Effectiveness of H1N1 vaccine for the prevention of pandemic influenza in Scotland, UK: a retrospective observational cohort study

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Summary

Background **A targeted vaccination programme for pandemic H1N1 2009 influenza was introduced in Scotland, UK, in October, 2009. We sought to assess the effectiveness of this vaccine in a sample of the Scottish population during the 2009–10 pandemic.**

Methods **We assessed the effectiveness of the Scottish pandemic H1N1 2009 influenza vaccination with a retrospective cohort design. We linked data of patient-level primary care, hospital records, death certification, and virological swabs to construct our cohort. We estimated vaccine effectiveness in a nationally representative sample of the Scottish population by establishing the risk of hospital admission and death (adjusted for potential confounders) resulting from influenza-related morbidity in vaccinated and unvaccinated patients and laboratory-confirmed cases of influenza H1N1 2009 in a subset of patients.**

Findings **Pandemic H1N1 2009 influenza vaccination began in week 43 of 2009 (Oct 21, 2009) and was given to 38 296 (15·5%, 95% CI 15·4–15·6) of 247 178 people by the end of the study period (Jan 31, 2010). 208 882 (85%) people were unvaccinated. There were 5207 emergency hospital admissions and 579 deaths in the unvaccinated population and 924 hospital admissions and 71 deaths in the vaccinated population during 23 893 359 person-days of observation. The effectiveness of H1N1 vaccination for prevention of emergency hospital admissions from influenza-related disorders was 19·5% (95% CI 0·8–34·7). The vaccine's effectiveness in preventing laboratory-confirmed influenza was 77·0% (95% CI 2·0–95·0).**

Interpretation **Pandemic H1N1 2009 influenza vaccination was associated with protection against pandemic influenza and a reduction in hospital admissions from influenza-related disorders in Scotland during the 2009–10 pandemic.**

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Introduction

In the past century there were three worldwide influenza epidemics (1918–19, 1957–58, and 1968–69). These epidemics resulted in substantial morbidity and mortality. 20 million to 40 million people died during the 1918–19 pandemic and about a million people died during each of the 1957–58 and 1968–69 pandemics. The lack of herd immunity to the new influenza viruses implicated (ie, H1N1, H2N2, and H3N2) could have been a key factor contributing to the high mortality.[1] The influenza A subtype H1N1 virus, which emerged in Mexico in March, 2009, was subsequently declared a pandemic by WHO in June, 2009.[2]

Production of pandemic H1N1 2009 influenza monovalent vaccines began soon after outbreaks in Europe and the USA, with two vaccines adopted by the UK's national immunisation programme: Pandemrix (GlaxoSmithKline Vaccines, Rixensart, Belgium), which requires one dose and Celvapan (Baxter Healthcare, Vienna, Austria), which requires two doses given at least 3 weeks apart; both are adjuvanted vaccines. Working in conjunction with the Scottish Government, the Chief Medical Officer for Scotland instituted a targeted vaccination programme[3] delivered through primary care.[4]

Vaccinations began in Scotland, UK, in late October, 2009, and these were initially offered to frontline health-care workers and pregnant women. Also targeted in this first phase were people with underlying health problems that put them at increased risk of serious illness or deaths from influenza-like illness. In December, 2009, the second phase of the immunisation programme targeted all children aged between 6 months and 5 years.

Observational studies can be used to estimate the effectiveness of health-care interventions in situations in which it is not ethical or feasible to mount more rigorous experimental studies, as was the case with the recent H1N1 pandemic.[5] Median monovalent pandemic H1N1 2009 influenza vaccine effectiveness for individuals younger than 65 years and presenting to sentinel primary-care practices and hospitals in five observational studies ranged from 60% (95% CI 27–78) to 93% (69–98).[6] Building on related pilot work,[4] we undertook an observational cohort study to assess the uptake and effectiveness of the pandemic H1N1 2009 vaccine in people from across Scotland registered with the Practice Team Information network, a sentinel surveillance network of primary care practices.

