BACKGROUND DOCUMENT

AIB Country Meeting

Adult Immunization in Finland: successes, lessons learned and the way forward

Helsinki, Finland
4 – 5 December 2024

Prepared by;
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Purpose of the background document

This pre-meeting background document contains a list of, AIB secretariat selected, abstracts/ references from a PubMed Medline and grey literature search on the adult immunization related topic(s) of the country meeting.

In addition, speakers from the different meeting sessions were asked to provide additional relevant and interesting references. The references are ranged by publication year (most recent first, search from earliest dates available to November 2024) and for each year in alphabetical order of the first author's name.

This document should guide you in the preparation of the meeting, it should not be considered as a complete literature review, but hopefully it will give an overview of what has been published on the topic(s) of the country meeting.

Inclusion of references in this document does not indicate that the AIB secretariat agrees with the content or correctness of the content.

Introduction

Meeting Objectives

- Review the structure of the healthcare system in Finland, focusing on how adult vaccination programs are integrated into the national vaccination plan. Analyze current policies and strategies for adult vaccination.
- Explore the integration of national healthcare registers in monitoring and evaluating vaccine coverage and effectiveness. Analyze the organization, distribution, and regulatory systems for adult vaccination at the national and regional level.
- Discuss the effectiveness of current surveillance systems in detecting and responding to vaccine-preventable diseases in adults.
- Understand the role of modeling and economic evaluations in shaping vaccine policy. Discuss how modelling studies can inform policy decisions and prioritization of vaccines.
- Address the factors influencing vaccine acceptance and strategies to increase demand among adults. Assess public attitudes and beliefs toward adult vaccination.
- Focus on existing vaccination strategies for specific population groups and the effectiveness of such programs. Discuss future directions for adult vaccination.

Intended Impact and Target Audience

AIB country meetings are organized to discuss country specific aspects of adult vaccination together with local experts. For these meetings, the AIB invites local academics, healthcare providers, public health representatives and policy makers to present on adult vaccination strategies implemented in the country, as well as educational and communicative initiatives aimed at increasing adult vaccine acceptance and coverage rates. The aim of these meetings is to establish a collaborative network of national experts of different fields, creating a platform for the exchange of knowledge and best practices in adult vaccination.

List of Abbreviations

AIB	Adult Immunization Board
CUBE	Finnish cultural, behavioural and media insights centre
VE	Vaccine effectiveness
THL	Finnish Institute for Health and Welfare
NVP	National vaccination program
KRAR (=NITAG)	National Advisory Committee on Vaccines
Kanta	Kanta Services are a set of digital services that store citizens' social welfare and health care data. This is different from the national registers.
Fimea	Finnish Medicines Agency
NVR	National Vaccination Register

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	2.2 National vaccination program in Finland	Mia Kontio
	2.3 Regulatory basis and organization of the vaccination program in Finland	Anni Virolainen-Julkunen
	2.4 Practical conducts of vaccinations in different wellbeing services counties	Kirsi Valtonen
Session 3: National registers in healthcare and their role in vaccine evaluation and monitoring	3.1 National registers including vaccination register and the national information resource plan	Jukka Jokinen
	3.2 Register-based surveillance of infectious diseases and comorbidities in Finland, present status and future	Tuija Leino
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	3.5 Vaccine safety monitoring	Petteri Hovi
	3.6 Finnish national registers in clinical trial settings	Tuomo Nieminen
Session 4: Epidemiology, Disease Burden, and Surveillance of Vaccine-Preventable Infections in Adults	4.1 Assessing the burden of Herpes zoster from the population-based, individually linkable, nationwide administrative register data	Heini Salo
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	vaccination on invasive pneumococcal disease in adults in Finland	
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Session 7: Adult Vaccination in Finland in specific situations and population groups; the way forward - panel discussion	7.1 Vaccinating risk groups against H5 avian influenza in Finland	Hanna Nohynek
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Part 2 Article references by session

Meeting title definitions

Adult immunization	Adult immunization refers to the administration of vaccines (active immunization) or antibodies (passive immunization) to individuals who are 18 years of age or older in order to protect them against various infectious diseases, before or after exposition. Source: AIB secretariat

Session 1: Opening, Introduction and Objectives

Session 1: Opening, introduction and objectives	1.1 Introduction of Adult Immunization Board	Pierre Van Damme and Paolo Bonanni
	1.2 Overview of the objectives of the meeting + Why is Finland interesting in context of adult vaccination	Arto Palmu

1.1 Introduction of Adult Immunization Board (AIB)

Potential questions/outcomes: What is the mission and objectives of the AIB? What is the operating procedure of the AIB? What is an AIB technical and country meeting? Who are the AIB advisors? How is the AIB funded?

1.1.1 AIB Technical meeting (April 2024) - Strategies for introducing and implementing vaccines for adults into National Immunization Programs in Europe: Exemplary Approaches and Key Insights (Peer-reviewed paper in preparation)

In April 2024, the Adult Immunization Board convened a technical meeting to explore the latest strategies and identify exemplary approaches regarding the implementation of vaccines for adults into Europe's National Immunization Programmes (NIPs). The meeting was built around 3 pillars: decision making for introducing a new vaccine, implementation, monitoring and evaluation. The increasing number of new and improved vaccines available in a context of competing health priorities warrants transparent and evidence-based decision-making processes for vaccine introduction. In Europe, burden of disease, vaccine efficacy or effectiveness, and safety are universally used decision-making criteria. While economic evaluations and the quality of evidence are being increasingly considered, public acceptance, equity, and operational criteria remain underutilised. Vaccine implementation requires careful planning and coordination. Implementation activities discussed during the meeting were vaccine targets, target population identification, communication, training of healthcare professionals, and the involvement of pharmacists. Once operational, NIPs are to be monitored in terms of safety, effectiveness, and impact. Implementation science and behavioural and cultural insights can be used to identify tangible interventions to improve vaccine uptake. As vaccine programmes in Europe shift towards a life-long approach, success stories and problem-solving strategies should continue to be identified and leveraged.

1.1.2 AIB Country meeting Italy (December 2023) – Bechini, A., Boccalini, S., Del Riccio, M., Pattyn, J., Hendrickx, G., Wyndham-Thomas, C., … Bonanni, P. (2024). Overview of adult immunization in Italy: Successes, lessons learned and the way forward. Human Vaccines & Immunotherapeutics

The exchange of knowledge and best practices in adult immunization are essential to improve vaccination strategies across the European region. Italy has made groundbreaking progress in the field, being one of the first countries to propose a life-course vaccination schedule, broadening the traditional focus on childhood immunization to include adults. All vaccines included in Italy's vaccination schedule are free of charge. Moreover, the country's National

Immunization Plan sets clear coverage targets, immunization priorities, and actions to reduce disparities. However, the fragmentation of its National Health System following the constitutional reform of 2001 has led to an increased complexity and regional inequalities regarding immunization. Other challenges the country faces include growing vaccine hesitancy, data gaps and underserved populations. This review describes Italy's adult immunization system, from policy to implementation. The successes, challenges and lessons learned were shared during the first Adult Immunization Board country meeting in Italy, where local experts, healthcare providers, public health representatives, and policymakers engaged in collaborative discussions and shared insights through case studies and presentations (December 2023). These insights are reviewed and discussed in this manuscript.

1.1.3 Pattyn J, Del Riccio M, Bechini A, Hendrickx G, Boccalini S, Van Damme P, Bonanni P. The Adult Immunization Board (AIB): A new platform to provide multidisciplinary guidelines for the implementation and optimization of adult immunization in Europe. Vaccine. 2024 Jan 1;42(1):1-3. doi: 10.1016/j.vaccine.2023.11.060. Epub 2023 Dec 3. PMID: 38044243.

1.1.4 Pattyn Jade, Bonanni Paolo, on behalf of the Adult Immunization Board working group. Assessing the health burden of vaccine-preventable infections in European adults: challenges and opportunities translated into action. Euro Surveill. 2023;28(48)

Abstract: Background - Accurate information on the health burden of vaccine-preventable infections (VPIs) is needed to support evidence-based vaccine policy recommendations and programs. The first technical meeting of the Adult Immunization Board (AIB) was dedicated to the assessment of health burden evidence of VPIs in European adults. Methods - The AIB technical meeting, held in Antwerp, Belgium, in April 2023, convened international experts on health burden of VPIs. Presentations by subject-matter experts and group discussions were held based on pre-defined meeting objectives, covering multiple topics on the availability and use of health burden evidence of adult VPIs in Europe. Results - Both opportunities and challenges were identified. Key points discussed included (1) the need for further harmonization of Burden of Disease (BoD) methodologies for cross-study and cross-country comparison, (2) the recognition that health burden studies require significant resources and high-quality data, and therefore improved infectious disease surveillance and collaborative efforts in Europe, (3) the important geographical differences and inequalities found at all levels of adult immunization in Europe that are to be considered when interpreting BoD results, and (4) the importance of tailored communication of VPI health burden data to each stakeholder for an effective translation into vaccine policy decisions. Conclusion - Several European initiatives promote health BoD harmonized methodologies and/or capacity building collaborations that are to be further built upon. Although VPI health burden data is available and is a key component in the evidence-based decision-making processes behind immunization strategies, data gaps remain, particularly for certain diseases and at-risk populations.

1.1.5 Adult Immunization Board website (link): www.adultimmunizationboard.org

All meeting materials (background document + slides + conclusions) are published on the AIB website. Summary meeting reports are published in peer-reviewed journals.

1.1.6 Adult Immunization Board video (link):
https://www.youtube.com/watch?v=4lbpByoI6Ow

1.2 Overview of the objectives of the meeting + Why is Finland interesting in the context of adult immunization / from the AIB perspective

Potential questions/outcomes: What are the objectives, topics of this AIB country meeting. Explain why a high amount of speakers are of the Finnish Institute for Health and Welfare (THL). Why is Finland interesting in the context of adult immunization? What has been achieved in Finland and what is the current landscape of policies and strategies regarding (adult) vaccination? What are the country's adult-specific challenges and what efforts are planned/ongoing?

Demographic and socioeconomic context in Finland, 2022

Demographic factors	Finland	EU
Population size	5 548 241	446 735 291
Share of population over age 65 (%)	23.1	21.1
Fertility rate[1] (2021)	1.5	1.5
Socioeconomic factors		
GDP per capita (EUR PPP[2])	38 679	35 219
Relative poverty rate[3] (%)	12.7	16.5
Unemployment rate (%)	6.8	6.2

1. Number of children born per woman aged 15-49. 2. Purchasing power parity (PPP) is defined as the rate of currency conversion that equalises the purchasing power of different currencies by eliminating the differences in price levels between countries. 3. Percentage of persons living with less than 60 % of median equivalised disposable income. Source: Eurostat Database.

Figure from OECD/European Observatory on Health Systems and Policies (2023), Finland: Country Health Profile 2023, State of Health in the EU, OECD Publishing, Paris/European Observatory on Health Systems and Policies, Brussels.

Session 2: Healthcare system and the adult vaccination program in Finland

Session 2: Healthcare system and the adult vaccination program in Finland	2.1 Finland: Health system summary	Ilmo Keskimäki
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2.1 Finland: Health system summary

Potential questions/outcomes: What are the key principles and objectives of the Finnish healthcare system when it comes to prevention, and how have they evolved over time? What are the key milestones or policy changes that have shaped the integration of prevention, especially immunization, within the Finnish healthcare system?

2.1.1 OECD/European Observatory on Health Systems and Policies (2023), Finland: Country Health Profile 2023, State of Health in the EU, OECD Publishing, Paris/European Observatory on Health Systems and Policies, Brussels.

This profile provides a concise and policy-focused overview of the state of health and the healthcare system in Finland, as a part of the broader series of Country Health Profiles from the State of Health in the EU initiative. It presents a succinct analysis encompassing the following key aspects: the current health status in Finland; the determinants of health, focusing on behavioural risk factors; the organization of the Finnish healthcare system; and an evaluation of the health system's effectiveness, accessibility, and resilience.

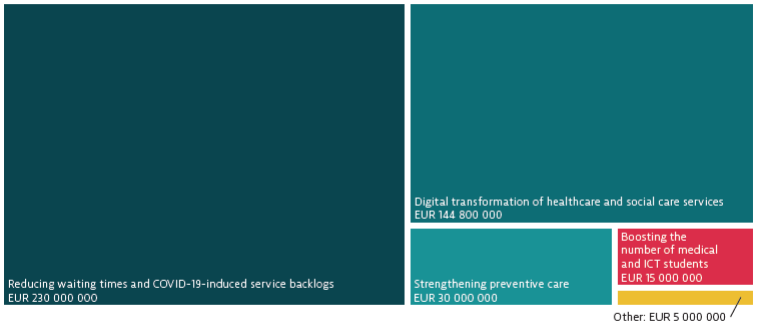
Conclusions:

- After two decades in the making, a major structural reform has led to a greater centralization and the establishment of counties as units responsible for health and social service provision in Finland from 2023.
- Since January 2023, primary and specialist healthcare and social services is organised into 21 well-being services counties (WBSCs) and the City of Helsinki.
- The reform also changes the key financing source for healthcare from municipalities to the national budget. Other financing channels have remained in place: the National Health Insurance system, which funds medicines and some other services; employers' expenditure on occupational healthcare; voluntary health insurance (VHI); and household out-of-pocket (OOP) payments
- The WBSCs will be funded based on revenue from the central government and to a smaller extent on fees collected from users. They will receive money depending on the simulated costs of service needs, the circumstances of the welfare areas, and the tasks of rescue services. The inputs for the simulations are based on the size of the population, health and social needs, language composition, and the health and well-being of the population.
- During the first two years of the pandemic, life expectancy in Finland fell only slightly, but the reduction in 2022 was much greater and the largest in over 50 years. This reduction was driven mainly by higher deaths from COVID-19, particularly among people aged over 80.
- About 35 % of all deaths in Finland in 2019 could be attributed to behavioural risk factors. Although progress has been achieved in reducing tobacco and alcohol consumption, obesity and overweight are growing public health concerns. In 2019, 20 % of adults were obese, up from 11 % in 2000, and the adult obesity rate was higher than in most EU countries. Overweight and obesity rates among adolescents in 2022 (24 %) were also higher than the EU average (21 %).
- Finland's health expenditure reached 10.3 % of GDP in 2021 – a large increase compared to 2019 due mainly to the increase in health spending during the first two years of the pandemic. Health spending as a share of GDP remained lower than the EU average in 2021 (11.0 %), however.
- In 2022, a larger proportion of the population (6.5 %) reported unmet medical care needs in Finland than the EU average (2.2 %), mostly related to waiting times.

- Shortages of health and long-term care workers are growing concerns, with employers having difficulties in recruiting many categories of staff, including general practitioners, nurses and homecare assistants. The Ministry of Social Affairs and Health launched a five-year programme in November 2021 to increase the supply of health and social care workers in response to population ageing. The main measures are to increase student intakes in health education and training programmes, review the division of roles and responsibilities between professions in health service delivery, make greater use of digital solutions, and improve working conditions to attract and retain more workers in the health and social care sector.
- Prevention expenditure accounted for about 5 % of overall health spending in 2021 – up from about 4 % before the pandemic.

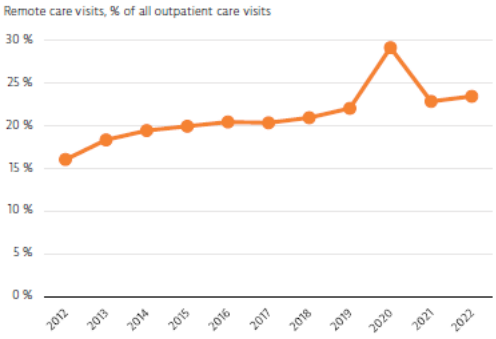
The figures below are a selection made by the AIB secretariat from: OECD/European Observatory on Health Systems and Policies (2023), Finland: Country Health Profile 2023, State of Health in the EU, OECD Publishing, Paris/European Observatory on Health Systems and Policies, Brussels.

Figure 26. Finland's Recovery and Resilience Plan prioritises addressing waiting times and digital transformation of the health system



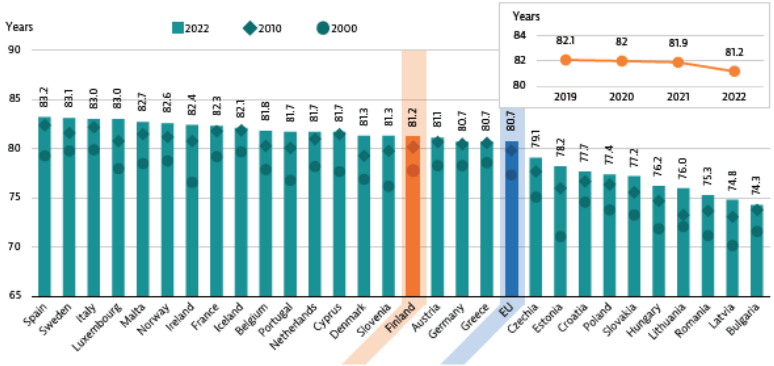
Notes: These figures refer to the original Recovery and Resilience Plan. The ongoing revision of the plan might affect its size and composition. Some elements have been grouped together to improve the chart's readability. The funding allocated to increasing the number of students in universities includes new places in medical education programmes, but also in information and communication technology (ICT) and engineering programmes.
Source: European Commission – Recovery and Resilience Scoreboard.

Figure 20. The share of outpatient teleconsultations in Finland peaked in 2020



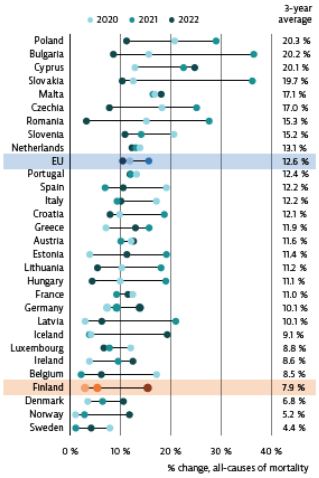
Source: Finnish Institute for Health and Welfare (2022).

Figure 1. Life expectancy in Finland was half a year higher than the EU average in 2022



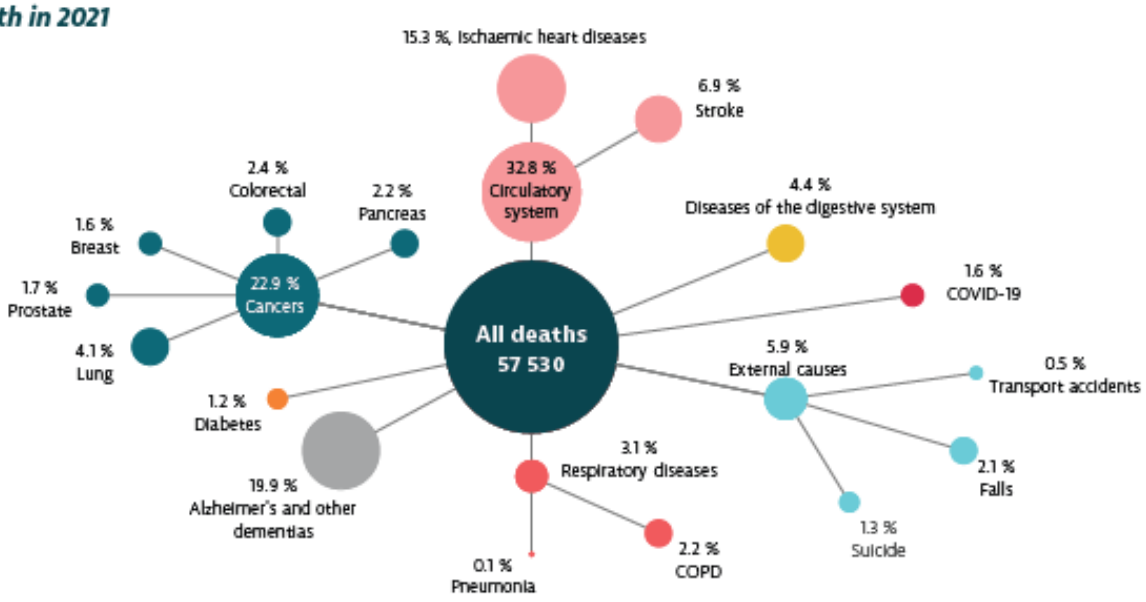
Notes: The EU average is weighted. The 2022 data are provisional estimates from Eurostat that may be different from national data and may be subject to revision. Data for Ireland refer to 2021.
Source: Eurostat Database.

Figure 3. Excess mortality in Finland was low in 2020 and 2021, but increased in 2022



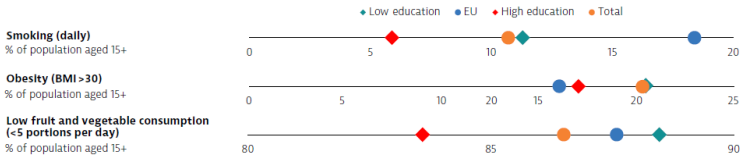
Note: Excess mortality is defined as the number of deaths from all causes above the average annual number of deaths over the previous five years before the pandemic (2015-19).
Source: OECD Health Statistics 2023, based on Eurostat data.

Figure 2. Circulatory diseases, cancer and Alzheimer and other dementias were the leading causes of death in 2021



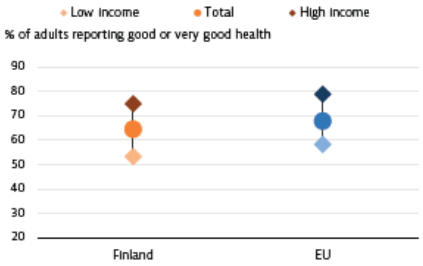
Note: COPD refers to chronic obstructive pulmonary disease.
Source: Eurostat Database (data refer to 2021).

Figure 9. People with lower education levels are more likely to smoke and be obese than the more highly educated



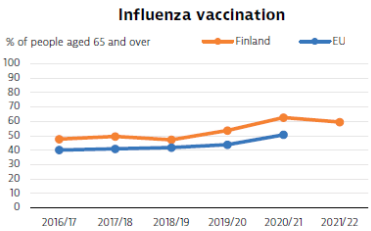
Note: Low education is defined as people who have not completed secondary education (ISCED 0-2), whereas high education is defined as people who have completed tertiary education (ISCED 5-8).
Source: Eurostat Database (based on EHIS 2019).

Figure 4. Inequalities in self-reported health by income level are large in Finland



Source: Eurostat Database, based on EU-SILC (data refer to 2022).

Figure 15. Influenza vaccination rates among older people rose substantially during the pandemic



Sources: OECD Health Statistics 2023 and Eurostat Database.

Proportion of people aged 65 and over with multiple chronic conditions

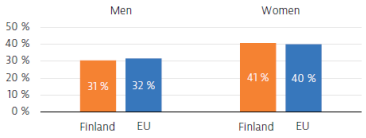
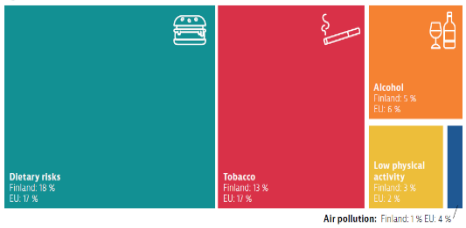
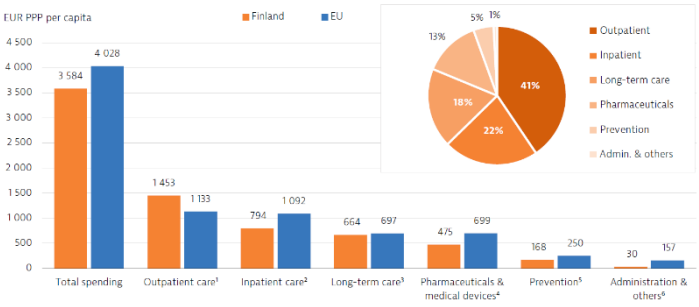


Figure 7. Over one third of deaths can be attributed to behavioural risk factors in Finland



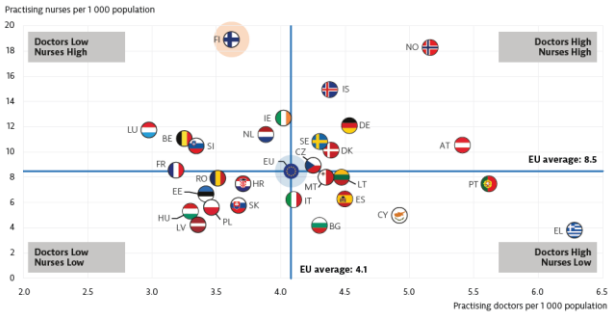
Notes: The overall number of deaths related to these risk factors is lower than the sum of each one taken individually, because the same death can be attributed to more than one risk factor. Dietary risks include 14 components, such as low fruit and vegetable intake, and high sugar-sweetened beverages consumption. Air pollution refers to exposure to $PM_{2.5}$ and ozone.
Sources: IHME (2020). Global Health Data Exchange (estimates refer to 2019).

Figure 11. Outpatient care is by far the largest health spending category in Finland



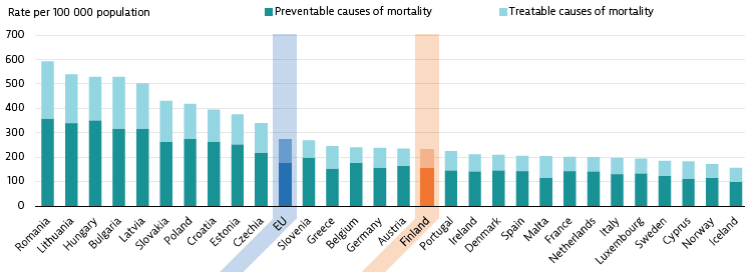
Notes: 1. Includes home care and ancillary services (e.g. patient transportation); 2. Includes curative-rehabilitative care in hospital and other settings; 3. Includes only the health component; 4. Includes only the outpatient market; 5. Includes only spending for organised prevention programmes; 6. Includes health system governance and administration and other spending. The EU average is weighted.
Sources: OECD Health Statistics 2023 (data refer to 2021).

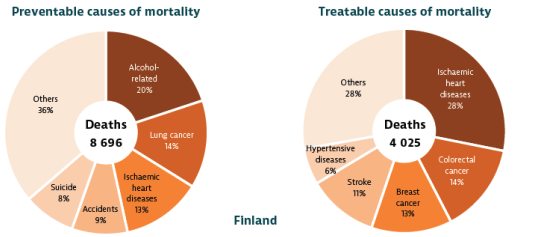
Figure 12. Finland has more nurses than other EU countries, but fewer doctors



Notes: The EU average is unweighted. The data on nurses include all categories of nurses (not only those meeting the EU Directive on the Recognition of Professional Qualifications). In Portugal and Greece, data refer to all doctors licensed to practise, resulting in a large overestimation of the number of practising doctors (e.g. of around 30 % in Portugal). In Greece, the number of nurses is underestimated as it only includes those working in hospitals.
Source: OECD Health Statistics 2023 (data refer to 2021 for most countries but to 2020 for Finland).

Figure 13. Avoidable mortality in Finland was lower than the EU average in 2020





Notes: Preventable mortality is defined as death that can be mainly avoided through public health and primary prevention interventions. Treatable (or amenable) mortality is defined as death that can be mainly avoided through healthcare interventions, including screening and treatment. Both indicators refer to premature mortality (under age 75). The lists attribute half of all deaths from some diseases (e.g. ischaemic heart disease, stroke, diabetes and hypertension) to the preventable mortality list and the other half to treatable causes, so there is no double-counting of the same death.
Source: Eurostat Database (data refer to 2020).

2.1.2 Tynkkynen LK, Keskimäki I, Karanikolos M, Litvinova Y (2023). Finland: Health system summary, 2023.

This Health system summary is based on the Finland: Health System Review published in 2019 in the Health Systems in Transition (HiT) series, and is significantly updated by the authors, including relevant reform updates highlighted by the Health Systems and Policies Monitor (HSPM) (www.hspm.org). For this edition, key data have been updated to those available in December 2022, unless otherwise stated. Health system summaries use a concise format to communicate central features of country health systems and analyse available evidence on the organization, financing and delivery of health care. They also provide insights into key reforms and the varied challenges testing the performance of the health system

2.1.3 L Tynkkynen, What a journey! – A short history of the Finnish health care and social service reform and administrative integration of health care and social services, European Journal of Public Health, Volume 33, Issue Supplement_2, October 2023, ckad160.125

Finland is a Nordic welfare state with universal access to tax-funded health care. While the health system performs relatively well when measured in terms of avoidable mortality, several measures indicate that access to care, especially primary care, is poor. There are also relatively large geographical and socioeconomic inequities in access, utilization, and quality of services. To tackle these issues, a process to reform the health system was initiated in the early 2000s. However, it was not until 2021 when the large-scale reform of the system was enacted and not until 2023 when the new structure was implemented. The process involved several different reform proposals which all shaped the outcome of the reform. The key feature in almost all the reform proposals and in the final reform plan has been fostering vertical integration in health care and horizontal integration of health and social services both at the level of administration and organization as well as through processes and patient

pathways. In this presentation we describe the history of the Finnish health & social care reform process and discuss, how integrated care as a policy idea & tool has shaped the reform agenda and reform proposals.

2.2 National vaccination program in Finland

Potential questions/outcomes: Which vaccines for adults are currently part of the national vaccination program (NVP) and for which populations? Which products are expected to be (re)evaluated (RSV? Booster TBE?) in the coming year? Are there specific catch-up programs for >18 year olds who have missed childhood/adolescent vaccinations (e.g. HPV, Varicella)? Is the life course immunization policy promoted in the NVP of Finland? What are the main differences in the national vaccination program compared to other EU-countries (TBE, HepB, Meningococcal, influenza for children etc.?)? All vaccinations in the NVP are currently voluntary? Was this always the case? Will this be the case in the future? How do the recommendations differ between COVID-19 and Influenza? Are people getting reminder letter for the Tdap vaccination?

