiliations & Notes Article Info

ARTICLES | JANUARY 10 2024

COVID-19 Vaccine Effectiveness Among Adolescents

Eero Poukka, MD; Niklas Worm Andersson, MD; Emilia Myrup Thiesson, MSc; Ulrike Baum, PhD; Nicklas Pihlström, MSc; Jori Perälä, MSc; Anja Bråthen Kristoffersen, PhD; Hinta Meijerink, PhD; Jostein Starrfelt, PhD; Rickard Ljung, PhD; Anders Hviid, Dr, MedSci

Comparative effectiveness of heterologous third dose vaccine schedules against severe covid-19 during omicron predominance in Nordic countries: population based cohort analyses

Niklas Worm Andersson, Emilia Myrup Thiesson, Ulrike Baum, Nicklas Pihlström, Jostein Starrfelt, Kristýna Faksová, Eero Poukka, Lars Christian Lund, Christian Holm Hansen, Mia Aakjær, Jesper Kjær, Catherine Cohet, Mathijs Goossens, Morten Andersen, Jesper Hallas, Hinta Meijerink, Rickard Ljung, Anders Hviid

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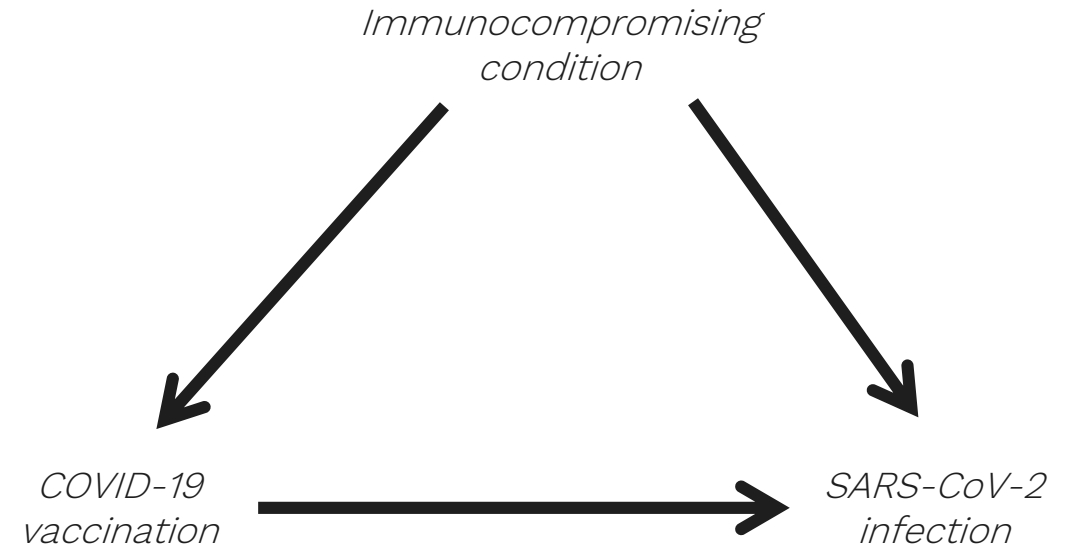
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Comparative effectiveness of monovalent XBB.1.5 containing covid-19 mRNA vaccines in Denmark, Finland, and Sweden: target trial emulation based on registry data

Niklas Worm Andersson, Emilia Myrup Thiesson, Nicklas Pihlström, Jori Perälä, Kristýna Faksová, Mie Agermose Gram, Eero Poukka, Tuija Leino, Rickard Ljung, Anders Hviid

Risk Groups: Why Identification Matters

- Special interest group
 - Low participation in RCTs
 - Waning VE – Recommendations for boosters?
- Confounding
 - Comorbidities, such as immunocompromising conditions, act as confounders in VE analyses



Identifying risk groups from registers

Risk group	Register
Elderly	Population Information System
Individuals with chronic disease	Care Register for Health Care (HILMO) Register of Primary Health Care Visits (AVO-HILMO) Special Reimbursement Register Prescription Centre
Healthcare workers (HCWs)	Registers of social welfare and healthcare professionals
Long-term care residents	Care Register for Social Care
Pregnant female	Register of Primary Health Care Visits (AVO-HILMO)*



