Health Protection Agency

Epidemiological report of pandemic (H1N1) 2009 in the UK

April 2009 – May 2010

HSC Public Health Agency

Health Protection Scotland

GIG CYMRU NHS WALES

RCGP Royal College of General Practitioners

Acknowledgements

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Summary

Following the emergence of the novel pandemic (H1N1) 2009 influenza virus in North America in April 2009, the first UK cases were reported on 27 April 2009. Several existing and new surveillance systems were used to investigate the first cases, to monitor the unfolding pandemic and to measure the impact and effectiveness of the various counter-measures that were implemented in the UK.

Most confirmed cases appeared to have experienced a largely typical influenza-like illness. A minority suffered serious disease. Children were most affected; adults aged over 50 years had evidence of some pre-existing immunity, with much lower clinical attack rates.

Two waves of pandemic activity, separated by the closure of schools over the summer, were observed. The first wave peaked in mid/late-July 2009. The regions most affected initially were the West Midlands, London and central Scotland, mainly due to several early large school-based outbreaks in the former two areas. England and Wales experienced higher activity levels in the first wave compared to Scotland and Northern Ireland, which may be due to earlier closure of Scottish and Northern Irish schools for summer holidays. The second wave started with the return to school in the autumn with a peak in mid-October 2009.

All viruses characterised were similar to the California/07/2009 strain. The pandemic (H1N1) 2009 virus was the main circulating strain: from week 20 2009 to week 20 2010, of 3059 influenza viruses detected by the HPA Respiratory Virus Unit, only 78 (2.5%) were non-pandemic viruses. Through GP sentinel surveillance, the highest weekly proportion of ILI cases positive for pandemic influenza was in Northern Ireland, where it reached 83% in week 44 (ending 1 November 2009). In England, the highest rate was 43% (week 43 2009), in Scotland 47% (week 45 2009) and in Wales 57% (week 42 2009).

The first reported UK death due to pandemic influenza occurred on 14 June 2009. The majority of hospitalisations and deaths were in people aged less than 65 years. The symptomatic case-fatality ratio was estimated to be 0.04%. People with an underlying medical condition, for which influenza vaccination is recommended by the Department of Health, did not seem to be at a greater risk of acquiring the infection, but were estimated to be 10 times more likely to be hospitalised and 18 times more likely to die than those without any underlying condition. In England, Wales and Scotland, no excess all-cause mortality was observed over the summer of 2009. In the 2009/10 winter season excess mortality was observed in weeks 52 and 53; influenza is unlikely to be the main explanation as all other influenza indicators showed low activity at the time and these deaths were concentrated in the elderly.

Antiviral drugs were offered to those presenting with clinical symptoms of influenza during the treatment phase in the UK. In England and Scotland the number of courses collected during the treatment phase covered about 2% of the population and in Northern Ireland enough were prescribed through primary and secondary care to cover 1.4% of the population. Of 6,379 viruses tested, only 45 (0.7%) were found to carry a mutation known to confer resistance to the antiviral drug oseltamivir. Most cases of resistance were thought to be treatment-induced. Antiviral drugs as treatment significantly reduced the median duration of illness and, as prophylaxis and treatment, reduced the household secondary attack rate.

Some side-effects attributed to the antiviral drugs were reported; mainly gastrointestinal symptoms.

There was no evidence that the 2008/09 seasonal influenza vaccine significantly affected risk of acquisition of pandemic (H1N1) 2009 infection. The UK 2009/10 seasonal influenza vaccination programme went ahead as normal. For all people aged over 65 years uptake ranged from 64% in Wales to 77% in Northern Ireland, and for those under 65 years in an underlying clinical risk group uptake ranging from 49% in Wales to 80% in Northern Ireland. The monovalent pandemic vaccine programme was initiated in October 2009, initially recommended for front-line health care workers and people of all ages with underlying medical conditions, including pregnancy. These recommendations were extended to all healthy children aged from 6 months to under 5 years in December 2009. The uptake of pandemic influenza vaccine in people at risk (including pregnant women) was 38% in England, 52-55% in Scotland and 42% in Wales. In Northern Ireland the uptake in this group (excluding pregnant women who had a 57% uptake) was 87%. Preliminary data from routine GP sentinel influenza surveillance in England and Scotland shows that pandemic influenza vaccine was effective in preventing confirmed influenza infection.

The post-pandemic phase was declared by WHO on 10 August, 2010. For the forthcoming 2010/11 season, the virus is expected to behave as a normal seasonal influenza virus, though vigilance for changes in the virus, the disease caused, or groups affected should be maintained.

Contents

Introduction

In the United Kingdom (UK), surveillance of influenza and other respiratory viruses is undertaken by the Health Protection Agency (HPA), Health Protection Scotland (HPS), Public Health Agency Northern Ireland and Public Health Wales. Data are collated from a variety of surveillance systems to provide timely information on which influenza strains are circulating, to ascertain which have epidemic potential, and to contribute towards the decision on influenza vaccine composition for the following season. Surveillance activities also produce timely reports[1] for health professionals, the media and the public on influenza activity and spread, burden of disease and the uptake and effectiveness of the main clinical counter-measures (in particular vaccination and antivirals).

Surveillance occurs throughout the year with a focus on the winter season between October (week 40) and May (week 20). Following the identification of the first cases of a novel swine influenza virus in April 2009 in Mexico and the United States[2;3], the UK embarked on an initial "containment" strategy during May and June (see Box 1). In an effort to mitigate the impact of the pandemic, during the containment phase all symptomatic cases were ascertained through enhanced surveillance, and those who met the clinical and epidemiological case definition, were followed up, laboratory confirmed and their close household and non-household contacts traced. *Antiviral drugs were recommended for early treatment of all confirmed cases and post-exposure p*rophylaxis offered to identified close contacts. Selective school closures were also recommended during the containment phase.

Box 1: Key actions during the containment and treatment only phases in the UK, adapted from[5]

Containment phase

- Diagnosis by laboratory confirmatory testing
- Suspected cases treated with antivirals and requested to self-isolate at home
- Household/close contacts of suspected cases traced
- Close contacts offered antiviral prophylaxis if index case laboratory confirmed; contacts advised to self-isolate only if they became clinically ill
- Risk assessment dependent closure of schools for 7 days if confirmed case(s) identified; treatment of clinically ill patients with antivirals
- Close contacts of confirmed/suspected cases in confirmed school outbreaks offered anti-viral prophylaxis

Treatment-only phase

- Diagnosis by clinical illness; laboratory testing not required
- Clinical cases offered antiviral treatment through consultation with healthcare professional or National Pandemic Flu Service (NPFS); emphasis on treatment for persons in higher risk groups
- Contacts of cases not offered prophylaxis apart from special circumstances (e.g. household member with serious underlying health problem)

In June 2009, WHO declared a global influenza pandemic[4], the first for over four decades.

In June, significant community transmission developed in a number of UK regions, in particular in London, the West Midlands and central Scotland. At the beginning of July 2009, with evidence of community transmission, the UK moved to a 'treatment-only phase' of cases to manage the pandemic. This phase focussed on provision of antivirals to people presenting with clinical respiratory illness (without the need for confirmatory testing) through primary and secondary care and the telephone and web-based National Pandemic flu Service (in England). Surveillance continued throughout this period to monitor trends, burden of disease and changes in the characteristics of the virus and the uptake and effectiveness of the pandemic influenza vaccine programme that was implemented in autumn 2010.

This report describes influenza activity in the UK from the beginning of the pandemic (end of April 2009) to week 20 2010 (ending 23 May 2010).

Methods

SOURCES OF DATA

A number of different data sources are traditionally used to monitor influenza activity in the UK. In response to the pandemic, some systems were enhanced and new ones were created to strengthen pandemic surveillance. Systems evolved as the UK moved through the different stages of the pandemic. Traditional seasonal influenza surveillance systems, along with several new influenza surveillance schemes, were utilised throughout the pandemic in the UK to provide a comprehensive assessment of this novel virus, to monitor its activity, to estimate impact and to measure the uptake, safety and effectiveness of the various counter-measures.

FIRST FEW 100 (FF100) SURVEILLANCE SYSTEM (NEW)

The FF100 system collected detailed demographic, exposure, clinical, treatment and outcome data for 392 of the first UK cases of laboratory confirmed pandemic (H1N1) 2009 and their close household and non-household contacts during the early part of the summer pandemic wave. Information was obtained through interviews and record reviews. Virological swabbing was undertaken when possible from symptomatic cases and blood samples for serological testing were sought from cases and their contacts[6].

The secondary household attack rate was calculated as the proportion of household contacts who became cases at two weeks. Uni- and multi-variable analyses were undertaken.

FLUZONE (NEW)

Fluzone was a case management system created by the HPA based on the generic clinical assessment information system HPZone. It was rapidly developed and rolled out to all English Health Protection Units and Flu Response Centres in summer 2009 during the containment phase. It was used in case management and follow-up of contacts, and also provided data on English cases by local area during this period.

FIELD EPIDEMIOLOGY STUDIES

A number of ad hoc field epidemiology investigations were undertaken by local Health Protection Units and their equivalents across the UK. These investigations occurred in various closed settings including schools and other venues.

SERO-EPIDEMIOLOGY STUDIES (NEW)

Serological analysis of serum samples was performed by the application of two assays – microneutralisation (MN) and haemagglutination inhibition (HI). These were designed and validated at the HPA Centre for Infections (CfI).

Serological assays were performed using NIBRG122, a reverse genetics version of a virus isolated from a human case (confirmed and isolated end of April 2009; A/England/195/2009) and antigenically representative for the pandemic viruses circulating

in the UK at that time. Recent infection was confirmed on the basis of 4-fold titre increase between an acute and convalescent serum sample by HI or MN. For unpaired sera (single convalescent serum samples from field studies or samples for sero-incidence study), the probability of recent infection was calculated based on the achievement of HI titres ≥32 (which correlates to a four-fold titre rise from a baseline titre of <8).

Serological samples for field epidemiological studies were collected as serum pairs where possible (acute and convalescent, separated by at least 14 days). In most cases, a single convalescent sample was obtained.

Population pre- and post-pandemic sero-prevalence and sero-incidence studies were undertaken. The HPA sero-epidemiology unit (SEU) and NHS chemical pathology laboratories in England provided the principal source of sera – using anonymised residual samples with information on age and month of sample. The SEU serum bank was examined from before the pandemic and at monthly intervals until the end of the pandemic[7].

A sero-prevalence study was also carried out in Scotland, using anonymised sera from residual diagnostic samples taken in March 2010[8].

CONSULTATION RATES FOR ILI WITH GPS

Clinical data are obtained from networks of general practitioner (GP) surgeries in the UK. Data reported are the weekly consultations for influenza-like illness (ILI) and other acute respiratory illnesses. These schemes use the number of patients registered with the participating GP as the denominator. In the UK, each country runs a national scheme. In addition, there is also a system (HPA/QSurveillance®) which includes practices from England, Northern Ireland and Wales, although the majority are from England. To aid interpretation of the consultation rates and comparison with previous years, thresholds have been defined for most GP-based schemes to indicate expected rates when influenza is not circulating widely (baseline levels), when normal seasonal levels of influenza are circulating in the winter season and when higher than expected or epidemic activity is occurring (see table 1). These thresholds have been set based on experience with several years of data.

Table 1: GP influenza surveillance system in the UK (click links in left-hand column for further information on the schemes from external websites)

Scheme (Country)	Baseline	Normal	Above Average	Case definition
RCGP (England)**	30	200	-	ILI
Public Health Wales	25	100	100-400	Influenza
PIPeR (Scotland)	50	-	-	ILI/ARI
PHA (Northern Ireland)	70	500	-	ILI/ influenza
HPA/QSurveillance® (UK*)	20	70	130	ILI

**** QSurveillance® is based on data from 43% of England's population, 11% of the population in Wales, 17% in Northern Ireland and 0% in Scotland; ** The thresholds for RCGP clinical data were lowered in 2004[8]***

COMMUNITY SYNDROMIC SURVEILLANCE

NHS Direct is a 24/7 nurse-led telephone health advice and information service in England and Wales. The NHS Direct/HPA surveillance scheme analyses data from this service. Key respiratory indicators are the proportion of callers reporting colds/flu and fever by age group and region[10]. In Scotland a similar system (NHS-24) operates.

In Northern Ireland there is no equivalent of NHS Direct/NHS-24. Data are collected from out-of-hours centres. During the 08/09 influenza season a pilot was undertaken with two of the seven primary care out-of-hours (OOH) centres. Data on total consultations and those for influenza/ILI, stratified by age, were extracted daily for the previous 24 hours and compared with sentinel consultation rates. This involved an auto-extraction process, with data being imported into a central repository. This process has now been extended to the remaining five centres.

On 23 July 2009 the National Pandemic Flu Service (NPFS) became operational in England only. Patients with uncomplicated ILI were asked to telephone or access the NPFS website rather than go to their GP. The service authorised antiviral drugs to people aged over one year, with ILI, who did not fall into a specified risk group. If they fell into one of these groups the individual was referred to the health service. NPFS replaced NHS Direct as the data source for community ILI syndromic surveillance. Data from NPFS provided information on the number of antiviral authorisations and collections.

In Northern Ireland, the number of antiviral courses, prescribed through primary and secondary care, was collated regionally on a weekly basis. In Scotland, the rate of antiviral prescriptions was analysed weekly.

MICROBIOLOGICAL SURVEILLANCE (ENHANCED)

Following development of a sensitive and specific H1N1 RT-PCR assay[11], all testing for pandemic (H1N1) 2009 was initially carried out at CfI. HPA regional laboratories forwarded all untypeable influenza A viruses to CfI for confirmation until a validated test had been developed and rolled out to them. Results of all tests from HPA laboratories for the novel virus (positive or negative) in England were reported to CfI, initially through standardised emailed spreadsheets. Reporting was later undertaken through the automated Datamart system for influenza and other respiratory viruses.

In addition, the National Laboratory Reporting Scheme (LabBase) comprises approximately 230 NHS, HPA and independent sector microbiology laboratories throughout England and Wales. This system reports positive results for human samples (from community and hospital settings) testing positive for pathogens. Trends in respiratory viruses including influenza, respiratory syncytial virus, rhinovirus and parainfluenza are examined.

A subset of ~50 general practices in the Royal College of General Practitioners (RCGP) Weekly Returns Service submit respiratory samples for virological testing from patients presenting with influenza-like illness in participating practices. Respiratory specimens, along with key demographic and epidemiological information about the patient and illness (e.g. use of antivirals and vaccination history), are submitted to the HPA CfI. A complementary sentinel primary care scheme of sampling is carried out by the HPA whereby respiratory specimens from patients presenting to their GP with an acute respiratory infection are

submitted to the local HPA Regional Microbiology Network (RMN) laboratory together with epidemiological information from the patient. Specimens are evaluated by PCR for influenza and other respiratory virus infections. Similar sentinel swabbing schemes through primary care operate in Scotland, Wales and Northern Ireland. Data from these schemes allow the calculation of the proportion of ILI cases consulting in primary care testing positive for influenza each week.

Beginning on 28 May 2009, a systematic sample of symptomatic callers to NHS Direct were asked to participate in a virological surveillance scheme. This involved self-sampling with nasal swabs. Swabs were then posted to HPA CfI for virological testing[12]. Virological self-sampling from NHS Direct stopped after week 30 and started through NPFS in week 32, until February 2010, when NHS Direct was used again.

HPA CfI undertakes antigenic and genetic characterisation of influenza isolates submitted for testing by HPA and NHS laboratories. Antigenic characterization of pandemic (H1N1) 2009 viruses circulating in the UK during 2009 was performed by haemagglutination inhibition (HI) assay using post-infection ferret antisera to A/California/07/2009 (vaccine strain), A/England/195/2009 (UK reference strain) and A/Brisbane/59/2007 (previous seasonal H1N1 vaccine strain). An isolate with a 4-fold or less change in reactivity to the reference strain is classed as being like the reference strain.

CfI also monitors the occurrence of anti-viral resistance in influenza isolates using a molecular marker for oseltamivir resistance (H275Y) and subsequent full phenotypic susceptibility testing. Cases found to be resistant were followed up through clinicians and microbiologists using a standard questionnaire.

To identify the role played by concurrent bacterial infections during the pandemic, an attempt was made to identify English pandemic (H1N1) 2009 cases who has also tested positive for a bacterial infection through record linkage.

ESTIMATED CASE NUMBERS (NEW)

The estimated number of symptomatic cases with ILI due to pandemic influenza, by English region and age group, was calculated each week using a statistical model. This used data from several surveillance sources including GP and NPFS age-specific consultation rates, age-specific positivity rates through sentinel virological schemes and estimated proportions consulting health care. The parameters altered over the pandemic period to take into account changes in policy (e.g. the introduction of NPFS and impact on proportion consulting health care) and changes in data[13]. An estimate of the total number of new symptomatic cases was given each week with the previous week estimates recalculated with updated data. There was uncertainty around the proportion of people with ILI symptoms who contacted their GP (or NPFS). To take this uncertainty into account a range of values were used resulting in a range of estimated symptomatic case numbers surrounding the central estimate.

HOSPITALISATION DATA (NEW)

During the initial part of the first wave, detailed information was collected for all laboratory confirmed cases as part of the FF100 project. Information collected included details of contact with the health care service and, where appropriate, of hospitalisation.

In England, after the closure of FF100, information on cases including possible hospitalisation was collected by Health Protection Units through the Fluzone system. Once the treatment phase started, not all suspected cases were tested for influenza infection, Acute Trusts reported to the Department of Health (DH) the number of confirmed or clinically suspected cases of pandemic (H1N1) 2009 admitted to local NHS hospitals. In October 2009, a web based reporting system was introduced by HPA and the Chief Medical Officer (CMO) across England to collect demographic, clinical and epidemiological information on all laboratory confirmed pandemic (H1N1) 2009 cases admitted to NHS trusts. In addition to collecting information prospectively, this system was used to collect information retrospectively on all laboratory confirmed cases admitted to hospital since the beginning of the pandemic. Information was collected on clinical details, underlying risk factors, use of antivirals and outcome of admission.

In Northern Ireland similar information on virologically confirmed hospitalised cases was forwarded, initially daily and subsequently weekly, by the hospital trusts to the Public Health Agency throughout the pandemic period.

In Scotland data on virologically confirmed hospitalised cases were collated by Health Protection Scotland.

In Wales similar data were collated by Public Health Wales Health Protection.

In addition, a detailed case note-based investigation was carried out in 55 hospitals across the UK. The Influenza Clinical Information Network (FLU-CIN) study collection in-dept clinical and demographic information on patients admitted to hospital with confirmed pandemic (H1N1) 2009 infection[14].

MORTALITY MONITORING (ENHANCED)

The Office for National Statistics (ONS) collates and reports to HPA estimated total all-cause death registrations on a weekly basis. This information is used to estimate excess all-cause all-age death registrations in England and Wales as compared to previous seasons each week. A statistical model is used based on the Serfling method, to establish a baseline of the expected weekly number of registered deaths[15]. If the observed number is above the upper limit of a 90% confidence interval around this expected number for at least one week, an excess is said to have occurred.

In addition to the ONS data, during the pandemic, the General Registry Office of England and Wales reported daily individual death registrations by age and registration district. This information was used to estimate excess all-cause mortality by age-group in England and Wales.

In Scotland the weekly total number of death registrations (overall and by age group) is compared to the expected number calculated using two methods; a Serfling cyclical model and a Gam model based upon previous winters.

The CMO undertook a confidential enquiry of confirmed pandemic (H1N1) 2009 deaths in England with reporting from all NHS trusts. In addition, individual pandemic (H1N1) 2009 deaths were ascertained through the various enhanced surveillance systems operated by

the HPA and reconciled. Similar information was gathered by health protection equivalents in Scotland, Wales and Northern Ireland. Information on cause of death, complications and underlying conditions was collected.

VACCINE UPTAKE MONITORING

Priority groups for pandemic (H1N1) 2009 vaccination were defined by the Joint Committee for Vaccination and Immunisation as those aged six months and up to 65 years in the current seasonal influenza vaccine clinical at-risk groups, all pregnant women, household contacts of immunocompromised individuals, and those aged 65 years and over in the current seasonal influenza vaccine clinical at-risk groups. These priority groups were offered pandemic vaccine from late October 2009. Following the DH announcement on phase two of the vaccination programme, healthy children aged six months and up to 5 years were offered pandemic vaccine from December 2009.

The DH recommended that all those aged 65 years and over and those aged 6 months to under 65 years falling in a clinical at risk group, be offered the seasonal 09/10 trivalent influenza vaccine. Clinical at risk groups include individuals with one of the following underlying medical condition: chronic respiratory disease, chronic heart disease, chronic renal disease, chronic liver disease, chronic neurological disease, diabetes or immunosuppression.

Uptake of both vaccines in the different eligible groups was monitored in England by the HPA through the DH web-portal ‘Immform’. Data on the eligible populations and the number of patients/health-care workers vaccinated were automatically extracted or manually outputted from GP and acute trust information systems and uploaded.

In Scotland, Wales and Northern Ireland similar data were collected using automated and manual methods.

VACCINE EFFECTIVENESS MONITORING

Estimates of vaccine effectiveness were made using data from GP sentinel virological schemes in England and Scotland. A swab negative case-control study of individuals with influenza-like-illness was undertaken. Those testing PCR positive for pandemic (H1N1) 2009 were cases and those testing negative were controls. Vaccine effectiveness was estimated as (1-OR).

DENOMINATOR DATA and MODELLING

Where population rates are presented, the population figures are from the ONS mid-2008 estimates, which are available by age and region[16].

In the case of rates by underlying medical condition, the population denominators are derived from the HPA-DH vaccine uptake surveys. These data provide information on the number of patients registered in primary care by specific underlying condition for people aged between six months and 65 years and for the 65-year or older group the overall number in a risk group is available. The estimate of the number of pregnant women is

derived from the annual maternities and number of miscarriages/abortions provided by ONS[17].

Where case-based rates are presented, the denominator used is the HPA estimated number of symptomatic cases (see above). To take into account the range of values used due to uncertainty around the case numbers, the case-rates are presented with a range; the upper and lower limits of 95% confidence intervals around the rates obtained using the low and high estimate of cases.

Follow-up of confirmed cases and their close household contacts in the FF100 project allowed an estimation of the overall household secondary attack rate (SAR), and of the impact of containment measures on the reproduction number (*R*)[18]. *R* is a measure of the transmissibility of the virus and sustained transmission requires $R>1$. Real-time modelling work also examined vaccination policy options for the Joint Committee of Vaccination and Immunisation.

Results

ENHANCED CASE FINDING AND EPIDEMIOLOGY STUDIES (CONTAINMENT PHASE to 1 JULY 2009)

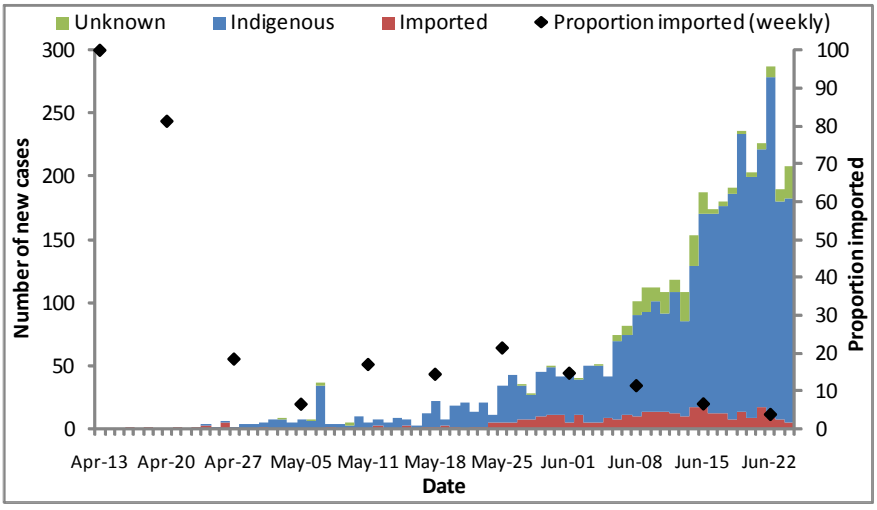
TIMING

The first cases of pandemic (H1N1) 2009 infection in the UK were reported on 27 April 2009, in a Scottish couple returning from a trip to Mexico[19;20]. Two days later, the first English case was reported in a person who had travelled on the same flight from Mexico.

In the first four weeks of the outbreak in the UK, transmission of the virus was sporadic and generally linked to travellers returning from affected areas (Mexico and the US) or to indigenous transmission to close contacts in school and household settings[5].

Sustained community transmission became established initially in Scotland (South Glasgow), the West Midlands and then London. In England, much of the transmission was linked to school outbreaks. By the end of the containment phase (1 July 2009), 7447 confirmed cases had been reported in the UK; 6162 (83%) in England, 1217 (16%) in Scotland and 34 (0.5%) each in Northern Ireland and Wales. Case numbers were doubling approximately every week at this stage. The proportion of cases who were imported (as opposed to infection acquired indigenously in the UK) decreased over the initial weeks to less than 5% by the end of June (figure 1).

Figure 1: Cases of pandemic (H1N1) 2009 by onset date and route of acquisition of infection and weekly proportion imported, UK (to 1 July 2009)



Datasources: Fluzone in England and equivalants in Scotland, Wales and Northern Ireland

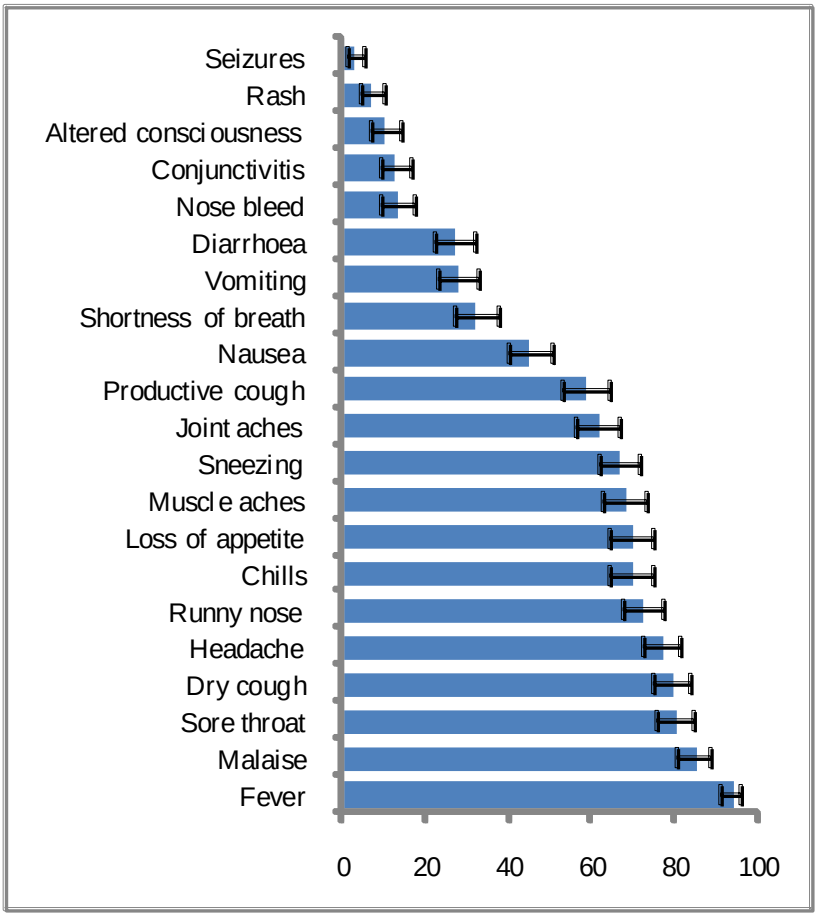
CLINICAL PRESENTATION

Most cases appear to have experienced an illness fairly typical for influenza.

Detailed investigation of 392 early laboratory-confirmed cases as part of the FF100 surveillance project found fever, malaise, dry cough, sore throat and headache to be the commonest (>70% of respondents) reported symptoms (figure 2). However, a greater proportion of cases reported gastrointestinal (diarrhoea and vomiting) than is usually seen with seasonal influenza. The median reported duration of illness was seven days (range 1-29 days)[21].

Asymptomatic infection is a well-recognised feature of seasonal influenza[22]. Serological studies of a boarding school outbreak of pandemic (H1N1) 2009 showed that sub-clinical infection occurred in about one third of those with serological evidence of infection [23].

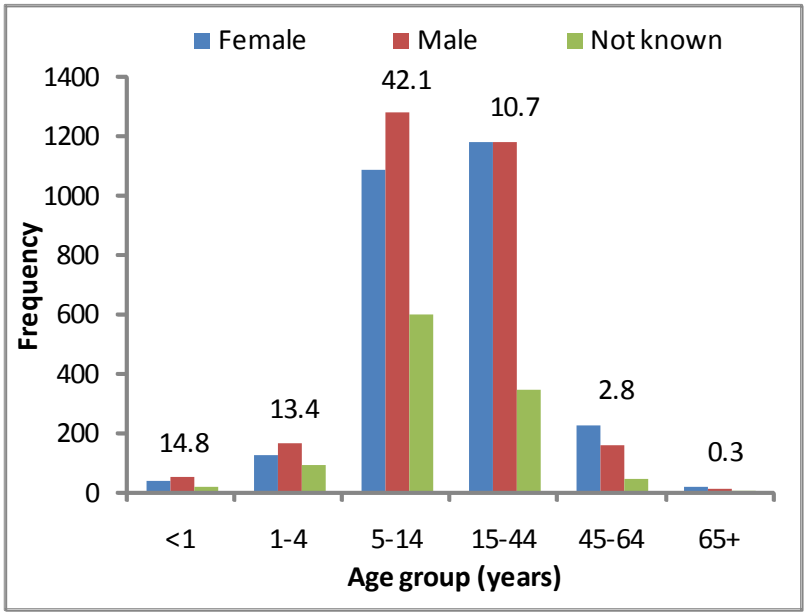
Figure 2: Proportion (%) of all UK FF100 cases of pandemic (H1N1) 2009 influenza reporting symptoms at any stage of illness, with binomial exact 95% confidence interval (adapted from[21])



GROUPS AFFECTED

During the containment phase, pandemic (H1N1) 2009 cases were identified aged from 0 to 90 years; the median age for confirmed cases up to 1 July 2009 was 14 years (IQR: 9 – 25 years). The 5-14 year age group had the highest cumulative population incidence rate (42.1 per 100,000) by 1 July 2009 (figure 3). The older age groups (aged over 45 years) had the lowest cumulative population incidence rates. At this stage, the median age varied by region; in London and the West Midlands, where there had been several large school-based outbreaks[24-26], it was 12 years while in other UK regions it ranged from 17 years (Scotland) to 25.5 years (North West England). There was an approximately equal distribution by gender (48% female).

Figure 3: Age and sex distribution of pandemic (H1N1) 2009 cases, UK with crude cumulative population rate per 100,000 (to 1 July 2009)



Cases of pandemic (H1N1) 2009 were not dispersed homogenously throughout England during the containment phase. Parts of London and the West Midlands region experienced high numbers of cases with rapid rates of increase in new cases from week to week early in the summer wave (figure 4, appendix 2). Both these areas showed the first increases in ILI reported through daily GP consultation rates before the end of the containment phase; about two weeks earlier than other areas of the country (figure 5).

Figure 4: location of UK cases of pandemic (H1N1) 2009 by week of report, June 2009

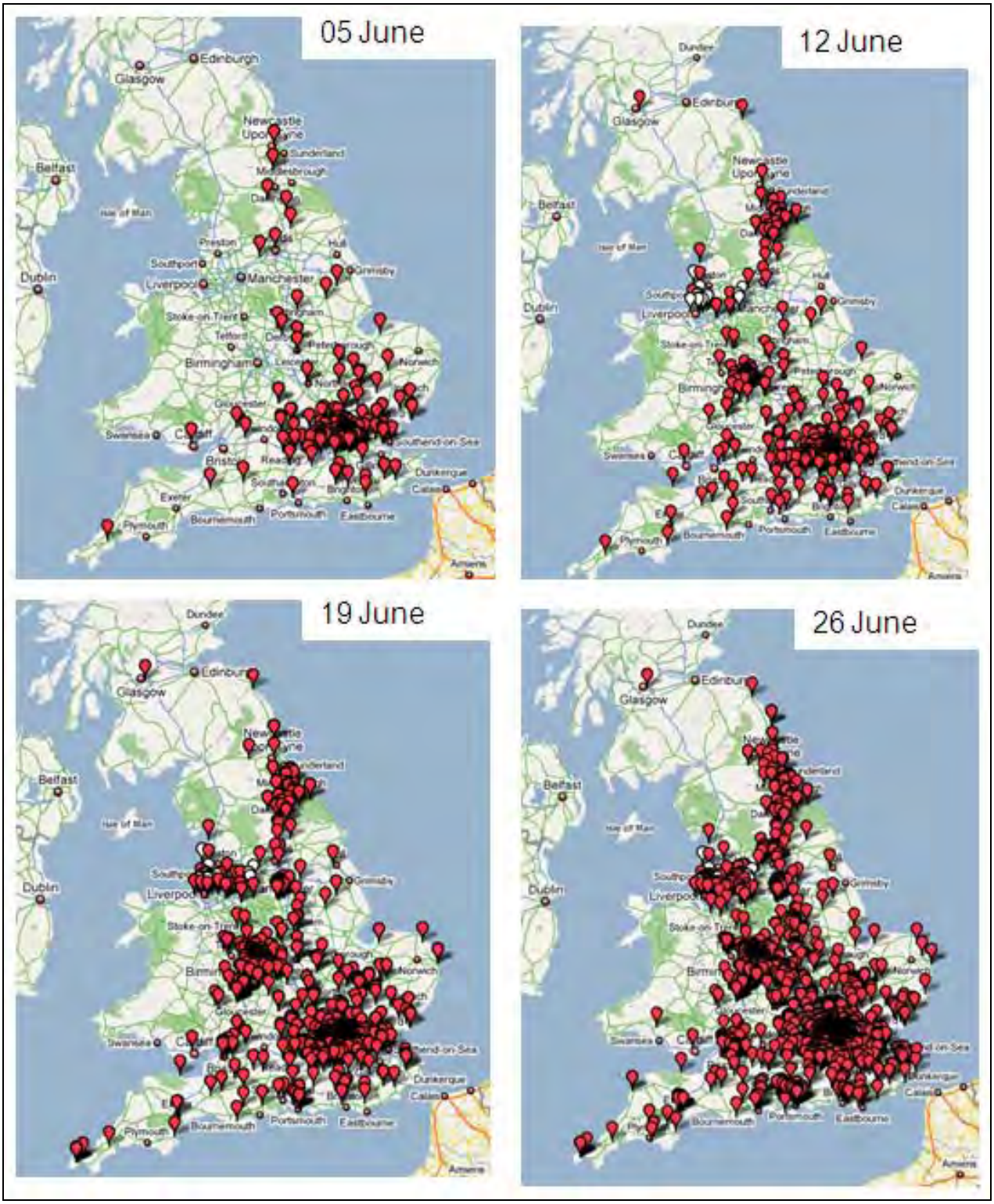
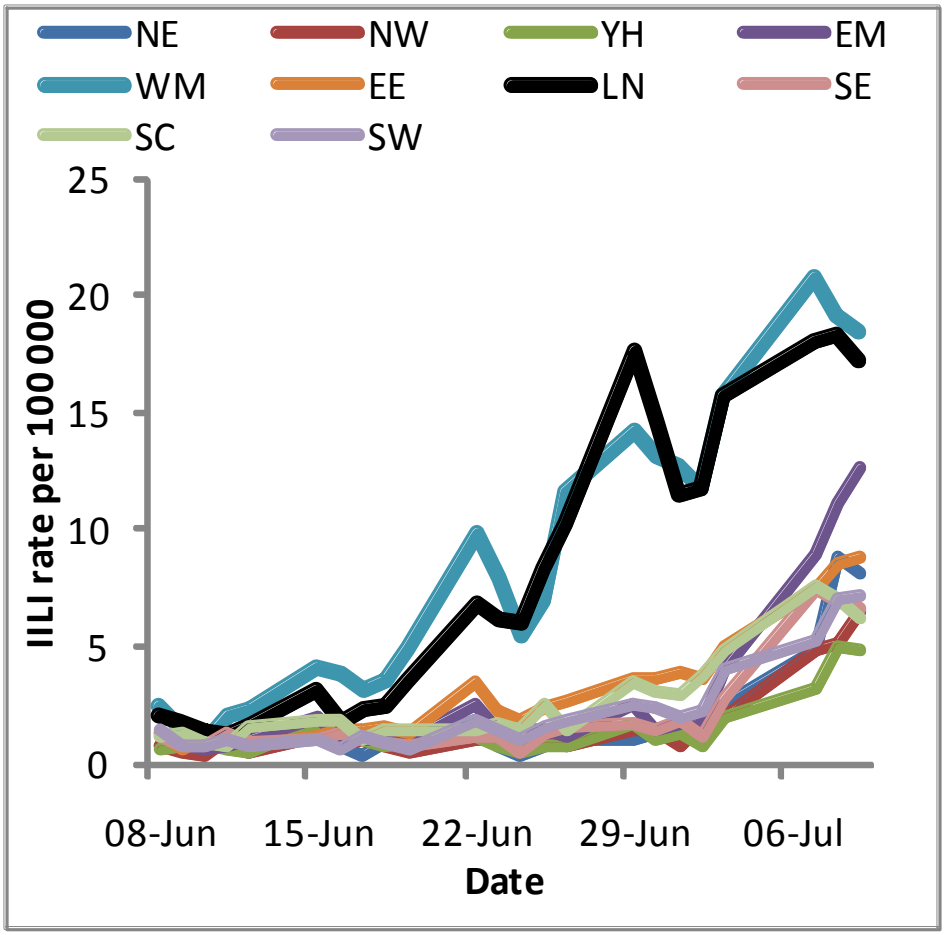


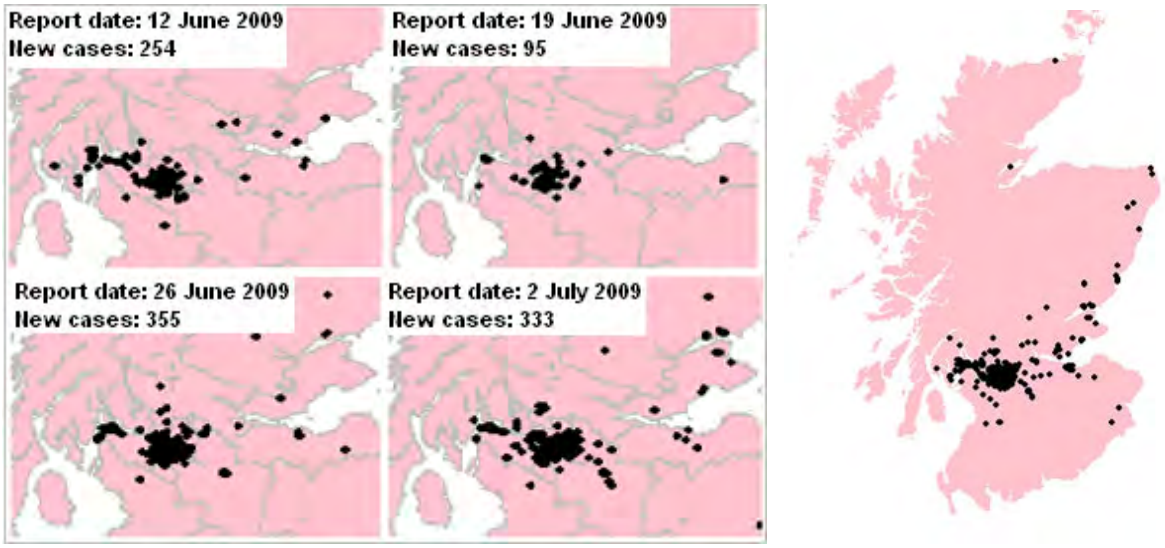
Figure 5: daily GP consultation rate for ILI through the HPA/QSurveillance system, by region*, June – July 2009



**EM: East Midlands, EE: East of England, LN: London, NE: North East, NW: North West, SC: South Central, SEC: South East Coast, SW: South West, WM: West Midlands, YH: Yorkshire and Humberside.*

In Scotland pandemic (H1N1) 2009 cases were initially clustered in the 'hotspot' areas of Greater Glasgow & Clyde in the West of the Central area of the country. Up to 2 July 2009 (after which point not all suspected cases were tested) the majority of cases were almost exclusively restricted to the Central Belt of Scotland although there was the start of gradual spread to beyond these limits (figure 6).

