Measuring the effect of influenza A(H1N1)pdm09: the epidemiological experience in the West Midlands, England during the 'containment' phase

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SUMMARY

The West Midlands was the first English region to report sustained community transmission during the 'containment' phase of the influenza A(H1N1)pdm09 pandemic in England. To describe the epidemiological experience in the region, West Midlands and national datasets containing laboratory-confirmed A(H1N1)pdm09 virus cases in the region during the 'containment' phase were analysed. The region accounts for about 10·5% of England's population, but reported about 42% of all laboratory-confirmed cases. Altogether 3063 cases were reported, with an incidence rate of 56/100 000 population. School-associated cases accounted for 25% of cases. Those aged <20 years, South Asian ethnic groups, and residents of urban and socioeconomically deprived areas were disproportionately affected. Imported cases accounted for 1% of known exposures. Regional R_0 central estimates between 1·41 and 1·43 were obtained. The West Midlands experience suggests that interpretation of transmission rates may be affected by complex interactions within and between sub-populations in the region.

Key words: Epidemiology, emerging infections, infectious disease, influenza, pandemic.

INTRODUCTION

In the UK and elsewhere early cases of a novel strain of swine influenza were identified in April 2009, first in Mexico and then North America, before rapidly spreading to other parts of the world [1].

Pre-existing pandemic plans were implemented, a number of these having an initial 'delay' or 'containment' phase designed to restrict spread of the pandemic virus [2]. Preparedness for this type of incident is crucial, requiring use of high-quality surveillance systems to guide operational decision-making [3].

In England, these systems reported the first laboratory-confirmed case of influenza A(H1N1) pdm09 on 29 April 2009, in a traveller returning from Mexico. By 2 July 2009, at the end of the containment phase, England had reported 6162 laboratory-confirmed cases [4]. By 9 July 2009, 335 hospitalised cases and 12 deaths due to pandemic influenza had been reported [5].

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This paper provides an epidemiological analysis of confirmed cases of A(H1N1)pdm09 virus in the West Midlands region, England, accounting for about 42% of laboratory-confirmed cases reported during the containment phase of the epidemic, and was also the first English region to report sustained community transmission [4].

METHODS

The Appendix (see Supplementary online material) provides the context for the study.

Ethical approval

This work was conducted as part of the public health response to pandemic influenza in England. As such no explicit ethical approval was necessary or sought.

Case definitions

The initial containment phase in England involved individual case management, including diagnostic sampling (nose or throat swabbing or both), antiviral treatment of all suspected cases, and prophylaxis of close contacts of laboratory-confirmed cases [2]. Suspected cases were those with a history of fever and acute respiratory illness, that in the 7 days prior to onset had either been in contact with a known confirmed case or had an epidemiological link to an area with evidence of sustained transmission (either abroad or latterly in the UK). A confirmed case was defined as a person with laboratory-confirmed influenza A(H1N1)pdm09 infection. Secondary cases were confirmed cases that had been in contact within 7 days of illness onset with a travel-associated confirmed case. Tertiary cases were confirmed cases that had been in contact within 7 days of illness onset with a secondary case. Sporadic cases were confirmed cases with no travel history or known contact with a confirmed case in the 7 days before onset of illness [6, 7].

Sources of surveillance data

During the containment phase response, data regarding suspected and confirmed cases of A(H1N1)pdm09 were entered by regional health protection staff into FluZone, a national surveillance database with case reporting and management functions [7]. Laboratory testing was conducted on respiratory samples from suspected cases (nasopharyngeal swabs), and the majority of specimens from cases in the West Midlands were tested for A(H1N1)pdm09 at the Health Protection Agency (HPA) laboratory, Heart of England Foundation Trust, Birmingham. Laboratory-confirmed cases of A(H1N1)pdm09 virus were reported to regional health protection staff who integrated these reports with demographic, clinical and contextual information on FluZone.

Socioeconomic deprivation was considered by assigning postcodes of residence recorded in Fluzone for confirmed cases to lower super output areas (LSOA), for which a deprivation score was assigned using the Index of Multiple Deprivation (IMD) 2007 [8]. Deprivation scores were grouped into quintiles, from the most affluent to the most deprived quintile. Cases were also mapped with ESRI software ArcGIS, version 10.0 (Environmental Systems Research Institute Inc., USA) using postcode data to assign them to local health areas (primary care trusts; PCTs).

