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Influenza surveillance in England and Wales using routine statistics

Development of 'cusum' graphs to compare 12 previous winters and to monitor the 1980/81 winter

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SUMMARY

Surveillance of influenza in England and Wales is made by monitoring weekly data. Principal indices are deaths, sickness-benefit claims (SBC), laboratory reports and observations from general practitioners (GPs). The 12 winters 1968/9 to 1979/80 have been studied to see which indices best described size and timing of influenza epidemics. A method of plotting the data (called cusums) is suggested which makes it easier to see the effect of small epidemics.

Cusums for GP statistics and respiratory deaths were found to be the most helpful indices for describing both size and timing of the epidemics, followed by total deaths and SBC, which were less specific to influenza, and influenza deaths, which lagged behind other indices. Deaths certified as pneumonia have been increasing over these years, whereas bronchitis deaths have been decreasing and these indices should not be used separately for monitoring.

The laboratory reporting system is important. It confirms the presence of influenza virus in the community and indicates prevalent strains. Because it is a voluntary system with no defined population base the reports are not reliable numerically for estimating relative size of epidemics or for developing cusums.

Cusum plots were unanimous in describing the winter of 1980/1 as one of little influenza activity.

INTRODUCTION

In 1977 the Communicable Disease Surveillance Centre (CDSC) assumed responsibility for influenza surveillance from the Department of Health and Social Security (DHSS) and the Welsh Office and now produces weekly influenza surveillance reports for England and Wales during epidemics. These reports are prepared using routine statistics on morbidity and mortality. Additional material on influenza abroad is provided by the World Health Organization. The reports give estimated current incidence together with anecdotal reports on outbreaks of particular interest. These surveillance reports are not published but are circulated in the weekly Communicable Disease Report (CDR).

Sometimes the progress of influenza elsewhere in the world can indicate the possibility of an approaching epidemic. However, influenza has proved unpredictable – for example, the newly emerged A/Hong Kong virus spread from the southern hemisphere and first arrived in Britain in the winter of 1968/9, but caused only a small outbreak. One winter later the same strain caused one of the largest post-war epidemics. This lack of predictability means that the study of influenza has to rely on close and frequent monitoring.

The first aim of the monitoring scheme is to decide when an epidemic has begun. It has been suggested that such decisions could be made by devising 'epidemic thresholds' for each index. These would be calculated using values of that index observed in past winters when there was no epidemic. However, there are few winters when influenza activity is negligible and therefore little data from which to estimate the distribution of indices in non-epidemic winters. Unpublished estimates of epidemic thresholds have proved unsatisfactory.

In the USA Serfling (1963) and later at the World Health Organization Assaad, Cockburn & Sundaresan (1973) have used sine-wave models fitted to weekly mortality data to evaluate expected levels of weekly deaths. These are dual purpose models which give estimates of excess mortality during past epidemics and give epidemic thresholds for current monitoring. Data from winters of moderate influenza activity have had to be included in order to have enough data to estimate the model. The standard errors, which are used to estimate epidemic thresholds, are affected by the constraints of a sine wave model, by non-normal distribution and by the fact that some 'outlying' data have been omitted. A new model for monitoring mortality statistics is being tried in the USA using time-series analysis (Choi & Thacker, 1981). This method gives fewer 'false alarms'. The approach would probably not be suitable for some of the UK indices, which remain at or close to zero during the summer months. In Moscow complete information is available on daily consultations and a much more detailed analysis is possible (Peretjagina, Antonova & Urbah, 1977).

A fresh appraisal of the monitoring of UK data is made in this paper. The aim of this study is to look at the last 12 winters, assess the impact of influenza retrospectively and then decide which indices would have best alerted us at the time to the beginning and size of the epidemic.

MATERIALS AND METHODS

Data sources

Frequent data are required for monitoring. The following indices are available weekly and have been collected since 1968 or before.

(*a*) *Morbidity statistics*

(i) Laboratory reports: confirmed influenza infections in England, Wales and Ireland reported to the Communicable Disease Surveillance Centre (CDSC) and previously to the Epidemiological Research Laboratory. Information is available on age, sex and symptoms of patient, area and on antigenic type of the virus for selected patients.

(ii) RCGP rates: practices scattered through the United Kingdom report consultations by diagnosis, including 'epidemic influenza', to the Birmingham

Research Unit of the Royal College of General Practitioners, where they are collated into weekly rates. (Population under surveillance has been about 150000–200000.)

