Influenza deaths in Leicestershire during the 1989–90 epidemic: implications for prevention

J. S. NGUYEN-VAN-TAM AND K. G. NICHOLSON

Infectious Diseases Unit, Groby Road Hospital, Leicester LE3 9QE

SUMMARY

There is an association between excess winter mortality and epidemics of influenza and it has been suggested that annual influenza vaccination should be offered to all over 65 years old as in the United States. This paper identifies the number of people dying from influenza in Leicestershire UK during the 1989–90 epidemic and the factors associated with a fatal outcome. The findings show that deaths attributed to influenza occur predominantly in very elderly people with underlying ill-health. The risk of influenzal death is greater in residential patients and increases substantially with the number of underlying medical conditions. The estimated death rates in vaccinated and non-vaccinated groups were not significantly different, but there were trends towards protection in both residential and non-residential groups. Influenza vaccine is not reaching the principal target groups and improved methods of influenza control are required.

INTRODUCTION

Deaths in excess of the normal winter increase are recorded regularly in association with influenza epidemics. The outbreak of influenza A in 1989–90 was the worst to have hit England and Wales since 1976 and may have been responsible, directly or indirectly, for about 26000 deaths [1].

Morbidity and mortality from influenza increase with age and presence of chronic disease [2] and the institutionalised elderly are thus placed at particular risk. The size of the elderly population in the United Kingdom is increasing and the number of those aged over 75 years is projected to increase by 358000 (9·9%) during the next decade [3]. Influenza vaccine offers 60–80% protection to healthy adults when vaccine and epidemic strains are closely related, but studies in elderly care homes reveal a mean protection of only 27% against influenza-like illness for influenza A (H_3N_2) vaccines, and 21% for influenza B vaccines [4]. Despite these poor results considerable reductions in the incidence of complications, including bronchopneumonia, hospital admission, and death, have been associated with the use of influenza vaccine in the elderly when vaccine and epidemic strains are closely related [5–8]. The Department of Health, the Welsh Office, and the Scottish Home and Health Department suggest that influenza vaccination be considered for elderly persons living in residential homes and long-stay hospitals, and for patients, especially the elderly, suffering with chronic pulmonary disease, chronic heart disease, chronic renal disease, diabetes and other less common

endocrine disorders, and conditions involving immunosuppressive therapy [9]. Only 10–20 % of elderly and high-risk patients are, however, immunized each year [10, 11]. Concern over vaccine safety and scepticism about vaccine efficacy are the most common reasons for poor vaccine uptake in both the United Kingdom and United States [10, 12].

Few data exist about deaths from influenza in the elderly in the United Kingdom, particularly with regard to vaccination status, place of residence and the presence or absence of chronic ill-health. We identified all certified influenza deaths that occurred in Leicestershire during the outbreak of influenza A/England/308/89 (H3N2) in 1989–90 to investigate the association with age, residential status, chronic ill-health, and history of immunization.

METHOD

Copies of death registrations for all patients aged ⩾ 65 years whose deaths in Leicestershire during September 1989 through March 1990 were certified as due to influenza, either as a primary or secondary cause, were provided by Leicestershire Health Authority. Access to general practitioner case notes for the deceased was gained through the Leicestershire Family Health Services Authority. The following data were obtained from the death register and general practitioner case-notes: basic demographic details; the usual place of residence classified into institutional and non-institutional (nursing and residential care homes, part III social services accommodation and long-stay hospital beds were classified as institutional, whereas all other residences, including warden-aided complexes, were considered non-institutional); the presence and severity of underlying chronic disease as identified from specific entries in the medical practitioners' notes, the drug history, the number of consultations with medical practitioners and hospital admissions before the final illness (chronic diseases and the drugs prescribed to treat them were classified according to the system affected); influenza vaccination since September 1985; and details of the final illness including the date of onset, number of consultations with the general practitioner, new drug prescriptions, admission to hospital, and place of death.