Methods

Study design

We constructed a cohort of patients by linking primary care, hospital records, and death certification datasets. We undertook a longitudinal study to assess vaccine effectiveness for preventing emergency hospital admissions and mortality from influenza-like illnesses, and also a nested case-control study (embedded within this cohort of patients) to assess vaccine effectiveness in prevention of laboratory-confirmed pandemic H1N1 2009 influenza.

Almost all individuals resident in Scotland are registered with a primary care practice, which provides a comprehensive array of health-care services, including the issuing of prescriptions. Nearly all specialist hospital care services are usually accessed through referral from primary care or, in emergency situations, through patients attending an emergency department. Primary-care-based physicians also provide and coordinate much of the care of patients discharged back into the community after a hospital admission.

We assessed the effectiveness of the Scottish pandemic H1N1 2009 influenza vaccination with a retrospective cohort design. The Practice Team Information network of 41 general practices covers a 5% representative sample of the Scottish population (n=247 178). These practices receive an annual financial incentive to electronically record all face-to-face contacts with patients.[7] Data from practices within Scotland are of high quality and useful for epidemiological research.[8–10] The completeness of capture of contacts and accuracy of clinical event coding in primary care was greater than 90%.[11] By use of the unique Community Health Index (CHI) number, general-practice patient-level data were extracted and then linked to the Scottish Morbidity Record catalogue, which has information on all inpatient hospital admissions within Scotland as well as information on death certification linked from the General Register Office for Scotland.[12] Hospital data are reliable from 1981, with completeness and accuracy rates exceeding 90%.[13] Additionally, we used the Health Protection Scotland dataset, which consists of all laboratory-confirmed cases of pandemic H1N1 2009 influenza from primary care. We established key characteristics of each identified patient in the cohort: sex, age (0–4, 5–14, 15–44, 45–64, 65–74, and 75 years or older), socioeconomic status (Carstairs' deprivation category scores[14] expressed as quintiles: 1 [most affluent] to 5 [most deprived]), clinical at-risk groups (ie, chronic respiratory disease, chronic heart disease, chronic kidney disease, chronic liver disease, chronic neurological disease, immunosuppression, and diabetes), pregnancy, and number of previous primary care consultations and hospital admissions (in the year before April, 2009).

Procedures

Vaccination uptake was extracted from primary care records; data on influenza, pneumonia, chronic obstructive pulmonary disease (COPD), and cardiovascular-related hospital admissions, and mortality (both individually and as composite outcomes, for emergency admissions) were extracted from the Scottish Morbidity Record and General Register Office for Scotland.[15] For comparison, we also assessed emergency hospital admissions for other serious morbidities in our population (eg, trauma, appendicitis, and hernia). For patients who remained unvaccinated and who had not been admitted to hospital, we defined the at-risk period of interest a priori as 103 days (ie, from Oct 21, 2009 [week 43 and the date of first vaccination in the dataset] to Jan 31, 2010 [week 4 and the study census endpoint; however, the vaccination programme continued beyond this point]). For patients who had been vaccinated, the risk period of interest after vaccination began 7 days after the vaccination date; individuals were classed as unvaccinated in the period before and for 7 days after vaccination.

We ignored hospital admissions before vaccination started (Oct 21, 2009), except when used to adjust for confounding. For example, if a person was admitted on Nov 1, 2009, was vaccinated on Nov 30, 2009, and then had another hospital admission on Dec 20, 2009, then we counted the first admission as unvaccinated and the second as vaccinated. All emergency admissions in the study period were counted and time at risk, therefore, only ended before the end of the study period if the patient died. This approach to analysis ensured that hospital admissions before vaccination could not be attributed to a vaccine effect.

