Epidemiology of Influenza in the United Kingdom 1996-2007

Introduction

The recent international concern related to an important outbreak of influenza A/H1N1, or swine flu, in Mexico has heightened awareness of the multifaceted and unpredictable behavior of the many viruses that can cause clinically important symptoms of influenza (1-3). In the United Kingdom (UK), influenza typically occurs seasonally from October through March. The size and virulence of outbreaks vary substantially over age, calendar time, and geography (4-6).

The availability of an accurate computerized record of medicines, vaccines, and clinical diagnoses recorded by more than 1,000 general practitioners from the 1990s to early 2007 allowed us to update the rate of influenza in the UK over an eleven-year period (July 1996 through June 2007) in relation to population demographics, calendar time, region, and general practice (7). The available information also documents the frequency of influenza vaccination in this population over these years.

Methods

Data Source

The study is based on around 350 UK general practices that have been providing standardized, computer-recorded, anonymous medical information since the early 1990s to the General Practice Research Database (GPRD). The source population, encompassing 3 million people annually, derives from these practices and has been followed from 1996 through 2007. It should be noted that the size of the population according to age and region has remained steady during this time since persons leaving a

practice due to death or transfer to a new practice are balanced by persons who are born or transfer into the practice. The comprehensive nature of the information on clinical diagnoses, vaccines, and drug exposure recorded in the database has been repeatedly validated and found to be of high quality for the purpose of conducting epidemiologic research (7-10). Numerous studies based on the database have addressed the safety and effectiveness of vaccines (11-15).

The general practitioners (GPs) who contribute to the database use office computers in their routine practice, have agreed to provide the information for research purposes, and have been trained to record medical information including demographic data, medical diagnoses, medicines, and vaccines in a standard format. Diagnoses and administrative events are recorded using Oxford Medical Information System (OXMIS) or Read codes. All patient and general practice information received by us is anonymized. We do receive the first two-digit postal code of each general practice. The distribution of age, gender, and geography in the practices is closely similar to that of the UK except that London is somewhat underrepresented (16). The UK population has been divided into eight regions by the GPRD group at the Medicines and Healthcare products Regulatory Agency (MHRA), which is responsible for data collection, storage and transmission to our office. The regions have been further subdivided into postal zones. In this report we identify the postal zones by the city, town, or county upon which they are based.

Estimation of Monthly Rates

We used a cohort design to estimate monthly age, region and general practice specific rates of clinically diagnosed influenza per 10,000 people at risk for the period July 1996 through June 2007.

Frequency of Influenza Vaccination

The frequency of influenza vaccination by age and calendar month for the period July 1996 through June 2007 was also derived directly from the computer-recorded information.

Data Analysis

As in our prior publication (7), we calculated monthly rates of influenza by dividing the number of cases of "influenza" or "influenza like symptoms" recorded by general practitioners in each calendar month by the number of people active in the practices (i.e. those who were at risk for influenza in that month). We provide the results according to age, calendar time, region and general practice.

Ethics Approval and Funding

The protocol for this study was reviewed and approved by the Independent Scientific Advisory Committee (ISAC) of the General Practice Research Database. This study was not funded.

Results

We identified more than 40,000 persons in the database who were diagnosed as having influenza during the eleven-year period of study. Since the database represents about 5% of the UK population (16), we estimate that there were more than 800,000 cases of influenza diagnosed nationwide during the eleven-year study period.

The monthly rates of influenza in the database are shown in Figure 1 for the period July 1996 through June 2007. The estimated extent of the seasonal activity has been previously labeled as baseline, normal seasonal activity, and higher than seasonal average (5-6). Few cases (rate <2 per 10,000 persons) were recorded in the spring and summer months from April through September in any year. Higher than seasonal average outbreaks were recorded in the database in the fall and winter (October through March) of 1996-1997 (6,885 cases), 1998-1999 (7,452 cases), and 1999-2000 (9,005 cases). In each year, the outbreak began in December, reached a peak in January, and lasted for less than two and a half months. Smaller outbreaks in 1997-1998 (3,502 cases) and 2000-2001 (3,940 cases) peaked in February (Figure 1).

From July 2001 through June 2007 the rate of influenza fell to background levels below 2,700 cases per season. In November of 2003, a brief outbreak in all regions totaled 1,007 cases, but the overall rate for the 2003-2004 season remained close to the normal background level (Figure 1) (17). During the eleven-year period, there were no seasons that reached epidemic activity (5-6).

The rates of influenza accumulated over the eleven-year period by month are shown in Figure 2 according to age and calendar month. The rates were highest on average for the months of December through February. The rates were regularly highest in those age 20-39 years, followed by those aged 40-54 and those aged 55-69 years. The

rates tended to be lowest in those 70 years of age or older. Exceptions occurred in October and January, where the highest rates were in the elderly and those aged 40-54, respectively. The seasonal rates according to region and calendar time are shown in Figure 3. The rates were consistently highest in Wales and Northern Ireland and consistently lowest in the Southern region. The dramatic decrease in rates in all years after 2001 is evident in all regions.