* Data quality is suboptimal, but improvements are expected in the future

VE against laboratory-confirmed SARS-CoV-2 infection among HCWs in 2021

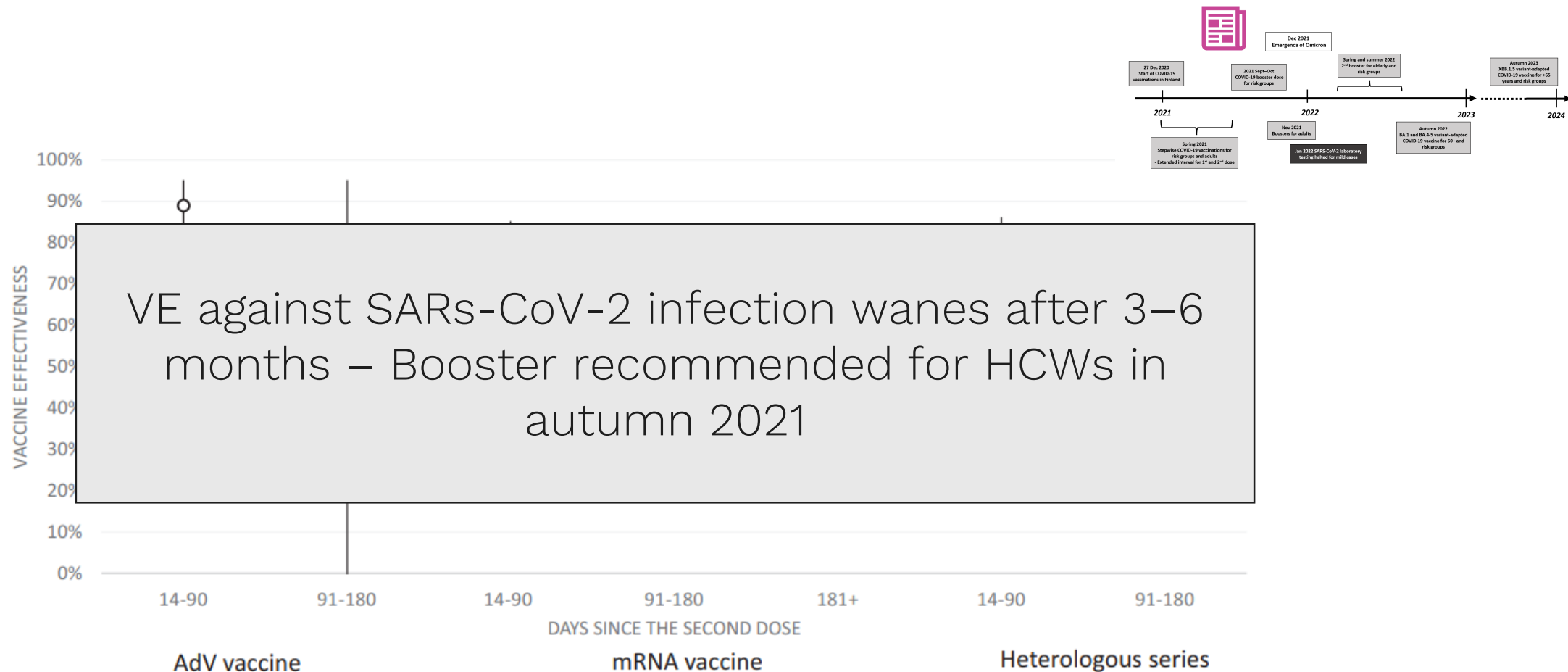
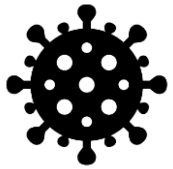


Fig. 2. Effectiveness of AdV (white), mRNA (black) and heterologous (grey) vaccine series against laboratory-confirmed SARS-CoV-2 infection among healthcare workers (N = 427 905) in Finland, 27 Dec 2020 – 26 Aug 2021. AdV = Adenovirus vector.