All confirmed cases in FluZone were classified as either 'South Asian' (a person of Indian, Pakistani or Bangladeshi origin) or 'non-South Asian' based on their first name and surname. This classification was carried out separately by two HPA staff of South Asian origin. Where there was disagreement, a third opinion was sought.

A regional schools database was established by regional staff to track school-related cases, recording counts of confirmed cases by school and school closure details.

Information on confirmed cases hospitalized in the West Midlands was obtained from the national Health Protection Agency Chief Medical Officer (HPA CMO) H1N1 hospitalization database [9].

Data presentation and analysis

Descriptive epidemiological data

Descriptive epidemiological data are presented as case counts and cumulative incidence rates, stratified by age group, sex, area of residence, socioeconomic deprivation category, ethnicity, exposure, and illness severity. Cumulative incidence rates were calculated using mid-2009 population estimates [10] with 95% confidence intervals (CIs) constructed using the Wilson score method.

For FluZone datasets, analysis considered those cases with illness onset from 16 April 2009 to 2 July 2009 inclusive, or where unknown, a laboratory confirmation date from 16 April 2009 to 6 July 2009 inclusive. The schools dataset considered cases with
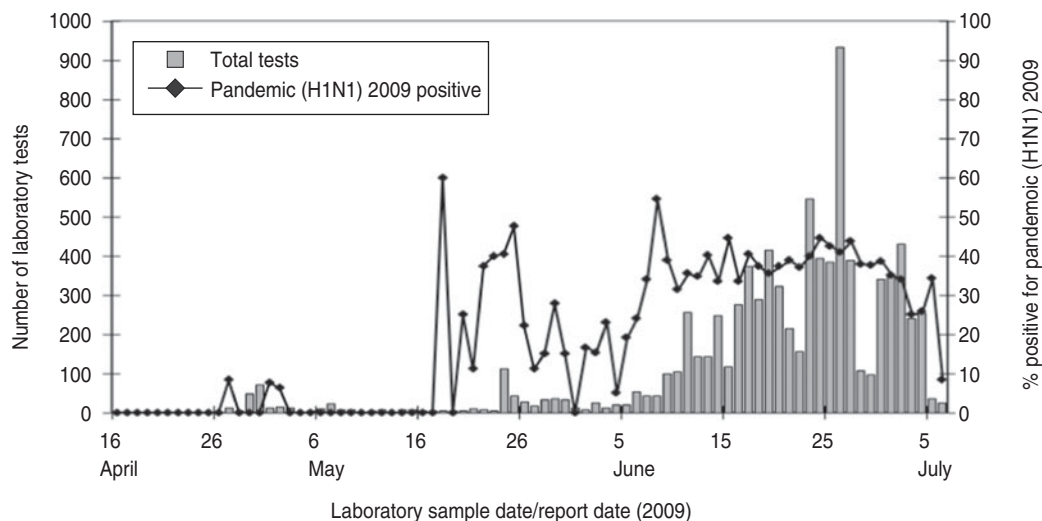
Fig. 1. Epidemic curve of laboratory-confirmed cases and proportion of positive pandemic (H1N1) 2009 laboratory results in the West Midlands with sample date/report date from 16 April to 6 July 2009 inclusive ($n = 3063$).

laboratory confirmation dates from 16 April 2009 to 2 July 2009. For hospital and laboratory data the period considered is from 16 April 2009 to 6 July 2009 inclusive, to capture cases with illness onset prior to and including 2 July 2009. Hospital data are presented by date of admission and laboratory data by specimen sample date, or, where unknown, date of laboratory test result. Summary estimates of the case hospitalization ratio uses numerator and denominator data from 16 April 2009 to 26 June 2009 inclusive, to capture those with symptom onset prior to and including 22 June 2009, before a change in management strategy was introduced in 'hotspot' areas by 23 June 2009.