(iii) Sickness benefit claims: weekly total certified absences in the insured working population of England and Wales. (A doctor's certificate is required for an absence of more than 3 days.)

(*b*) *Mortality statistics*

Selected mortality figures for England and Wales are published weekly by the Office of Population Censuses and Surveys in the *Weekly Monitor*:

(i) total deaths (all causes, excluding stillbirths),
(ii) pneumonia deaths (except secondary to accidents and to other infections),
(iii) bronchitis deaths (acute and chronic),
(iv) influenza deaths (influenza and influenzal pneumonia),
(v) respiratory deaths = (ii) + (iii) + (iv).

These data all relate to England and Wales, although some also include Scotland and Ireland. The winter period studied is the last 9 weeks of one year and the first 21 weeks of the next. The weekly period covered by the indices varies as shown in Table 1. Provisional data for all indices is usually available on Wednesday, when the CDR goes to press.

CUSUM method of plotting indices

A way of plotting data in order to clarify when small as well as large rises are occurring has been developed for use in quality control in the industrial situation (van Dobben de Bruyn, 1968). A baseline for the variable being measured is accepted as the normal and cumulated deviations of successive measurements from this baseline are plotted. The plot is called a 'cusum' – cumulative summation. For example, if X_1 deaths are observed in the first week of surveillance, X_2 in the second week, etc., and if B_1 is the baseline level (the expected level in the absence of an influenza epidemic) in week 1, B_2 in week 2, etc., then:

$$\begin{aligned}\text{cusum value for week } 1 &= X_1 - B_1,\\ \text{cusum value for week } 2 &= (X_1 - B_1) + (X_2 - B_2),\\ \text{cusum value for week } 3 &= (X_1 - B_1) + (X_2 - B_2) + (X_3 - B_3), \text{ etc.}\end{aligned}$$

If there is no outbreak then the cusum values should hover close to zero. If there is an epidemic then the cusum will rise above zero, rising sharply during the height of the epidemic and levelling off at the end.

Choosing baselines for cusums

Regression analyses of SBC, total deaths and respiratory deaths that give measures of excess morbidity and mortality attributable to influenza have already been reported (Clifford *et al.* 1977; Tillett, Smith & Clifford, 1980). These studies have been used to calculate an average rank for each winter from 1968/9 to 1979/80 with respect to the effects of influenza. The analyses showed that there were insignificant excess deaths and SBC in the two winters 1970/1 and 1979/80, and therefore these data have been used to estimate baselines for cusums. In addition annual adjustments have been made to baseline estimates to take account of time

Table 1. *Period covered and availability of indices*

Source of information	Period covered by weekly report	Day on which provisional information is made available by telephone	Day on which provisional information is published or circulated
Laboratory reports (collated at CDSC)	Saturday to Friday	Monday, i.e. 3 days after period covered	Friday, i.e. 7 days after period covered
Mortality Statistics (OPCS Monitor)	Saturday to Friday	Wednesday, i.e. 5 days after period covered	Friday, i.e. 7 days after period covered
Sickness Benefit Claims (OPCS Monitor)	Wednesday to Tuesday	Monday, i.e. 6 days after period covered	Friday, i.e. 10 days after period covered
RCGP Rates	Wednesday to Tuesday	Friday, i.e. 3 days after period covered	Friday, i.e. 10 days after period covered

trends in SBC and total deaths indicated by the regression analyses. (Regression models themselves cannot be used for monitoring purposes because they use 4-weekly rather than weekly data.)

RESULTS

Retrospective study of 12 *winters* (1968/9 *to* 1979/80)

Weekly indices

In each winter Influenza A virus was isolated from at least a few patients. The first winter, 1968/9, saw the arrival in Britain of the H_3N_2 virus A subtype, and it is still circulating in 1981. Several variants of this H_3N_2 subtype have emerged over the years. In 1977/8 the H_1N_1 subtype returned to circulate concurrently with H_3N_2. It is still being isolated in 1981. Most of the adult population is immune to H_1N_1 virus and it has not yet been associated with a major epidemic since its return. Influenza B virus was usually found less frequently than A and does not often cause nationwide epidemics, being mainly confined to children. An exception was the winter of 1978/9, when there was evidence of Influenza B causing more illness among adults than Influenza A (Anon., 1979).