Figure 6: Maps of Scotland showing new laboratory confirmed cases reported to HPS by week of report and the total to 2 July 2009 (n=1238)



FIELD INVESTIGATIONS

Health protection teams across the UK initiated a number of field investigations of outbreaks in closed settings. In one early school outbreak in England, 91 symptomatic cases were identified between 15 April and 15 May 2009 of which 33 were confirmed to be positive for pandemic (H1N1) 2009. In this outbreak an overall virologically confirmed attack rate in the school pupils of 2% was observed, though in the most affected age group this increased to 15%. Transmission was documented in several households of the pupils with a 17% virologically confirmed secondary attack rate in household contacts[24].

A large, late-recognised, outbreak of pandemic (H1N1) 2009 infection in an English primary school had a 30% clinical attack rate in the pupils, with a virologically confirmed attack rate of 13% overall (ranging from 5.1% to 23% in different age groups). The symptoms reported were generally mild: predominantly fever, nasal congestion and sore throat[25].

TRANSMISSION

The overall household secondary attack rate (SAR) (for virologically confirmed pandemic (H1N1) 2009) in the FF100 was estimated as 8.2% (95% CI 6.4 – 10.3%) during the containment phase. This was significantly affected by the use of antivirals to treat index cases and as prophylaxis for close household contacts. There was also evidence of a differing SAR by age group; with the rates in children and young adults significantly higher than the rate in adults aged over 50 years (table 2)[27].

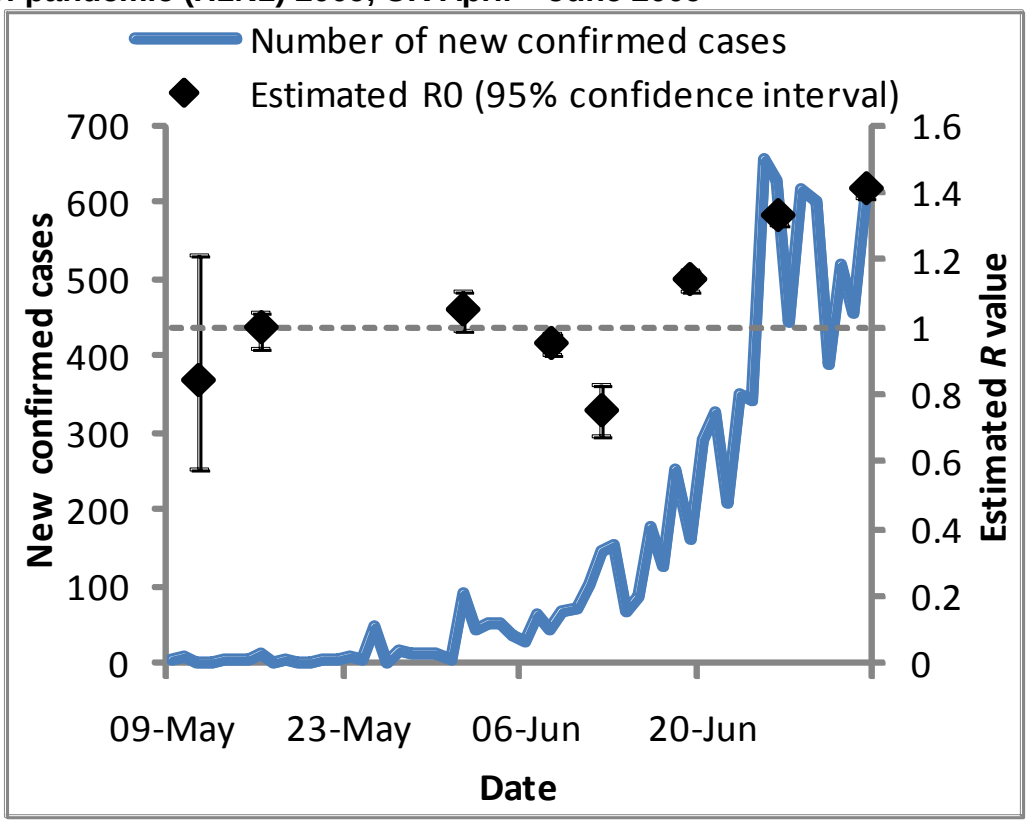
R was estimated to be close to 1 but with considerable uncertainty from early May until mid June, after which it was consistently above 1 (figure 7). This fluctuation in the estimate is to be expected due to stochastic effects (randomness) being significant when numbers of infected individuals are low.

Table 2: Uni- and multi-variable analysis of SAR by gender, age group and prophylaxis and treatment for virologically-confirmed cases (adapted from[27])

Variable level	Crude (uni-variable) SAR	Adjusted (multi-variable) OR (95% CI)	p-value
Male	37/364 (10.2%)	Baseline	0.94%
Female	25/381 (6.6%)	1.0 (0.5 - 2.0)	
<16 year	40/212 (18.9%)	14.2 (3.0 - 67.1)	<0.001
16-49 years	20/378 (5.3%)	2.8 (0.6 - 13.4)	
50+ years	2/171 (1.2%)	Baseline	
No prophylaxis	45/132 (34.1%)	Baseline	<0.001
AV prophylaxis	8/455 (1.8%)	0.03 (0.02 - 0.09)	
>48 hours*	48/453 (10.6%)	Baseline	0.004
≤48 hours*	14/308 (4.5%)	0.3 (0.13 - 0.68)	
Total	62/761 (8.1%)		

** Index case treated with antiviral drugs*

Figure 7: Estimated R by date of estimation with the number of new confirmed cases of pandemic (H1N1) 2009, UK April – June 2009



ROUTINE AND ENHANCED INFLUENZA SURVEILLANCE SYSTEMS (April 2009 – May 2010)

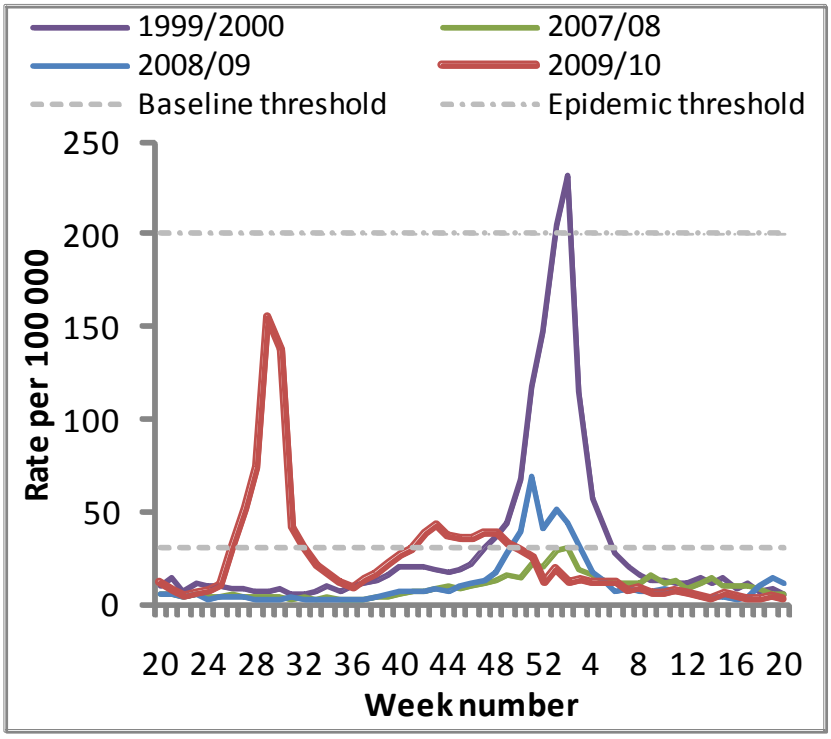
CLINICAL

Weekly GP clinical surveillance schemes in England, Scotland, Wales and Northern Ireland:

With the onset of widespread community transmission, the RCGP weekly ILI rate in England exceeded the baseline level of 30 consultations per 100,000 in week 27 (ending 5 July 2009) when it increased from 29.6 to 51.9 per 100,000. It peaked in week 29 (ending 19 July 2009) at 155.3 per 100 000 and remained above the baseline level until week 33 (ending 16 August 2009) when it decreased from 30.9 to 21.2 per 100,000. It decreased until week 36 (reaching 8.6 per 100,000 at the lowest point) after which it began to increase again, exceeding the baseline in week 42 (ending 18 October 2009) when it increased from 29.1 to 42.8 per 100,000. This was the highest rate observed in the autumn, though the rate remained above the baseline for several weeks. It finally fell below this level in weeks 50 (29.7 per 100,000) and 51 (24.7 per 100,000) (figure 8).

Observed trends in primary care consultations were likely affected by the NPFS which operated in England between 23 July 2009 (the RCGP peak week) and 11 February 2010. In addition, most state schools in England started their summer holidays in the week ending 26 July.

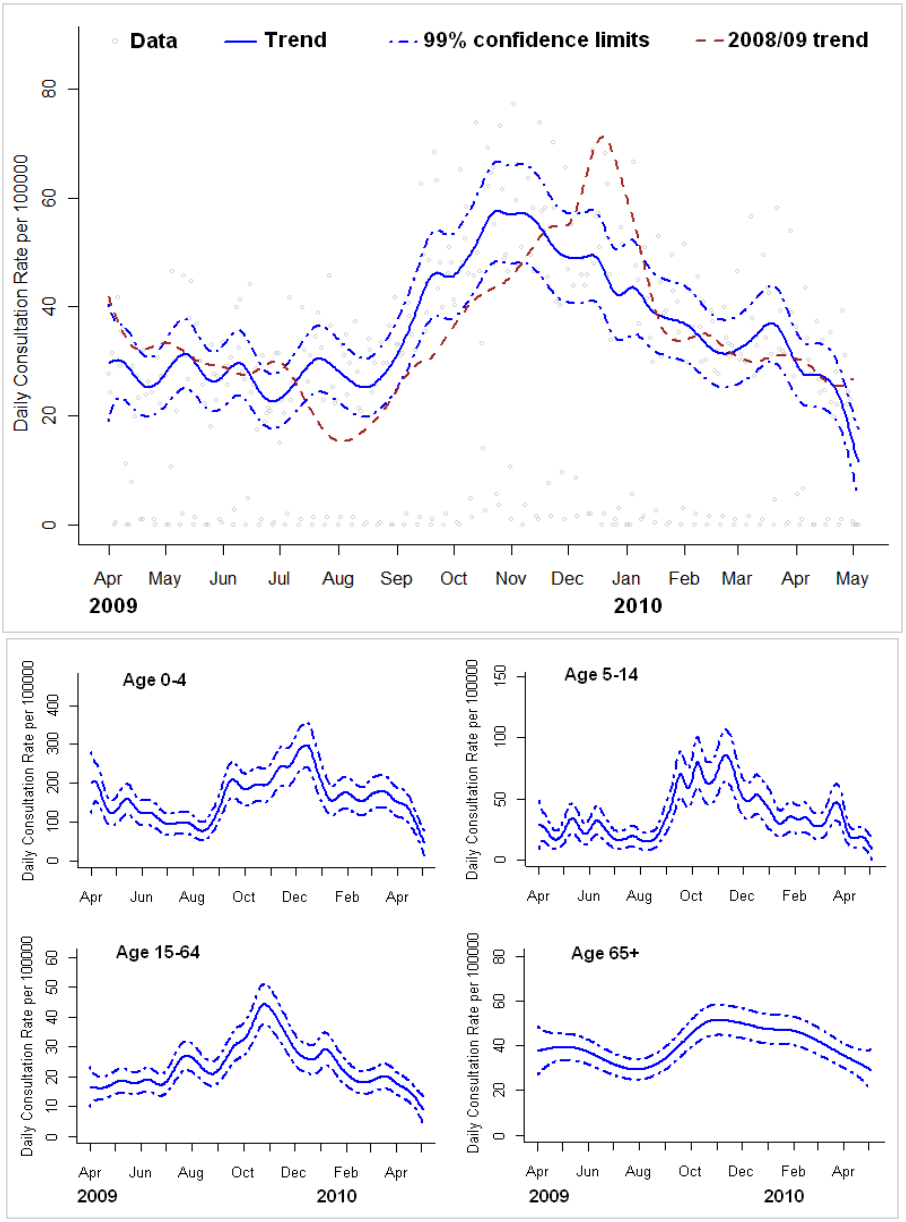
Figure 8: Royal College of General Practitioners weekly influenza-like illness rate per 100,000, May 2009 – May 2010



A summer peak has not been observed since the start of the RCGP weekly returns service in 1966. The 2009 summer peak ILI consultation rate was lower than that observed during the 1999/2000 winter season (231.1 per 100,000) but higher than the peak seen in the 2008/09 winter season (68.5 per 100,000) which was associated with moderately high activity mainly due to circulation of influenza A (H3).

In Scotland there was little distinction between the summer and autumn pandemic waves according to the GP ILI/ARI rate. A gradual increase was observed over the summer but the baseline of 50 per 100,000 was only exceeded in week 39 (ending 27 September 2009) when it increased from 48.6 to 51.8 per 100,000. Note that schools in Scotland finished earlier than England in week 27 (ending 5 July 2009). The highest rate observed was 66.1 per 100,000 in week 43 (ending 25 October 2009). The rate decreased to below the baseline level in week 2 (ending 17 January) when it decreased from 51.8 to 39.5 per 100,000 (figure 9). The Scottish ILI/ARI rate did not exceed the 2008/09 peak rate of 92 per 100,000. The younger age groups had the highest rates.

Figure 9: Health Protection Scotland: PIPeR daily ILI rate per 100,000 overall and by age group*, April 2009 – May 2010

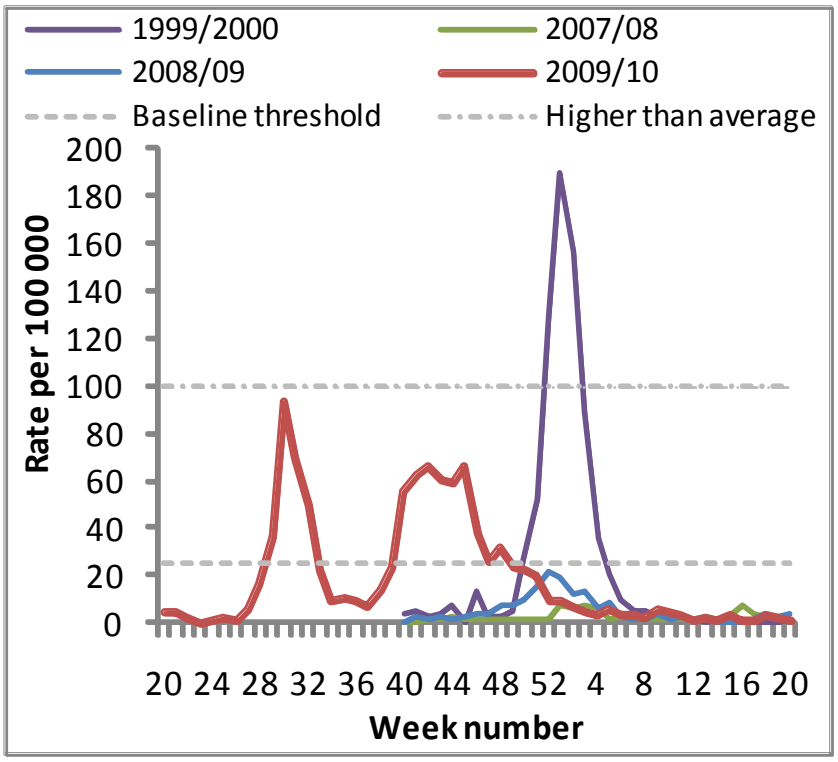


**Note differing scales on age break-down figures.*

In Wales, the influenza primary care consultation rate showed a similar pattern to the RCGP ILI rate in England. The baseline level of 25 per 100,000 was exceeded for the first time in nine years in week 29 (ending 19 July 2009) when it increased from 15.8 to 36 per 100,000. The rate climbed to a peak of 92.8 per 100,000 in week 30 and rapidly declined to below the baseline by week 33 (ending 16 August 2009). For most Welsh schools, the summer term ended in week 29 (ending 19 July 2009).

After week 37 (ending 13 September 2009), the rate began to increase again exceeding the baseline once more in week 40 (ending 4 October 2009) when it increased from 22.8 to 54.8 per 100,000. A second peak of 66.2 per 100,000 was observed in week 42 (ending 18 October 2009), after which the rate declined to below the baseline level by week 49 (ending 6 December 2009) (figure 10). The highest Welsh ILI consultation rate exceeded the level seen in the 2008/09 winter (21.5 per 100,000), but was half as high as the level observed in 1999/2000 (189.5 per 100,000).

Figure 10: Wales: weekly influenza rate per 100,000, May 2009 – May 2010

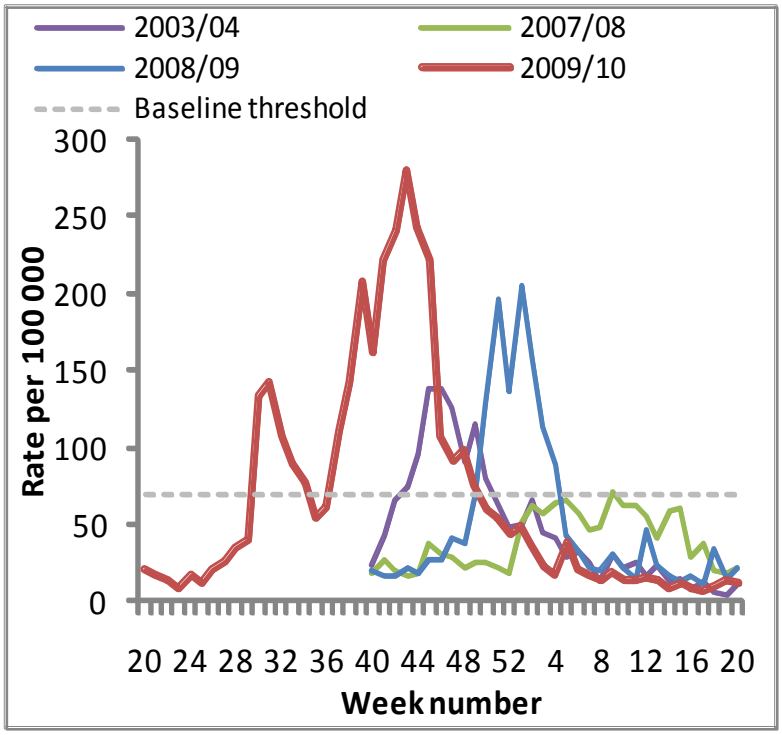


In Northern Ireland, the combined influenza/ILI rate peaked in the summer at 142.5 per 100,000 in week 31 (ending 2 August 2009). A provisional threshold of 70 per 100,000 was set for the 2009/10 influenza season and the rate was above this level for five weeks over the summer wave. The Northern Ireland school year ended in week 27 (ending 5 July 2009).

The threshold was also exceeded in the autumn in week 37 (ending 13 September 2009) when it increased from 61.9 to 113.8 per 100,000. A second peak of 280.6 per 100,000 was observed in week 43 (ending 25 October 2009) at a higher level than the summer. The rate declined to below the new baseline level by week 50 (ending 13 December 2009) (figure

11). The rate exceeded the level observed in previous years; 204.9 per 100,000 in 2008/09, though it should be noted that this system was not operational during the last large UK epidemic in 1999/2000.

Figure 11: Northern Ireland: weekly influenza/ILI rate per 100,000, May 2009 – May 2010



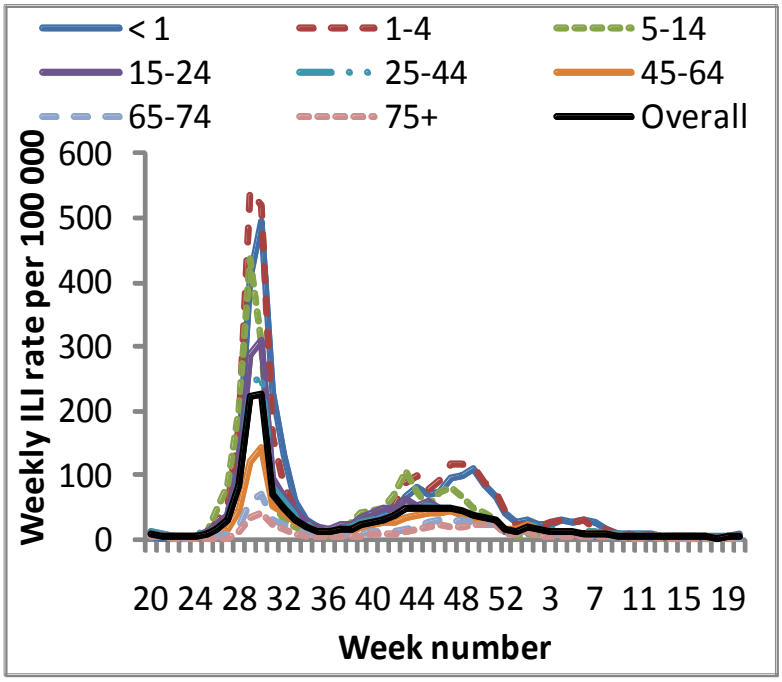
Weekly GP clinical surveillance through the HPA/QSurveillance system (England, Wales and Northern Ireland)

The weekly ILI rate for England, Wales and Northern Ireland (no Scottish data are available) through the HPA/QSurveillance system showed a similar pattern to the RCGP ILI rate. A peak of 226 per 100,000 was observed in week 30 (ending 26 July 2009), after which the rates decreased until week 36 then increased to a second peak of 50.5 per 100,000 in week 47 (ending 22 November 2009). Similar to the RCGP scheme, the autumn wave was much lower and flatter; the rate was around 50 per 100,000 from week 43 to week 48 (figure 12). This GP consultation rate was also affected by the use of the NPFS from 23 July 2009 to 11 February 2010.

By age group, the highest rate was seen in the 1-4 year group in week 29 (ending 12 July) at 541.2 per 100,000, followed by 493 per 100,000 in the under one year group in week 30 and 437.1 per 100,000 in the 5-14 year olds in week 29 (the week before English school summer holidays). All age groups peaked in week 29 or 30 in the summer wave; however a different pattern was seen in the autumn wave. The 5-14 year group peaked earliest at 105.2 per 100,000 in week 43 (ending 25 October 2009 – which was the week before the English school half-term holiday), followed by the 1-4 year group at 118.2 per 100,000 in week 47 (ending 22 November) and the under one year group at 108.9 per 100,000 in week

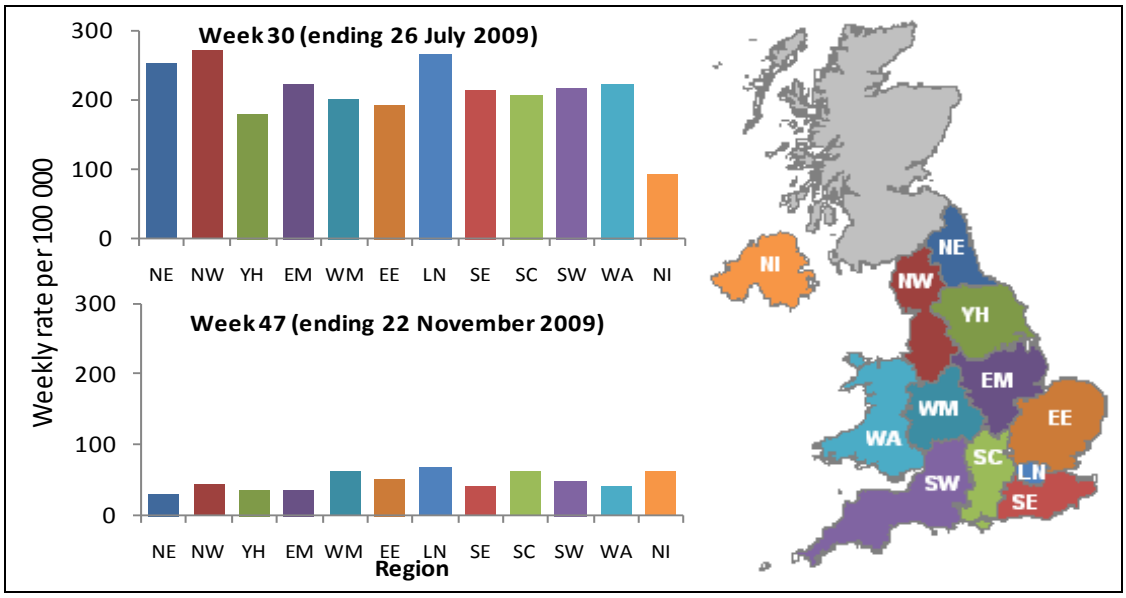
49 (ending 6 December). The lowest rates in both waves were in the older age groups over 45 years of age (figure 12)

Figure 12: Weekly ILI consultation rate through the HPA/QSurveillance system, by age group, E, W NI, May 2009 – May 2010



The London and West Midlands Strategic Health Authorities (SHA) were the first to show increases in the ILI rate, but most regions peaked in week 29 or 30 in the summer wave (appendix 2). The highest regional rate was observed in London at 310 per 100,000. In the autumn wave, the rates peaked in the Northern regions in week 43 (ending 25 October 2009), with the highest in the North East (67.3 per 100,000). Most of the central and southern regions peaked later in week 47 (ending 22 November 2009) with the highest in London at 67.3 per 100,000 (figure 13).

Figure 13: GP ILI rates through HPA/QSurveillance system by region in the peak weeks (peak of overall rate), E, W, NI

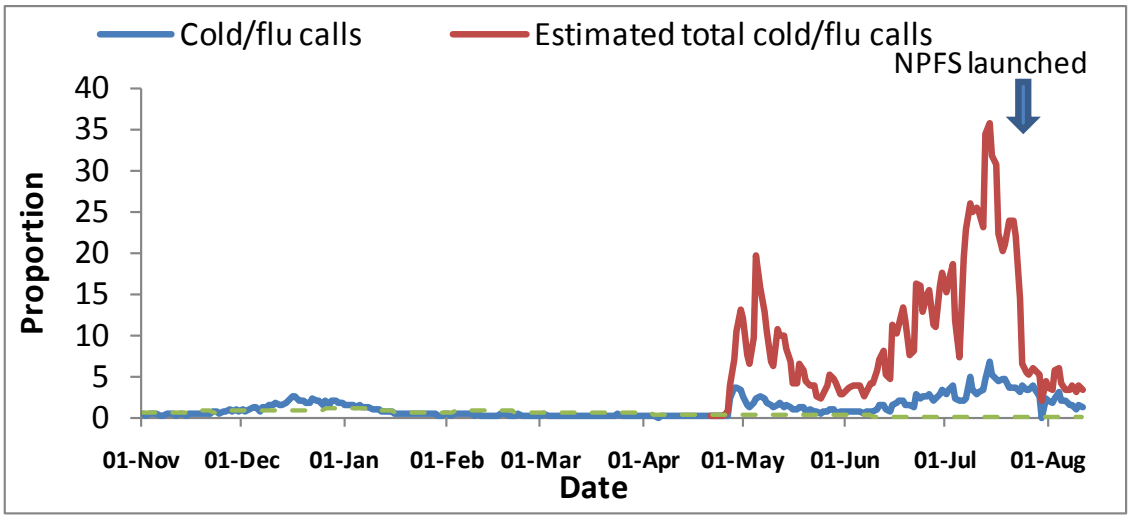


Syndromic Surveillance in the community through call/out-of-hours centres

Following the initial reports of the pandemic and the first confirmed cases in the UK at the beginning of May 2009, an early increase in cold/flu calls to NHS Direct in England and Wales was observed with a peak on 5 May 2009. This is thought to be in part due to media coverage (figure 14)

There was a further rise in cold-flu calls from early July, commensurate with evidence of community transmission. The proportion of cold/flu calls rose to a peak of 35.9% on 14 July 2009. A marked decline was then observed coinciding with the launch of the NPFS on 23 July 2009. NPFS, rather than NHS Direct, handled the majority of calls from people with an ILI in England (figure 14).

Figure 14: Daily proportion of calls due to colds/flu through NHS Direct, England and Wales, November 2008 – August 2009



From the launch of NPFS in July 2009 to February 2010, when it ceased operation, a total of 2,401,043 assessments were carried out. As a result, 1,635,948 authorisations for antivirals were issued, and 1,079,179 courses of antiviral treatment were collected in England. Assessments, authorisations and collections peaked when the service was first launched in July 2009 followed by a steady decline. In the autumn wave the peak occurred in week 43 (ending 25 October 2009) when 137,739 assessments were completed, 98,590 antiviral authorisations were issued and 66,218 antiviral courses were collected (figure 15).

In Scotland, similar to what was seen in England and Wales; there was an increase in the proportion of cold/flu calls to NHS24 during early May 2009 at a time when there was considerable media attention. A similar pattern was evident in June that may reflect the increased publicity following outbreaks in schools and the first UK death reported from Scotland, rather than evidence of widespread community transmission. Call volumes for cold/flu then increased again during July in Scotland and peaked in early August, about two weeks before the return of the schools from the summer holiday. The proportion of calls due to colds/flu increased in the beginning of October followed by a fall in early November, probably resulting from the effect of the school half-term holiday in October, before increasing once more and peaking at the end of November (figure 16).

Figure 15: Number of assessments completed, antivirals authorised and collected through the National Pandemic Flu Service, England July 2009 – February 2010

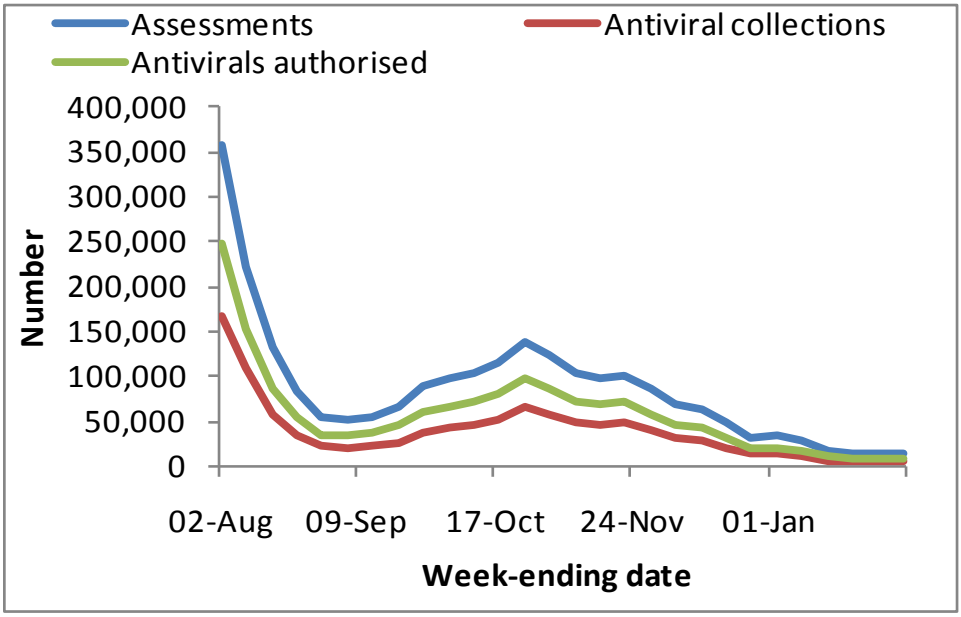
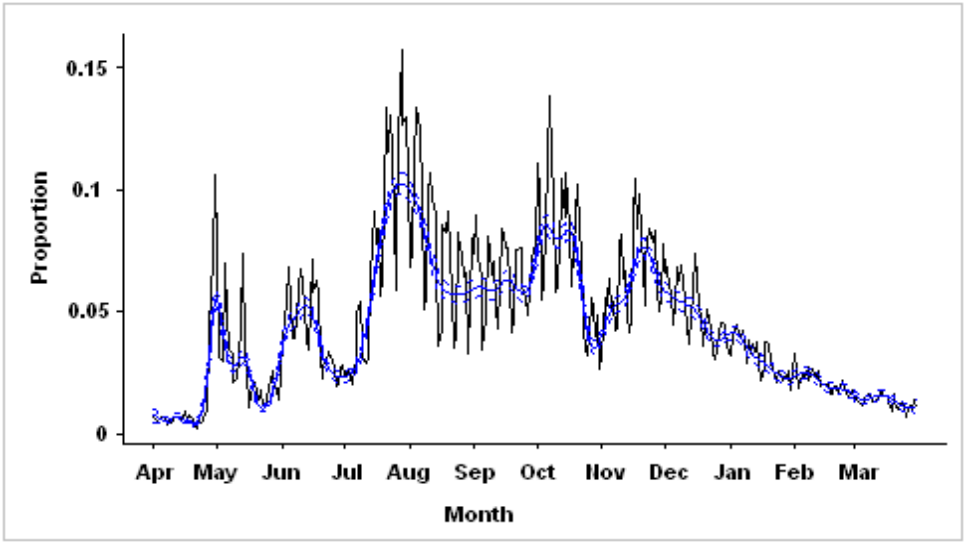


Figure 16: Daily proportion of calls due to colds/flu through NHS 24, Scotland, April 2009 – April 2010

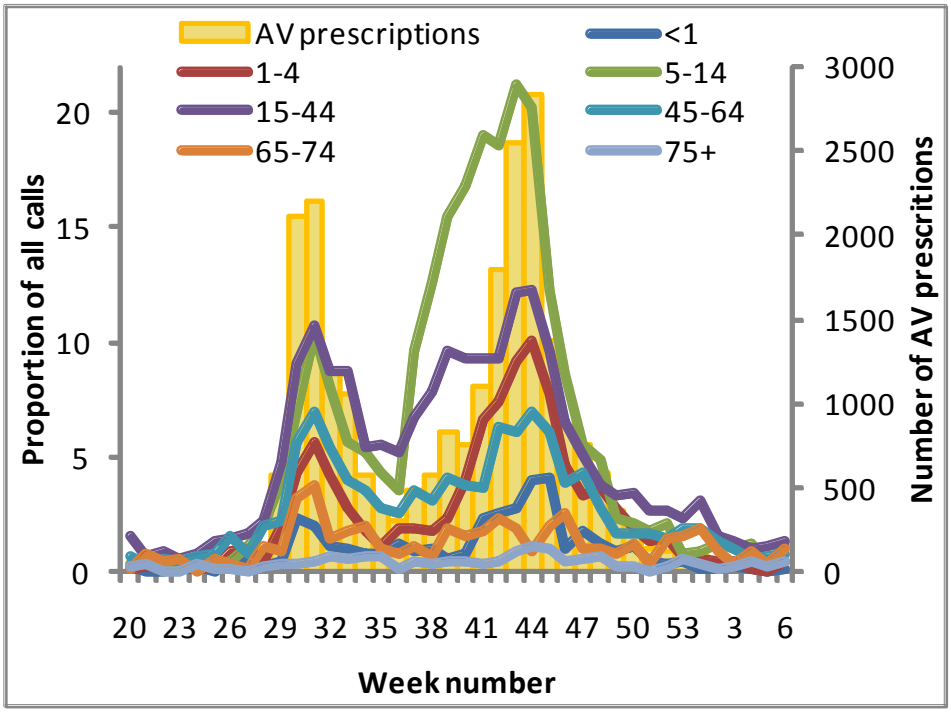


In Scotland antiviral prescribing was restricted to general practice in the treatment phase. A total of 98,000 courses of antivirals were issued across the entire pandemic. Antiviral prescribing patterns were broadly consistent with the increasing trends seen in General Practice consultations and hospital admissions. The rate of antiviral prescribing corresponded to the peak of Scotland's GP consultation rate in week 46.

In Northern Ireland, out-of-hours (OOH) consultation rates peaked initially in week 33 (49.6/100,000) when 7.5% of OOH consultations were due to influenza/ILI and then again in week 43 (rate 77.5/100,000) when 10.2% were due to influenza/ILI. In the first wave the highest proportion of OOH consultations due to influenza/ILI by age band was in the 15-44 year age group closely followed by the 5-14 year age group. This was in contrast to the second wave, when the proportion of influenza/ILI calls was markedly higher in the 5-14 year group. In week 43, 21.2% of OOH consultations in this age group were due to influenza/ILI (figure 17).

Trends in antiviral prescriptions closely corresponded to sentinel consultation rates and OOH calls, though the early increase in calls in the 5-14 year group was not mirrored by the prescription data (figure 17).

Figure 17: Weekly proportion of calls due to influenza/ILI of total calls to out-of-hours centres by age group and total number of antiviral prescriptions, Northern Ireland, May 2009 – February 2010

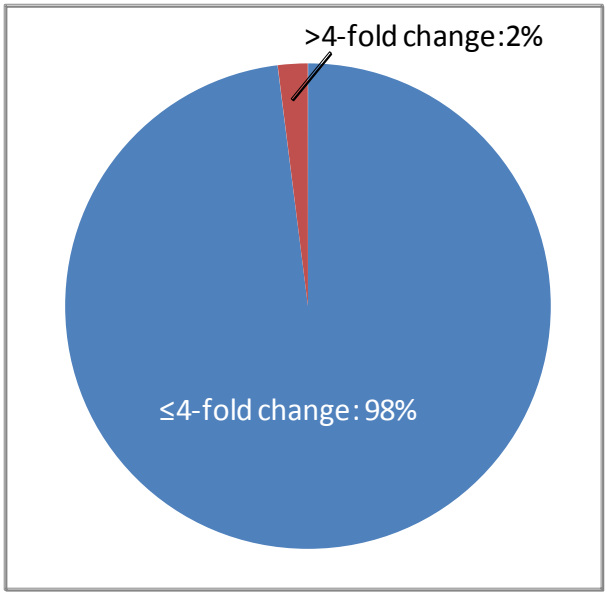


MICROBIOLOGICAL

A total of 29,228 (20,595 in England, 6,600 in Scotland, 1,369 in Northern Ireland and 664 in Wales) virologically confirmed cases of pandemic (H1N1) 2009 were reported up to 1 June 2010 (note: from July 2009 onwards, not all suspected cases were tested).