2.2.1 Authorized vaccines for adults in Finland

Figure 1: Marketing authorization granted vaccines for adults in Finland. Data received via Fimea (Contact person: Mäenpää Tero)

<2000	Hepatitis B
	Polio
	Hepatitis A
	Varicella
	Typhoid
	Yellow fever
	Hib
	TBE
	MMR
2000-2005	Tdap
	Pneumococcal
	TB
	Cholera
2006-2010	Herpes Zoster
	HPV
	JE
	P Influenza
	Men AWCY
2011-2015	Men B
	Smallpox/ (Mpox)
2016-2020	Dengue
	Ebola
	COVID-19
2021-present	RSV
	Rabies
	Chikungunya

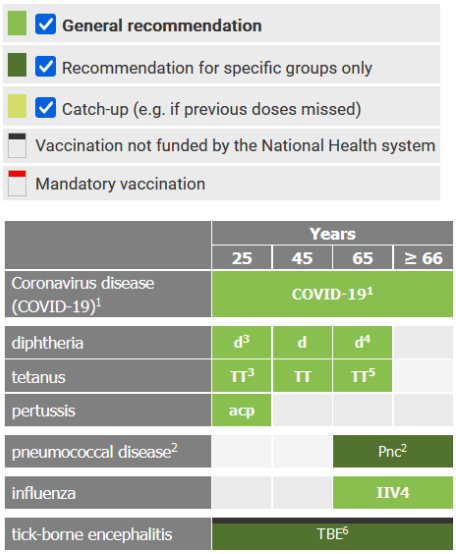
This figure shows an overview of currently available vaccines for adults in Finland approved by Fimea, the Finnish Medicines Agency. The dates of approvals can differ from implementation dates and some vaccines in the list may have been available before, but the types of these vaccines were withdrawn and replaced by new forms (e.g. rabies). Finland currently approved vaccines against >25 different infectious diseases. The national vaccination programme does not include all vaccines. Vaccines can be purchased with a doctor's prescription and then obtained from a health centre. Vaccines can also be obtained from a private health clinic, for example before travelling abroad.

2.2.2 Essential programme on Immunization

Building on the momentum of the smallpox eradication effort, the Expanded Programme on Immunization (EPI) was launched in 1974 to ensure that all children, in all countries, benefited from life-saving vaccines. This programme has evolved into what is now commonly known as the Essential Programme on Immunization. Today every country in the world has a national immunization programme and vaccines are viewed as one of the safest, most cost-effective, and successful public health interventions to prevent deaths and improve lives. Since the initial focus on protection against six childhood vaccine-preventable diseases (Bacillus Calmette-Guérin (BCG), diphtheria, pertussis, tetanus, polio, and measles) over four decades ago, the addition of new vaccines has increased the breadth of protection

provided by immunization, to include vaccinations for protection of older children, adolescents and adults. There are now 13 vaccines (antigens) recommended by WHO for the EPI programme. They are: Bacillus Calmette-Guérin (BCG), diphtheria, pertussis, tetanus, Haemophilus influenzae type B (Hib), Hepatitis B (HepB), polio, measles, rubella, pneumococcal disease (PNC), rotavirus (Rota), human papillomavirus (HPV), and COVID-19 (for adults). Committed to its goal of universal access to all relevant vaccines for all at risk, EPI continues to work in synergy with other public health programmes to control infectious diseases and achieve better health for all populations everywhere.

2.2.3 The national vaccination program, ECDC Vaccine schedule. (Last update 15-01-2024 Vaccination Programme)



1. for updated information refer to https://thl.fi/fi/web/infektiotaudit-ja-rokotukset/rokotteet-a-o/koronavirusrokotteet-eli-covid-19-rokotteet-ohjeita-ammattilaisille
2. for more information on pneumococcal vaccination and target groups refer to https://thl.fi/fi/web/infektiotaudit-ja-rokotukset/rokotteet-a-o/pneumokokkirokotteet
3. Thereafter Td booster every 10 years with or without vaccination against poliomyelitis (IPV) in case of travel to endemic areas and when previous IPV dose was given more than 5 years before
4. Then every 10 years.
5. Then every 10 years.
6. TBE for to those living permanently on island of Åland

info outdated: more already included in the NVP

The goal of the national vaccination programme is to protect Finnish citizens as well as possible from diseases that are preventable through vaccination. The national vaccination programme only uses vaccines that have a marketing authorisation, and the vaccinations are voluntary and free of charge. The vaccines within the vaccination programme are funded from the state budget.

2.2.4 THL website: Vaccination programme for children and adults https://thl.fi/en/topics/infectious-diseases-and-vaccinations/information-about-vaccinations/vaccination-programme-for-children-and-adults

The aim of the national vaccination programme (NVP) is to provide the best possible protection for the Finnish population against vaccine-preventable diseases. The NVP started to take shape in the late 1950s when well-baby clinics covered almost the whole country. Vaccinations are free-of-charge and voluntary.

When a new vaccine is considered for inclusion into the NVP in Finland the following topics are evaluated:

- The expected public health benefit
- The safety of the vaccine for an individual and the safety of the vaccination programme at the population level

- The cost-effectiveness of the vaccination programme
    - An economic evaluation is needed to support the decision-making process. The decision-makers have not specified an explicit range of cost-effectiveness threshold values below which an intervention would automatically be accepted and lead to funding.

The vaccination programme is affected by:

- changes in the incidence of infectious diseases preventable by vaccinations
- protection provided by vaccines and changes in the effectiveness of protection
- vaccine development, changes in vaccines and new vaccines
- changes in the severity of the disease, related secondary diseases and long-term adverse effects
- changes in risk groups
- adverse effects after vaccinations.

Vaccines are scheduled in a manner that enables achieving adequate protection at the right time with minimum vaccine doses and adverse effects.

Vaccines <u>for adults</u> included in the national vaccination programme

1) COVID-19 (not included in the NVP -> endemic vaccine)
2) Td(ap)
    a. Diphtheria, tetanus and pertussis vaccine, or Tdap vaccine, for adolescents and adults
    b. Diphtheria and tetanus vaccine, or dT vaccine, for adults
3) Pneumococcal vaccines
4) Influenza vaccine
5) TBE vaccine
6) Polio vaccine
7) Mpox (not included in the NVP -> endemic vaccines)
8) MMR and varicella vaccine
9) Hib vaccine
10) Hepatitis vaccines
11) Meningococcal vaccines

<u>1) COVID-19:</u>

- Vaccine group:
    - This autumn, the booster dose is recommended to the following groups:
        - elderly residents of care homes or elderly clients who use home care services regularly;
        - persons aged 75 and over; and
        - persons of all ages with severe immunodeficiency.
        - The vaccine should also be offered to all persons aged 65 and over and all persons aged 18 and over with any condition that increases the risk of severe COVID-19
    - It is recommended that the vaccination should first be offered to the elderly residents of care homes and elderly clients who use home care services regularly, all persons aged 80 and over and all persons with severe immunodeficiency. It is also recommended that persons aged 75–79 should be vaccinated earlier than in previous autumns.

  - Persons aged 65 and above and persons aged 18 and above who are in a risk group can be vaccinated against the coronavirus later when the influenza vaccine is offered.

  - Going forward, the recommended basic series of COVID-19 vaccines is:
    - For persons aged 18 and over and for persons aged 12 and over who are in a risk group: one dose of the COVID-19 vaccine instead of the previous three doses.
    - For persons with severe immunodeficiency: two doses.
    - For persons who have received a stem cell transplant: 2–3 doses based on the individual's situation.

- Vaccines: Finland has received Comirnaty vaccines (Pfizer), which have been updated to target the JN.1 variant of the coronavirus as recommended by the European Medicines Agency EMA. The administration of COVID-19 vaccines is recommended to start in September.

2) Td(ap):

- Vaccine group:
  - Adults must personally make sure that they have received at least three tetanus, diphtheria and polio vaccines as a primary series. The tetanus, diphtheria and pertussis vaccinations given during childhood and youth are boosted in adulthood.
  - A Tdap vaccine should be administered to recipients aged 25 years
  - A Td vaccine booster is administered at the ages of 45 and 65 years, and subsequently every 10 years
  - DTaP vaccine must be given every five years to those continuously working with children aged under 12 months in social and healthcare units.
  - Since 2015, the Tdap vaccine has been offered to those starting their military service if more than 5 years have elapsed since their most recent Td or Tdap vaccination.
  - In case of an accident, the patient's vaccination protection can be boosted with the dT vaccine if necessary. For the immunisation of school-age children, the DTaP vaccine should be used.
  - The Tdap vaccine can also be administered to other adults when they need to be protected against not only tetanus and diphtheria but also whooping cough. In this case, the person receiving the vaccination will pay for the vaccine
- Vaccines: diTekiBooster (25 yrs.), diTeBooster (other age groups) - AJ Vaccines A/S

3) Pneumococcal disease:

- Vaccine group:
  - Some underlying medical conditions increase the risk of developing severe pneumococcal disease. This is why people in risk groups get the pneumococcal vaccine as part of the national vaccination programme. These risk groups are:
    - All stem cell transplant recipients
    - under 75-year-olds with severe kidney disease
    - under 75-year-olds with severe immunodeficiency

        - 65–84-year-olds who have asthma or chronic obstructive pulmonary disease.
- Vaccines: PCV13 (Prevenar 13, Pfizer) and PPV23 (Pneumovax 23, MSD)

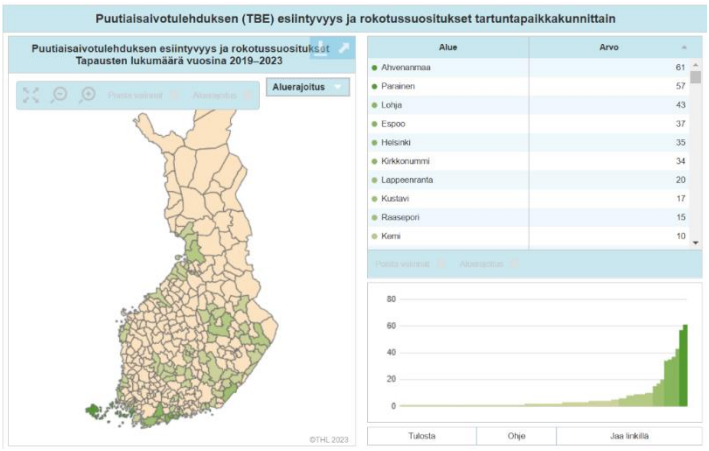
4) Influenza:

- Vaccine group:
    - all persons aged 65 and above
    - children aged under 7
    - those who are pregnant
    - those in risk groups because of their illness or treatment
    - men/women starting their (voluntary) military service
    - social welfare, health care and pharmaceutical service personnel who participate in the immediate care or maintenance of patients and clients
    - the close family and friends of people at especially high risk of severe influenza.
    - Persons who live or stay for long periods in institutional conditions, including prisons and reception centres, are also entitled to a free vaccination.
- Vaccines: The 2024–2025 influenza season uses the injectable VaxigripTetra (Sanofi Pasteur) vaccine for all age groups. Fluad Tetra vaccine (Seqirus) containing the M59 adjuvant is offered to people aged 85 and above and people aged 50 and above with severe immunodeficiency. This vaccine is likely to provide them with somewhat better and longer-lasting protection than the VaxigripTetra vaccine, which does not contain an adjuvant. For children aged 2–6, the Fluenz nasal spray vaccine is also available. The administration of influenza vaccines is recommended to start in October, which is earlier than in previous autumns.
- Vaccination coverage 2023-2024: According to the vaccination register, the influenza vaccination coverage was 30% in the entire population of Finland on 9 February 2024. The coverage varied somewhat in different age groups: it was 41% for children aged under 2 years, 29% for children between the ages of 2 and 6, 8% for school-aged children (7–17 years old), 22% for the working-age population (18–64 years), 60% for people aged 65–79, and 66% for people aged 80 and older.
- Vaccination effectiveness: Once a sufficient number of laboratory-confirmed influenza cases have been found, preliminary calculations of the effectiveness of vaccines can be made by combining register data. According to the data, the effectiveness of the influenza vaccines in use in season 2023-2024 against laboratory-confirmed influenza in people aged 65 or over is fairly good, 54%. This age group comprises approximately 1.3 million people. In children aged under 7 years, the effectiveness is also fairly good, 45%. There are around 300,000 of them. In influenza cases that led to hospitalization, the effectiveness of vaccines was slightly lower: 41% of those aged 65 or over, and slightly higher for those under 7, 63%.

5) TBE:

- Vaccine group: The national vaccination programme offers a free vaccine to persons aged 3 years and over who have a municipality of residence in Finland and who have a permanent home or a holiday house in (only those who are planning to spend time in nature for at least 4 weeks in summer need the vaccine):
    - Southern districts of Kemi
    - Simo
    - Kotka Archipelago

  - Sammonlahti district in Lappeenranta
  - Preiskari island off Raahe
  - Parainen
  - Lohjanjärvi archipelago area
  - Kustavi
  - Luoma region of Kirkkonummi
  - In parts of the Sipoo Archipelago
  - Those permanently resident in the Åland Islands are also entitled to a free vaccine.
- A person who has not been previously vaccinated is entitled to three free doses. A person whose primary vaccination series has not been completed also receives the booster vaccinations free of charge as part of the national programme.
- Booster doses: Administration of the first booster dose after three years is recommended. Subsequently, boosters are administered as follows if exposure to the TBE virus continues:
  - to those who received the booster when aged under 50, the next booster dose is given after 10 years
  - to those who received the booster when aged 50 to 60, boosters are given every 5 years
  - to those who received the booster when aged over 60, the next booster doses are given every 3 years
  - to persons with weakened immune system due to treatment or an illness, a booster dose should be administered every 3 years.
  - Boosters for those who have received the series of three doses are not currently included in the national vaccination programme.
- <u>Vaccines:</u> TicoVac (Pfizer) or Encepur (Bavarian Nordic A/S)



https://www.thl.fi/ttr/gen/atlas/html/atlas.html?show=tbe_riskienarviointi

<u>6) Polio:</u>

  - <u>Vaccine groups</u>
    - The IPV polio vaccine (2 doses) is administered to adults who are protected against diphtheria and tetanus but who have insufficient or no protection against polio
    - Boosters are not normally needed after the primary series. In some unique cases polio is given as a booster for persons
      - travelling to countries where polio occurs

        - for persons arriving in Finland after staying over four weeks in a country where polio occurs
    - Vaccine: Imovax Polio

7) MMR:

    - Vaccine groups:
        - All children and adults must have immunity against measles, mumps and rubella, either through having had the disease or protection provided by MMR vaccinations.
        - The MMR vaccine should be administered if a person is not fully protected against one of these diseases. The vaccine is part of the national vaccination programme and free for everyone.
        - It is particularly important to ensure that the following groups have protection against the MMR diseases:
            - healthcare personnel
            - foreign students
            - immigrant children and adolescents
            - those born in Finland between 1965 and 1975.
        - If a person has not had the MMR diseases or received two doses of the MMR vaccine, their protection should be complemented. If the situation is unclear, the vaccine is administered.
    - Vaccines: Priorix (GSK) and M-M-RVAXPRO (Merck Sharp & Dohme B.V.)

8) Mpox:

    - Vaccine groups: A vaccine is offered to:
        - people who have been exposed
        - people in close personal contact with a person who has been diagnosed with the virus and those at high risk of infection.
        - It is recommended that those at risk, who do not have the protection provided by having had the disease or having had two vaccine doses, still be vaccinated to prevent infections. Risk groups include:
            - Men who have sex with men and who have had several occasional sexual partners during past six months
            - Men who use HIV preventive PrEP medication and have sex with men
            - Men who are awaiting PrEP treatment and have sex with men
    - Vaccines: Imvanex (Bavarian Nordic A/S)

9) Hib vaccine

    - Vaccine groups:
        - National vaccination program
            - Stem cell transplant recipients are the only medical special group who receive a free Hib vaccine. In their case, it is included in the primary series of vaccinations administered as DTaP-IPV-Hib vaccine (5-in-1).
        - Risk groups not included in national vaccination program but recommended. The vaccines for people in these groups are paid for by either the treatment provider or the recipient.

- splenectomy patients or those with abnormal spleen function
- organ transplant patients
- patients using complement activation inhibitors, eculizumab

- Vaccines: Act-HIB (Sanofi Pasteur)

10) Hepatitis vaccines

- Vaccine groups
  - Serious infections caused by hepatitis are rare in Finland, which is why vaccines against it are not included in the national vaccination programme for children, unlike in some other EU/EEA countries. On the other hand, vaccines are offered in a targeted manner for a variety of reasons to persons belonging to high-risk groups.
  - Hepatitis B vaccines are offered in the national programme to those belonging to certain at-risk groups.
    - haemophiliacs receiving regular treatment
    - intravenous drug users
    - persons close to intravenous drug users, including family members, sexual partners and housemates
    - men who have sex with men
    - newborn children and sexual partners of, and those living in the same household with, persons with a hepatitis B infection and asymptomatic HBsAg positive persons
    - sex workers
    - students exposed to infection risk during internships
    - persons at risk of hepatitis B infection resulting from a needlestick injury or other blood exposure and who have been exposed in environments other than the workplace
    - children aged under 5 years at a day care centre when a child in the group is known to be HBsAg positive
    - newborn infants when at least one of the parents comes from a country where hepatitis B is common
    - newborn infants of mothers with a hepatitis C infection.
  - Hepatitis A vaccines are offered in the national program to those belonging to certain at-risk groups:
    - haemophiliacs receiving regular treatment
    - intravenous drug users
    - persons close to intravenous drug users, including family members, sexual partners and housemates
    - men who have sex with men
  - Occupational healthcare services vaccinate those who are exposed to hepatitis A or B infections at work.
  - Travellers may also need hepatitis vaccines. They can ask for a prescription and purchase the vaccine in a pharmacy.
- Vaccines: Hepatitis A → Havrix 1440 ELISA U/ml (GSK) and hepatitis B → HBVAXPRO (Merck Sharp & Dohme B.V.)

11) Meningococcal vaccines

- Vaccine groups Serious infections caused by meningococcus are rare in Finland, which is why vaccines against it are not included in the national vaccination programme for children, unlike in some other EU/EEA countries. On the other hand, vaccines are offered in a targeted manner for a variety of reasons to persons belonging to high-risk groups.

  1/ Vaccination AWCY and B of medical risk groups:
  - a complement deficiency (C3, C5-C9, properdin, factor D, factor H)
  - ekulizumab (Soliris) or ravulizumab (Ultomiris) medication to prevent complement activation.
  - spleen deficiency
  - spleen failure, including patients with sickle-cell anaemia and patients with chronic graft-versus-host disease following stem cell transplantation

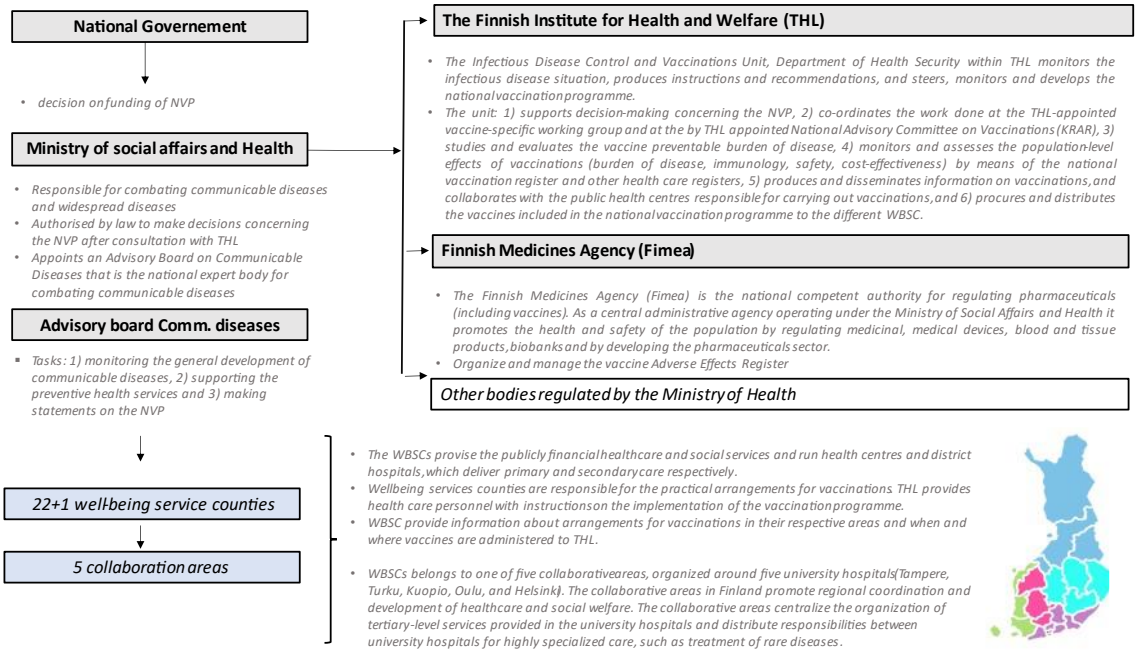
Men ACWY vaccines may be administered as a booster dose to previously vaccinated persons aged 12 months or over who have previously been vaccinated with the either the same or a different kind of meningococcal conjugate vaccine or meningococcal polysaccharide vaccine. For patients who have had their spleen removed or who have a complement deficiency or sickle-cell anaemia, booster doses are recommended every five years. The protection afforded by Meningococcus ACWY vaccines against the serogroup A disease may be of short duration. Therefore, the administering of booster doses can be considered earlier if the risk of exposure to group A meningococcus is particularly high and more than three years have elapsed since the previous dose. MenB vaccines Bexsero and Trumenba vaccines are not interchangeable.

2/ Vaccinations of close contacts
3/ Vaccination of conscripts starting their military service
4/ Vaccinations for tourists and travellers A normal tourist usually does not need meningococcal vaccinations. However, vaccines may be recommended to some tourists or other travellers on the basis of an individual risk assessment. The vaccines are paid for by the traveller themselves or by their employer.

- Vaccines: meningococcus ACWY (Nimenrix, Pfizer) and meningococcus B (Bexsero, GSK).

2.3 Regulatory basis and organization of vaccination program in Finland

Potential questions/outcomes: What regulatory basis exist and how is vaccination organized in Finland (focus on Adult Immunization). What new directions does the program plan to take for the future? What was the experience of Finland with the COVID-19 EU joint procurement programme



2.3.1 PhD Heini Salo – Introduction Economic evaluations in adopting new vaccines in the Finnish national vaccination programme

Decision-making

When the need for an evaluation is acknowledged, for example, because a new vaccine is coming into the market or there is a potential change in the benefit-risk ratio of the vaccination programme (e.g. change in disease incidence, vaccine effectiveness or safety), a vaccine-specific working group is established by THL (different from the KRAR). The working group is composed of national experts on vaccines and vaccinations, infectious diseases, epidemiology and health economics. It may also consult individual experts or pharmaceutical companies if needed. The working group carefully evaluates the potential vaccination programme according to four criteria given by :

1. expected public health benefit
2. safety of vaccine for an individual
3. safety of the vaccination programme at the population level
4. cost effectiveness

To be able to determine the expected public health benefit, the working group needs data on the burden of disease in Finland, the efficacy of the vaccine in the target group and the effect of vaccinations on the whole population. The incidence of the infectious disease, mortality, life years lost and the use of health care services are estimated from health care registers. Also, health-related quality-of-life losses due to the disease are estimated. To evaluate the direct and indirect effect of vaccinations on the population, a dynamic transmission model of the disease is required. The effectiveness among the vaccinated and unvaccinated (potential indirect effects) population is evaluated separately.

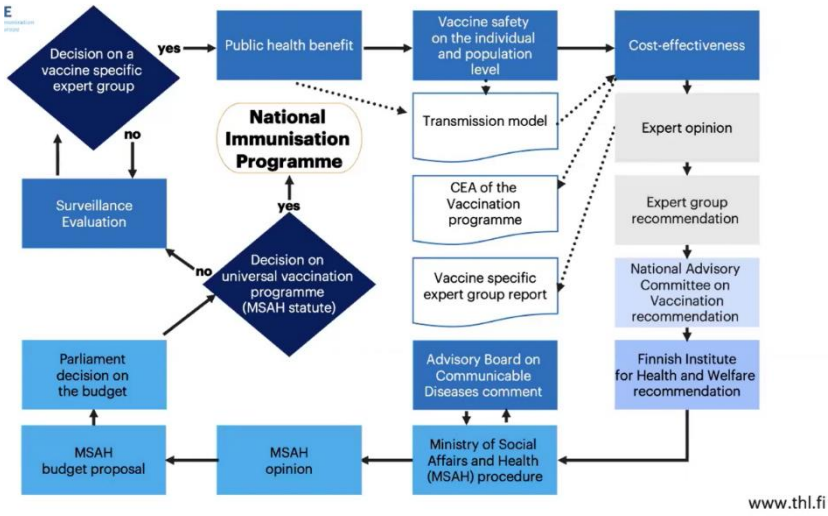
In some cases, the expected public health benefit can be considerable only in a sub-population with a higher risk of disease than the general population. For example, individuals with certain medical conditions have a higher risk of complications associated with influenza and people living in some geographical areas are more likely to contract tick-borne encephalitis than the population in general.

The safety of the vaccine for an individual and the safety of the vaccination programme at the population level are evaluated. The population-level safety of a vaccination programme may be jeopardized through indirect effects of vaccinations (e.g. shift of disease to older age groups or replacement of the eliminated microbe by another capable of causing disease). These potential indirect effects in the population can be investigated using dynamic transmission models.

For a new vaccine to be accepted into the NVP it must have been assessed to be cost effective. Yet, the decision-makers have not specified an explicit range of threshold values in Finland for a cost per QALY gained what should be considered cost-effective. This may jeopardize the transparency of decision-making. The cost-effectiveness analyses are done in the Department of Health Security at THL. In order to maintain the independence of the analyses, they have been financed by the State Budget. The cost-effectiveness analyses can be done from the health care provider perspective and from the societal perspective, if deemed helpful to the decision-making. The effectiveness of the vaccination programme is measured both in life years gained (LYGs) and quality-adjusted life years (QALYs) gained.

A Working Group recommendation is presented to the National Advisory Committee on Vaccination (KRAR) summing up the expert opinion. THL gives its recommendation to Ministry of Social affairs and Health (MSAH) after hearing the expert opinion of the Working Group and KRAR. The decision on the introduction of a new vaccine into the NVP is finally made by MSAH when it has received the THL recommendation and consulted its Advisory Board on Communicable Diseases. The decision on funding is made by the Finnish Parliament. After the decision making process has been completed, it is the responsibility of THL to implement any changes.

Illustration of the current decision-making process for adopting a new vaccine into the NVP.



Resources, costs, and funding of the national vaccination programme

The vaccines of the NVP are purchased centrally and funded by the government budget. Due to the introduction of new vaccines, government budget appropriations for vaccine purchases have increased from EUR 5.3 million in 2001 to EUR 10.6 million in 2007 and further to EUR 22.9 million in 2014.

The budget appropriation is used for the:

- purchase, storage and distribution of vaccines
- guidance on vaccine usage
- investigation of the epidemiological and immunological impact, coverage and safety of vaccinations as well as the development of their surveillance systems
- management of obligatory storing system
- the payment of the Finnish Cooperative for Pharmaceutical Injury Indemnities
- procurement costs.

All vaccines for the NVP are purchased according to an open EU-tender procedure. The storage and distribution of vaccines is outsourced to a wholesale distributor of pharmaceutical products. Vaccines are distributed to hospital pharmacies and pharmaceutical centres, which reallocate the vaccines to the municipal health care centres where the vaccinations are carried out.

When the introduction of a new vaccine into the NVP is considered, THL researchers and experts compile the data that the vaccine-specific working group needs to be able to form the required expert opinion. Approximately 4 full-time equivalent employees (equivalent to EUR 240 000) are allocated annually to the evaluation of vaccination programmes at THL.

The work of the members of vaccine-specific working groups that are not THL employees is not included in this figure. Each member is compensated for a meeting by a nominal fee totalling from EUR 1200 to EUR 26 000 per working group.

In addition to the cost of vaccines there are also other costs related to the introduction of a new vaccine. These costs include the administrative costs of vaccinating, e.g. supplies and time nurses spend on the routine activities of vaccinating, as well as on information dissemination. THL provides information on the new vaccine programme to health care workers and to target groups. It is essential to assess the feasibility and acceptability among health care workers and those to be vaccinated to achieve a good vaccination coverage. Approximately 4 full-time equivalent employees (equivalent to EUR 240 000) are allocated annually to the implementation of vaccination programmes at THL. In addition, wider media campaigns have been launched for seasonal influenza and HPV vaccination programmes. The annual costs of the materials (e. g. posters, handouts, and brochures) for the seasonal influenza vaccination campaign have been on average EUR 27 000. In 2015–2016 the costs of materials were considerably higher (EUR 60 000) after the live attenuated influenza vaccine (LAIV) was implemented for two-year-olds for the first time. Half of the costs were accounted for by a survey of public health nurses and parental knowledge and attitudes towards intranasal LAIV. In addition to these marginal costs, there are fixed costs that are covered by the already existing public health care system that carries out vaccinations in the NVP in Finland.

According to the Communicable Diseases Act (1986/583, revision 2010/1244), THL shall monitor the efficiency and effects of the vaccines used for the prevention of communicable diseases. The surveillance of infectious diseases is conducted through health care registers held by THL. The National Infectious Diseases Register is based on the notifications of cases of generally hazardous or notifiable communicable diseases. In 2016 eight full-time equivalent employees (equivalent to EUR 480 000) are allocated annually to maintain the National Infectious Diseases Register at THL. The Care Register for Health Care (former Hospital Discharge Register) contains data on inpatient care and secondary outpatient care. The National Vaccination Register is used in the follow-up of vaccination coverage, safety, and effectiveness. The Vaccine Adverse Effects Register is a spontaneous vaccine safety

surveillance system relying on passive reporting of events suspected by reporters to be vaccine related. THL keeps all the before-mentioned registers.