Fig. 1 shows weekly values of the main indices during the 12 winters studied. Correlation between the indices is apparent and reflects influenza activity. An upward trend in laboratory reports in relation to other indices can be seen by comparing the large outbreaks of 1969/70 and 1975/6. The latter saw smaller rises in deaths, RCGP rate and sickness-benefit claims (SBC) than the former whereas laboratory reports totalled 3093 in 1975/6 and only 1923 in 1969/70. This is because the amount of virology done and the numbers of laboratories reporting have increased gradually over the period (Morris, 1981). Moreover in 1971 a surveillance scheme was introduced in which volunteer GP's send regular swabs from patients with respiratory infections to their local laboratory. This has increased the proportion of influenza cases being formally diagnosed and reported. Changes in techniques also affect reporting. The large numbers of reports of Influenza B virus in 1978/9 are now shown in Fig. 1 but are probably reflected in the rises in other indices.

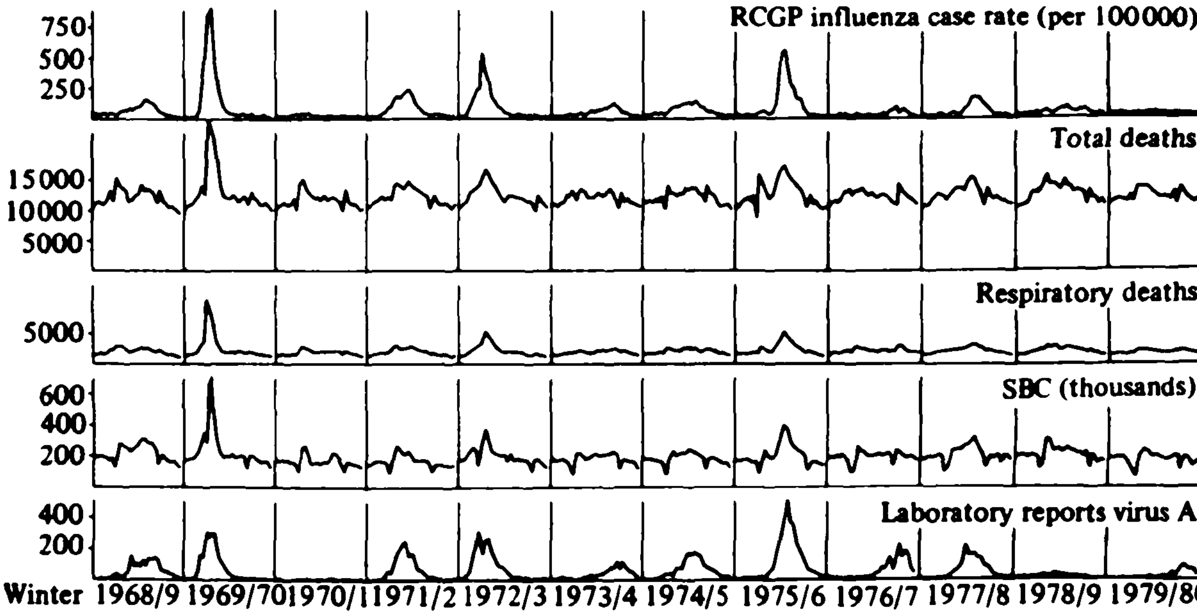

Fig. 1. Weekly indices of morbidity and mortality.

The RCGP epidemic influenza rate shows a rise in every winter, suggesting that this clinical diagnosis may follow a basic seasonal pattern even in the absence of an influenza epidemic. Seasonal patterns are evident for all the other indices shown – SBC, total and respiratory deaths. SBC are exceptionally low in weeks that include public holidays (Christmas, New Year and Easter).

The effect of large influenza epidemics is clear from Fig. 1 – for example, the large rises in 1969/70, 1972/3 and 1975/6. In other winters it is more difficult to judge the size of the epidemics from the data as plotted.

Cusum plots

Cusum plots were found to be satisfactory for RCGP rate, total, respiratory and influenza deaths and SBC (Fig. 2). The cusums usually hovered close to zero before influenza was prevalent, rose during epidemics and then levelled off to become approximately horizontal again.

It can be seen from Fig. 2 that cusum rises with RCGP rate and influenza deaths occur only during epidemics. Total-deaths cusums, however, are more erratic. For example, there was a sharp rise early in the winter of 1973/4 and a sustained rise in 1976/7. Respiratory-deaths cusums appear more specific than total deaths to influenza epidemics, although they reflect to a lesser extent some of the 'non-influenza' rises in total deaths. (Both these rises mentioned coincided with spells of colder-than-average weather. The winter epidemics of Parainfluenza viruses 1 and 2 were unusually large in 1976/7, as judged by laboratory reports.)

