Vaccine effectiveness of live attenuated and trivalent inactivated influenza vaccination in 2010/11 to 2015/16: the SIVE II record linkage study

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Scientific summary

The SIVE II record linkage study

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Scientific summary

Background

Globally, there are 90 million new cases of influenza and 1 million cases of influenza-associated severe acute lower respiratory infection per annum among children. National influenza vaccination programmes, delivered by primary care in the community, are important to reduce influenza-related illness, and hence the considerable investment in this approach. Previously, these programmes targeted older people (i.e. those aged ≥ 65 years) and people with chronic disease (e.g. asthma) who are susceptible to serious illness from influenza. Children are also thought to be important in the transmission of influenza to the populations at risk of serious complications from influenza, and diminished circulation of the virus has been predicted to improve herd immunity. Using evidence generated from epidemiological modelling, and following advice from the UK Joint Committee for Vaccination and Immunisation, from September 2013 the seasonal influenza vaccination programme was extended. In addition to the seasonal trivalent influenza vaccine (TIV), the live attenuated influenza vaccine (LAIV) is offered to all children aged 2–11 years (except children clinically severely immunocompromised owing to conditions or immunosuppressive therapy or oral steroids and children with severe asthma), by primary care clinicians in general practice (GP) and in schools in Scotland.

Objectives

Building on prior work, approaches used were further refined as part of three National Institute for Health Research Health Technology Assessment and Health Services and Delivery Research projects [Simpson CR, Ritchie LD, Robertson C, Sheikh A, McMenamin J. Vaccine effectiveness in pandemic influenza – primary care reporting (VIPER): an observational study to assess the effectiveness of the pandemic influenza A (H1N1)v vaccine. *Health Technol Assess* 2010;**14**(34); Simpson CR, Lone N, Kavanagh K, Ritchie LD, Robertson C, Sheikh A, *et al.* Trivalent inactivated seasonal influenza vaccine effectiveness for the prevention of laboratory confirmed influenza in a Scottish population 2000–2009. *Euro Surveill* 2015;**20**:ii–21043; and Simpson CR, Lone N, McMenamin J, Gunson R, Robertson C, Ritchie LD, Sheikh A. Early estimation of pandemic influenza Antiviral and Vaccine Effectiveness (EAVE): use of a unique community and laboratory national data-linked cohort study. *Health Technol Assess* 2015;**19**(79)]. The study determined seasonal influenza vaccine uptake and effectiveness in the Scottish population. This involved the interrogation of data from 230 GPs (a sample of 25% of Scotland's practices) linked to the Health Protection Scotland virology database (Electronic Communication of Surveillance in Scotland), the Information Services Division hospital and mortality records (General Register Office for Scotland Death Certification and Scottish Morbidity Record 01) and the Child Health Services Programme/Scottish Immunisation & Recall Service.

The primary objective was to evaluate:

- early estimates of the uptake and effectiveness of LAIV administered to children (from 2013).

The secondary objectives were to evaluate the:

- vaccine effectiveness of seasonal TIV among older people (aged ≥ 65 years)
- vaccine effectiveness of seasonal TIV among those people with at-risk diseases (e.g. asthma) and aged < 65 years

- validity of using laboratory-confirmed influenza tests from non-Sentinel primary care and secondary care compared with Sentinel primary care practices
- validity of using laboratory-confirmed respiratory syncytial virus as a negative-control outcome
- adverse events associated with vaccination.

Methods

The setting for this project was 230 participating GPs based throughout Scotland.

Data on vaccination and other patient characteristics from GPs were linked using NHS Scotland's unique patient identifier, the Community Health Index number, to the Scottish Morbidity Record catalogue (inpatient hospitalisations) and mortality within Scotland and virological real-time reverse-transcription polymerase chain reaction (RT-PCR) data. Vaccine uptake was derived from the electronic GP record and vaccine effectiveness was calculated using information from linked virological swab data, using a logistic regression model adjusted for the effects of sex, age and socioeconomic status. In addition, the cohort method was used to estimate the proportion of influenza-like illness (ILI), acute respiratory disease and other non-specific clinical outcomes, such as hospitalisation or death from influenza, between vaccinated and unvaccinated cases.