The Vaccine Adverse Effects Register is transferred to the care of the Finnish Medicines Agency when the new Communicable Diseases Act entered into force in March 2017. The epidemiological surveillance of adverse effects remains at THL.

2.3.2 Website Ministry of Social Affairs and Health – vaccinations https://stm.fi/en/vaccinations

- Decision-making by the Ministry of Social Affairs and Health concerning the vaccination programme is made with the support of the Finnish Institute for Health and Welfare (THL).

2.4 Practical conducts of vaccinations in different wellbeing services counties

Potential questions/outcomes: How is vaccination practically organized for different vaccines for adults in different wellbeing service counties? Are campaigns the same in different counties? Who can vaccinate in the different counties? Can pharmacist vaccinate in the different counties? What are the current main challenges? What changes do WBSC aim to make/see in the future?

2.4.1 Well-being service counties – MSAH website https://stm.fi/en/wellbeing-services-counties

The responsibility for organising healthcare, social welfare and rescue services was transferred from municipalities and joint municipal authorities to wellbeing services counties on 1 January 2023. There are 21 wellbeing services counties, and the division into counties is mainly based on the division into regions. The region of Uusimaa is divided into four wellbeing services counties. The City of Helsinki will continue to be responsible for organising health, social and rescue services. The HUS Group will be responsible for demanding specialised healthcare duties separately laid down by law.

The wellbeing services counties were established under the reform of healthcare, social welfare and rescue services, which has been one of the most significant administrative reforms in Finnish history. The reform was necessary to ensure equal services, reduce inequalities in health and wellbeing and curb the growth in costs. The wellbeing services counties are self-governing. Their funding is based on central government funding, and they do not, as of yet, have the right to levy taxes. Differences in the service needs of the counties are taken into account when determining funding.

The duties of the wellbeing services counties include:

- Primary healthcare
- Specialised healthcare
- Social welfare
- Services for children, young people and families
- Services for working-age people
- Mental health and substance abuse services
- Services for persons with disabilities
- Student welfare

- Rescue services
- Prehospital emergency medical services

Cooperation between the wellbeing services counties and the municipalities will focus on promoting health and wellbeing, thus reducing the need for healthcare and social welfare services. In addition, private operators along with organisations and associations will supplement public health and social services. The municipalities will remain responsible for child daycare, education, sports and culture, for example.

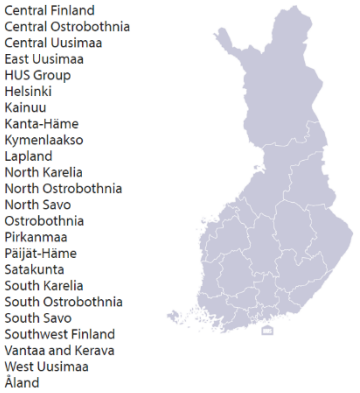
County elections and decision-making

Each wellbeing services county has a county council responsible for the county's activities and finances. County councillors are elected in county elections held in each wellbeing services county. The next county elections will be held in 2025. Each wellbeing services county also has three bodies through which residents can exert influence: youth council, council for older people, and disability council. County residents may also exert influence by submitting initiatives.

Wellbeing services counties and their municipalities

1. The wellbeing services county of South Karelia consists of the following municipalities: Imatra, Lappeenranta, Lemi, Luumäki, Parikkala, Rautjärvi, Ruokolahti, Savitaipale, and Taipalsaari.
2. The wellbeing services county of South Ostrobothnia consists of the following municipalities: Alajärvi, Alavus, Evijärvi, Ilmajoki, Isojoki, Isokyrö, Karijoki, Kauhajoki, Kauhava, Kuortane, Kurikka, Lappajärvi, Lapua, Seinäjoki, Soini, Teuva, Vimpeli, and Ähtäri.
3. The wellbeing services county of South Savo consists of the following municipalities: Enonkoski, Hirvensalmi, Juva, Kangasniemi, Mikkeli, Mäntyharju, Pertunmaa, Pieksämäki, Puumala, Rantasalmi, Savonlinna, and Sulkava.
4. The wellbeing services county of East Uusimaa consists of the following municipalities: Askola, Lapinjärvi, Loviisa, Myrskylä, Porvoo, Pukkila, and Sipoo.
5. The wellbeing services county of Kainuu consists of the following municipalities: Hyrynsalmi, Kajaani, Kuhmo, Paltamo, Puolanka, Ristijärvi, Sotkamo, and Suomussalmi.
6. The wellbeing services county of Kanta-Häme consists of the following municipalities: Forssa, Hattula, Hausjärvi, Humppila, Hämeenlinna, Janakkala, Jokioinen, Loppi, Riihimäki, Tammela, and Ypäjä.
7. The wellbeing services county of Central Ostrobothnia consists of the following municipalities: Halsua, Kannus, Kaustinen, Kokkola, Lestijärvi, Perho, Toholampi, and Veteli.
8. The wellbeing services county of Central Finland consists of the following municipalities: Hankasalmi, Joutsa, Jyväskylä, Jämsä, Kannonkoski, Karstula, Keuruu, Kinnula, Kivijärvi, Konnevesi, Kyyjärvi, Laukaa, Luhanka, Multia, Muurame, Petäjävesi, Pihtipudas, Saarijärvi, Toivakka, Uurainen, Viitasaari, and Äänekoski.
9. The wellbeing services county of Central Uusimaa consists of the following municipalities: Hyvinkää, Järvenpää, Nurmijärvi, Mäntsälä, Tuusula, and Pornainen.
10. The wellbeing services county of Kymenlaakso consists of the following municipalities: Hamina, Kotka, Kouvola, Miehikkälä, Pyhtää, and Virolahti.
11. The wellbeing services county of Lapland consists of the following municipalities: Enontekiö, Inari, Kemi, Kemijärvi, Keminmaa, Kittilä, Kolari, Muonio, Pelkosenniemi, Pello, Posio, Ranua, Rovaniemi, Salla, Savukoski, Simo, Sodankylä, Tervola, Tornio, Utsjoki, and Ylitornio.

12. The wellbeing services county of West Uusimaa consists of the following municipalities: Espoo, Hanko, Ingå, Karkkila, Kauniainen, Kirkkonummi, Lohja, Raseborg, Siuntio, and Vihti.
13. The wellbeing services county of Pirkanmaa consists of the following municipalities: Akaa, Hämeenkyrö, Ikaalinen, Juupajoki, Kangasala, Kihniö, Kuhmoinen, Lempäälä, Mänttä-Vilppula, Nokia, Orivesi, Parkano, Pirkkala, Punkalaidun, Pälkäne, Ruovesi, Sastamala, Tampere, Urjala, Valkeakoski, Vesilahti, Virrat, and Ylöjärvi.
14. The wellbeing services county of Ostrobothnia consists of the following municipalities: Kaskinen, Korsnäs, Kristinestad, Kronoby, Laihia, Larsmo, Malax, Korsholm, Närpes, Pedersöre, Jakobstad, Nykarleby, Vaasa, and Vörå.
15. The wellbeing services county of North Karelia consists of the following municipalities: Heinävesi, Ilomantsi, Joensuu, Juuka, Kitee, Kontiolahti, Lieksa, Liperi, Nurmes, Outokumpu, Polvijärvi, Rääkkylä, and Tohmajärvi.
16. The wellbeing services county of North Ostrobothnia consists of the following municipalities: Alavieska, Haapajärvi, Haapavesi, Hailuoto, Ii, Kalajoki, Kempele, Kuusamo, Kärsämäki, Liminka, Lumijoki, Merijärvi, Muhos, Nivala, Oulainen, Oulu, Pudasjärvi, Pyhäjoki, Pyhäjärvi, Pyhäntä, Raahe, Reisjärvi, Sievi, Siikajoki, Siikalatva, Taivalkoski, Tyrnävä, Utajärvi, Vaala, and Ylivieska.
17. The wellbeing services county of North Savo consists of the following municipalities: Iisalmi, Joroinen, Kaavi, Keitele, Kiuruvesi, Kuopio, Lapinlahti, Leppävirta, Pielavesi, Rautalampi, Rautavaara, Siilinjärvi, Sonkajärvi, Suonenjoki, Tervo, Tuusniemi, Varkaus, Vesanto, and Vieremä.
18. The wellbeing services county of Päijät-Häme consists of the following municipalities: Asikkala, Hartola, Heinola, Hollola, Iitti, Kärkölä, Lahti, Orimattila, Padasjoki, and Sysmä.
19. The wellbeing services county of Satakunta consists of the following municipalities: Eura, Eurajoki, Harjavalta, Huittinen, Jämijärvi, Kankaanpää, Karvia, Kokemäki, Merikarvia, Nakkila, Pomarkku, Pori, Rauma, Siikainen, Säkylä, and Ulvila.
20. The wellbeing services county of Vantaa and Kerava consists of the cities of Vantaa and Kerava.
21. The wellbeing services county of Southwest Finland consists of the following municipalities: Aura, Kaarina, Kimitoön, Koski Tl, Kustavi, Laitila, Lieto, Loimaa, Marttila, Masku, Mynämäki, Naantali, Nousiainen, Oripää, Paimio, Pargas, Pyhäranta, Pöytyä, Raisio, Rusko, Salo, Sauvo, Somero, Taivassalo, Turku, Uusikaupunki, and Vehmaa.



The City of Helsinki and Aland do not form wellbeing services counties but are responsible for organising health, social and rescue services in their areas.

2.4.2 Ekezie W, Awwad S, Krauchenberg A, Karara N, Dembiński Ł, Grossman Z, Del Torso S, Dornbusch HJ, Neves A, Copley S, Mazur A, Hadjipanayis A, Grechukha Y, Nohynek H, Damnjanović K, Lazić M, Papaevangelou V, Lapii F, Stein-Zamir C, Rath B, For The ImmuHubs Consortium. Access to Vaccination among Disadvantaged, Isolated and Difficult-to-Reach Communities in the WHO European Region: A Systematic Review. Vaccines (Basel). 2022 Jun 28;10(7):1038.

Vaccination has a significant impact on morbidity and mortality. High vaccination coverage rates are required to achieve herd protection against vaccine-preventable diseases. However,

limited vaccine access and hesitancy among specific communities represent significant obstacles to this goal. This review provides an overview of critical factors associated with vaccination among disadvantaged groups in World Health Organisation European countries. Initial searches yielded 18,109 publications from four databases, and 104 studies from 19 out of 53 countries reporting 22 vaccine-preventable diseases were included. Nine groups representing the populations of interest were identified, and most of the studies focused on asylum seekers, refugees, migrants and deprived communities. Recall of previous vaccinations received was poor, and serology was conducted in some cases to confirm protection for those who received prior vaccinations. Vaccination coverage was lower among study populations compared to the general population or national average. Factors that influenced uptake, which presented differently at different population levels, included health service accessibility, language and vaccine literacy, including risk perception, disease severity and vaccination benefits. Strategies that could be implemented in vaccination policy and programs were also identified. Overall, interventions specific to target communities are vital to improving uptake. More innovative strategies need to be deployed to improve vaccination coverage among disadvantaged groups.

Session 3: National registers in healthcare and their role in vaccine evaluation and monitoring

Session 3: National registers in healthcare and their role in vaccine evaluation and monitoring	3.1 National registers including vaccination register and the national information resource plan	Jukka Jokinen
	3.2 Register-based surveillance of infectious diseases and comorbidities in Finland; present status and future	Tuija Leino
	3.3 Real time-based study on register data for seasonal influenza vaccination	Ulrike Baum
	3.4 COVID-19 vaccine effectiveness (VE) in risk groups	Eero Poukka
	3.5 Vaccine safety monitoring	Petteri Hovi
	3.6 Finnish national registers in clinical trial settings	Tuomo Nieminen

3.1 National registers including vaccination register and the national information resource plan

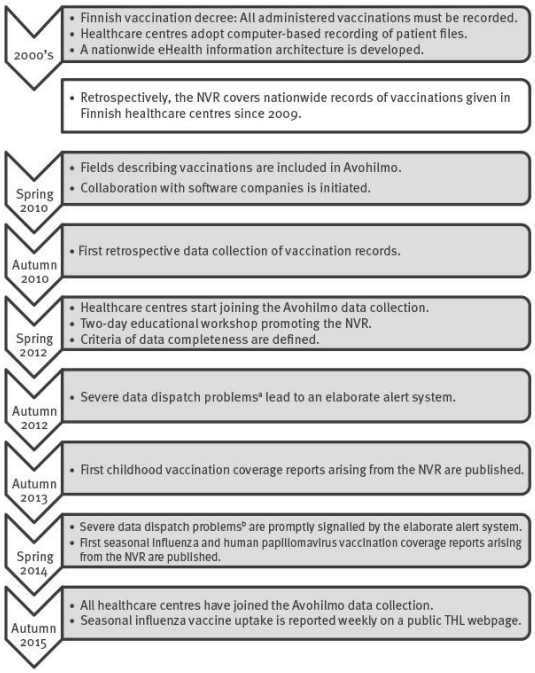
Potential questions/outcomes: Since when are the national registers operational? What main changes were made over the years? Are vaccinations at specialist medical care and private health care also well registered? Is coverage monitored for all 10 VPD in adults in Finland? If a new vaccine is included in the NVP, how long does it take to include in the vaccination register? How does adult immunization in Finland benefit from the digital transformation of the health system/ the register? Are there similar registers in other European countries? Why

has Finland successfully implemented these registers, while others have faced challenges? What lessons can be drawn from Finland's approach, and how does Finland ensure the safety and security of these systems?

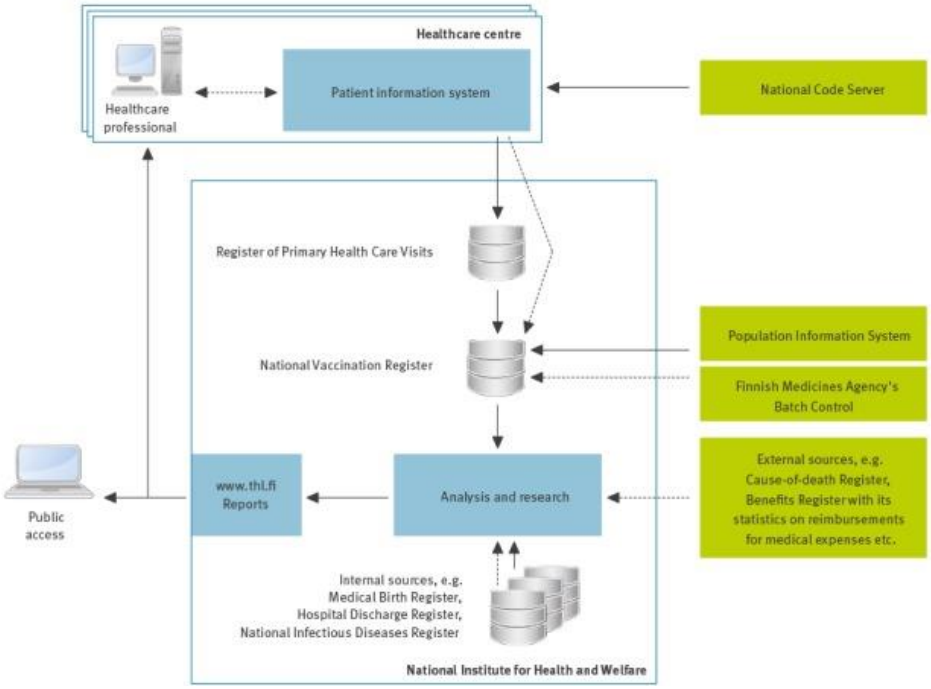
3.1.1 Vuokko, R., Vakkuri, A. and Palojoki, S. (2021). "Harmonization of Finnish Vaccination Data." Stud Health Technol Inform 281: 709-713.

Vaccination information is needed at individual and at population levels, as it is an important part of public health measures. In Finland, a vaccination data structure has been developed for centralized information services that include patient access to information. Harmonization of data with national vaccination registry is ongoing. New requirements for vaccination certificates have emerged because of COVID-19 pandemic. We explore, what is the readiness of Finnish development of vaccination data structures and what can be learned from Finnish harmonization efforts in order to accomplish required level of interoperability.

3.1.2 Baum U, Sundman J, Jääskeläinen S, Nohynek H, Puumalainen T, Jokinen J. Establishing and maintaining the National Vaccination Register in Finland. Euro Surveill. 2017 Apr 27;22(17):30520.



Computerised, population-based vaccination registers are valuable tools for assessing the vaccine uptake and impact in populations. However, reliable impact assessment is only possible if the data quality can be reviewed and monitored continuously. This report describes the establishment and maintenance of the National Vaccination Register (NVR) in Finland. Currently, the NVR covers nationwide records of vaccinations given within the frame of the National Vaccination Programme since 2009. All vaccinations registered in the NVR contain a record of the personal identity code, the administered vaccine, and the date of vaccination. The vaccine lot number is the key component for recording and identifying vaccinations, because of its broad availability across patient information systems and its importance in vaccine safety monitoring. Vaccination records are accumulated and updated daily into the NVR, and their completeness is monitored monthly to assess deficiencies in data entry and data collection. Additionally, an alert system reports unexpected changes in data accumulation prompting the validation of observed changes in vaccination coverage. The presented process documentation may serve as basis to improve the design and quality of other vaccination or healthcare registers and aims to inspire the set-up of vaccination registers in those countries which still do not have one.



3.1.3 THL Website: Finnish National Vaccination Register and monitoring of the vaccination programme

The Finnish Institute for Health and Welfare (THL) maintains a Finnish national vaccination register. Vaccination data are collected directly from patient record systems. The vaccination register covers vaccinations given in public primary health care. The data is also obtained on vaccinations administered in specialist medical care and private health care.

Purposes of the national vaccination register

The Finnish Institute for Health and Welfare monitors and evaluates the coverage of the national vaccination programme through the national vaccination register.

You cannot check the vaccination data of an individual person in the vaccination register.

The vaccination register can be used to

- produce data about national and regional vaccination coverage
- monitor changes in vaccination coverage in nearly real time
- examine vaccination coverage per population group and specific time period.

The Finnish Institute for Health and Welfare monitors the impacts of the vaccination programme together with municipal health care professionals. The vaccination register enables health centres to

- obtain information about local vaccination coverage
- compare their own vaccination coverage with the coverage in nearby municipalities and Finland as a whole
- assess the vaccination protection of the population in their region and develop local vaccination activities.

The introduction of the vaccination register has enabled eliminating laborious and slow sampling studies and the reporting system for influenza vaccinations, which produced information with a delay.

The vaccination register produces knowledge on the benefits of vaccination and is used to monitor the safety of vaccinations

Monitoring the vaccination programme

The need to reform the vaccination programme is continuously assessed based on monitoring and research data. The need for reform is also assessed when a new vaccine is introduced to the market.

The Public Health Solutions unit conducts research related to vaccines funded by the private sector or jointly funded.

3.2 Register-based surveillance of infectious diseases and comorbidities in Finland; present status and future

Potential questions/outcomes: How is the register-based surveillance of infectious diseases and co-morbidities used? What are the current main challenges for VPD in adults? With which European expert networks do you work? Which updates are planned for the future?

3.2.1 Finnish National Infectious Diseases Register https://thl.fi/en/topics/infectious-diseases-and-vaccinations/surveillance-and-registers/finnish-national-infectious-diseases-register

Approximately 140,000 cases of infectious diseases are reported to the National Infectious Diseases Register each year. The register data are used to prevent, monitor, control and research infectious diseases. In addition to the National Infectious Diseases Register, several other systems are used to monitor the disease situation. THL also engages in extensive international cooperation with European expert networks.

Surveillance and registers in Finland:

- Finnish National Infectious Diseases Register
- Disease-specific monitoring systems
- Finnish National Vaccination Register and monitoring of the vaccination programme
- Surveillance of healthcare-associated infections
- Surveillance of antimicrobial resistance
- Wastewater monitoring

The public statistical database of the National Infectious Diseases Register provides access to statistical data by hospital district, age group and gender, on an annual and monthly basis. In addition to the number of cases, the register provides information about incidence, or the number of cases relative to 100,000 residents. Data in the register may also be disclosed for research purposes in return for a research permit. Data have been collected since 1995.

Doctors and dentists must file a communicable disease notification for some of the cases of generally hazardous or monitored communicable diseases listed in the Communicable Diseases Decree. There are around 40 of such diseases.

Microbiology laboratories file a notification of the microbes they find to the National Infectious Diseases Register. The laboratories must submit a notification of findings of around 70 specific pathogens and all findings in blood or cerebrospinal fluid.

Notifications of the findings are filed online using a communicable disease notification or submitted directly from the laboratory's electronic information system.

THL's specialist laboratories examine and monitor samples. The research and monitoring activities are based on the Communicable Diseases Act and Decree.
Communicable Diseases Act (Finlex)

Statistical database of the National Infectious Diseases Register

Detailed statistics on the numbers and incidence of infectious diseases are available in the online service of the National Infectious Diseases Register. When examining the figures, it should be kept in mind that they are also influenced by the share of patients who seek health care and the number of microbiological examinations carried out to identify the cause. The rates are also affected by changes in diagnostic practice and methods. The incidence presented in the statistics refers to the number of cases per 100,000 inhabitants.

Scientific research

The Finnish Institute for Health and Welfare may disclose data from the National Infectious Diseases Register for research purposes. Using the data of the National Infectious Diseases Register always requires a research permit. Before applying for a permit, you should familiarise yourself with the register content by viewing the list of microbes and the publicly available statistics of the National Infectious Diseases a Register.

A favourable statement from the controller must be attached to the permit application.

3.3 Real time-based study on register data for seasonal influenza vaccination

Potential questions/outcomes: Which studies have been conducted related to S. Influenza using the register. What were the main outcomes for the NVP? Which studies are done yearly and which other studies are planned in the future? Will do HD vs. SD study be repeated no COVID-19 is over? Will Finland change to trivalent vaccines in season 2025-2026? If yes, which studies will be conducted? What are the advantages and the risks in using these registers for studies? Are there specific cases were register data cannot be used? To what extent can data from the Finnish registry be used for other countries' vaccination programs? Do you have any examples?

3.3.1 Ulrike Baum, Niina Ikonen, Oskari Luomala, et al. The epidemiology of influenza during the COVID-19 pandemic in Finland -- A summary and interpretation of surveillance data from 2019 to 2024. Authorea. November 02, 2024.

The Finnish influenza surveillance system monitors the influenza prevalence, disease burden, vaccine uptake and effectiveness. Since the start of the COVID-19 pandemic the publication of the yearly surveillance report has been paused. Therefore, this paper summarizes the past five seasons based on surveillance data from 2019 to 2024 and describes the epidemiology of influenza during the COVID-19 pandemic in Finland. Clinical surveillance showed that the 2019/20 epidemic ended concomitantly with the introduction of COVID-19 containment measures in March 2020, in 2020/21 influenza was absent, and the 2021/22 epidemic peaked exceptionally late. Influenza activity has roughly returned to pre-pandemic levels since 2022/23, when there were 13,728 and 2,172 laboratory-confirmed influenza A and influenza B cases, 1,485 and 179 of which were hospitalized due to influenza. Virological surveillance confirmed that circulation of the influenza B/Yamagata lineage had ceased. One to two million influenza vaccinations were given each season. While the percentage of vaccinated children younger than seven years was constant (ranging from 31% to 37%), the percentage of vaccinated people aged 65 years and above increased from 48% in 2019/20 to 63% in 2021/22 and has remained moderately high. The vaccine effectiveness against hospitalization due to laboratory-confirmed influenza in young children and elderly people was 68% (95% confidence interval: 38%; 83%) and 42% (34%; 50%) in 2022/23 and slightly lower in 2023/24. The COVID-19 pandemic had two hopefully lasting effects on the epidemiology of influenza: elimination of the influenza B/Yamagata lineage and improved influenza vaccination coverage among the elderly population in Finland.

3.3.2 Palmu AA, Pepin S, Syrjänen RK, Mari K, Mallett Moore T, Jokinen J, Nieminen H, Kilpi T, Samson SI, De Bruijn I. High-Dose Quadrivalent Influenza Vaccine for Prevention of Cardiovascular and Respiratory Hospitalizations in Older Adults. Influenza Other Respir Viruses. 2024 Apr;18(4):e13270.

Background: We assessed the relative vaccine effectiveness (rVE) of high-dose quadrivalent influenza vaccine (QIV-HD) versus standard-dose quadrivalent influenza vaccine (QIV-SD) in preventing respiratory or cardiovascular hospitalizations in older adults. Methods: FinFluHD was a phase 3b/4 modified double-blind, randomized pragmatic trial. Enrolment of 121,000 adults ≥65 years was planned over three influenza seasons (October to December 2019-2021). Participants received a single injection of QIV-HD or QIV-SD. The primary endpoint was first occurrence of an unscheduled acute respiratory or cardiovascular hospitalization (ICD-10 primary discharge J/I codes), from ≥14 days post-vaccination until May 31. The study was terminated after one season due to COVID-19; follow-up data for 2019-2020 are presented. Results: 33,093 participants were vaccinated (QIV-HD, n = 16,549; QIV-SD, n = 16,544); 529 respiratory or cardiovascular hospitalizations (QIV-HD, n = 257; QIV-SD, n =

272) were recorded. The rVE of QIV-HD versus QIV-SD to prevent respiratory/cardiovascular hospitalizations was 5.5% (95% CI, -12.4 to 20.7). When prevention of respiratory and cardiovascular hospitalizations were considered separately, rVE estimates of QIV-HD versus QIV-SD were 5.4% (95% CI, -28.0 to 30.1) and 7.1% (95% CI, -15.0 to 25.0), respectively. Serious adverse reactions were <0.01% in both groups. Conclusions: Despite insufficient statistical power due to the impact of COVID-19, rVE point estimates demonstrated a trend toward a benefit of QIV-HD over QIV-SD. QIV-HD was associated with lower respiratory or cardiovascular hospitalization rates than QIV-SD, with a comparable safety profile. Adequately powered studies conducted over multiple influenza seasons are needed to determine statistical significance of QIV-HD compared with QIV-SD against preventing respiratory and cardiovascular hospitalizations.

3.3.3 Stuurman AL, Carmona A, Biccler J, Descamps A, Levi M, Baum U, Mira-Iglesias A, Bellino S, Hoang U, de Lusignan S, Bonaiuti R, Lina B, Rizzo C, Nohynek H, Díez-Domingo J; DRIVE Study Contributors. Brand-specific estimates of influenza vaccine effectiveness for the 2021-2022 season in Europe: results from the DRIVE multi-stakeholder study platform. Front Public Health. 2023 Jul 20;11:1195409.

Introduction: Development of Robust and Innovative Vaccine Effectiveness (DRIVE) was a European public-private partnership (PPP) that aimed to provide annual, brand-specific estimates of influenza vaccine effectiveness (IVE) for regulatory and public health purposes. DRIVE was launched in 2017 under the umbrella of the Innovative Medicines Initiative (IMI) and conducted IVE studies from its pilot season in 2017-2018 to its final season in 2021-2022. Methods: In 2021-2022, DRIVE conducted four primary care-based test-negative design (TND) studies (Austria, Italy, Iceland, and England; involving >1,000 general practitioners), nine hospital-based TND studies (France, Iceland, Italy, Romania, and Spain, for a total of 21 hospitals), and one population-based cohort study in Finland. In the TND studies, patients with influenza-like illness (primary care) or severe acute respiratory infection (hospital) were enrolled, and laboratory tested for influenza using RT-PCR. Study contributor-specific IVE was calculated using logistic regression, adjusting for age, sex, and calendar time, and pooled by meta-analysis. Results: In 2021-2022, pooled confounder-adjusted influenza vaccine effectiveness (IVE) estimates against laboratory-confirmed influenza (LCI) overall and per type and subtype/lineage was produced, albeit with wide confidence intervals (CI). The limited circulation of influenza in Europe did not allow the network to reach the optimal sample size to produce precise IVE estimates for all the brands included. The most significant IVE estimates were 76% (95% CI 23%-93%) for any vaccine and 81% (22%-95%) for Vaxigrip Tetra in adults ≥65 years old and 64% (25%-83%) for Fluenz Tetra in children (TND primary care setting), 85% (12%-97%) for any vaccine in adults 18-64 years (TND hospital setting), and 38% (1%-62%) in children 6 months-6 years (population-based cohort, mixed setting). Discussion: Over five seasons, DRIVE collected data on >35,000 patients, more than 60 variables, and 13 influenza vaccines. DRIVE demonstrated that estimating brand-specific IVE across Europe is possible, but achieving sufficient sample size to obtain precise estimates for all relevant stratifications remains a challenge. Finally, DRIVE's network of study contributors and lessons learned have greatly contributed to the development of the COVID-19 vaccine effectiveness platform COVIDRIVE.

3.3.4 Halme J, Syrjänen RK, Baum U, Palmu AA. Effectiveness of trivalent influenza vaccines against hospitalizations due to laboratory-confirmed influenza a in the elderly: Comparison of test-negative design with register-based designs. Vaccine. 2022 Jul 29;40(31):4242-4252.

Introduction: Measuring influenza vaccine effectiveness (IVE) seasonally is important and has been conducted utilizing several observational study designs. The active test-negative design has been most widely used and the validity of passive register-based studies has been debated. We aimed to explore the potential differences, advantages, and weaknesses of different study designs in estimating influenza vaccine effectiveness. Methods: We compared three study designs in estimating IVE against hospitalization in the elderly aged 65 years or more over three influenza seasons 2015/16, 2016/17 and 2017/18. Designs compared were active test-negative design (TND), register-based cohort design and register-based case-control design with different selection criteria for cases and controls. Results: Adjusted IVE estimates for the three consecutive seasons 2015-18 in active test-negative design were 82% (95% confidence interval 26, 96), 21% (-179, 77), 15% (-113, 66). For case-control design, estimates from different analyses ranged in 2015/16 from 47% (-16, 76) to 52% (-48, 84), in 2016/17 from 10% (-42, 43) to 29% (-20, 58), and in 2017/18 from -27% (-91, 15) to 1% (-40, 30). In the cohort design, the adjusted IVE estimates were 48% (-9, 75), 29% (1, 49), 13% (-21, 37) for the three seasons. Conclusions: The register-based cohort design produced results more concordant with the active test-negative design than the case-control design. Furthermore, the register-based cohort design yielded most precise estimates with narrower confidence intervals. In Finland with the availability of near real-time nationwide register data, the register-based cohort design is the method of choice to continue the annual surveillance of influenza vaccine effectiveness.