Information regarding the overall size and composition of the elderly population of Leicestershire at the time of the epidemic was obtained from the Office of Population Censuses and Surveys and the Leicestershire Census of the Elderly [13, 14]. The number of deaths from all causes in the elderly during December 1989 through January 1990 and their residential status prior to death were obtained from Leicestershire Health Authority death registrations.

For the purposes of estimating frequency of influenza mortality among institutionalised persons with chronic disease, the numbers of persons at risk with none, one, two, or three or more chronic medical conditions were estimated from the medical records of 162 elderly residents of 11 homes for the elderly in Leicestershire [15]. To estimate the probability of influenza mortality among non-residential people without chronic illness and those with lung or heart disease, the numbers of persons in each category were derived from a Market and Opinion Research Institute survey of 756 adults aged 65 or over who were interviewed in 148 constituency sampling points throughout Great Britain between 19–23 and

26–30 April 1990 for the Influenza Monitoring and Information Bureau. To estimate the influenza-associated mortality among vaccinees and non-vaccinees, the numbers of persons at risk in residential and non-residential settings were calculated from the medical records of elderly residents of homes for the elderly in Leicestershire and the immunization rates of the elderly population covered by 127 medical practices in the Trent Region [10, 15].

The data were analysed using SPSS-X and EPI-INFO programmes. Fisher's exact and Chi-squared tests. Wherever quoted, confidence limits are given at 95%.

RESULTS

Age, residential status, and cause of death

Forty-seven deaths between 8 December 1989 and 29 January 1990 were registered with influenza as the primary or contributory cause. Influenza was reported as the cause of death for 18 men and 29 women aged 67–97 years (mean 83·7; S.D. 7·0 years); 41 (87%) were aged $\geqslant$ 75 years. Fig. 1 shows the chronology of the deaths and consultation rates for influenza as reported by the Royal College of General Practitioner spotter practices.

Twenty (42·6%) of the 47 patients whose deaths were wholly or partly attributed to influenza lived in institutional care. At the time of the epidemic an estimated 128700 persons aged $\geqslant$ 65 years lived in Leicestershire and 6000 of these were receiving institutional care. Between 1 December 1989 and 31 January 1990 there were 1594 deaths from all causes among people in Leicestershire aged $\geqslant$ 65 years; 370 (23·2%) of these occurred in people receiving institutional care. Twenty (5·4%) of the 370 institutional deaths during the epidemic were attributed to influenza as compared with 27 (2·2%) of the 1224 deaths in private or warden-aided residences ($\chi^2 = 9·1$; $P = 0·0026$). The risk of dying from certified influenza associated with institutional living was 2·45 (confidence limits 1·39–4·32).

Pneumonia, entered on the death certificate at Ia (i.e. directly leading to death), and influenza, entered at Ib (i.e. directly leading to Ia), were recorded as the cause of death for 25 (53%) of the 47 cases. Of these 25, 10 had either heart failure ($n = 2$), ischaemic heart disease ($n = 1$), depression ($n = 1$), Alzheimer's disease ($n = 1$), chronic obstructive airways' disease ($n = 2$); old age ($n = 2$), and alcoholism ($n = 1$) as a subsidiary cause of death, i.e. entered at Ic (directly leading to Ib), or II (other conditions contributing to the death, but not related to the disease causing it), on the death certificate. Influenza was certified as the principal cause of death (i.e. entered at Ia) for 9 (19%) cases; 4 of these 9 cases had heart failure ($n = 1$), dementia ($n = 2$), and cerebrovascular, cardiovascular and renal disease ($n = 1$) as complications. The remaining 13 (28%) cases had heart failure ($n = 7$), myocardial infarction ($n = 3$), respiratory failure ($n = 2$), and cardiorespiratory failure ($n = 1$) as principal causes of death (i.e. certified as Ia), and influenza was certified as Ib for 3, Ic for 7, and II for 3.