COVID-19 outcomes in registers



Laboratory-confirmed
SARS-CoV-2
- National Infectious Diseases
Register



Hospitalisation due to
COVID-19
- Care Register for Health Care



ICU admission due to COVID-19
- Finnish Intensive Care Consortium's
Quality Register for Intensive Care



Death due to COVID-19
- Death certificates

COVID-19 severity

Consequences of Omicron's emergence

Testing in Preomicron period

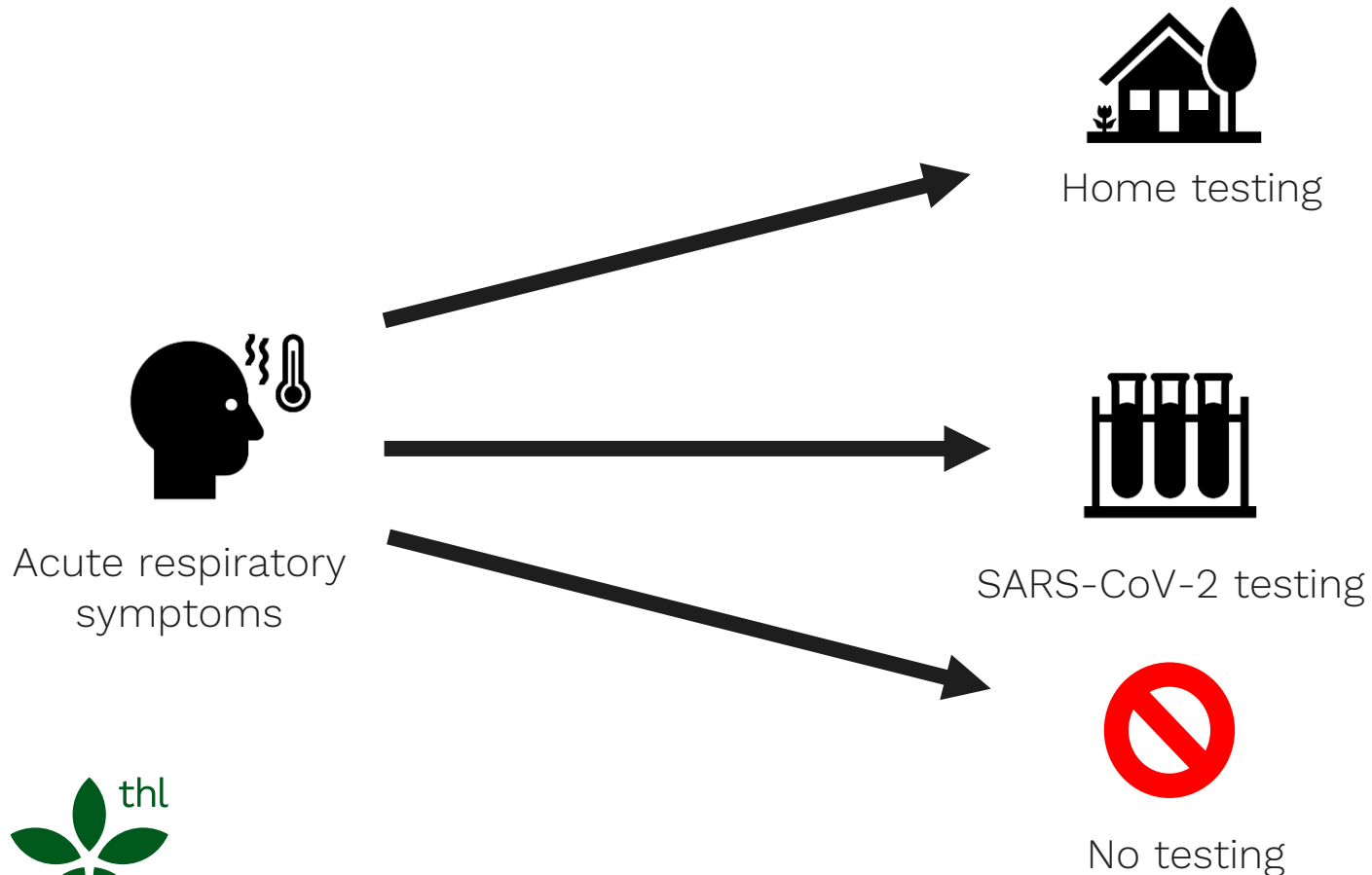


Extensive testing = Almost all
SARS-CoV-2 infections
detected