3.3.5 Baum U, Kulathinal S, Auranen K. Spotlight influenza: Estimation of influenza vaccine effectiveness in elderly people with assessment of residual confounding by negative control outcomes, Finland, 2012/13 to 2019/20. Euro Surveill. 2021 Sep;26(36):2100054.

Background Cohort studies on vaccine effectiveness are prone to confounding bias if the distribution of risk factors is unbalanced between vaccinated and unvaccinated study subjects. Aim We aimed to estimate influenza vaccine effectiveness in the elderly population in Finland by controlling for a sufficient set of confounders based on routinely available register data. Methods For each of the eight consecutive influenza seasons from 2012/13 through 2019/20, we conducted a cohort study comparing the hazards of laboratory-confirmed influenza in vaccinated and unvaccinated people aged 65-100 years using individual-level medical and demographic data. Vaccine effectiveness was estimated as 1 minus the hazard ratio adjusted for the confounders age, sex, vaccination history, nights hospitalised in the past and presence of underlying chronic conditions. To assess the adequacy of the selected set of confounders, we estimated hazard ratios of off-season hospitalisation for acute respiratory infection as a negative control outcome. Results Each analysed cohort comprised around 1 million subjects, of whom 37% to 49% were vaccinated. Vaccine effectiveness against laboratory-confirmed influenza ranged from 16% (95% confidence interval (CI): 12-19) to 48% (95% CI: 41-54). More than 80% of the laboratory-confirmed cases were hospitalised. The adjusted off-season hazard ratio estimates varied between 1.00 (95% CI: 0.94-1.05) and 1.08 (95% CI: 1.01-1.15), indicating that residual confounding was absent or negligible. Conclusion Seasonal influenza vaccination reduces the hazard of severe influenza disease in vaccinated elderly people. Data about age, sex, vaccination history and utilisation of hospital care proved sufficient to control confounding.

3.3.6 Baum U, Auranen K, Kulathinal S, Syrjänen R, Nohynek H, Jokinen J. Cohort study design for estimating the effectiveness of seasonal influenza vaccines in real time based on register data: The Finnish example. Scand J Public Health. 2020 May;48(3):316-322.

This paper presents the principles of implementing register-based cohort studies as currently applied for real-time estimation of influenza vaccine effectiveness in Finland. All required

information is retrieved from computerised national registers and deterministically linked via the unique personal identity code assigned to each Finnish resident. The study cohorts comprise large subpopulations eligible for a free seasonal influenza vaccination as part of the National Vaccination Programme. The primary outcome is laboratory-confirmed influenza. Each study subject is taken to be at risk of experiencing the outcome from the onset of the influenza season until the first of the following three events occurs: outcome, loss to follow up or end of season. Seasonal influenza vaccination is viewed as time-dependent exposure. Accordingly, each subject may contribute unvaccinated and vaccinated person-time during their time at risk. The vaccine effectiveness is estimated as one minus the influenza incidence rate ratio comparing the vaccinated with the unvaccinated within the study cohorts. Data collection in register-based research is an almost fully automated process. The effort, resources and the time spent in the field are relatively small compared to other observational study designs. This advantage is pivotal when vaccine effectiveness estimates are needed in real time. The paper outlines possible limitations of register-based cohort studies. It also addresses the need to explore how national and subnational registers available in the Nordic countries and elsewhere can be utilised in vaccine effectiveness research to guide decision making and to improve individual health as well as public health.

3.4.7 Hergens MP, Baum U, Brytting M, Ikonen N, Haveri A, Wiman Å, Nohynek H, Örtqvist Å. Mid-season real-time estimates of seasonal influenza vaccine effectiveness in persons 65 years and older in register-based surveillance, Stockholm County, Sweden, and Finland, January 2017. Euro Surveill. 2017 Feb 23;22(8):30469. doi: 10.2807/1560-7917.ES.2017.22.8.30469. Erratum in: Euro Surveill. 2017 Mar 2;22(9):30475

Systems for register-based monitoring of vaccine effectiveness (VE) against laboratory-confirmed influenza (LCI) in real time were set up in Stockholm County, Sweden, and Finland, before start of the 2016/17 influenza season, using population-based cohort studies. Both in Stockholm and Finland, an early epidemic of influenza A(H3N2) peaked in week 52, 2016. Already during weeks 48 to 50, analyses of influenza VE in persons 65 years and above showed moderately good estimates of around 50%, then rapidly declined by week 2, 2017 to 28% and 32% in Stockholm and Finland, respectively. The sensitivity analyses, where time since vaccination was taken into account, could not demonstrate a clear decline, neither by calendar week nor by time since vaccination. Most (68%) of the samples collected from vaccinated patients belonged to the 3C.2a1 subclade with the additional amino acid substitution T135K in haemagglutinin (64%) or to subclade 3C.2a with the additional haemagglutinin substitutions T131K and R142K (36%). The proportion of samples containing these alterations increased during the studied period. These substitutions may be responsible for viral antigenic change and part of the observed VE drop. Another possible cause is poor vaccine immunogenicity in older persons. Improved influenza vaccines are needed, especially for the elderly.

3.4 COVID-19 vaccine effectiveness (VE) in risk groups

Potential questions/outcomes: Which studies have been conducted related to COVID-19 using the register. What were the main outcomes for the NVP? Which studies are done yearly and which other studies are planned in the future? What are the advantages and the risks in using these registers for studies (which ones are specifically for COVID-19)? Are there specific cases were register data cannot be used? To what extent can data from the Finnish registry be used for other countries' vaccination programs? Do you have any examples? How to use negative control outcomes/exposures for detecting residual confounding?

3.4.1 Comparative effectiveness of bivalent BA.4–5 or BA.1 mRNA booster vaccines among immunocompromised individuals across three Nordic countries: A nationwide cohort study
Gram, Mie Agermose et al. Journal of Infection, Volume 89, Issue 4, 106261

Objectives - To estimate the effectiveness and waning of the bivalent BA.4–5 or BA.1 mRNA booster vaccine against Covid-19-related hospitalization and death in immunocompromised individuals. Methods - Nationwide analyses across Nordic countries from 1 September 2022 to 31 October 2023 using a matched cohort design. Individuals boosted with a BA.4–5 or BA.1 vaccine were matched 1:1 with unboosted individuals. The outcomes of interest were country-combined vaccine effectiveness (VE) estimates against Covid-19-related hospitalization and death at day 270 of follow-up. Waning was assessed in 45-day intervals. Results - A total of 352,762 BA.4–5 and 191,070 BA.1 booster vaccine doses were included. At day 270, the comparative VE against Covid-19-related hospitalization was 34.2% (95% CI, 7.1% to 61.3%) for the bivalent BA.4–5 vaccine and 42.6% (95% CI, 31.3% to 53.9%) for the BA.1 vaccine compared with matched unboosted. The comparative VE against Covid-19-related death was 53.9% (95% CI, 38.6% to 69.3%) for the bivalent BA.4–5 vaccine and 57.9% (95% CI, 48.5% to 67.4%) for the BA.1 vaccine. Conclusions - In immunocompromised individuals, vaccination with bivalent BA.4–5 or BA.1 booster lowered the risk of Covid-19-related hospitalization and death over a follow-up period of 9 months. The effectiveness was highest during the first months since vaccination with subsequent gradual waning.

3.4.2 Poukka E, Perälä J, Nohynek H, Goebeler S, Auranen K, Leino T, Baum U. 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 Sep;29(37):2300587.

Background Long-term effectiveness data on bivalent COVID-19 boosters are limited. Aim We evaluated the long-term protection of bivalent boosters against severe COVID-19 among ≥ 65-year-olds in Finland. Methods In this register-based cohort analysis, we compared the risk of three severe COVID-19 outcomes among ≥ 65-year-olds who received a bivalent booster (Original/Omicron BA.1 or Original/BA.4-5; exposed group) between 1/9/2022 and 31/8/2023 to those who did not (unexposed). We included individuals vaccinated with at least two monovalent COVID-19 vaccine doses before 1/9/2022 and ≥ 3 months ago. The analysis was divided into two periods: 1/9/2022-28/2/2023 (BA.5 and BQ.1.X predominating) and 1/3/2023-31/8/2023 (XBB predominating). The hazards for the outcomes between exposed and unexposed individuals were compared with Cox regression. Results We included 1,191,871 individuals. From 1/9/2022 to 28/2/2023, bivalent boosters were associated with a reduced risk of hospitalisation due to COVID-19 (hazard ratio (HR): 0.45; 95% confidence interval (CI): 0.37-0.55), death due to COVID-19 (HR: 0.49; 95% CI: 0.38-0.62), and death in which COVID-19 was a contributing factor (HR: 0.40; 95% CI: 0.31-0.51) during 14-60 days since vaccination. From 1/3/2023 to 31/8/2023, bivalent boosters were associated with lower risks of all three severe COVID-19 outcomes during 61-120 days since a bivalent booster (e.g. HR: 0.53; 95% CI: 0.39-0.71 for hospitalisation due to COVID-19); thereafter no notable risk reduction was observed. No difference was found between Original/Omicron BA.1 and Original/BA.4-5 boosters. Conclusion Bivalent boosters initially reduced the risk of severe COVID-19 outcomes by ca 50% among ≥ 65-year-olds, but protection waned over time. These findings help guide vaccine development and vaccination programmes.

3.4.3 Poukka E, Auranen K, Baum U. Non-COVID-19 hospitalisation as a negative control outcome in COVID-19 vaccine effectiveness studies. Lancet Infect Dis. 2024 May;24(5):e275.

3.4.4 **Comparative effectiveness of the monovalent XBB.1.5-containing covid-19 mRNA vaccine across three Nordic countries** Niklas Worm Andersson, Emilia Myrup Thiesson, Nicklas Pihlström, Jori Perälä, Kristýna Faksová, Mie Agermose Gram, Eero Poukka, Tuija Leino, Rickard Ljung, Anders Hviid medRxiv 2024.05.08.24307058

Objective To estimate the effectiveness of vaccination with a monovalent XBB.1.5-containing covid-19 mRNA vaccine against severe covid-19 across three Nordic countries. Design Nationwide cohort studies, using target trial emulation. Setting Denmark, Finland, and Sweden, from 1 October 2023 to 29 February 2024. Participants Individuals aged ≥65 years who had previously received at least four covid-19 vaccine doses. Main outcome measures: Cumulative incidences of covid-19 hospital admission and death for 12 weeks after immunisation (defined as 1 week after vaccination) among recipients of an XBB.1.5-containing covid-19 mRNA vaccine and matched non-recipients. Cumulative incidences were used to calculate comparative vaccine effectiveness (1-risk ratio) and risk differences.
Results During autumn and winter 2023-2024, a total of 1,867,448 1:1 matched pairs of XBB-containing covid-19 mRNA vaccine recipients and non-recipients were included (mean age 75.4 years, standard deviation 7.4 years). The comparative vaccine effectiveness was 60.6% (95% confidence interval, 46.1% to 75.1%) against covid-19 hospital admission (930 v 2,551 events) and 77.9% (69.2% to 86.7%) against covid-19 related death (301 v 1,326 events) at 12 weeks of follow-up. This corresponded to 191.1 (95% confidence interval, 50.2 to 332.1) covid-19 hospital admissions and 109.2 (100.2 to 118.1) deaths prevented per 100,000 individuals vaccinated with an XBB.1.5-containing vaccine. The comparative vaccine effectiveness was similar across sex, age (65-74/≥75 years), number of previous covid-19 vaccine doses received, and seasonal influenza vaccination co-administration subgroups and periods of either omicron XBB- or BA.2.86-sublineage dominance. While the protection was highest during the first weeks after vaccination, it was well-preserved at end of week 12 of follow-up. Conclusion Among adults aged ≥65 years, vaccination with a monovalent XBB.1.5-containing covid-19 mRNA vaccine reduced the rates of covid-19 related hospital admission and death during autumn and winter 2023-2024 across three Nordic countries.

3.4.5 Andersson NW, Thiesson EM, Baum U, Pihlström N, Starrfelt J, Faksová K, Poukka E, Meijerink H, Ljung R, Hviid A. **Comparative effectiveness of bivalent BA.4-5 and BA.1 mRNA booster vaccines among adults aged ≥50 years in Nordic countries: nationwide cohort study.** BMJ. 2023 Jul 25;382:e075286.

Objective: To estimate the effectiveness of the bivalent mRNA booster vaccines containing the original SARS-CoV-2 and omicron BA.4-5 or BA.1 subvariants as the fourth dose against severe covid-19. Design: Nationwide cohort analyses, using target trial emulation. Setting: Denmark, Finland, Norway, and Sweden, from 1 July 2022 to 10 April 2023. Participants: People aged ≥50 years who had received at least three doses of covid-19 vaccine (that is, a primary course and a first booster). Main outcome measures: The Kaplan-Meier estimator was used to compare the risk of hospital admission and death related to covid-19 in people who received a bivalent Comirnaty (Pfizer-BioNTech) or Spikevax (Moderna) BA.4-5 or BA.1 mRNA booster vaccine as a fourth dose (second booster) with three dose (first booster) vaccinated people and between four dose vaccinated people. Results: A total of 1 634 199 people receiving bivalent BA.4-5 fourth dose booster and 1 042 124 receiving bivalent BA.1 fourth dose booster across the four Nordic countries were included. Receipt of a bivalent BA.4-5 booster as a fourth dose was associated with a comparative vaccine effectiveness against admission to hospital with covid-19 of 67.8% (95% confidence interval 63.1% to 72.5%) and a risk difference of -91.9 (95% confidence interval -152.4 to -31.4) per 100 000 people at three months of follow-up compared with having received three doses of vaccine (289 v 893 events). The corresponding comparative vaccine effectiveness and risk difference for bivalent

BA.1 boosters (332 v 977 events) were 65.8% (59.1% to 72.4%) and -112.9 (-179.6 to -46.2) per 100 000, respectively. Comparative vaccine effectiveness and risk difference against covid-19 related death were 69.8% (52.8% to 86.8%) and -34.1 (-40.1 to -28.2) per 100 000 for bivalent BA.4-5 booster (93 v 325 events) and 70.0% (50.3% to 89.7%) and -38.7 (-65.4 to -12.0) per 100 000 for BA.1 booster (86 v 286) as a fourth dose. Comparing bivalent BA.4-5 and BA.1 boosters as a fourth dose directly resulted in a three month comparative vaccine effectiveness and corresponding risk difference of -14.9% (-62.3% to 32.4%) and 10.0 (-14.4 to 34.4) per 100 000 people for admission to hospital with covid-19 (802 v 932 unweighted events) and -40.7% (-123.4% to 42.1%) and 8.1 (-3.3 to 19.4) per 100 000 for covid-19 related death (229 v 243 unweighted events). The comparative vaccine effectiveness did not differ across sex and age (</≥70 years) and seemed to be sustained up to six months from the day of vaccination with modest waning. Conclusion: Vaccination with bivalent BA.4-5 or BA.1 mRNA booster vaccines as a fourth dose was associated with reduced rates of covid-19 related hospital admission and death among adults aged ≥50 years. The protection afforded by the bivalent BA.4-5 and BA.1 boosters did not differ significantly when directly compared, and any potential difference would most likely be very small in absolute numbers.

3.4.6 Tiirinki H, Viita-Aho M, Tynkkynen LK, Sovala M, Jormanainen V, Keskimäki I. COVID-19 in Finland: Vaccination strategy as part of the wider governing of the pandemic. Health Policy Technol. 2022 Jun;11(2):100631.

Objectives: To analyze the vaccination strategy as part of wider public governing of the COVID-19 pandemic in Finland. Methods: The study provides a synthesis of vaccination strategy and health policy measures, as well as economic challenges, in the COVID-19 pandemic in Finland. The analysis is based on the systematic collection and reviewing of documents and reports. The review was complemented with relevant pandemic and vaccination monitoring data from Finland. Results: The vaccination strategy approved by the Finnish Government in December 2020 prioritised various risk groups and health and social care professionals attending to COVID-19 patients. The Government has purchased COVID-19 vaccines through the EU joint procurement programme. Vaccinations were organised by municipalities and offered free of charge. The Government recommends universal vaccinations, including foreign residents and undocumented migrants. In 2021, the Government adopted a revised COVID-19 hybrid strategy, which aimed to dismantle wide restrictions as a means to control the epidemic. Despite high vaccination coverage, the Omicron variant became widespread in the population. The economic consequences of the pandemic have been less severe than expected. Conclusions: In the approach to manage the pandemic, the vaccination strategy has a central role. Finland has probably benefitted from the EU joint vaccine procurement programme. The rapid launch of the vaccinations was supported by the existing vaccination capacity in municipalities. High vaccine coverage was seen as a key in opening society. Although a relatively high vaccination rate was not able to stop the spread of Omicron in late 2021, it has efficiently curbed serious cases and kept the death rate low.

3.4.7 Baum U, Poukka E, Leino T, Kilpi T, Nohynek H, Palmu AA. High vaccine effectiveness against severe COVID-19 in the elderly in Finland before and after the emergence of Omicron. BMC Infect Dis. 2022 Nov 5;22(1):816.

Background: The elderly are highly vulnerable to severe COVID-19. Waning immunity and emergence of Omicron have caused concerns about reduced effectiveness of COVID-19 vaccines. The objective was to estimate vaccine effectiveness (VE) against severe COVID-19 among the elderly. Methods: This nationwide, register-based cohort analysis included all residents aged 70 years and over in Finland. The follow-up started on December 27, 2020,

and ended on March 31, 2022. The outcomes of interest were COVID-19-related hospitalization and intensive care unit (ICU) admission timely associated with SARS-CoV-2 infection. VE was estimated as one minus the hazard ratio comparing the vaccinated and unvaccinated and taking into account time since vaccination. Omicron-specific VE was evaluated as the effectiveness observed since January 1, 2022. Results: The cohort included 896,220 individuals. Comirnaty (BioNTech/Pfizer) VE against COVID-19-related hospitalization was 93% (95% CI 89-95%) and 85% (95% CI 82-87%) 14-90 and 91-180 days after the second dose; VE increased to 95% (95% CI 94-96%) 14-60 days after the third dose. VE of other homologous and heterologous three dose series was similar. Protection against severe COVID-19 requiring ICU treatment was even better. Since January 1, 2022, Comirnaty VE was 98% (95% CI 92-99%) and 92% (95% CI 87-95%) 14-90 and 91-180 days after the second and 98% (95% CI 95-99%) 14-60 days after the third dose. Conclusions: VE against severe COVID-19 is high among the elderly. It waned slightly after two doses, but a third restored the protection. VE against severe COVID-19 remained high even after the emergence of Omicron.

3.4.8 Salo H, Lehtonen T, Auranen K, Baum U, Leino T. Predictors of hospitalisation and death due to SARS-CoV-2 infection in Finland: A population-based register study with implications to vaccinations. Vaccine. 2022 May 26;40(24):3345-3355.

Introduction: The aim of this study was to investigate how age and underlying medical conditions affect the risk of severe outcomes following SARS-CoV-2 infection and how they should be weighed while prioritising vaccinations against COVID-19. Methods: This population-based register study includes all SARS-CoV-2 PCR-test-positive cases until 24 Feb 2021, based on the Finnish National Infectious Diseases Register. The cases were linked to other registers to identify presence of predisposing factors and severe outcomes (hospitalisation, intensive care treatment, death). The odds of severe outcomes were compared in those with and without the pre-specified predisposing factors using logistic regression. Furthermore, population-based rates were compared between those with a given predisposing factor and those without any of the specified predisposing factors using negative binomial regression. Results: Age and various comorbidities were found to be predictors of severe COVID-19. Compared to 60-69-year-olds, the odds ratio (OR) of death was 7.1 for 70-79-year-olds, 26.7 for 80-89-year-olds, and 55.8 for ≥ 90-year-olds. Among the 20-69-year-olds, chronic renal disease (OR 9.4), malignant neoplasms (5.8), hematologic malignancy (5.6), chronic pulmonary disease (5.4), and cerebral palsy or other paralytic syndromes (4.6) were strongly associated with COVID-19 mortality; severe disorders of the immune system (8.0), organ or stem cell transplant (7.2), chronic renal disease (6.7), and diseases of myoneural junction and muscle (5.5) were strongly associated with COVID-19 hospitalisation. Type 2 diabetes and asthma, two very common comorbidities, were associated with all three outcomes, with ORs from 2.1 to 4.3. The population-based rate of SARS-CoV-2 infection decreased with age. Taking the 60-69-year-olds as reference, the rate ratio was highest (3.0) for 20-29-year-olds and < 1 for 70-79-year-olds and 80-89-year-olds. Conclusion: Comorbidities predispose for severe COVID-19 among younger ages. In vaccine prioritisation both the risk of infection and the risk of severe outcomes, if infected, should be considered.

3.4.9 Poukka E, Baum U, Palmu AA, Lehtonen TO, Salo H, Nohynek H, Leino T. Cohort study of Covid-19 vaccine effectiveness among healthcare workers in Finland, December 2020 - October 2021. Vaccine. 2022 Jan 31;40(5):701-705.

Recently, Covid-19 vaccine effectiveness has decreased especially against mild disease due to emergence of the Delta variant and waning protection. In this register-based study among

healthcare workers in Finland, the vaccine effectiveness of two-dose mRNA vaccine series against SARS-CoV-2 infection decreased from 82% (95% CI 79-85%) 14-90 days after vaccination to 53% (43-62%) after 6 months. Similar trend was observed for other series. Waning was not observed against Covid-19 hospitalization. These results facilitate decision-making of booster doses for healthcare workers.

3.4.10 Baum U, Poukka E, Palmu AA, Salo H, Lehtonen TO, Leino T. 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. PLoS One. 2021 Nov 18;16(11):e0258704

Background: In Finland, both mRNA and adenovirus vector (AdV) Covid-19 vaccines have been used after the vaccination campaign started on December 27, 2020. Vaccination of the elderly and chronically ill was prioritized and the interval between doses set to 12 weeks. The objective of this interim analysis was to evaluate first and second dose vaccine effectiveness (VE) in a real-world setting. Methods: During the first five months of the campaign, a register-based cohort study was conducted in the Finnish elderly aged 70+ years and those aged 16-69 years with medical conditions predisposing to severe Covid-19 (chronically ill). Using Cox regression, VE against SARS-CoV-2 infection and Covid-19 hospitalisation was estimated comparing the hazard in the vaccinated with that in the unvaccinated. Results: The cohorts included 901092 elderly (89% vaccinated) and 774526 chronically ill (69% vaccinated) individuals. Three weeks after the first dose, mRNA VE against infection was 45% (95% confidence interval, 36-53%) and 40% (26-51%) in elderly and chronically ill; mRNA VE against hospitalisation was 63% (49-74%) and 82% (56-93%). In chronically ill, AdV VE was 42% (32-50) and 62% (42-75%) against infection and hospitalisation, respectively. One week after the second dose, mRNA VE against infection was 75% (65-82%) and 77% (65-85%) in elderly and chronically ill; mRNA VE against hospitalisation was 93% (70-98%) and 90% (29-99%). Conclusions: Covid-19 vaccines protect against SARS-CoV-2 infection and Covid-19 hospitalisation. A single dose provides moderate protection in elderly and chronically ill, although two doses are clearly superior.

3.5 Vaccine safety monitoring

Potential questions/outcomes: How are the registers helping to monitor vaccines for adults safety? Which studies have been conducted and what were the outcome relevant for the NVP and public health? Are there general lessons learned from this research?

3.5.1 Hviid A, Nieminen TA, Pihlström N, Gunnes N, Dahl J, Karlstad Ø, Gulseth HL, Sundström A, Husby A, Hansen JV, Ljung R, Hovi P. Booster vaccination with SARS-CoV-2 mRNA vaccines and myocarditis in adolescents and young adults: a Nordic cohort study. Eur Heart J. 2024 Apr 14;45(15):1327-1335.

Background and aims: The SARS-CoV-2 mRNA vaccines are associated with an increased risk of myocarditis. This association appears to be strongest in male adolescents and younger males and after the second dose. The aim was to evaluate the risk of myocarditis following SARS-CoV-2 mRNA booster vaccination in 12-to-39-year-olds. Methods: A multinational cohort study was conducted using nationwide register data in Denmark, Finland, Norway, and Sweden and comprising all 8.9 million individuals residing in each of the four countries. Participants were followed for an inpatient diagnosis of myocarditis. In each of the four countries, Poisson regression was used to estimate adjusted incidence rate ratios (IRRs) of myocarditis comparing vaccination schedules, with associated 95% confidence intervals (CIs).

Country-specific results were combined in meta-analyses. Results: A total of 8.9 million residents were followed for 12 271 861 person-years and 1533 cases of myocarditis were identified. In 12-to-39-year-old males, the 28-day acute risk period following the third dose of BNT162b2 or mRNA-1273 was associated with an increased incidence rate of myocarditis compared to the post-acute risk period 28 days or more after the second dose [IRR 2.08 (95% CI 1.31-3.33) and 8.89 (2.26-35.03), respectively]. For females, the corresponding IRR was only estimable for BNT162b2, 3.99 (0.41-38.64). The corresponding absolute risks following the third dose of BNT162b2 and mRNA-1273 in males were 0.86 (95% CI 0.53-1.32) and 1.95 (0.53-4.99) myocarditis events within 28 days per 100 000 individuals vaccinated, respectively. In females, the corresponding absolute risks following the third dose of BNT162b2 were 0.15 (0.04-0.39) events per 100 000 individuals vaccinated. No deaths occurred within 30 days of vaccine-related cases. Conclusions: The results suggest that a booster dose is associated with increased myocarditis risk in adolescents and young adults. However, the absolute risk of myocarditis following booster vaccination is low.

3.5.2 Faksova K, Walsh D, Jiang Y, Griffin J, Phillips A, Gentile A, Kwong JC, Macartney K, Naus M, Grange Z, Escolano S, Sepulveda G, Shetty A, Pillsbury A, Sullivan C, Naveed Z, Janjua NZ, Giglio N, Perälä J, Nasreen S, Gidding H, Hovi P, Vo T, Cui F, Deng L, Cullen L, Artama M, Lu H, Clothier HJ, Batty K, Paynter J, Petousis-Harris H, Buttery J, Black S, Hviid A. COVID-19 vaccines and adverse events of special interest: A multinational Global Vaccine Data Network (GVDN) cohort study of 99 million vaccinated individuals. Vaccine. 2024 Apr 2;42(9):2200-2211

Background: The Global COVID Vaccine Safety (GCoVS) Project, established in 2021 under the multinational Global Vaccine Data Network™ (GVDN®), facilitates comprehensive assessment of vaccine safety. This study aimed to evaluate the risk of adverse events of special interest (AESI) following COVID-19 vaccination from 10 sites across eight countries. Methods: Using a common protocol, this observational cohort study compared observed with expected rates of 13 selected AESI across neurological, haematological, and cardiac outcomes. Expected rates were obtained by participating sites using pre-COVID-19 vaccination healthcare data stratified by age and sex. Observed rates were reported from the same healthcare datasets since COVID-19 vaccination program rollout. AESI occurring up to 42 days following vaccination with mRNA (BNT162b2 and mRNA-1273) and adenovirus-vector (ChAdOx1) vaccines were included in the primary analysis. Risks were assessed using observed versus expected (OE) ratios with 95 % confidence intervals. Prioritised potential safety signals were those with lower bound of the 95 % confidence interval (LBCI) greater than 1.5. Results: Participants included 99,068,901 vaccinated individuals. In total, 183,559,462 doses of BNT162b2, 36,178,442 doses of mRNA-1273, and 23,093,399 doses of ChAdOx1 were administered across participating sites in the study period. Risk periods following homologous vaccination schedules contributed 23,168,335 person-years of follow-up. OE ratios with LBCI > 1.5 were observed for Guillain-Barré syndrome (2.49, 95 % CI: 2.15, 2.87) and cerebral venous sinus thrombosis (3.23, 95 % CI: 2.51, 4.09) following the first dose of ChAdOx1 vaccine. Acute disseminated encephalomyelitis showed an OE ratio of 3.78 (95 % CI: 1.52, 7.78) following the first dose of mRNA-1273 vaccine. The OE ratios for myocarditis and pericarditis following BNT162b2, mRNA-1273, and ChAdOx1 were significantly increased with LBCIs > 1.5. Conclusion: This multi-country analysis confirmed pre-established safety signals for myocarditis, pericarditis, Guillain-Barré syndrome, and cerebral venous sinus thrombosis. Other potential safety signals that require further investigation were identified.

3.5.3 Machado, M. A. d. A., Gandhi-Banga, S., Gallo, S., Cousseau, T. G., Byrareddy, R. M., Nissilä, M., Schelling, J. and Monfredo, C. (2024). "Enhanced passive safety surveillance of

high-dose and standard-dose quadrivalent inactivated split-virion influenza vaccines in Germany and Finland during the 2022/23 influenza season." Human Vaccines & Immunotherapeutics 20(1): 2322196.