Medical and drug histories of fatal cases

General practitioner notes were available for 42 cases, 18 out of 20 residential cases and 24 of 27 non-residential cases, and another was known from the death certificate to have suffered with Alzheimer's disease and to have lived in a
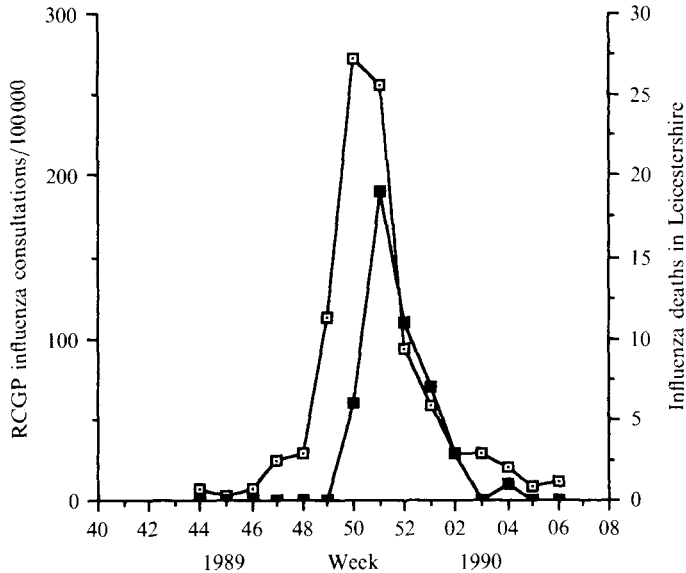
Fig. 1. Temporal relationship between certified influenza deaths in Leicestershire and the consultation rate (per 100000 population) for influenza in RCGP spotter practices in England and Wales. □, No. of influenza consultations; ■, influenza deaths in Leicestershire.

psychogeriatric hospital for many years. Thus some diagnostic information was available for 43 cases (19 of 20 residential, and 24 of 27 non-residential), but drug and immunization histories were only available for 42 cases with GP notes. The records of 40 of 43 (93%) patients revealed a history of one or more chronic medical problems; 15 (35%) had disease affecting 1 body system, 17 (39%) had 2 systems affected, 7 (16%) had 3 systems affected, and 1 (2%) had 4 body systems affected. Overall, 27 patients (63%) had cardiovascular disease, 11 (26%) had respiratory disease, and 16 (37%) had CNS problems, mainly dementia, Parkinson's disease, and a history of a cerebrovascular accident.

Only 5 of the 42 patients (12%) were taking no regular medication; 12 (29%) took 1 drug regularly, 10 (24%) took 2, 16 (38%) took 3 or more, and the average number of drugs taken per patient was 2·6. Cardiovascular medication was prescribed most frequently, to 25 (60%) of the 42 patients.

Thirty-nine (91%) of the 43 patients were seen by their general practitioner at least once in the 12 months before the final illness; the mean number of medical consultations during this period was 6·2 (s.d. 4·9). Eight patients (19%) were admitted to hospital during the 12 months before their final illness and 22 (51%) were admitted to either a hospital, nursing home, or other institution. Twenty-two were admitted to hospital at least once in the preceding 5 years.

Immunization status

Ten (24%) of 42 cases received influenza vaccine in 1989. The interval between vaccination and death ranged from 3–78 days (mean 39·7; s.d. 23·1), 3 were vaccinated in December when the outbreak was apparent nationally but 7 were vaccinated ≥ 21 days before death. Six of the 10 vaccinees were immunized during

Table 1. *Influenza-associated death rates during the 1989–90 influenza A epidemic*

Status	No. of influenza deaths	Estimated no. in population*	Deaths per 10^5†
Residential patients:			
(a) With 1 medical condition	8	2334	343
(b) With 2 medical conditions	5	1002	499
(c) With $\geqslant$ 3 medical conditions	6	222	2703
(d) With lung disease	5	1590	314
(e) With heart disease	12	1668	719
Non-residential patients:			
(f) Without medical condition	3	45399	6·6
(g) With lung disease	6	51534	11·6
(h) With heart disease	15	65031	23·1

 * Population estimates derived from the Office of Population Censuses and Surveys [13], the Leicestershire Census of the Elderly [14], analysis of the medical records of residents of 11 homes for the elderly in Leicestershire [15], immunization rates of the elderly population in the Trent Region [10], and a MORI survey of 756 adults in 148 constituency sampling points throughout Great Britain.
 † For (a), (b), and (c) χ^2 for trend $P < 0\cdot0005$; $P = 0\cdot06$ for (f) versus (h); $P \leqslant 0\cdot00002$ for (d) versus (g), and (e) versus (h) (Fisher's exact tests).