→ VE against laboratory-
confirmed SARS-CoV-2
infection accurate

Consequences of Omicron's emergence

Testing in Omicron period



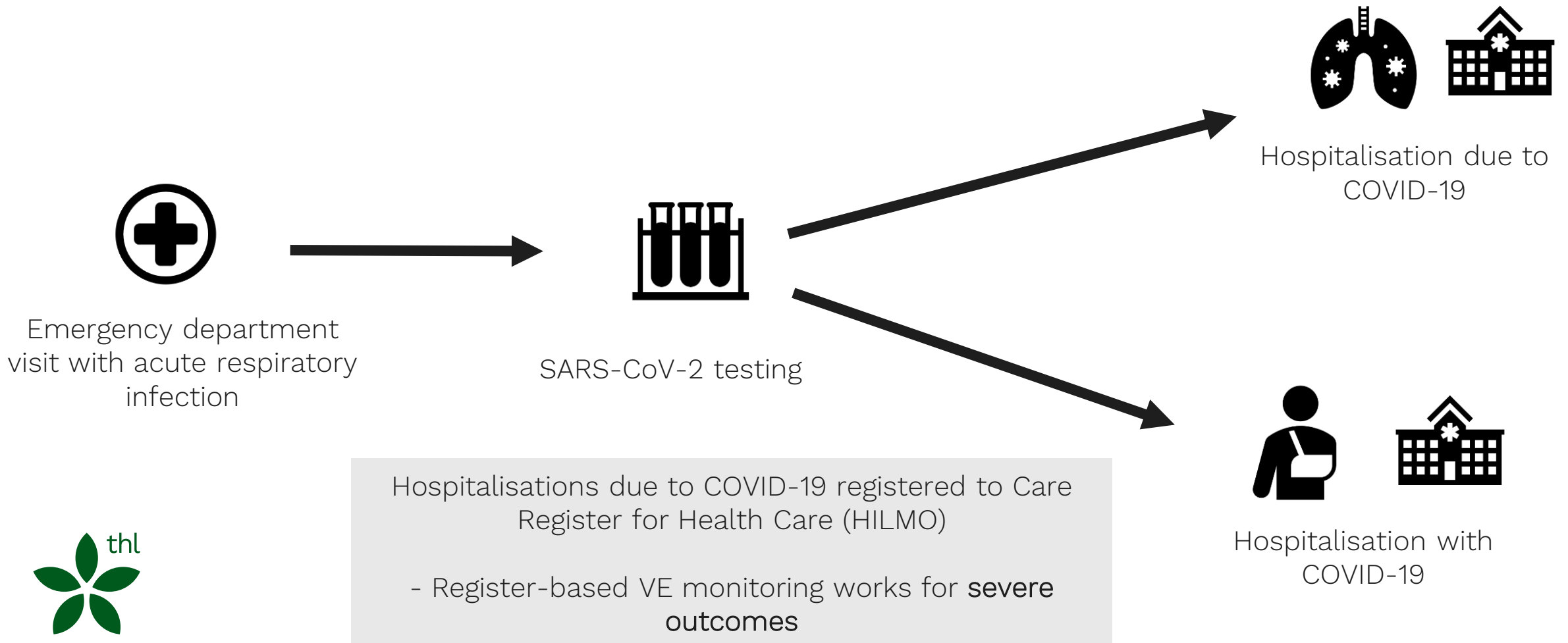
SARS-CoV-2 testing for severe cases =
Most of SARS-CoV-2 cases not detected

Consequences

- 1) VE against laboratory-confirmed SARS-CoV-2 cases challenging
 - TND superior compared to register-based cohort studies
- 2) Confounding due to recent and unregistered SARS-CoV-2 infection ("immune booster")
 - This confounding difficult to address