Satisfactory baselines were not found for calculating cusums for laboratory reports since there was an upward trend in such reports during the period studied. Cusums are available for the other constituents of respiratory deaths – pneumonia and bronchitis deaths. Pneumonia-death cusums tended to be too low at the beginning of the 12-year period and too high at the end, whereas bronchitis deaths tended to be too high at the beginning and too low at the end. This is due to an upward trend in pneumonia deaths and a downward trend in bronchitis deaths (for example, the ratio of pneumonia to bronchitis was 1·6 in 1970/1 and 2·7 in

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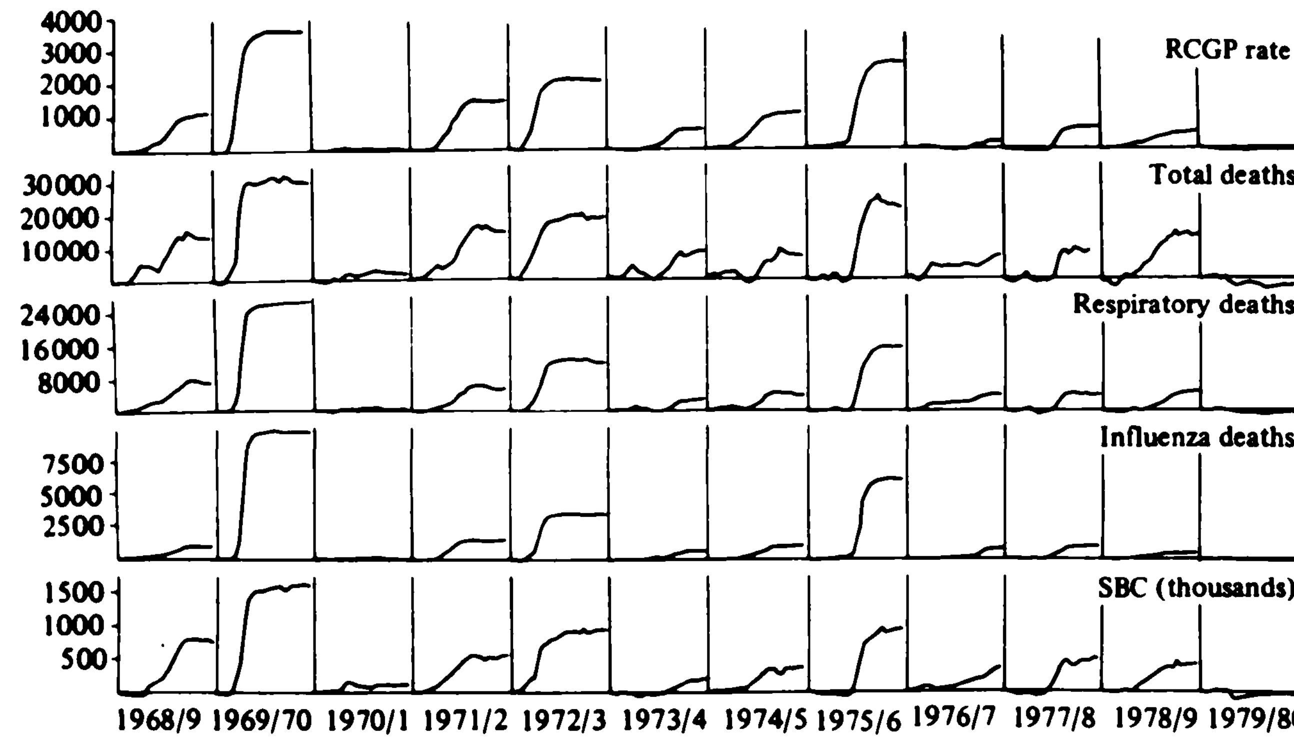

Fig. 2. Cusums of RCGP influenza rate, total, respiratory and influenza deaths and sickness benefit claims.

1979/80). These trends could be built into the baseline values to improve the accuracy of the cusums, but, since part of the trend may be due to changing habits in recording cause of death, it is thought more realistic to concentrate on combined respiratory deaths.

Size of epidemics as measured by height of cusums

The height achieved by a cusum during the winter period is taken as an indicator of the total impact of influenza on that index. Rankings of the heights of the cusums in the 12 winters have been made for the five indices and are shown in Table 2. The average ranks given by estimated excess deaths and SBC are also shown.