Influenza Vaccination

The frequency of influenza vaccination over time is shown in Figure 4 according to age. From 1996 through September of 2000 about 35%-45% of persons 70 years or older and 18%-22% of those age 55-69 years received at least one influenza vaccination. These frequencies rose rapidly in October 2000 after the government initiated a policy to vaccinate the elderly and others at high risk for influenza (18-19). By 2005, the vaccination frequency in the Database practices reached 90% and 50% in those at least 70 years and 55-69 years of age, respectively. About 64% of vaccinations were given in the month of October, 25% in November, and 5% in December. More than 75% of people received at least two influenza vaccinations and 16% were vaccinated eight or more times during the eleven-year period.

Comment

The recent serious outbreak of influenza A/H1N1 that began in Mexico in April of 2009 raised widespread concern throughout the world that a virulent pandemic might ensue. The strain of virus responsible for the initial outbreak is a previously unidentified

subtype of H1N1 that is reported to be the result of a novel re-assortment of influenza A from avian, swine, and human strains (1). The extent and virulence of the spread and clinical consequences of the outbreak in Mexico were initially uncertain and on April 25, 2009 the World Health Organization declared the swine influenza outbreak in North America a "public health emergency of international concern" (1).

This concern was shared in the UK, where urgent nationwide surveillance for potential H1N1 influenza cases and stockpiling of anti-viral drugs were intensified (1,20). This concern prompted us to update information on the rate of influenza in the UK for the years 1996 through 2007 in order to provide some background for considering the possible spread of Influenza A/H1N1 in the UK (7). As of 9 June 2009, 675 cases of swine influenza had been confirmed and an additional 300 were under investigation (21).

In the past two decades outbreaks of influenza in the UK have been restricted to the fall and winter months of October through March (4-6). The severity, age, and geographic distribution have varied from season to season. The largest outbreak considered to be "epidemic" occurred in the 1989-1990 season (5-6). Three outbreaks in the 1996-1997, 1998-1999 and 1999-2000 seasons were described as "higher than seasonal average" (5-6). Other small outbreaks prior to 2001 are described as "normal seasonal activity". Since October 2001, the seasonal rate of influenza has remained at an unusually low level (22). If an important outbreak of influenza were to now occur in May or June in the UK, this would be highly unusual.

A previously undetected virus (A/H1N2) was identified in the UK 2001-2002 influenza season (23-24). Nevertheless, the level of influenza in that season remained low

(24). This experience indicates that circulation of a previously undetected influenza virus strain does not necessarily lead to a substantial public health matter.

In addition to providing nationwide estimates of influenza rates, the current study identified the variety of outbreaks in relation to age, calendar time, and region. Real time identification and detailed evaluation of such outbreaks could provide for rapid, cost efficient identification of their source and nature in terms of the identification of the responsible influenza virus, and allow for the initiation of public health measures to mitigate the outbreak.

The monthly rates of influenza derived from 350 practices in the GPRD are closely similar to the weekly rates reported from the UK Royal College of General Practitioners based in 96 sentinel surveillance centers (5-6,17,22), as was the case in our prior publication (7). The concordance between the two data sources lends support to the reliability of both sources of information (25). A certain proportion of patients with influenza may not have seen their GP and may have treated themselves at home while subjects with severe symptoms, complications, high fever, advanced age and/or preexisting comorbidities are presumably more likely to see their GP for influenza symptoms than the "average" population. Therefore, our assessment of influenza incidence based on data from the GPRD is likely to underestimate the true rate. On the other hand, there is also some misclassification with regard to the correct diagnosis of influenza in the general practice setting since influenza is a somewhat subjective diagnosis that is based on a combination of symptoms during a given time period when influenza is likely to occur, which may lead to an overestimate of the real rate of influenza. It is not possible to estimate to what extent these sources of misclassification

may counterbalance each other, and while we recognize that there is likely to be some misclassification in a large computer-based survey like this, the rates in this study are consistent with other published rates (5-6,17,22).

Following a comprehensive review of published studies, Simonson et al concluded that the effectiveness of the influenza vaccine in the elderly is still under debate (26). In the current population-based database a major increase in influenza vaccination frequency in October 2001 was associated with a dramatic decrease in the rate of influenza in all age groups that began in October 2001 has continued through March 2007. Whether this time trend association is coincidental or, at least in part, due to increased influenza vaccination remains to be determined.

In summary, these data provide useful estimates of the rate of influenza and influenza vaccination in the UK. The availability of this source of data could be an important basis for plans to locate and respond to the otherwise unpredictable natural occurrence of a potential outbreak in the UK in the near future.

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Figure 1. Monthly rate of influenza for July 1996 through June 2007. Seasonal activity labels from Goddard et al (6).



Figure 2. Monthly rate of influenza accumulated from July 1996 – June 2007 by month and age group.



Figure 3. Seasonal rate of influenza by region.



Figure 4. Frequency of influenza vaccination by age group and calendar time.