Reproductive number (R_0) estimates

The R_0 for the West Midlands was estimated. A log-linear fit was performed to the cumulative number of laboratory-confirmed cases with laboratory sample/report dates 4–25 June 2009 inclusive, and symptom onset dates 1–17 June 2009 inclusive. The early exponential growth rate r was estimated as the slope of this fit, and R_0 was then calculated using methods presented by Wallinga & Lipsitch [11]:

$$R_0 = 1 + rT_c,$$

T_c is the serial interval, or the average time between infection in one case and transmission to a subsequent case. This quantity has been estimated through quantitative meta-analysis as $T_c = 3 \cdot 0$ (95% CI 2·4–3·6) days [12].

The time periods were chosen to be late enough that early chance events were unlikely to influence the estimate, and the epidemic had settled into exponential growth; and early enough that the report rate had not declined due to health system capacity and changes in management protocols. To test this, we made use of the idea of an effective growth rate (r_{eff}) on day t, given a previous observation T days ago:

$$r_{eff}(t) = (1/T)\ln(C(t)/C(t-T)),$$

where $C(t)$ is the incidence on day t and $\ln()$ is the natural logarithm. Semi-parametric, splinal fits of these effective daily growth rate estimates showed a reasonably constant value of r during the time period fitted for.

RESULTS

Diagnostic testing

From 16 April 2009 to 6 July 2009 (end of the containment phase) the West Midlands regional HPA laboratories had tested 8524 specimens for suspected A(H1N1)pdm09, of which 3063 (35·9%) were positive. The majority (81%) of test results were reported from 10 June to 2 July 2009 (Fig. 1), during this period weekly positivity rates ranged from 31·4% to 44·6% (mean 38·6%). Due to changes in management practices from 23 June 2009 onwards, case ascertainment is incomplete. From 16 April 2009 to 26 June 2009 inclusive (capturing cases with illness onset prior to 23 June 2009), there were 2276 reported laboratory-confirmed cases in the West Midlands.
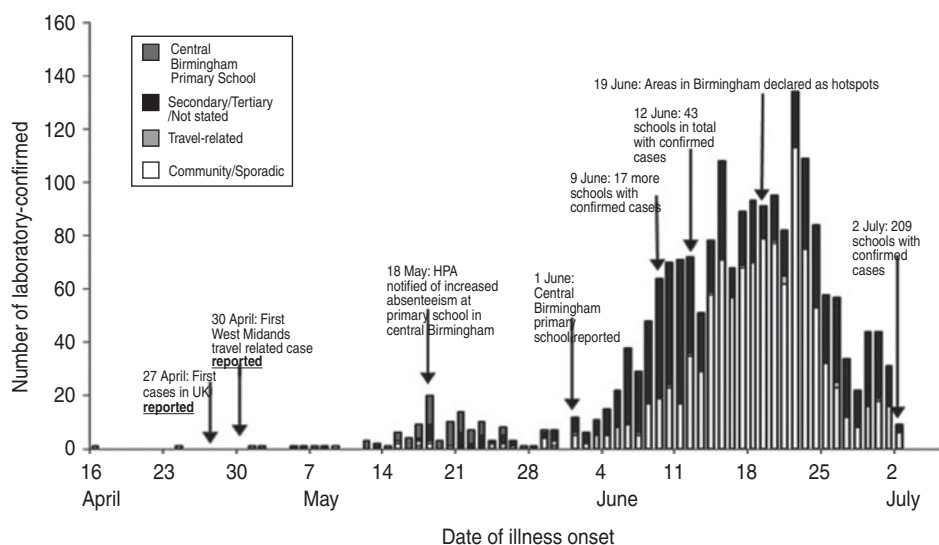
Fig. 2. Laboratory-confirmed pandemic (H1N1) 2009 cases in the West Midlands during the containment phase by illness onset date and route of transmission ($n = 1967$). Includes cases in the FluZone dataset ($n = 1962$) meeting dataset definitions criteria and a further five cases from the initial primary school outbreak who met the criteria, but were not included in the FluZone database.

Epidemiological characteristics

The cumulative incidence rate for laboratory-confirmed cases was 56/100 000 (95% CI 54–58) population (16 April 2009 to 6 July 2009). The median age of confirmed cases was 12 years (range <1 month to 80 years), with 70% (2096/2978) of cases aged <20 years, and school-aged children (5–16 years) accounting for 55·5% (1653/2798) of all cases. The cumulative incidence of confirmed illness was highest in children aged 5–9 years (247/100 000 population).