In the absence of any agreed markers of frailty or functional status and robust methods for matching vaccinated and unvaccinated patients, we did a post-hoc sensitivity analysis. We limited our study population to patients younger than 65 years (ie, with age as a surrogate marker for frailty) with underlying disease (ie, patients with at least one clinical at-risk disease to help minimise differences between vaccinated and unvaccinated patients

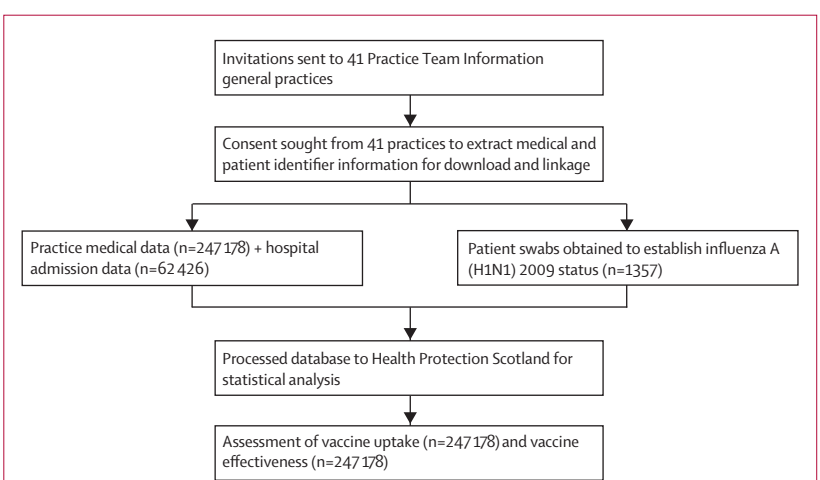

Figure 1: **Study profile**

by selecting a homogeneous group of patients targeted for vaccination) and used the longitudinal study design we described to assess vaccine effectiveness for preventing emergency hospital admissions and mortality from influenza-like illnesses in this population.

	Number of patients	Vaccine uptake
Sex		
Female	124 560 (50·4%)	21 260 (17·1%, 16·9–17·3)
Male	122 618 (49·6%)	17 036 (13·9%, 13·7–14·1)
Age group (years)		
0–4	13 950 (5·6%)	4089 (29·3%, 28·6–30·1)
5–15	26 076 (10·5%)	1711 (6·6%, 6·3–6·9)
15–44	104 343 (42·2%)	7953 (7·6%, 7·5–7·8)
45–64	64 674 (26·2%)	11 983 (18·5%, 18·3–18·8)
65–74	20 584 (8·3%)	6769 (32·9%, 32·2–33·5)
≥75	17 551 (7·1%)	5791 (33·0%, 32·3–33·7)
Deprivation quintile		
1	27 198 (11·0%)	3673 (13·5%, 13·1–13·9)
2	24 481 (9·9%)	3664 (15·0%, 14·5–15·4)
3	68 060 (27·5%)	11 683 (17·2%, 16·9–17·4)
4	61 385 (24·8%)	9101 (14·8%, 14·5–15·1)
5*	66 054 (26·7%)	10 175 (15·4%, 15·1–15·7)
At-risk comorbidity	61 141 (24·7%)	26 050 (42·6%, 42·2–43·0)
Pregnancy	2314 (2·2%)†	837 (36·2%, 34·2–38·1)

Data are number (% within category) or number (%, 95% CI). *Most socioeconomically deprived. †Pregnancy percentage refers to the proportion of women aged 15–44 years who were pregnant during the study period.