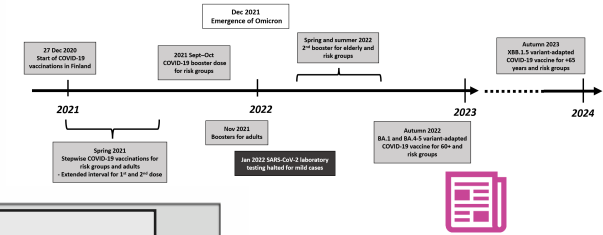
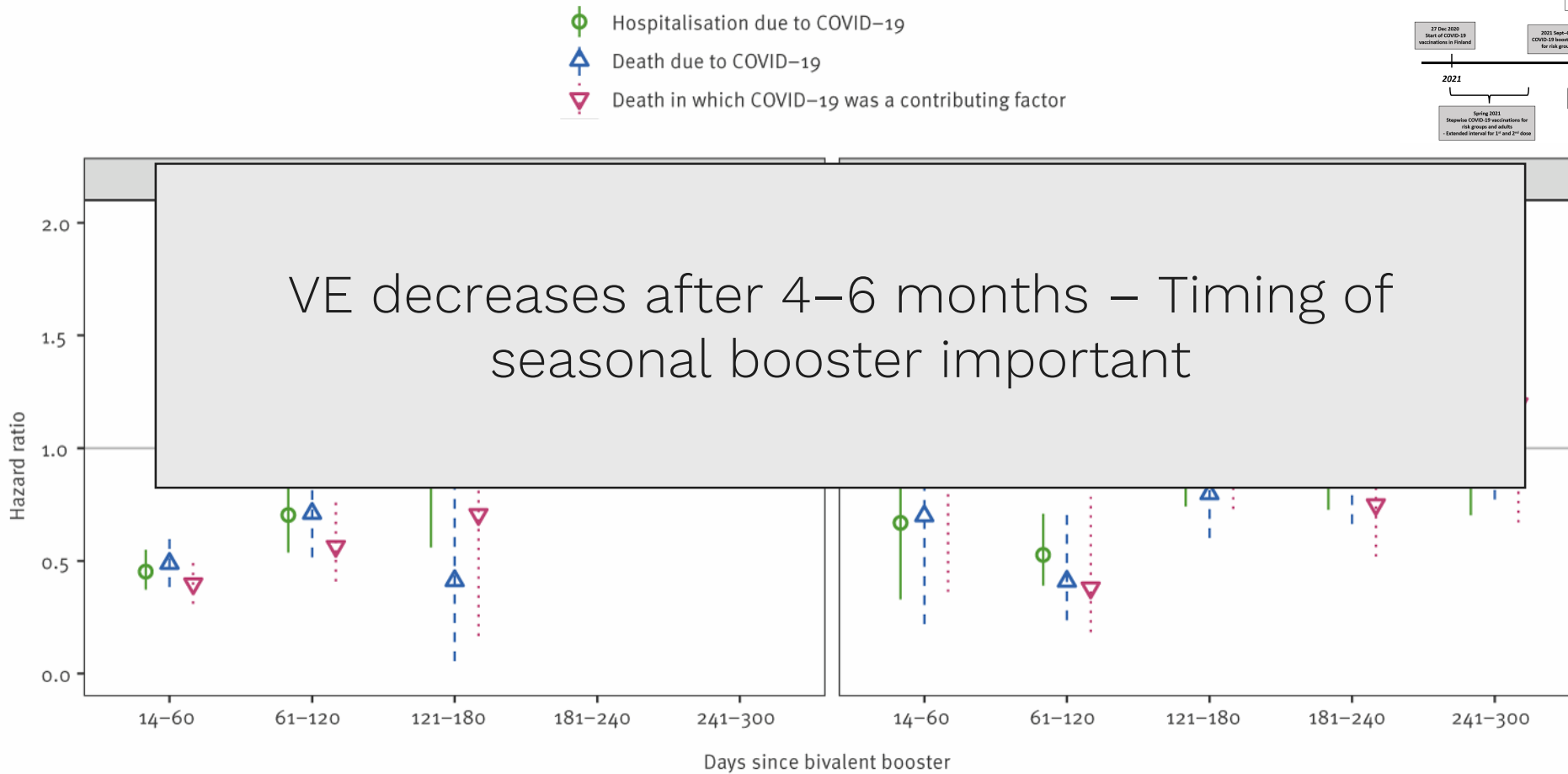
Consequences of Omicron's emergence

