THL DRIVE protocol, season 2021/22

Objectives

To provide aggregated data for Finland-specific and pooled analysis answering the objectives

- IVE against medically-attended (any reason) laboratory-confirmed influenza
  - overall and by vaccine brand
  - in children aged 0.5-6 years and elderly aged 65-100 years
  - overall and by influenza virus type

Study design

Register-based, population-based cohort study, prospective but non-concurrent

Study setting

Finland, ~5.5 inhabitants (citizens and permanent residents)

From https://thl.fi/en/web/infectious-diseases-and-vaccinations/vaccines-a-to-z/influenza-vaccine:

> A free influenza vaccine is available as part of the national vaccination programme to those for whom influenza is an essential health risk, or who gain significant health benefits from the vaccination. Groups entitled to a free influenza vaccination are
>
> - social, healthcare and medical care personnel
> - pregnant women
> - everyone aged 65 and over
> - children aged under 7
> - those belonging to at-risk groups because of an illness or treatment
> - those close to a person susceptible to serious influenza
> - men starting their military service and women starting their voluntary military service
>
> Persons who live or stay for long periods in institutional conditions, including prisons and reception centres, are also entitled to a free vaccination.
>
> During the influenza season 2021–2022, the vaccination programme offers
>
> - injectable VaxigripTetra vaccine for all age groups
> - FluenzTetra nasal spray vaccine for children aged from 2 to 6 years

During influenza season 2021–2022, the virus strains in VaxigripTetra and FluenzTetra vaccines are

- A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus
- A/Hong Kong/2671/2019 (H3N2)-like virus
- B/Washington/02/2019-like virus (Victoria lineage)
- B/Phuket/3073/2013-like virus (Yamagata lineage)

Study period

04.10.2021 (week 40) - 29.04.2022

Study population and individual follow-up

Children aged 0.5-6 years on 31.12.2021 as recorded in the Population Information System

Respectively, children born 2015-2019 in Fluenz Tetra analysis

Elderly aged 65-100 years on 31.12.2021 as recorded in the Population Information System

Follow-up from 04.10.2021 till • outcome of interest, • death, • vaccination with an influenza vaccine other than the one of interest, or • 30.04.2022, whatever comes first

Excluding the population with presumably incomplete vaccination records in 2021-22 and 2020-21 (see the National Vaccination Register's data quality assessment)

Excluding FinFluHD trial participants

Outcome definitions

Laboratory-confirmed influenza (as recorded in the National Infectious Diseases Register) dated to the day the respiratory sample was taken

- By virus type: • overall (any influenza-positive test), • influenza type A (positive tests), • influenza type B (positive tests)

Laboratory-confirmed influenza cases are considered as inpatient cases if they were hospitalized (>= 24h) for any reason starting or ongoing on the day of laboratory confirmation.

Exposure definition

Vaccination with the vaccine of interest during study period

Vaccination dates and vaccine brands as recorded in the National Vaccination Register

Time-varying variable as described in core protocol: unvaccinated, partially vaccinated, vaccinated

Potential confounders and effect modifiers

Children

- Age
- Sex
- Influenza vaccination in 2020/21
- Presence of at least one chronic condition before 04.10.2021
- Number of hospitalisations in 2020 (counting consecutive visits as one hospitalisation)
- Number of primary care consultations in the last 12 months before 04.10.2021 (without identifying/ removing follow-up visits)

Elderly

- Age
- Sex
- Influenza vaccination in 2020/21
- Presence of at least one chronic condition before 04.10.2021
- Number of hospitalisations in 2020 (counting consecutive visits as one hospitalisation)
- Number of primary care consultations in the last 12 months before 04.10.2021 (without identifying/ removing follow-up visits)

Data management

Data are extracted from the respective registers and linked on the individual-level through a unique person identifier

Vaccination and influenza records that cannot be linked with the individuals included in the cohort(s) are removed

Records with implausible dates (e.g. records of vaccination or influenza dated to before birth or after death) are removed

The National Vaccination Register's data quality assessment is applied

The data sets containing linked individual-level data relevant for the aggregation will be archived at THL in rokostat database schema influvaik

- season_20212022_children_study

  • id • age_years • sex • dob • death • deathdate • seasvacn6 • seasvacn5 • seasvacn4 • seasvacn3 • seasvacn2 • seasvacn1 • inflvac • inflvacdate • inflvac2 • inflvacdate2 • iivtype• iivtypedate • iivtype2 • iivtypedate2 • notiivtype

• notiivtypedate • vaxigriptetra • vaxigriptetradate • vaxigriptetra2 • vaxigriptetra2 • notvaxigriptetra • notvaxigriptetradate • fluenztetra • fluenztetradate • notfluenztetra • notfluenztetradate • infl • infldate • inflA • inflAdate • inlfB • inflBdate • chronic1 • nhosp • nprim • icd10liver • icd10diabe • icd10cardi • icd10cance • icd10immun • icd10lungd • icd10anemi • icd10renal• icd10demen • icd10strok • icd10rheum • icd10obesi •

- season_20212022_elderly_study

  • id • age_years • sex • dob • death • deathdate • seasvacn1 • inflvac • inflvacdate • vaxigriptetra • vaxigriptetradate • notvaxigriptetra • notvaxigriptetradate • infl • infldate • inflA • inflAdate • inlfB • inflBdate • chronic1 • nhosp • nprim • icd10liver • icd10diabe • icd10cardi • icd10cance • icd10immun • icd10lungd • icd10anemi • icd10renal• icd10demen • icd10strok • icd10rheum • icd10obesi •

The aggregated data set will be shared (http://apps.p-95.com/essa1/) and archived at THL in http://opus.thl.fi/group/rokostat/influvaik/drive/

- thl_20212022_aggregation.csv

  age • sex • seasvacn1 • chronic1 • nhosp • nprim • week • exposure • events • events_hosp • persondays • population • exp • out

Code book:

age	age in years
sex	as in D7.2 core protocol Annex 1
seasvacn1	received influenza vaccination in 2020/21 (0 : no, 1 : yes, fully vaccinated, 2 : yes, partially vaccinated, 9 : not applicable due to young age)
chronic1	as in D7.2 core protocol Annex 1
nhosp	number of hospitalisations in 2020 (0 : 0, 1 : 1-2, 2 : >2)
nprim	number of primary care consultations in last 12 months (0 : 0, 1 : 1-5, 2 : >5)
week	calendar week 2021/22
exposure	vaccination with the vaccine of interest (0 : unvaccinated, 1 : partially vaccinated, 2 : fully vaccinated)
events	number of outcome of interest occurrences
events_hosp	number of hospitalized outcome of interest occurrences
persondays	number of person-days
population	number of individuals who exited the cohort from that respective stratum
exp	exposure of interest (inflvac : any influenza vaccine, vaxigriptetra : Vaxigrip Tetra, fluenztetra: Fluenz Tetra)
out	outcome of interest (infl : any influenza, inflA : influenza A, inflB : influenza B)

Ethical approval

This analysis plan for the season 2021/22 is part of the study **'Influenssan tautitaakka ja rokotteiden vaikuttavuuden seuranta kansallisten terveysrekisterien pohjalta'** (The disease burden and surveillance of influenza vaccine effectiveness based on national health registers), which has received a favourable opinion from the Institutional review board (IRB) of the National Institute for Health and Welfare 2.6.2016. No additional approval is needed, because only aggregated data or vaccine effectiveness figures will be shared with DRIVE partners.