Table 1: **Pandemic influenza A H1N1 2009 vaccine uptake**

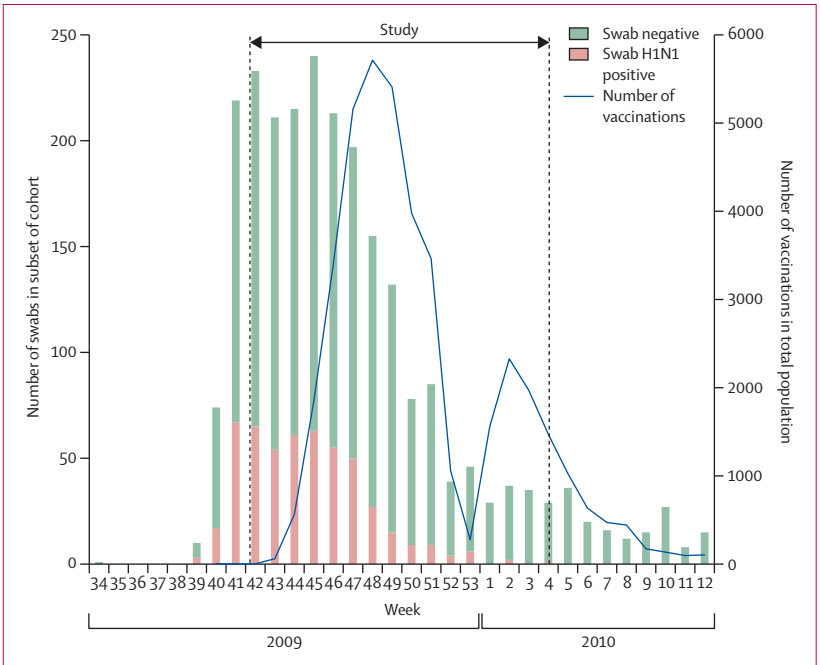

Figure 2: **Pandemic influenza A H1N1 2009 vaccinations (in the total population) and swab positivity (in the cohort of patients)**

During 2009, as part of the Scottish Government's response to pandemic influenza, we undertook a national programme, which included the use of Practice Team Information practices to test patients for pandemic H1N1 2009 influenza. This sentinel scheme encouraged general practitioners to swab at least the first symptomatic patient (who might have had mild symptoms) and at least two vaccinated patients each day up to a maximum of ten patients per practice for pandemic H1N1 2009 influenza. We also included results, for the patients in our study, from swabbing done in primary and secondary care for routine diagnostic purposes outside the sentinel scheme. RT-PCR tests were done by the West of Scotland Specialist Virology Centre (Glasgow, UK). More specifically, a rapid, specific, and sensitive multiplex RT-PCR assay that detects all influenza A types and simultaneously identifies samples that contain the pandemic influenza A H1N1 2009 virus was used for all submitted samples.[16] The virology centre is a WHO-accredited testing centre for influenza and conformed to the WHO standard for influenza testing. To calculate vaccine effectiveness, patient swab data were linked with the Community Health Index number, allowing characteristics of patients such as vaccination status to be established from general practice and hospital admission data.

Statistical analysis

We calculated adjusted odds ratios to assess differences in vaccine uptake rates by age, sex, and deprivation quintile. Illness and mortality rate ratios (RRs) are the ratio of the rate of first emergency admission to hospital or death in vaccinated patients compared with the rate of first emergency admission to hospital or death among those who did not receive the vaccine. This RR is a direct measure of vaccine effectiveness.

The unadjusted estimate of vaccine effectiveness was (1–RR)×100. Adjusted RRs of vaccine effectiveness for prevention of first hospital admission or death were derived from Poisson regression creating a Cox proportional hazards model, adjusting for age, sex, deprivation, previous number of hospital and general practice consultations, pregnancy, and clinical at-risk group. An adjustment to the SE of the estimated effect to account for clustering of patients within practices was done with the survey package in R (version 2.14) for the hospital admission endpoints.

For estimates of vaccine effectiveness, we did a nested case-control study design with information derived from linked virological swab data. A generalised additive logistic regression model[17] was fitted adjusting for the effects of week during the study period, age, sex, deprivation, previous number of primary care consultations, pregnancy, and being in a clinical at-risk group. Some of these patients did not receive the pandemic H1N1 2009 influenza vaccine; some received the vaccine, but after they were tested; and others received the vaccine before they were tested. We therefore

measured vaccine effectiveness by comparing swabs taken after vaccination from individuals who were vaccinated with swabs taken from all those who were not vaccinated at the time the swab was taken (people who were unvaccinated at the time of swab and who were then subsequently vaccinated count as unvaccinated in our analysis as do people who were never vaccinated). We assessed only the first dose when two doses were given.