Of the five cusums RCGP rate and influenza deaths show very close correlation with the ranking of epidemics given by excesses. Respiratory and total deaths both gave high ranking to the winter of 1978/9, in which there was exceptionally cold weather. Deviations in temperature from the seasonal average were found to correlate with numbers of deaths and this factor was accounted for in the previously published regression models and therefore did not distort the estimated excess deaths associated with influenza. Total-deaths cusums correlated the least well with previous rankings and the cusum graph was less smooth than for the other indices (Fig. 2). However, there was complete agreement between the indices about which were the three largest and which the two smallest epidemics.

For total deaths, respiratory deaths and SBC the final values of the cusums at the end of the winter give an estimate of the excess over the number expected when there is insignificant influenza. The accuracy of these estimates is not known, but comparison can be made with the estimates from the regression analyses, for which standard errors have been published. Results of this comparison are satisfactory. Each cusum estimate differs from the regression estimate by less than one standard error, except for deaths in 1978/9. This was the winter of exceptionally cold

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Table 2. *Ranking of cusums for weekly indices compared with average ranks given by excess morbidity and mortality estimates*

Winter	Average rank from regression estimates	Cusums: RCGP rate	Total deaths	Respiratory deaths	Influenza deaths	SBC
1969/70	1·0	1	1	1	1	1
1975/76	2·0	2	2	2	2	2
1972/73	3·3	3	3	3	3	3
1071/72	4·3	4	4	5	4	5
1968/69	4·3	5	6	4	5	4
1974/75	6·0	6	9	7	6	7
1077/78	7·3	7	8	8	7	6
1973/74	8·7	8	7	10	9	10
1976/77	8·7	10	10	9	8	9
1978/79	9·3	9	5	6	10	8
1970/71	11·0	11	11	11	11	11
1979/80	12·0	12	12	12	12	12

weather and the regression analysis estimated that about 4500 deaths could be accounted for by the lower-than-average temperatures in that winter (Tillett, Smith & Clifford, 1980).

Early warning of epidemics

The most useful indices for giving early warning of an epidemic will be those for which the cusums rise promptly and clearly at the beginning of an outbreak and for which the rises are specific to influenza.

Figs. 3 and 4 show the timings of the three largest epidemics as shown by the most promising of the weekly indices. In order to compare the rates at which the indices rose, each cusum has been plotted as a percentage of the final level reached in that epidemic. Laboratory reports are also included in Fig. 3 and are plotted as the cumulative percentage of the total reports during the winter period. Of the three epidemics, 1969/70 was the largest and most explosive and all the indices rose at the same time. The winters of 1975/6 and 1972/3 saw epidemics which, though smaller in size, were spread over a longer period and therefore differences between the indices were more evident.

Fig. 3 shows indices of morbidity. The initial rises during the first 2 or 3 weeks of an epidemic were seen in all indices but were more marked with the RCGP rate. It is of interest that laboratory reports start increasing at the same time or at most 1 week behind the RCGP rate, even though there is a median time-interval of 2–3 weeks between a swab being taken from the patient and the report of a positive isolation being made by the laboratory. SBC show a more erratic course than other indices when the epidemic period includes public holidays (e.g. week 51 of 1972) and were slower to rise at the beginning of the 1975/6 epidemic. This may reflect possible delays between onset of illness, obtaining a doctor's certificate and submitting it to the DHSS.

Fig. 4 shows mortality indices. Total-deaths cusums rose slightly ahead of the other indices in the early weeks of all three epidemics although the rises for

