Development of Robust and Innovative Vaccine Effectiveness

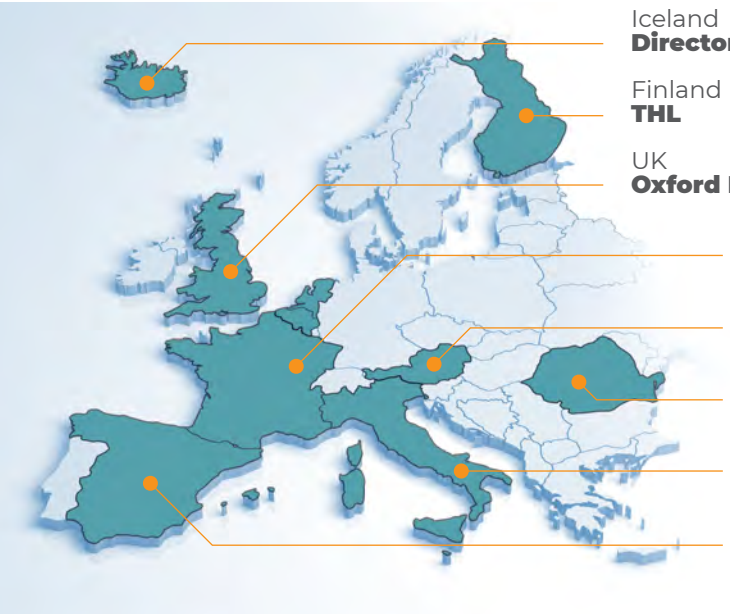
DRIVE

Monitoring vaccine performance after regulatory approval and immunization programme implementation is critical for guiding health authorities. Generating real-world evidence (RWE) to assess the benefit/risk of their marketed vaccines is an obligation for vaccines companies. Meanwhile combined efforts are needed to provide robust vaccine monitoring estimates in real-life conditions and account for the diversity and heterogeneity observed in Europe on virus circulation, vaccines technology and uptake, populations, and settings.

To respond to this endeavour in the context of monitoring seasonal influenza vaccine performance, the Innovative Medicines Initiative (IMI - https://www.imi.europa.eu/) launched a public-private partnership in July 2017 named the Development of Robust and Innovative Vaccine Effectiveness (DRIVE - https://www.drive-eu.org/) to establish a long-term collaborative platform and generate robust, high-quality and brand-specific effectiveness estimates for influenza vaccines used in the EU each season.

DRIVE involved 16 partners from seven European countries, coming from public health institutes, universities, research institutes, small-medium enterprises, patients' associations, and vaccine companies. Over the project's 5 years, DRIVE reached significant milestones by generating relevant brand-specific IVE estimates and was successful in demonstrating the value of collaboration in establishing a RWE infrastructure for vaccine effectiveness in Europe.

> *DRIVE, in which brand-specific influenza vaccine effectiveness (IVE) studies are implemented by independent study sites, paid with combined public and private funds, under the oversight of an independent scientific committee, is an example of a PPP model in which the insights and experience from the public and private sectors can jointly contribute to success, while avoiding conflicts of interest.*
>
> *DRIVE Independent Scientific Committee members*



Consortium Members

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Iceland
Embætti landlæknis

Romania
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CIRI-IT: Centro Interuniversitario per la Ricerca sull'Influenza e le altre Infezioni Trasmissibili – 5 hospitals; **Directorate of Health**, Iceland – 200 GPs and 1 hospital. **FISABIO:** Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana – 4 hospitals; **HUGTiP:** Hospital Universitario Germans Trias i Pujol – 1 hospital; **HULP:** Hospital Universitario La Paz – 1 hospital; **Practitioners HUS:** Hospital Universitario Salamanca – 1 hospital ; **HUVH:** Hospital Universitario Vall d'Hebron – 1 hospital; **ISS:** Istituto Superiore di Sanità – 245 GPs; **IREIVAC:** Innovative clinical research network in vaccinology – 5 hospitals; **MUV:** Medical University of Vienna – 250 GPs; **NIID:** National Institute for Infectious Diseases – Matei Bals – 1 hospital; **Oxford-RCGP RSC:** University of Oxford – Royal College of General Research & Surveillance Centre - 450 GPs; **THL:** Finnish Institute for Health and Welfare – nationwide register based cohort.

Seasonal influenza in Europe

50 million seasonal influenza cases are detected every year in the EU/EEA, affecting up to 11% of the population. This can result in 1**5,000–70,000 Europeans dying of causes associated with this illness (1)**.

Despite the typically brief duration of symptoms, influenza has a **significant annual economic and healthcare burden**. The direct and indirect costs of an seasonal influenza epidemic have been assessed to range from €6-14 billion annually (2).

Currently, there are 12 influenza vaccines on the European market built using different technologies for different population groups, but **as seasonal flu viruses mutate, their effectiveness can also vary**.