95% CIs for the RR and tests of the differences between two rates were done with the "midp method" in the "rateratio" function and the "rate2by2.test" function, respectively, with the "epitools" package in R (version 2.9.0).[18] For small samples, 95% CIs for the RRs based on likelihood scores (a non-iterative method) were estimated with the Excel 2010 workbook.[19,20]

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

38 296 (15·5%, 95% CI 15·4–15·6) of 247 178 people were given pandemic H1N1 2009 influenza vaccination by the end of the study (Jan 31, 2010; figure 1, table 1). Vaccination began in week 43 of 2009 (Oct 21, 2009; figure 2). Most individuals received Pandemrix (37 530 [99%]), the rest Celvapan (766 [1%]). Uptake rates were highest in patients younger than 5 years of age and older than 65 years of age, pregnant women, and those with one or more chronic disease that put them in an at-risk category (table 1).

There were 6131 emergency hospital admissions for any cause during 23 893 359 person-days of observation, giving an incidence for emergency hospital admissions of 25·7 (95% CI 25·0–26·3) per 100 000 person-days. During the study period, there were 32 emergency hospital admissions for influenza and pneumonia in patients who received the vaccine (table 2). Patients who were vaccinated had a higher rate of hospital admission for the composite outcome (ie, influenza, pneumonia, COPD, or cardiovascular-related disease) than did their unvaccinated counterparts. Vaccinated patients were also more likely to be admitted to hospital for other causes. After adjustment for confounding, significant findings consistent with protection in recipients of pandemic H1N1 2009 influenza vaccine were evident for prevention of an emergency admission for the composite outcome (table 3). The vaccine effectiveness for the prevention of H1N1-related hospital admission in patients younger than 65 years with underlying disease was 19·8% (95% CI –17·8 to 45·4).

During the study period, there were 650 deaths from any cause (579 in unvaccinated patients [89%] and 71 in vaccinated patients [11%]), giving a mortality rate of 2·7 (95% CI 2·5–2·9) per 100 000 person-days. No deaths resulted solely from influenza. There were 28 deaths (4%) from pneumonia and 272 deaths (42%)

	Number of events	Rate per 100 000 person-days*	Crude risk ratio (95% CI)
Influenza			
No	31	0·14	1·00
Yes	2	0·11	0·86 (0·13–2·84)
Pneumonia			
No	136	0·62	1·00
Yes	30	1·69	2·75 (1·82–4·03)
COPD			
No	265	1·20	1·00
Yes	98	5·51	4·60 (3·63–5·78)
CRH			
No	412	1·86	1·00
Yes	86	4·83	2·60 (2·05–3·26)
Influenza and pneumonia			
No	167	0·76	1·00
Yes	32	1·80	2·39 (1·61–3·44)
Influenza, pneumonia, and COPD			
No	432	1·95	1·00
Yes	130	7·30	3·74 (3·06–4·54)
Influenza, pneumonia, COPD, and CRH			
No	844	3·82	1·00
Yes	216	12·13	3·18 (2·73–3·69)
Trauma-associated emergency admission†			
No	925	4·18	1·00
Yes	118	6·63	1·59 (1·30–1·91)
Any emergency admission			
No	5207	23·55	1·00
Yes	924	51·90	2·20 (2·05–2·36)

COPD=chronic obstructive pulmonary disease. CRH=cardiovascular-related hospital admission. *Vaccinated days at risk: yes=4 080 450; no=33 602 271. †Trauma (including fractures), appendicitis, and hernia.

Table 2: **Emergency hospital admissions and pandemic influenza A (H1N1) 2009 vaccination status**

	Hospital admissions		Mortality	
	Adjusted vaccine effectiveness*	p value	Adjusted vaccine effectiveness*	p value
Influenza	9·42% (–470·32 to 85·61)	0·92	NA†	NA
Pneumonia	16·63% (–44·23 to 51·81)	0·51	66·92% (–42·32 to 92·31)	0·14
COPD	7·44% (–28·03 to 33·08)	0·64	64·35% (5·45 to 86·56)	0·038
Cardiovascular-related disease	32·26% (10·07 to 49·98)	0·007	45·10% (11·97 to 65·76)	0·013
Influenza and pneumonia	13·68% (–56·57 to 52·41)	0·63	NA†	NA
Influenza, pneumonia, and COPD	7·34% (–24·89 to 31·25)	0·62	64·31% (6·34 to 86·40)	0·036
Influenza, pneumonia, COPD, and cardiovascular-related disease	19·54% (0·80 to 34·74)	0·04	51·53% (22·87 to 69·54)	0·0022