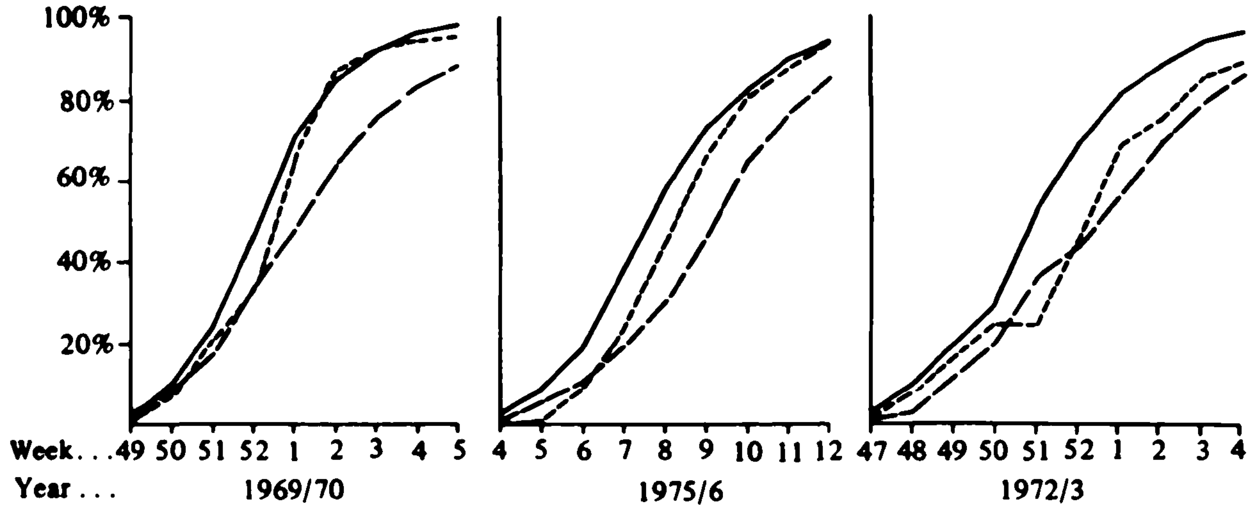

Fig. 3. Weekly rises in morbidity indices during three large epidemics. —, RCGP: % of final cusum level. – –, laboratory reports: % of total. ---, Sickness Benefit Claims: % of final cusum level.

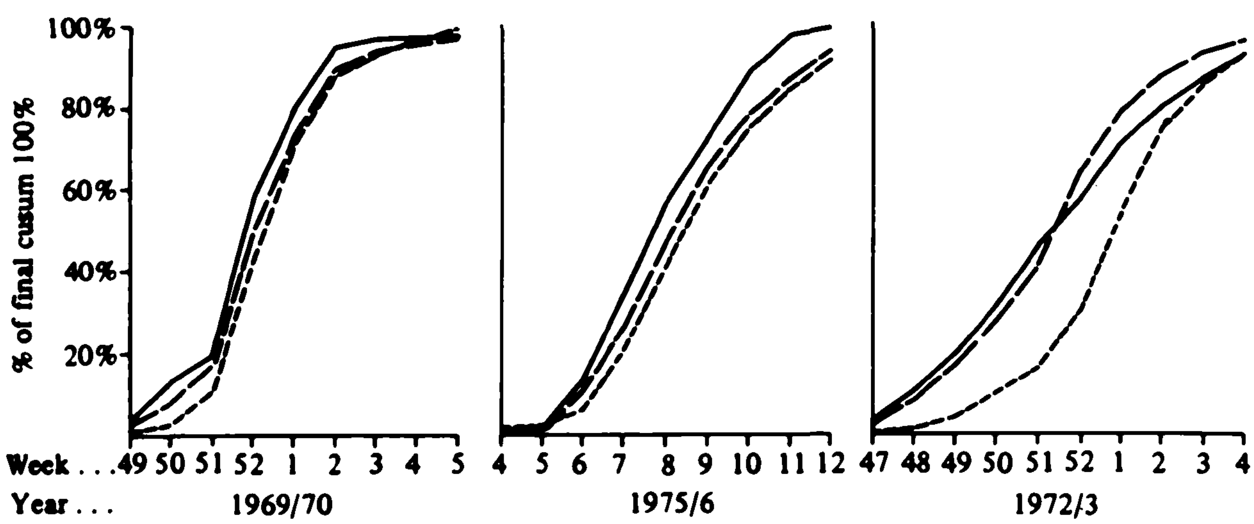

Fig. 4. Weekly rises in mortality indices during three large epidemics. —, Total deaths; — —, respiratory deaths; - - - -, influenza deaths.

respiratory deaths were close in size and timing. Influenza deaths were always slower to make the initial rises, especially in 1972/3. It seems unlikely that deaths due only to influenza or influenzal pneumonia should occur after a longer interval from onset of influenza than deaths where other respiratory or non-respiratory disease were involved as well as influenza. The slight lag in number of influenza deaths recorded may be due to the way in which death certificates are completed. The word 'influenza' may be less likely to appear on a death certificate until the epidemic is well publicized.

Winters with smaller epidemics have been studied in the same way as shown in Figs. 3 and 4. RCGP rate is the most consistent index, with laboratory reports rising at about the same time and influenza deaths tending to lag behind slightly. Although total and respiratory deaths and SBC cusums rose in the smaller epidemics their course is more erratic than in the larger epidemics.