Characterisation of sentinel and non-sentinel pandemic (H1N1) 2009 viruses revealed that the majority of UK isolates were antigenically similar to the A/California/07/2009 vaccine strain. There were sporadic identifications of viruses with a greater than four-fold change in reactivity to A/California/07/2009 antiserum (2% of all isolates tested, figure 18); this change did not appear to correlate with specific amino acid substitutions in the haemagglutinin (HA) gene.

Figure 18: Antigenic reactivity with A/California/07/2009 antiserum, UK isolates, April 2009 – May 2010



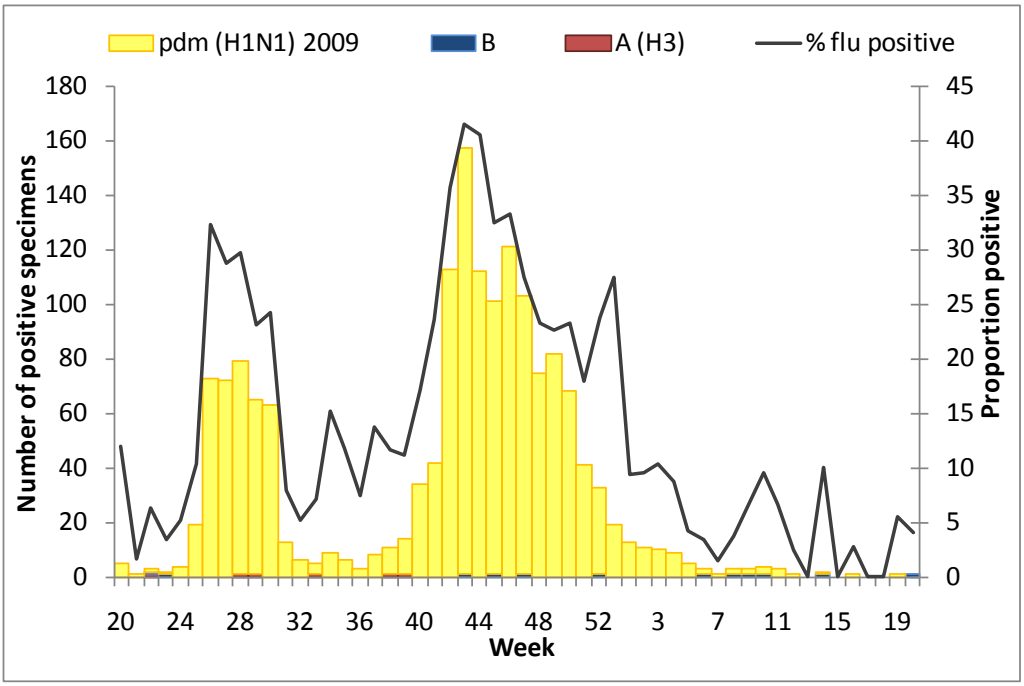
Genetic analysis of the HA gene of UK pandemic (H1N1) 2009 viruses from 2009 indicates that they are similar to the pandemic vaccine strain, A/California/07/2009. UK viruses clustered together with viruses isolated in geographically distant places, showing that there was global circulation of pandemic influenza lineages (appendix 3). The diversity seen among these viruses was less that that seen for seasonal influenza, with only 12 amino acids of difference between the two most distant viruses. All UK viruses isolated after June 2009 are characterised by substitution S203T. Other amino acid changes at residues D222E, or E374K, or N370H were also observed in the HA sequence of some UK and non-UK pandemic viruses.

From week 20 2009 to week 20 2010, an additional 78 non-pandemic influenza viruses were detected by CfI: six A (H1), four of which were detected from May to July 2009; 51 A (H3), 90% detected before October 2009 and 21 influenza B, the majority detected between January and May 2010.

Sentinel virological schemes

The proportion of samples taken by GPs in the two English sentinel schemes (RCGP/HPA and HPA/RMN schemes) positive for influenza showed two peaks corresponding to the summer and autumn waves. Unlike GP consultations, the number of positive samples and proportion positive reached higher levels in the autumn wave compared to the summer wave (figure 19). The positivity peaked at 41.2% in week 43 (ending 25 October 2009), when 156 of 379 samples were positive for pandemic (H1N1) 2009. A similar pattern was observed for the NHS Direct/NPFS schemes, with a summer and higher autumn peak (figure 19). The highest proportion positive through NHS Direct/NPFS was observed in week 44 (31.3%).

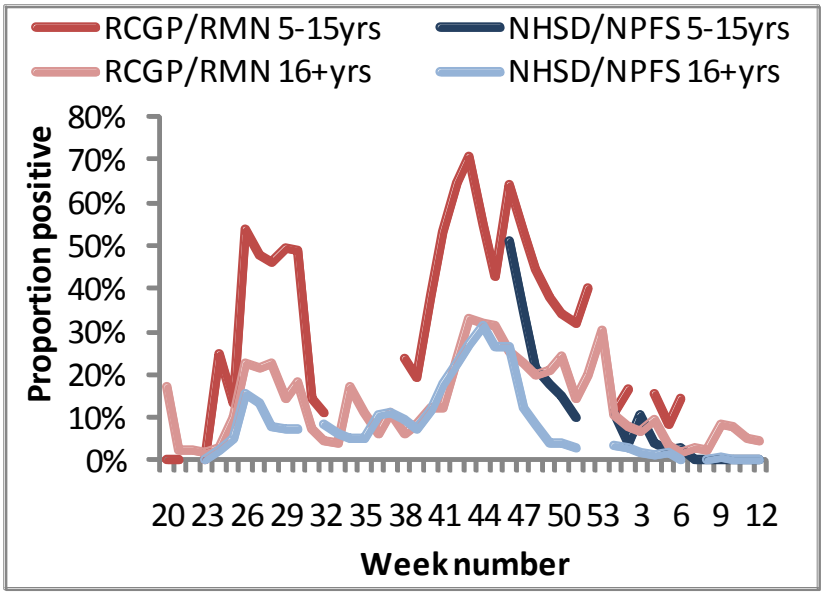
Figure 19: Samples positive for influenza through English GP sentinel virological schemes, May 2009 – May 2010



Very few specimens through the GP and self-sampling schemes tested positive for other influenza subtypes: from week 20 2009 to week 20 2010, only six influenza A (H3) and 12 influenza B viruses were detected.

The overall positivity rates through the NHS Direct and the NPFS self-sampling schemes were consistently lower than that through the GP schemes. However, children aged less than 16 years were not sampled until week 46 through NPFS; after age adjustment, the positivity rates for the GP and self-sampling schemes were largely similar (figure 20).

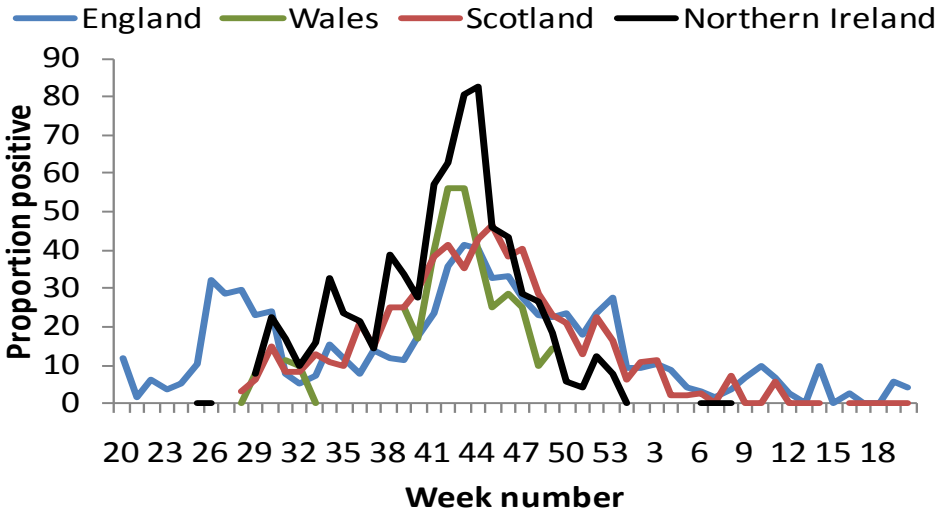
Figure 20: Samples positive for influenza through English GP and NHS Direct/NPFS sentinel virological schemes by age group, May 2009 – March 2010



NB. Sampling of children aged 5-15 years commenced through NPFS in week 46 (ending 15 November); weekly proportion positive omitted when fewer than five samples tested.

Few samples were positive for influenza through the primary care sentinel schemes in Scotland, Wales and Northern Ireland during the summer wave (figure 21). In Scotland additional sentinel swabbing centres were recruited to submit 500 samples per week across the containment phase to allow any differences within the 14 Scottish NHS boards to be identified on a weekly basis. The positivity rate increased from week 30 (ending 26 July 2009) to a peak of 46.5% positive (236/508) in week 45 (ending 8 November 2009). In Wales, a peak of 56.3% (9/16 samples positive) was observed in week 42, corresponding to the GP consultation rate peak. In Northern Ireland a peak of 82.9% (34/41 samples positive) was observed in week 44, one week after the peak in clinical activity, though the virological data from Northern Ireland is based on week of report.

Figure 21: Proportion of sentinel samples positive for influenza through GP-based schemes in the UK, by week May 2009 – May 2010



NB. All data is based on week sample was taken from the patient except in Northern Ireland, where it is the week of the reported result from the laboratory; weekly proportion positive omitted when fewer than 5 samples tested.

Antiviral resistance

From the beginning of the pandemic to 23 May 2010, a total of 6,379 pandemic (H1N1) 2009 viruses were analysed for the marker commonly associated with resistance to oseltamivir in seasonal influenza (H275Y). The viruses tested came from a cross-section of patients from all regions in the UK, age groups and from both community and hospital sources. The first two cases with viruses carrying this mutation were reported in week 38 (ending 20 September).

To date, a total of 45 (0.7%) pandemic cases have been found to carry this mutation in the UK; 15 of these 45 viruses have been tested phenotypically and confirmed to be resistant to oseltamivir while retaining sensitivity to zanamivir. Three hundred and thirty-eight of the 6,379 viruses have been fully tested for susceptibility to oseltamivir; all except the 15 described above have been found to be sensitive. Further information was available for 37 of the 45 resistant cases; 26 (70.3%) were male and 11 female, the ages ranged from 0 to 55 years with a median of 48 years. Thirty-one (83.8%) of the cases had an underlying medical condition: 23 (74.2%) were immunosuppressed and eight had another underlying

illness. Ten (22.2%) resistant cases are known to have died. In the majority (30 cases, 81%) of cases, resistance was treatment induced[28], although probable person-to- person transmission was documented in an outbreak in a hospital ward in Wales in November 2009[29].

Other respiratory viruses

The number of specimens reported to be positive for other respiratory viruses from hospital and regional laboratories across England and Wales was higher throughout the pandemic compared to the previous year (figure 22). This is likely to be due to increased collection and testing of respiratory samples during the pandemic from individuals presenting with acute respiratory illness to health services. There was a notable increase in rhinovirus detections over the autumn of 2009 and detections of parainfluenza were at higher levels in April 2010 than in the previous year. Detections of respiratory syncytial virus (RSV) were at slightly higher levels than the previous winter season. The peak of RSV detections was slightly later (1,164 in week 51) compared to the 2008/09 winter (759 in week 48). The highest number of detections was in children aged less than 5 years of age (figure 23).

Figure 22: Reports of samples positive for other respiratory viruses by week of specimen, England and Wales (LabBase), May 2008 – May 2010

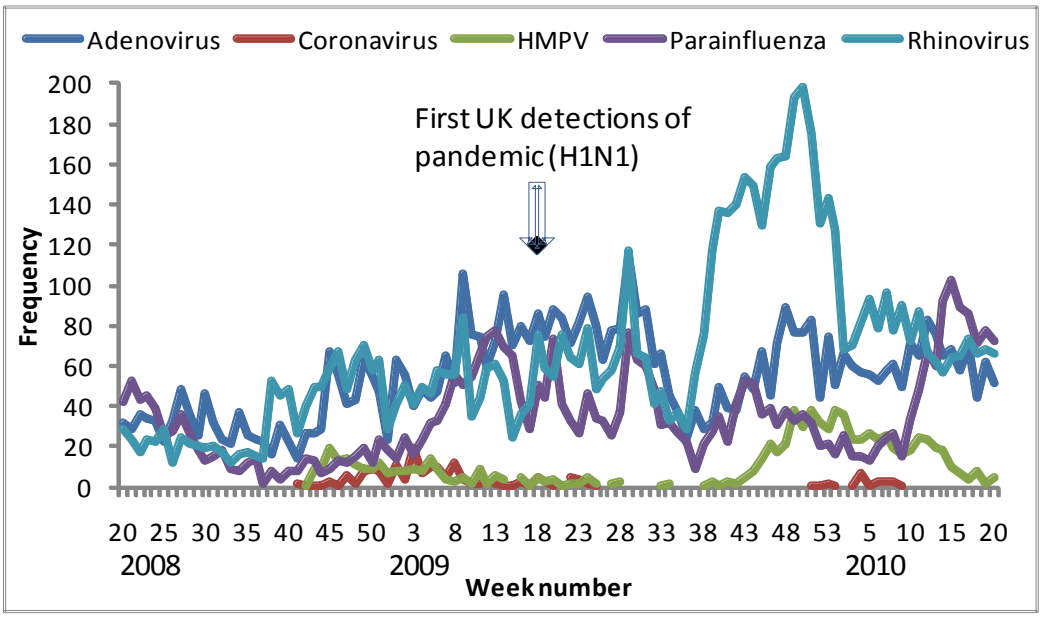
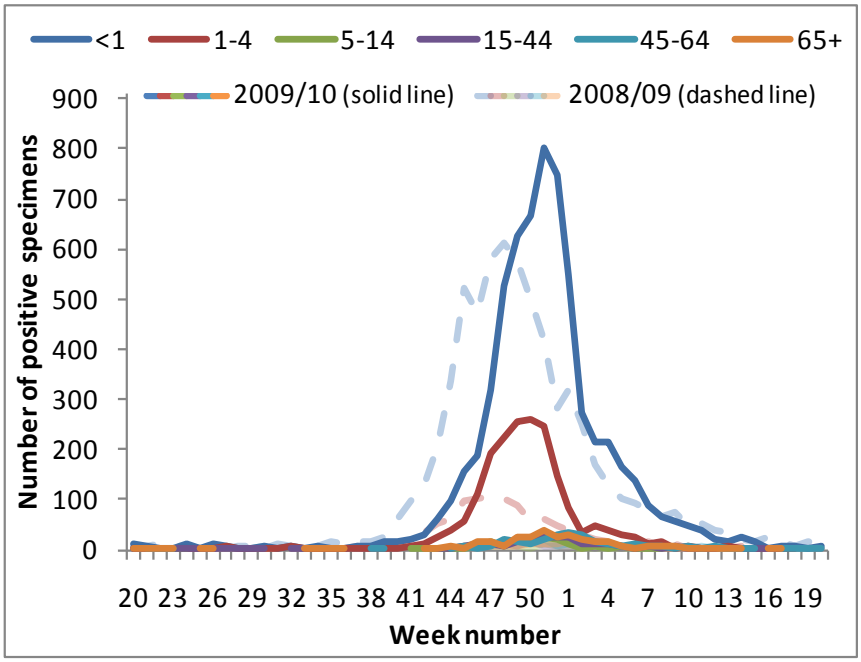
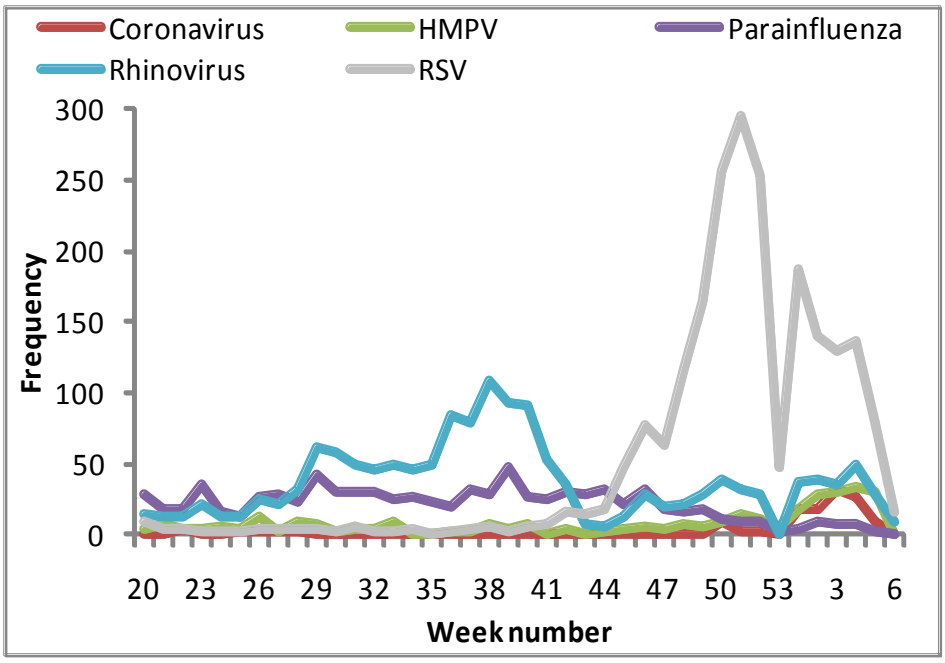


Figure 23: Reports of samples positive for respiratory syncytial virus by age group and week of specimen, England and Wales (LabBase), May 2009 – May 2010



In Scotland there was also an increase in rhinovirus detections between weeks 35 and 42 (August – October 2009). From January to March, RSV was the predominant pathogen seen, with low levels of HMPV, rhinovirus and coronavirus (figure 24).

Figure 24: Reports of samples positive for other respiratory viruses by week of specimen, Scotland May 2009 – February 2010



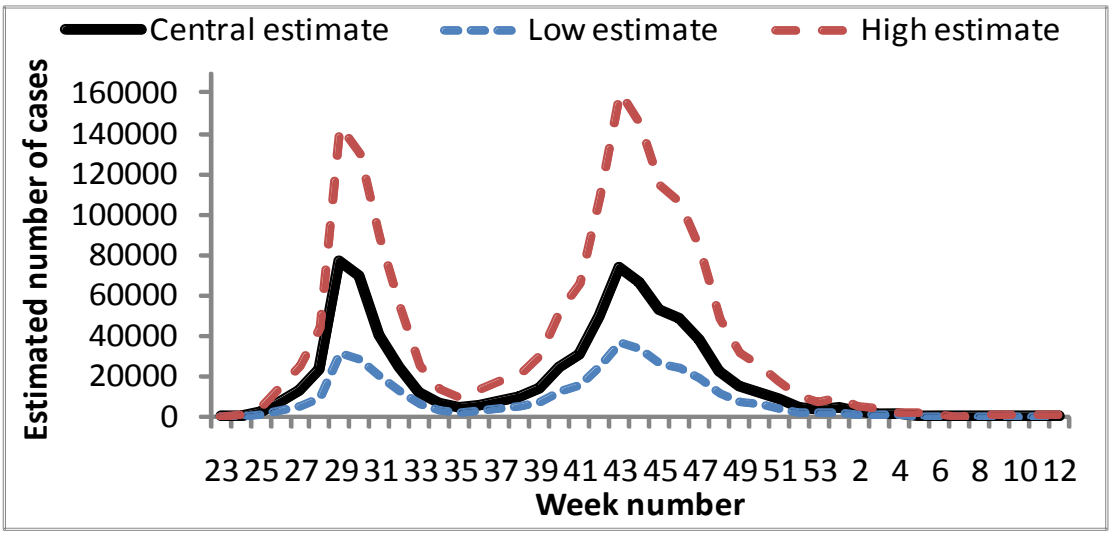
Concurrent bacterial infections

Concurrent bacterial infections (CBI) were not identified as a major feature of the pandemic. Among 20,288 confirmed English pandemic (H1N1) 2009 cases reported, a total of 76 associated CBI cases (0.4%) were identified: 39 were due to *S. pneumoniae*, 34 due to *S. aureus*, and three due to *S. pyogenes*. Twenty-four of these associated CBI cases (0.9%) were hospitalised, and 16 (4.8%) were fatal [30].

ESTIMATED CLINICAL CASES

From 7 June 2009 to 28 March 2010, a total of 784,000 (range 372,000 – 1,638,000) clinical cases of ILI due to pandemic (H1N1) 2009 were estimated to have occurred in England. The summer and autumn waves are thought to have peaked with a similar number of new cases; in week 29 (ending 19 July 2009) with an estimated 77,000 (range 31,000 – 143,000) new clinical cases and in week 43 (ending 25 October 2009) with an estimated 74,000 (range 37,000 – 160,000) clinical cases (figure 25)[31].

Figure 25: Estimated number of clinical cases in England June 2009 – March 2010



SERO-EPIDEMIOLOGY

Serological analysis of English residual population samples taken in 2008 (before the pandemic) showed that protective antibody titres increased significantly with age (*F* test $p<0{\cdot}0001$) with 31.3% (52 of 166; 24.8—38.7) of samples from adults aged 80 years or older with haemagglutination inhibition titre 1:32 or more[7]. The presence of such cross-reactive antibody in older birth cohorts explains why younger people were predominantly affected through both pandemic waves in the UK.

Comparing the proportion of English samples with haemagglutination inhibition titre equal to or above the putative threshold of 1:32 before (baseline) and after the first pandemic wave, in all regions children aged under 15 years showed a significant increase from baseline (6.3%, 1.8—12.9). In London and the West Midlands, which experienced early and intense pandemic activity compared to the rest of England, the difference between baseline and September 2009, was 21.3% (95% CI 8.8—40.3) for children younger than 5 years of age,

42.0% (26.3—58.2) for 5—14-year-olds, and 20.6% (1.6—42.4) for 15—24-year-olds. No difference between baseline and September was observed in older age groups[7]. Additional analyses for other regions and the post-second wave situation are pending.
In Scotland, serology data suggests that the proportion of people infected during the two pandemic waves varied by region, with samples from Glasgow showing a lower proportion positive than Aberdeen and Edinburgh[8].

SEVERITY INDICATORS

HOSPITALISATION

The number of people reported to be hospitalised in NHS trusts in England with suspected pandemic (H1N1) 2009 showed two peaks similar to the other surveillance indicators. The highest hospitalisation rate was consistently in children aged less than 5 years. Between July 2009 and February 2010, when this surveillance system was operational, an overall cumulative rate of 221.7 per 100,000 population (95% CI 216.4 – 227.1) was observed in children under 5 years, which was 6 times higher than in the 16-64 year group (rate ratio 5.9, 95% CI 5.7 – 6.1). The rate in the under 5 year group peaked at 17.8 (95% CI 16.3 – 19.4) per 100,000 population in week 49 when it was 10 times higher (95% CI 8.9 – 11.2) than the rate in the 16-64 year age group.

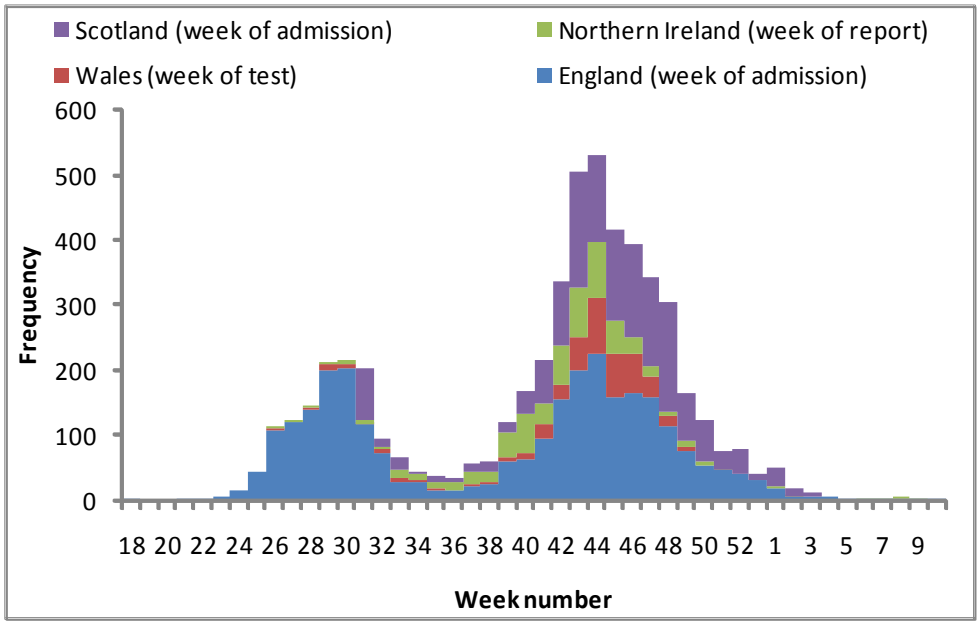
A total of 2,831 patients were reported as hospitalised with confirmed pandemic (H1N1) 2009 infection in England from the beginning of the pandemic to April 2010 through the HPA/CMO reporting system in 129 acute hospital trusts (figure 26). Thirty-eight per cent of the cases were admitted in the summer pandemic wave. In total, 55.5% of hospitalised cases with available information were reported to have an underlying risk factor for severe disease including pregnancy and obesity[32].

In Northern Ireland there were 580 hospital admissions of confirmed pandemic (H1N1) 2009 of which 51 (8.8%) occurred during the first wave (weeks 21 – 35) (figure 25), with four admissions to ICU (3.9%) The proportion of admissions of confirmed cases to ICU in the second wave was 9.1%. While the weekly hospitalisation trend closely corresponded to sentinel consultation rates in the second wave this was less so during the first wave when there were comparatively few hospitalisations. Admission rates were highest in the 0-4 year age group (109.5 per 100,000) followed by the 5-14 age group (admission rate 51.5 per 100,000)[33].

In Scotland a total of 1542 patients were hospitalised with confirmed pandemic (H1N1) 2009 infection over the period of the pandemic. The peak week for admission was week 43 (ending 25 October 2009) (figure 26).

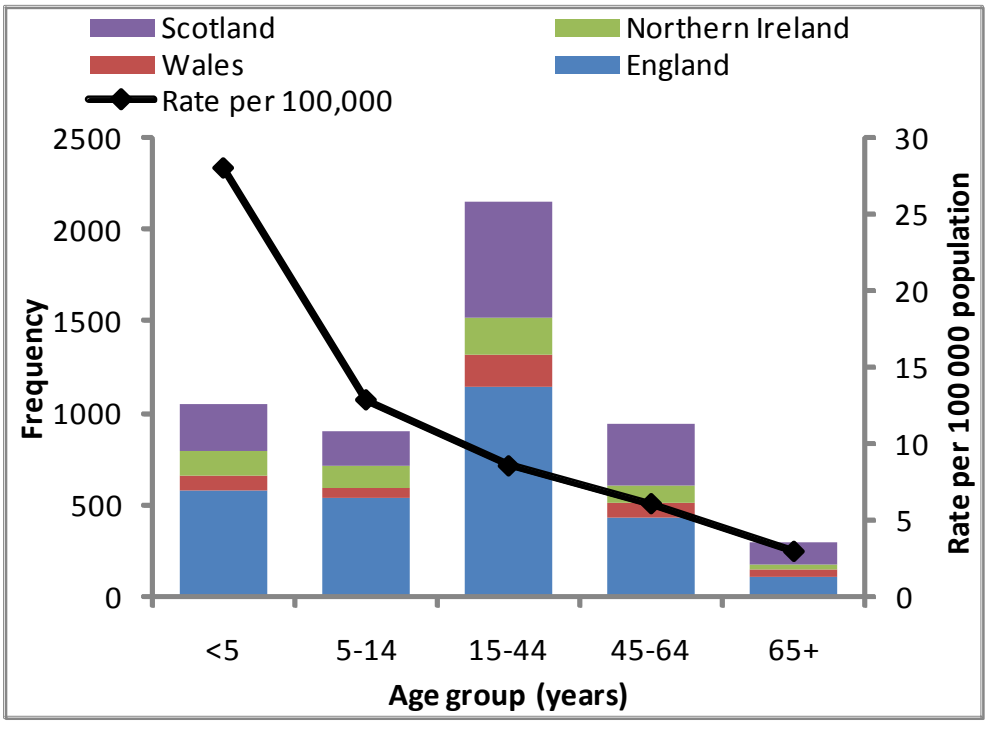
In Wales 423 patients were hospitalised with virologically confirmed pandemic (H1N1) 2009. Similar to Northern Ireland, there were few hospitalisations during the first pandemic wave; the peak of hospital admissions in Wales (by week of test) was week 44 (ending 1 November 2009) when there were 83 hospitalisations (figure 26).

Figure 26: Number of hospitalisations for confirmed pandemic (H1N1) 2009 by week and country, April 2009 – March 2010, UK



Across the UK, the hospitalisation rate decreased with age with children aged under 5 years having the highest population hospitalisation rate (28 per 100,000 for the entire UK) (figure 27).

Figure 27: Number and rate of hospitalisations with confirmed pandemic (H1N1) 2009 by age group and country, April 2009 – March 2010, UK

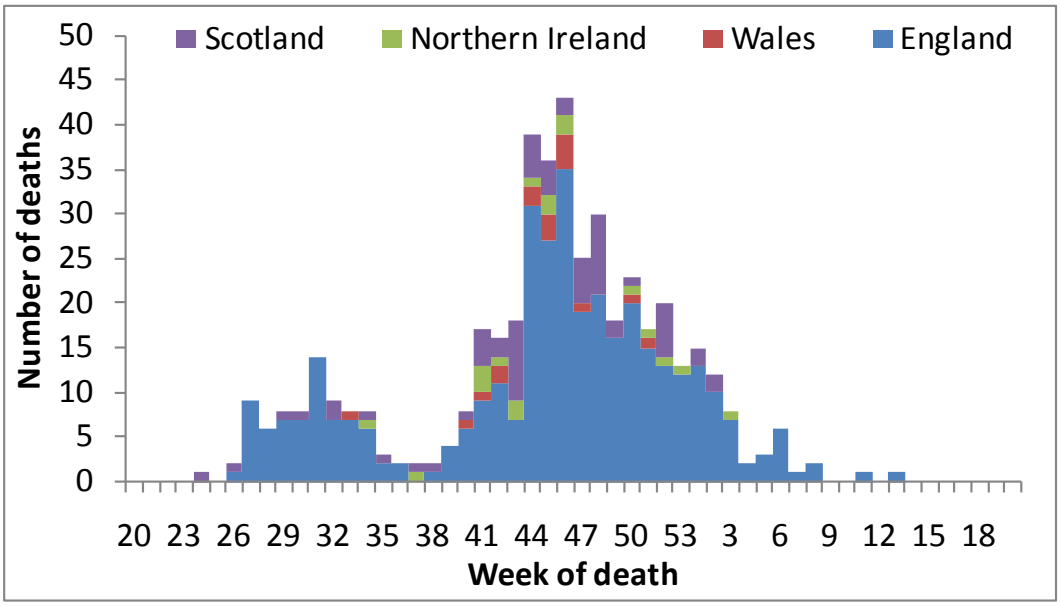


The FLU-CIN study collected information on 631 patients admitted to 55 UK hospitals with confirmed pandemic (H1N1) 2009 infection in the first wave. This in-depth study found that non-white and pregnant patients were over-represented and 45% of patients had an underlying medical condition. Of the 29 patients who died, 59% were previously healthy[14].

MORTALITY

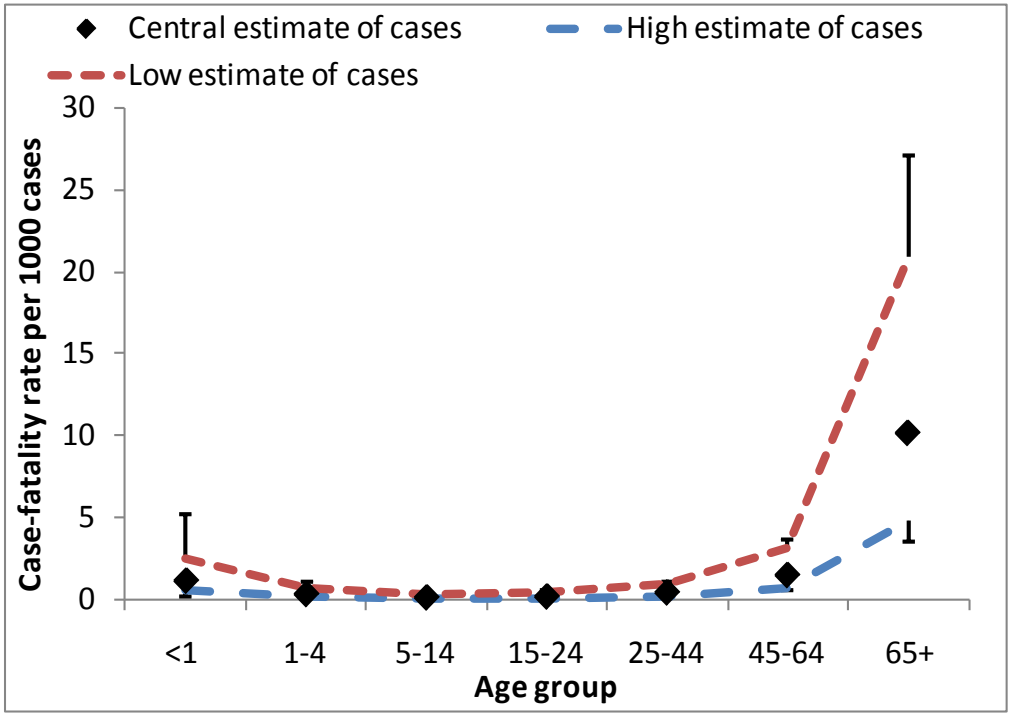
The first death due to pandemic (H1N1) 2009 in the UK occurred on 14 June 2009. A total of 474 deaths with confirmed pandemic (H1N1) 2009 (either laboratory confirmed or with mention on the death certificate) were reported in the UK up to 15 April 2010 (359 in England, 69 in Scotland, 18 in Northern Ireland and 28 in Wales). A number of deaths occurred in the spring/summer of 2009 but the majority (83%) occurred over the autumn/winter (figure 28). Seventy-two per cent of fatal cases were reported to have an underlying risk factor for severe disease[34]. [34]

Figure 28: deaths due to pandemic (H1N1) 2009 by week of death and country, UK May 2009 – May 2010 (adapted from[34])



The symptomatic case-fatality ratio was estimated to be 0.04%[34]. The majority of deaths occurred in people aged under 65 years old (85% of English deaths), though the estimated case fatality rate was much higher in older adults aged 65 years or over, in whom infection was much less common (figure 29).

Figure 29: Estimated case fatality rate by age group, England, June 2009 – April 2010



In England and Wales, no excess of weekly death registrations above the threshold was observed over the summer of 2009. In the 2009/10 winter season 3,261 (95% CI 2,993 – 3,530) excess deaths were estimated to have occurred in weeks 52 and 53 (table 3); this is unlikely to be due to influenza, as all other influenza indicators were showing low activity at that time.

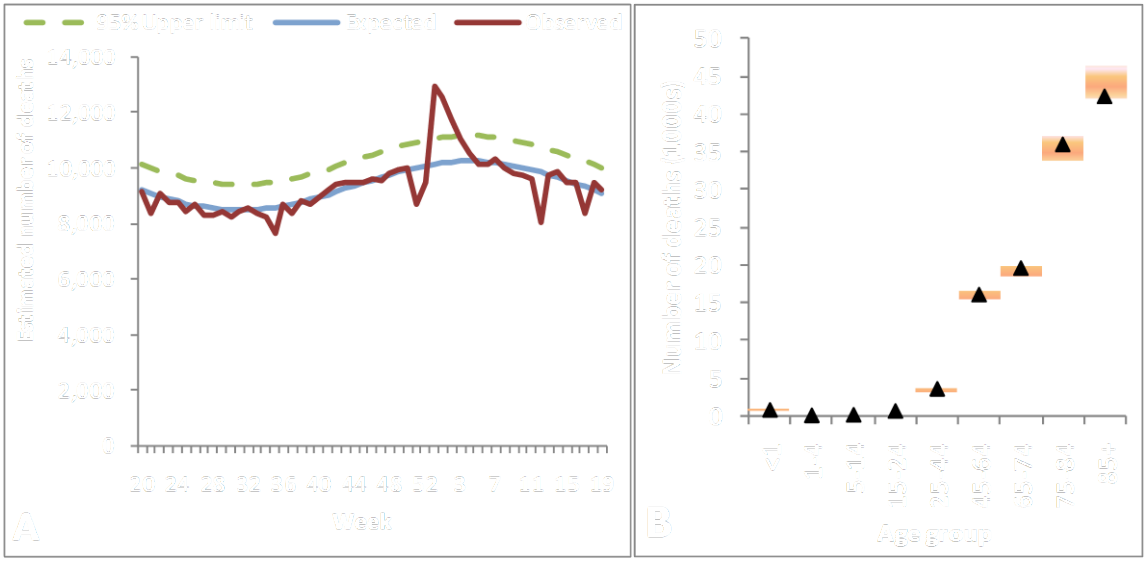
Table 3: Annual excess all-cause mortality by influenza season, 1999-2010

Season	Excess (95% CI)	Total no. of deaths	% deaths in excess
1999/2000	21227 (20690 - 21764)	395,507	5.4%
2000/2001	746 (478 - 1015)	383,805	0.2%
2001/2002	6824 (6556 - 7093)	388,552	1.8%
2002/2003	6392 (6123 - 6660)	386,946	1.7%
2003/2004	4873 (4336 - 5410)	377,242	1.3%
2004/2005	1860 (1591 - 2128)	372,259	0.5%
2005/2006	Not detected	361,910	0.0%
2006/2007	Not detected	318,775	0.0%
2007/2008	457 (0 - 994)	321,853	0.1%
2008/2009	10146 (9878 - 10588)	327,334	3.1%
Summer 2009	Not detected	170,231	0.0%
2009/2010	3261 (2992 - 3529)	315,931	1.0%

It is notable that this excess occurred in a period when the UK experienced a prolonged cold snap. Closure of registry offices over bank holidays was also temporally associated with an artefactual dip and subsequent increase at the end of December and the beginning of April (figure 30A).