Hospitalisation due to vs with COVID-19 in Omicron period



VE among elderly aged 65+ years during 9/2022 – 8/2023

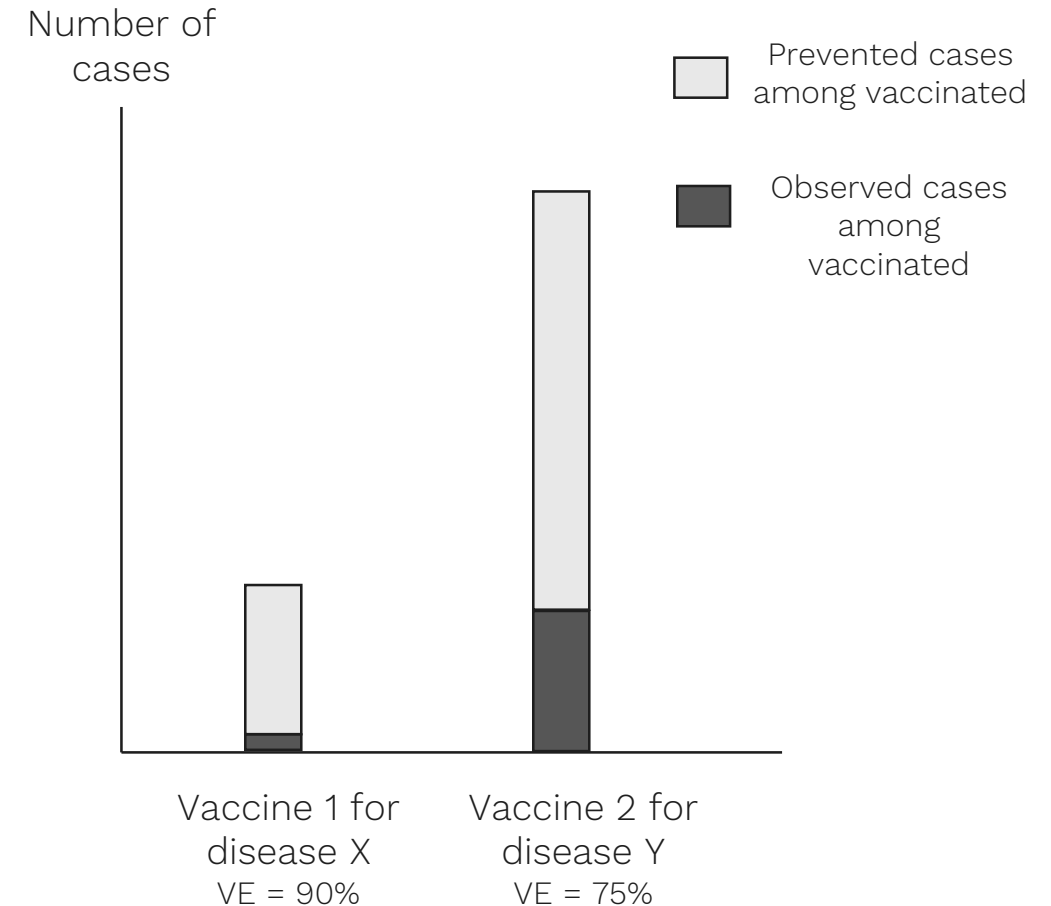
BA.4-5 or BA.1 booster vs non-booster with at least 2 COVID-19 doses



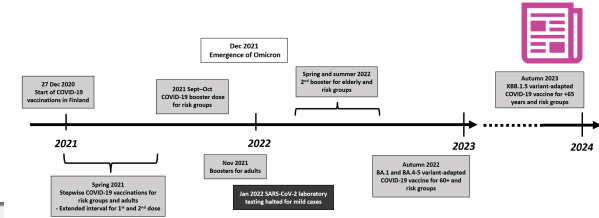
Poukka Eero, Perälä Jori, Nohynek Hanna, Goebeler Sirkka, Auranen Kari, Leino Tuija, Baum Ulrike. Relative effectiveness of bivalent boosters against severe COVID-19 outcomes among people aged ≥ 65 years in Finland, September 2022 to August 2023. Euro Surveill. 2024;29(37):pii=2300587. <https://doi.org/10.2807/1560-7917.ES.2024.29.37.2300587>