Enhanced Passive Safety Surveillance (EPSS) was conducted for quadrivalent inactivated split-virion influenza vaccines (IIV4) in Germany (high dose [HD]) and Finland (standard dose [SD]) for the northern hemisphere (NH) 2022/23 influenza season. The primary objective was to assess adverse events following immunization (AEFI) occurring ≤7 days post-vaccination. In each country, the EPSS was conducted at the beginning of the NH influenza season. Exposure information was documented using vaccination cards (VC), and AEFI were reported via an electronic data collection system or telephone. AEFI were assessed by seriousness and age group (Finland only). The vaccinee reporting rate (RR) was calculated as the number of vaccinees reporting ≥ 1 AEFI divided by the total vaccinees. In Germany, among 1041 vaccinees, there were 31 AEFI (ten vaccinees) during follow-up, including one serious AEFI. Of 16 AEFI (six vaccinees) with reported time of onset, 15 occurred ≤7 days post-vaccination (RR 0.58%, 95% confidence interval [CI] 0.21, 1.25), which was lower than the 2021/22 season (RR 1.88%, 95% CI: 1.10, 3.00). In Finland, among 1001 vaccinees, there were 142 AEFI (51 vaccinees) during follow-up, none of which were serious. Of 133 AEFI (48 vaccinees) with time of onset reported, all occurred ≤7 days post-vaccination (RR 4.80%, 95% CI: 3.56, 6.31), which was similar to the 2021/22 season (RR 4.90%, 95% CI: 3.65, 6.43). The EPSS for HD-IIV4 and for SD-IIV4 in the 2022/23 influenza season did not suggest any clinically relevant changes in safety beyond what is known/expected for IIV4s.

3.5.4 Salmon DA, Lambert PH, Nohynek HM, Gee J, Parashar UD, Tate JE, Wilder-Smith A, Hartigan-Go KY, Smith PG, Zuber PLF. Novel vaccine safety issues and areas that would benefit from further research. BMJ Glob Health. 2021 May;6(Suppl 2):e003814.

Vaccine licensure requires a very high safety standard and vaccines routinely used are very safe. Vaccine safety monitoring prelicensure and postlicensure enables continual assessment to ensure the benefits outweigh the risks and, when safety problems arise, they are quickly identified, characterised and further problems prevented when possible. We review five vaccine safety case studies: (1) dengue vaccine and enhanced dengue disease, (2) pandemic influenza vaccine and narcolepsy, (3) rotavirus vaccine and intussusception, (4) human papillomavirus vaccine and postural orthostatic tachycardia syndrome and complex regional pain syndrome, and (5) RTS,S/adjuvant system 01 malaria vaccine and meningitis, cerebral malaria, female mortality and rebound severe malaria. These case studies were selected because they are recent and varied in the vaccine safety challenges they elucidate. Bringing these case studies together, we develop lessons learned that can be useful for addressing some of the potential safety issues that will inevitably arise with new vaccines.

3.6 Finnish national registers in clinical trial settings

Potential questions/outcomes: How are registers used for clinical research? Give examples of candidate vaccines for adults (focus on other vaccines than COVID-19/Influenza, previous talks). What are the added values and the potential pitfalls?

3.6.1 FIMEA website: https://fimea.fi/en/-/possibility-to-access-finnish-institute-for-health-and-welfare-register-data-in-clinical-trials-from-1-january-2024-onwards

Act on the National Institute for Health and Welfare and the Act on Clinical Trials on Medicinal Products are updated on 1 January 2024. After the change, the sponsor, their representative, researcher and a member of the research group have the right to obtain data from the Care Register for Health Care (Hilmo), the Register of Primary Health Care Visits (AvoHilmo) and on microbial findings from the Finnish National Infectious Diseases Register from the National Institute for Health and Welfare, if this information is essential for carrying out the trial. In order to assess essentialness, the use of the data must be justified in the study protocol, for example in terms of the experimental design or methodology of the clinical trial. The register intended for use in data retrieval should also be included in the study protocol. More detailed information will be filled in in application for the National Institute of Health and Welfare (additional instructions will be available).

Disclosure of data for a clinical trial requires a positive decision of the clinical trial, which also includes an authorisation subject to conditions. Once the use of the register data has been justified in the study protocol and is available for inspection, a note on the use of register data is recorded in Fimea's positive decision: "According to the research plan, the purpose of the research is to utilise the register data referred to in section 34 of the Act on Clinical Trials on Medicinal Products. Fimea and Tukija have assessed the use of the data in relation to the requirement laid down in Articles 3(b) and 6(1)(b)(i) of the EU Clinical Trials Regulation on the reliability and robustness of the data produced in clinical trials and consider the use of the data to be essential for the experimental design of the trial." If Fimea or Tukija finds that there are not sufficient grounds for using register data, additional questions will be asked during the assessment phase of the trial. If the use of register data is not considered justified even after the responses, the use of the data will not be authorised. As usual, participants sign their consent to take part in the clinical trial. However, this right of access to register data may also be exercised in emergency clinical trials if the trial has received such authorisation. The patient information document template can be found on the Tukija website (pdf, in Finnish).

Session 4: Epidemiology, Disease Burden, and Surveillance of Vaccine Preventable Infections in Adults

Session 4: Epidemiology, Disease Burden, and Surveillance of Vaccine-Preventable Infections in Adults	4.1 Assessing the burden of Herpes zoster from the population-based, individually linkable, nationwide administrative register data	Heini Salo
	4.2 National Surveillance of RSV in Finland	Toni Lehtonen
	4.3 Population impact of infant pneumococcal vaccination on invasive pneumococcal disease in adults in Finland	J Pekka Nuorti
	4.4 Immune surveillance for vaccine-preventable diseases	Merit Melin

4.1 Assessing the burden of Herpes zoster from the population-based, individually linkable, nationwide administrative register data

Potential questions/outcomes: What is the epidemiology and burden of herpes zoster (are there data gaps)? What is the main reason that THL doesn't has a recommended use of the herpes zoster (shingles) vaccine. Is this expected to change in the near future? Do you expect an impact of the childhood vaccination program? Can this affect current recommendations? If yes, how?

4.1.1 Poster at EuGMS (funding by GSK) - Heinonen SE. Health and economic burden of herpes zoster in older adults in Finland: a retrospective database study

A two-dose varicella vaccination programme at the age of 18 months and 6 years started in September 2017 in Finland with catch-up vaccinations, based on earlier modelling results, for children <12 years (born in 2006 or later) with no history of varicella. Nationwide population-based register data were used to assess the age-specific vaccination coverage and the annual incidence rates of varicella cases contacting public primary health care in 2014-2020. Age-specific incidence rates after (2022) and before (2014-2016) the implementation of the vaccination programme was compared by incidence rate ratios (IRR) with 95 % confidence interval. In 2019-2022, the first-dose coverage of varicella vaccination among children following the routine vaccination programme ranged from 85 to 87 % (children born in 2016 or later). The second-dose coverage was 58 % for the children born in 2016. The coverage of the catch-up vaccinations ranged from 18 % (children born in 2006) to 82 % (children born in 2015) for the first dose and from 10 % to 64 % for the second dose in the respective birth cohorts. In 2022, compared to the pre-vaccination period (2014-2016) the annual incidence rate of varicella cases contacting public primary health care declined in all age groups. The reduction ranged from 92 % to 98 % among the children eligible for the vaccinations (born 2006 or later). The 87 % reduction in the incidence rate among the unvaccinated children < 1 year suggests the indirect effect of the vaccinations. Introducing varicella vaccinations with catch-up was associated with rapid reduction in the varicella cases contacting primary health care in all ages. However, the coverage of the routine programme needs to be improved further as presently susceptibles accumulate and enable thus further outbreaks in coming decades.

4.1.2 Salo H, Perälä J, Hannila-Handelberg T, Sarvikivi E, Luomala O, Ollgren J, Leino T. Decline in varicella cases contacting primary health care after introduction of varicella vaccination in Finland - A population-based register study. Vaccine. 2023 Oct 13;41(43):6535-6541.

A two-dose varicella vaccination programme at the age of 18 months and 6 years started in September 2017 in Finland with catch-up vaccinations, based on earlier modelling results, for children <12 years (born in 2006 or later) with no history of varicella. Nationwide population-based register data were used to assess the age-specific vaccination coverage and the annual incidence rates of varicella cases contacting public primary health care in 2014-2020. Age-specific incidence rates after (2022) and before (2014-2016) the implementation of the vaccination programme was compared by incidence rate ratios (IRR) with 95 % confidence interval. In 2019-2022, the first-dose coverage of varicella vaccination among children following the routine vaccination programme ranged from 85 to 87 % (children born in 2016

or later). The second-dose coverage was 58 % for the children born in 2016. The coverage of the catch-up vaccinations ranged from 18 % (children born in 2006) to 82 % (children born in 2015) for the first dose and from 10 % to 64 % for the second dose in the respective birth cohorts. In 2022, compared to the pre-vaccination period (2014-2016) the annual incidence rate of varicella cases contacting public primary health care declined in all age groups. The reduction ranged from 92 % to 98 % among the children eligible for the vaccinations (born 2006 or later). The 87 % reduction in the incidence rate among the unvaccinated children < 1 year suggests the indirect effect of the vaccinations. Introducing varicella vaccinations with catch-up was associated with rapid reduction in the varicella cases contacting primary health care in all ages. However, the coverage of the routine programme needs to be improved further as presently susceptibles accumulate and enable thus further outbreaks in coming decades.

4.1.3 Poletti P, Melegaro A, Ajelli M, Del Fava E, Guzzetta G, Faustini L, Scalia Tomba G, Lopalco P, Rizzo C, Merler S, Manfredi P. Perspectives on the impact of varicella immunization on herpes zoster. A model-based evaluation from three European countries. PLoS One. 2013 Apr 17;8(4):e60732.

The introduction of mass vaccination against Varicella-Zoster-Virus (VZV) is being delayed in many European countries because of, among other factors, the possibility of a large increase in Herpes Zoster (HZ) incidence in the first decades after the initiation of vaccination, due to the expected decline of the boosting of Cell Mediated Immunity caused by the reduced varicella circulation. A multi-country model of VZV transmission and reactivation, is used to evaluate the possible impact of varicella vaccination on HZ epidemiology in Italy, Finland and the UK. Despite the large uncertainty surrounding HZ and vaccine-related parameters, surprisingly robust medium-term predictions are provided, indicating that an increase in HZ incidence is likely to occur in countries where the incidence rate is lower in absence of immunization, possibly due to a higher force of boosting (e.g. Finland), whereas increases in HZ incidence might be minor where the force of boosting is milder (e.g. the UK). Moreover, a convergence of HZ post vaccination incidence levels in the examined countries is predicted despite different initial degrees of success of immunization policies. Unlike previous model-based evaluations, our investigation shows that after varicella immunization an increase of HZ incidence is not a certain fact, rather depends on the presence or absence of factors promoting a strong boosting intensity and which might or not be heavily affected by changes in varicella circulation due to mass immunization. These findings might explain the opposed empirical evidences observed about the increases of HZ in sites where mass varicella vaccination is ongoing.

4.1.4 Karhunen M, Leino T, Salo H, Davidkin I, Kilpi T, Auranen K. Modelling the impact of varicella vaccination on varicella and zoster. Epidemiol Infect. 2010 Apr;138(4):469-81. doi: 10.1017/S0950268809990768. Epub 2009 Oct 2. PMID: 19796447.

It has been suggested that the incidence of herpes zoster may increase due to lack of natural boosting under large-scale vaccination with the varicella vaccine. To study the possibility and magnitude of such negative consequences of mass vaccination, we built a mathematical model of varicella and zoster epidemiology in the Finnish population. The model was based on serological data on varicella infection, case-notification data on zoster, and new knowledge about close contacts relevant to transmission of infection. According to the analysis, a childhood programme against varicella will increase the incidence of zoster by one to more than two thirds in the next 50 years. This will be due to increase in case numbers in the 35

years age groups. However, high vaccine coverage and a two-dose programme will be very effective in stopping varicella transmission in the population.

4.2 National Surveillance of RSV in Finland

Potential questions/outcomes: What is the epidemiology and burden of RSV in adults in Finland? Are there gaps in the data? Can the data from RSV be compared with influenza/COVID-19. What are the main challenges?

4.2.1 Poukka E, van Roekel C, Turunen T, Baum U, Kramer R, Begier E, Presser L, Teirlinck A, Heikkinen T, Knol M, Nohynek H; PROMISE Investigators. Effectiveness of Vaccines and Monoclonal Antibodies Against Respiratory Syncytial Virus: Generic Protocol for Register-Based Cohort Study. J Infect Dis. 2024 Mar 1;229(Supplement_1):S84-S91.

Several immunization products are currently being developed against respiratory syncytial virus (RSV) for children, pregnant females, and older adults, and some products have already received authorization. Therefore, studies to monitor the effectiveness of these products are needed in the following years. To assist researchers to conduct postmarketing studies, we developed a generic protocol for register-based cohort studies to evaluate immunization product effectiveness against RSV-specific and nonspecific outcomes. To conduct a study on the basis of this generic protocol, the researchers can use any relevant databases or healthcare registers that are available at the study site.

4.2.2 Deng S, Guo L, Cohen C, Meijer A, Moyes J, Pasittungkul S, Poovorawan Y, Teirlinck A, van Boven M, Wanlapakorn N, Wolter N, Paget J, Nair H, Li Y; Respiratory Virus Global Epidemiology Network and the PROMISE Investigators. Impact of Subgroup Distribution on Seasonality of Human Respiratory Syncytial Virus: A Global Systematic Analysis. J Infect Dis. 2024 Mar 1;229(Supplement_1):S25-S33.

Background: Previous studies reported inconsistent findings regarding the association between respiratory syncytial virus (RSV) subgroup distribution and timing of RSV season. We aimed to further understand the association by conducting a global-level systematic analysis. Methods: We compiled published data on RSV seasonality through a systematic literature review, and unpublished data shared by international collaborators. Using annual cumulative proportion (ACP) of RSV-positive cases, we defined RSV season onset and offset as ACP reaching 10% and 90%, respectively. Linear regression models accounting for meteorological factors were constructed to analyze the association of proportion of RSV-A with the corresponding RSV season onset and offset. Results: We included 36 study sites from 20 countries, providing data for 179 study-years in 1995-2019. Globally, RSV subgroup distribution was not significantly associated with RSV season onset or offset globally, except for RSV season offset in the tropics in 1 model, possibly by chance. Models that included RSV subgroup distribution and meteorological factors explained only 2%-4% of the variations in timing of RSV season. Conclusions: Year-on-year variations in RSV season onset and offset are not well explained by RSV subgroup distribution or meteorological factors. Factors including population susceptibility, mobility, and viral interference should be examined in future studies.

4.2.3 Osei-Yeboah R, Spreeuwenberg P, Del Riccio M, Fischer TK, Egeskov-Cavling AM, Bøås H, van Boven M, Wang X, Lehtonen T, Bangert M, Campbell H, Paget J; Respiratory Syncytial Virus Consortium in Europe (RESCEU) Investigators. Estimation of the Number of

Respiratory Syncytial Virus-Associated Hospitalizations in Adults in the European Union. J Infect Dis. 2023 Nov 28;228(11):1539-1548.

Background: Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infections in adults that can result in hospitalizations. Estimating RSV-associated hospitalization is critical for planning RSV-related healthcare across Europe. Methods: We gathered RSV-associated hospitalization estimates from the RSV Consortium in Europe (RESCEU) for adults in Denmark, England, Finland, Norway, Netherlands, and Scotland from 2006 to 2017. We extrapolated these estimates to 28 European Union (EU) countries using nearest-neighbor matching, multiple imputations, and 2 sets of 10 indicators. Results: On average, 158 229 (95% confidence interval [CI], 140 865-175 592) RSV-associated hospitalizations occur annually among adults in the EU (≥18 years); 92% of these hospitalizations occur in adults ≥65 years. Among 75-84 years, the annual average is estimated at 74 519 (95% CI, 69 923-79 115) at a rate of 2.24 (95% CI, 2.10-2.38) per 1000. Among ≥85 years, the annual average is estimated at 37 904 (95% CI, 32 444-43 363) at a rate of 2.99 (95% CI, 2.56-3.42). Conclusions: Our estimates of RSV-associated hospitalizations in adults are the first analysis integrating available data to provide the disease burden across the EU. Importantly, for a condition considered in the past to be primarily a disease of young children, the average annual hospitalization estimate in adults was lower but of a similar magnitude to the estimate in young children (0-4 years): 158 229 (95% CI, 140 865-175 592) versus 245 244 (95% CI, 224 688-265 799).

4.2.4 Kenmoe S, Chu HY, Dawood FS, Milucky J, Kittikraisak W, Matthewson H, Kulkarni D, Suntarattiwong P, Frivold C, Mohanty S, Havers F, Li Y, Nair H; PROMISE Investigators. Burden of Respiratory Syncytial Virus-Associated Acute Respiratory Infections During Pregnancy. J Infect Dis. 2024 Mar 1;229(Supplement_1):S51-S60.

Background: With the licensure of maternal respiratory syncytial virus (RSV) vaccines in Europe and the United States, data are needed to better characterize the burden of RSV-associated acute respiratory infections (ARI) in pregnancy. The current study aimed to determine among pregnant individuals the proportion of ARI testing positive for RSV and the RSV incidence rate, RSV-associated hospitalizations, deaths, and perinatal outcomes. Methods: We conducted a systematic review, following PRISMA 2020 guidelines, using 5 databases (Medline, Embase, Global Health, Web of Science, and Global Index Medicus), and including additional unpublished data. Pregnant individuals with ARI who had respiratory samples tested for RSV were included. We used a random-effects meta-analysis to generate overall proportions and rate estimates across studies. Results: Eleven studies with pregnant individuals recruited between 2010 and 2022 were identified, most of which recruited pregnant individuals in community, inpatient and outpatient settings. Among 8126 pregnant individuals, the proportion with ARI that tested positive for RSV ranged from 0.9% to 10.7%, with a meta-estimate of 3.4% (95% confidence interval [CI], 1.9%-54%). The pooled incidence rate of RSV among pregnant individuals was 26.0 (95% CI, 15.8-36.2) per 1000 person-years. RSV hospitalization rates reported in 2 studies were 2.4 and 3.0 per 1000 person-years. In 5 studies that ascertained RSV-associated deaths among 4708 pregnant individuals, no deaths were reported. Three studies comparing RSV-positive and RSV-negative pregnant individuals found no difference in the odds of miscarriage, stillbirth, low birth weight, and small size for gestational age. RSV-positive pregnant individuals had higher odds of preterm delivery (odds ratio, 3.6 [95% CI, 1.3-10.3]). Conclusions: Data on RSV-associated hospitalization rates are limited, but available estimates are lower than those reported in older adults and young children. As countries debate whether to include RSV vaccines in maternal vaccination programs, which are primarily intended to protect infants, this information could be useful in shaping vaccine policy decisions.

4.2.5 van Boven M, Teirlinck AC, Meijer A, Hooiveld M, van Dorp CH, Reeves RM, Campbell H, van der Hoek W; RESCEU Investigators. Estimating Transmission Parameters for Respiratory Syncytial Virus and Predicting the Impact of Maternal and Pediatric Vaccination. J Infect Dis. 2020 Oct 7;222(Suppl 7):S688-S694

Background: Respiratory syncytial virus (RSV) is a leading cause of respiratory tract illness in young children and a major cause of hospital admissions globally. Methods: Here we fit age-structured transmission models with immunity propagation to data from the Netherlands (2012-2017). Data included nationwide hospitalizations with confirmed RSV, general practitioner (GP) data on attendance for care from acute respiratory infection, and virological testing of acute respiratory infections at the GP. The transmission models, equipped with key parameter estimates, were used to predict the impact of maternal and pediatric vaccination. Results: Estimates of the basic reproduction number were generally high (R0 > 10 in scenarios with high statistical support), while susceptibility was estimated to be low in nonelderly adults (<10% in persons 20-64 years) and was higher in older adults (≥65 years). Scenario analyses predicted that maternal vaccination reduces the incidence of infection in vulnerable infants (<1 year) and shifts the age of first infection from infants to young children. Conclusions: Pediatric vaccination is expected to reduce the incidence of infection in infants and young children (0-5 years), slightly increase incidence in 5 to 9-year-old children, and have minor indirect benefits.

4.3 Population impact of infant pneumococcal vaccination on invasive pneumococcal disease in adults in Finland

Potential questions/outcomes: What is the disease burden of pneumococcal disease in older adults (are there gaps in the data?). Based on the burden of disease, what are the recommendations regarding vaccination in the adult population? Are any changes expected in the near future? What are the indirect herd effects of the infant pneumococcal vaccination in older age groups? Currently PCV13 (Prevenar 13) and PPV23 (Pneumovax) are used, do you expect changes in the near future?

4.3.1 Narciso, A.R., Dookie, R., Nannapaneni, P. et al. Streptococcus pneumoniae epidemiology, pathogenesis and control. Nat Rev Microbiol (2024).

Infections caused by Streptococcus pneumoniae (also known as pneumococci) pose a threat to human health. Pneumococcal infections are the most common cause of milder respiratory tract infections, such as otitis and sinusitis, and of more severe diseases, including pneumonia (with or without septicaemia) and meningitis. The introduction of pneumococcal conjugate vaccines in the childhood vaccination programme in many countries has led to a notable decrease of severe invasive pneumococcal disease in vaccinated children. However, infections caused by non-vaccine types have concurrently increased, causing invasive pneumococcal disease in unvaccinated populations (such as older adults), which has hampered the effect of these vaccines. Moreover, emerging antibiotic resistance is threatening effective therapy. Thus, new approaches are needed for the treatment and prevention of pneumococcal infections, and recent advances in the field may pave the way for new strategies. Recently, several important findings have been gained regarding pneumococcal epidemiology, genomics and the effect of the introduction of pneumococcal conjugate vaccines and of the COVID-19 pandemic. Moreover, elucidative pathogenesis studies have shown that the interactions between pneumococcal virulence factors and host receptors may be exploited for new

therapies, and new vaccine candidates have been suggested. In this Review, we summarize some recent findings from clinical disease to basic pathogenesis studies that may be of importance for future control strategies.

4.3.2 Arya S, Norton N, Kaushik P, Brandtmüller A, Tsoumani E. Recent changes to adult national immunization programs for pneumococcal vaccination in Europe and how they impact coverage: A systematic review of published and grey literature. Hum Vaccin Immunother. 2023 Dec 15;19(3):227ppn9394.

Despite widespread use of pneumococcal vaccines throughout Europe, the burden of pneumococcal disease (PD) in adults is considerable. To mitigate this burden, National Immunization Technical Advisory Groups (NITAGs) and Health Technology Assessment (HTA) agencies assess the value of different vaccine for protecting against PD. The aim of this review was to assess the evidence and rationales used by NITAGs/HTA agencies, when considering recent changes to National Immunization Programs (NIPs) for adults, and how identified changes affected vaccine coverage rates (VCRs). A systematic review was conducted of published literature from PubMed® and Embase®, and gray literature from HTA/NITAG websites from the last 5 y, covering 31 European countries. Evidence related to NIP recommendations, epidemiology (invasive PD, pneumonia), health economic assessments and VCRs were collected and synthesized. Eighty-four records providing data for 26 countries were identified. Of these, eight described explicit changes to NIPs for adults in seven countries. Despite data gaps, some trends were observed; first, there appears to be a convergence of NIP recommendations in many countries toward sequential vaccination, with a pneumococcal conjugate vaccine (PCV), followed by pneumococcal polysaccharide vaccine 23. Second, reducing economic or healthcare burden were common rationales for implementing changes. Third, most health economic analyses assessing higher-valency PCVs for adults found its inclusion in NIPs cost-effective. Finally, higher coverage rates were seen in most cases where countries had expanded their NIPs to cover at-risk populations. The findings can encourage agencies to improve surveillance systems and work to reach the NIP's target populations more effectively.

4.3.3 Presentation by Heini Salo at AIB technical meeting in Antwerp 21/04/2023 Examples of how health burden estimates are used to recommend adult vaccines in national vaccination programmes Example NITAG (N-Europe): Finland

4.3.4 Nuorti JP, Rinta-Kokko H, Toropainen M, Siira L, Nohynek H, Palmu AA. Long-term population impact of infant 10-valent pneumococcal conjugate vaccination on invasive pneumococcal disease in adults in Finland. Vaccine. 2022 Sep 29;40(41):5950-5958.

Background: Limited data are available on long-term indirect effects of ten-valent pneumococcal conjugate vaccine (PCV10) programmes. We evaluated changes in invasive pneumococcal disease (IPD) incidence, mortality, and serotype distribution in adults up to 9 years after infant PCV10 introduction. Methods: Culture-confirmed IPD cases ≥18 years (n = 5610; 85% were pneumonia) were identified through national, population-based laboratory surveillance; data were linked with population registry to conduct nationwide follow-up study. In a time-series model, we compared serotype-specific IPD incidence and associated 30-day mortality rates before and after PCV10 by using negative binomial regression models. Results: During pre-PCV10 period (7/2004-6/2010), overall IPD incidence in adults ≥18 years increased yearly by 4.8%. After adjusting for trend and seasonality, the observed PCV10

serotype IPD incidence in 7/2018-6/2019 was 90% (12/100,000 person-years) lower than the expected rate without PCV10 program. Non-PCV10 serotype incidence was 40% (4.4/100,000 person-years) higher than expected; serotypes 3, 19A, 22F, and 6C accounted for most of the rate increase. However, incidence of non-PCV10 IPD levelled off by end of follow-up. The observed-expected incidence rate-ratio (IRR) was 0·7 (95 %CI 0·5-0.8) for all IPD and 0·7 (95 %CI 0·3-1·3) for IPD-associated 30-day mortality. Case-fatality proportion decreased from 11·9% to 10.0% (p < 0.01). In persons ≥65 years, the IRR was 0·7 (95 %CI 0·5-0.95). Conclusions: Significant indirect effects were seen for vaccine-serotype IPD and for overall IPD in all adult age groups. For non-vaccine IPD, the incidence stabilized 5 years after infant PVC10 program introduction, resulting in a steady state in which non-vaccine IPD accounted for nearly 90% of overall IPD. Substantial pneumococcal disease burden remains in older adults.

4.3.5 Rinta-Kokko H, Nurhonen M, Auranen K. Impact and effectiveness of a conjugate vaccine against invasive pneumococcal disease in Finland - a modelling approach. Hum Vaccin Immunother. 2021 Jun 3;17(6):1834-1843.

The evaluation of the public health impact of a vaccination program is essential in monitoring its policy relevance. Vaccine impact (VI) is usually assessed in a before-after design, in which data on disease burden without vaccination program is required from a historical reference period. It takes into account the indirect effects and therefore aims to describe the public health performance of the vaccination program in the population. Vaccine effectiveness (VE), measured in parallel settings, quantifies the benefit for an individual of being vaccinated but does not address the indirect effects of a vaccination program. The motivation of this paper is to gain insight into patterns of how VI and VE have manifested under large-scale use of a ten-valent pneumococcal conjugate vaccine in Finnish children. We construct a simple pseudo-dynamic model that mimics typical post-vaccination trends in the incidences of pneumococcal carriage and invasive disease in children when the proportion of vaccine-type carriage decreases. In the context of the model, we define the parameters of interest for VI and VE and explore how their expected values evolve over time. For comparison, we demonstrate the application of VI and VE estimation by using register data.

4.3.6 Hanquet G, Krizova P, Valentiner-Branth P, Ladhani SN, Nuorti JP, Lepoutre A, Mereckiene J, Knol M, Winje BA, Ciruela P, Ordobas M, Guevara M, McDonald E, Morfeldt E, Kozakova J, Slotved HC, Fry NK, Rinta-Kokko H, Varon E, Corcoran M, van der Ende A, Vestrheim DF, Munoz-Almagro C, Latasa P, Castilla J, Smith A, Henriques-Normark B, Whittaker R, Pastore Celentano L, Savulescu C; SpIDnet/I-MOVE+ Pneumo Group. Effect of childhood pneumococcal conjugate vaccination on invasive disease in older adults of 10 European countries: implications for adult vaccination. Thorax. 2019 May;74(5):473-482.

Background: Pneumococcal conjugate vaccines (PCVs) have the potential to prevent pneumococcal disease through direct and indirect protection. This multicentre European study estimated the indirect effects of 5-year childhood PCV10 and/or PCV13 programmes on invasive pneumococcal disease (IPD) in older adults across 13 sites in 10 European countries, to support decision-making on pneumococcal vaccination policies. Methods: For each site we calculated IPD incidence rate ratios (IRR) in people aged ≥65 years by serotype for each PCV10/13 year (2011-2015) compared with 2009 (pre-PCV10/13). We calculated pooled IRR and 95% CI using random-effects meta-analysis and PCV10/13 effect as (1 - IRR)*100. Results: After five PCV10/13 years, the incidence of IPD caused by all types, PCV7 and additional PCV13 serotypes declined 9% (95% CI -4% to 19%), 77% (95% CI 67% to 84%) and 38% (95% CI 19% to 53%), respectively, while the incidence of non-PCV13 serotypes increased 63% (95% CI 39% to 91%). The incidence of serotypes included in PCV13 and not

in PCV10 decreased 37% (95% CI 22% to 50%) in six PCV13 sites and increased by 50% (95% CI -8% to 146%) in the four sites using PCV10 (alone or with PCV13). In 2015, PCV13 serotypes represented 20-29% and 32-53% of IPD cases in PCV13 and PCV10 sites, respectively. Conclusion: Overall IPD incidence in older adults decreased moderately after five childhood PCV10/13 years in 13 European sites. Large declines in PCV10/13 serotype IPD, due to the indirect effect of childhood vaccination, were countered by increases in non-PCV13 IPD, but these declines varied according to the childhood vaccine used. Decision-making on pneumococcal vaccination for older adults must consider the indirect effects of childhood PCV programmes. Sustained monitoring of IPD epidemiology is imperative.

4.3.7 Linkevicius M, Cristea V, Siira L, Mäkelä H, Toropainen M, Pitkäpaasi M, Dub T, Nohynek H, Puumalainen T, Rintala E, Laaksonen ME, Feuth T, Grönroos JO, Peltoniemi J, Frilander H, Lindström I, Sane J. Outbreak of invasive pneumococcal disease among shipyard workers, Turku, Finland, May to November 2019. Euro Surveill. 2019 Dec;24(49):1900681.