Data are % (95% CI) unless stated otherwise. NA=not applicable. COPD=chronic obstructive pulmonary disease. *Adjusted for age, sex, deprivation, previous number of primary care and hospital consultations, pregnancy, at-risk comorbidity, and clustering of patients within practices. †No deaths from influenza occurred.

Table 3: **Vaccine effectiveness in reducing emergency admissions to hospital and mortality for all patients**

	Total patients (rate per 1000 patients, 95% CI)	Swab positivity (95% CI)	Adjusted odds ratio (95% CI)*
Sex			
Female	778 (6·25, 5·81–6·68)	25·06% (22·15–28·23)	1·00
Male	579 (4·72, 4·34–5·11)	24·53% (21·20–28·19)	1·01% (0·76–1·34)
Age (years)			
0–4	292 (20·93, 18·56–23·31)	17·47% (13·54–22·24)	1·00
5–14	206 (7·90, 6·83–8·97)	45·63% (38·98–52·45)	3·15% (2·02–4·93)
15–44	524 (5·02, 4·59–5·45)	28·05% (24·38–32·05)	1·57% (1·06–2·33)
45–64	247 (3·82, 3·34–4·29)	16·19% (12·12–21·30)	0·77% (0·47–1·25)
65–74	55 (2·67, 1·97–3·38)	7·27% (2·86–17·26)	0·32% (0·11–0·98)
≥75	33 (1·88, 1·24–2·52)	3·03% (0·16–15·32)	0·10% (0·01–0·76)
Deprivation quintile			
1	131 (4·82, 3·99–5·64)	18·32% (12·63–25·81)	1·00
2	175 (7·15, 6·09–8·20)	22·86% (17·26–29·62)	1·24% (0·68–2·27)
3	343 (5·04, 4·51–5·57)	30·61% (25·97–35·68)	1·82% (1·07–3·10)
4	338 (5·51, 4·92–6·09)	22·78% (18·63–27·54)	1·22% (0·71–2·10)
5†	370 (5·60, 5·03–6·17)	24·60% (20·48–29·23)	1·50% (0·88–2·57)
At-risk comorbidity			
No	940 (5·05, 4·73–5·37)	24·57% (21·93–27·43)	1·00
Yes	417 (6·82, 6·17–7·47)	25·42% (21·48–29·81)	1·13% (0·83–1·55)
Pregnancy			
No	293 (5·95, 5·24–6·65)	24·60% (22·36–27·00)	1·00
Yes	36 (14·15, 9·80–18·51)	33·33% (20·22–49·67)	1·40% (0·64–3·05)

*Adjusted for age, sex, deprivation, previous number of primary care and hospital consultations, pregnancy, at-risk comorbidity, and clustering of patients within practices. †Most socioeconomically deprived.

Table 4: **Adjusted odds ratio of laboratory-confirmed pandemic influenza A H1N1-2009**

from the composite outcome; three of these deaths from pneumonia and 34 from the composite outcome were in vaccinated patients. Vaccinated patients were less likely to die from the composite outcome than were unvaccinated patients (table 3). Vaccine effectiveness for prevention of H1N1-related death in patients younger than 65 years with underlying disease was 51·2% (95% CI –35·1 to 82·4).

