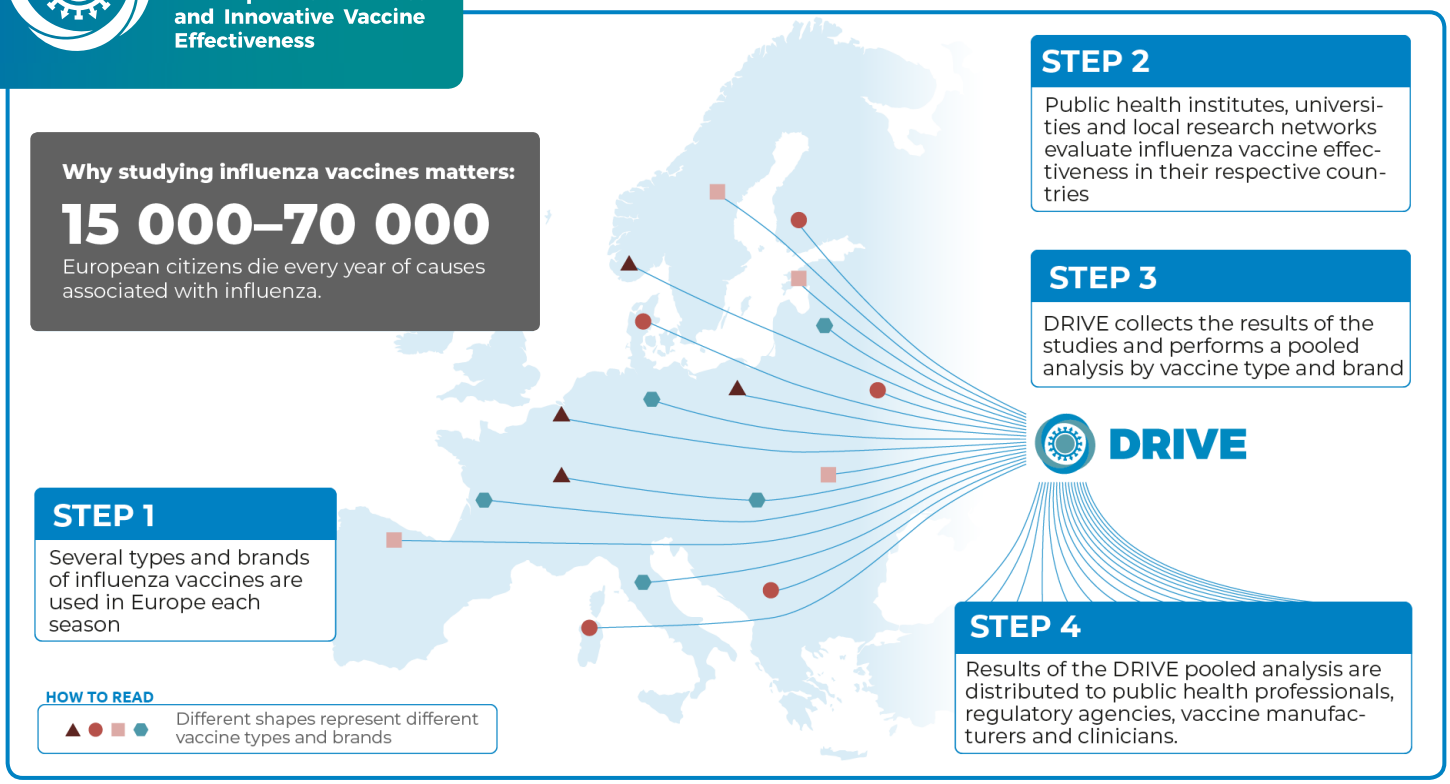


BRAND-SPECIFIC INFLUENZA VACCINE EFFECTIVENESS:

Building a network, season 2018-2019

Background

THE NEED FOR INFORMATION ON BRAND-SPECIFIC VACCINE EFFECTIVENESS

Although vaccination is the best way to protect against influenza, several factors affect how well vaccines work in a given influenza season and among different groups of people. These factors may be seasonal characteristics or the vaccine recipient's immune response or the type vaccine which they received.

Europe-wide research is needed to understand how different influenza vaccines perform during each influenza season. The DRIVE (Developing of Robust and Innovative Vaccine Effectiveness) consortium aims to build a robust research platform for studying annual brand-specific influenza vaccine performance, known as "vaccine effectiveness" (VE).