We report an outbreak of invasive pneumococcal disease and pneumococcal pneumonia among shipyard workers, in Turku, Southwest Finland. In total, 31 confirmed and six probable cases were identified between 3 May and 28 November 2019. Streptococcus pneumoniae serotypes 12F, 4 and 8 were isolated from blood cultures of 25 cases. Occupational hygiene measures and vaccination of ca 4,000 workers are underway to control the outbreak at the shipyard.

4.3.8 Jokinen J, Snellman M, Palmu AA, Saukkoriipi A, Verlant V, Pascal T, Devaster JM, Hausdorff WP, Kilpi TM. Testing Pneumonia Vaccines in the Elderly: Determining a Case Definition for Pneumococcal Pneumonia in the Absence of a Gold Standard. Am J Epidemiol. 2018 Jun 1;187(6):1295-1302.

Clinical assessments of vaccines to prevent pneumococcal community-acquired pneumonia (CAP) require sensitive and specific case definitions, but there is no gold standard diagnostic test. To develop a new case definition suitable for vaccine efficacy studies, we applied latent class analysis (LCA) to the results from 7 diagnostic tests for pneumococcal etiology on clinical specimens from 323 elderly persons with radiologically confirmed pneumonia enrolled in the Finnish Community-Acquired Pneumonia Epidemiology study during 2005–2007. Compared with the conventional use of LCA, which is mainly to determine sensitivities and specificities of different tests, we instead used LCA as an appropriate instrument to predict the probability of pneumococcal etiology for each CAP case based on individual test profiles, and we used the predictions to minimize the sample size that would be needed for a vaccine efficacy trial. When compared with the conventional laboratory criteria of encapsulated pneumococci in culture, in blood culture or high-quality sputum culture, or urine antigen positivity, our optimized case definition for pneumococcal CAP resulted in a trial sample size that was almost 20,000 subjects smaller. We believe that the novel application of LCA detailed here to determine a case definition for pneumococcal CAP could also be similarly applied to other diseases without a gold standard.

4.3.9 Okasha O, Rinta-Kokko H, Palmu AA, Ruokokoski E, Jokinen J, Nuorti JP. Population-level impact of infant 10-valent pneumococcal conjugate vaccination on adult pneumonia hospitalisations in Finland. Thorax. 2018 Mar;73(3):262-269.

Introduction: Limited data are available on population-level herd effects of infant 10-valent pneumococcal conjugate vaccine (PCV10) programmes on pneumonia. We assessed national

trends in pneumococcal and all-cause pneumonia hospitalisations in adults aged ≥18 years, before and after infant PCV10 introduction in 2010. Methods: Monthly hospitalisation rates of International Statistical Classification of Diseases, 10th revision (ICD-10)-coded primary discharge diagnoses compatible with pneumonia from 2004-2005 to 2014-2015 were calculated with population denominators from the population register. Trends in pneumonia before and after PCV10 introduction were assessed with interrupted time-series analysis. Rates during the PCV10 period were estimated from adjusted negative binomial regression model and compared with those projected as continuation of the pre-PCV10 trend. All-cause hospitalisations were assessed for control purposes. Results: Before PCV10, the all-cause pneumonia rate in adults aged ≥18 years increased annually by 2.4%, followed by a 4.7% annual decline during the PCV10 period. In 2014-2015, the overall all-cause pneumonia hospitalisation rate was 109.3/100 000 (95% CI 96.5 to 121.9) or 15.4% lower than the expected rate. A significant 6.7% decline was seen in persons aged ≥65 years (131.5/100 000), which translates to 1456 fewer pneumonia hospitalisations annually. In comparison, hospitalisations other than pneumonia decreased by 3.5% annually throughout the entire study period. Conclusion: These national data suggest that herd protection from infant PCV10 programme has reversed the increasing trend and substantially decreased all-cause pneumonia hospitalisations in adults, particularly the elderly.

4.4 Immune surveillance for vaccine-preventable diseases

Potential questions/outcomes: What studies have been done focused on immunity generated by SARS-CoV-2 infections and vaccines? Which other adult VPI are monitored via immune surveillance in Finland and what is the added value (e.g., COVID-19 booster recommendations). What can we expect in the future?

4.4.1 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.

Data on immune responses following COVID-19 booster vaccinations and subsequent infections in the immunocompromised are limited. We studied antibody responses after the fourth dose and subsequent infections to define patient groups benefiting most from boosters. Fourth vaccine (booster) doses were, in Finland, first recommended for severely immunocompromised individuals, whom we invited to participate in our study in 2022. We assessed spike protein-specific IgG and neutralizing antibodies (NAb) against the ancestral and Omicron BA.1 strains one month after the fourth dose from 488 adult participants and compared them to the levels of 35 healthy controls after three doses. We used Bayesian generalized linear modeling to assess factors explaining antibody levels and assessed vaccine-induced and hybrid immunity six months after the last vaccine dose. Chronic kidney disease (CKD) and immunosuppressive therapy (IT) were identified as factors explaining sub-optimal antibody responses. The proportion of participants with a normal antibody response and NAbs was significantly lower regarding CKD patients compared to the controls. By the 6-month sampling point, one-third of the participants became infected (documented by serology and/or molecular tests), which notably enhanced antibody levels in most immunocompromised participants. Impaired antibody responses, especially NAbs against the Omicron lineage, suggest limited protection in individuals with CKD and highlight the need for alternative pharmaceutical preventive strategies. Vaccination strategies should take into account the development of robust hybrid immunity responses also among the immunocompromised.

4.4.2 Nieminen TA, Auranen K, Kulathinal S, Härkänen T, Melin M, Palmu AA, Jokinen J. Underreporting of SARS-CoV-2 infections during the first wave of the 2020 COVID-19 epidemic in Finland-Bayesian inference based on a series of serological surveys. PLoS One. 2023 Jun 23;18(6):e0282094.

In Finland, the first wave of the COVID-19 epidemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) took place from March to June 2020, with the majority of COVID-19 cases diagnosed in the Helsinki-Uusimaa region. The magnitude and trend in the incidence of COVID-19 is one way to monitor the course of the epidemic. The diagnosed COVID-19 cases are a subset of the infections and therefore the COVID-19 incidence underestimates the SARS-CoV-2 incidence. The likelihood that an individual with SARS-CoV-2 infection is diagnosed with COVID-19 depends on the clinical manifestation as well as the infection testing policy and capacity. These factors may fluctuate over time and the underreporting of infections changes accordingly. Quantifying the extent of underreporting allows the assessment of the true incidence of infection. To obtain information on the incidence of SARS-CoV-2 infection in Finland, a series of serological surveys was initiated in April 2020. We develop a Bayesian inference approach and apply it to data from the serological surveys, registered COVID-19 cases, and external data on antibody development, to estimate the time-dependent underreporting of SARS-Cov-2 infections during the first wave of the COVID-19 epidemic in Finland. During the entire first wave, there were 1 to 5 (95% probability) SARS-CoV-2 infections for every COVID-19 case. The underreporting was highest before April when there were 4 to 17 (95% probability) infections for every COVID-19 case. It is likely that between 0.5%-1.0% (50% probability) and no more than 1.5% (95% probability) of the adult population in the Helsinki-Uusimaa region were infected with SARS-CoV-2 by the beginning of July 2020.

4.4.3 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.

Studying the prevalence of SARS-CoV-2 specific antibodies (seroprevalence) allows for assessing the impact of epidemic containment measures and vaccinations and estimating the number of infections regardless of viral testing. We assessed antibody-mediated immunity to SARS-CoV-2 induced by infections and vaccinations from April 2020 to December 2022 in Finland by measuring serum IgG to SARS-CoV-2 nucleoprotein (N-IgG) and spike glycoprotein from randomly selected 18-85-year-old subjects (n = 9794). N-IgG seroprevalence remained at <7% until the last quartile (Q) of 2021. After the emergence of the Omicron variant, N-IgG seroprevalence increased rapidly and was 31% in Q1/2022 and 54% in Q4/2022. Seroprevalence was highest in the youngest age groups from Q2/2022 onwards. We did not observe regional differences in seroprevalence in 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. In conclusion, major shifts in the COVID-19 pandemic and resulting population immunity could be observed by serological testing.

4.4.4 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.

Background: Previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection primes the immune system; thus individuals who have recovered from infection have enhanced immune responses to subsequent vaccination (hybrid immunity). However, it remains unclear how well hybrid immunity induced by severe or mild infection can cross-neutralize emerging variants. We aimed to compare the strength and breadth of antibody responses in vaccinated recovered and uninfected subjects. Methods: We measured spike-specific immunoglobulin (Ig)G and neutralizing antibodies (NAbs) from vaccinated subjects including 320 with hybrid immunity and 20 without previous infection. From 29 subjects with a previous severe or mild infection, we also measured NAb responses against Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), and Omicron (B.1.1.529/BA.1) variants following vaccination. Results: A single vaccine dose induced 2-fold higher anti-spike IgG concentrations and up to 4-fold higher neutralizing potency of antibodies in subjects with a previous infection compared with vaccinated subjects without a previous infection. Hybrid immunity was more enhanced after a severe than a mild infection, with sequentially decreasing NAb titers against Alpha, Beta, Delta, and Omicron variants. We found similar IgG concentrations in subjects with a previous infection after 1 or 2 vaccine doses. Conclusions: Hybrid immunity induced strong IgG responses, particularly after severe infection. However, the NAb titers were low against heterologous variants, especially against Omicron.

4.4.5 Dub T, Solastie A, Hagberg L, Liedes O, Nohynek H, Haveri A, Virta C, Vara S, Lasander M, Ekström N, Österlund P, Lind K, Valtonen H, Hemmilä H, Ikonen N, Lukkarinen T, Palmu AA, Melin M. High secondary attack rate and persistence of SARS-CoV-2 antibodies in household transmission study participants, Finland 2020-2021. Front Med (Lausanne). 2022 Jul 28;9:876532.

Background: Household transmission studies offer the opportunity to assess both secondary attack rate (SAR) and persistence of SARS-CoV-2 antibodies over time. Methods: In Spring 2020, we invited confirmed COVID-19 cases and their household members to four visits, where we collected nasopharyngeal and serum samples over 28 days after index case onset. We calculated SAR based on the presence of SARS-CoV-2 neutralizing antibodies (NAb) and assessed the persistence of NAb and IgG antibodies (Ab) against SARS-CoV-2 spike glycoprotein and nucleoprotein. Results: SAR was 45% (39/87), including 35 symptomatic secondary cases. During the initial 28-day follow-up, 62% (80/129) of participants developed NAb. Of those that seroconverted, 90% (63/70), 85% (63/74), and 78% (45/58) still had NAb to early B-lineage SARS-CoV-2 3, 6, and 12 months after the onset of the index case. Anti-spike IgG Ab persisted in 100% (69/69), 97% (72/74), and 93% (55/59) of seroconverted participants after 3, 6, and 12 months, while anti-nucleoprotein IgG Ab levels waned faster, persisting in 99% (68/69), 78% (58/74), and 55% (39/71) of participants, respectively. Conclusion: Following detection of a COVID-19 case in a household, other members had a high risk of becoming infected. NAb to early B-lineage SARS-CoV-2 persisted for at least a year in most cases.

4.4.6 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.

The emergence of SARS-CoV-2 Omicron variant (B.1.1.529) with major spike protein mutations has raised concern over potential neutralization escape and breakthrough infections among vaccinated and previously SARS-CoV-2-infected subjects. We measured cross-protective antibodies against variants in health care workers (HCW, n = 20) and nursing home

residents (n = 9) from samples collected at 1-2 months, following the booster (3rd) dose. We also assessed the antibody responses in subjects infected before the Omicron era (n = 38) with subsequent administration of a single mRNA vaccine dose. Following booster vaccination, HCWs had high IgG antibody concentrations to the spike protein and neutralizing antibodies (NAb) were detectable against all variants. IgG concentrations among the elderly remained lower, and some lacked NAbs against the Beta and Omicron variants. NAb titers were significantly reduced against Delta, Beta, and Omicron compared to WT virus regardless of age. Vaccination induced high IgG concentrations and variable titers of cross-reactive NAbs in previously infected subjects, whereas NAb titers against Omicron were barely detectable 1 month postinfection. High IgG concentrations with cross-protective neutralizing activity were detected after three Coronavirus Disease 2019 (COVID-19) vaccine doses in HCWs. However, lower NAb titers seen in the frail elderly suggest inadequate protection against Omicron breakthrough infections, yet protection against severe COVID-19 is expected.

Session 5: Modeling and economic evaluation studies to support decision-making

Session 5: Modeling and economic evaluation studies to support decision-making	5.1 Modeling to support decision making on vaccination programs	Simopekka Vänskä
	5.2 Using health economic analysis to assess the monetary value of the quality criterion in national vaccine tenders	Heini Salo

5.1 Modeling to support decision making on vaccination programs

Potential questions/outcomes: Address the ways that modeling can help guide and optimize vaccine strategies (give examples for vaccines for adults in Finland). Are modeling results accepted/understood by policy makers? Identify limitations and areas for improvement in current vaccination modeling practices in Finland/Europe.

5.1.1 Lehtinen M, Elfström M, Vänskä S, Dillner J. Elimination of cervical cancer by refined vaccination and screening. Int J Cancer. 2024 Oct 25.

5.1.2 Lehtinen M, Bruni L, Elfström M, Gray P, Logel M, Mariz FC, Baussano I, Vänskä S, Franco EL, Dillner J. Scientific approaches toward improving cervical cancer elimination strategies. Int J Cancer. 2024 May 1;154(9):1537-1548.

At the 2023 EUROGIN workshop scientific basis for strategies to accelerate the elimination of cervical cancer and its causative agent, human papillomavirus (HPV) were reviewed. Although some countries have reached key performance indicators toward elimination (>90% of girls HPV vaccinated and >70% of women HPV screened), most are yet to reach these targets, implying a need for improved strategies. Gender-neutral vaccination, even with moderate vaccination coverage was highlighted as a strategy to achieve elimination more rapidly. It is more resilient against major disturbances in vaccination delivery, such as what happened during the coronavirus pandemic. Further, an analysis of ethical/legal issues indicated that female-restricted vaccination is problematic. Extended catch-up of vaccination with

concomitant screening, and outreach to vulnerable groups were highlighted. Although birth cohorts with high coverage of HPV vaccination at school are protected against HPV, and HPVs have a very low reproductive rate in women above age 35, adult women below age 30 have inadequate direct protection. In addition to herd protection from gender-neutral vaccination, this group can be protected by offering concomitant catch-up HPV vaccination and HPV screening. Furthermore, hepatitis B vaccination experiences indicate that elimination cannot be achieved without prioritizing vulnerable/migrant populations. The long-lasting durability of vaccination-induced antibody responses suggests prolonged protection with HPV vaccines when adequately administrated. Finally, cost-effectiveness modelling suggests that high-coverage HPV vaccination in multiple population segments will be resource-saving due to reduced need for screening. In summary, the workshop found that strategically optimal deployment of vaccination will accelerate elimination of HPV and cervical cancer.

5.1.3 Qendri V, Bogaards JA, Baussano I, Lazzarato F, Vänskä S, Berkhof J. The cost-effectiveness profile of sex-neutral HPV immunisation in European tender-based settings: a model-based assessment. Lancet Public Health. 2020 Nov;5(11):e592-e603. doi: 10.1016/S2468-2667(20)30209-7. Erratum in: Lancet Public Health. 2020 Dec;5(12):e638.

Background: In many European countries, human papillomavirus (HPV) vaccine uptake among girls has remained below target levels, supporting the scope for vaccination of boys. We aimed to investigate if sex-neutral HPV vaccination can be considered cost-effective compared with girls-only vaccination at uptake levels equal to those among girls and under tender-based vaccination costs achieved throughout Europe. Methods: We investigated the cost-effectiveness of sex-neutral HPV vaccination in European tender-based settings. We applied a Bayesian synthesis framework for health economic evaluation to 11 countries (Austria, Belgium, Croatia, Estonia, Italy, Latvia, the Netherlands, Poland, Slovenia, Spain, and Sweden), accommodating country-specific information on key epidemiological and economic parameters, and on current HPV vaccination programmes. We used projections from three independently developed HPV transmission models to tailor region-specific herd effects. The main outcome measures in the comparison of sex-neutral with girls-only vaccination were cancer cases prevented and incremental cost-effectiveness ratios (ICERs), defined as the cost in international dollars (I$) per life-year gained. Findings: The total number of cancer cases to be prevented by vaccinating girls at currently realised vaccine uptake varied from 318 (95% CI 197-405) per cohort of 200 000 preadolescents (100 000 girls plus 100 000 boys) in Croatia (under 20% uptake of the 9-valent vaccine) to 1904 (1741-2101) in Estonia (under 70% uptake of the 9-valent vaccine). Vaccinating boys at equal coverage increased these respective numbers by 168 (95% CI 121-213) in Croatia and 467 (391-587) in Estonia. Sex-neutral vaccination was likely to be cost-effective, with ICERs of sex-neutral compared with girls-only vaccination varying from I$4300 per life-year gained in Latvia (95% credibility interval 3450-5160; 40% uptake) to I$25 720 per life-year gained in Spain (21 380-30 330; 80% uptake). At uniform 80% uptake, a favourable cost-effectiveness profile was retained for most of the countries investigated (Austria, Belgium, Italy, Latvia, the Netherlands, Slovenia, Spain, and Sweden). Interpretation: Sex-neutral HPV vaccination is economically attractive in European tender-based settings. However, tendering mechanisms need to ensure that vaccination of boys will remain cost-effective at high vaccine uptake rates.

5.1.4 Carter A, Msemburi W, Sim SY, Gaythorpe KAM, Lambach P, Lindstrand A, Hutubessy R. Modeling the impact of vaccination for the immunization Agenda 2030: Deaths averted due to vaccination against 14 pathogens in 194 countries from 2021 to 2030. Vaccine. 2024 Apr 8;42 Suppl 1:S28-S37.

Background: The Immunization Agenda 2030 (IA2030) Impact Goal 1.1. aims to reduce the number of future deaths averted through immunization in the next decade. To estimate the potential impact of the aspirational coverage targets for IA2030, we developed an analytical framework and estimated the number of deaths averted due to an ambitious vaccination coverage scenario from 2021 to 2030 in 194 countries. Method: A demographic model was used to determine annual age-specific mortality estimates associated with vaccine coverage rates. For ten pathogens (Hepatitis B virus, Haemophilus influenzae type B, human papillomavirus, Japanese encephalitis, measles, Neisseria meningitidis serogroup A, Streptococcus pneumoniae, rotavirus, rubella, yellow fever), we derived single measures of country-, age-, and pathogen-specific relative risk of deaths conditional upon coverage rates, leveraging the data from 18 modeling groups as part of the Vaccine Impact Model Consortium (VIMC) for 110 countries. We used a logistic regression model to extrapolate the relative risk estimates to countries that were not modeled by VIMC. For four pathogens (diphtheria, tetanus, pertussis and tuberculosis), we used estimates from the Global Burden of Disease 2019 study and existing literature on vaccine efficacy. A future scenario defining years of vaccine introduction and scale-up needed to reach aspirational targets was developed as an input to estimate the long-term impact of vaccination taking place from 2021 to 2030. Findings: Overall, an estimated 51.5 million (95 % CI: 44.0-63.2) deaths are expected to be averted due to vaccinations administered between the years 2021 and 2030. With immunization coverage projected to increase over 2021-2030 an average of 5.2 million per year (4.4-6.3) deaths will be averted annually, with 4.4 million (3.9-5.1) deaths be averted for the year 2021, gradually rising to 5.8 million (4.9-7.5) deaths averted in 2030. The largest proportion of deaths is attributed to Measles and Hepatitis B accounting for 18.8 million (17.8-20.0) and 14.0 million (11.5-16.9) of total deaths averted respectively. Interpretation: The results from this global analysis demonstrate the substantial potential mortality reductions achievable if the IA2030 targets are met by 2030. Deaths caused by vaccine preventable diseases disproportionately affect LMICs in the African region.

5.2 Using health economic analysis to assess the monetary value of the quality criterion in national vaccine tenders

Potential questions/outcomes: How are economic evaluations used in assessing the quality criteria in national vaccine tenders. Give an example of the tendering process (e.g. pneumococcal conjugate vaccine? What is expected in the future?

5.2.1 https://en.opasnet.org/w/Tendering_process_for_pneumococcal_conjugate_vaccine

5.2.2 El Banhawi H., Chowdhury S., Neri M., Radu P., Besley S., Bell E., Brassel S., Steuten L., (2024) Socio-Economic Value of Adult Immunisation Programmes. OHE Contract Research (funded by IFPMA). Available from https://www.ifpma.org/publications/the-socio-economic-value-of-adult-immunisation-programmes-ohe/

This report provides evidence for adult immunisation programmes across ten countries and four vaccines showing that adult immunisation programmes offset their costs multiple times through benefits to individuals, the healthcare system, and wider society. In particular, benefit-cost analysis of the same vaccines showed that adult vaccines can return up to 19

times their initial investment to society, when their significant benefits beyond the healthcare system are monetised. This is the equivalent of billions of dollars in net monetary benefits to society, or more concretely, up to $4637 for one individual's full vaccination course. Despite increasing recognition of the broader value of vaccination, substantial evidence gaps remain, leading to underestimation of vaccine value and risking suboptimal policy decisions. Governments are recommended to adopt a prevention-first mindset to help ease increasing pressures on health systems and society, with adult immunisation playing a crucial role in enabling us to live longer, healthier, and more productive lives. Download this OHE report, commissioned by IFPMA, to learn more about the socio-economic value of adult vaccination programmes on individual lives and societies at large.

5.2.3 Salo H, Sakalauskaitė M, Lévy-Bruhl D, Lindstrand A, Valentiner-Branth P, Wichmann O, Puumalainen T. Prices of paediatric vaccines in European vaccination programmes. Vaccine X. 2023 Sep 20;15:100392.

Objective: To compare the vaccine prices per vaccinated child under 18 and vaccine funding and procurement systems in the national vaccination programmes (NVPs) in Europe. Methods: The on-line survey targeted to NVP managers collected data referred to the information available on 31 December 2016. The prices of vaccines were categorised into three groups. The price per child 1) fully vaccinated comprised all vaccines and doses offered in the NVP; 2) vaccinated with standard vaccines comprised the vaccines included in the NVP in all countries; 3) vaccinated with recent vaccines comprised the pneumococcal conjugate, human papillomavirus and rotavirus vaccines. Results: In the 23 out of 32 countries that answered the survey, 17 funded the vaccines by taxes and six by social insurance. 18 countries procured the vaccines through public tenders or negotiations. Five countries purchased the vaccines by healthcare providers and reimbursed from the health insurance system.In the countries with vaccine procurement through public tenders the price per child vaccinated with standard vaccines ranged from €59 to €117 when using pentavalent and from €98 to €220 when using hexavalent vaccines. The mean price per child vaccinated with recent vaccines was €130 for the countries that offered pneumococcal conjugate and human papillomavirus vaccines and €142 for the countries that in addition included rotavirus vaccine.In the countries that purchased the vaccines by healthcare providers and reimbursed from the health insurance system the price per child vaccinated with standard vaccines ranged from €136 to €427. Conclusions: The vaccine prices differ notably in Europe. Prices were lower in countries where vaccines in the NVP were tax-funded and nationally or regionally procured. Improved procurement systems could lead to substantial savings or possibilities to introduce more vaccines into the NVP.

5.2.4 Salo H, Kilpi T. National vaccination program - a success story of public health and economy. Duodecim. 2017

The savings in treatment costs generated by disease cases prevented by the national vaccination program exceed the costs of the vaccination program by at least 60 million euros. In addition, other costs due to contracting the illness are avoided. Vaccinations serve the purpose of both increasing well-being and releasing resources for other uses. Financial support of vaccinations through the health insurance system would be costly and targetted to those with the ability to pay. Public funds should be directed to the development of a vaccination program. New vaccines coming on the market are expensive. Adding a new vaccine to the vaccination program is based on scientific evidence-based expert assessments and cost-effectiveness. In addition to preliminary assessments carried out in support of

decision-making, the National Institute of Health and Welfare monitors by using population-based health registers the effectiveness and cost-effectiveness of the vaccination program. From the standpoint of transparency of decision-making it would be preferred that the decision-makers define a willingness to pay threshold below which an intervention would be accepted and lead to funding.

5.2.5 PhD Heini Salo – Introduction Economic evaluations in adopting new vaccines in the Finnish national vaccination programme

A direct quote from my PhD thesis (Summary, Discussion, page 86): In Finland, the economic evaluation of the vaccination programme has been part of the decision-making process since 2001. After 2003 there are **five vaccinations** that have been considered for the Finnish NVP and for which an economic evaluation has been conducted. Vaccinations of all **children** aged 6–36 months with **influenza** vaccine were estimated to be cost-saving (II) and the vaccine was accepted into the NVP in **2007**. Infant's **rotavirus** and **pneumococcal** vaccinations were accepted into the NVP in **2008** and **2010** with a cost per QALY gained of EUR 25 000 (230, 231) and EUR 20 490 (232), respectively. Vaccinations of all girls aged 11–13 years with **HPV** vaccine was estimated to be cost-saving (219) and was accepted into the NVP in **2013**. **Varicella** vaccinations were concluded to be acceptably cost-effective with a cost per QALY gained of EUR 15 000 (233). Vaccinations were included in the Government's budget proposal in August 2016 and they will start in **2017**. All these results of economic evaluations are from the **health care provider perspective**.

5.2.6 Ultsch B, Damm O, Beutels P, Bilcke J, Brüggenjürgen B, Gerber-Grote A, Greiner W, Hanquet G, Hutubessy R, Jit M, Knol M, von Kries R, Kuhlmann A, Levy-Bruhl D, Perleth M, Postma M, Salo H, Siebert U, Wasem J, Wichmann O. Methods for Health Economic Evaluation of Vaccines and Immunization Decision Frameworks: A Consensus Framework from a European Vaccine Economics Community. Pharmacoeconomics. 2016 Mar;34(3):227-44.

Background: Incremental cost-effectiveness and cost-utility analyses [health economic evaluations (HEEs)] of vaccines are routinely considered in decision making on immunization in various industrialized countries. While guidelines advocating more standardization of such HEEs (mainly for curative drugs) exist, several immunization-specific aspects (e.g. indirect effects or discounting approach) are still a subject of debate within the scientific community. Objective: The objective of this study was to develop a consensus framework for HEEs of vaccines to support the development of national guidelines in Europe. Methods: A systematic literature review was conducted to identify prevailing issues related to HEEs of vaccines. Furthermore, European experts in the field of health economics and immunization decision making were nominated and asked to select relevant aspects for discussion. Based on this, a workshop was held with these experts. Aspects on 'mathematical modelling', 'health economics' and 'decision making' were debated in group-work sessions (GWS) to formulate recommendations and/or--if applicable--to state 'pros' and 'contras'. Results: A total of 13 different aspects were identified for modelling and HEE: model selection, time horizon of models, natural disease history, measures of vaccine-induced protection, duration of vaccine-induced protection, indirect effects apart from herd protection, target population, model calibration and validation, handling uncertainty, discounting, health-related quality of life, cost components, and perspectives. For decision making, there were four aspects regarding the purpose and the integration of HEEs of vaccines in decision making as well as the variation of parameters within uncertainty analyses and the reporting of results from HEEs. For each

aspect, background information and an expert consensus were formulated. Conclusions: There was consensus that when HEEs are used to prioritize healthcare funding, this should be done in a consistent way across all interventions, including vaccines. However, proper evaluation of vaccines implies using tools that are not commonly used for therapeutic drugs. Due to the complexity of and uncertainties around vaccination, transparency in the documentation of HEEs and during subsequent decision making is essential.

5.2.7 Ultsch B, Damm O, Beutels P, Bilcke J, Brüggenjürgen B, Gerber-Grote AU, Greiner W, Hanquet G, Harder T, Hutubessy R, Jit M, Knol M, Kuhlmann A, von Kries R, Levy-Bruhl D, Perleth M, Postma MJ, Salo H, Siebert U, Wasem J, Weidemann F, Wichmann O. Methods for Health Economic Evaluations of Vaccines - Results from an International Expert-Workshop. Value Health. 2014 Nov;17(7):A552

Objectives - Health economic evaluations (HEEs) of vaccines are commonly considered during immunization introduction decision-making processes in most industrialized countries. Despite the availability of guidelines advocating more standardization for such HEEs, there are still several infection/immunization-specific particularities that are debated in the scientific community. An international expert-workshop was convened to identify good practices for (i) how to conduct HEEs of vaccines and (ii) how to consider results of HEE in vaccine introduction decision-making. Methods - A systematic literature search was conducted to identify prevailing opinions and remaining issues of HEE in vaccination. Twenty-two experts in the field of health economics and immunization decision-making were invited to a workshop and were asked to answer a survey-questionnaire based on the systematic literature search beforehand to inform the preparation of group work sessions (GWS). In GWS, issues focusing on 'mathematical modeling', 'health economics', and 'decision-making' were discussed and summarized. Results - The GWS (based on systematic literature search) included topics such as cost-components, quality of life (QoL), discounting, and perspectives leading to suggestions such as including caregiver QoL impact and applying decreasing time-related discount rates. Since vaccination often causes indirect effects, the use of dynamic models is required and exceptions should be justified. In order to facilitate transparent decision-making, the results of HEE should present parameter and methodological uncertainty as well as cumulative and time-specific figures. The majority of countries in Europe use results from HEEs in an informal judgment-process without willingness to pay (WTP) threshold. The expert-group emphasized that transparency should be maximized in decision-making process. Conclusions - The deliberations led to suggestions on several HEE issues. However, vaccines not always need to be considered differently in HEE since other interventions might share similar characteristics. Transparency in the conduct and presentation of HEE, and subsequent decision-making is essential, especially in the absence of explicit WTP thresholds.