1357 patients were swabbed and then tested with RT-PCR. Although all groups were represented, these patients tended to be younger, female, and more likely to have an at-risk comorbidity or be pregnant than the general population (table 4). Pandemic influenza positivity peaked in week 41 and began to decline in week 46 (figure 2) with a total of 337 people testing positive for H1N1, giving a pandemic H1N1 2009 influenza positive rate of 24·8% (95% CI 22·6–27·2). The last H1N1 positive test was in week 4 of 2010 (Jan 31, the endpoint of our study). The adjusted odds ratios in table 4 show that during our study patients older than 65 years were less likely to test positive for H1N1 (when compared with children younger than 5 years). Of the 289 patients who were vaccinated and swabbed, two patients (swabbed after vaccination) tested positive for pandemic H1N1 2009 influenza. Of the 1068 unvaccinated patients, 335 tested positive for influenza. Vaccine effectiveness was 77·0% (95% CI 2·0–95·0).

Discussion

In our nationally representative cohort there were fewer hospital admissions and deaths from influenza-like illnesses in patients who were given an influenza A H1N1 2009 vaccine. Our findings suggest that our estimate for vaccine effectiveness (77·0%, 95% CI 2·0–95·0) is greater than recent estimates of vaccine effectiveness in case-control studies undertaken in the UK (72%, 21–90) and in a multicentre European study (71·9%, 45·6–85·5; panel).[21,22] However, our estimate is lower than the adjusted vaccine effectiveness reported in a nested case-control study within a cohort of the Spanish population in Navarre (89·0%, 36·0–100·0).[23] The vaccine effectiveness for prevention of influenza-like illnesses in our study is at least similar to the effectiveness of the seasonal influenza vaccine in preventing hospital admissions for influenza and pneumonia in elderly patients (14–27%),[24,25] influenza-like illness (27%) in all patients,[26] acute respiratory disease and cardiovascular disease (97%) in high-risk patients,[27] and medically attended acute respiratory illness in children (18% in those aged 18 months to 18 years).[28] Our estimate of vaccine effectiveness for prevention of hospital admissions for influenza-like illnesses for patients younger than 65 years with underlying disease was lower than that reported in a similar group by use of laboratory-confirmed hospital admissions for H1N1.[29]

Retrospective ascertainment of vaccination status is necessarily less reliable than prospective clarification, but the use of data derived from health records is more reliable than self-reporting methods,[30] as is the electronic recording of uptake rates in this sample of the Scottish population. Also, the small size of the Scottish population made it feasible to collate centrally almost all cases of H1N1 disease allowing for completeness of reporting.

Observational studies can be used to assess the effects of health-care interventions without affecting the care provided or the patients.[5] Therefore, when used in the assessment of vaccination programmes, these studies have high external validity and broad generalisability. Non-randomised studies such as ours are limited by the extent to which differences between vaccinated and non-vaccinated people might exist, in both their likelihood of receiving vaccination and in their subsequent care and follow-up.

We have, where possible, attempted to limit the effect of any bias caused by the preferential receipt of vaccine by relatively healthy individuals by adjusting for the effect of underlying disorders and consultations with primary care and hospital admission before the influenza season.[31] However, we were unable to undertake a review of case notes to gather information, including functional status gathered when patients were assessed in primary care and in hospital;[32] rather we were only able to use the parameters available from the linkage to adjust for confounding and do a post-hoc sensitivity analysis. With age as a surrogate

marker for frailty, our analysis showed similar effect sizes (albeit non-significant because of the smaller population) for the protection against H1N1-related hospital admissions and death for patients younger than 65 years of age with underlying disease (to help minimise differences between the vaccinated and unvaccinated patients by selecting a homogeneous group of patients targeted for vaccination).

A study to identify measures of functional status with routine data is underway.[33] The potential population effect of the pandemic vaccination programme could be underestimated because there was a significant mismatch between vaccine availability and vaccine uptake,[34] such that some cases of influenza accrued before the vaccine had been given (including a small outbreak of H1N1 influenza in the summer of 2009) and had an opportunity to exert an effect. The subset of our cohort tested for laboratory-confirmed influenza was younger, female, had an at-risk comorbidity, and was more likely to be pregnant than the general population; however, this largely represented those patients who consulted with primary care for influenza-like illnesses.[35] However, we accounted for these differences in our model as adjustment factors. Lastly, the relative lack of vaccine effectiveness against other respiratory viral infections would add further credibility to the results of this study; however, this interpretation is outside the scope of our present study and needs to be assessed in further work.