[1] ECDC. European Centre for Disease Prevention and Control Factsheet for health professionals. Available from: http://ecdc.europa.eu/en/healthtopics/seasonal_influenza/basic_facts/Pages/factsheet_professionals_seasonal_influenza.aspx. [Accessed 7 July 2022]

[2] Preaud, E., Durand, L., Macabeo, B. et al. Annual public health and economic benefits of seasonal influenza vaccination: a European estimate. BMC Public Health 14, 813 (2014). https://doi.org/10.1186/1471-2458-14-813

DRIVE Achievements

An agile, efficient, and cost-effective study platform

This large study platform includes 13 sites covering 21 hospitals and more than 1,000 general practices in seven EU countries (Spain, Italy, France, UK, Romania, Austria, Iceland) and one nationwide population-based cohort, in Finland. Data from those sites were collected following a common protocol and pooled to enhance sample size and geographical coverage. IVE results were delivered two months after the end of the influenza season (from end of April to early July). An average of 800K EUR -1M EUR was paid per season to sites for conducting IVE studies.

A transparent public-private partnership model

DRIVE partners sought to foster an atmosphere that was conducive to scientific discussions, sound study conduct, transparency and Independent Scientific Committee (ISC) oversight, while assuring effective control of possible conflicts of interest. DRIVE had a multi-stakeholder scientific collaboration strategy in which each partner contributed important added values, synergy in resource allocation and cohesiveness in communication.

Representative influenza vaccine estimates

In the 2021/22 season, 8 out of 12 of influenza vaccines used in the EU were captured by the DRIVE study platform. DRIVE has performed test negative design (TND) studies has during five influenza seasons (2017 – 2022) to include more than 35,000 severe acute respiratory infection (SARI) patients, approximately 60 variables, and 13 influenza vaccines. Moreover, it has also performed nation-wide cohort studies in Finland. The platform was unique compared to others in offering consistently brand-specific IVE results for each season in the EU.

A regulatory pathway

There is no uniform procedure to reach out to regulatory agencies as a consortium. The DRIVE consortium met with the European Medicines Agency (EMA) to unify vaccination performance data and reporting standards. This encouraged a discussion about vaccination monitoring implementation and results interpretation, including authorities' expectations about vaccine effectiveness robustness and what they consider informed results for decision-making.

Sharing of scientific insights

Seasonal IVE results were posted online, discussed at annual meetings, and submitted to the EMA for regulatory evaluation. Public and private partners created scientific communications and awareness campaigns on the outcomes of project. DRIVE communication activities resulted in 73 website posts, 34 event participations, 26 newsletters and 21 publications (of which 5 were peer-reviewed).

Key Learnings

- DRIVE established a public-private collaboration platform to undertake influenza vaccine effectiveness assessments. These independent studies led by public partners indicate that **cooperation with vaccine companies is compatible with transparent scientific collaboration**.
- DRIVE is a multi-disciplinary platform that **fosters scientific collaboration and debates about governance, public health involvement, and conflict of interest control.**
- DRIVE has created a framework for researchers, including external stakeholders, to **conduct secondary analyses utilizing the DRIVE dataset**.
- DRIVE established a proof of concept for future vaccine evaluation at EU level involving collaboration of all stakeholders.

> ***Providing evidence of effects of a vaccine has always been under the responsibility of the manufacturer, but once the vaccine is adopted in public health extended immunization programs the responsibility is to be shared between the public and the private sector. This is why a Public-Private collaboration is expected to be the suitable approach to monitor the effects of each vaccine and of the public health choice. A wider collaboration among multiple stakeholders, following well defined protocol and transparent procedures, as in DRIVE, has been shown to be able to produce robust and scientific sounded evidence, in the interest of the target populations.***
>
> *DRIVE Independent Scientific Committee members*

Perspectives

On 8 June 2022, at the final DRIVE Annual Forum, European stakeholders and public institution representatives gathered to discuss the benefits of public-private partnership-generated RWE for vaccine monitoring. During the meeting, DRIVE successes were acknowledged, and the initiative was described as scientifically sound with transparent governance mechanisms. Furthermore, open and transparent collaboration between the public institutions and vaccine companies was deemed of vital importance in fighting vaccine hesitancy and growing infodemics.

The roundtable summary can be found here: https://www.drive-eu.org/public-roundtable/. DRIVE efforts to find a reliable method of assessing vaccine effectiveness have also been highlighted in an article published on the innovative health initiative website which can be found here: https://www.ihi.europa.eu/news-events/DRIVE.

The COVID-19 pandemic has accelerated open data and access practices. It has also proven the necessity for quickly available near real-time evidence in health emergencies. DRIVE provided a viable setup to build a COVID-19 spin-off in only 9 months (see https://covidrive.eu/). COVIDRIVE exemplifies the importance of having existing RWE infrastructure and stakeholders' collaboration in place, for a rapid scale-up to address emergency use during a pandemic.

As the DRIVE IMI project ended in June 2022, it is expected that such successful public-private collaboration model will be considered in the ongoing conversation about vaccine monitoring framework in the EU, coordinated by the EMA and European Centre for Disease Control (ECDC).

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For further information or requests, please email info@drive-eu.org