Session 6: Vaccine acceptance and demand

Session 6: Vaccine acceptance and demand	6.1 Finns' relationship to vaccinations	Aapo Kuusipalo
	6.2 The Finland's cultural, behavioural and media insights centre (CUBE)	Tuukka Tammi

6.1 Finns' relationship to vaccinations

Potential questions/outcomes: Provide an overview of recent findings related to the Finn's relationship to vaccination. What are the key factors influencing vaccine confidence among the Finnish population? Are there regional and/or socio-economic variations in vaccine confidence? How do these findings inform public health strategies to address vaccine hesitancy? What specific recommendations have been proposed to counteract vaccine hesitancy? Can you share examples of successful interventions or campaigns that have been implemented based on specific recommendations? How is the vaccine confidence in the Finnish healthcare providers (HCPs)?

6.1.1 Ferrara M, Langiano E, Esposito M, Lo Moro G, Lombardi R, Vuolanto P, De Vito E. Key factors in complex public health interventions to address vaccine hesitancy using a multidisciplinary approach: the VAX-TRUST project. Health Educ Res. 2024 Aug 23:cyae027.

The VAX-TRUST project addresses vaccine hesitancy in seven European countries with a systematic and evidence-based approach. Interventions, targeting healthcare professionals, draw from behavioural and social theories. A checklist, inspired by the TIDieR (Template for Intervention Description and Replication), ensures a detailed description of actions, transparency and replicability. The intervention development process begins with collaborative meetings and systematic revisions, concluding with external evaluations for replicability in diverse public health contexts. This study aims to provide valuable insights for future complex interventions in public health, based on lessons learnt to reduce the risk of vaccine-preventable diseases. The analysis of educational interventions within the VAX-TRUST project has led to the definition of precise guidelines to ensure their replicability and adaptation to various contexts, attempting to establish a universally applicable approach. Active participant engagement and consideration of local social dynamics, beyond information transmission, have emerged as key factors to improve intervention effectiveness. Various educational tools and collaboration with academic institutions have contributed to strengthening credibility.

6.1.2 McCready J, Erfani G, Comparcini D, Cicolini G, Mikkonen K, Keisala J, Tomietto M; Sigma IMPACT Research team. Profiling vaccine hesitancy in nursing to tailor public healthcare policies: A cross-sectional international study. J Nurs Scholarsh. 2024 Aug 14.

Introduction: Vaccine hesitancy is a complex issue of global concern. As nurses play a vital role in delivering patient care and shaping public opinions on vaccines, interventions to address vaccine hesitancy in nursing are imperative. As such, identifying profiles of characteristics and attitudes contributing to hesitancy may help identify specific areas of focus to target tailored global vaccination uptake campaigns. The purpose of this study was to profile the characteristics and attitudes contributing to hesitancy toward COVID-19 and Influenza vaccines in the nursing community. Design: This multisite, cross-sectional study recruited 1967 registered nurses and 1230 nursing students from the United Kingdom, Finland, and Italy between March and September 2023. Methods: Data collection involved an online survey adopting the Vaccination Attitudes Examination (VAX) Scale, the Bergen Social Media Addiction Scale, and questions pertaining to sociodemographic and occupational characteristics. A k-means cluster analysis was used to identify various clusters of hesitancy based on the VAX Scale. One-way ANOVA and chi-square tests were used to identify significant differences in sociodemographic characteristics, occupational factors, vaccination attitudes, and social media usage between the clusters. Results: Three distinct clusters were identified. Profile A showed high vaccine confidence, profile B displayed slight hesitancy, and profile C reported high levels of hesitancy. In profile C, higher levels of vaccine hesitancy were identified in younger, less experienced nurses with lower educational attainment. While older nurses

with higher educational attainment, who were in senior roles, were more vaccine-confident and had a consistent history of accepting the Influenza and COVID-19 vaccinations (profile A). The study found Italian nurses highly hesitant (profile C), British nurses highly confident (profile A), and Finnish nurses evenly distributed between confident, slightly hesitant, and highly hesitant (profiles A, B, and C, respectively). In addition, more frequent usage of Instagram and TikTok was associated with vaccine hesitancy (profiles B and C), and LinkedIn and X were more common among vaccine-confident individuals (profile A). Conclusions: This study has identified specific sociodemographic and occupational factors that are related to vaccine hesitancy in an international sample of nurses. Additionally, attitudes contributing to hesitancy were identified, with worries about unforeseen future effects of the vaccine being identified as a critical attitude that may undermine confidence and increase hesitancy in nursing. This study also sheds light on the influence that social media platforms have on vaccine hesitancy and, as such, indicates which platforms are effective to disseminate vaccination campaigns to global nursing communities. Clinical relevance: Global vaccination campaigns should focus on specific profiles and clusters to promote vaccination in the international nursing community. Empowering nurses early in their careers will help to instill positive vaccination behaviors, ensuring a sustained uptake of vaccinations throughout the individual's career and beyond, with an impact on promoting vaccination at the public health level as well

6.1.3 Hämäläinen A, Patovirta RL, Vuorinen S, Leppäaho-Lakka J, Kilpinen S, Sieberns J, Ruotsalainen E, Koivula I, Hämäläinen S. COVID-19 vaccination among health care workers in Finland: coverage, perceptions and attitudes. Scand J Public Health. 2024 May;52(3):309-315.

Aims: In this study, we examined the voluntary COVID-19 vaccine coverage among health care workers (HCWs) working in close patient contact. HCWs' beliefs about COVID-19 infection, their opinions of vaccination and reasons for having or declining the COVID-19 vaccination were also evaluated. Methods: In October 2021, a cross-sectional observational study was carried out in five hospitals in Central and Eastern Finland. The anonymous and voluntary survey was targeted at 5120 doctors and nurses working in close patient contact. Results: Some 1837 responses were included in the study. Ninety-seven per cent of the respondents had received at least one COVID-19 vaccine and 68% of the respondents agreed that all HCWs working in close patient contact should be vaccinated against COVID-19. Vaccination coverage and support for vaccination were higher among older HCWs and doctors. HCWs' main reasons for having the COVID vaccine were willingness to protect themselves, their family and their patients from COVID-19. Concerns about adverse reactions to the COVID-19 vaccine was the main reason for declining it. Conclusions: The overall COVID-19 vaccination coverage and support for vaccinations among HCWs working in close patient contact were high without actual mandatory policies being introduced. Prioritising HCWs for COVID-19 vaccinations and widespread vaccine availability, as well as low general vaccine hesitancy and high seasonal influenza vaccination coverage among the study population were check marks in achieving high COVID-19 vaccination coverage rapidly.

6.1.4 Lasander M, Elo K, Joronen K, Dub T. Barriers to vaccine acceptance in the adult population of mainland Finland, 2021. Epidemiol Infect. 2024 Mar 15;152:e54. doi: 10.1017/S0950268824000463. Erratum in: Epidemiol Infect. 2024 May 23;152:e79.

There has been a lack of information on vaccine acceptance for Finnish adults. We conducted a secondary analysis of cross-sectional data collected through the Finnish Medicines Agency

Medicine Barometer 2021 survey (response rate: 20.6%). We described and explained vaccine acceptance by investigating the associations between socio-demographic factors and statements using logistic regression and conducted a factor analysis. The majority of respondents (n = 2081) considered vaccines to be safe (93%), effective (97%), and important (95%). However, 20% and 14% felt they did not have enough information about vaccines and vaccine-preventable diseases (VPDs), respectively. Respondents aged 18-39 were 2.8 times more likely to disagree that they had enough information about VPDs compared to respondents aged 60-79 ($p < 0.001$), while respondents with poorer self-perceived health were 1.8 times more likely to declare not having enough information about vaccines ($p < 0.001$). We generated three-factor dimensions from the eight statements. They were related to 'Confidence and attitudes towards vaccines', 'Access to information on vaccines and VPDs', and 'Debate on vaccine issues', which may reflect the underlying thinking patterns. Access to and understanding of information about vaccines and VPDs need to be improved for Finnish adults to increase vaccine acceptance and uptake, thus preventing the spread of VPDs.

6.1.5 Hartonen T, Jermy B, Sõnajalg H, Vartiainen P, Krebs K, Vabalas A; FinnGen; Estonian Biobank Research Team; Leino T, Nohynek H, Sivelä J, Mägi R, Daly M, Ollila HM, Milani L, Perola M, Ripatti S, Ganna A. Nationwide health, socio-economic and genetic predictors of COVID-19 vaccination status in Finland. Nat Hum Behav. 2023 Jul;7(7):1069-1083. doi: 10.1038/s41562-023-01591-z. Epub 2023 Apr 20.

Understanding factors associated with COVID-19 vaccination can highlight issues in public health systems. Using machine learning, we considered the effects of 2,890 health, socio-economic and demographic factors in the entire Finnish population aged 30-80 and genome-wide information from 273,765 individuals. The strongest predictors of vaccination status were labour income and medication purchase history. Mental health conditions and having unvaccinated first-degree relatives were associated with reduced vaccination. A prediction model combining all predictors achieved good discrimination (area under the receiver operating characteristic curve, 0.801; 95% confidence interval, 0.799-0.803). The 1% of individuals with the highest predicted risk of not vaccinating had an observed vaccination rate of 18.8%, compared with 90.3% in the study population. We identified eight genetic loci associated with vaccination uptake and derived a polygenic score, which was a weak predictor in an independent subset. Our results suggest that individuals at higher risk of suffering the worst consequences of COVID-19 are also less likely to vaccinate.

6.1.7 Lohiniva AL, Hussein I, Lehtinen JM, Sivelä J, Hyökki S, Nohynek H, Nuorti P, Lyytikäinen O. Qualitative Insights into Vaccine Uptake of Nursing Staff in Long-Term Care Facilities in Finland. Vaccines (Basel). 2023 Feb 23;11(3):530.

Vaccine hesitancy and refusal have undermined COVID-19 vaccination efforts of nursing staff. This study aimed to identify behavioral factors associated with COVID-19 vaccine uptake among unvaccinated nursing staff in long-term care facilities (LTCF) in Finland. Methodology: The study was based on the Theoretical Domains Framework. Data were collected through qualitative in-depth interviews among nursing staff and managers of LTCFs. The analysis was based on thematic analysis. We identified seven behavioral domains, with several themes, that reduced the staff's intention to get vaccinated: knowledge (information overload, inability to identify trustworthy information sources, lack of vaccine-specific and understandable scientific information), beliefs about consequences (incorrect perceptions about the vaccine

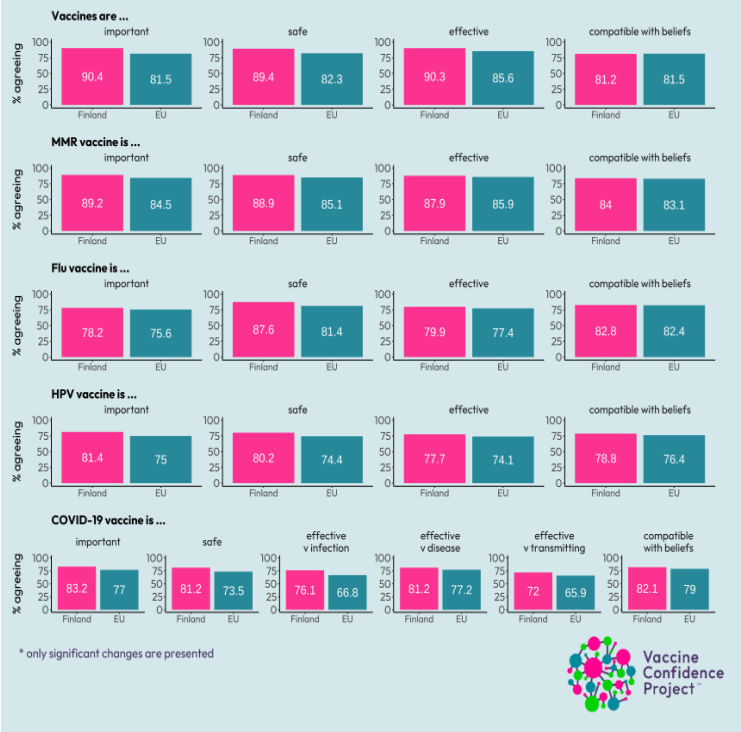
effectiveness, and lack of trust in the safety of the vaccine), social influences (influence of family and friends), reinforcement (limited abilities of the management to encourage vaccination), beliefs about capabilities (pregnancy or desire to get pregnant), psychological factors (coping with changing opinion), and emotions (confusion, suspicion, disappointment, and fatigue). We also identified three behavioral domains that encouraged vaccine uptake: social influences (trust in health authorities), environmental context and resources (vaccination logistics), and work and professional role (professional pride). The study findings can help authorities to develop tailored vaccine promotion strategies for healthcare workers in LTCFs.

6.1.9 Lohiniva, A. L., Pensola, A., Hyokki, S., Sivela, J., Harma, V. and Tammi, T. (2023). "Identifying factors influencing COVID-19 vaccine uptake in Finland - a qualitative study using social media data." Front Public Health 11: 1138800.

Introduction: Vaccine demand creation requires understanding what is driving the uptake of the vaccine. Qualitative research methods are paramount to gaining a localized understanding of behavioral drivers and barriers to vaccine uptake, but they are often underutilized. Methods: This is a qualitative study that used public comments on the Facebook and Twitter posts of the Finnish Institute for Health and Welfare (THL) as data sources to identify behavioral drivers for COVID-19 vaccine uptake in Finland. The participatory data analysis utilized thematic analysis and the Theoretical Domains 29 Framework (TDF). NVIVO was used to assist in the coding process. Results: The greatest number of FB and Twitter comments were linked with six TDF domains: knowledge, environmental context and resources, beliefs in consequences, beliefs in capabilities, social and professional role, and social influences. The domains included 15 themes that were interlinked. The knowledge domain overlapped with all other domains. Discussion: By using public discourse on Facebook and Twitter, and rapid qualitative data analysis methods within a behavioral insight framework, this study adds to the emerging knowledge about behavioral drivers of COVID-19 vaccines that can be used by public health experts to enhance the uptake of vaccines during future pandemics and epidemics.

6.1.10 - State of Vaccine Confidence in the EU (2022)

Vaccine confidence in Finland is high compared to other countries. The latest data we have for Finland is from surveys conducted in 2022 which showed that 88% of people feel that vaccines are safe and 89% think they are effective. 89% of those surveyed said they believe it's important for children to have vaccines and 79% feel that vaccines are compatible with their religious beliefs. Confidence in vaccines in Finland has declined since the first surveys carried out there. In 2015, 95% of people felt that vaccines were safe while 96% thought they were effective. 98% said they believed it was important for children to have vaccines and 86% felt that vaccines were compatible with their religious beliefs.



6.1.11 Sääksvuori L, Betsch C, Nohynek H, Salo H, Sivelä J, Böhm R. Information nudges for influenza vaccination: Evidence from a large-scale cluster-randomized controlled trial in Finland. PLoS Med. 2022 Feb 9;19(2):e1003919.

Background: Vaccination is the most effective means of preventing the spread of infectious diseases. Despite the proven benefits of vaccination, vaccine hesitancy keeps many people from getting vaccinated. Methods and findings: We conducted a large-scale cluster randomized controlled trial in Finland to test the effectiveness of centralized written reminders (distributed via mail) on influenza vaccination coverage. The study included the entire older adult population (aged 65 years and above) in 2 culturally and geographically distinct regions with historically low (31.8%, n = 7,398, mean age 75.5 years) and high (57.7%, n = 40,727, mean age 74.0 years) influenza vaccination coverage. The study population was randomized into 3 treatments: (i) no reminder (only in the region with low vaccination coverage); (ii) an individual-benefits reminder, informing recipients about the individual benefits of vaccination; and (iii) an individual- and social-benefits reminder, informing recipients about the additional social benefits of vaccination in the form of herd immunity. There was no control treatment group in the region with high vaccination coverage as general reminders had been sent in previous years. The primary endpoint was a record of influenza vaccination in the Finnish National Vaccination Register during a 5-month follow-up period (from October 18, 2018 to March 18, 2019). Vaccination coverage after the intervention in the region with historically low coverage was 41.8% in the individual-benefits treatment, 38.9% in the individual- and social-benefits treatment and 34.0% in the control treatment group. Vaccination coverage after the intervention in the region with historically high coverage was 59.0% in the individual-benefits treatment and 59.2% in the individual- and social-benefits treatment. The effect of receiving any type of reminder letter in comparison to control treatment group (no reminder) was 6.4 percentage points (95% CI: 3.6 to 9.1, p < 0.001). The effect of reminders was particularly large among individuals with no prior influenza vaccination (8.8 pp, 95% CI: 6.5

to 11.1, p < 0.001). There was a substantial positive effect (5.3 pp, 95% CI: 2.8 to 7.8, p < 0.001) among the most consistently unvaccinated individuals who had not received any type of vaccine during the 9 years prior to the study. There was no difference in influenza vaccination coverage between the individual-benefit reminder and the individual- and social-benefit reminder (region with low vaccination coverage: 2.9 pp, 95% CI: -0.4 to 6.1, p = 0.087, region with high vaccination coverage: 0.2 pp, 95% CI: -1.0 to 1.3, p = 0.724). Study limitations included potential contamination between the treatments due to information spillovers and the lack of control treatment group in the region with high vaccination coverage. Conclusions: In this study, we found that sending reminders was an effective and scalable intervention strategy to increase vaccination coverage in an older adult population with low vaccination coverage. Communicating the social benefits of vaccinations, in addition to individual benefits, did not enhance vaccination coverage. The effectiveness of letter reminders about the benefits of vaccination to improve influenza vaccination coverage may depend on the prior vaccination history of the population.

6.1.12 Hammer, C. C., Cristea, V., Dub, T. and Sivela, J. (2021). "High but slightly declining COVID-19 vaccine acceptance and reasons for vaccine acceptance, Finland April to December 2020." Epidemiol Infect 149: e123

We investigated likelihood to vaccinate and reasons for and against accepting a coronavirus disease 2019 (COVID-19) vaccine among adult residents of Finland. Vaccine acceptance declined from 70% in April to 64% in December 2020. Complacency and worry about side effects were main reasons against vaccination while concern about severe disease was a strong motive for vaccination. Convenience of vaccination and recommendations by healthcare workers were identified as enablers for vaccination among those aged under 50 years. Understanding barriers and enablers behind vaccine acceptance is decisive in ensuring a successful implementation of COVID-19 vaccination programmes, which will be key to ending the pandemic.

6.1.13 Väliverronen, E., Sivelä, J. and Nohynek, H. (2020). "Suomalaisten suhde rokotuksiin – mitä tuoreet kyselytutkimukset kertovat." Sosiaalilääketieteellinen Aikakauslehti 57(3). ("Finns' relationship to vaccinations - what recent surveys tell us." Social Medicine Journal)

English summary: The review presents recent surveys mapping the vaccination attitudes of Finns and makes a descriptive analysis based on them. In light of the survey results, Finns have very strong confidence in the effectiveness and safety of vaccines in an international comparison. The data from the national vaccination register on the development of vaccination coverage also do not support the claims that are sometimes made in the public about a significant increase in refusal of vaccinations. However, more research data on Finns' attitude to vaccinations is needed, especially on regional variation. Qualitative research on vaccination attitudes is also needed alongside questionnaire surveys.

6.1.14 Karlsson, L. C., Lewandowsky, S., Antfolk, J., Salo, P., Lindfelt, M., Oksanen, T., Kivimaki, M. and Soveri, A. (2019). "The association between vaccination confidence, vaccination behavior, and willingness to recommend vaccines among Finnish healthcare workers." PLoS One 14(10): e0224330.

Information and assurance from healthcare workers (HCWs) is reported by laypeople as a key factor in their decision to get vaccinated. However, previous research has shown that, as in the general population, hesitancy towards vaccines exists among HCWs as well. Previous studies further suggest that HCWs with a higher confidence in vaccinations and vaccine providers are more willing to take the vaccines themselves and to recommend vaccines to

patients. In the present study with 2962 Finnish HCWs (doctors, head nurses, nurses, and practical nurses), we explored the associations between HCWs' vaccination confidence (perceived benefit and safety of vaccines and trust in health professionals), their decisions to accept vaccines for themselves and their children, and their willingness to recommend vaccines to patients. The results showed that although the majority of HCWs had high confidence in vaccinations, a notable share reported low vaccination confidence. Moreover, in line with previous research, HCWs with higher confidence in the benefits and safety of vaccines were more likely to accept vaccines for their children and themselves, and to recommend vaccines to their patients. Trust in other health professionals was not directly related to vaccination or recommendation behavior. Confidence in the benefits and safety of vaccines was highest among doctors, and increased along with the educational level of the HCWs, suggesting a link between confidence and the degree of medical training. Ensuring high confidence in vaccines among HCWs may be important in maintaining high vaccine uptake in the general population.

6.1.15 Sivela, J. Launis, V. Jääskeläinen, S. Puumalainen, T. Nohynek, H. (2018). "Käsitykset rokotuksista ja rokotuskattavuuteen vaikuttavat tekijät". Laakarilehti, Science. pp. 648 - 652 (Perceptions of vaccinations and factors affecting vaccination coverage)

English summary: Vaccine attitudes and factors affecting vaccine coverage On average, the level of vaccine coverage in Finland is good. However, pockets of low coverage exist in certain areas. To a certain extent, the low coverage is a result of vaccine hesitancy. Vaccine hesitancy is a term developed by the WHO Strategy Advisory Group of Experts (SAGE) on Immunization. Vaccine attitudes are considered to exist on a continuum between total acceptance and complete refusal, with most people having a positive attitude towards vaccination. A crucial aspect about vaccine hesitancy is that it also encompasses other reasons behind low vaccine coverage than so-called ideological vaccine refusal. Factors related to complacency (when the perceived risk of vaccine-preventable diseases is low and vaccination is not considered a necessary preventive action), and convenience (when the quality and degree of vaccination services affects the decision to be vaccinated) can also have a considerable effect on vaccination coverage. Mandatory vaccinations have been publicly discussed as a possibility to ensure good coverage. However, mandatory vaccination includes many risks that may, in the end, be harmful when it comes to People's attitudes towards both vaccinations and the health care system in general. Therefore, mandatory vaccinations are not considered a constructive way to handle vaccine hesitancy in Finland. Good vaccination coverage can be ensured through various actions and interventions. A well-functioning national vaccination program (NVP) forms the foundation for operations and actions aiming to maintain good coverage. Nevertheless, there is an increasing need for both research-based knowledge about determinants that affect vaccination coverage and vaccine-related behavior and research-based actions and strategies.

6.2 The Finland's cultural, behavioural and media insights centre (CUBE)

Potential questions/outcomes: Explain Finland's CUBE and how its helping to improve adult immunization in the country.

6.2.1 THL website: https://thl.fi/en/about-us/organisation/departments-and-units/communications-and-influencing/cultural-behavioral-and-media-insights-centre-cube-

The Cultural, Behavioural and Media Insights Centre (CUBE) researches and develops influencing through information in an era where citizens' perceptions and attitudes as well as the phenomena of a digitalising media society, such as the spread of misinformation, disinformation and polarised information, have a significant impact on their health and wellbeing.

The Cultural, Behavioural and Media Insights Centre (CUBE):

- researches wellbeing and health promotion and the relevant policies
- researches the impacts of the media environment on building and disseminating perceptions related to health and wellbeing
- produces data and understanding of factors affecting people's behaviour, perceptions and activities
- develops and monitors more effective and sustainable measures to promote health and wellbeing
- provides special behavioural and cultural-social competence for health studies
- monitors and promotes the effectiveness of research-based information and communications.

The goal is to improve our understanding of different social factors that affect people's behaviour. Research-based information is used to promote choices that support wellbeing and health in different population groups and to promote the relevant research-based decision-making. The Cultural, Behavioural and Media Insights Centre (CUBE) operates under THL's communications and influencing unit and acts as a horizontal partner in THL's expert and research work. CUBE is extensively networked and actively engages in cooperation with both Finnish and international partners.

Example of projects and activities population groups and to promote the relevant research-based decision-making. The Cultural, Behavioural and Media Insights Centre (CUBE) operates under THL's communications

- Crisis Narratives
- EU-Joint Action on Vaccination (EU-Jav)
- Addressing vaccine hesitancy in Europe (VAX-TRUST)
- Mediating Expertise – MEX group (University of Helsinki)
- Ilmastotuuppaus.fi (In English)
- After Action Review (ECDC)

Session 7: Adult Vaccination in Finland in specific situations and population groups; the way forward - panel discussion

Session 7: Adult Vaccination in Finland in specific situations and population groups; the way forward - panel discussion	7.1 Vaccinating risk groups against H5 avian influenza in Finland	Hanna Nohynek
	7.2 Vaccination of healthcare providers in Finland	Mia Kontio

	7.3 Vaccinations in Finnish military conscripts, example pertussis booster vaccine	Tuula Hannila Handelberg
	7.4 Vaccination of migrants in Finland	Idil Hussein
	7.5 Travel vaccines for the Finnish	Anu Kantele

7.1 Vaccinating risk groups against H5 avian influenza in Finland

Potential questions/outcomes: Who is targeted as risk groups for vaccination against H5? Which vaccine(s) are given (is it voluntary?), why specifically these vaccines? Which other control measures are in place? What is the uptake? What are the lessons learned until now? What might change in the future?

7.1.1 Nohynek H, Helve OM. One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland. Euro Surveill. 2024 Jun;29(25):2400383.

7.1.2 Anniina Virkku, Erika Lindh, Laura Kalin-Mänttäri, Merit Melin, Hanna Nohynek, Niina Ikonen. Avian influenza vaccinations in Finland. Finnish Institute for Health and Welfare (THL). Discussion Paper 43/2024. 12 pages. Helsinki 2024. ISBN 978-952-408-340-9 (online publication)

Avian influenza viruses of the subtype H5 have been spreading in bird populations around the world since 1996, causing sporadic infections in mammals and humans. Since 2020, a highly pathogenic avian influenza H5N1 virus has become established in bird populations in Europe, causing extensive outbreaks in both wild birds and in poultry. The virus has increasingly caused spill-over infections in mammals and on a few occasions, epidemics in mammal populations. In 2023, the A(H5N1) avian influenza virus caused an extensive epidemic in farmed fur animals in Finland and exposed more than 500 people to the virus. Dense and large animal populations in which the virus can spread rapidly are an ideal platform for the evolution of influenza viruses. From a public health perspective, the spread of the virus in farmed fur animals is particularly concerning due to the susceptibility of the animal hosts to seasonal influenza viruses. Simultaneous infections with human and avian influenza viruses may, through a process known as reassortment, produce viruses with mixed genes and novel properties. Variants arisen through reassortment may be transmitted more efficiently between humans and evade previous population immunity. In particular, minks are regarded as highly potent springboard for pandemic influenza, facilitating the adaptation of avian influenza viruses through adaptive mutations and reassortment to mammals and humans. Because of the exceptional epidemic situation and the risk of H5N1 evolving into a pandemic virus, Finland has procured avian influenza vaccines for persons who are at risk of exposure to avian influenza. The H5N8 avian influenza vaccine was granted a marketing authorisation in the EU in April 2024. The vaccine manufacturer has modified the previous authorised zoonotic avian influenza vaccine to better match the H5 virus lineage that occurred in Europe in 2023. The aim of the vaccinations is to protect persons at risk of being exposed to H5N1 from severe disease and to mitigate viral evolution into forms with increased transmissibility in the human population, and consequently the emergence of a novel pandemic. THL has defined the target groups for the avian influenza vaccinations in cooperation with the Finnish Food Authority. The vaccine will be offered to persons aged 18 or over who because of their work or other circumstances are at increased risk of contracting avian influenza. They include

persons who are in contact with fur animals or poultry, official veterinarians, and laboratory workers who handle samples that may contain avian influenza virus. The aim is to implement a two-dose vaccination series for persons in the target groups during July and August 2024, before the autumn influenza season begins.

7.1.3 Lindh E, Lounela H, Ikonen N, Kantala T, Savolainen-Kopra C, Kauppinen A, Österlund P, Kareinen L, Katz A, Nokireki T, Jalava J, London L, Pitkäpaasi M, Vuolle J, Punto-Luoma AL, Kaarto R, Voutilainen L, Holopainen R, Kalin-Mänttäri L, Laaksonen T, Kiviranta H, Pennanen A, Helve O, Laamanen I, Melin M, Tammiranta N, Rimhanen-Finne R, Gadd T, Salminen M. Highly pathogenic avian influenza A(H5N1) virus infection on multiple fur farms in the South and Central Ostrobothnia regions of Finland, July 2023. Euro Surveill. 2023

Since mid-July 2023, an outbreak caused by highly pathogenic avian influenza A(H5N1) virus clade 2.3.4.4b genotype BB is ongoing among farmed animals in South and Central Ostrobothnia, Finland. Infections in foxes, American minks and raccoon dogs have been confirmed on 20 farms. Genetic analysis suggests introductions from wild birds scavenging for food in farm areas. Investigations point to direct transmission between animals. While no human infections have been detected, control measures are being implemented to limit spread and human exposure.

7.1.4 Kareinen L, Tammiranta N, Kauppinen A, Zecchin B, Pastori A, Monne I, Terregino C, Giussani E, Kaarto R, Karkamo V, Lähteinen T, Lounela H, Kantala T, Laamanen I, Nokireki T, London L, Helve O, Kääriäinen S, Ikonen N, Jalava J, Kalin-Mänttäri L, Katz A, Savolainen-Kopra C, Lindh E, Sironen T, Korhonen EM, Aaltonen K, Galiano M, Fusaro A, Gadd T. Highly pathogenic avian influenza A(H5N1) virus infections on fur farms connected to mass mortalities of black-headed gulls, Finland, July to October 2023. Euro Surveill. 2024 Jun;29(25):2400063.