Gender was not known for 58/2978 cases (1·9%). Of the remaining cases, 50·1% (1463/2920) were women, and 49·9% (1457/2920) were men. This distribution was not consistent across all age groups. In those aged ≥20 years, a significantly higher proportion of cases were women (60·3%, 95% CI 56·9–63·5 compared to 37·9%, 95% CI 34·7–41·3 in men), the opposite was true for those aged <20 years (53·4%, 95% CI 51·2–55·5 in men compared to 44·6%, 95% CI 42·5–46·7 in women).

Laboratory-confirmed cases were reported from all health areas (PCTs) in the West Midlands region. The majority of cases (66·9%, 1991/2978) lived in Birmingham or the surrounding urban areas comprising the West Midlands metropolitan area. The number of confirmed cases within more rural areas of the region was low.

Socioeconomic indices could be identified for 92% (2754/2978) of cases and marked social inequalities were seen. A significantly greater proportion of con-firmed cases were from the most socioeconomically deprived quintile in the region (1837/2754; 66·7%, 95% CI 64·9–68·5), compared to the most affluent quintile (170/2754; 6·2%, 95% CI 5·3–7·1).

The majority of cases (2753/2978, 92%) were classified into one of two ethnic groups. A significantly greater proportion of laboratory-confirmed cases were reported in South Asian individuals (1595/2753; 57·9%, 95% CI 56·1–59·8), than non-South Asian (1158/2753; 42·1%, 95% CI 40·2–43·9).

Exposure

Exposure history (Fig. 2) was available for 89% (1747/1967) of cases in FluZone with a recorded date of illness onset. The majority of cases (56%, 1105/1967) were classified as sporadic, and others as secondary or tertiary (32%, 622/1967). Only a minority were travel-related cases (1%, 27/1967). For the remaining 11% of cases (220/1967) the route of transmission was not recorded. Of the travel-related cases, 13 (48%, 13/27) reported travel to the USA and three to Mexico.

Three hundred and forty-four schools contacted the HPA during the containment phase to report unusual patterns of pupil or staff absenteeism. Of these, 209 (61%) had at least one laboratory-confirmed case, 127 (61%) were primary schools. Sixty-five (19%) schools were closed at some time from 16 April 2009 to 2 July 2009 inclusive. About one third (35%, 23/65) of schools were closed as an outbreak
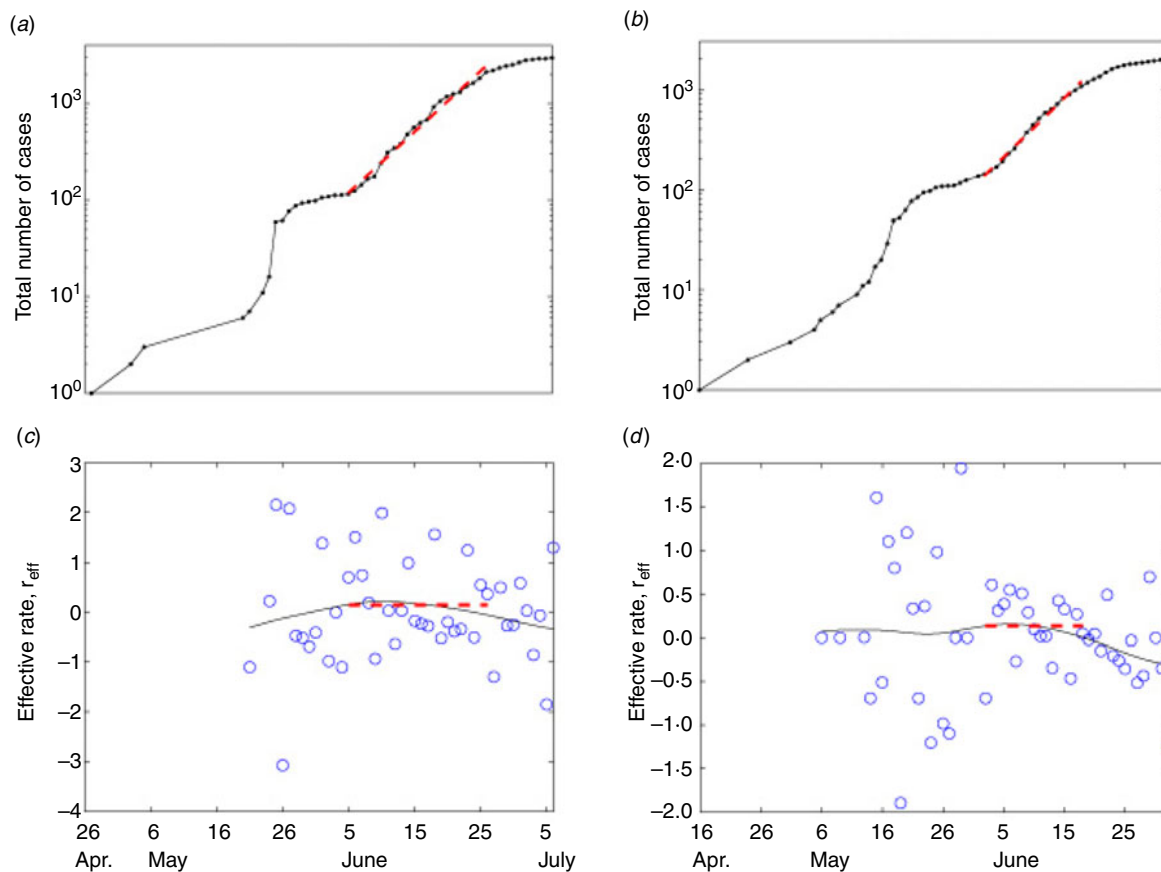
Fig. 3 [*colour online*]. Fitting R_0 (*a*, *b*) through log-linear fitting and (*c*, *d*) through splinal (smoothing parameter = 0·1%) methods for (*a*, *c*) laboratory sample/report dates and (*b*, *d*) symptom onset dates.