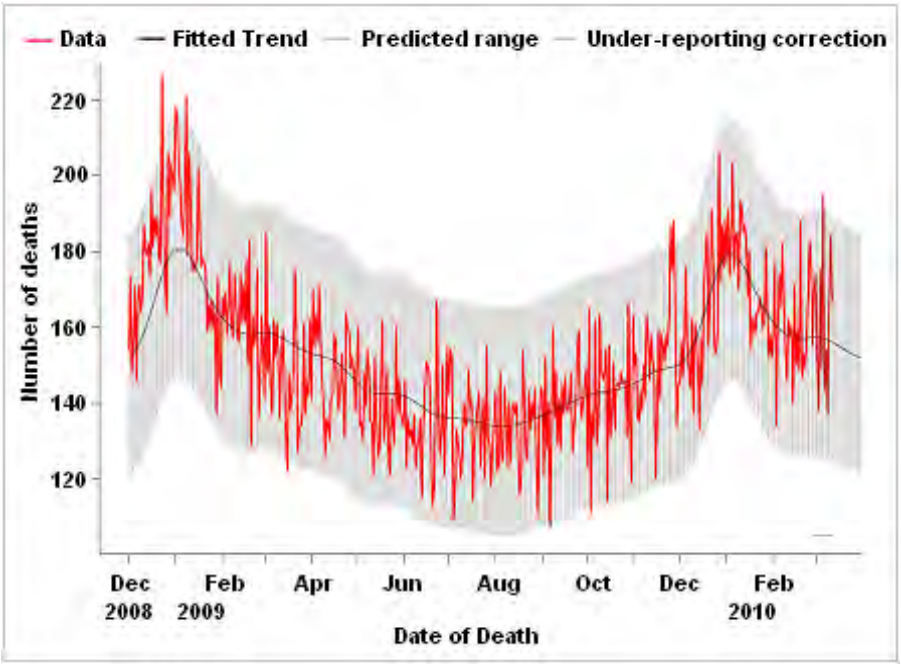
Analysis of daily mortality data made available from the General Registry Office (England and Wales) by age-group over the two pandemic waves shows that there was no evidence of any age-specific excess mortality throughout the pandemic prior to the Christmas excess (figure 30B).

Figure 30: A: all cause mortality from ONS (England and Wales) with expected number of deaths (HPA), May 2009 – May 2010; B: Age-specific mortality monitoring (GRO), shaded areas show expected range, week 37-49 (Autumn wave) England and Wales



The number of weekly Scottish deaths remained within expected ranges over the 2009 summer. There was an increase above expected levels at the end of December/ beginning of January and a slight excess of deaths at end of November. The overall pattern was similar to what was seen in England and Wales, with the excess coinciding with low influenza activity and cold weather (figure 31).

Figure 31: all cause mortality (Scotland) with expected number of deaths through Serfling and GAM methods (HPS), April 2009 – May 2010



RISK GROUPS

Data from the FF100 surveillance project showed that people with underlying medical conditions, such as chronic respiratory, neurological or heart disease were not at significantly greater risk of clinical infection in the early stages of the pandemic[21]. In England, people aged between 6 months and less than 65 years with an underlying condition were 10 times more likely to be hospitalised with confirmed pandemic (H1N1) 2009 infection compared to people of the same age without an underlying condition, and 18 times more likely to die from the infection[32;34]. The underlying conditions with the highest risk of hospitalisation with pandemic (H1N1) 2009 infection were immunosuppression, chronic renal disease and chronic neurological disease (including stroke)[32]. For death, the risks were highest for chronic neurological disease (excluding stroke), chronic liver disease and immunosuppression[34]. Pregnant women were not at an elevated risk of becoming cases, but were 5 times more likely to be hospitalised and seven times more likely to die, once infected, compared to females of child-bearing age (15-44 years) with no underlying condition (table 4)[34].

Table 4: Rate ratios for hospitalisation and mortality by risk group, England adapted from [32] and [34]

	Hospitalisations					Deaths				
	N	Rate ratio	95% confidence interval			N	Rate ratio	95% confidence interval		
Total	2,463					361				
Total aged 65 or over	104					56				
Any risk factor (65y+)	67	2.8	1.7	–	4.5	44	6.0	2.7	–	13.4
No risk factor (65y+)	23	Baseline				7	Baseline			
Total aged 6m-65y	2,258					300				
Any risk factor (6m-65y)	1,033	10.3	9.4	–	11	190	18.7	14.5	–	24.1
No risk factor (6m-65y)	1,028	Baseline				84	Baseline			
Chronic renal disease	58	17.2	13	–	22	16	37.7	22.0	–	64.5
Chronic heart disease	85	5.9	4.7	–	7.4	26	16.7	10.8	–	25.9
Chronic respiratory disease	601	12	11	–	13	51	11.7	8.3	–	16.6
Chronic liver disease	22	8.7	5.7	–	13	23	70.8	44.4	–	112.8
Diabetes	78	4.3	3.4	–	5.4	23	9.8	6.1	–	15.6
Immunosuppression	135	18.5	15	–	22	48	56.0	39.0	–	80.4
Stroke/TIA*				–		3	7.2	2.3	–	23.0
Chronic neurological disease*	123	14.3	12	–	17	66	115.8	85.2	–	157.5
Total females of childbearing age (15-44years)	585					63				
Females of childbearing age with no risk factor	291	Baseline				22	Baseline			
Pregnant (F15-44 only)	145	5.1	4.2	–	6.1	10	7.0	3.3	–	14.8

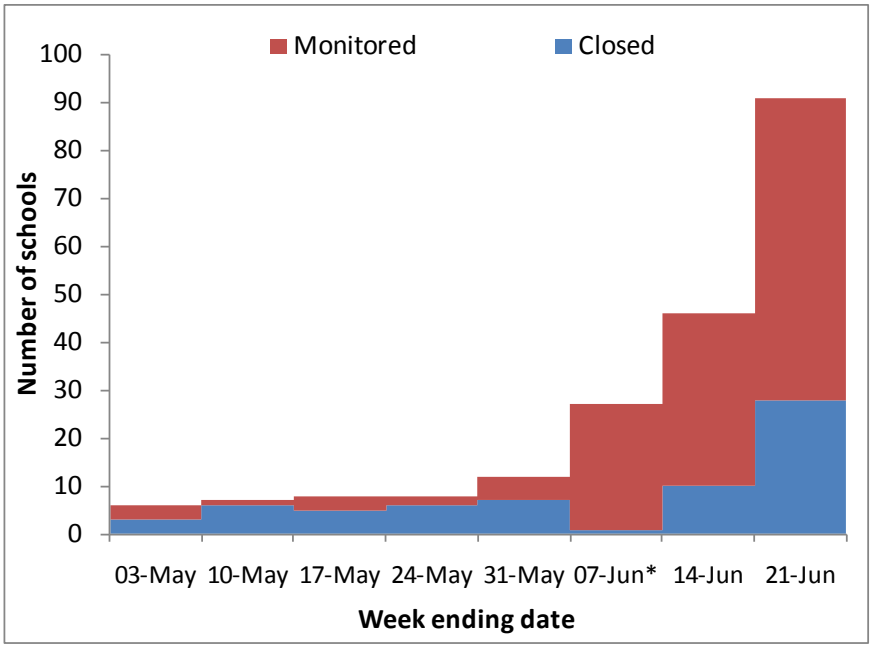
** Strokes are included under neurological disease for the hospitalisation data but are separate for mortality data*

INTERVENTIONS

SCHOOL CLOSURES

At the beginning of the pandemic, many schools were advised to temporarily close if there were confirmed cases of pandemic (H1N1) 2009 among staff or students. Antiviral prophylaxis was also given to close contacts of confirmed cases as part of the containment strategy. Up to the end of the containment phase, 74 schools in England were reported to have been closed due to pandemic (H1N1) 2009 and 417 schools reported confirmed cases to HPA. Figure 32 shows the increasing number of schools in England affected each week from the beginning of May to 21 June 2009. In Northern Ireland there were 26 school outbreaks with the last being during week 5 2010; none of these schools were closed due to the outbreak. In Scotland there were 29 school closures during the containment phase.

Figure 32: Number of schools affected by pandemic influenza, England; May – June 2009



** Half-term holiday for most schools in England; Monitored: confirmed or suspected cases in the school but remaining open, Closed: partially or total suspension of classes due to confirmed or suspected cases of pandemic influenza.*

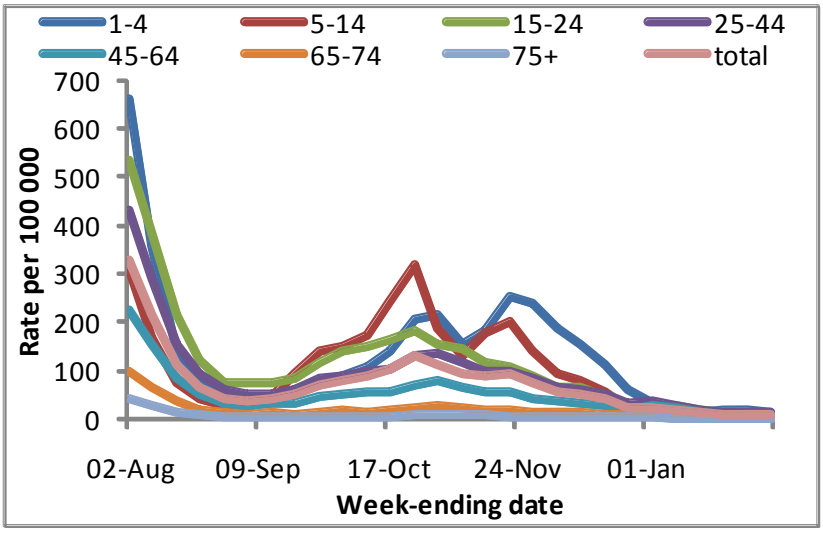
Whether individual school closures had significant effects on transmission is unclear [personal communication, H Maguire]. The closure of all UK schools for the summer holiday is likely to have played a large part in interrupting transmission over this period.

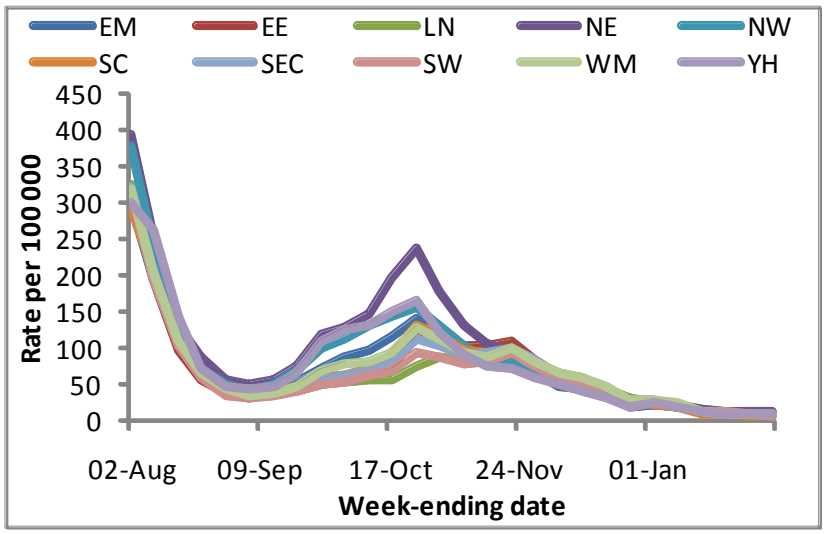
ANTIVIRALS

Uptake: Of the 365 UK FF100 cases with information available, 335 (91.8%) reported receiving treatment with antiviral drugs[21]. Of 656 contacts with available information, 595 (90.7%) reported receiving antiviral drugs[27].

Sixty-eight per cent of assessments through the NPFS (1,645,948 of 2,401,043) resulted in an authorisation for antiviral drugs being issued; of these 66% (1,079,179 [2.1% of the population]) were collected. The population rate of collection varied by region and age group. In the summer wave the rate of collection was notably higher in the North East compared to other regions and the rates were highest in children aged 1-4 and 5-14 (figure 33). Babies aged less than one year were the only age group not considered by NPFS and were always referred to their GP, as were those with underlying risk factors for severe disease.

Figure 33: weekly rate of antiviral collection, per 100,000 population through NPFS by region* and age group, August 2009 – March 2010, England





**EM: East Midlands, EE: East of England, LN: London, NE: North East, NW: North West, SC: South Central, SEC: South East Coast, SW: South West, WM: West Midlands, YH: Yorkshire and Humberside.*

A total of 24,160 courses of antivirals were issued through primary and secondary care in Northern Ireland (1.4% of the population).

In Scotland, 98,000 courses of antivirals were issued (1.9% of the population).

Effectiveness: Data from the FF100 study showed that the household secondary attack rate was significantly affected by the use of antivirals with a 92% reduction in virologically confirmed secondary attack rate at two weeks[27].

Impact: Modelling data from cases identified during the containment phase suggest that treatment of cases in association with prophylaxis of their close contacts reduced the reproduction number by an estimated 16% (95% CI 12 – 20%) in those who received the intervention; the overall population-level effect will have been smaller than this, as most affected individuals did not seek care [18].

Safety: Forty-one (12.2%) of the 335 FF100 cases who took antiviral drugs, reported side-effects which they attributed to antiviral treatment. More adults aged 16 or older (25 of 140 – 15%) than children (16 of 153 – 9.5%) reported an adverse event. Of the 17 who had specified the severity of the adverse event, 15 (88.2%) graded it as moderate and two as severe. Gastrointestinal symptoms were the most commonly reported adverse events, reported by 30 of the 41 cases reporting side-effects (11 (37.0%) children and 19 adults)[21].

VACCINATION

Pandemic vaccine uptake: In England, 37.6% of patients in clinical risk groups, including pregnant women, and 23.6% of healthy children aged six months to 5 years received the swine influenza monovalent vaccine (Pandemrix, dose 1) by 31 March 2010 [35].
In Northern Ireland and Scotland uptake was higher in all groups compared to the England data with 86.5% of people in Northern Ireland aged under 65 years in a risk group receiving the vaccine (though this does not include pregnant women of whom 57.1% received the vaccine). Welsh vaccine uptake was similar to that of England (table 5).

Table 5: Pandemic vaccine uptake, dates, by country and risk group, UK

	England*	Northern Ireland**	Scotland*	Wales***
<65 years at risk	**37.6%**	**86.5%**	**52.1% - 54.5%**	**42.1%**
Pregnant women	**Inc. above**	**57.1%**	**Inc. above**	**Inc. above**
Children <5 years	**23.6%**	**38.3%**	**44.6%**	**26.1%**
>65 years at risk	**40.4%**	**74.9%**	**56.2% - 57.4%**	**45.0%**
Health care workers	**40.3%**	**47.7%**	**55.1%**	**N/A**

** to 31 March 2010; ** to 28 February 2010, except pregnancy which is to 30 November 2009; ***to June 2010*

Pandemic vaccine effectiveness: Data from the sentinel primary care schemes in Scotland and England, gave an adjusted monovalent influenza vaccine effectiveness in excess of 70%[36].

Pandemic vaccine cost-effectiveness modelling: Modelling estimated that vaccination of high-risk groups would prevent about 45 deaths (80% credibility interval 26-67) in England, and save around 2900 quality adjusted life years (QALYs) (80% credibility interval 1600-4500). Such a vaccination programme was estimated to be cost-effective assuming the cost of the vaccine was treated as a sunk cost. Extending vaccination to school-age children was found to be the most cost-effective intervention in the model[37]. Due to the timing of the programme in relation to pandemic activity, it was unable to prevent more cases and deaths.

Seasonal vaccine uptake: In England, the uptake of the 2009/10 seasonal influenza vaccine in those aged 65 years and over reached 72.4%; a slight decrease compared to the previous season (74.1%). In those aged under 65 years falling in a clinical risk group, uptake increased from 47.1% in 2008/09 to 51.6% in 2009/10[38]. In Northern Ireland, the uptake in over 65 year-olds was similar to the previous season (77%); there was a slight decrease in Scotland (75% vs. 76.3%) and an increase in Wales (63.5% vs. 59.5%) (table 6).

Table 6: Seasonal vaccine uptake, dates, by country, UK

	England	**Northern Ireland**	**Scotland**	**Wales**
>65 years 2009/10 season	**72.4%**	**77.0%**	**75.0%**	**63.5%**
>65 years 2008/09 season	*74.1%*	*76.8%*	*76.3%*	*59.5%*
<65 years at risk 2009/10 season	**51.6%**	**80.0%**	**53.4%**	**49.1%**
<65 years at risk 2008/09 season	*47.1%*	*74.0%*	*47.8%*	*40.8%*

Seasonal vaccine effectiveness: There was no evidence that the 2008/09 nor 2009/10 seasonal influenza vaccines had any significant effect on infection with pandemic influenza[39;40].

Season vaccine 2010/11 season: The World Health Organization recommended that the 2010/11 northern hemisphere vaccine contain an A/California/7/2009 (H1N1)-like virus (pandemic), an A/Perth/16/2009 (H3N2)-like virus and a B/Brisbane/60/2008-like virus[41]. In the UK, pregnant women who have not previously received the pandemic vaccine are recommended to receive the trivalent vaccine, in addition to the normal groups (over 65 year-olds, those in risk groups, HCWs, carers etc.). There are also some groups who are recommended to receive the monovalent pandemic vaccine[42].

Discussion and conclusions

Following the emergence of pandemic (H1N1) 2009 in North America in April 2009, imported cases of this novel virus were quickly identified across the UK. The first cases were mainly travellers returning from Mexico or the United States and secondary cases linked to indigenous transmission among close contacts in households and schools. Two waves of pandemic activity were observed, separated by the closure of schools for summer holidays, which appears to have reduced transmission (appendix 1). Community transmission was initially observed in London and the West Midlands following large school outbreaks. Cases were reported from all UK regions in the summer wave, though there was a variable level of transmission; all regions of the UK were affected in a more uniform way during the autumn wave. Most cases were reported to have a mild illness consistent with influenza. Severe disease, hospitalisations and deaths were reported in a minority of cases, particularly among those with underlying clinical disease. There was an overall low case-fatality ratio, particularly compared to previous pandemics. Clinical counter-measures were employed across the UK, with evidence that antivirals were effective in reducing transmission and disease severity. Pandemic vaccine was effective, though uptake only increased in the second half of the autumn wave.

Although the first European cases of pandemic (H1N1) 2009 were confirmed in Spain on April 27 2009 and most European countries had reported cases by the end of May 2009[43], the UK and Ireland were the only European countries reporting high influenza activity during the summer of 2009[44]. In this respect there was greater similarity with other northern hemisphere countries such as the USA and Canada. Indeed, the UK has significantly more air traffic from North America compared to most European countries and thus experienced multiple introductions during spring 2009 onwards, which may be one of the explanatory factors. The main wave of pandemic influenza activity in Europe occurred in the autumn, with many countries, including the UK, reporting levels of activity higher and earlier than in recent seasons[45].

Evidence gathered from the FF100 project showed that most cases experienced a mild, typical influenza-like illness, with fever and respiratory symptoms reported most frequently[21]. A significant proportion of cases reported gastrointestinal symptoms – an observation that was also seen in other geographic settings, including those where antivirals (a potential confounding factor) were used less widely [46]. To optimise its positive predictive value, a strict case definition was used initially based on clinical (fever and respiratory symptoms) and epidemiological (recent travel to an affected area or contact with a confirmed or suspected case) criteria. This meant that people who did not fulfil these definitions, for example cases with milder clinical symptoms, may not have been tested; they would have been missed, underestimating the number of infections.

Compared to seasonal influenza, pandemic (H1N1) 2009 tended to affect younger people. Serological studies have demonstrated evidence of widespread infection in the population during the pandemic particularly in younger age-groups. People older than 50 years of age had evidence of cross-reactive H1N1 antibodies due to exposures to influenza A (H1N1) prior to 1957, explaining the lower age-specific attack rates in this group [7;8]. Other sero-epidemiology studies elsewhere have demonstrated similar findings[47].

The UK's containment approach recommended the use of antiviral drugs for all symptomatic confirmed cases and their close contacts. This may have slowed the initial spread of the virus, as suggested by transmission and modelling studies, but any impact is likely to have been small. Furthermore, use of antivirals in the early treatment of cases significantly reduced the severity of illness – in terms of duration of illness[21], risk of hospitalisation[14] and risk of ICU admission[32]. Despite this intervention, a number of patients were hospitalised and died due to pandemic influenza. Although people aged over 65 were less likely to acquire the infection, once infected they were more likely to have a more severe outcome compared to younger cases. People with underlying clinical conditions were also more likely to have a severe outcome, as would be expected with seasonal influenza. As has been found in other countries, pregnant women were also at higher risk of severe outcomes[48]. A significant minority of hospitalised and fatal cases did not have any underlying condition.

On 10 August 2010, the Director-General of the World Health Organization announced that the world had moved into the post-pandemic period[49]. For the forthcoming 2010/11 season, the pandemic (H1N1) 2009 virus is expected to behave as a normal seasonal influenza virus, continuing to circulate, perhaps along with other seasonal influenza viruses, for some years to come. The WHO has recommended vigilance regarding future activity due to the pandemic (H1N1) 2009 virus, particularly as it is likely that the virus will continue to cause serious disease in a minority of younger age groups and people in high-risk groups[50].

With the declaration of the post-pandemic phase, the focus is on normalisation of influenza surveillance. There is still, however, a requirement to monitor influenza activity for a potential resurgence and to ensure any possible increase in clinical indicators is rapidly identified and investigated. As outlined, during the pandemic a number of additional surveillance systems were developed to provide a more complete picture of influenza and broader respiratory virus activity. Several of these will be incorporated into the standard suite of influenza surveillance activities and be maintained beyond the current pandemic in particular a sentinel hospital pilot surveillance system for severe disease and the laboratory denominator surveillance system for influenza and other respiratory viruses.

In conclusion, pandemic (H1N1) 2009 caused moderate to high levels of influenza activity in the UK during summer 2009, a period when activity is usually at low levels, and in the autumn of 2009. Although the illness caused was generally mild, there were significant hospitalisations and intensive care admissions and some fatalities, particularly among younger people and those with underlying clinical risk factors. In some areas large proportions of the community are thought to have been infected, though this is likely to vary across the country. The pandemic virus was consistently the predominant influenza virus circulating and appeared to replace previously circulating A (H1N1) viruses. Experience from the 2010 winter season in the Southern Hemisphere suggests that H1N1 will continue to circulate in the coming winter season in the Northern Hemisphere, possibly with other seasonal influenza viruses. Unless there is significant antigenic drift, impact is unlikely to be as large as that observed in 2009/10.

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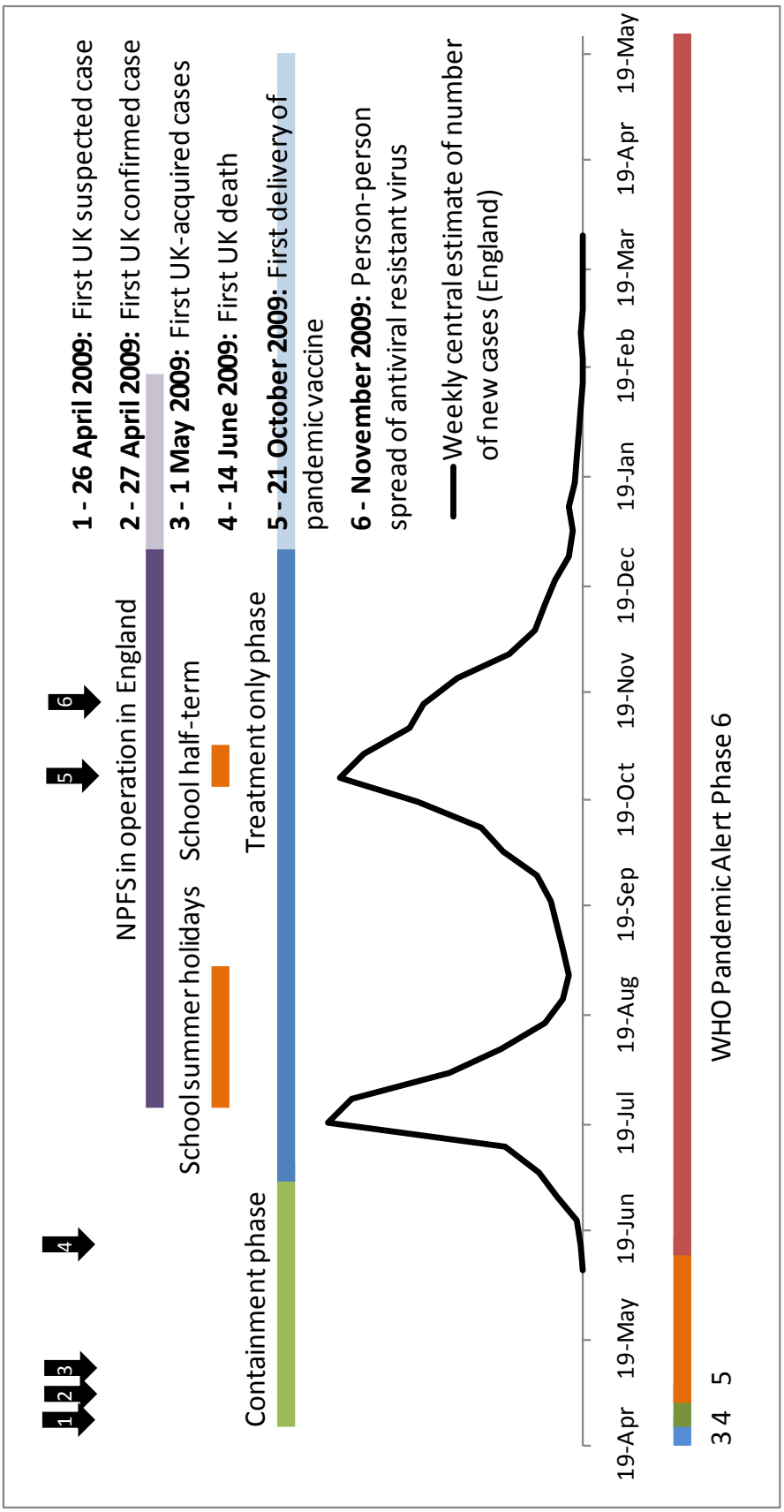
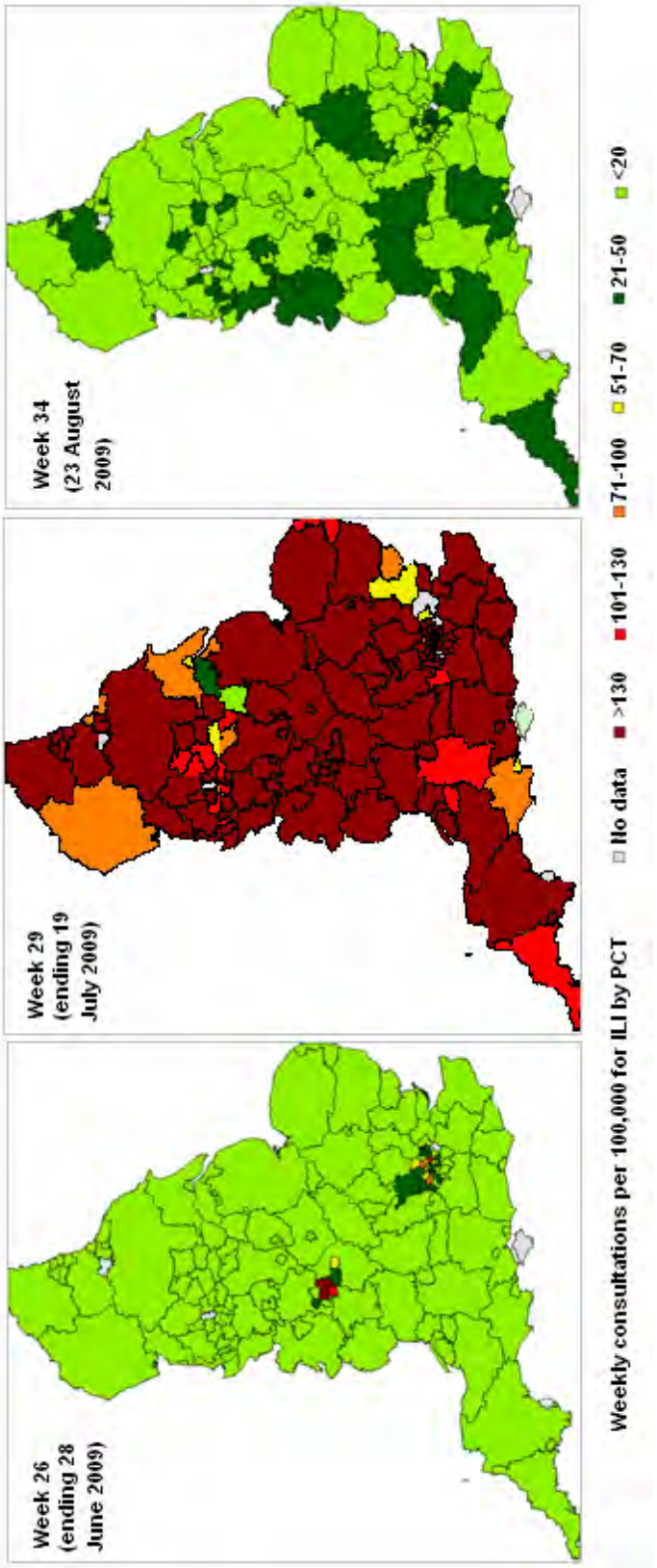
Appendix 1

Timeline of key epidemiological events of the pandemic in the UK, with HPA estimated number of clinical cases (England), April 2009 – May 2010.



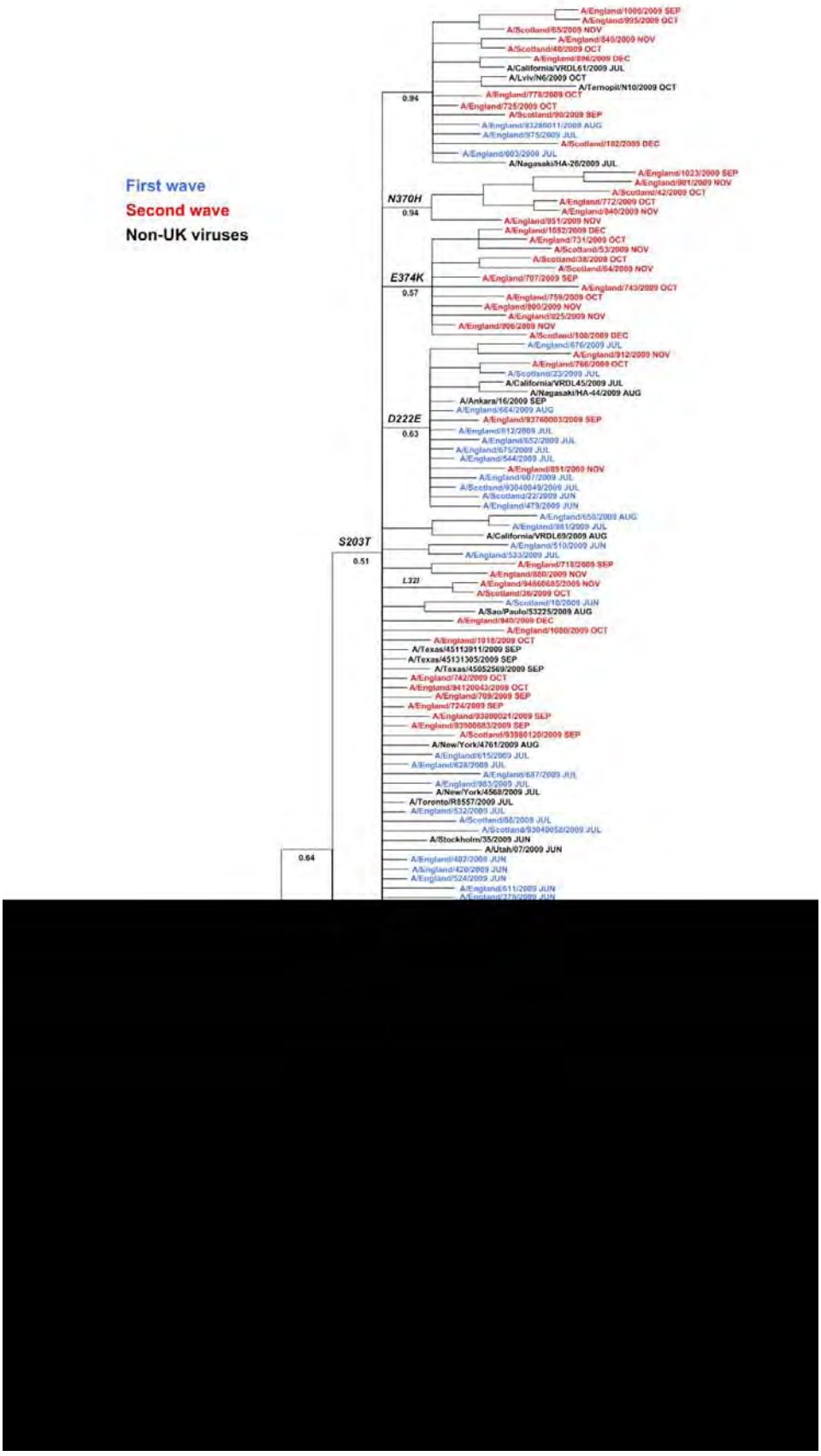
Appendix 2

PCT maps from HPA/QSurveillance system displaying GP incidence rates for ILI per 100,000. The maps illustrate the initial spread in the West Midlands and London regions during week 26, the widespread ILI activity during the peak of the first wave (week 29) and the cessation of activity following the first wave (week 34).



Appendix 3

Phylogenetic tree for pandemic (H1N1) 2009 HA sequences, April – December 2009.



References

(1) Health Protection Agency (2009). National weekly influenza report. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1246433639498.

(2) Centers for Disease Control and Prevention (2009). Swine influenza A (H1N1) infection in two children--Southern California, March-April 2009. MMWR Morbidity and Mortality Weekly Report 58: 400-402. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0421a1.htm.

(3) Centers for Disease Control and Prevention (2009). Outbreak of swine-origin influenza A (H1N1) virus infection - Mexico, March-April 2009. MMWR Morbidity and Mortality Weekly Report 58: 467-470. Available online: http://www.cdc.gov/mmwR/preview/mmwrhtml/mm58d0430a2.htm.

(4) World Health Organization (2009). Transcript of statement by Margaret Chan, Director-General of the World Health Organization, 11 June 2009. Available online: http://www.who.int/mediacentre/influenzaAH1N1_presstranscript_20090611.pdf.

(5) Health Protection Agency (2009). Pandemic (H1N1) 2009 in England: an overview of initial epidemiological findings and implications for the second wave. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1258560552857.

(6) Health Protection Agency (2009). The First Few Hundred (FF100) Project: Epidemiological Protocols for Comprehensive Assessment of Early Swine Influenza Cases in the United Kingdom. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1257260453727.

(7) Miller E, Hoschler K, Hardelid P et al (2010). Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet 375: 1100-1108. Available online: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)62126-7/abstract.

(8) Adamson WE, Maddi S, Robertson C et al (2010). 2009 pandemic influenza A(H1N1) virus in Scotland: geographically variable immunity in Spring 2010, following the winter outbreak. Euro Surveill 15: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19590.

(9) Goddard NL, Kyncl J, Watson JM (2003). Appropriateness of thresholds currently used to describe influenza activity in England. Commun Dis Public Health 6: 238-245.

(10) Cooper DL, Verlander NQ, Elliot AJ et al (2009). Can syndromic thresholds provide early warning of national influenza outbreaks? J Public Health (Oxf) 31: 17-25. Available online: http://jpubhealth.oxfordjournals.org/cgi/content/full/31/1/17?view=long&pmid=18032426.

(11) Ellis J, Iturriza M, Allen R et al (2009). Evaluation of four real-time PCR assays for detection of influenza A(H1N1)v viruses. Eurosurveillance 14: pii: 19230. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19230.

(12) Elliot AJ, Powers C, Thornton A et al (2009). Monitoring the emergence of community transmission of influenza A/H1N1 2009 in England: a cross sectional opportunistic survey of self sampled telephone callers to NHS Direct. BMJ 339: b3403. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2733951/?tool=pubmed.

(13) Health Protection Agency (2009). Method used to estimate new pandemic (H1N1) 2009 influenza cases in England in the week 3 August to 9 August 2009. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1250150839845.

(14) Nguyen-Van-Tam JS, Openshaw PJ, Hashim A et al (2010). Risk factors for hospitalisation and poor outcome with pandemic A/H1N1 influenza: United Kingdom first wave (May-September 2009). Thorax 65: 645-651. Available online: http://thorax.bmj.com/content/65/7/645.long.

(15) Serfling RE (1963). Methods for current statistical analysis of excess pneumonia-influenza deaths. Public Health Rep 78: 494-506.

(16) Office of National Statistics (2009). Population estimates for UK, England and Wales, Scotland and Northern Ireland. Available online: http://www.statistics.gov.uk/hub/release-calendar/index.html?newquery=*&uday=0&umonth=0&uyear=0&title=Population+Estimates+for+UK%2C+England+and+Wales%2C+Scotland+and+Northern+Ireland&pagetype=calendar-entry.

(17) Office of National Statistics (2009). Birth Statistics. Available online: http://www.statistics.gov.uk/downloads/theme_population/FM1-37/FM1_37_2008.pdf.

(18) Ghani AC, Baguelin M, Griffin J et al (2009). The Early Transmission Dynamics of H1N1pdm Influenza in the United Kingdom. PLoS Curr Influenza RRN1130. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2780827/?tool=pubmed.

(19) Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales et al (2009). Epidemiology of new influenza A (H1N1) virus infection, United Kingdom, April-June 2009. Eurosurveillance 14: pii:19232. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19232.

(20) Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales et al (2009). Epidemiology of new influenza A(H1N1) in the United Kingdom, April-May 2009. Eurosurveillance 14: pii: 19213. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19213.

(21) McLean E, Pebody RG, Campbell C et al (2010). Pandemic (H1N1) 2009 influenza in the UK: Clinical and epidemiological findings from the First Few Hundred (FF100) cases in the United Kingdom. Epidemiol Infect doi:10.1017/S0950268810001366.

Available online: http://journals.cambridge.org/action/displayFulltext?type=6&fid=7828773&jid=&volumeId=&issueId=-1&aid=7828772&bodyId=&membershipNumber=&societyETOCSession=&fulltextType=RA&fileId=S0950268810001366.

(22) Carrat F, Vergu E, Ferguson NM et al (2008). Time lines of infection and disease in human influenza: a review of volunteer challenge studies. Am J Epidemiol 167: 775-785. Available online: http://aje.oxfordjournals.org/cgi/content/full/167/7/775?view=long&pmid=18230677.

(23) Ihekweazu C (2010). Clinical spectrum of disease caused by novel Pandemic (H1N1) 2209 in a closed population setting: a sero-epidemiological study. Slide session at the International Conference on Emerging Infectious Diseases, Atlanta 2010.

(24) Calatayud L, Kurkela S, Neave PE et al (2009). Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. Epidemiology and Infection 138: 183-191. Available online: http://journals.cambridge.org/action/displayFulltext?type=6&fid=6879892&jid=&volumeId=&issueId=02&aid=6879888&bodyId=&membershipNumber=&societyETOCSession=&fulltextType=RA&fileId=S0950268809991191 .

(25) Health Protection Agency West Midlands H1N1v Investigation Team (2009). Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. Eurosurveillance 14: pii: 19264. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19264.

(26) Smith A, Coles S, Johnson S et al (2009). An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. Euro Surveill 14: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19263.

(27) Pebody RG, Collaborative UK FF100 Group (2010). Effectiveness of anti-virals in reducing household transmission of Pandemic Influenza A (h1N1) 2009 in the United Kingdom during the"Containment" phase. Poster presented at the International Conference on Emerging Infectious Diseases, Atlanta 2010.

(28) Calatayud L (2010). Oseltamivir resistant pandemic (H1N1) 2009 virus infection in England and Scotland, 2009- 2010. Presentation at Health Protection Conference 2010.