Absolute vs relative risk difference

- VE is the most commonly used measure of vaccination benefits
 - Allows for comparisons between results from different studies
- For policymaking absolute risk measures are as important
 - Which group benefits the most from the vaccination
 - Case-control and TND studies cannot measure these effects
 - Dependent on several factors like follow-up time, background incidence etc
 - Difficult to compare between studies



Absolute vs relative risk difference



NNV < 75 years of age = 1481 (95% CI 1000–2865)
 NNV ≥ 75 years of age = 400 (95% CI 267–801)

Conclusion: Vaccination for individuals aged 75 years or more offers greater benefits compared to vaccinating those under 75 years

at 24 weeks of follow-up, comparing the omicron XBB.1.5 subvariant, aged 2023 to 21 April 2024*

	Difference (95% CI) per 100 individuals	Comparative vaccine effectiveness (%; 95% CI)
Men	-190.0 (-271.6 to -108.4)	60.2 (50.5 to 70.0)
Age <75 years	-67.5 (-100.1 to -34.9)	60.3 (51.9 to 68.7)
Age ≥75 years	-249.5 (-374.3 to -124.8)	57.6 (47.8 to 67.5)

	Sweden	Denmark, Finland, and Sweden
Men	574/147 923	1443/145 927
Age <75 years	226/172 332	563/171 845
Age ≥75 years	859/152 606	2072/149 090



Comparative effectiveness of monovalent XBB.1.5 containing covid-19 mRNA vaccines in Denmark, Finland, and Sweden: target trial emulation based on registry data

Niklas Worm Andersson^{1,2}, Emilia Myrup Thiesson¹, Niklas Pihlström,^{2,3} Jori Perälä,⁴ Kristýna Faksová¹, Mie Agermose Gram,¹ Eero Poukka,^{4,5} Tuija Leino,⁴ Rickard Ljung^{1,2,3}, Anders Hviid^{1,6}

Conclusions

Strengths and limitations of COVID-19 VE monitoring in Finland

- Strengths:
 - Near real-time VE monitoring
 - Identifying risk groups
 - VE estimation within these groups
 - Confounding
 - Wide range of outcomes
 - Compatible with Nordic countries
 - Capability to estimate relative and absolute differences
- Limitations:
 - VE against mild COVID-19 difficult
 - Improving identifying selected risk groups
 - Pregnant females



Thank you!

Extra sildes



Negative control outcomes

Negative Controls

A Tool for Detecting Confounding and Bias in Observational Studies

Marc Lipsitch,^{a,b,c} Eric Tchetgen Tchetgen,^{a,c,d} and Ted Cohen^{a,c,e}

- Observational studies have possibility of residual confounding
- Negative control outcomes and exposures can detect residual confounding
 - Negative controls cannot exclude possibility of residual confounding
- Negative control outcome criteria
 - 1) Same confounders affect the association between exposure – outcome and exposure – negative control outcome
 - 2) No causal relationship between the exposure and negative control outcome
- Association between the exposure and negative control outcome could indicate residual confounding



Negative control outcome

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Supplementary Table S8. Sensitivity analysis of the risk of negative control outcomes at 24 weeks of follow-up comparing XBB.1.5-containing vaccine recipients with non-recipients aged ≥ 65 years in Denmark, Finland, and Sweden, 1 October 2023 to 21 April 2024.

	Contributing countries	Events / person-years		Risk difference (95% CI) per 100,000 individuals	Comparative vaccine effectiveness (95% CI)
		XBB.1.5-containing vaccine recipients	XBB.1.5-containing vaccine non-recipients		
Diverticular disease	DK, FI, SE	2343 / 296,055	2198 / 293,838	22.0 (-54.3 to 98.3)	-6.4 (-28.8 to 16.1)
Clavicle fracture	DK, FI, SE	186 / 313,189	200 / 310,765	-2.6 (-11.9 to 6.7)	10.0 (-17.9 to 37.9)
Lower back pain	DK, FI, SE	2045 / 299,492	1889 / 297,158	16.1 (-2.9 to 35.0)	-6.8 (-26.1 to 12.5)