Table 2. *Influenza-associated death rates during the 1989–90 influenza A epidemic in vaccinated and non-vaccinated groups*

Status	No. of influenza deaths	Estimated no. in population*	Deaths per 10^5†
Residential patients:			
Vaccinated	7	2686	261
Non-vaccinated	11	3314	332
Non-residential patients:			
Vaccinated	3	23927	12·5
Non-vaccinated	21	98773	21·3

 * Population estimates derived from the Office of Population Censuses and Surveys [13], the Leicestershire Census of the Elderly [14], analysis of the medical records of residents of 11 homes for the elderly in Leicestershire [15], and immunization rates of the elderly population in the Trent Region [10].
 † $P \geqslant 0\cdot3$ for both comparisons of vaccinated and non-vaccinated groups.

the 1988–9 season and 4 of these were also vaccinated during the 1987–8 season. Only 1 of the 33 who were not vaccinated during 1989 received vaccine during the previous 5 years. Vaccination was considerably more common among institutional than non-institutional patients, but the difference was not statistically different (7 of 18 (39%) versus 3 of 24 (12·5%); $P = 0\cdot11$, Fisher's exact test).

Risk of influenza associated mortality

Estimated rates of influenza-associated mortality during the influenza A epidemic according to residential status and presence of chronic conditions are summarized in Table 1. Among residential patients there were consistent and substantially increased rates of death with increased presence of chronic conditions. These ranged from 343 influenza deaths per 100000 among those with

one chronic disease to 2703 per 100000 in persons with 3 or more chronic medical conditions (χ^2 for trend 12·4, $P < 0·0005$). The death rates of 314 and 719 per 100000 for residential patients with lung and heart disease represent increases of 27- and 31-fold respectively over the rates for non-residential patients ($P < 0·00002$, Fisher's exact test).

Estimated rates of influenza mortality among vaccinees and non-vaccinated persons in both residential and non-residential settings are shown in Table 2. Among both residential and non-residential persons there were trends towards lower mortality in vaccinees (21% lower among residential people, 41% lower among the non-residential), but neither difference was statistically significant.

DISCUSSION

Before discussing our observations it is important to consider the potential strengths and limitations of the study. We focused on the certified deaths in Leicestershire that were attributed partly or wholly to influenza by clinicians, without laboratory or post-mortem confirmation of the diagnosis. Although this approach sacrifices specificity of diagnosis, it nevertheless considers cases that contributed to the excess mortality of 26000 that occurred in England and Wales during the 1989–90 influenza epidemic which was the worst to hit the United Kingdom since 1976 [1]. Regarding the 47 deaths in this report, several points are of particular note, first, that during confirmed community epidemics, as occurred in Leicestershire, the clinical diagnostic rate as later assessed by serology averages about 80% [16–20] and secondly the mean consultation rate during the final illness was 2·3 visits per patient, so death certifications were supported by clinical observation over several days for most patients and the diagnostic rate is therefore likely to be high. Thus our results, based on a total population of 892000, are especially relevant to the role of general medical practitioners in preventing deaths directly attributed to epidemic influenza.