(29) Gulland A (2009). First cases of spread of oseltamivir resistant swine flu between patients are reported in Wales. BMJ 339: b4975. Available online: http://www.bmj.com/cgi/content/full/339/nov23_2/b4975?view=long&pmid=19933735 .

(30) Degail M (2010). Concurrent invasive bacterial infections in confirmed Pandemic (H1N1) 2009 influenza cases in England, 2009- 2010. Presentation at Health Protection Conference 2010 Available online: http://www.healthprotectionconference.org.uk/.

(31) Evans B, Charlett A, McLean E et al (2010). H1N1 case number estimates for England - first and second waves 2009. Poster presentation at 'H1N1: The world responds to a 21st century pandemic conference', London 2010.

(32) Campbell C, Mytton OT, McLean E (2010). Two waves of hospitalisation with pandemic influenza in England. Submitted for publication.

(33) Sfetcu O (2010). Hospitalised patients with 2009 H1N1 influenza in Northern Ireland (NI), June 2009-February 2010. Poster presentation at 'H1N1: The world responds to a 21st century pandemic conference', London 2010.

(34) Pebody RG, McLean E, Zhao H et al (2010). Pandemic Influenza A (H1N1) 2009 and mortality in the United Kingdom: risk factors for death, April 2009 to March 2010. Euro Surveill 15: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19571.

(35) Sethi M, Begum F, Gates P et al (2010). National pandemic H1N1 influenza vaccine uptake in clinical risk groups in England – winter season 2009/10. Poster presentation at Health Protection Conference 2010.

(36) Pebody RG (2010). Epidemiology of the 2009 H1N1 pandemic. Presentation at Health Protection Conference 2010 Available online: http://www.healthprotectionconference.org.uk/.

(37) Baguelin M, van Hoek AJ, Jit M et al (2010). Vaccination against pandemic influenza A/H1N1v in England: a real-time economic evaluation. Vaccine 28: 2370-2384. Available online: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD4-4Y6V99S-1&_user=8810565&_coverDate=03%2F11%2F2010&_rdoc=1&_fmt=high&_orig=search&_sort=d&_docanchor=&view=c&_acct=C000046143&_version=1&_urlVersion=0&_userid=8810565&md5=d2880d48d4e4cb6977d5a4983f258d19 .

(38) Begum F, Pebody RG on behalf of the Health Protection Agency and Department of Health (2010). Seasonal influenza vaccine uptake among the 65 years and over and under 65 years at risk in England, Winter season 2009-10. Available online: http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_118542.pdf.

(39) Hardelid P, Fleming D, McMenamin J et al (2010). Effectiveness of pandemic and seasonal influenza vaccine in preventing pandemic influenza A (H1N1) 2009 infection in England and Scotland 2009-2010. Submitted for publication.

(40) Pebody RG, Andrews N, Waight P et al (2010). No effect of 2008/09 seasonal influenza vaccination on the risk of pandemic H1N1 2009 influenza infection in the UK. Submitted for publication.

(41) World Health Organization (2010). Recommended viruses for influenza vaccines for use in the 2010-2011 northern hemisphere influenza season. Available online: http://www.who.int/csr/disease/influenza/recommendations2010_11north/en/index.html.

(42) Davies S, Beasley C, Ridge K (2010). The influenza immunisation programme 2010/11. Professional letter, Department of Health website. Available online: http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Professionalletters/Chiefmedicalofficerletters/DH_116507.

(43) World Health Organization (2009). Pandemic (H1N1) 2009: Countries, territories and areas with lab confirmed cases and number of deaths as reported to WHO as of 27 May 2009. WHO website. Available online: http://gamapserver.who.int/mapLibrary/Files/Maps/GlobalSubnationalMasterGradcolour_weekly_20090527.png.

(44) European Centre for Disease Prevention and Control (2009). Weekly electronic bulletin Week 32: 03 August 2009 - 09 August 2009. ECDC website. Available online: http://ecdc.europa.eu/en/activities/surveillance/EISN/Newsletter/SUN_EISN_INFL_Bulletin_2009week32.pdf.

(45) European Centre for Disease Prevention and Control (2009). Weekly influenza surveillance overview: week 40. ECDC website. Available online: http://ecdc.europa.eu/en/publications/Publications/091016_EISN_Weekly_Influenza_Surveillance_Overview.pdf.

(46) Dawood FS, Jain S, Finelli L et al (2009). Emergence of a novel swine-origin influenza A (H1N1) virus in humans. New England Journal of Medicine 360: 2605-2615. Available online: http://www.nejm.org/doi/full/10.1056/NEJMoa0903810.

(47) Centers for Disease Control and Prevention (2009). Serum cross-reactive antibody response to a novel influenza A (H1N1) virus after vaccination with seasonal influenza vaccine. MMWR Morbidity and Mortality Weekly Report 58: 521-524. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5819a1.htm.

(48) Centers for Disease Control and Prevention (2009). Novel influenza A (H1N1) virus infections in three pregnant women - United States, April-May 2009. MMWR Morb Mortal Wkly Rep 58: 497-500. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5818a3.htm.

(49) World Health Organization (2010). H1N1 in post-pandemic period. Director-General's opening statement at virtual press conference. Available online: http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html.

(50) World Health Organization (2010). WHO recommendations for the post-pandemic period. Available online: http://www.who.int/csr/disease/swineflu/notes/briefing_20100810/en/index.html.

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Summary

Following the emergence of the novel pandemic (H1N1) 2009 influenza virus in North America in April 2009, the first UK cases were reported on 27 April 2009. Several existing and new surveillance systems were used to investigate the first cases, to monitor the unfolding pandemic and to measure the impact and effectiveness of the various counter-measures that were implemented in the UK.

Most confirmed cases appeared to have experienced a largely typical influenza-like illness. A minority suffered serious disease. Children were most affected; adults aged over 50 years had evidence of some pre-existing immunity, with much lower clinical attack rates.

Two waves of pandemic activity, separated by the closure of schools over the summer, were observed (appendix 1). The first wave peaked in mid/late-July 2009. The regions most affected initially were the West Midlands, London and central Scotland, mainly due to several early large school-based outbreaks in the former two areas. England and Wales experienced higher activity levels in the first wave compared to Scotland and Northern Ireland, which may be due to earlier closure of Scottish and Northern Irish schools for summer holidays. The second wave started with the return to school in the autumn with a peak in mid-October 2009.

All viruses characterised were similar to the California/07/2009 strain. The pandemic (H1N1) 2009 virus was the main circulating strain: from week 20 2009 to week 20 2010, of 3059 influenza viruses detected by the HPA Respiratory Virus Unit, only 78 (2.5%) were non-pandemic viruses. Through GP sentinel surveillance, the highest weekly proportion of ILI cases positive for pandemic influenza was in Northern Ireland, where it reached 83% in week 44 (ending 1 November 2009). In England, the highest rate was 43% (week 43 2009), in Scotland 47% (week 45 2009) and in Wales 57% (week 42 2009).

The first reported UK death due to pandemic influenza occurred on 14 June 2009. The majority of hospitalisations and deaths were in people aged less than 65 years. The symptomatic case-fatality ratio was estimated to be 0.04%. People with an underlying medical condition, for which influenza vaccination is recommended by the Department of Health, did not seem to be at a greater risk of acquiring the infection, but were estimated to be 10 times more likely to be hospitalised and 18 times more likely to die than those without any underlying condition. In England, Wales and Scotland, no excess all-cause mortality was observed over the summer of 2009. In the 2009/10 winter season excess mortality was observed in weeks 52 and 53; influenza is unlikely to be the main explanation as all other influenza indicators showed low activity at the time and these deaths were concentrated in the elderly.

Antiviral drugs were offered to those presenting with clinical symptoms of influenza during the treatment phase in the UK. In England and Scotland the number of courses collected during the treatment phase covered about 2% of the population and in Northern Ireland enough were prescribed through primary and secondary care to cover 1.4% of the population. Of 6,379 viruses tested, only 45 (0.7%) were found to carry a mutation known to confer resistance to the antiviral drug oseltamivir. Most cases of resistance were thought to be treatment-induced. Antiviral drugs as treatment significantly reduced the median duration of illness and, as prophylaxis and treatment, reduced the household secondary attack rate.

Some side-effects attributed to the antiviral drugs were reported; mainly gastrointestinal symptoms.

There was no evidence that the 2008/09 seasonal influenza vaccine significantly affected risk of acquisition of pandemic (H1N1) 2009 infection. The UK 2009/10 seasonal influenza vaccination programme went ahead as normal. For all people aged over 65 years uptake ranged from 64% in Wales to 77% in Northern Ireland, and for those under 65 years in an underlying clinical risk group uptake ranging from 49% in Wales to 80% in Northern Ireland. The monovalent pandemic vaccine programme was initiated in October 2009, initially recommended for front-line health care workers and people of all ages with underlying medical conditions, including pregnancy. These recommendations were extended to all healthy children aged from 6 months to under 5 years in December 2009. The uptake of pandemic influenza vaccine in people at risk (including pregnant women) was 38% in England, 52-55% in Scotland and 42% in Wales. In Northern Ireland the uptake in this group (excluding pregnant women who had a 57% uptake) was 87%. Preliminary data from routine GP sentinel influenza surveillance in England and Scotland shows that pandemic influenza vaccine was effective in preventing confirmed influenza infection.

The post-pandemic phase was declared by WHO on 10 August, 2010. For the forthcoming 2010/11 season, the virus is expected to behave as a normal seasonal influenza virus, though vigilance for changes in the virus, the disease caused, or groups affected should be maintained.

Contents

Introduction

In the United Kingdom (UK), surveillance of influenza and other respiratory viruses is undertaken by the Health Protection Agency (HPA), Health Protection Scotland (HPS), Public Health Agency Northern Ireland and Public Health Wales. Data are collated from a variety of surveillance systems to provide timely information on which influenza strains are circulating, to ascertain which have epidemic potential, and to contribute towards the decision on influenza vaccine composition for the following season. Surveillance activities also produce timely reports[1] for health professionals, the media and the public on influenza activity and spread, burden of disease and the uptake and effectiveness of the main clinical counter-measures (in particular vaccination and antivirals).

Surveillance occurs throughout the year with a focus on the winter season between October (week 40) and May (week 20). Following the identification of the first cases of a novel swine influenza virus in April 2009 in Mexico and the United States[2;3], the UK embarked on an initial "containment" strategy during May and June (see Box 1). In an effort to mitigate the impact of the pandemic, during the containment phase all symptomatic cases were ascertained through enhanced surveillance, and those who met the clinical and epidemiological case definition, were followed up, laboratory confirmed and their close household and non-household contacts traced. Antiviral drugs were recommended for early treatment of all confirmed cases and post-exposure prophylaxis offered to identified close contacts. Selective school closures were also recommended during the containment phase.

Box 1: Key actions during the containment and treatment only phases in the UK, adapted from[5]

Containment phase

- Diagnosis by laboratory confirmatory testing
- Suspected cases treated with antivirals and requested to self-isolate at home
- Household/close contacts of suspected cases traced
- Close contacts offered antiviral prophylaxis if index case laboratory confirmed; contacts advised to self-isolate only if they became clinically ill
- Risk assessment dependent closure of schools for 7 days if confirmed case(s) identified; treatment of clinically ill patients with antivirals
- Close contacts of confirmed/suspected cases in confirmed school outbreaks offered anti-viral prophylaxis

Treatment-only phase

- Diagnosis by clinical illness; laboratory testing not required
- Clinical cases offered antiviral treatment through consultation with healthcare professional or National Pandemic Flu Service (NPFS); emphasis on treatment for persons in higher risk groups
- Contacts of cases not offered prophylaxis apart from special circumstances (e.g. household member with serious underlying health problem)

In June 2009, WHO declared a global influenza pandemic[4], the first for over four decades.

In June, significant community transmission developed in a number of UK regions, in particular in London, the West Midlands and central Scotland. At the beginning of July 2009, with evidence of community transmission, the UK moved to a 'treatment-only phase' of cases to manage the pandemic. This phase focussed on provision of antivirals to people presenting with clinical respiratory illness (without the need for confirmatory testing) through primary and secondary care and the telephone and web-based National Pandemic flu Service (in England). Surveillance continued throughout this period to monitor trends, burden of disease and changes in the characteristics of the virus and the uptake and effectiveness of the pandemic influenza vaccine programme that was implemented in autumn 2010.

This report describes influenza activity in the UK from the beginning of the pandemic (end of April 2009) to week 20 2010 (ending 23 May 2010).

Methods

SOURCES OF DATA

A number of different data sources are traditionally used to monitor influenza activity in the UK. In response to the pandemic, some systems were enhanced and new ones were created to strengthen pandemic surveillance. Systems evolved as the UK moved through the different stages of the pandemic. Traditional seasonal influenza surveillance systems, along with several new influenza surveillance schemes, were utilised throughout the pandemic in the UK to provide a comprehensive assessment of this novel virus, to monitor its activity, to estimate impact and to measure the uptake, safety and effectiveness of the various counter-measures.

FIRST FEW 100 (FF100) SURVEILLANCE SYSTEM (NEW)

The FF100 system collected detailed demographic, exposure, clinical, treatment and outcome data for 392 of the first UK cases of laboratory confirmed pandemic (H1N1) 2009 and their close household and non-household contacts during the early part of the summer pandemic wave. Information was obtained through interviews and record reviews. Virological swabbing was undertaken when possible from symptomatic cases and blood samples for serological testing were sought from cases and their contacts[6].

The secondary household attack rate was calculated as the proportion of household contacts who became cases at two weeks. Uni- and multi-variable analyses were undertaken.

FLUZONE (NEW)

Fluzone was a case management system created by the HPA based on the generic clinical assessment information system HPZone. It was rapidly developed and rolled out to all English Health Protection Units and Flu Response Centres in summer 2009 during the containment phase. It was used in case management and follow-up of contacts, and also provided data on English cases by local area during this period.

FIELD EPIDEMIOLOGY STUDIES

A number of ad hoc field epidemiology investigations were undertaken by local Health Protection Units and their equivalents across the UK. These investigations occurred in various closed settings including schools and other venues.

SERO-EPIDEMIOLOGY STUDIES (NEW)

Serological analysis of serum samples was performed by the application of two assays – microneutralisation (MN) and haemagglutination inhibition (HI). These were designed and validated at the HPA Centre for Infections (CfI).

Serological assays were performed using NIBRG122, a reverse genetics version of a virus isolated from a human case (confirmed and isolated end of April 2009; A/England/195/2009) and antigenically representative for the pandemic viruses circulating

in the UK at that time. Recent infection was confirmed on the basis of 4-fold titre increase between an acute and convalescent serum sample by HI or MN. For unpaired sera (single convalescent serum samples from field studies or samples for sero-incidence study), the probability of recent infection was calculated based on the achievement of HI titres ≥32 (which correlates to a four-fold titre rise from a baseline titre of <8).

Serological samples for field epidemiological studies were collected as serum pairs where possible (acute and convalescent, separated by at least 14 days). In most cases, a single convalescent sample was obtained.

Population pre- and post-pandemic sero-prevalence and sero-incidence studies were undertaken. The HPA sero-epidemiology unit (SEU) and NHS chemical pathology laboratories in England provided the principal source of sera – using anonymised residual samples with information on age and month of sample. The SEU serum bank was examined from before the pandemic and at monthly intervals until the end of the pandemic[7].

A sero-prevalence study was also carried out in Scotland, using anonymised sera from residual diagnostic samples taken in March 2010[8].

CONSULTATION RATES FOR ILI WITH GPS

Clinical data are obtained from networks of general practitioner (GP) surgeries in the UK. Data reported are the weekly consultations for influenza-like illness (ILI) and other acute respiratory illnesses. These schemes use the number of patients registered with the participating GP as the denominator. In the UK, each country runs a national scheme. In addition, there is also a system (HPA/QSurveillance®) which includes practices from England, Northern Ireland and Wales, although the majority are from England. To aid interpretation of the consultation rates and comparison with previous years, thresholds have been defined for most GP-based schemes to indicate expected rates when influenza is not circulating widely (baseline levels), when normal seasonal levels of influenza are circulating in the winter season and when higher than expected or epidemic activity is occurring (see table 1). These thresholds have been set based on experience with several years of data.

Table 1: GP influenza surveillance system in the UK (click links in left-hand column for further information on the schemes from external websites)

Scheme (Country)	Baseline	Normal	Above Average	Case definition
RCGP (England)**	30	200	-	ILI
Public Health Wales	25	100	100-400	Influenza
PIPeR (Scotland)	50	-	-	ILI/ARI
PHA (Northern Ireland)	70	500	-	ILI/ influenza
HPA/QSurveillance® (UK*)	20	70	130	ILI

**** QSurveillance® is based on data from 43% of England's population, 11% of the population in Wales, 17% in Northern Ireland and 0% in Scotland; ** The thresholds for RCGP clinical data were lowered in 2004[8]***

COMMUNITY SYNDROMIC SURVEILLANCE

NHS Direct is a 24/7 nurse-led telephone health advice and information service in England and Wales. The NHS Direct/HPA surveillance scheme analyses data from this service. Key respiratory indicators are the proportion of callers reporting colds/flu and fever by age group and region[10]. In Scotland a similar system (NHS-24) operates.

In Northern Ireland there is no equivalent of NHS Direct/NHS-24. Data are collected from out-of-hours centres. During the 08/09 influenza season a pilot was undertaken with two of the seven primary care out-of-hours (OOH) centres. Data on total consultations and those for influenza/ILI, stratified by age, were extracted daily for the previous 24 hours and compared with sentinel consultation rates. This involved an auto-extraction process, with data being imported into a central repository. This process has now been extended to the remaining five centres.

On 23 July 2009 the National Pandemic Flu Service (NPFS) became operational in England only. Patients with uncomplicated ILI were asked to telephone or access the NPFS website rather than go to their GP. The service authorised antiviral drugs to people aged over one year, with ILI, who did not fall into a specified risk group. If they fell into one of these groups the individual was referred to the health service. NPFS replaced NHS Direct as the data source for community ILI syndromic surveillance. Data from NPFS provided information on the number of antiviral authorisations and collections.

In Northern Ireland, the number of antiviral courses, prescribed through primary and secondary care, was collated regionally on a weekly basis. In Scotland, the rate of antiviral prescriptions was analysed weekly.

MICROBIOLOGICAL SURVEILLANCE (ENHANCED)

Following development of a sensitive and specific H1N1 RT-PCR assay[11], all testing for pandemic (H1N1) 2009 was initially carried out at CfI. HPA regional laboratories forwarded all untypeable influenza A viruses to CfI for confirmation until a validated test had been developed and rolled out to them. Results of all tests from HPA laboratories for the novel virus (positive or negative) in England were reported to CfI, initially through standardised emailed spreadsheets. Reporting was later undertaken through the automated Datamart system for influenza and other respiratory viruses.

In addition, the National Laboratory Reporting Scheme (LabBase) comprises approximately 230 NHS, HPA and independent sector microbiology laboratories throughout England and Wales. This system reports positive results for human samples (from community and hospital settings) testing positive for pathogens. Trends in respiratory viruses including influenza, respiratory syncytial virus, rhinovirus and parainfluenza are examined.

A subset of ~50 general practices in the Royal College of General Practitioners (RCGP) Weekly Returns Service submit respiratory samples for virological testing from patients presenting with influenza-like illness in participating practices. Respiratory specimens, along with key demographic and epidemiological information about the patient and illness (e.g. use of antivirals and vaccination history), are submitted to the HPA CfI. A complementary sentinel primary care scheme of sampling is carried out by the HPA whereby respiratory specimens from patients presenting to their GP with an acute respiratory infection are

submitted to the local HPA Regional Microbiology Network (RMN) laboratory together with epidemiological information from the patient. Specimens are evaluated by PCR for influenza and other respiratory virus infections. Similar sentinel swabbing schemes through primary care operate in Scotland, Wales and Northern Ireland. Data from these schemes allow the calculation of the proportion of ILI cases consulting in primary care testing positive for influenza each week.

Beginning on 28 May 2009, a systematic sample of symptomatic callers to NHS Direct were asked to participate in a virological surveillance scheme. This involved self-sampling with nasal swabs. Swabs were then posted to HPA CfI for virological testing[12]. Virological self-sampling from NHS Direct stopped after week 30 and started through NPFS in week 32, until February 2010, when NHS Direct was used again.

HPA CfI undertakes antigenic and genetic characterisation of influenza isolates submitted for testing by HPA and NHS laboratories. Antigenic characterization of pandemic (H1N1) 2009 viruses circulating in the UK during 2009 was performed by haemagglutination inhibition (HI) assay using post-infection ferret antisera to A/California/07/2009 (vaccine strain), A/England/195/2009 (UK reference strain) and A/Brisbane/59/2007 (previous seasonal H1N1 vaccine strain). An isolate with a 4-fold or less change in reactivity to the reference strain is classed as being like the reference strain.

CfI also monitors the occurrence of anti-viral resistance in influenza isolates using a molecular marker for oseltamivir resistance (H275Y) and subsequent full phenotypic susceptibility testing. Cases found to be resistant were followed up through clinicians and microbiologists using a standard questionnaire.

To identify the role played by concurrent bacterial infections during the pandemic, an attempt was made to identify English pandemic (H1N1) 2009 cases who has also tested positive for a bacterial infection through record linkage.

ESTIMATED CASE NUMBERS (NEW)

The estimated number of symptomatic cases with ILI due to pandemic influenza, by English region and age group, was calculated each week using a statistical model. This used data from several surveillance sources including GP and NPFS age-specific consultation rates, age-specific positivity rates through sentinel virological schemes and estimated proportions consulting health care. The parameters altered over the pandemic period to take into account changes in policy (e.g. the introduction of NPFS and impact on proportion consulting health care) and changes in data[13]. An estimate of the total number of new symptomatic cases was given each week with the previous week estimates recalculated with updated data. There was uncertainty around the proportion of people with ILI symptoms who contacted their GP (or NPFS). To take this uncertainty into account a range of values were used resulting in a range of estimated symptomatic case numbers surrounding the central estimate.

HOSPITALISATION DATA (NEW)

During the initial part of the first wave, detailed information was collected for all laboratory confirmed cases as part of the FF100 project. Information collected included details of contact with the health care service and, where appropriate, of hospitalisation.

In England, after the closure of FF100, information on cases including possible hospitalisation was collected by Health Protection Units through the Fluzone system. Once the treatment phase started, not all suspected cases were tested for influenza infection, Acute Trusts reported to the Department of Health (DH) the number of confirmed or clinically suspected cases of pandemic (H1N1) 2009 admitted to local NHS hospitals. In October 2009, a web based reporting system was introduced by HPA and the Chief Medical Officer (CMO) across England to collect demographic, clinical and epidemiological information on all laboratory confirmed pandemic (H1N1) 2009 cases admitted to NHS trusts. In addition to collecting information prospectively, this system was used to collect information retrospectively on all laboratory confirmed cases admitted to hospital since the beginning of the pandemic. Information was collected on clinical details, underlying risk factors, use of antivirals and outcome of admission.

In Northern Ireland similar information on virologically confirmed hospitalised cases was forwarded, initially daily and subsequently weekly, by the hospital trusts to the Public Health Agency throughout the pandemic period.

In Scotland data on virologically confirmed hospitalised cases were collated by Health Protection Scotland.

In Wales similar data were collated by Public Health Wales Health Protection.

In addition, a detailed case note-based investigation was carried out in 55 hospitals across the UK. The Influenza Clinical Information Network (FLU-CIN) study collection in-dept clinical and demographic information on patients admitted to hospital with confirmed pandemic (H1N1) 2009 infection[14].

MORTALITY MONITORING (ENHANCED)

The Office for National Statistics (ONS) collates and reports to HPA estimated total all-cause death registrations on a weekly basis. This information is used to estimate excess all-cause all-age death registrations in England and Wales as compared to previous seasons each week. A statistical model is used based on the Serfling method, to establish a baseline of the expected weekly number of registered deaths[15]. If the observed number is above the upper limit of a 90% confidence interval around this expected number for at least one week, an excess is said to have occurred.

In addition to the ONS data, during the pandemic, the General Registry Office of England and Wales reported daily individual death registrations by age and registration district. This information was used to estimate excess all-cause mortality by age-group in England and Wales.

In Scotland the weekly total number of death registrations (overall and by age group) is compared to the expected number calculated using two methods; a Serfling cyclical model and a Gam model based upon previous winters.

The CMO undertook a confidential enquiry of confirmed pandemic (H1N1) 2009 deaths in England with reporting from all NHS trusts. In addition, individual pandemic (H1N1) 2009 deaths were ascertained through the various enhanced surveillance systems operated by

the HPA and reconciled. Similar information was gathered by health protection equivalents in Scotland, Wales and Northern Ireland. Information on cause of death, complications and underlying conditions was collected.

VACCINE UPTAKE MONITORING

Priority groups for pandemic (H1N1) 2009 vaccination were defined by the Joint Committee for Vaccination and Immunisation (JCVI) as those aged six months and up to 65 years in the current seasonal influenza vaccine clinical at-risk groups, all pregnant women, household contacts of immunocompromised individuals, and those aged 65 years and over in the current seasonal influenza vaccine clinical at-risk groups. These priority groups were offered pandemic vaccine from late October 2009. Following the DH announcement on phase two of the vaccination programme, healthy children aged six months and up to 5 years were offered pandemic vaccine from December 2009.

The JCVI recommended that all those aged 65 years and over and those aged 6 months to under 65 years falling in a clinical at risk group, be offered the seasonal 09/10 trivalent influenza vaccine. Clinical at risk groups include individuals with one of the following underlying medical condition: chronic respiratory disease, chronic heart disease, chronic renal disease, chronic liver disease, chronic neurological disease, diabetes or immunosuppression.

Uptake of both vaccines in the different eligible groups was monitored in England by the HPA through the DH web-portal „Immform". Data on the eligible populations and the number of patients/health-care workers vaccinated were automatically extracted or manually outputted from GP and acute trust information systems and uploaded.

In Scotland, Wales and Northern Ireland similar data were collected using automated and manual methods.

VACCINE EFFECTIVENESS MONITORING

Estimates of vaccine effectiveness were made using data from GP sentinel virological schemes in England and Scotland. A swab negative case-control study of individuals with influenza-like-illness was undertaken. Those testing PCR positive for pandemic (H1N1) 2009 were cases and those testing negative were controls. Vaccine effectiveness was estimated as (1-OR).

DENOMINATOR DATA and MODELLING

Where population rates are presented, the population figures are from the ONS mid-2008 estimates, which are available by age and region[16].

In the case of rates by underlying medical condition, the population denominators are derived from the HPA-DH vaccine uptake surveys. These data provide information on the number of patients registered in primary care by specific underlying condition for people aged between six months and 65 years and for the 65-year or older group the overall number in a risk group is available. The estimate of the number of pregnant women is derived from the annual maternities and number of miscarriages/abortions provided by ONS[17].

Where case-based rates are presented, the denominator used is the HPA estimated number of symptomatic cases (see above). To take into account the range of values used due to uncertainty around the case numbers, the case-rates are presented with a range; the upper and lower limits of 95% confidence intervals around the rates obtained using the low and high estimate of cases.

Follow-up of confirmed cases and their close household contacts in the FF100 project allowed an estimation of the overall household secondary attack rate (SAR), and of the impact of containment measures on the reproduction number (*R*)[18]. *R* is a measure of the transmissibility of the virus and sustained transmission requires $R>1$. Real-time modelling work also examined vaccination policy options for the Joint Committee of Vaccination and Immunisation.

Results

ENHANCED CASE FINDING AND EPIDEMIOLOGY STUDIES (CONTAINMENT PHASE to 1 JULY 2009)

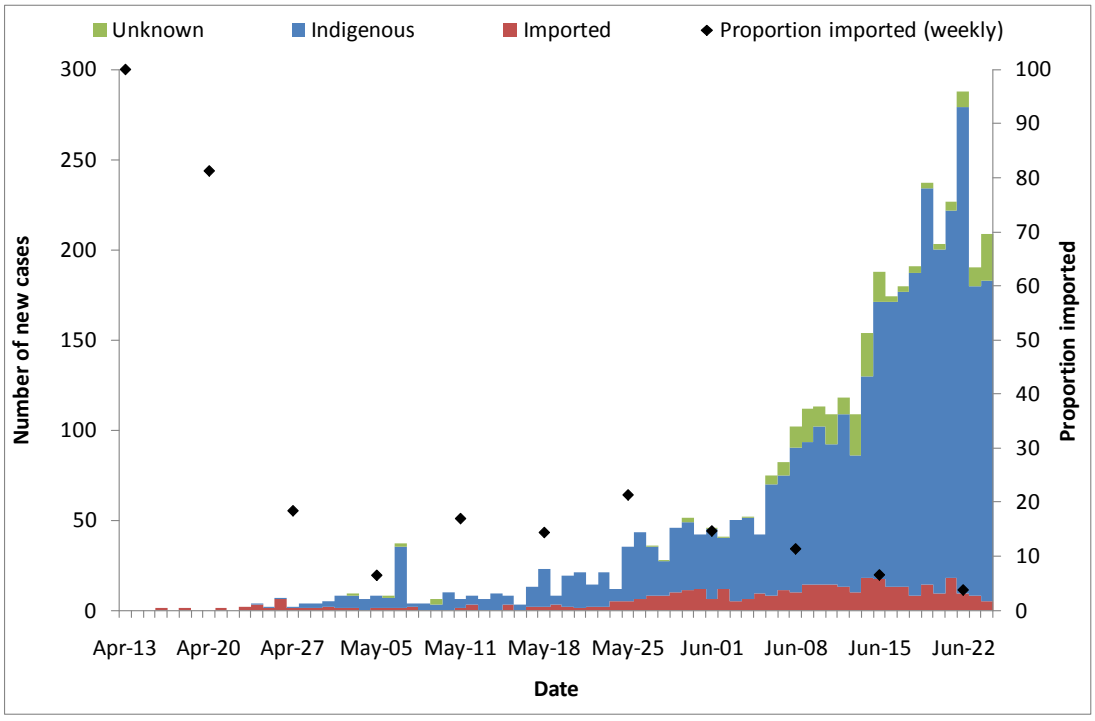
TIMING

The first cases of pandemic (H1N1) 2009 infection in the UK were reported on 27 April 2009, in a Scottish couple returning from a trip to Mexico[19;20]. Two days later, the first English case was reported in a person who had travelled on the same flight from Mexico.

In the first four weeks of the outbreak in the UK, transmission of the virus was sporadic and generally linked to travellers returning from affected areas (Mexico and the US) or to indigenous transmission to close contacts in school and household settings[5].

Sustained community transmission became established initially in Scotland (South Glasgow), the West Midlands and then London. In England, much of the transmission was linked to school outbreaks. By the end of the containment phase (1 July 2009), 7447 confirmed cases had been reported in the UK; 6162 (83%) in England, 1217 (16%) in Scotland and 34 (0.5%) each in Northern Ireland and Wales. Case numbers were doubling approximately every week at this stage. The proportion of cases who were imported (as opposed to infection acquired indigenously in the UK) decreased over the initial weeks to less than 5% by the end of June (figure 1).

Figure 1: Cases of pandemic (H1N1) 2009 by onset date and route of acquisition of infection and weekly proportion imported, UK (to 1 July 2009)



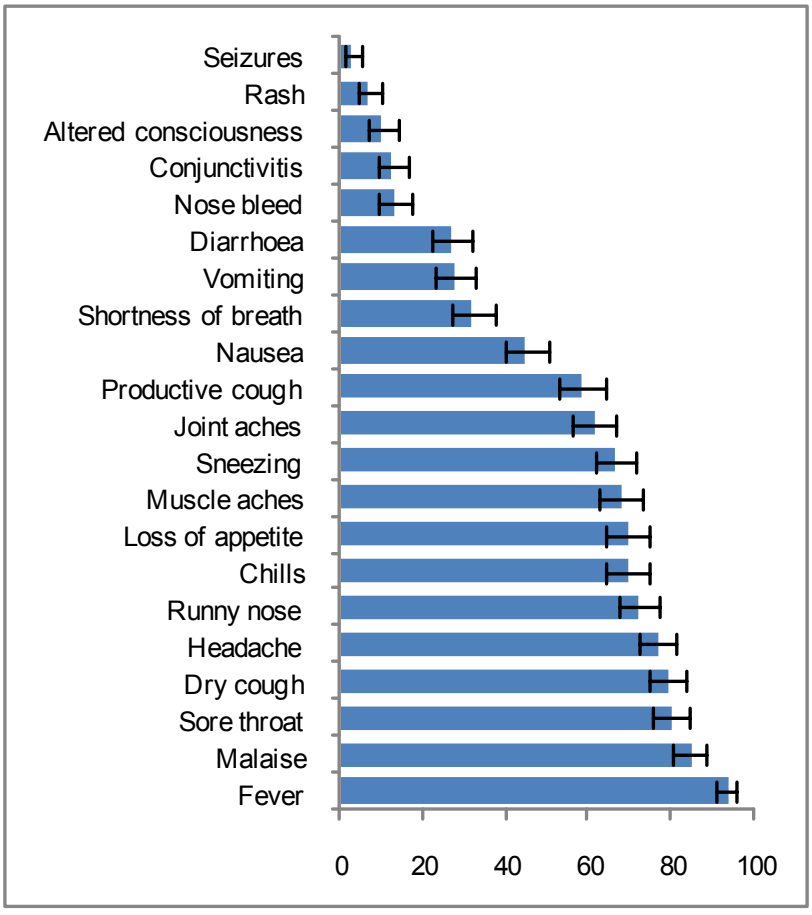
CLINICAL PRESENTATION

Most cases appear to have experienced an illness fairly typical for influenza.

Detailed investigation of 392 early laboratory-confirmed cases as part of the FF100 surveillance project found fever, malaise, dry cough, sore throat and headache to be the commonest (>70% of respondents) reported symptoms (figure 2). However, a greater proportion of cases reported gastrointestinal (diarrhoea and vomiting) than is usually seen with seasonal influenza. The median reported duration of illness was seven days (range 1-29 days)[21].

Asymptomatic infection is a well-recognised feature of seasonal influenza[22]. Serological studies of a boarding school outbreak of pandemic (H1N1) 2009 showed that sub-clinical infection occurred in about one third of those with serological evidence of infection [23].

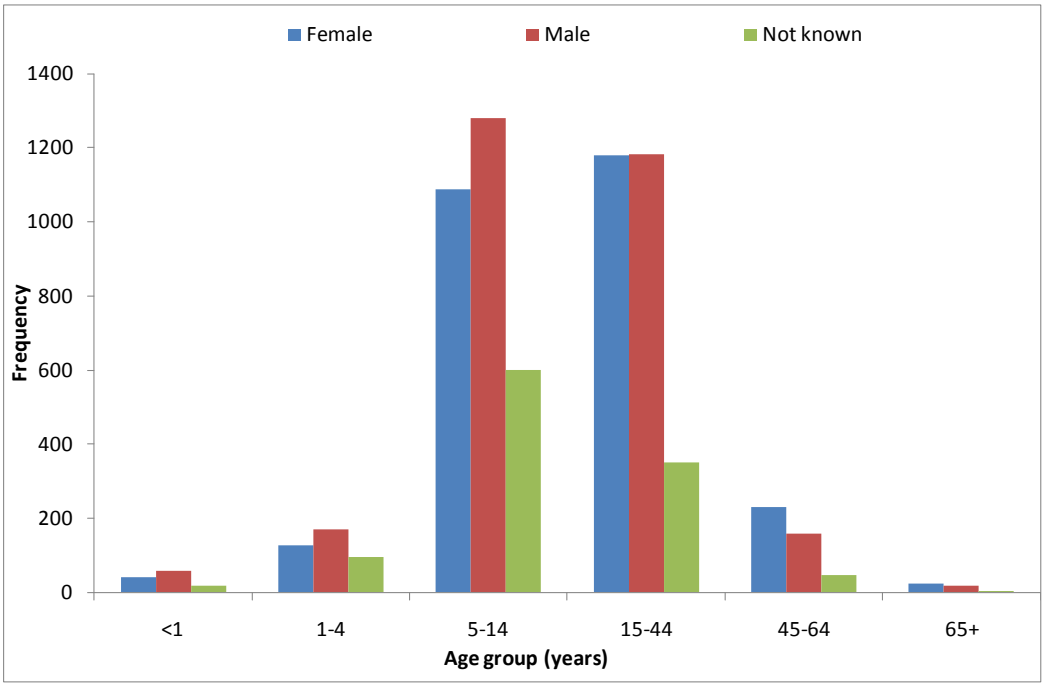
Figure 2: Proportion (%) of all UK FF100 cases of pandemic (H1N1) 2009 influenza reporting symptoms at any stage of illness, with binomial exact 95% confidence interval (adapted from[21])



GROUPS AFFECTED

During the containment phase, pandemic (H1N1) 2009 cases were identified aged from 0 to 90 years; the median age for confirmed cases up to 1 July 2009 was 14 years (IQR: 9 – 25 years). The 5-14 year age group had the highest cumulative population incidence rate (42.1 per 100,000) by 1 July 2009 (figure 3). The older age groups (aged over 45 years) had the lowest cumulative population incidence rates. At this stage, the median age varied by region; in London and the West Midlands, where there had been several large school-based outbreaks[24-26], it was 12 years while in other UK regions it ranged from 17 years (Scotland) to 25.5 years (North West England). There was an approximately equal distribution by gender (48% female).

Figure 3: Age and sex distribution of pandemic (H1N1) 2009 cases, UK with crude cumulative population rate per 100,000 (to 1 July 2009)



Cases of pandemic (H1N1) 2009 were not dispersed homogenously throughout England during the containment phase. Parts of London and the West Midlands region experienced high numbers of cases with rapid rates of increase in new cases from week to week early in the summer wave (figure 4, appendix 2). Both these areas showed the first increases in ILI reported through daily GP consultation rates before the end of the containment phase; about two weeks earlier than other areas of the country (figure 5).