Highly pathogenic avian influenza (HPAI) has caused widespread mortality in both wild and domestic birds in Europe 2020-2023. In July 2023, HPAI A(H5N1) was detected on 27 fur farms in Finland. In total, infections in silver and blue foxes, American minks and raccoon dogs were confirmed by RT-PCR. The pathological findings in the animals include widespread inflammatory lesions in the lungs, brain and liver, indicating efficient systemic dissemination of the virus. Phylogenetic analysis of Finnish A(H5N1) strains from fur animals and wild birds has identified three clusters (Finland I-III), and molecular analyses revealed emergence of mutations known to facilitate viral adaptation to mammals in the PB2 and NA proteins. Findings of avian influenza in fur animals were spatially and temporally connected with mass mortalities in wild birds. The mechanisms of virus transmission within and between farms have not been conclusively identified, but several different routes relating to limited biosecurity on the farms are implicated. The outbreak was managed in close collaboration between animal and human health authorities to mitigate and monitor the impact for both animal and human health.

7.2 Vaccination of healthcare providers in Finland

Potential questions/outcomes: What is understood in Finland under health care providers? Which vaccine(s) are given (are there (semi-)mandatory vaccines?), why specifically these vaccines? What is the vaccine uptake among HCWs? What are the lessons learned until now? What might change in the future?

7.2.1 Savulescu C, et al. Muñoz-Almagro C, Milagro A, Bacci S, Nardone A; VEBIS HCW VE study group; Collaborators in VEBIS HCW study group. Effectiveness of the autumn 2023 COVID-19 vaccine dose in hospital-based healthcare workers: results of the VEBIS healthcare worker vaccine effectiveness cohort study, seven European countries, season 2023/24. Euro Surveill. 2024 Oct;29(44):2400680.

COVID-19 vaccination recommendations include healthcare workers (HCWs). We measured COVID-19 vaccine effectiveness (CVE) of the autumn 2023 dose against laboratory-confirmed SARS-CoV-2 infection in a prospective cohort study of 1,305 HCWs from 13 European hospitals. Overall CVE was 22% (95% CI: -17 to 48), 49% (95% CI: -8 to 76) before and -11% (95% CI: -84 to 34) after the start of BA.2.86/JN.1 predominant circulation. Autumn 2023 COVID-19 vaccination led to a moderate-to-low reduction in SARS-CoV-2 infection incidence in HCWs. Monitoring of CVE is crucial for COVID-19 prevention.

7.2.2 Hammer CC, Lyytikäinen O, Arifulla D, Toura S, Nohynek H. High influenza vaccination coverage among healthcare workers in acute care hospitals in Finland, seasons 2017/18, 2018/19 and 2019/20. Euro Surveill. 2022 Apr;27(17):2100411.

Background Influenza vaccination is widely recommended for healthcare workers (HCWs) in European countries, but the coverage is not always satisfactory. In Finland, a new act was introduced in March 2017, according to which it is the employer's responsibility to appoint only vaccinated HCWs for servicing vulnerable patients. Aim We determined the influenza vaccination coverage among HCWs in Finnish acute care hospitals in three influenza seasons after introduction of the act. Methods We analysed data collected by an internet-based survey sent annually to all Finnish acute care hospitals and described the influenza vaccination coverage among HCWs during seasons 2017/18, 2018/19 and 2019/20. We calculated mean coverage per healthcare district and season. Results In season 2017/18, 38 of 39 hospitals, in 2018/19, 35 of 36 hospitals and in 2018/19 31 of 33 hospitals provided data. The mean influenza vaccination coverage was 83.7% (SD: 12.3) in season 2017/18, 90.8% (SD: 8.7) in 2018/19 and 87.6% (SD: 10.9) in season 2019/20. There was no significant increase or decrease in the mean coverage across the three seasons. The differences between districts were only significant in 2018/19 ($p < 0.005$). Conclusions The coverage of influenza-vaccinated HCWs in Finnish hospitals was high in all three seasons and the current legal situation (semi-mandatory system) in Finland seems to provide a good background for this. Data collection should be maintained and improved for further monitoring.

7.2.3 Dub T, Søborg B, Andersen PH, Gudnason T, Nøkleby H, Lindstrand A, Carlsson RM, Nohynek H. Immunisation of healthcare workers in the Nordic countries: Variation in recommendations and practices and a lack of assessment. Euro Surveill. 2021 Jan;26(4):1900555.

Healthcare workers (HCWs) are at increased risk of both exposure and transmission of infectious disease. Two European Union (EU) directives state that health services are responsible for assessing their employees' potential exposure to infectious diseases and offering immunisation free of charge. We assessed current policy for immunisation of HCWs and the availability of vaccine coverage data in the Nordic countries by surveying national vaccination experts in Denmark, Finland, Iceland, Norway and Sweden, as well as Swedish county medical officers (CMOs). All national experts and 17 of 21 Swedish CMOs responded. All EU countries had transposed the European directives into national law, while Norway and Iceland had similar national legislation. Recommendations or guidelines were issued in

Denmark, Finland, Iceland, Norway and 15 of 17 responding Swedish counties. The range of diseases covered differed by countries and Swedish counties. HCW vaccine coverage data were not systematically collected; incomplete estimates were only available for Finland and two Swedish counties. In conclusion, recommendations or guidelines exist in the Nordic countries, but their impact cannot be assessed, as vaccine uptake among HCWs is not currently measured. Systematic collection of data is a necessary step towards improving HCW immunisation policy and practice in the Nordic countries.

7.2.4 Hämäläinen A, Patovirta RL, Mauranen E, Hämäläinen S, Koivula I. Support among healthcare workers for the new mandatory seasonal influenza vaccination policy and its effects on vaccination coverage. Ann Med. 2021 Dec;53(1):384-390.

Introduction: Finland was the first European country to introduce a nation-wide mandatory seasonal influenza vaccination policy for healthcare workers (HCWs) by mandating that administrators of health care institutions only employ vaccinated HCWs. In this study, we examine the effects of the new policy and the view of HCWs on the new policy. Methods: A cross-sectional observational study was conducted in Kuopio University Hospital among HCWs working in close patient contact. The statistics on vaccination coverage were obtained from the hospital's own databases, where employees were asked to self-report their suitability for work. An anonymous survey was sent to HCWs in 2015-2016 (n = 987) and 2018-2019 (n = 821). Results: Vaccination coverage increased from 59.5 to 99.6%, according to the hospital's own records. Among the survey respondents, the seasonal influenza vaccination coverage of HCWs increased from 68.2 to 95.4%. 83.8% of doctors and 49.4% of nurses supported the new policy. 12.7% of doctors and 41.5% of nurses found the new mandate coercive or that it restricted their self-determination. Conclusions: Our study confirms the positive effects of mandating the administrators of health care institutions to only employ vaccinated HCWs. The majority (57.9%) of all HCWs supported the new policy, with doctors being more compliant than nurses. Key messages Finland became the first European country to mandate influenza vaccination for HCWs by mandating that administrators of health care institutions only employ vaccinated HCWs. After the new act, the vaccination coverage of HCWs increased close to 100%. Most of the HCWs supported the new act and did not find it coercive.

7.2.5 Koivisto, K., Puhakka, L., Lappalainen, M., Blomqvist, S., Saxen, H. and Nieminen, T. (2017). "Immunity against vaccine-preventable diseases in Finnish pediatric healthcare workers in 2015." Vaccine 35(12): 1608-1614.

Healthcare workers (HCWs) pose a risk to themselves and their patients if not protected against vaccine-preventable diseases. Alarmingly, lacking immunity has been reported in several studies. We assessed the immunity against vaccine-preventable diseases in 157 pediatric HCWs in Helsinki Children's Hospital. The HCWs enrolled answered a questionnaire and gave a serum sample. Antibodies were measured with EIA against MMR-diseases, tetanus and diphtheria toxins, Hepatitis B (HBV), Hepatitis A (HAV), varicella zoster and pertussis toxin. Neutralizing antibodies against poliovirus 1, 2 and 3 were measured. All of the HCWs had antibodies against tetanus and 89.8% against diphtheria. All had measurable levels of polio antibodies to all three polioviruses. 41% had suboptimal levels of antibodies against at least one of the antigens tested: MMR-viruses, diphtheria, HBV or polio. Measles, mumps and rubella antibodies were detectable in 81.5%, 89.2% and 93%, respectively. Only one HCW had no varicella-antibodies. Hepatitis B surface antibodies (HBsAb) were detected in 89.8% of the nurses. 67.5% had HAV-antibodies. A poor correlation between detected antibody levels and reported vaccination history was noticed, indicating a need for a universal record system for registering the vaccines given to each individual.

7.3 Vaccinations in Finnish military conscripts, example pertussis booster vaccine

Potential questions/outcomes: Give some background about the Finnish military conscripts and the vaccines that are included before starting their program (is it voluntary?), Why specifically these vaccines? What is the uptake? What are the lessons learned until now? What might change in the future?

7.3.1 Article on recent adenovirus outbreak in Finnish Military
https://www.iltalehti.fi/politiikka/a/14655f60-1d8d-4b31-ab43-099ac48ff7d6
https://puolustusvoimat.fi/-/adenovirustilanne-puolustusvoimissa
https://ruotuvaki.fi/-/adenovirukselta-suojautuminen-on-varusmiesten-ja-henkilokunnan-yhteispelia

7.3.2 Zöldi V, Sane J, Nohynek H, Virkki M, Hannila-Handelberg T, Mertsola J. Decreased incidence of pertussis in young adults after the introduction of booster vaccine in military conscripts: Epidemiological analyses of pertussis in Finland, 1995-2015. Vaccine. 2017 Sep 18;35(39):5249-5255. doi: 10.1016/j.vaccine.2017.08.008. Epub 2017 Aug 18. PMID: 28823620.

Introduction: In 2005, in Finland, the whole-cell pertussis vaccine was replaced by acellular given at 3-5-12months, and boosters at 4 and 11-15years of age. From July 2012, military conscripts have been offered a pertussis booster dose. Conscription is mandatory for Finnish men, and >95% were 19-21years old when enrolled during 2012-2015. We describe the epidemiology of pertussis in Finland during 1995-2015, and show the indirect effect of the booster in conscripts on pertussis incidence in the Finnish population. Materials and methods: We extracted data on laboratory confirmed notified pertussis cases from the National Infectious Diseases Register. We calculated annual incidence using as denominator population data and incidence rate ratios (IRR) using Poisson regression. Results: The overall pertussis incidence peaked in 2004 (31/100,000) and was lowest in 2015 (3.0/100,000), with 66 reported cases in <3months infants in 2004 versus 6 in 2015. The majority of the cases were female (59%) with a male-to-female case ratio of 1:1.5. Cases were spread throughout the year with highest incidence during August-February. Among the 19- to 21-year-olds in the general population, incidence decreased from 49/100,000 in 2011 to 0.51/100,000 in 2015 (IRR=0.01; 95%CI, 0.00-0.16). Among the same age group, comparing the 3.5-year period before and after July 2012, incidence decreased from 33/100,000 to 5.3/100,000 (IRR=0.16; 95%CI, 0.06-0.40) in males and from 16/100,000 to 5.0/100,000 (IRR=0.31; 95%CI, 0.11-0.84) in females. Conclusions: Implementation of the pertussis booster dose in Finnish military conscripts was followed by a significant decrease in pertussis incidence both among the 19- to 21-year-old males and females, possibly reflecting herd immunity effect. Together with booster doses in adolescents this has resulted in low incidence in the whole population including infants. Our results support the implementation of the booster dose for conscripts. We recommend continuing monitoring pertussis epidemiology to optimize pertussis vaccination strategies in Finland.

7.3.3 Mölsä M, Hemmilä H, Rönkkö E, Virkki M, Nikkari S, Ziegler T. Molecular characterization of adenoviruses among finnish military conscripts. J Med Virol. 2016 Apr;88(4):571-7

Although adenoviruses were identified as important respiratory pathogens many years ago, little information is available concerning the prevalence of different adenovirus serotypes, which are circulating and causing epidemics in Finnish military training centers. Over a period of five years from 2008 to 2012, 3577 respiratory specimens were collected from military conscripts presenting with symptoms compatible with acute respiratory tract infection. Upon initial testing for certain respiratory viruses by real-time PCR, 837 of these specimens were identified as adenovirus-positive. For 672 of these specimens, the serotype of the adenovirus responsible was successfully determined by DNA sequencing. Serotypes 1, 2, 3, and 4 were detected in 1, 3, 181, and 487 samples, respectively. Adenovirus epidemics were observed during each year of this study. Based on these findings, adenovirus vaccination should be considered for military conscripts in the Finnish Defence Forces.

7.3.4 Jounio U, Saukkoriipi A, Bratcher HB, Bloigu A, Juvonen R, Silvennoinen-Kassinen S, Peitso A, Harju T, Vainio O, Kuusi M, Maiden MC, Leinonen M, Käyhty H, Toropainen M. Genotypic and phenotypic characterization of carriage and invasive disease isolates of Neisseria meningitidis in Finland. J Clin Microbiol. 2012 Feb;50(2):264-73.

The relationship between carriage and the development of invasive meningococcal disease is not fully understood. We investigated the changes in meningococcal carriage in 892 military recruits in Finland during a nonepidemic period (July 2004 to January 2006) and characterized all of the oropharyngeal meningococcal isolates obtained (n = 215) by using phenotypic (serogrouping and serotyping) and genotypic (porA typing and multilocus sequence typing) methods. For comparison, 84 invasive meningococcal disease strains isolated in Finland between January 2004 and February 2006 were also analyzed. The rate of meningococcal carriage was significantly higher at the end of military service than on arrival (18% versus 2.2%; $P < 0.001$). Seventy-four percent of serogroupable carriage isolates belonged to serogroup B, and 24% belonged to serogroup Y. Most carriage isolates belonged to the carriage-associated ST-60 clonal complex. However, 21.5% belonged to the hyperinvasive ST-41/44 clonal complex. Isolates belonging to the ST-23 clonal complex were cultured more often from oropharyngeal samples taken during the acute phase of respiratory infection than from samples taken at health examinations at the beginning and end of military service (odds ratio [OR], 6.7; 95% confidence interval [95% CI], 2.7 to 16.4). The ST-32 clonal complex was associated with meningococcal disease (OR, 17.8; 95% CI, 3.8 to 81.2), while the ST-60 clonal complex was associated with carriage (OR, 10.7; 95% CI, 3.3 to 35.2). These findings point to the importance of meningococcal vaccination for military recruits and also to the need for an efficacious vaccine against serogroup B isolates.

7.4 Vaccination of migrants in Finland

Potential questions/outcomes: Give some background about the strategies to vaccinate migrants in Finland. Which vaccines are check during the initial health examination? What is the uptake? What are the lessons learned until now? What might change in the future?

7.4.1 THL National study on the health, welfare and services of the foreign-born population – MoniSuomi 2022 Key observations to support decision-making

The National study on the health, welfare and services of the foreign-born population - MoniSuomi 2022 is a population study for the adult population with a foreign background

(hereafter immigrant). The aim of the study is to examine health, well-being and service experiences and factors affecting these. Key results are presented in a web-based phenomenon report in which these can be examined nationally by country of origin, gender and age group as well as specifically in the wellbeing services counties studied. It is now also possible for the first time to view the change over time between 2018 and 2022. The results of the MoniSuomi study increase knowledge, understanding and discussion on the immigrant population in Finland and provide tools for decisions-making and planning. In addition, participation in the study has given immigrants the opportunity to influence and highlight their experiences.

Main Findings:

- On average, the immigrant population in Finland is doing well. The majority have at least one friend in Finland and a moderately strong experience of inclusion and the safety of their daily lives.
- Most immigrants also felt their health was good and reported fewer long-term illnesses than the total population on average.
- Discrimination experiences are particularly common in the immigrant population, as 43% had experienced discrimination within the previous 12 months.
- Between 2018 and 2022, the need for physician, nurse and dentist appointment services increased significantly.
- The MoniSuomi study reinforces previous data that there are still major differences in the health, welfare, experiences of inclusion and access to services in the context of groups from different countries of origin and between men and women.

7.4.2 Safarov N, Kemppainen L, Wrede S, Kouvonen A. Self-identified barriers to health services among migrants 50 years of age or older: population-based survey study of Russian speakers in Finland. BMC Health Serv Res. 2024 Feb 27;24(1):252.

Background: The compounded effect of a migratory background and ageing increases the risk of unequal medical treatment opportunities. The aim of this article is to investigate the social determinants of barriers to health services. Methods: The study uses population-based survey data of Russian-speaking migrants (50 + years) residing in Finland (n = 1082, 57% of men, mean age 63 years). Multiple correspondence analysis was performed as a dimension reduction procedure on six barriers to health services. Multiple ordinary least-squares linear regression was used for the predicted score of the barriers as an outcome variable. Results: Most of the sociodemographic characteristics were not associated with barriers to health services, except gender, as women tended to face more disadvantages. Migration-related factors, such as the need for interpreters for health services and experienced discrimination, were associated with an increased likelihood of reporting barriers to health services. Using the internet as a primary source of health information was associated with more access barriers to health services. Conclusions: Migrants 50 years of age or older face multiple barriers to health services. Given that the healthcare needs increase with age, addressing this issue becomes crucial, necessitating improved access to health services for older migrants.

7.4.3 Bastola K, Nohynek H, Lilja E, Castaneda AE, Austero S, Kuusio H, Skogberg N. Incidence of SARS-CoV-2 Infection and Factors Associated With Complete COVID-19 Vaccine Uptake Among Migrant Origin Persons in Finland. Int J Public Health. 2023 May 3;68:1605547..

Objective: We examined incidence of SARS-CoV-2 infection, COVID-19 vaccine uptake and factors associated with complete COVID-19 vaccine uptake among persons of migrant origin in Finland. Methods: Data on laboratory-confirmed SARS-CoV-2 infection and COVID-19 vaccine doses between March 2020 and November 2021 were linked to FinMonik register sample (n = 13,223) and MigCOVID (n = 3,668) survey data using unique personal identifier. Logistic regression was the main method of analyses. Results: Among FinMonik sample, complete COVID-19 vaccine uptake was lower among persons of Russia/former Soviet Union, Estonia, and rest of Africa and higher among persons of Southeast Asia, rest of Asia, and the Middle East/North Africa than among persons originating from Europe/North America/Oceania. Male sex, younger age, migration age (<18 years) and shorter length of residence were associated with lower vaccine uptake among FinMonik sample, whereas younger age, being economically inactive, poorer language skills, experiences of discrimination and psychological distress were associated with lower vaccine uptake among MigCOVID sub-sample. Conclusion: Our Findings point to a further need of tailored and targeted communication and community outreach strategies to increase vaccine uptake among persons of migrant origin.

7.4.4 Ekezie, W., Awwad, S., Krauchenberg, A., Karara, N., Dembinski, L., Grossman, Z., Del Torso, S., Dornbusch, H. J., Neves, A., Copley, S., Mazur, A., Hadjipanayis, A., Grechukha, Y., Nohynek, H., Damnjanovic, K., Lazic, M., Papaevangelou, V., Lapii, F., Stein-Zamir, C., Rath, B. and For The ImmuHubs, C. (2022). "Access to Vaccination among Disadvantaged, Isolated and Difficult-to-Reach Communities in the WHO European Region: A Systematic Review." Vaccines (Basel) 10(7).

Vaccination has a significant impact on morbidity and mortality. High vaccination coverage rates are required to achieve herd protection against vaccine-preventable diseases. However, limited vaccine access and hesitancy among specific communities represent significant obstacles to this goal. This review provides an overview of critical factors associated with vaccination among disadvantaged groups in World Health Organisation European countries. Initial searches yielded 18,109 publications from four databases, and 104 studies from 19 out of 53 countries reporting 22 vaccine-preventable diseases were included. Nine groups representing the populations of interest were identified, and most of the studies focused on asylum seekers, refugees, migrants and deprived communities. Recall of previous vaccinations received was poor, and serology was conducted in some cases to confirm protection for those who received prior vaccinations. Vaccination coverage was lower among study populations compared to the general population or national average. Factors that influenced uptake, which presented differently at different population levels, included health service accessibility, language and vaccine literacy, including risk perception, disease severity and vaccination benefits. Strategies that could be implemented in vaccination policy and programs were also identified. Overall, interventions specific to target communities are vital to improving uptake. More innovative strategies need to be deployed to improve vaccination coverage among disadvantaged groups.

7.4.5 Tuomisto K, Tiittala P, Keskimäki I, Helve O. Refugee crisis in Finland: Challenges to safeguarding the right to health for asylum seekers. Health Policy. 2019 Sep;123(9):825-832.

In 2015 Finland received an unprecedented number of asylum seekers, ten times more than in any previous year. This surge took place at a time the Finnish Government was busily undergoing a wide-range health and social care reform amid growing nationalist and populist

sentiments. Our aim is to explore the governance of a parallel health system for asylum seekers with a right-to-health approach. We concentrated on three right to health features most related to the governance of asylum seeker health care, namely Formal recognition of the right to health, Standards and Coordination mechanisms. Through our qualitative review, we identified three major hurdles in the governance of the system for asylum seekers: 1) Ineffectual and reactive national level coordination and stewardship; 2) Inadequate legislative and supervisory frameworks leading to ineffective governance; 3) Discrepancies between constitutional rights to health, legal entitlements to services and guidance available. This first-time large-scale implementation of the policies exposed weaknesses in the legal framework and the parallel health system. We recommend the removal of the parallel system and the integration of asylum seekers' health services to the national public health care system.

7.4.6 Giambi C, Del Manso M, Marchetti G, Olsson K, Adel Ali K, Declich S; Venice survey working group. Immunisation of migrants in EU/EEA countries: Policies and practices. Vaccine. 2019 Aug 23;37(36):5439-5451.

In recent years various EU/EEA countries have experienced an influx of migrants from low and middle-income countries. In 2018, the "Vaccine European New Integrated Collaboration Effort (VENICE)" survey group conducted a survey among 30 EU/EEA countries to investigate immunisation policies and practices targeting irregular migrants, refugees and asylum seekers (later called "migrants" in this report). Twenty-nine countries participated in the survey. Twenty-eight countries reported having national policies targeting children/adolescent and adult migrants, however vaccinations offered to adult migrants are limited to specific conditions in seven countries. All the vaccinations included in the National Immunisation Programme (NIP) are offered to children/adolescents in 27/28 countries and to adults in 13/28 countries. In the 15 countries offering only certain vaccinations to adults, priority is given to diphtheria-tetanus, measles-mumps-rubella and polio vaccinations. Information about the vaccines given to child/adolescent migrants is recorded in 22 countries and to adult migrants in 19 countries with a large variation in recording methods found across countries. Individual and aggregated data are reportedly not shared with other centres/institutions in 13 and 15 countries, respectively. Twenty countries reported not collecting data on vaccination uptake among migrants; only three countries have these data at the national level. Procedures to guarantee migrants' access to vaccinations at the community level are available in 13 countries. In conclusion, although diversified, strategies for migrant vaccination are in place in all countries except for one, and the strategies are generally in line with international recommendations. Efforts are needed to strengthen partnerships and implement initiatives across countries of origin, transit and destination to develop and better share documentation in order to guarantee a completion of vaccination series and to avoid unnecessary re-vaccination. Development of migrant-friendly strategies to facilitate migrants' access to vaccination and collection of vaccination uptake data among migrants is needed to meet existing gaps.

7.4.7 THL website: https://thl.fi/en/topics/infectious-diseases-and-vaccinations/diseases-and-disease-control/prevention-of-infectious-diseases-among-migrants

Some of the people who have migrated to Finland come from areas where it has not been possible to implement comprehensive vaccination programs in recent years. The need for vaccination of people who have migrated to Finland is assessed in connection with the initial health examination. If necessary, the immunisation is completed. Children are vaccinated according to national vaccination program and adults when it is considered necessary for the

protection of individuals and population. The vaccines for risk groups are offered for those children and adults, who belong to risk groups.

7.4.8 https://river-eu.org/countries/finland/

In Finland, all children and young adults are eligible for vaccines included in the national vaccination programme free of charge. Vaccination coverage is high in Finland, mainly because vaccinations are widely available as they are an integrated part of the child's health care visits. Trust is an important factor in terms of facilitating vaccine uptake. Around 80 % of Somali migrants said they trust the Finnish healthcare system.

7.5 Travel vaccines for the Finnish

Potential questions/outcomes: Give some background about the strategies to vaccinate Finnish travelers. What is the uptake? What are the lessons learned until now? What might change in the future?

7.5.1 Palojoki, S., Vakkuri, A. and Vuokko, R. (2021). "The European Cross-Border Health Data Exchange: Focus on Clinically Relevant Data." Stud Health Technol Inform 281: 442-446.

The eHealth Digital Service Infrastructure (eHDSI) is an infrastructure ensuring the continuity of care for European citizens while they are travelling abroad in the EU. We present the Finnish readiness of implementing datasets of diagnosis, vaccinations and medication summary in a case study, and discuss challenges emerging from the national perspective. International harmonized standards are a key element in the smooth development of European information exchange.

7.5.2 Mäkelä HMM, Cristea V, Sane JA. Lack of perception regarding risk of dengue and day-active mosquitoes in Finnish travellers. Infect Dis (Lond). 2020 Sep;52(9):651-658.

Background: An increasing number of international travellers are at risk for dengue infection. We analysed the characteristics of Finnish travellers with recently acquired dengue infections. Methods: Notified dengue infections from 2016 to 2019 were obtained from the Finnish National Infectious Disease Register. We developed a questionnaire and invited individuals diagnosed with dengue to provide information on countries and areas of infection, travel characteristics, risk perception and use of protective measures. Results: Almost all infections (94%, 127/135) were acquired in Asian countries, most in Thailand (78/135, 58%). The Maldives had the highest crude risk after adjusting for the number of travellers (55.6/100,000). Most trips were pre-booked holidays (93/111, 84%) and 62% (69/111) had a duration of 14-21 days with time spent mostly on the beach (78/111, 70%). The majority of travellers were not aware of the risk of dengue infection before travelling (67/111, 60%) and had not sought pre-travel advice (72/111, 65%). The majority applied some protective measures (71/111, 64%) but mainly after sunset (64/111, 58%).Conclusions: Most dengue infections in Finnish travellers were acquired at popular destinations in Southeast Asia, especially Thailand. Our study showed that there was low awareness regarding the risk of contracting the infection. In addition, many travellers reported inadequate use of protective measures. This calls for further public health actions, such as raising awareness of day-active mosquitoes, of risk at popular travelling destinations and the correct way of applying anti-vectorial measures

Session 8: Breakout groups

Session 8: Breakout groups

Session 9: Vaccine clinical trial environment

Potential questions/outcomes: Is Finland conducting a lot of vaccine clinical trials (phase 1/2/3). Is this changing over time? Are there specific trends observed? What insights can observational field studies offer compared to the 'gold standard' of clinical trials, especially when these studies consistently align in their findings (despite well-known confounding issues). This is particularly relevant for influenza vaccines, where clinical trials are possible but undoubtedly complex.

Session 9 – Vaccine clinical trial environment	Vaccine clinical trial environment; history, current and future	Arto Palmu

9.1 Article from HUS: Increasing drug research is only possible with significant special support and national cooperation 8 May 2023

9.2 Identifying WHO global priority endemic pathogens for vaccine research and development (R&D) using multi-criteria decision analysis (MCDA): an objective of the Immunization Agenda 2030 Hasso-Agopsowicz, Mateusz et al.eBioMedicine, Volume 0, Issue 0, 105424

A new World Health Organization (WHO) study published today in eBioMedicine names 17 pathogens that regularly cause diseases in communities as top priorities for new vaccine development. The WHO study is the first global effort to systematically prioritize endemic pathogens based on criteria that included regional disease burden, antimicrobial resistance risk and socioeconomic impact. The study reconfirms longstanding priorities for vaccine research and development (R&D), including for HIV, malaria, and tuberculosis – three diseases that collectively take nearly 2.5 million lives each year. The study also identifies pathogens such as Group A streptococcus and Klebsiella pneumoniae as top disease control priorities in all regions, highlighting the urgency to develop new vaccines for pathogens increasingly resistant to antimicrobials. "Too often global decisions on new vaccines have been solely driven by return on investment, rather than by the number of lives that could be saved in the most vulnerable communities," said Dr Kate O'Brien, Director of the Immunization, Vaccines and Biologicals Department at WHO. "This study uses broad regional expertise and data to assess vaccines that would not only significantly reduce diseases that greatly impact communities today but also reduce the medical costs that families and health systems face." WHO asked international and regional experts to identify factors that are most important to them when deciding which vaccines to introduce and use. The analysis of those preferences, combined with regional data for each pathogen, resulted in top 10 priority pathogens for each WHO region. The regional lists where then consolidated to form the global list, resulting in 17

priority endemic pathogens for which new vaccines need to be researched, developed and used. This new WHO global priority list of endemic pathogens for vaccine R&D supports the Immunization Agenda 2030's goal of ensuring that everyone, in all regions, can benefit from vaccines that protect them from serious diseases. The list provides an equitable and transparent evidence base to set regional and global agendas for new vaccine R&D and manufacturing, and is intended to give academics, funders, manufacturers and countries a clear direction for where vaccine R&D could have the most impact. This global prioritization exercise for endemic pathogens, complements the WHO R&D blueprint for epidemics, which identified priority pathogens that could cause future epidemics or pandemics, such as COVID-19 or severe acute respiratory syndrome (SARS).The findings of this new report on endemic pathogens are part of WHO's work to identify and support the research priorities and needs of immunization programmes in low- and middle-income countries, to inform the global vaccine R&D agenda, and to strategically advance development and uptake of priority vaccines, particularly against pathogens that cause the largest public health burden and greatest socioeconomic impact.

WHO Priority endemic pathogens list

Vaccines for these pathogens are at different stages of development.

Pathogens where vaccine research is needed

- Group A streptococcus
- Hepatitis C virus
- HIV-1
- Klebsiella pneumoniae

Pathogens where vaccines need to be further developed

- Cytomegalovirus
- Influenza virus (broadly protective vaccine)
- Leishmania species
- Non-typhoidal Salmonella
- Norovirus
- Plasmodium falciparum (malaria)
- Shigella species
- Staphylococcus aureus

Pathogens where vaccines are approaching regulatory approval, policy recommendation or introduction

- Dengue virus
- Group B streptococcus
- Extra-intestinal pathogenic E. coli
- Mycobacterium tuberculosis
- Respiratory syncytial virus (RSV)