management intervention, 21 (32%) for operational reasons (such as high staff absence), and one to protect children with particular medical needs. Reasons for closure were not stated for the remaining schools. School-associated cases comprised 25% (95% CI 24–27) of all cases (778/3063) in the region.

Severity of illness

There were 195 cases hospitalized from 16 April 2009 to 6 July 2009 inclusive, the highest admission incidence was reported in the 0–4 years age group: 14/100 000 (95% CI 11–18) population. Of the 195 admissions, 110 (56%) were women, of whom 12 (11%) were pregnant. Ten admitted cases (5% of hospitalized cases) required intensive-care admission, four (2%) required high-dependency unit admission. Ninety-five (48%) admitted cases had chronic disease conditions, 18 (9%) having more than one condition. The most commonly reported comorbidities were asthma (24%, 47/195) and chronic respiratory disease (8%, 15/195). Five of the 10 intensive-care admissions had

underlying chronic disease comorbidities and there was one death in hospital, in a patient with more than one comorbidity. From 16 April 2009 to 26 June 2009 (capturing all case-patients with illness onset prior to but not including 23 June 2009), there were 115 hospital admissions in laboratory-confirmed case-patients, giving a reported case-patient hospitalization incidence of 5% (115/2276).

Estimates of R_0

Examination of laboratory sample/report dates gave exponential growth estimates of $r = 0.144$ (95% CI 0·137–0·152) days^{-1} and $R_0 = 1.43$ (95% CI 1·34–1·52) days^{-1}. Symptom onset dates gave exponential growth rate estimates of $r = 0.136$ (95% CI 0·129–0·143) days^{-1} and $R_0 = 1.41$ (95% CI 1·33–1·49) days^{-1}. The application of splinal methods shows that there is some evidence of a reduction in r during the periods considered, probably due to increasing difficulty of case ascertainment and changes in management strategies, but this does not bias the log-linear fit (Fig. 3).

DISCUSSION

The West Midlands was greatly impacted by influenza A(H1N1)pdm09 and, its epidemiological experience differed from that seen elsewhere in England. Although the West Midlands region accounts for about 10·5% of England's population, it was disproportionately affected compared to other English regions during the containment phase, reporting 42% of all laboratory-confirmed cases, and was the first English region to report sustained community transmission [4].

The highest incidence of confirmed cases was in the 5–9 years age group, and 25% of the disease burden was school-associated, particularly in primary schools. Certain population groups were disproportionately affected: those aged <20 years; residents of Birmingham and surrounding urban areas; those living in the most deprived areas of the region; and people from the South Asian ethnic minority group. Imported cases accounted for 1% of known exposures. There was a 5% case hospitalization ratio and one death. The links with transmission in school-aged children and within deprived communities were also features of the London experience [13].