The observation that all influenza deaths in Leicestershire involved persons older than 65 years of age is compatible with past influenza mortality patterns for England and Wales (WHO, World Health Statistics Annuals, 1977–89). Moreover, the findings that only 3 of the 43 cases for whom comprehensive data were available involved persons without chronic disease is in agreement with the study in Portland, Oregon, USA, by Barker and Mullooly [21]. The fatal influenza cases in Leicestershire had a mean age of 83·7 years; 91% were seen by their medical practitioners at least once during the preceding 12 months and the average number of medical consultations during this period was 6·2; half were admitted to either a hospital, nursing home, or other institute during the preceding 12 months, and 43% were living in an institution at the onset of the final illness. Although many deaths occurred among the debilitated elderly, approximately half had chronic disease but were considered medically stable and functioning independently, indicating a need to improve vaccines, vaccine delivery, and chemoprophylaxis with amantadine or rimantadine.

The estimated rates of influenza-associated death among sub-groups of the population summarized in Table 1 provide a quantitative basis for setting priorities for prophylaxis. The absence of any influenza deaths among persons

younger than 65 years and the rate of only 6·6 per 100000 healthy, non-residential persons aged 65 years and older suggests that such persons should be given relatively low priority. Our data are compatible with the mortality patterns documented by Barker and Mullooly [21] and, regardless of questionable vaccine efficacy, do not support the view that the current British immunization policy should be extended to include all healthy people aged $\geqslant$ 65 years, as this would evidently have little impact on deaths attributed to influenza.

Among non-residential people with heart disease the death rate increased substantially compared to those without underlying chronic ill-health but was still comparatively low at 23·1 per 100000. The death rates of 314 and 719 per 100000 for residential patients with lung and heart disease represent increases of 27- and 31-fold respectively over the rates for non-residential patients and reflect the greater debility of residential individuals and opportunities for cross-infection in institutions. In the residential facilities there were consistent and substantial increased rates of death with increased presence of chronic disease, ranging from 343 per 100000 with one chronic disease to 2703 per 100000 (i.e., almost 3%) in persons with 3 or more chronic conditions.

Altogether 24% of the deceased were vaccinated against influenza and 17% received vaccine more than 3 weeks before death. Because the number of influenza deaths was small there were no significant differences between the immunization rates for residential and non-residential persons. However the immunization rate of 39% for residential patients was compatible with that of 45% for residents of 11 homes for the elderly in Leicester [15], and the rate of 12·5% for non-residential patients was comparable to the rate of 19·5% for all people aged $\geqslant$ 65 years in Trent Region [10].

Vaccine effectiveness in reducing deaths was estimated by comparing the perceived death rates for vaccinated and non-vaccinated people using recent surveys of immunization status of elderly people in Leicester and the Trent Region [10, 15]. Previous serological studies have shown that there was a good match between the A/Shanghai/11/87 (H_3N_2) vaccine component and the A/England/308/89 (H_3N_2) wild-type strain responsible for the 1989–90 epidemic [22]. Assuming that there were no differences between vaccinated and non-vaccinated groups in exposure to influenza virus nor in the way in which they were treated, then the value of vaccination in both residential and non-residential settings – despite the good match between vaccine and wild-type strains – remains unproven. However, it is acknowledged that there were trends towards lower mortality among both residential and non-residential vaccinees (21% and 41% reductions respectively) and that the reductions in deaths may be due to vaccination, but given the epidemic and immunization levels of 1989–90, almost 100000 residential and 600000 non-residential elderly people would be needed to achieve statistically significant results.

Previous studies have found a decreased incidence of complications of influenza or influenza-like illness, including bronchopneumonia, hospital admission, and death in people receiving influenza vaccine compared to non-vaccinees [5–8]. None of these studies were truly randomized and since doctors are likely to vaccinate active medically-stable patients with chronic ill-health rather than inactive, severely debilitated individuals – whom we have found to be at greatest risk from

influenza – it is possible that the apparent beneficial effect of vaccine in previous studies is related more to selection of patients for vaccination, or subsequent antibiotic therapy, than to the protective effect of vaccine. Until the failure of vaccination is established by large well-designed prospective studies we believe that vaccine delivery to current target groups should be improved, the prophylactic use of amantadine should be more widespread [23], and that the search for improved influenza vaccines should continue.

ACKNOWLEDGEMENTS

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