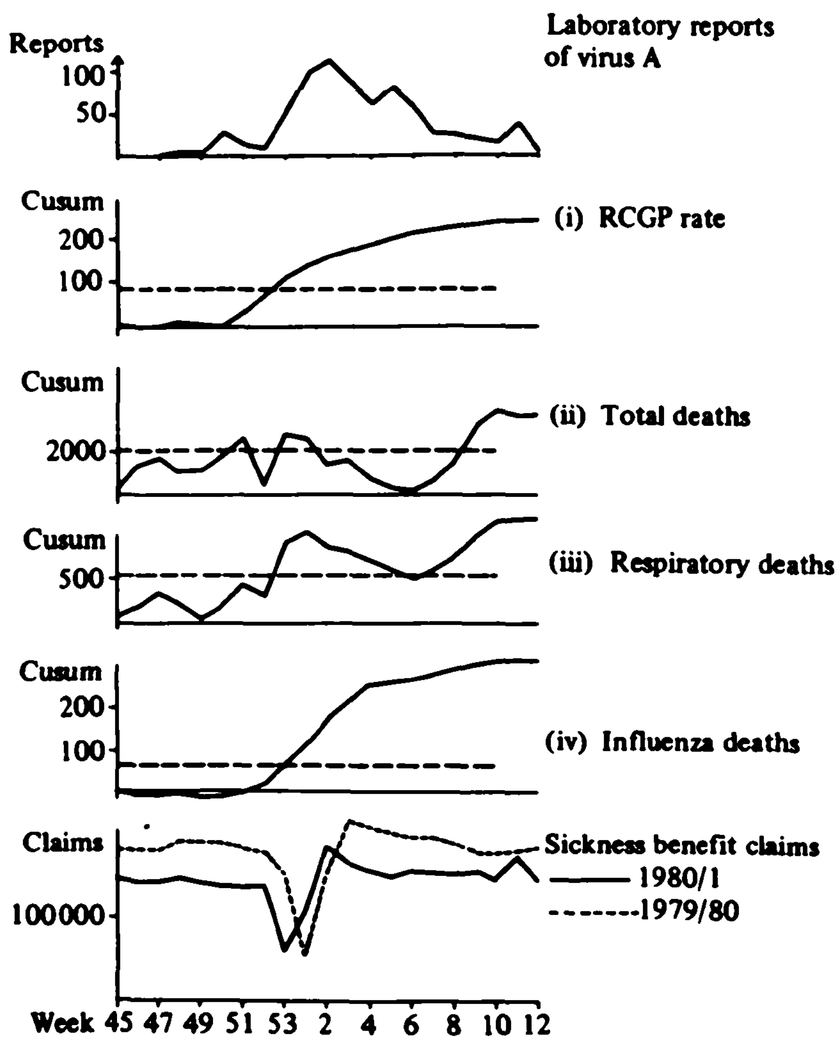

Fig. 5. Weekly surveillance 1980/1. The dashed line on the cusums indicates the 1970/1 level.

Prospective surveillance of the 1980/1981 *winter*

The cusums for RCGP rate, total, respiratory and influenza deaths and SBC together with a plot of laboratory reports, were used week by week to monitor influenza.

Laboratory reports of influenza increased early in the winter and indicated some influenza activity just before, and for a few weeks after, the Christmas holiday. Reporting was low during the holiday weeks. Fig. 5 also shows cusums for four indices, plotted on a larger scale than Fig. 2. The graphs show the levels reached by the cusums in 1970/1, which was a winter of insignificant influenza and was ranked 11th out of the past 12 winters in respect of amount of influenza activity. All four 1980/1 cusums passed this level in week 51 or 53 but none of them passed the level reached by the cusum in the winter ranked 10. The 1980/1 RCGP rate cusum, however, equalled that of 1976/7. It is concluded that these four indices described a very small amount of influenza activity in 1980/1, which ranked 11th out of the 13 winters 1968/9 to 1980/1.

The RCGP rate and the influenza-deaths cusums reflected this small epidemic the most clearly – influenza deaths lagging behind RCGP rate in making the initial rise. Total deaths were erratic, affected by the Christmas holiday, and the small rise was not sustained. The respiratory-deaths cusum was not smooth either, but showed more indication of a definite rise. Both these mortality indices rose again in weeks 7 and 8 following a spell of colder weather.

When the SBC cusum was plotted it fell rapidly below zero, indicating that the baseline was too large. The regression analysis of trend was made using data up to 1979/80 and predicted a fall of 5000 per week in SBC for the 1980/1 baseline compared with 1979/80. Looking at the bottom graph of Fig. 5 it can be seen that the difference between the 2 years is approximately 40000 per week. This may be accounted for by the increase in unemployment and short-time working. Fig. 5 shows actual SBC claims in the two winters. Little influence of influenza is apparent in the 1980/1 SBC.