Figure 4: location of UK cases of pandemic (H1N1) 2009 by week of report, June 2009

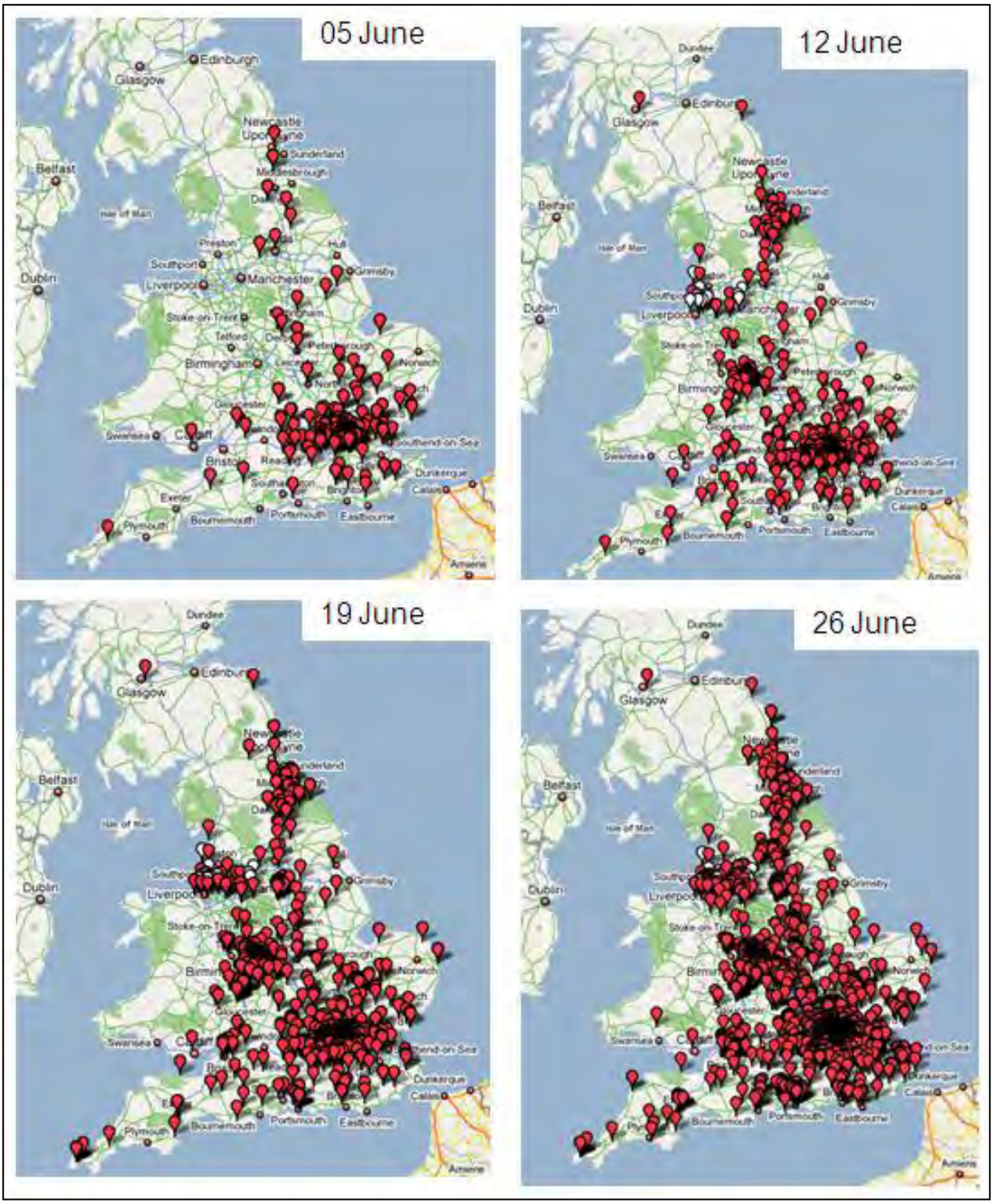
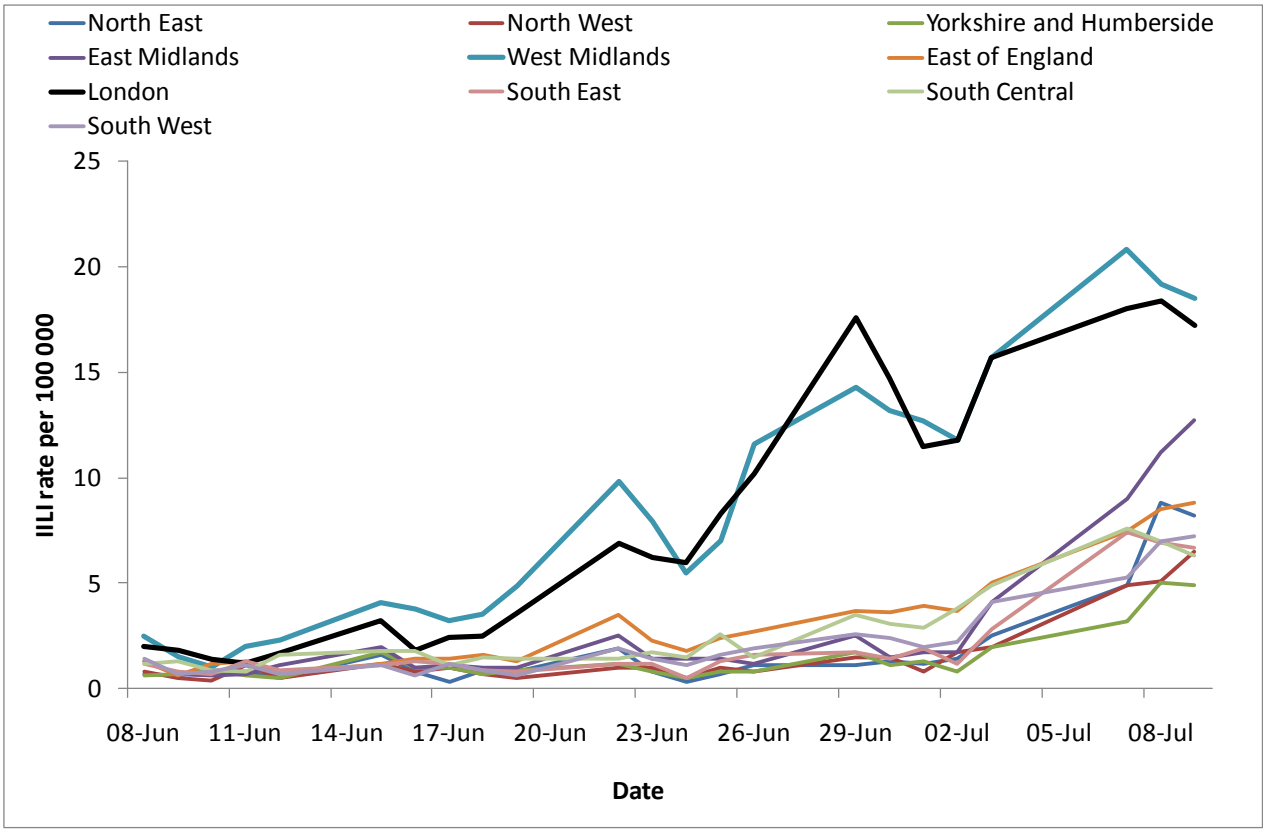


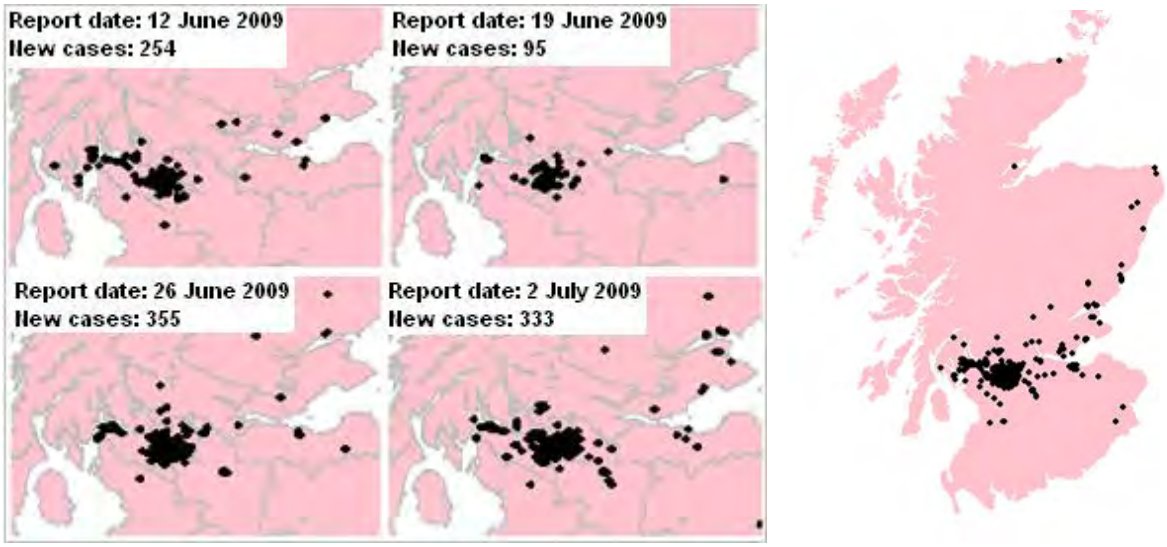
Figure 5: daily GP consultation rate for ILI through the HPA/QSurveillance system, by region*, June – July 2009



**EM: East Midlands, EE: East of England, LN: London, NE: North East, NW: North West, SC: South Central, SEC: South East Coast, SW: South West, WM: West Midlands, YH: Yorkshire and Humberside.*

In Scotland pandemic (H1N1) 2009 cases were initially clustered in the ‗hotspot' areas of Greater Glasgow & Clyde in the West of the Central area of the country. Up to 2 July 2009 (after which point not all suspected cases were tested) the majority of cases were almost exclusively restricted to the Central Belt of Scotland although there was the start of gradual spread to beyond these limits (figure 6).

Figure 6: Maps of Scotland showing new laboratory confirmed cases reported to HPS by week of report and the total to 2 July 2009 (n=1238)



FIELD INVESTIGATIONS

Health protection teams across the UK initiated a number of field investigations of outbreaks in closed settings. In one early school outbreak in England, 91 symptomatic cases were identified between 15 April and 15 May 2009 of which 33 were confirmed to be positive for pandemic (H1N1) 2009. In this outbreak an overall virologically confirmed attack rate in the school pupils of 2% was observed, though in the most affected age group this increased to 15%. Transmission was documented in several households of the pupils with a 17% virologically confirmed secondary attack rate in household contacts[24].

A large, late-recognised, outbreak of pandemic (H1N1) 2009 infection in an English primary school had a 30% clinical attack rate in the pupils, with a virologically confirmed attack rate of 13% overall (ranging from 5.1% to 23% in different age groups). The symptoms reported were generally mild: predominantly fever, nasal congestion and sore throat[25].

TRANSMISSION

The overall household secondary attack rate (SAR) (for virologically confirmed pandemic (H1N1) 2009) in the FF100 was estimated as 8.2% (95% CI 6.4 – 10.3%) during the containment phase. This was significantly affected by the use of antivirals to treat index cases and as prophylaxis for close household contacts. There was also evidence of a differing SAR by age group; with the rates in children and young adults significantly higher than the rate in adults aged over 50 years (table 2)[27].

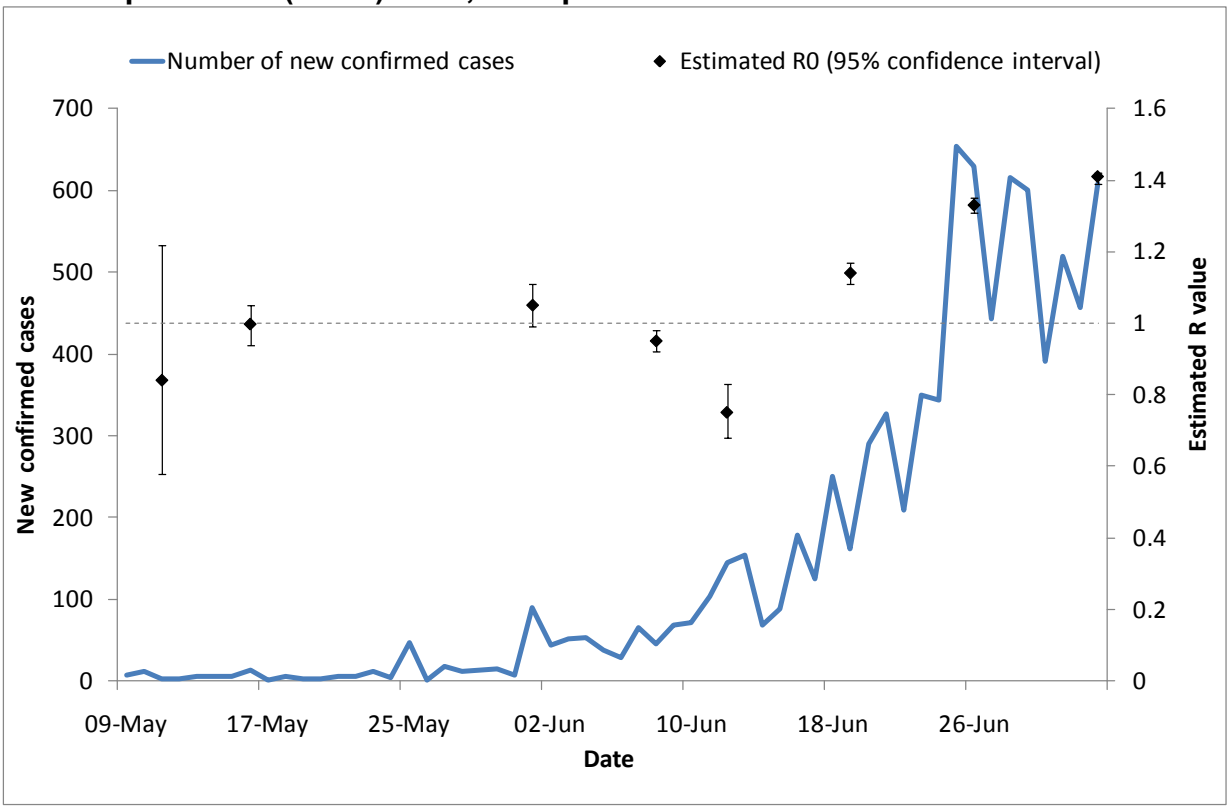
R was estimated to be close to 1 but with considerable uncertainty from early May until mid June, after which it was consistently above 1 (figure 7). This fluctuation in the estimate is to be expected due to stochastic effects (randomness) being significant when numbers of infected individuals are low.

Table 2: Uni- and multi-variable analysis of SAR by gender, age group and prophylaxis and treatment for virologically-confirmed cases (adapted from[27])

Variable level	Crude (uni-variable) SAR	Adjusted (multi-variable) OR (95% CI)	p-value
Male	37/364 (10.2%)	Baseline	0.94%
Female	25/381 (6.6%)	1.0 (0.5 - 2.0)	
<16 year	40/212 (18.9%)	14.2 (3.0 - 67.1)	<0.001
16-49 years	20/378 (5.3%)	2.8 (0.6 - 13.4)	
50+ years	2/171 (1.2%)	Baseline	
No prophylaxis	45/132 (34.1%)	Baseline	<0.001
AV prophylaxis	8/455 (1.8%)	0.03 (0.02 - 0.09)	
>48 hours*	48/453 (10.6%)	Baseline	0.004
≤48 hours*	14/308 (4.5%)	0.3 (0.13 - 0.68)	
Total	62/761 (8.1%)		

** Index case treated with antiviral drugs*

Figure 7: Estimated R by date of estimation with the number of new confirmed cases of pandemic (H1N1) 2009, UK April – June 2009



ROUTINE AND ENHANCED INFLUENZA SURVEILLANCE SYSTEMS (April 2009 – May 2010)

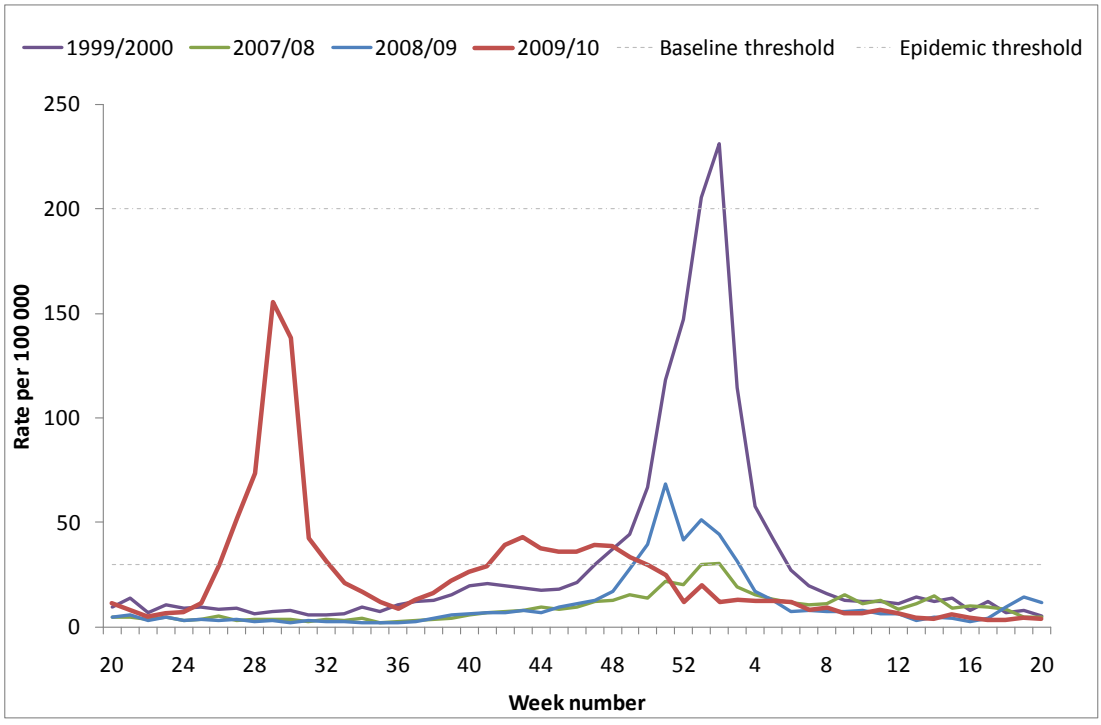
CLINICAL

Weekly GP clinical surveillance schemes in England, Scotland, Wales and Northern Ireland:

With the onset of widespread community transmission, the RCGP weekly ILI rate in England exceeded the baseline level of 30 consultations per 100,000 in week 27 (ending 5 July 2009) when it increased from 29.6 to 51.9 per 100,000. It peaked in week 29 (ending 19 July 2009) at 155.3 per 100 000 and remained above the baseline level until week 33 (ending 16 August 2009) when it decreased from 30.9 to 21.2 per 100,000. It decreased until week 36 (reaching 8.6 per 100,000 at the lowest point) after which it began to increase again, exceeding the baseline in week 42 (ending 18 October 2009) when it increased from 29.1 to 42.8 per 100,000. This was the highest rate observed in the autumn, though the rate remained above the baseline for several weeks. It finally fell below this level in weeks 50 (29.7 per 100,000) and 51 (24.7 per 100,000) (figure 8).

Observed trends in primary care consultations were likely affected by the NPFS which operated in England between 23 July 2009 (the RCGP peak week) and 11 February 2010. In addition, most state schools in England started their summer holidays in the week ending 26 July.

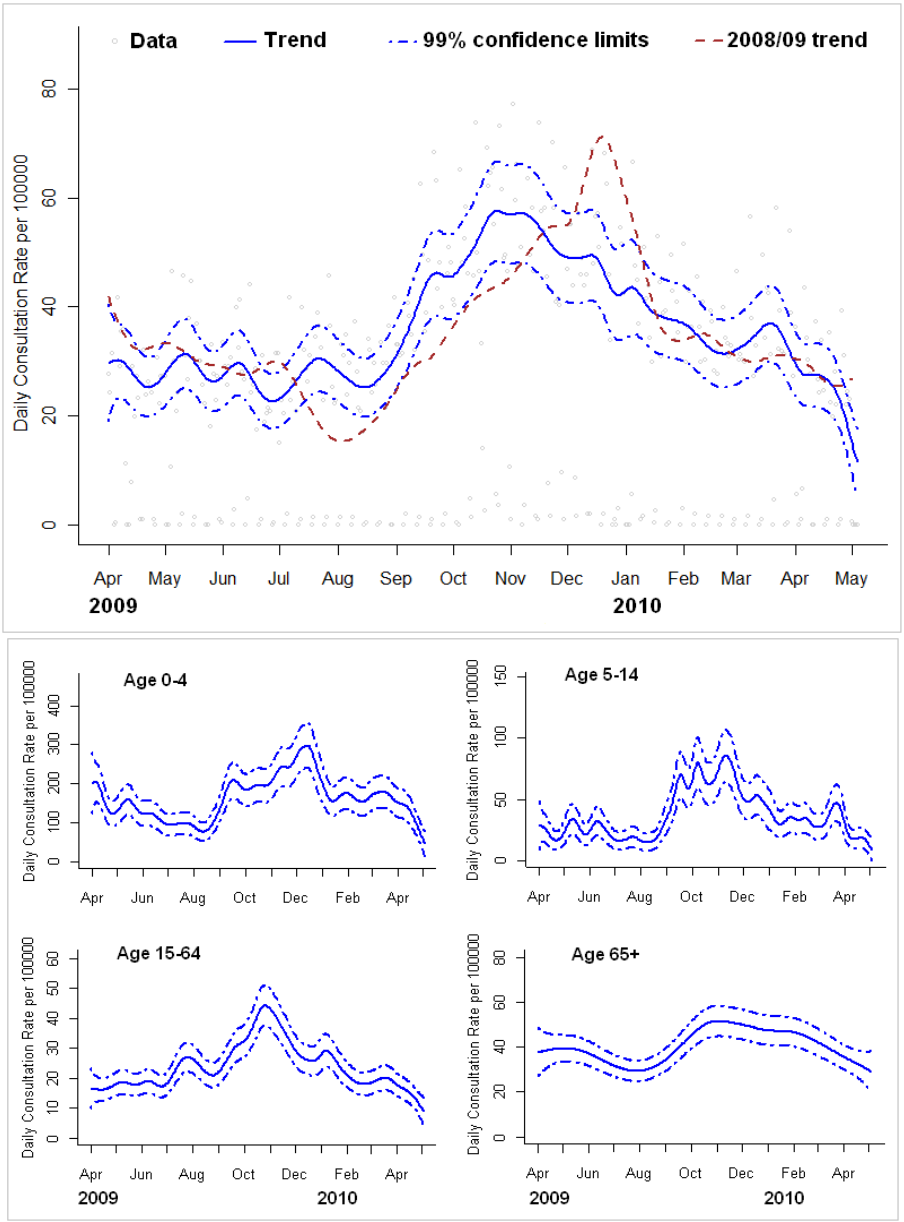
Figure 8: Royal College of General Practitioners weekly influenza-like illness rate per 100,000, May 2009 – May 2010



A summer peak has not been observed since the start of the RCGP weekly returns service in 1966. The 2009 summer peak ILI consultation rate was lower than that observed during the 1999/2000 winter season (231.1 per 100,000) but higher than the peak seen in the 2008/09 winter season (68.5 per 100,000) which was associated with moderately high activity mainly due to circulation of influenza A (H3).

In Scotland there was little distinction between the summer and autumn pandemic waves according to the GP ILI/ARI rate. A gradual increase was observed over the summer but the baseline of 50 per 100,000 was only exceeded in week 39 (ending 27 September 2009) when it increased from 48.6 to 51.8 per 100,000. Note that schools in Scotland finished earlier than England in week 27 (ending 5 July 2009). The highest rate observed was 66.1 per 100,000 in week 43 (ending 25 October 2009). The rate decreased to below the baseline level in week 2 (ending 17 January) when it decreased from 51.8 to 39.5 per 100,000 (figure 9). The Scottish ILI/ARI rate did not exceed the 2008/09 peak rate of 92 per 100,000. The younger age groups had the highest rates.

Figure 9: Health Protection Scotland: PIPeR daily ILI rate per 100,000 overall and by age group*, April 2009 – May 2010

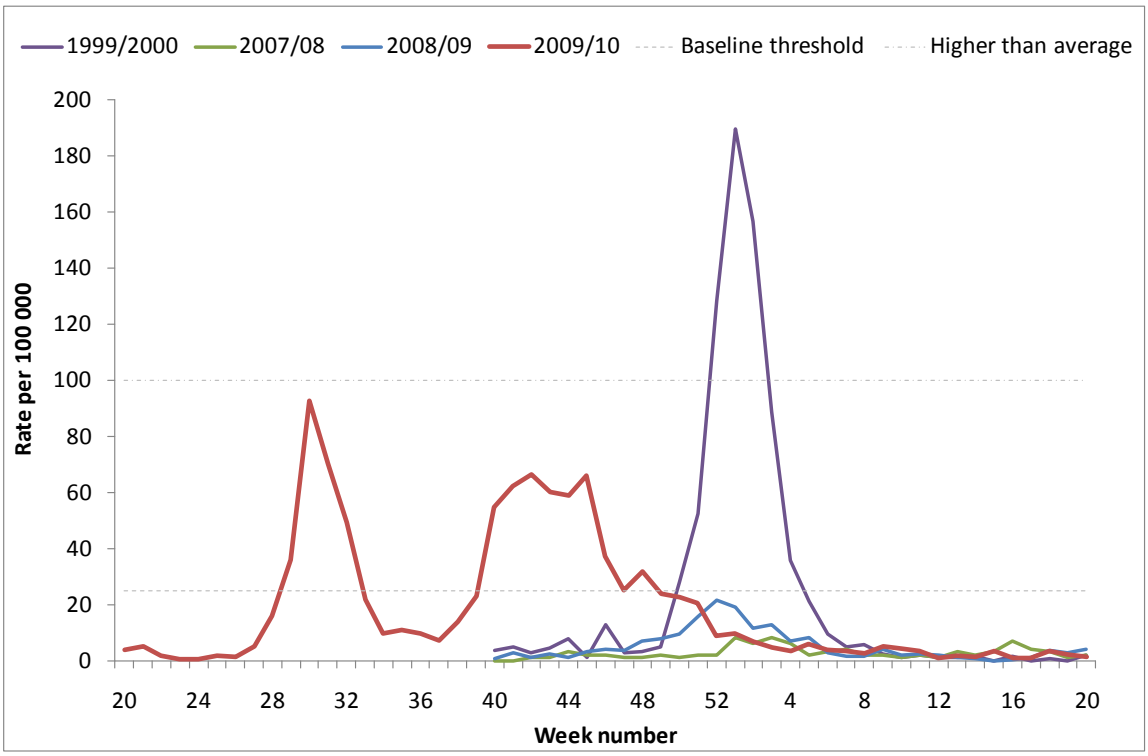


*Note differing scales on age break-down figures.

In Wales, the influenza primary care consultation rate showed a similar pattern to the RCGP ILI rate in England. The baseline level of 25 per 100,000 was exceeded for the first time in nine years in week 29 (ending 19 July 2009) when it increased from 15.8 to 36 per 100,000. The rate climbed to a peak of 92.8 per 100,000 in week 30 and rapidly declined to below the baseline by week 33 (ending 16 August 2009). For most Welsh schools, the summer term ended in week 29 (ending 19 July 2009).

After week 37 (ending 13 September 2009), the rate began to increase again exceeding the baseline once more in week 40 (ending 4 October 2009) when it increased from 22.8 to 54.8 per 100,000. A second peak of 66.2 per 100,000 was observed in week 42 (ending 18 October 2009), after which the rate declined to below the baseline level by week 49 (ending 6 December 2009) (figure 10). The highest Welsh ILI consultation rate exceeded the level seen in the 2008/09 winter (21.5 per 100,000), but was half as high as the level observed in 1999/2000 (189.5 per 100,000).

Figure 10: Wales: weekly influenza rate per 100,000, May 2009 – May 2010

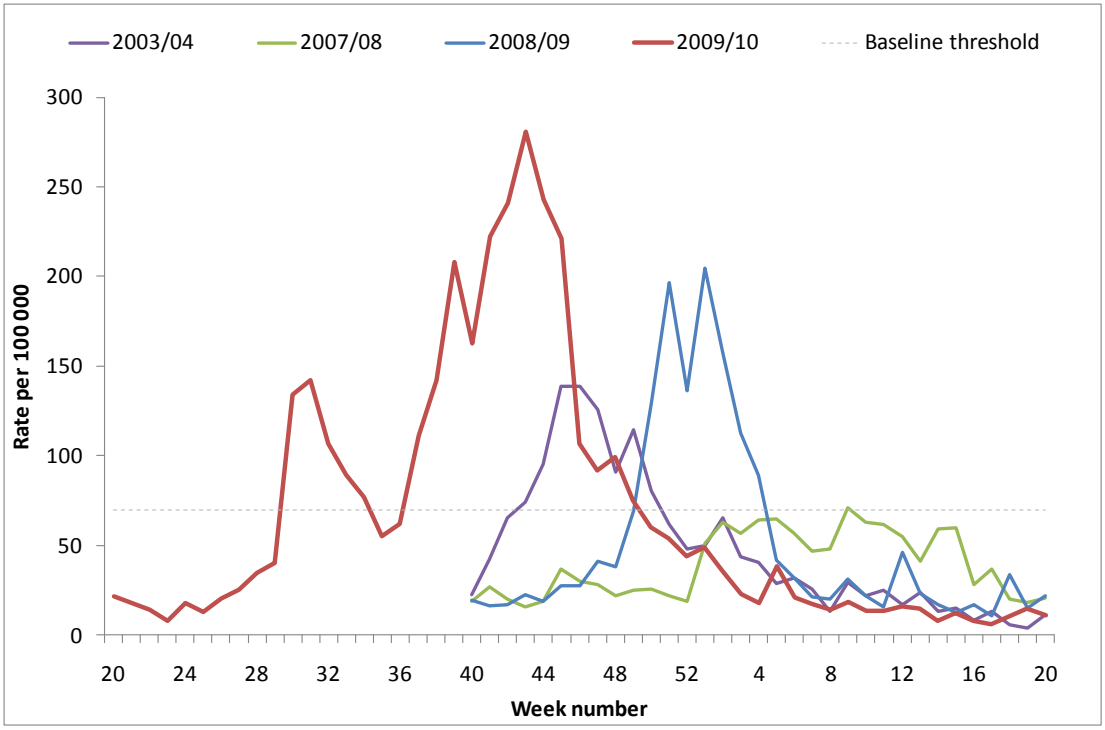


In Northern Ireland, the combined influenza/ILI rate peaked in the summer at 142.5 per 100,000 in week 31 (ending 2 August 2009). A provisional threshold of 70 per 100,000 was set for the 2009/10 influenza season and the rate was above this level for five weeks over the summer wave. The Northern Ireland school year ended in week 27 (ending 5 July 2009).

The threshold was also exceeded in the autumn in week 37 (ending 13 September 2009) when it increased from 61.9 to 113.8 per 100,000. A second peak of 280.6 per 100,000 was observed in week 43 (ending 25 October 2009) at a higher level than the summer. The rate declined to below the new baseline level by week 50 (ending 13 December 2009) (figure

11). The rate exceeded the level observed in previous years; 204.9 per 100,000 in 2008/09, though it should be noted that this system was not operational during the last large UK epidemic in 1999/2000.

Figure 11: Northern Ireland: weekly influenza/ILI rate per 100,000, May 2009 – May 2010



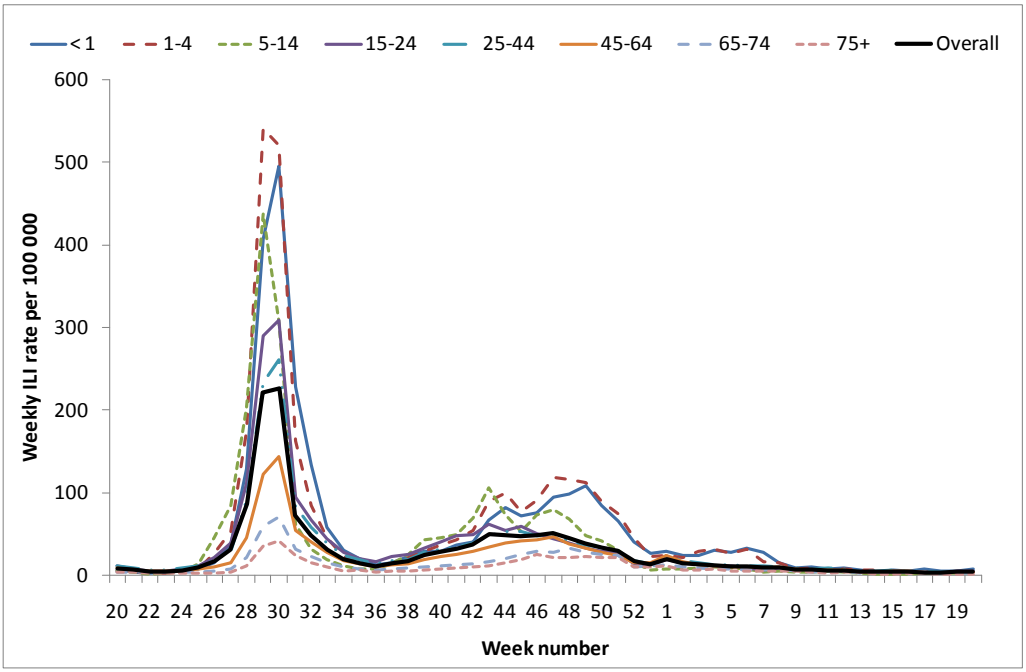
Weekly GP clinical surveillance through the HPA/QSurveillance system (England, Wales and Northern Ireland)

The weekly ILI rate for England, Wales and Northern Ireland (no Scottish data are available) through the HPA/QSurveillance system showed a similar pattern to the RCGP ILI rate. A peak of 226 per 100,000 was observed in week 30 (ending 26 July 2009), after which the rates decreased until week 36 then increased to a second peak of 50.5 per 100,000 in week 47 (ending 22 November 2009). Similar to the RCGP scheme, the autumn wave was much lower and flatter; the rate was around 50 per 100,000 from week 43 to week 48 (figure 12). This GP consultation rate was also affected by the use of the NPFS from 23 July 2009 to 11 February 2010.

By age group, the highest rate was seen in the 1-4 year group in week 29 (ending 12 July) at 541.2 per 100,000, followed by 493 per 100,000 in the under one year group in week 30 and 437.1 per 100,000 in the 5-14 year olds in week 29 (the week before English school summer holidays). All age groups peaked in week 29 or 30 in the summer wave; however a different pattern was seen in the autumn wave. The 5-14 year group peaked earliest at 105.2 per 100,000 in week 43 (ending 25 October 2009 – which was the week before the English school half-term holiday), followed by the 1-4 year group at 118.2 per 100,000 in week 47 (ending 22 November) and the under one year group at 108.9 per 100,000 in week

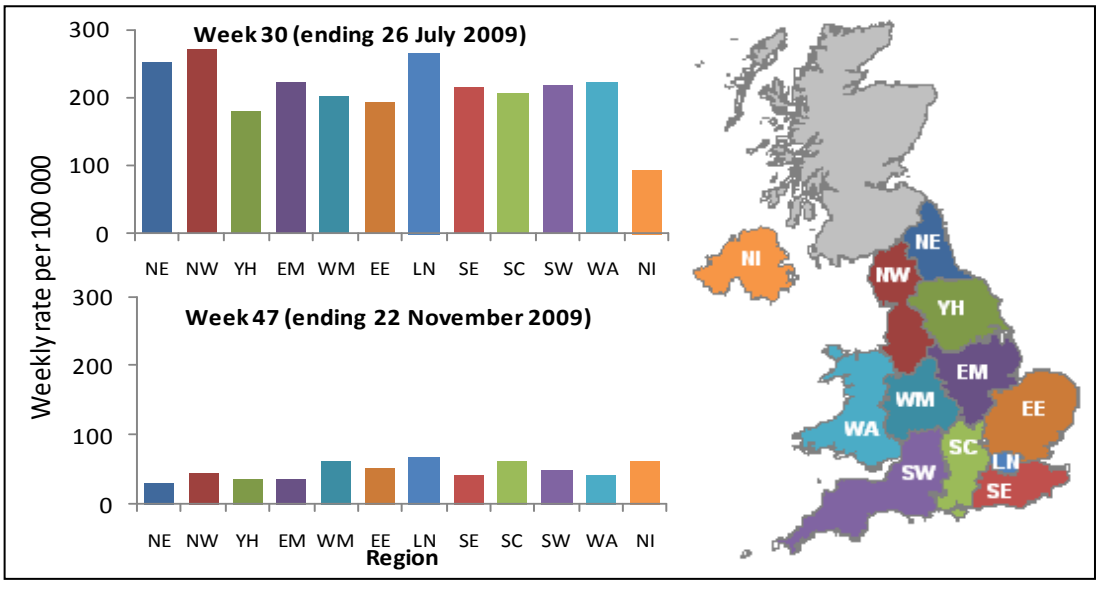
49 (ending 6 December). The lowest rates in both waves were in the older age groups over 45 years of age (figure 12)

Figure 12: Weekly ILI consultation rate through the HPA/QSurveillance system, by age group, E, W NI, May 2009 – May 2010



The London and West Midlands Strategic Health Authorities (SHA) were the first to show increases in the ILI rate, but most regions peaked in week 29 or 30 in the summer wave (appendix 2). The highest regional rate was observed in London at 310 per 100,000. In the autumn wave, the rates peaked in the Northern regions in week 43 (ending 25 October 2009), with the highest in the North East (67.3 per 100,000). Most of the central and southern regions peaked later in week 47 (ending 22 November 2009) with the highest in London at 67.3 per 100,000 (figure 13).

Figure 13: GP ILI rates through HPA/QSurveillance system by region in the peak weeks (peak of overall rate), E, W, NI

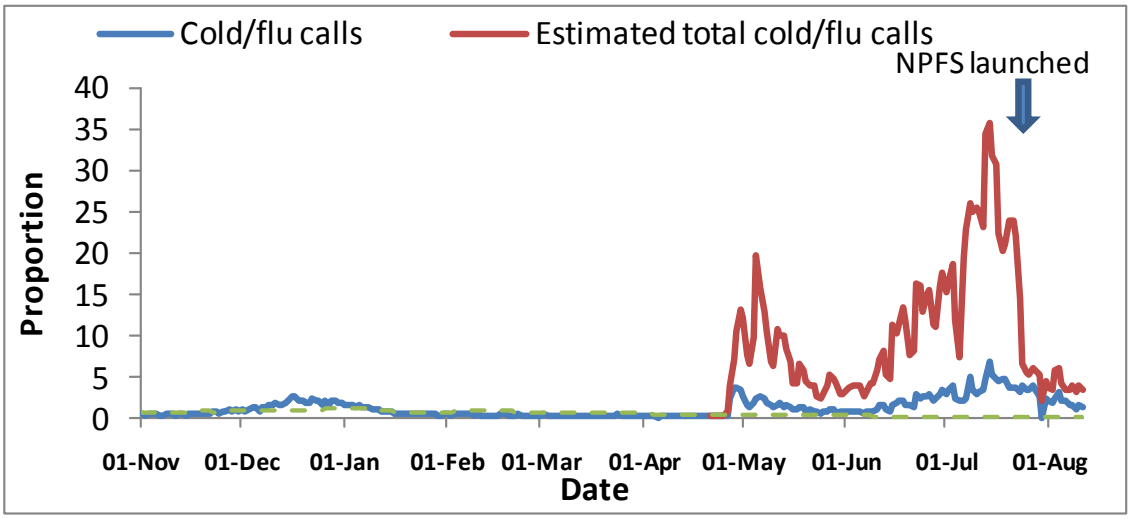


Syndromic Surveillance in the community through call/out-of-hours centres

Following the initial reports of the pandemic and the first confirmed cases in the UK at the beginning of May 2009, an early increase in cold/flu calls to NHS Direct in England and Wales was observed with a peak on 5 May 2009. This is thought to be in part due to media coverage (figure 14)

There was a further rise in cold-flu calls from early July, commensurate with evidence of community transmission. The proportion of cold/flu calls rose to a peak of 35.9% on 14 July 2009. A marked decline was then observed coinciding with the launch of the NPFS on 23 July 2009. NPFS, rather than NHS Direct, handled the majority of calls from people with an ILI in England (figure 14).