In 2017, the EU research project DRIVE was launched as a 5-year public-private partnership, aiming to set up a network of sufficient size to obtain meaningful vaccine effectiveness estimates. Public partners design and carry out the vaccine effectiveness studies.

The DRIVE project has been initially launched to address a guideline issued in 2017 by the European Medicines Agency (EMA), requesting effectiveness evaluation for all influenza vaccines used in the EU as part of the regulatory requirements.

Results of the DRIVE analysis are distributed to public health professionals, regulatory agencies, vaccine manufacturers and clinicians to enhance the understanding of the benefit of influenza vaccination. DRIVE also makes the results publicly available.

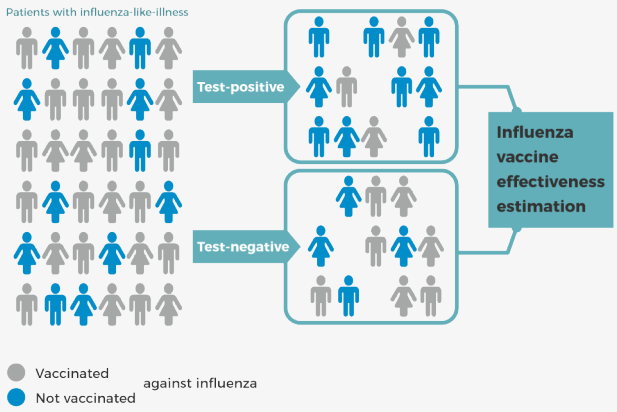
Studies

In 2017/18, DRIVE conducted a pilot study involving 5 study sites in 5 European countries to help establish the research platform. In 2018/19, improvements to the study design were made and the DRIVE network grew to include 13 study sites in 6 countries.

Progress

Two types of study design are used to assess influenza vaccine effectiveness.

Test-negative studies

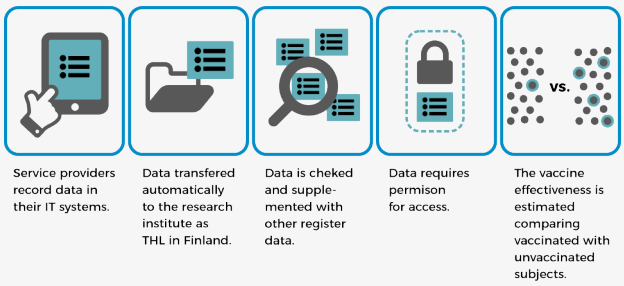


During **test-negative design studies**, patients with influenza-like symptoms who visit the general practitioner or hospital are tested for influenza and have their vaccination status recorded.

Influenza vaccine effectiveness is then estimated by comparing the proportions of people who test positive for influenza among those vaccinated vs. not vaccinated against influenza.

For example, if 4 out of 10 vaccinated people test positive for influenza (40%) and 8 out of 10 non-vaccinated people test positive for influenza (80%), the vaccine effectiveness is estimated to be 50%. Vaccine effectiveness is thus a percentage which indicates the proportionate reduction of cases among those who receive vaccination compared to those who don't.

Register-based studies



During influenza season 2018/19, data was collected from general practitioner consultations (primary care network sites) in Austria, Italy, and the UK, and from hospital sites in Finland, Italy, Romania and Spain. Data from these study sites were pooled to obtain VE estimates for three age groups using a test-negative study design.

Another type of study design uses Register-based cohort studies, which makes use of already collected data from vaccination registers and other electronic health care databases to generate vaccine effectiveness estimates.

In 2018/19, the Finnish registers (such as the vaccination register and the infectious disease register) were used to access data on influenza vaccination by type, brand, age of recipient, and whether or not the patient became infected with influenza, which was confirmed by laboratory testing. The large amount of high-quality data available enabled the calculation of robust brand-specific estimates for the two influenza vaccines available in Finland during the season 2018/19.

DRIVE has included results from studies using these different designs which were conducted in general practitioner or hospital clinics among people of all ages. The studies also looked at the different influenza viruses which were circulating in Europe.

INFLUENZA VACCINE EFFECTIVENESS ESTIMATES IN THE SEASON 2018/19

The 2018/19 influenza season was mild and it was a challenge to the DRIVE consortium to collect enough data to study vaccine effectiveness in much detail.