DISCUSSION

Influenza in England and Wales is monitored using weekly routine data. The behaviour of these data during the 12 winters 1968/9 to 1979/80 has been studied. Because there has been a significant amount of influenza in 10 of the 12 winters and because the epidemics started at different times each winter and developed at different rates, no attempt has been made to fit probability models to the distribution of these data. Instead a descriptive statistical method – a cusum plot – has been used for which it might be possible to develop significance tests when more data are available.

Weekly baseline values for each index have been estimated using winters of insignificant influenza and incorporating long-term trends as indicated by a previous study using regression analysis. Accuracy in baseline estimates should improve when more data are available from 'no influenza' winters. Cusums are sensitive to changes in baseline levels and it is important that long-term trends be checked each year.

The cusum graphs have been assessed with respect to estimating the size of epidemics, the promptness with which they rise at the beginning of an epidemic and the specificity of their rises to influenza activity.

Firstly, there was fairly good agreement about relative sizes of the 12 epidemics. The successful indices being RCGP rate, total deaths, respiratory deaths, influenza deaths and SBC. The other constituents of respiratory deaths – pneumonia and bronchitis deaths – are not suitable on their own because of opposite trends, which are cancelled out when all respiratory deaths are added together. SBC by cause are not available weekly. Laboratory reports are affected by the amount of diagnostic virology done, which has changed over the years, and by changes in techniques.

Secondly, for early warning of epidemics all cusums rose at approximately the same time but RCGP rate and total deaths have tended to be slightly ahead of other indices. SBC and respiratory deaths also seem good early indicators. Influenza-deaths cusums tend to lag a little behind other mortality indices. Laboratory reports have been seen to rise at the same time, or at most 1 week after, the RCGP rate, although most of the patients to whom the laboratory reports relate had their illnesses 1, 2 or 3 weeks before the week of reporting. Therefore, although RCGP rate of 'epidemic influenza' has emerged as a consistently valuable index, it is clear that an earlier warning could be possible. It seems that the first cases in an epidemic are not being recorded as 'epidemic influenza' but may appear under other respiratory categories, rather in the way that influenza deaths seem to increase after the epidemic has gained momentum and therefore publicity. RCGP 'influenza-like' and 'total respiratory' illnesses have been considered as additional indices. However, they rise and fall frequently in association with causes other than influenza. In retrospect they can be seen to have risen slightly ahead of the 'epidemic influenza' rate in some large epidemics, but it would have been impossible to interpret these rises at the time.

Thirdly, RCGP epidemic influenza rate and influenza deaths cusums were the most specific to influenza. Respiratory deaths were intermediate and total deaths and SBC were the least specific. SBC are the most affected by public holidays. Exceptionally cold weather results in rises in total and respiratory deaths cusums. With more data and experience it should be possible to build into the cusum method an adjustment for temperature changes.

In the future it is suggested that the five cusums be plotted weekly and that concurrent rises in RCGP rate and respiratory or total deaths, when laboratory reports confirm the presence of influenza virus, should be taken as an indication that an epidemic is beginning. This will be confirmed if influenza deaths rise. Allowance must be made for the effects of excessively cold weather on mortality and therefore most weight should be given to the RCGP index. The consistent behaviour of this index has already been reported by the RCGP Research Unit (1977).

The winter of 1980/1 has been used as a trial for monitoring influenza with cusum plots. The cusums for the four indices RCGP rate, total, respiratory and influenza deaths were unanimous in describing the epidemic as the 11th largest in the 13 winters 1968/9 to 1980/1. Therefore the size was little larger than the 1970/1 level, which was regarded as insignificant. Most activity appeared to be from week 50 to week 4, although laboratory report forms analysed by date of collection of specimen indicated illness increasing from week 48. The SBC cusum could not be used because the baseline estimated in advance was inadequate. The annual trend has been far more erratic for this index than for any other. Laboratory reports confirmed the presence and timing of influenza and indicated that both H_1N_1 and H_3N_2 types were circulating. Many reports came from school-children. A new reporting scheme, which has been under way for two winters, should help to monitor this age group. Volunteers from the Medical Officers of Schools Association are reporting on illnesses among boarding-school children and these reports are being collated at CDSC. In the 1980/1 winter the influenza rate was higher at the end of the autumn term and beginning of the spring term than it had been in the previous winter. As more years of data are available this should become a valuable addition to the influenza monitoring indices.

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