Figure 14: Daily proportion of calls due to colds/flu through NHS Direct, England and Wales, November 2008 – August 2009



From the launch of NPFS in July 2009 to February 2010, when it ceased operation, a total of 2,401,043 assessments were carried out. As a result, 1,635,948 authorisations for antivirals were issued, and 1,079,179 courses of antiviral treatment were collected in England. Assessments, authorisations and collections peaked when the service was first launched in July 2009 followed by a steady decline. In the autumn wave the peak occurred in week 43 (ending 25 October 2009) when 137,739 assessments were completed, 98,590 antiviral authorisations were issued and 66,218 antiviral courses were collected (figure 15).

In Scotland, similar to what was seen in England and Wales; there was an increase in the proportion of cold/flu calls to NHS24 during early May 2009 at a time when there was considerable media attention. A similar pattern was evident in June that may reflect the increased publicity following outbreaks in schools and the first UK death reported from Scotland, rather than evidence of widespread community transmission. Call volumes for cold/flu then increased again during July in Scotland and peaked in early August, about two weeks before the return of the schools from the summer holiday. The proportion of calls due to colds/flu increased in the beginning of October followed by a fall in early November, probably resulting from the effect of the school half-term holiday in October, before increasing once more and peaking at the end of November (figure 16).

Figure 15: Number of assessments completed, antivirals authorised and collected through the National Pandemic Flu Service, England July 2009 – February 2010

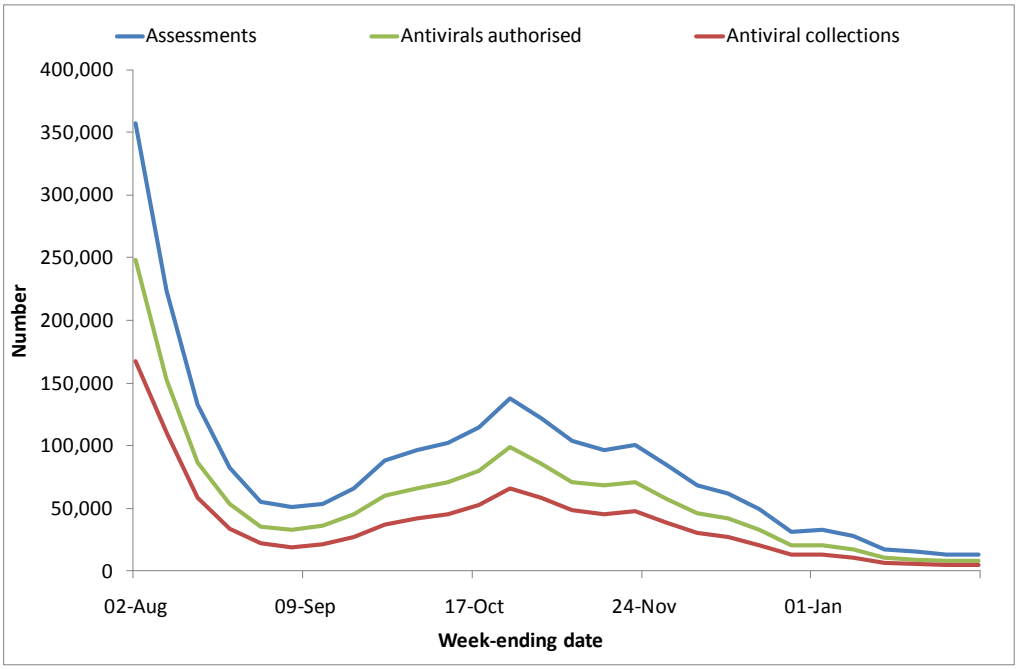
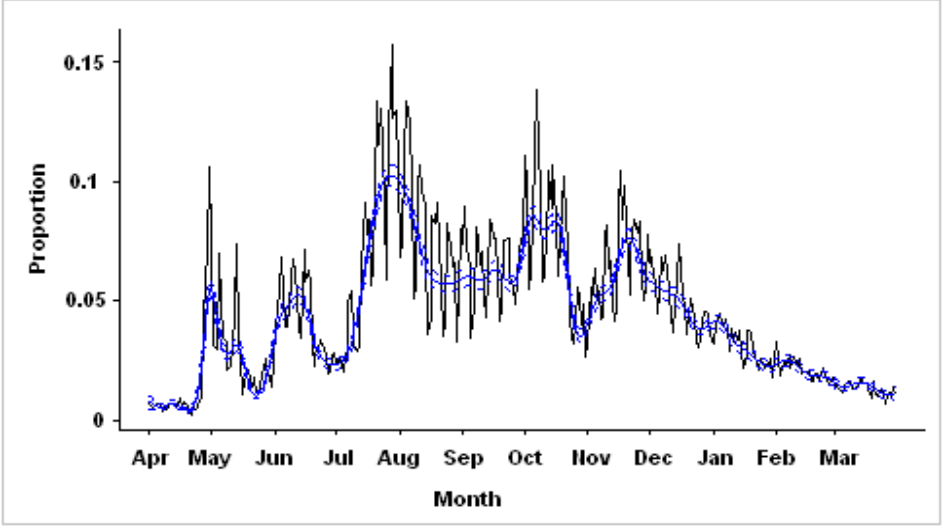


Figure 16: Daily proportion of calls due to colds/flu through NHS 24, Scotland, April 2009 – April 2010

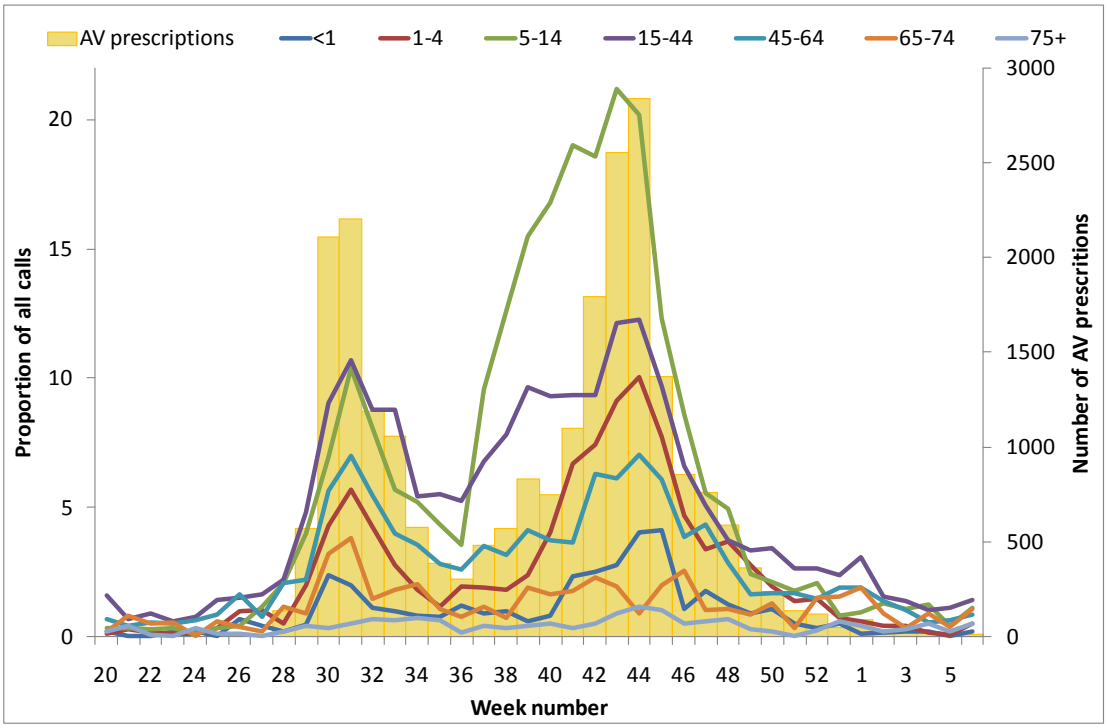


In Scotland antiviral prescribing was restricted to general practice in the treatment phase. A total of 98,000 courses of antivirals were issued across the entire pandemic. Antiviral prescribing patterns were broadly consistent with the increasing trends seen in General Practice consultations and hospital admissions. The rate of antiviral prescribing corresponded to the peak of Scotland‘s GP consultation rate in week 46.

In Northern Ireland, out-of-hours (OOH) consultation rates peaked initially in week 33 (49.6/100,000) when 7.5% of OOH consultations were due to influenza/ILI and then again in week 43 (rate 77.5/100,000) when 10.2% were due to influenza/ILI. In the first wave the highest proportion of OOH consultations due to influenza/ILI by age band was in the 15-44 year age group closely followed by the 5-14 year age group. This was in contrast to the second wave, when the proportion of influenza/ILI calls was markedly higher in the 5-14 year group. In week 43, 21.2% of OOH consultations in this age group were due to influenza/ILI (figure 17).

Trends in antiviral prescriptions closely corresponded to sentinel consultation rates and OOH calls, though the early increase in calls in the 5-14 year group was not mirrored by the prescription data (figure 17).

Figure 17: Weekly proportion of calls due to influenza/ILI of total calls to out-of-hours centres by age group (lines) and total number of antiviral prescriptions (bars), Northern Ireland, May 2009 – February 2010

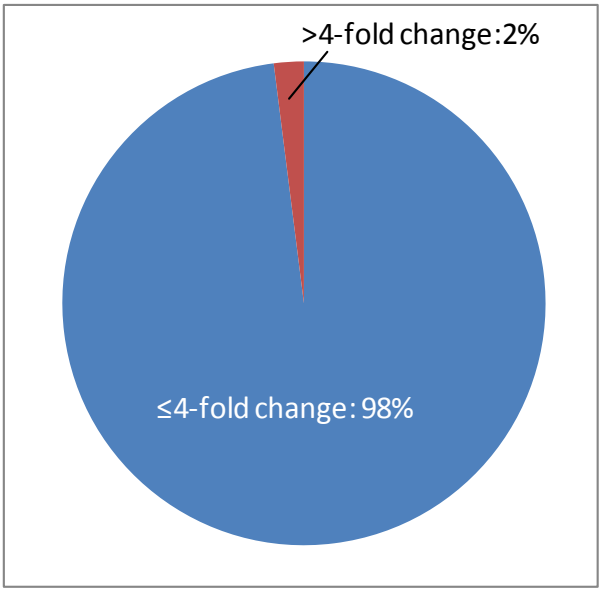


MICROBIOLOGICAL

A total of 29,228 (20,595 in England, 6,600 in Scotland, 1,369 in Northern Ireland and 664 in Wales) virologically confirmed cases of pandemic (H1N1) 2009 were reported up to 1 June 2010 (note: from July 2009 onwards, not all suspected cases were tested).

Characterisation of sentinel and non-sentinel pandemic (H1N1) 2009 viruses revealed that the majority of UK isolates were antigenically similar to the A/California/07/2009 vaccine strain. There were sporadic identifications of viruses with a greater than four-fold change in reactivity to A/California/07/2009 antiserum (2% of all isolates tested, figure 18); this change did not appear to correlate with specific amino acid substitutions in the haemagglutinin (HA) gene.

Figure 18: Antigenic reactivity with A/California/07/2009 antiserum, UK isolates, April 2009 – May 2010



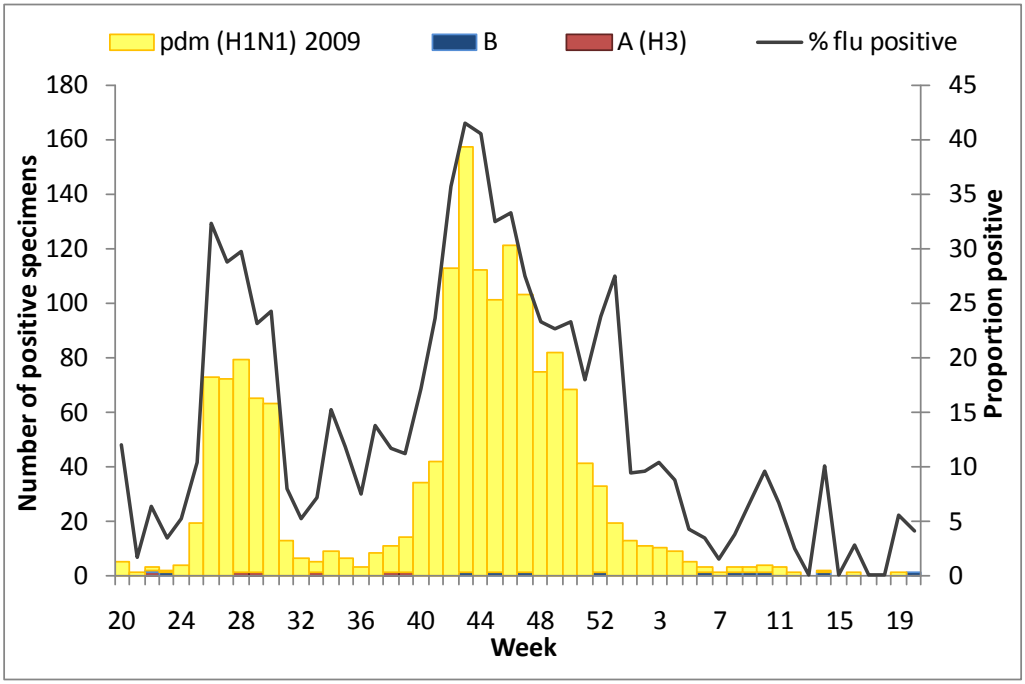
Genetic analysis of the HA gene of UK pandemic (H1N1) 2009 viruses from 2009 indicates that they are similar to the pandemic vaccine strain, A/California/07/2009. UK viruses clustered together with viruses isolated in geographically distant places, showing that there was global circulation of pandemic influenza lineages (appendix 3). The diversity seen among these viruses was less that that seen for seasonal influenza, with only 12 amino acids of difference between the two most distant viruses. All UK viruses isolated after June 2009 are characterised by substitution S203T. Other amino acid changes at residues D222E, or E374K, or N370H were also observed in the HA sequence of some UK and non-UK pandemic viruses.

From week 20 2009 to week 20 2010, an additional 78 non-pandemic influenza viruses were detected by CfI: six A (H1), four of which were detected from May to July 2009; 51 A (H3), 90% detected before October 2009 and 21 influenza B, the majority detected between January and May 2010.

Sentinel virological schemes

The proportion of samples taken by GPs in the two English sentinel schemes (RCGP/HPA and HPA/RMN schemes) positive for influenza showed two peaks corresponding to the summer and autumn waves. Unlike GP consultations, the number of positive samples and proportion positive reached higher levels in the autumn wave compared to the summer wave (figure 19). The positivity peaked at 41.2% in week 43 (ending 25 October 2009), when 156 of 379 samples were positive for pandemic (H1N1) 2009. A similar pattern was observed for the NHS Direct/NPFS schemes, with a summer and higher autumn peak (figure 19). The highest proportion positive through NHS Direct/NPFS was observed in week 44 (31.3%).

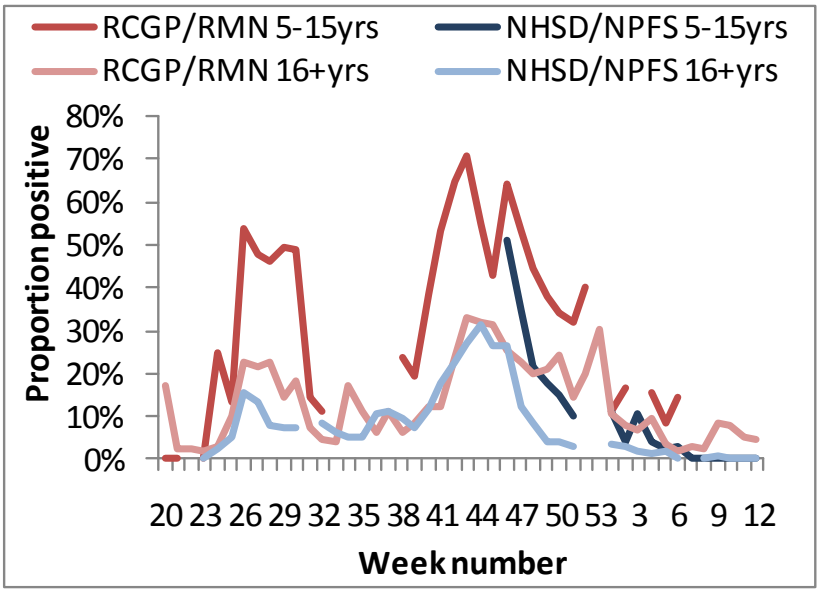
Figure 19: Samples positive for influenza through English GP sentinel virological schemes, May 2009 – May 2010



Very few specimens through the GP and self-sampling schemes tested positive for other influenza subtypes: from week 20 2009 to week 20 2010, only six influenza A (H3) and 12 influenza B viruses were detected.

The overall positivity rates through the NHS Direct and the NPFS self-sampling schemes were consistently lower than that through the GP schemes. However, children aged less than 16 years were not sampled until week 46 through NPFS; after age adjustment, the positivity rates for the GP and self-sampling schemes were largely similar (figure 20).

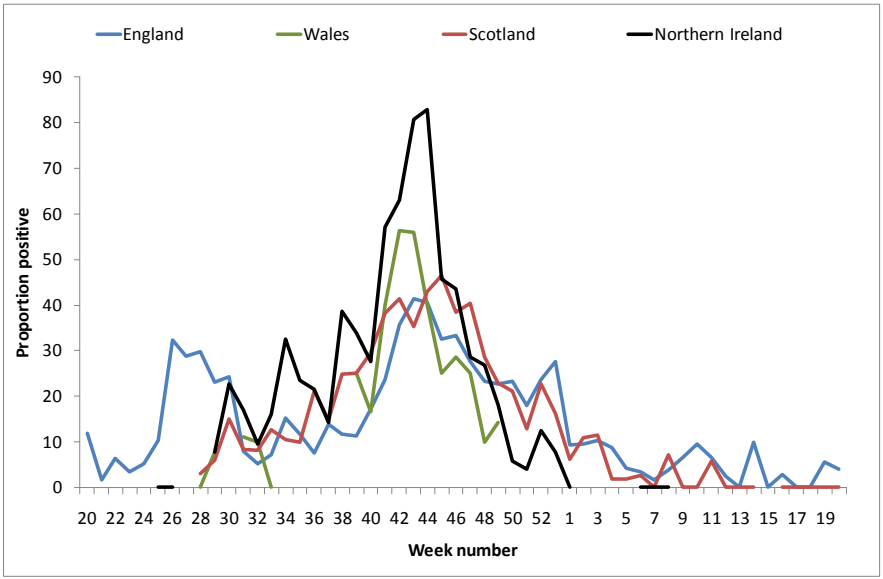
Figure 20: Samples positive for influenza through English GP and NHS Direct/NPFS sentinel virological schemes by age group, May 2009 – March 2010



NB. Sampling of children aged 5-15 years commenced through NPFS in week 46 (ending 15 November); weekly proportion positive omitted when fewer than five samples tested.

Few samples were positive for influenza through the primary care sentinel schemes in Scotland, Wales and Northern Ireland during the summer wave (figure 21). In Scotland additional sentinel swabbing centres were recruited to submit 500 samples per week across the containment phase to allow any differences within the 14 Scottish NHS boards to be identified on a weekly basis. The positivity rate increased from week 30 (ending 26 July 2009) to a peak of 46.5% positive (236/508) in week 45 (ending 8 November 2009). In Wales, a peak of 56.3% (9/16 samples positive) was observed in week 42, corresponding to the GP consultation rate peak. In Northern Ireland a peak of 82.9% (34/41 samples positive) was observed in week 44, one week after the peak in clinical activity, though the virological data from Northern Ireland is based on week of report.

Figure 21: Proportion of sentinel samples positive for influenza through GP-based schemes in the UK, by week May 2009 – May 2010



NB. All data is based on week sample was taken from the patient except in Northern Ireland, where it is the week of the reported result from the laboratory; weekly proportion positive omitted when fewer than 5

Antiviral resistance

From the beginning of the pandemic to 23 May 2010, a total of 6,379 pandemic (H1N1) 2009 viruses were analysed for the marker commonly associated with resistance to oseltamivir in seasonal influenza (H275Y). The viruses tested came from a cross-section of patients from all regions in the UK, age groups and from both community and hospital sources. The first two cases with viruses carrying this mutation were reported in week 38 (ending 20 September).

To date, a total of 45 (0.7%) pandemic cases have been found to carry this mutation in the UK; 15 of these 45 viruses have been tested phenotypically and confirmed to be resistant to oseltamivir while retaining sensitivity to zanamivir. Three hundred and thirty-eight of the 6,379 viruses have been fully tested for susceptibility to oseltamivir; all except the 15 described above have been found to be sensitive. Further information was available for 37 of the 45 resistant cases; 26 (70.3%) were male and 11 female, the ages ranged from 0 to 55 years with a median of 48 years. Thirty-one (83.8%) of the cases had an underlying medical condition: 23 (74.2%) were immunosuppressed and eight had another underlying

illness. Ten (22.2%) resistant cases are known to have died. In the majority (30 cases, 81%) of cases, resistance was treatment induced[28], although probable person-to- person transmission was documented in an outbreak in a hospital ward in Wales in November 2009[29].

Other respiratory viruses

The number of specimens reported to be positive for other respiratory viruses from hospital and regional laboratories across England and Wales was higher throughout the pandemic compared to the previous year (figure 22). This is likely to be due to increased collection and testing of respiratory samples during the pandemic from individuals presenting with acute respiratory illness to health services. There was a notable increase in rhinovirus detections over the autumn of 2009 and detections of parainfluenza were at higher levels in April 2010 than in the previous year. Detections of respiratory syncytial virus (RSV) were at slightly higher levels than the previous winter season. The peak of RSV detections was slightly later (1,164 in week 51) compared to the 2008/09 winter (759 in week 48). The highest number of detections was in children aged less than 5 years of age (figure 23).

Figure 22: Reports of samples positive for other respiratory viruses by week of specimen, England and Wales (LabBase), May 2008 – May 2010

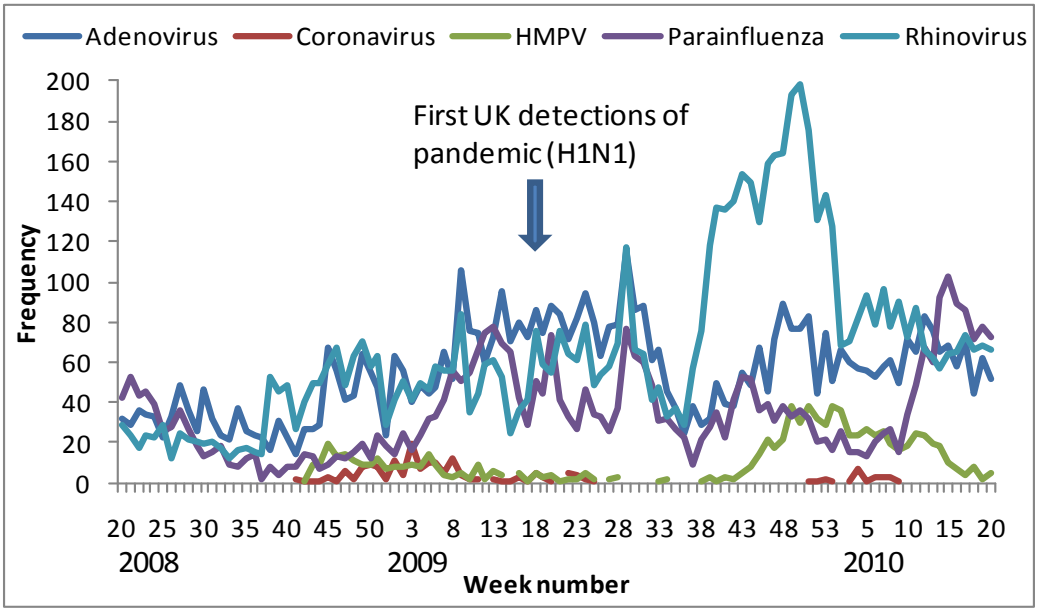
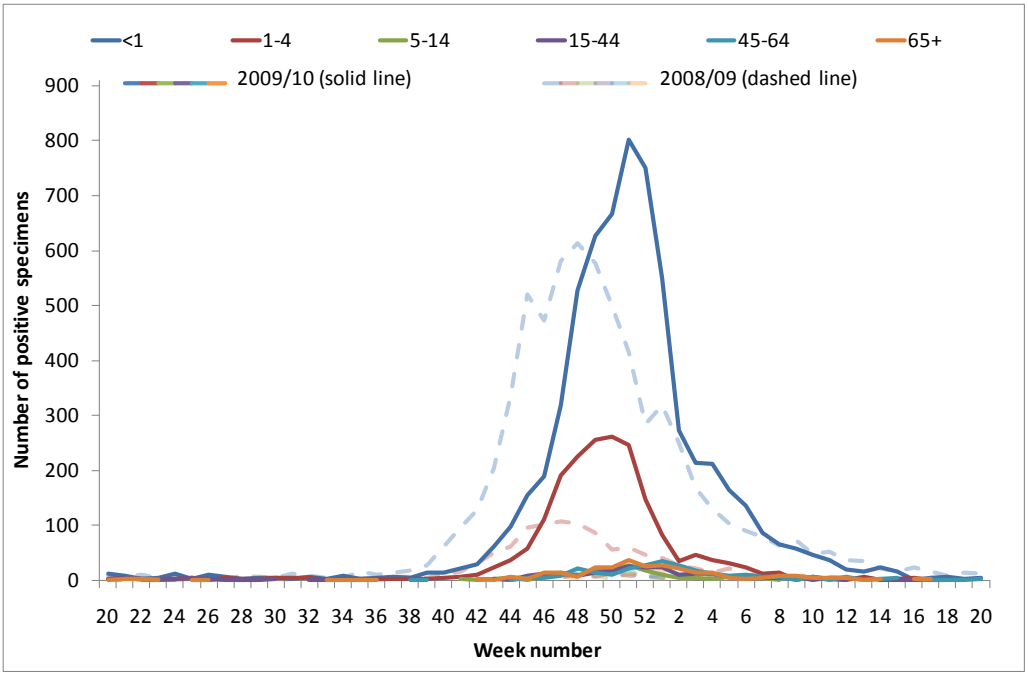
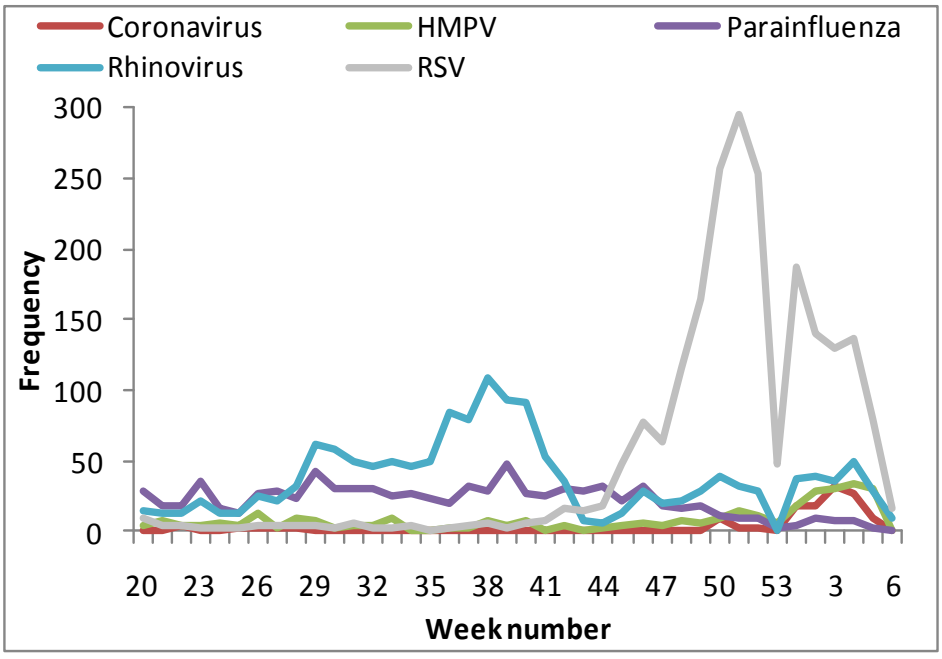


Figure 23: Reports of samples positive for respiratory syncytial virus by age group and week of specimen, England and Wales (LabBase), May 2009 – May 2010



In Scotland there was also an increase in rhinovirus detections between weeks 35 and 42 (August – October 2009). From January to March, RSV was the predominant pathogen seen, with low levels of HMPV, rhinovirus and coronavirus (figure 24).

Figure 24: Reports of samples positive for other respiratory viruses by week of specimen, Scotland May 2009 – February 2010



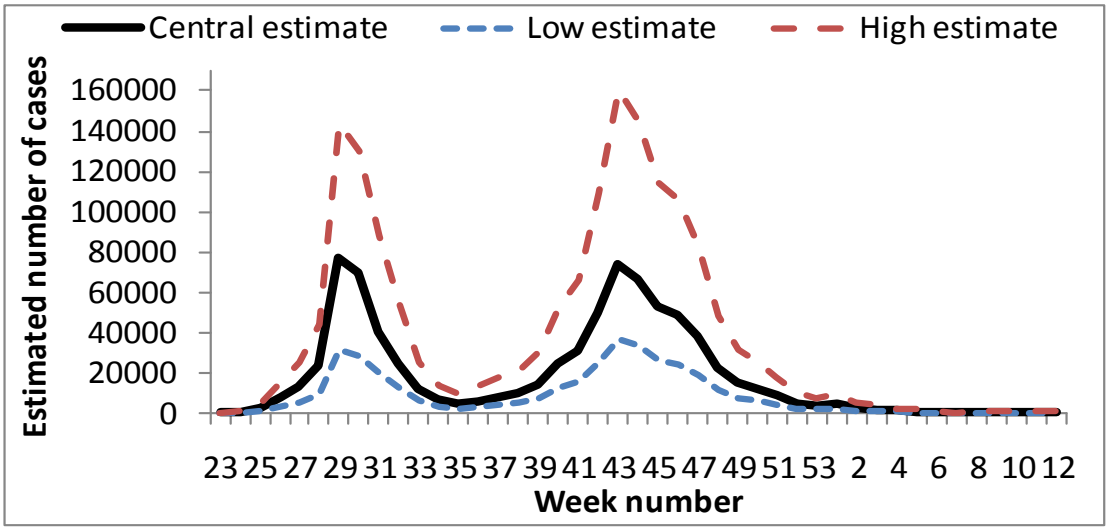
Concurrent bacterial infections

Concurrent bacterial infections (CBI) were not identified as a major feature of the pandemic. Among 20,288 confirmed English pandemic (H1N1) 2009 cases reported, a total of 76 associated CBI cases (0.4%) were identified: 39 were due to *S. pneumoniae*, 34 due to *S. aureus*, and three due to *S. pyogenes*. Twenty-four of these associated CBI cases (0.9%) were hospitalised, and 16 (4.8%) were fatal [30].

ESTIMATED CLINICAL CASES

From 7 June 2009 to 28 March 2010, a total of 784,000 (range 372,000 – 1,638,000) clinical cases of ILI due to pandemic (H1N1) 2009 were estimated to have occurred in England. The summer and autumn waves are thought to have peaked with a similar number of new cases; in week 29 (ending 19 July 2009) with an estimated 77,000 (range 31,000 – 143,000) new clinical cases and in week 43 (ending 25 October 2009) with an estimated 74,000 (range 37,000 – 160,000) clinical cases (figure 25)[31].

Figure 25: Estimated number of clinical cases in England June 2009 – March 2010



SERO-EPIDEMIOLOGY

Serological analysis of English residual population samples taken in 2008 (before the pandemic) showed that protective antibody titres increased significantly with age (*F* test $p<0{\cdot}0001$) with 31.3% (52 of 166; 24.8—38.7) of samples from adults aged 80 years or older with haemagglutination inhibition titre 1:32 or more[7]. The presence of such cross-reactive antibody in older birth cohorts explains why younger people were predominantly affected through both pandemic waves in the UK.

Comparing the proportion of English samples with haemagglutination inhibition titre equal to or above the putative threshold of 1:32 before (baseline) and after the first pandemic wave, in all regions children aged under 15 years showed a significant increase from baseline (6.3%, 1.8—12.9). In London and the West Midlands, which experienced early and intense pandemic activity compared to the rest of England, the difference between baseline and September 2009, was 21.3% (95% CI 8.8—40.3) for children younger than 5 years of age,

42.0% (26.3—58.2) for 5—14-year-olds, and 20.6% (1.6—42.4) for 15—24-year-olds. No difference between baseline and September was observed in older age groups[7]. Additional analyses for other regions and the post-second wave situation are pending.
In Scotland, serology data suggests that the proportion of people infected during the two pandemic waves varied by region, with samples from Glasgow showing a lower proportion positive than Aberdeen and Edinburgh[8].

SEVERITY INDICATORS

HOSPITALISATION

The number of people reported to be hospitalised in NHS trusts in England with suspected pandemic (H1N1) 2009 showed two peaks similar to the other surveillance indicators. The highest hospitalisation rate was consistently in children aged less than 5 years. Between July 2009 and February 2010, when this surveillance system was operational, an overall cumulative rate of 221.7 per 100,000 population (95% CI 216.4 – 227.1) was observed in children under 5 years, which was 6 times higher than in the 16-64 year group (rate ratio 5.9, 95% CI 5.7 – 6.1). The rate in the under 5 year group peaked at 17.8 (95% CI 16.3 – 19.4) per 100,000 population in week 49 when it was 10 times higher (95% CI 8.9 – 11.2) than the rate in the 16-64 year age group.

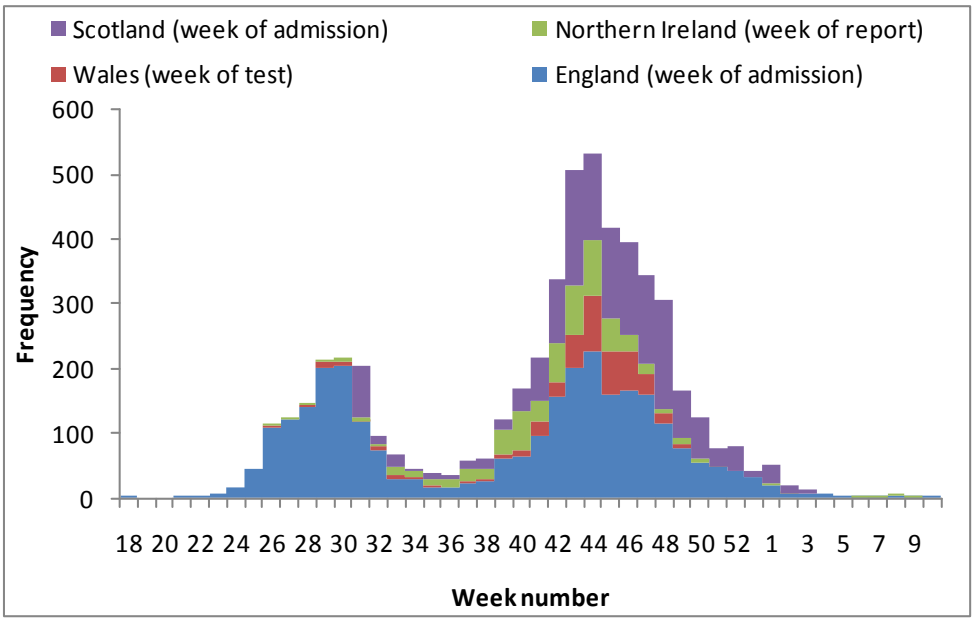
A total of 2,831 patients were reported as hospitalised with confirmed pandemic (H1N1) 2009 infection in England from the beginning of the pandemic to April 2010 through the HPA/CMO reporting system in 129 acute hospital trusts (figure 26). Thirty-eight per cent of the cases were admitted in the summer pandemic wave. In total, 55.5% of hospitalised cases with available information were reported to have an underlying risk factor for severe disease including pregnancy and obesity[32].

In Northern Ireland there were 580 hospital admissions of confirmed pandemic (H1N1) 2009 of which 51 (8.8%) occurred during the first wave (weeks 21 – 35) (figure 25), with four admissions to ICU (3.9%) The proportion of admissions of confirmed cases to ICU in the second wave was 9.1%. While the weekly hospitalisation trend closely corresponded to sentinel consultation rates in the second wave this was less so during the first wave when there were comparatively few hospitalisations. Admission rates were highest in the 0-4 year age group (109.5 per 100,000) followed by the 5-14 age group (admission rate 51.5 per 100,000)[33].

In Scotland a total of 1542 patients were hospitalised with confirmed pandemic (H1N1) 2009 infection over the period of the pandemic. The peak week for admission was week 43 (ending 25 October 2009) (figure 26).

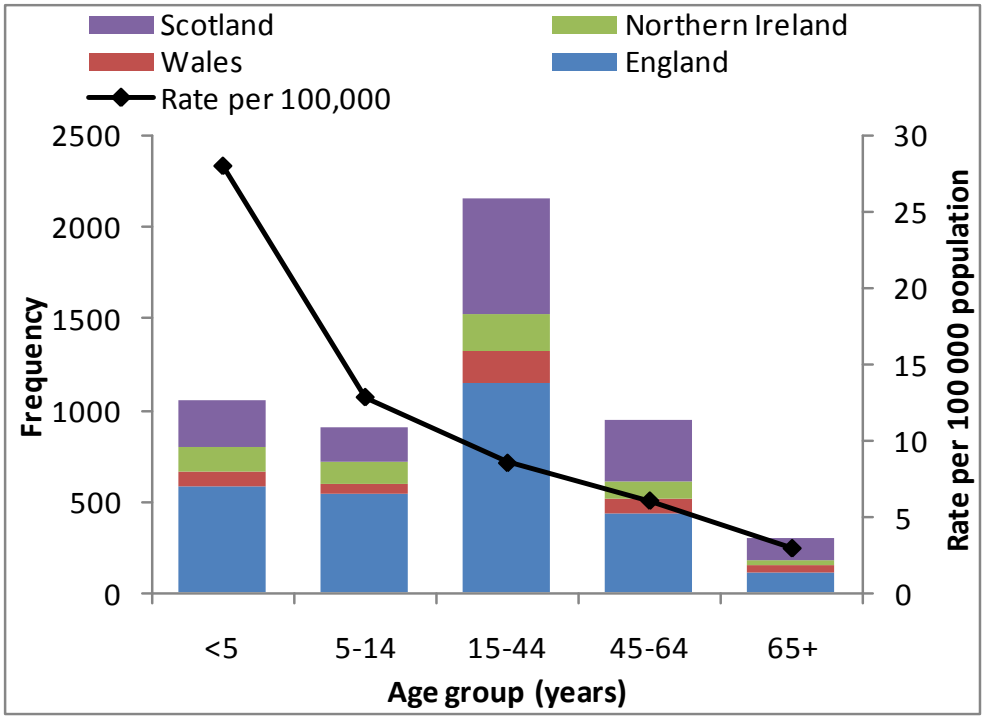
In Wales 423 patients were hospitalised with virologically confirmed pandemic (H1N1) 2009. Similar to Northern Ireland, there were few hospitalisations during the first pandemic wave; the peak of hospital admissions in Wales (by week of test) was week 44 (ending 1 November 2009) when there were 83 hospitalisations (figure 26).