The results from the single outcome of emergency admission for cardiovascular-related illness or the use of the less specific composite outcome (emergency hospital admission due to influenza, pneumococcal disease, COPD, and cardiovascular disease, and death) should also be treated with some caution because not all these events are attributable to influenza, especially deaths related to COPD and cardiovascular disease, which were common in elderly patients who had relatively low levels of pandemic-associated illness. Furthermore, these outcomes are more prone to the healthy vaccine effect. For instance, within the high-risk group, patients at lower risk of heart disease and non-smokers (at lower risk of COPD) might be more likely to be vaccinated. However, researchers have already assessed the role of influenza in the generation of cardiac-related disorders (eg, myocarditis) and have shown an association between influenza epidemics and increased cardiovascular mortality and a decrease in cardiovascular mortality in high-risk patients following vaccination with influenza vaccine.[36–38]

That we used a sample of practices in Scotland means that our data could be subject to fluctuations as a result of any factors that have an effect locally, such as changes to the way that the primary care practices taking part in the Practice Team Information project manage their services.[11] However, apart from a reduction in precision, the small sample size, or other associated factors, are unlikely to have a substantial effect on our overall estimates of vaccine effectiveness. Also, conventionally, the seasonal influenza vaccine is thought to need 14 days to establish a protective effect; however, evidence from studies in progress (involving Health Protection Scotland [Glasgow, UK] and the Health Protection Agency [London, UK]) shows that 7 days is probably sufficient for the pandemic H1N1 2009 influenza vaccine. A sensitivity analysis with the 14-day cutoff period was done with similar estimates of vaccine effectivness (data not shown).

Evidence from swabs gathered from patients in the cohort presenting with respiratory symptoms in general practice suggests that the introduction of pandemic H1N1 2009 influenza vaccine in Scotland was associated with a high degree of protection against pandemic H1N1 2009 influenza. Additionally, we showed that the vaccine was associated with a reduction in both emergency hospital admissions and mortality from the combined category of influenza, pneumonia, COPD, and cardiac disorders and is likely to have reduced the burden of pandemic influenza on health-care providers. These findings help strengthen the international evidence base for the effectiveness of H1N1 vaccination programmes and the future distribution of pandemic influenza vaccine. Policy makers ought to be encouraged that the vaccine effectiveness estimates we obtained are similar to those for seasonal influenza; however, there were disappointing rates of uptake in the very young and pregnant women who were most susceptible to the pandemic.

Panel: Research in context

Systematic review

We searched PubMed for articles published up to Jan 31, 2012, with the search terms "H1N1 and vaccine effectiveness". 21 studies were identified. The effectiveness of monovalent pandemic H1N1 2009 influenza vaccine for prevention of laboratory-confirmed influenza in individuals younger than 65 years and who presented to sentinel primary care practices and hospitals in five observational studies ranged from 60% to 93%.[6] Adjusted vaccine effectiveness in a nested case-control study within a whole population cohort of the Spanish population in Navarre was 89% (95% CI 36–100) in preventing H1N1 and 32% for reduction of influenza-like illnesses.[23] Two case-control studies showed H1N1 vaccine effectiveness to be 72% (95% CI 21–90) in the UK and 72% (95% CI 46–86) in other multicentre studies in Europe.[21,22]

Interpretation

Our findings help strengthen the international evidence base for the effectiveness of H1N1 vaccination programmes and the future distribution of pandemic influenza vaccines. Policy makers ought to be encouraged that our vaccine estimates obtained are similar to those reported for seasonal influenza.

Contributors

CRS was principal investigator and led the writing of this report. LDR and AS helped to design the study and commented on drafts of the report. CR and JM helped to design the study, undertake the analyses, and write the report.

For the **HTA monograph report** see http://www.hta.ac.uk/fullmono/mon1434.pdf

Conflicts of interest

We declare that we have no conflicts of interest.

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