The reported incidence of 56/100 000 population confirmed cases during the containment phase in the West Midlands greatly underestimates the true incidence, as it reflects only those who sought medical attention and assumes a perfect diagnostic test. HPA case estimates for the West Midlands during the containment phase (up to and including 5 July 2009) suggest that the estimated incidence in the West Midlands was higher than other English regions with the exception of London [14]. These case estimates have also been shown to underestimate the likely true incidence, due to inaccuracies in assumptions regarding consultation behaviours, a significant proportion of asymptomatic and mildly symptomatic cases, the comparatively low virulence of the organism, and the effects of control measures [14–16]. The age and sex distribution of cases reported in the West Midlands during the containment phase is consistent with the national distribution [17], which is to be expected as the West Midlands contributed substantially to national rates. Although the distribution of cases by sex was equal overall, there were significantly more women affected in older age groups, also consistent with the national pattern [17]. This may partly reflect differences in symptom reporting behaviours [18], and increased exposure in caregiving roles [19].

Incidence was highest in younger age groups, consistent with the 1957 (H2N2) pandemic but different from the 1918 pandemic, which affected young adults, and the 1968 (H3N2) pandemic, which affected all age groups [20–22]. In the West Midlands, the recent pandemic was probably driven by the large number of school outbreaks, and school-associated cases, attributable to children's extensive contact networks and infection susceptibility [20, 23]. Although there is strong evidence that closing schools can reduce peak and cumulative incidence, the cost-effectiveness of different school-closure strategies requires further evaluation given the social and economic impact of such measures relative to the severity of a particular pandemic [24–26]. In this study, about one third of school closures were initiated for operational reasons (e.g. staff absence). Future modelling or evaluative work regarding school closures should take this into account.

Cases occurred in all parts of the region but were disproportionately clustered in urban areas, people of South Asian ethnic origin and in people living in the most deprived neighbourhoods. Data from London and the West Midlands are similar with regard to the greater number of cases reported from socioeconomically deprived areas compared to other areas, and the links between deprivation and mortality due to A(H1N1)pdm09 have been demonstrated [13, 27]. Although there is one study that provides evidence of increased mortality in South Asian children admitted to hospital as a result of A(H1N1)pdm09 [28], comparable data from other parts of England with regard to ethnic differences in A(H1N1)pdm09 morbidity are lacking. However, research from other countries reports similar findings to ours in ethnic minority groups [29]. Although not fully understood these findings may reflect community-specific mixing patterns, health-seeking behaviour and socioeconomic status.

In the West Midlands, the proportion of imported cases (1%) appears very low compared to other reports (range 2–78%) [2, 30]. The reasons for these differences are unclear, but incomplete ascertainment of imported cases is one hypothesized explanation. The low proportion of imported cases identified in this study is similar to the 2% reported by Fielding *et al.* in Victoria, Australia [30]. They proposed that a low proportion of imported cases suggests early establishment and rapid spread of influenza A(H1N1)pdm09 virus as a result of early silent importations prior to recognition of the first case. They

Table 1. *Challenges and lessons learnt from measuring the effect of influenza A(H1N1)pdm09 in the West Midlands during the containment phase of the pandemic*

- Influenza viruses are unpredictable and past influenza pandemics were poor predictors of geographical zone of emergence and severity of influenza A(H1N1)pdm09 virus.
- Extent to which the information obtained could be used at a regional level in real-time was limited by pragmatic considerations dictated by the circumstances in which data were collected, e.g. data collected in real time provided supporting evidence of sustained community transmission in the region; however, more detailed analyses presented here were carried out following the pandemic.
- Based on evidence provided by local data there is a need to allow local flexibility with regard to tailoring response and control activities to local needs without undermining national plans.
- There is value in investing in pandemic planning strategies and exercise and strengthening public health infrastructure as a means of anticipating information and decision-making needs required to detect and respond to novel infectious disease threats.
- Integrating existing influenza surveillance systems with newly established systems offered a more robust and comprehensive means of monitoring influenza A(H1N1)pdm09; however, changes made to surveillance systems during the course of a pandemic should be avoided.
- Access is required to timely and high-quality surveillance data in order to determine: trends; extent of severity of infection; when to change policy and guidelines; and in order to support modelling studies.
- Effective, efficient and timely integration and communication of data from surveillance systems are important for decision-making.
- Interpretation of R_0 may be influenced by the structure of the population through which it is spreading and similar reproductive numbers may not result in epidemics of similar sizes and timings.
- Collecting school-related data and hospital data was challenging and surveillance systems had to be established to meet specific information needs.
- Value of a database with both reporting and case-management functions and, of flexible information management systems that can be strengthened and expanded to meet key information needs was demonstrated.
- Accurate and rapid laboratory diagnosis and communication of results are critical for public health surveillance and response operations.
- Surge capacity for laboratories, diagnostic services and the public health response need to be identified in advance.