In the test-negative studies, pooled vaccine estimates for any influenza vaccine against any influenza for children ranged from 38-48%. In adults this range was 40-45%. Amongst older people the range was 18%-27%.

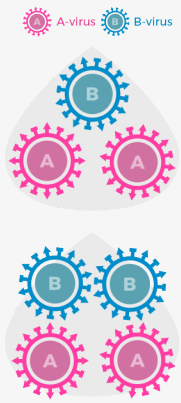
Types of Influenza

There are 2 types of influenza which causes seasonal epidemics in humans almost every winter in Europe – Influenza A and Influenza B.

Influenza vaccines protect against 2 types (or strains) of influenza A virus and either 1 or 2 different strains of Influenza B virus.

Types of influenza vaccines in Europe:

- 2 × A strains + 1 × B strain
  = trivalent influenza vaccine (three strains)
- 2 × A strains + 2 × B strains
  = quadrivalent influenza vaccine (four strains)



Overall, seven influenza vaccine brands were reported to have been used according to the data collected. For two of the brands, robust vaccine effectiveness estimates were obtained from the Finnish cohort study due to access to a large vaccination register. In children up to 6 years, vaccine effectiveness was estimated at 36% for the quadrivalent nasal vaccine Fluenz Tetra, and at 54% for the quadrivalent vaccine VaxigripTetra. In people of 65 years and older, vaccine effectiveness was estimated at 30% for VaxigripTetra.

However, even when combining the data from the various test-negative studies, it was not possible to generate robust vaccine effectiveness estimates for other brands and types of influenza vaccines due to the limited amount of data available for each type, brand, and age group.

Therefore these estimations should be interpreted with caution. Vaccine effectiveness is expected to vary from season to season due to the changing nature of the structure of the influenza virus and to be less effective in older adults compared to younger people due to the effects of ageing on the immune system. It's also important to note that vaccination can reduce the severity of influenza symptoms of those who do become infected.

The amount of data required to obtain robust vaccine effectiveness estimates for all influenza vaccine brands and types across different groups and settings is large, particularly in milder influenza seasons, as was the case in 2018/19. DRIVE will continue generating access to larger amounts of data by expanding the number of sites participating in test-negative studies; exploring the possibility of accessing data from a greater number of vaccination registers and other electronic healthcare databases; and encouraging greater data sharing amongst public health institutes, as well as health and medical research organisations across Europe.

Want to contribute?

If you or your institution are interested in joining DRIVE or contributing data to DRIVE, please visit **www.drive-eu.org** or get in touch at **info@drive.eu**.

Links:

- The report
- The consortium members

Appendices

APPENDIX 1.0:
TEST NEGATIVE STUDIES, VE AGAINST ANY LABORATORY CONFIRMED INFLUENZA.

In this study, 'Children' were 6 months - 17 years of age.
In this study, 'Older people' were over the age of 65.

Age group	Pooled VE estimates	95% Confidence Interval
Children	38 % - 48 %	(-65 - 81), (0 - 78)
Adult	40 % - 45 %	(2 - 63), (18 - 63)
Older people	18 % - 27 %	(-85 - 71), (6 - 44)

APPENDIX 2.0:
FINNISH REGISTER BASED COHORT STUDY, VE AGAINST ANY LABORATORY CONFIRMED INFLUENZA A.

	VE estimate (any vaccine)	95% Confidence Interval (any vaccine)	Pooled VE estimates for Fluenz Tetra	95% Confidence Interval for Fluenz Tetra	Pooled VE estimates for VaxigriTetra	95% Confidence Interval for VaxigripTetra
Children*	44 %	(36 - 51)	36 %	(24 - 45)	54 %	(43 - 62)
Older people	30 %	(25 - 35)	N/A	N/A	30 %	(25 - 35)

'Children' up to 6 yeards old* / 'Older people' over the age of 65 / N/A: not applicable
*Children 2-6y for Fluenz Tetra; Children 6m-6y for VaxigripTetra.

WHY STUDYING INFLUENZA VACCINES MATTERS?

According to the European Centre for Disease Prevention and Control (ECDC), seasonal influenza causes 4–50 million symptomatic cases in Europe each year, and 15.000–70.000 European citizens die every year of causes associated with influenza. The yearly economic and healthcare burden of influenza is substantial.

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https://www.imi.europa.eu

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