

# Early estimation of pandemic influenza Antiviral and Vaccine Effectiveness (EAVE): use of a unique community and laboratory national data-linked cohort study

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## Scientific summary

### The EAVE study

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# Scientific summary

## Background

During the 20th and 21st centuries, there have been four pandemics (global epidemics) of influenza (1918–19, 1957–8, 1968–9, 2009–10) producing very large numbers of clinical cases and a large numbers of deaths (with an estimated 20–40 million, 1 million, 1 million and 0.25 million deaths, respectively). This was owing to the population having little immunity to the novel influenza viruses involved (H1N1, H2N2 and H3N2). Immunisation programmes delivered in primary health-care settings have been shown to be acceptable (as evidenced by previous high uptake rates) and effective, and this will therefore be the mainstay of disease prevention in any new influenza pandemic.

After the introduction of any new pandemic influenza, as well as front-line health-care workers, any new vaccination will be targeted at those who are considered to be at increased risk of serious illness or death from influenza infection, for example (1) those with any underlying medical conditions (e.g. chronic renal disease, immunosuppression resulting from disease or treatment, chronic heart disease, chronic respiratory disease); (2) those who may lack herd immunity (cross-reactivity) from exposure to previous pandemics or vaccinations; and (3) novel risk groups that are uniquely at risk because of a tropism exhibited by the virus. These national vaccination strategies have been shown to represent a potentially important approach to reduce both influenza-related illness and death, hence the considerable investment in this approach in many parts of the world.

## Objectives

Building on prior work, we aimed to enhance a previously used data linkage approach, which allowed the effectiveness of the 2009 H1N1 influenza pandemic vaccine to be determined. We wished to create a pandemic influenza reporting platform. We anticipate that the platform will allow rapid extraction and linkage of general practice clinical, prescribing and vaccination data from sentinel general practices to virology laboratory information [serology and real-time polymerase chain reaction (RT-PCR) test results].

The objective of the platform is that, once a new pandemic is under way, the following should be rapidly determined:

- the uptake and effectiveness of any new pandemic vaccine (if) available
- the analysis of any protective effect conferred by antiviral drugs
- the clinical attack rate of pandemic influenza in general practice,

and, with stored serological information, determine:

- the existence of any protective effect provided by previous exposure to, and vaccination from, A/H1N1 pandemic or seasonal influenza/identification of susceptible groups.

## Methods

The setting for this project was 41 participating general practices based throughout Scotland. The pre-pandemic phase of this project aimed to: complete all ethical, privacy and governance approvals; set up and test the data extraction systems; and create a repository of serology samples from patients registered with practices. Secure general practice data extraction systems supported by Trusted Third Party Albasoft Ltd have been tested.

Data on vaccination and other patient characteristics from general practice can be linked using the NHS Scotland's unique patient identifier – the Community Health Index number to the Scottish Morbidity Record catalogue, which has information on all inpatient hospitalisations and mortality within Scotland, virological RT-PCR data and serological information collected from patients with influenza-like illness (ILI) by general practices. The West of Scotland Specialist Virology Centre (WoSSVC) will store 2000 biochemistry samples from a subset of participating practices within NHS Lothian and Greater Glasgow and Clyde Health Board areas.

In the event of any new pandemic influenza data, statistical scripts have been created that can calculate odds and risk ratios (adjusted for age, sex and deprivation) for differences in proportions of vaccine uptake between different groups of patients and for investigating trends in vaccine uptake. For vaccine effectiveness using information from linked virological swab data, a logistic regression model will be fitted, adjusting for the effects of sex, age, socioeconomic status and being in an at-risk morbidity group. In addition, using the cohort method, the proportion of ILI, acute respiratory disease and other adverse outcomes, such as hospitalisation or death from influenza, between vaccinated and unvaccinated cases will be ascertained. These data will also be used to determine the clinical attack rate of pandemic influenza.

To determine the existence of any protective effect provided by previous exposure to, and vaccination from, A/H1N1 pandemic or seasonal influenza/identification of susceptible groups, serology samples are linked to general practice data (which provide patient information on patient vaccination status, demographics and comorbidities/pregnancy). They will then be tested (once a validated haemagglutination inhibition assay has been developed) prior to the introduction of any vaccination. A seropositive result will be determined using the universally accepted cut-off point of a 1 : 40 dilution for a panel of influenza strains. These tests will be undertaken by the WoSSVC in Glasgow. A binomial analysis and logistic regression will be used to determine differences in seropositivity rates owing to age, sex, comorbidity and vaccination status. Results will be expressed as the mean seropositivity rate with 95% confidence intervals.

## Conclusions

A new sentinel system capable of rapidly determining the estimated incidence of pandemic influenza, and pandemic influenza vaccine and antiviral uptake and effectiveness in preventing influenza and influenza-related clinical outcomes, has been created. We have all of the required regulatory approvals to allow rapid activation of the sentinel systems in the event of a pandemic. Of the 41 practices expressing an interest in participating, 40 have completed all of the necessary paperwork to take part in the reporting platform. The data extraction tool has been installed in these practices. Data extraction and deterministic linkage systems have been tested. Four biochemistry laboratories have been recruited, and systems for serology collection and linkage of samples to general practice data have been put in place.

## Study registration

This study is registered as ISRCTN55398410.

## Funding details

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## This report

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