Results

Two-fifths (40%) of preschool-aged children and three-fifths (60%) of primary school-aged children registered in the study's practices were vaccinated. Uptake varied among groups [e.g. most affluent vs. most deprived in 2- to 4-year-olds, odds ratio 1.76, 95% confidence interval (CI) 1.70 to 1.82]. LAIV-adjusted vaccine effectiveness among children (aged 2–11 years) for preventing RT-PCR laboratory-confirmed influenza was 21% (95% CI –19% to 47%) in 2014/15 and 58% (95% CI 39% to 71%) in 2015/16. No significant adverse events were associated with LAIV. Among at-risk 18- to 64-year-olds, significant TIV effectiveness was found for four of the six seasons with the highest vaccine effectiveness in 2010/11 (53%, 95% CI 21% to 72%). The seasons with non-significant vaccine effectiveness had low levels of circulating influenza virus (2011/12, 5%; 2013/14, 9%). For people aged ≥ 65 years, TIV effectiveness was positive in all six seasons, but in only one of the six seasons (2013/14) was significance achieved (57%, 95% CI 20% to 76%). An analysis of age groups found significant vaccine effectiveness for people aged 65–74 years with asthma (53%, 95% CI 13% to 74%) and chronic kidney disease (60%, 95% CI 17% to 81%). Furthermore, significant vaccine effectiveness was found in those aged 75–84 years with chronic respiratory disease against influenza A(H3N2) (52%, 95% CI 11% to 74%) and in those with asthma against influenza B (86%, 95% CI 32% to 97%). Among the oldest age group (i.e. people aged ≥ 85 years), significant vaccine effectiveness was found for those with chronic respiratory disease (20%, 95% CI 2% to 34%), chronic heart disease (27%, 95% CI 3% to 45%), asthma (54%, 95% CI 43% to 62%), diabetes mellitus (34%, 95% CI 9% to 51%) and impaired immune function (42%, 95% CI 3% to 65%). TIV in adults was also found to be safe.

In the cohort analysis for people aged ≥ 65 years, adjusted vaccine effectiveness for reducing primary care consultations for ILIs was not significant in 2012/13 (vaccine effectiveness –64%, 95% CI –72% to –56%) and in 2013/14 (–28%, 95% CI –34% to –23%). However, statistically significant protective vaccine effectiveness was observed in hospitalisation due to influenza and pneumonia, ranging from 17% (95% CI 16% to 19%) in 2010/11 to 28% (95% CI 26% to 29%) in 2013/14. Vaccine effectiveness for death attributable to influenza and pneumonia was statistically significant and ranged from 32% (95% CI 31% to 33%) in 2010/11 to 40% (95% CI 39% to 41%) in 2015/16.

Conclusions

Few countries' health systems allow for the integrated and accessible data recording that made this study possible and made it feasible to centrally collate almost all hospitalisations and deaths attributed to influenza, allowing for completeness of reporting. Using these data, LAIV was found to be safe and effective in decreasing RT-PCR-confirmed influenza in children. TIV was safe and significantly effective (in most seasons) for 18- to 64-year-olds, with positive vaccine effectiveness in most seasons for those aged ≥ 65 years, although this was significant in only one season. Higher vaccine effectiveness was found among younger adults with asthma. This should strengthen the evidence base for health-care practitioners involved in distributing LAIV. TIV immunisation for at-risk adults aged < 65 years in primary health-care settings is effective. The finding of limited vaccine effectiveness in people aged ≥ 65 years supports the recent UK Joint Committee on Vaccination and Immunisation recommendation to introduce adjuvanted vaccine for those in this age group from the 2018/19 season.

Recommendations for research

The monitoring of the LAIV programme with enhanced Sentinel swabbing of preschool- and primary school-aged children should continue. Replication of vaccine effectiveness and safety in LAIV and TIV in other countries that have these influenza vaccine programmes is now required to confirm the results of this study. The Joint Committee on Vaccination and Immunisation has recommended the use of adjuvanted injectable vaccine for those aged ≥ 65 years from season 2018/19 onwards. A future study will be required to evaluate this vaccine.

Trial registration

This trial is registered as ISRCTN88072400.

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This report

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