further suggest that early establishment is characterized by a rapid increase in cases with no travel history and a low median age during the most intense phase of the pandemic indicating amplification in young age groups, features seen in the West Midlands.

In England, the West Midlands had the highest regional number of admissions reported in the HPA CMO hospitalization database for the week beginning 13 April 2009 to the week beginning 6 July 2009 (defined to capture admissions in those with laboratory confirmation from 16 April to 6 July 2009 inclusive), reporting a higher number of admissions than the cumulative total for other English regions. Although time periods of concern are not directly comparable during the containment phase, the 5% case hospitalization ratio in laboratory-confirmed cases in the West Midlands, is similar to cumulative 'worst-case' scenarios, used in national pre-pandemic planning, assuming no effective treatment [3, 31]. However, it is higher than updated planning assumptions for the early pandemic [32], probably to reflect case ascertainment bias [14], resulting in over-inflated hospitalization incidence estimates.

The estimated rate of spread (R_0) of influenza A(H1N1)pdm09 in the West Midlands was about 1·4. This is similar to that reported elsewhere and for transmissibility reported for the 1957 and 1968 pandemics, but less than that for the 1918 pandemic [33]. The West Midlands R_0 of A(H1N1)pdm09 is not markedly different from reported initial estimates for England and Wales (range 1·2–1·5 for period 31 May 2009 to 7 June 2009 inclusive) [23], and on its own does not explain why the West Midlands was reportedly disproportionately affected in the early stages of the pandemic. However, when the other epidemiological features previously described are considered it suggests that potentially a unique combination of complex population contact patterns, in addition to chance events, acted to establish and sustain early exponential growth in the West Midlands compared to other parts of England.

Support for this multifactorial explanation of our results may be found by utilizing the ideas of Watts *et al.* regarding the role of population interaction structure [34]. Using hierarchical metapopulation modelling, which envisages population structure as a

hierarchy of sub-populations or communities, they suggest that the nature of an epidemic is highly sensitive to the structure of the population through which it is spreading. The concentration of transmission in school-aged children and the unpredictable nature of interaction between individuals in different sub-populations or communities, suggests that similar reproductive numbers may result in epidemics of different sizes and timings [34]. We propose this as one possible hypothesis for the early establishment of the first pandemic wave in the West Midlands in 2009. Other explanations could relate to links between the West Midlands and other parts of the UK to which travellers from Mexico returned, the intensity of transmission within schools, and large household sizes (linking schools together). It should also be noted that the predominance of cases in South Asian ethnic groups, in urban deprived areas and transmission in school children may well have been much more significant than transmission within the region as a whole.

Limitations and lessons learned

There are challenges in collecting, using and interpreting surveillance data to measure the effect of a pandemic. In the West Midlands a variety of surveillance systems were used to measure the local impact of the pandemic, and although each has its limitations, by integrating local and national surveillance systems, a more robust means of measuring the impact of A(H1N1)pdm09 was established. Some of the challenges encountered and lessons learnt are summarized in Table 1. A number of these are consistent with previous reports and are likely to apply to other public health emergencies or outbreaks of novel infections [3, 35–37].

CONCLUSION

Overall, the nature of the West Midlands experience appears to have been due to a number of factors, and highlights how interpretation of overall reported incidence and transmission rates may be affected by complex population interactions. Further analysis of the West Midlands experience will help strengthen future public health responses to novel infectious disease outbreaks or pandemics.

SUPPLEMENTARY MATERIAL

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0950268813001234.

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DECLARATION OF INTEREST

None.

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