Figure 26: Number of hospitalisations for confirmed pandemic (H1N1) 2009 by week and country, April 2009 – March 2010, UK



Across the UK, the hospitalisation rate decreased with age with children aged under 5 years having the highest population hospitalisation rate (28 per 100,000 for the entire UK) (figure 27).

Figure 27: Number and rate of hospitalisations with confirmed pandemic (H1N1) 2009 by age group and country, April 2009 – March 2010, UK

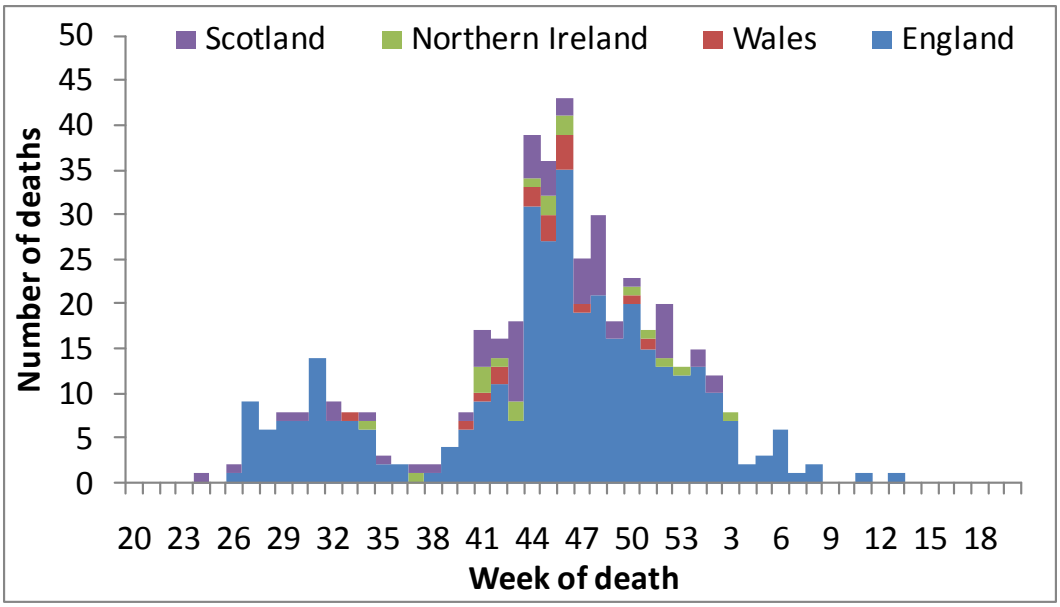


The FLU-CIN study collected information on 631 patients admitted to 55 UK hospitals with confirmed pandemic (H1N1) 2009 infection in the first wave. This in-depth study found that non-white and pregnant patients were over-represented and 45% of patients had an underlying medical condition. Of the 29 patients who died, 59% were previously healthy[14].

MORTALITY

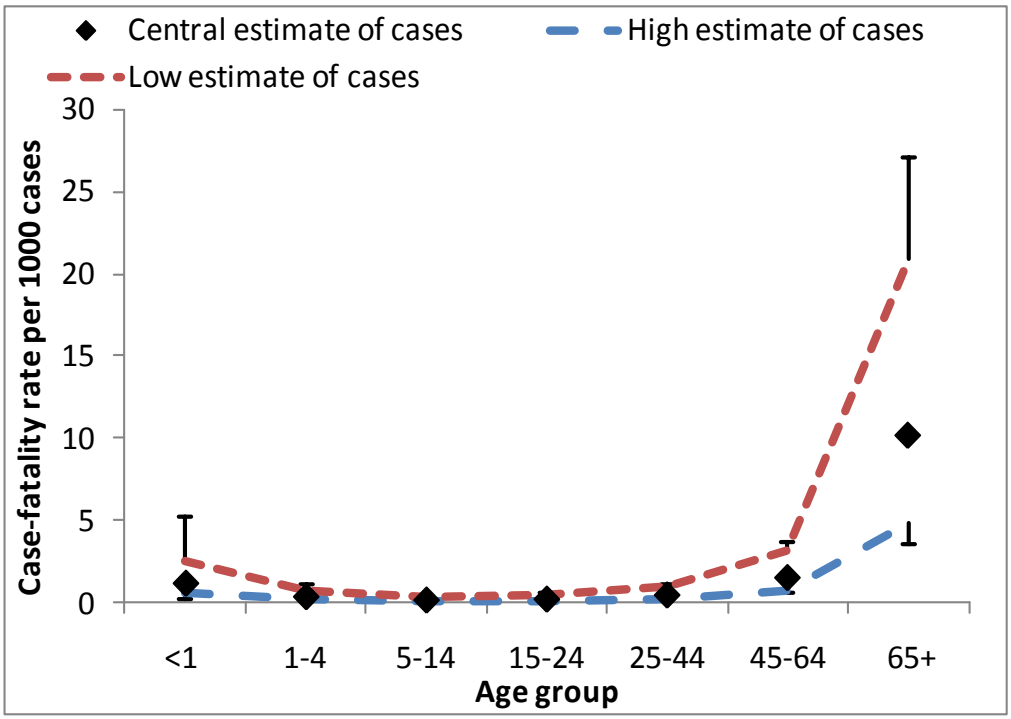
The first death due to pandemic (H1N1) 2009 in the UK occurred on 14 June 2009. A total of 474 deaths with confirmed pandemic (H1N1) 2009 (either laboratory confirmed or with mention on the death certificate) were reported in the UK up to 15 April 2010 (359 in England, 69 in Scotland, 18 in Northern Ireland and 28 in Wales). A number of deaths occurred in the spring/summer of 2009 but the majority (83%) occurred over the autumn/winter (figure 28). Seventy-two per cent of fatal cases were reported to have an underlying risk factor for severe disease[34]. [34]

Figure 28: deaths due to pandemic (H1N1) 2009 by week of death and country, UK May 2009 – May 2010 (adapted from[34])



The symptomatic case-fatality ratio was estimated to be 0.04%[34]. The majority of deaths occurred in people aged under 65 years old (85% of English deaths), though the estimated case fatality rate was much higher in older adults aged 65 years or over, in whom infection was much less common (figure 29).

Figure 29: Estimated case fatality rate by age group, England, June 2009 – April 2010



In England and Wales, no excess of weekly death registrations above the threshold was observed over the summer of 2009. In the 2009/10 winter season 3,261 (95% CI 2,993 – 3,530) excess deaths were estimated to have occurred in weeks 52 and 53 (table 3); this is unlikely to be due to influenza, as all other influenza indicators were showing low activity at that time.

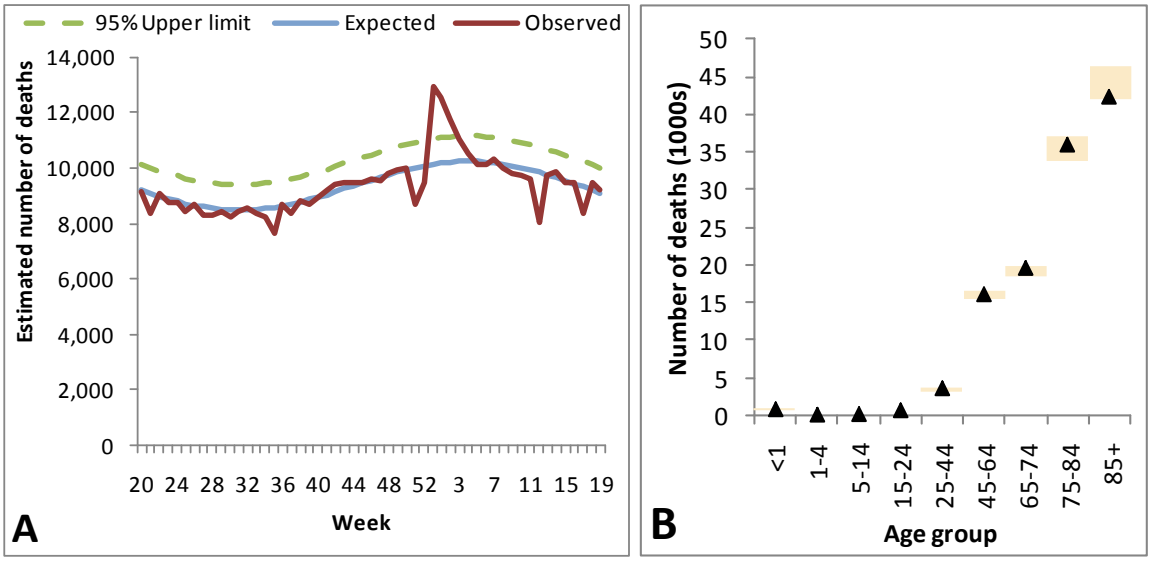
Table 3: Annual excess all-cause mortality by influenza season, 1999-2010

Season	Excess (95% CI)	Total no. of deaths	% deaths in excess
1999/2000	21227 (20690 - 21764)	395,507	5.4%
2000/2001	746 (478 - 1015)	383,805	0.2%
2001/2002	6824 (6556 - 7093)	388,552	1.8%
2002/2003	6392 (6123 - 6660)	386,946	1.7%
2003/2004	4873 (4336 - 5410)	377,242	1.3%
2004/2005	1860 (1591 - 2128)	372,259	0.5%
2005/2006	Not detected	361,910	0.0%
2006/2007	Not detected	318,775	0.0%
2007/2008	457 (0 - 994)	321,853	0.1%
2008/2009	10146 (9878 - 10588)	327,334	3.1%
Summer 2009	Not detected	170,231	0.0%
2009/2010	3261 (2992 - 3529)	315,931	1.0%

It is notable that this excess occurred in a period when the UK experienced a prolonged cold snap. Closure of registry offices over bank holidays was also temporally associated with an artefactual dip and subsequent increase at the end of December and the beginning of April (figure 30A).

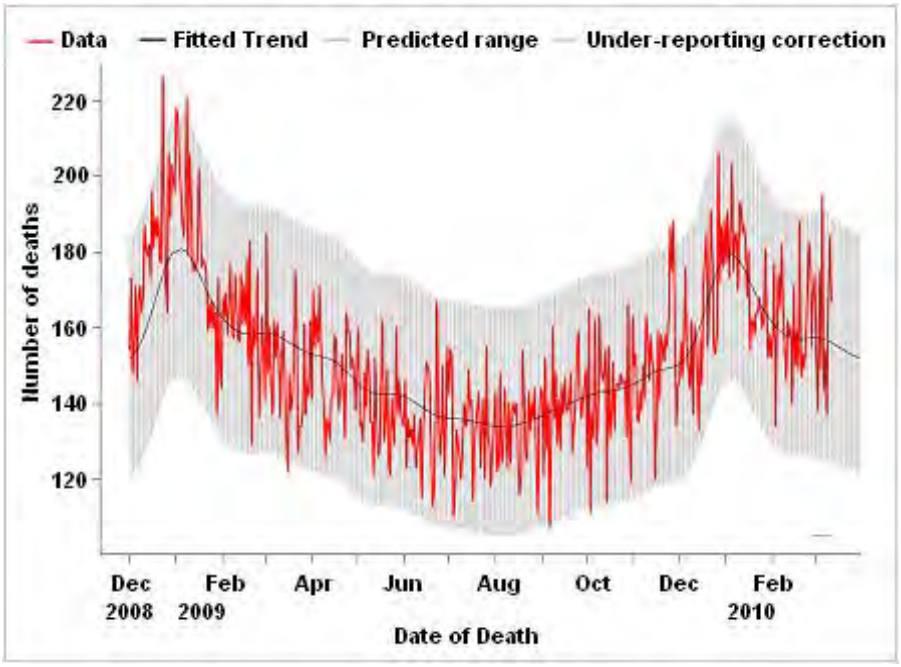
Analysis of daily mortality data made available from the General Registry Office (England and Wales) by age-group over the two pandemic waves shows that there was no evidence of any age-specific excess mortality throughout the pandemic prior to the Christmas excess (figure 30B).

Figure 30: A: all cause mortality from ONS (England and Wales) with expected number of deaths (HPA), May 2009 – May 2010; B: Age-specific mortality monitoring (GRO), shaded areas show expected range, week 37-49 (Autumn wave) England and Wales



The number of weekly Scottish deaths remained within expected ranges over the 2009 summer. There was an increase above expected levels at the end of December/ beginning of January and a slight excess of deaths at end of November. The overall pattern was similar to what was seen in England and Wales, with the excess coinciding with low influenza activity and cold weather (figure 31).

Figure 31: all cause mortality (Scotland) with expected number of deaths through the GAM method (HPS), April 2009 – May 2010



RISK GROUPS

Data from the FF100 surveillance project showed that people with underlying medical conditions, such as chronic respiratory, neurological or heart disease were not at significantly greater risk of clinical infection in the early stages of the pandemic[21]. In England, people aged between 6 months and less than 65 years with an underlying condition were 10 times more likely to be hospitalised with confirmed pandemic (H1N1) 2009 infection compared to people of the same age without an underlying condition, and 18 times more likely to die from the infection[32;34]. The underlying conditions with the highest risk of hospitalisation with pandemic (H1N1) 2009 infection were immunosuppression, chronic renal disease and chronic neurological disease (including stroke)[32]. For death, the risks were highest for chronic neurological disease (excluding stroke), chronic liver disease and immunosuppression[34]. Pregnant women were not at an elevated risk of becoming cases, but were 5 times more likely to be hospitalised and seven times more likely to die, once infected, compared to females of child-bearing age (15-44 years) with no underlying condition (table 4)[34].

Table 4: Rate ratios for hospitalisation and mortality by risk group, England adapted from [32] and [34]

	Hospitalisations			Deaths		
	N	Rate ratio	95% confidence interval	N	Rate ratio	95% confidence interval
Total	2,463			361		
Total aged 65 or over	104			56		
Any risk factor (65y+)	67	2.8	1.7 — 4.5	44	6.0	2.7 — 13.4
No risk factor (65y+)	23	Baseline		7	Baseline	
Total aged 6m-65y	2,258			300		
Any risk factor (6m-65y)	1,033	10.3	9.4 — 11	190	18.7	14.5 — 24.1
No risk factor (6m-65y)	1,028	Baseline		84	Baseline	
Chronic renal disease	58	17.2	13 — 22	16	37.7	22.0 — 64.5
Chronic heart disease	85	5.9	4.7 — 7.4	26	16.7	10.8 — 25.9
Chronic respiratory disease	601	12	11 — 13	51	11.7	8.3 — 16.6
Chronic liver disease	22	8.7	5.7 — 13	23	70.8	44.4 — 112.8
Diabetes	78	4.3	3.4 — 5.4	23	9.8	6.1 — 15.6
Immunosuppression	135	18.5	15 — 22	48	56.0	39.0 — 80.4
Stroke/TIA*			—	3	7.2	2.3 — 23.0
Chronic neurological disease*	123	14.3	12 — 17	66	115.8	85.2 — 157.5
Total females of childbearing age (15-44years)	585			63		
Females of childbearing age with no risk factor	291	Baseline		22	Baseline	
Pregnant (F15-44 only)	145	5.1	4.2 — 6.1	10	7.0	3.3 — 14.8

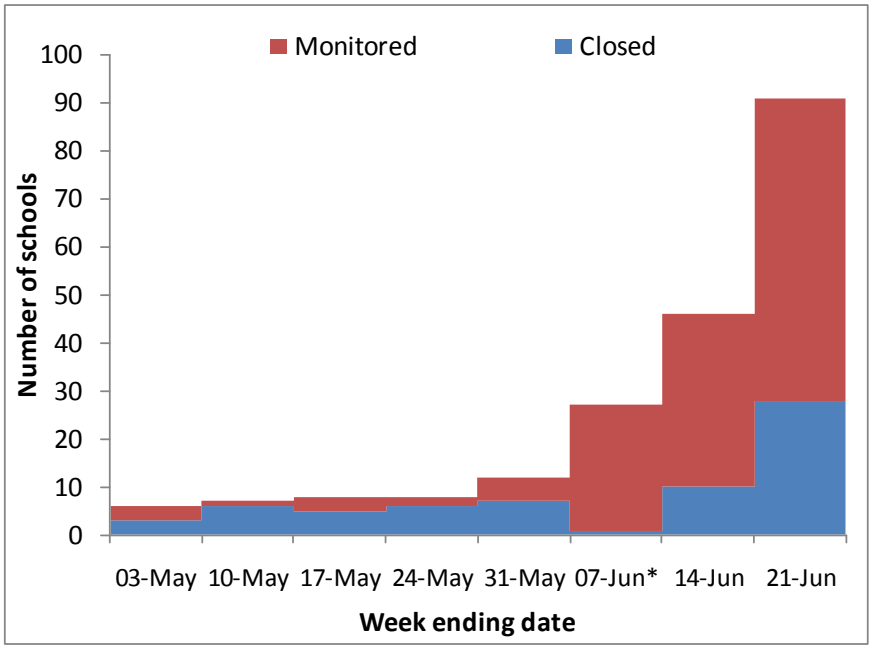
** Strokes are included under neurological disease for the hospitalisation data but are separate for mortality data*

INTERVENTIONS

SCHOOL CLOSURES

At the beginning of the pandemic, many schools were advised to temporarily close if there were confirmed cases of pandemic (H1N1) 2009 among staff or students. Antiviral prophylaxis was also given to close contacts of confirmed cases as part of the containment strategy. Up to the end of the containment phase, 74 schools in England were reported to have been closed due to pandemic (H1N1) 2009 and 417 schools reported confirmed cases to HPA. Figure 32 shows the increasing number of schools in England affected each week from the beginning of May to 21 June 2009. In Northern Ireland there were 26 school outbreaks with the last being during week 5 2010; none of these schools were closed due to the outbreak. In Scotland there were 29 school closures during the containment phase.

Figure 32: Number of schools affected by pandemic influenza, England; May – June 2009



** Half-term holiday for most schools in England; Monitored: confirmed or suspected cases in the school but remaining open, Closed: partially or total suspension of classes due to confirmed or suspected cases of pandemic influenza.*

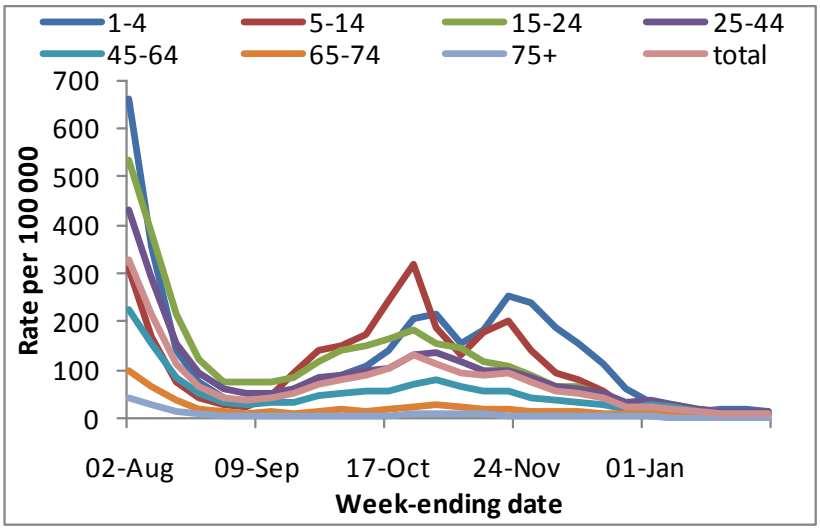
Whether individual school closures had significant effects on transmission is unclear [personal communication, H Maguire]. The closure of all UK schools for the summer holiday is likely to have played a large part in interrupting transmission over this period.

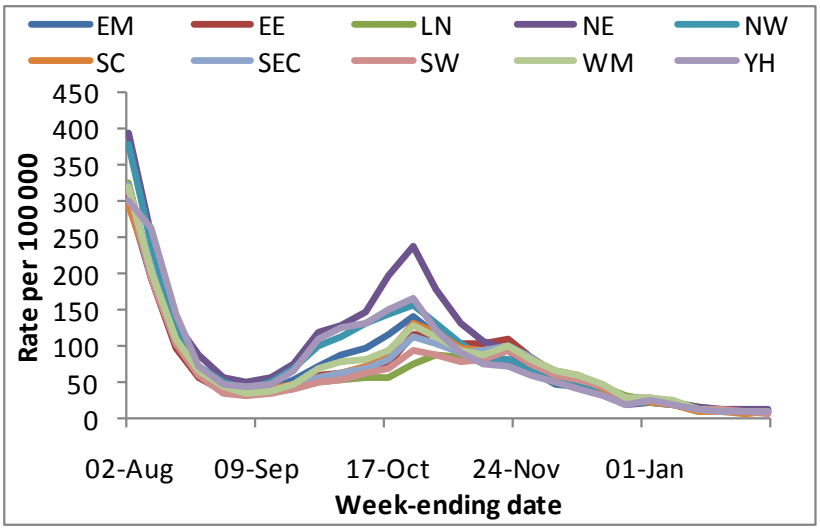
ANTIVIRALS

Uptake: Of the 365 UK FF100 cases with information available, 335 (91.8%) reported receiving treatment with antiviral drugs[21]. Of 656 contacts with available information, 595 (90.7%) reported receiving antiviral drugs[27].

Sixty-eight per cent of assessments through the NPFS (1,645,948 of 2,401,043) resulted in an authorisation for antiviral drugs being issued; of these 66% (1,079,179 [2.1% of the population]) were collected. The population rate of collection varied by region and age group. In the summer wave the rate of collection was notably higher in the North East compared to other regions and the rates were highest in children aged 1-4 and 5-14 (figure 33). Babies aged less than one year were the only age group not considered by NPFS and were always referred to their GP, as were those with underlying risk factors for severe disease.

Figure 33: weekly rate of antiviral collection, per 100,000 population through NPFS by region* and age group, August 2009 – March 2010, England





**EM: East Midlands, EE: East of England, LN: London, NE: North East, NW: North West, SC: South Central, SEC: South East Coast, SW: South West, WM: West Midlands, YH: Yorkshire and Humberside.*

A total of 24,160 courses of antivirals were issued through primary and secondary care in Northern Ireland (1.4% of the population).

In Scotland, 98,000 courses of antivirals were issued (1.9% of the population).

Effectiveness: Data from the FF100 study showed that the household secondary attack rate was significantly affected by the use of antivirals with a 92% reduction in virologically confirmed secondary attack rate at two weeks[27].

Impact: Modelling data from cases identified during the containment phase suggest that treatment of cases in association with prophylaxis of their close contacts reduced the reproduction number by an estimated 16% (95% CI 12 – 20%) in those who received the intervention; the overall population-level effect will have been smaller than this, as most affected individuals did not seek care [18].

Safety: Forty-one (12.2%) of the 335 FF100 cases who took antiviral drugs, reported side-effects which they attributed to antiviral treatment. More adults aged 16 or older (25 of 140 – 15%) than children (16 of 153 – 9.5%) reported an adverse event. Of the 17 who had specified the severity of the adverse event, 15 (88.2%) graded it as moderate and two as severe. Gastrointestinal symptoms were the most commonly reported adverse events, reported by 30 of the 41 cases reporting side-effects (11 (37.0%) children and 19 adults)[21].

VACCINATION

Pandemic vaccine uptake: In England, 37.6% of patients in clinical risk groups, including pregnant women, and 23.6% of healthy children aged six months to 5 years received the swine influenza monovalent vaccine (Pandemrix, dose 1) by 31 March 2010 [35].
In Northern Ireland and Scotland uptake was higher in all groups compared to the England data with 86.5% of people in Northern Ireland aged under 65 years in a risk group receiving the vaccine (though this does not include pregnant women of whom 57.1% received the vaccine). Welsh vaccine uptake was similar to that of England (table 5).

Table 5: Pandemic vaccine uptake, dates, by country and risk group, UK

	England*	Northern Ireland**	Scotland*	Wales***
<65 years at risk	**37.6%**	**86.5%**	**52.1% - 54.5%**	**42.1%**
Pregnant women	**Inc. above**	**57.1%**	**Inc. above**	**Inc. above**
Children <5 years	**23.6%**	**38.3%**	**44.6%**	**26.1%**
>65 years at risk	**40.4%**	**74.9%**	**56.2% - 57.4%**	**45.0%**
Health care workers	**40.3%**	**47.7%**	**55.1%**	**N/A**

** to 31 March 2010; ** to 28 February 2010, except pregnancy which is to 30 November 2009; ***to June 2010*

Pandemic vaccine effectiveness: Data from the sentinel primary care schemes in Scotland and England, gave an adjusted monovalent influenza vaccine effectiveness in excess of 70%[36].

Pandemic vaccine cost-effectiveness modelling: Modelling estimated that vaccination of high-risk groups would prevent about 45 deaths (80% credibility interval 26-67) in England, and save around 2900 quality adjusted life years (QALYs) (80% credibility interval 1600-4500). Such a vaccination programme was estimated to be cost-effective assuming the cost of the vaccine was treated as a sunk cost. Extending vaccination to school-age children was found to be the most cost-effective intervention in the model[37]. Due to the timing of the programme in relation to pandemic activity, it was unable to prevent more cases and deaths.

Seasonal vaccine uptake: In England, the uptake of the 2009/10 seasonal influenza vaccine in those aged 65 years and over reached 72.4%; a slight decrease compared to the previous season (74.1%). In those aged under 65 years falling in a clinical risk group, uptake increased from 47.1% in 2008/09 to 51.6% in 2009/10[38]. In Northern Ireland, the uptake in over 65 year-olds was similar to the previous season (77%); there was a slight decrease in Scotland (75% vs. 76.3%) and an increase in Wales (63.5% vs. 59.5%) (table 6).

Table 6: Seasonal vaccine uptake, dates, by country, UK

	England	Northern Ireland	Scotland	Wales
>65 years 2009/10 season	**72.4%**	**77.0%**	**75.0%**	**63.5%**
>65 years 2008/09 season	*74.1%*	*76.8%*	*76.3%*	*59.5%*
<65 years at risk 2009/10 season	**51.6%**	**80.0%**	**53.4%**	**49.1%**
<65 years at risk 2008/09 season	*47.1%*	*74.0%*	*47.8%*	*40.8%*

Seasonal vaccine effectiveness: There was no evidence that the 2008/09 nor 2009/10 seasonal influenza vaccines had any significant effect on infection with pandemic influenza[39;40].

Season vaccine 2010/11 season: The World Health Organization recommended that the 2010/11 northern hemisphere vaccine contain an A/California/7/2009 (H1N1)-like virus (pandemic), an A/Perth/16/2009 (H3N2)-like virus and a B/Brisbane/60/2008-like virus[41]. In the UK, pregnant women who have not previously received the pandemic vaccine are recommended to receive the trivalent vaccine, in addition to the normal groups (over 65 year-olds, those in risk groups, HCWs, carers etc.). There are also some groups who are recommended to receive the monovalent pandemic vaccine[42].

Discussion and conclusions

Following the emergence of pandemic (H1N1) 2009 in North America in April 2009, imported cases of this novel virus were quickly identified across the UK. The first cases were mainly travellers returning from Mexico or the United States and secondary cases linked to indigenous transmission among close contacts in households and schools. Two waves of pandemic activity were observed, separated by the closure of schools for summer holidays, which appears to have reduced transmission (appendix 1). Community transmission was initially observed in London and the West Midlands following large school outbreaks. Cases were reported from all UK regions in the summer wave, though there was a variable level of transmission; all regions of the UK were affected in a more uniform way during the autumn wave. Most cases were reported to have a mild illness consistent with influenza. Severe disease, hospitalisations and deaths were reported in a minority of cases, particularly among those with underlying clinical disease. There was an overall low case-fatality ratio, particularly compared to previous pandemics. Clinical counter-measures were employed across the UK, with evidence that antivirals were effective in reducing transmission and disease severity. Pandemic vaccine was effective, though uptake only increased in the second half of the autumn wave.

Although the first European cases of pandemic (H1N1) 2009 were confirmed in Spain on April 27 2009 and most European countries had reported cases by the end of May 2009[43], the UK and Ireland were the only European countries reporting high influenza activity during the summer of 2009[44]. In this respect there was greater similarity with other northern hemisphere countries such as the USA and Canada. Indeed, the UK has significantly more air traffic from North America compared to most European countries and thus experienced multiple introductions during spring 2009 onwards, which may be one of the explanatory factors. The main wave of pandemic influenza activity in Europe occurred in the autumn, with many countries, including the UK, reporting levels of activity higher and earlier than in recent seasons[45].

Evidence gathered from the FF100 project showed that most cases experienced a mild, typical influenza-like illness, with fever and respiratory symptoms reported most frequently[21]. A significant proportion of cases reported gastrointestinal symptoms – an observation that was also seen in other geographic settings, including those where antivirals (a potential confounding factor) were used less widely [46]. To optimise its positive predictive value, a strict case definition was used initially based on clinical (fever and respiratory symptoms) and epidemiological (recent travel to an affected area or contact with a confirmed or suspected case) criteria. This meant that people who did not fulfil these definitions, for example cases with milder clinical symptoms, may not have been tested; they would have been missed, underestimating the number of infections.

Compared to seasonal influenza, pandemic (H1N1) 2009 tended to affect younger people. Serological studies have demonstrated evidence of widespread infection in the population during the pandemic particularly in younger age-groups. People older than 50 years of age had evidence of cross-reactive H1N1 antibodies due to exposures to influenza A (H1N1) prior to 1957, explaining the lower age-specific attack rates in this group [7;8]. Other sero-epidemiology studies elsewhere have demonstrated similar findings[47].

The UK‘s containment approach recommended the use of antiviral drugs for all symptomatic confirmed cases and their close contacts. This may have slowed the initial spread of the virus, as suggested by transmission and modelling studies, but any impact is likely to have been small. Furthermore, use of antivirals in the early treatment of cases significantly reduced the severity of illness – in terms of duration of illness[21], risk of hospitalisation[14] and risk of ICU admission[32]. Despite this intervention, a number of patients were hospitalised and died due to pandemic influenza. Although people aged over 65 were less likely to acquire the infection, once infected they were more likely to have a more severe outcome compared to younger cases. People with underlying clinical conditions were also more likely to have a severe outcome, as would be expected with seasonal influenza. As has been found in other countries, pregnant women were also at higher risk of severe outcomes[48]. A significant minority of hospitalised and fatal cases did not have any underlying condition.

On 10 August 2010, the Director-General of the World Health Organization announced that the world had moved into the post-pandemic period[49]. For the forthcoming 2010/11 season, the pandemic (H1N1) 2009 virus is expected to behave as a normal seasonal influenza virus, continuing to circulate, perhaps along with other seasonal influenza viruses, for some years to come. The WHO has recommended vigilance regarding future activity due to the pandemic (H1N1) 2009 virus, particularly as it is likely that the virus will continue to cause serious disease in a minority of younger age groups and people in high-risk groups[50].

With the declaration of the post-pandemic phase, the focus is on normalisation of influenza surveillance. There is still, however, a requirement to monitor influenza activity for a potential resurgence and to ensure any possible increase in clinical indicators is rapidly identified and investigated. As outlined, during the pandemic a number of additional surveillance systems were developed to provide a more complete picture of influenza and broader respiratory virus activity. Several of these will be incorporated into the standard suite of influenza surveillance activities and be maintained beyond the current pandemic in particular a sentinel hospital pilot surveillance system for severe disease and the laboratory denominator surveillance system for influenza and other respiratory viruses.

In conclusion, pandemic (H1N1) 2009 caused moderate to high levels of influenza activity in the UK during summer 2009, a period when activity is usually at low levels, and in the autumn of 2009. Although the illness caused was generally mild, there were significant hospitalisations and intensive care admissions and some fatalities, particularly among younger people and those with underlying clinical risk factors. In some areas large proportions of the community are thought to have been infected, though this is likely to vary across the country. The pandemic virus was consistently the predominant influenza virus circulating and appeared to replace previously circulating A (H1N1) viruses. Experience from the 2010 winter season in the Southern Hemisphere suggests that H1N1 will continue to circulate in the coming winter season in the Northern Hemisphere, possibly with other seasonal influenza viruses. Unless there is significant antigenic drift, impact is unlikely to be as large as that observed in 2009/10.

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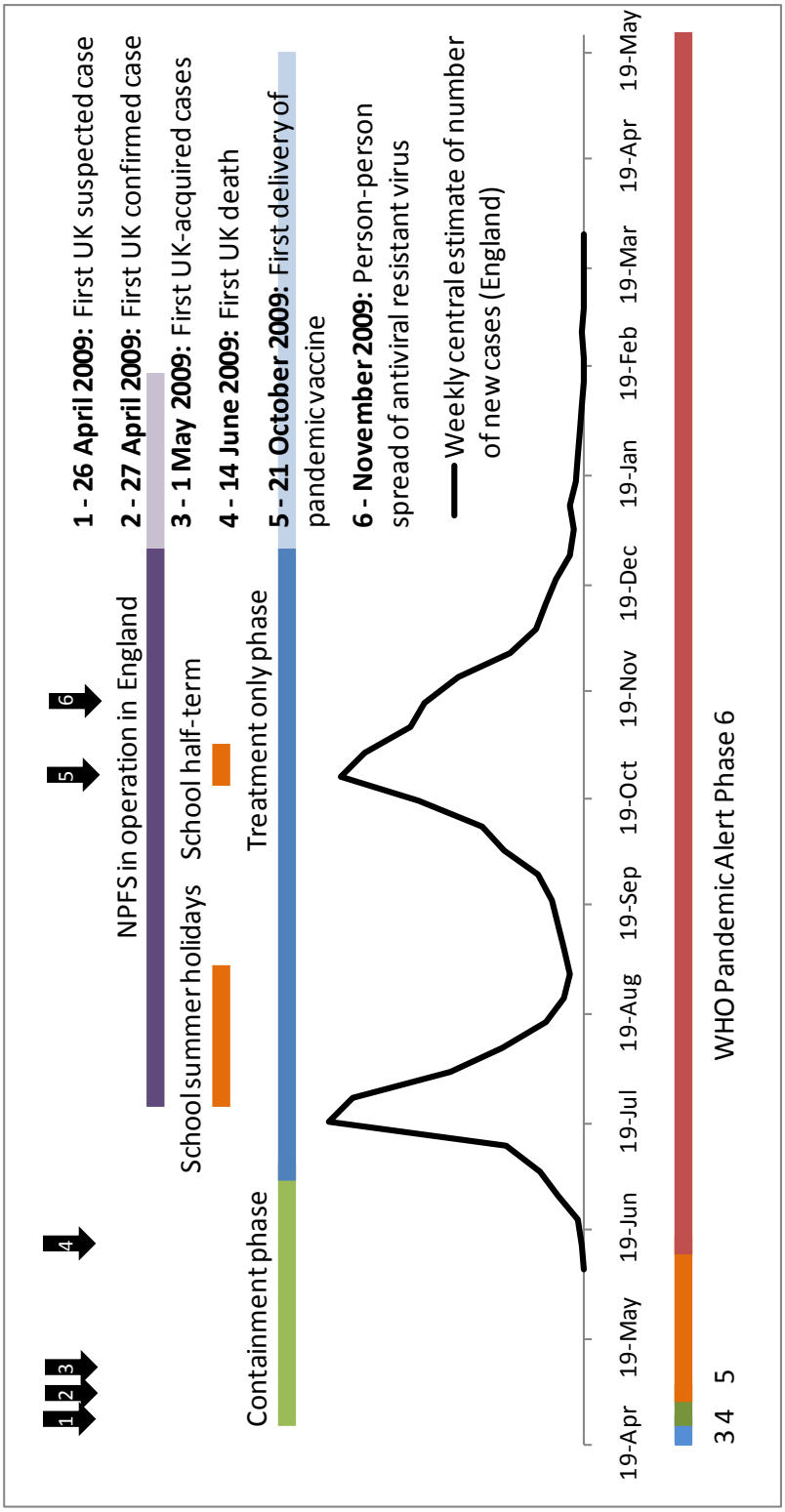
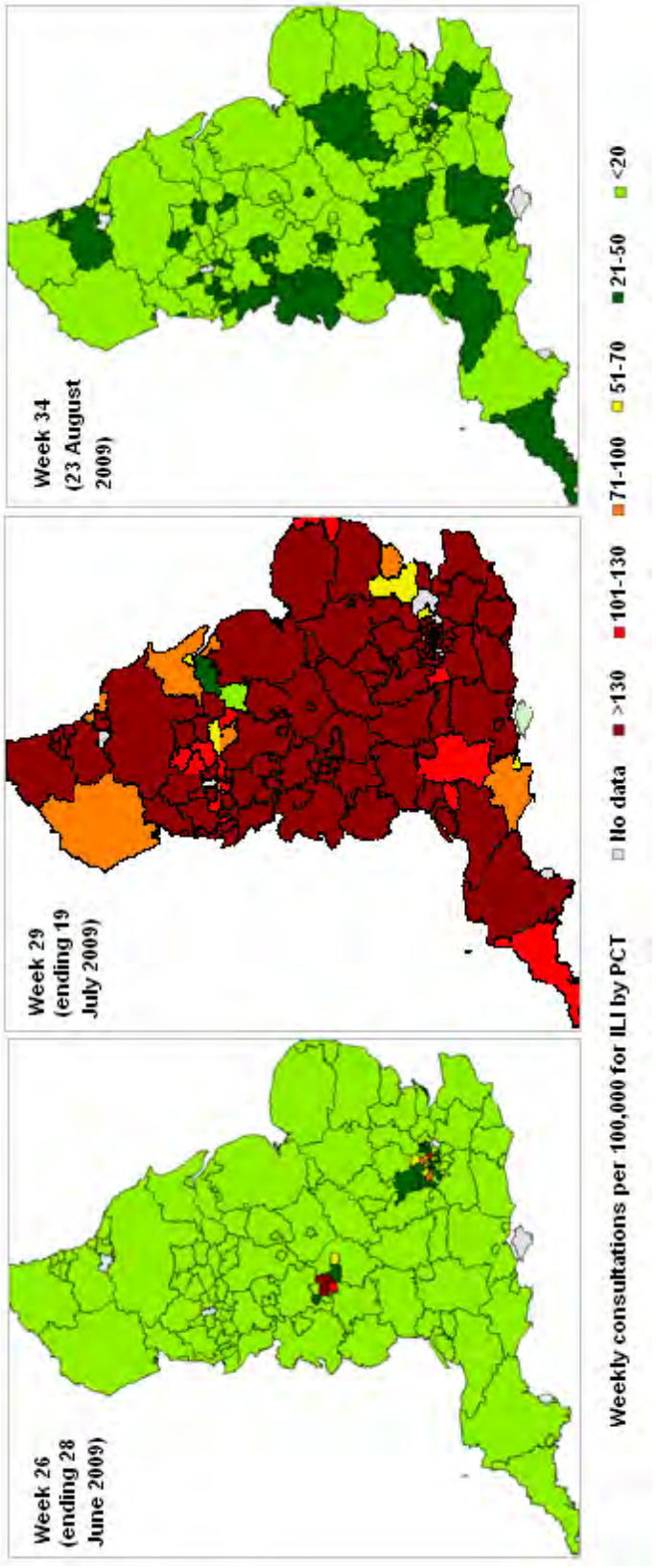
Appendix 1

Timeline of key epidemiological events of the pandemic in the UK, with HPA estimated number of clinical cases (England), April 2009 – May 2010.



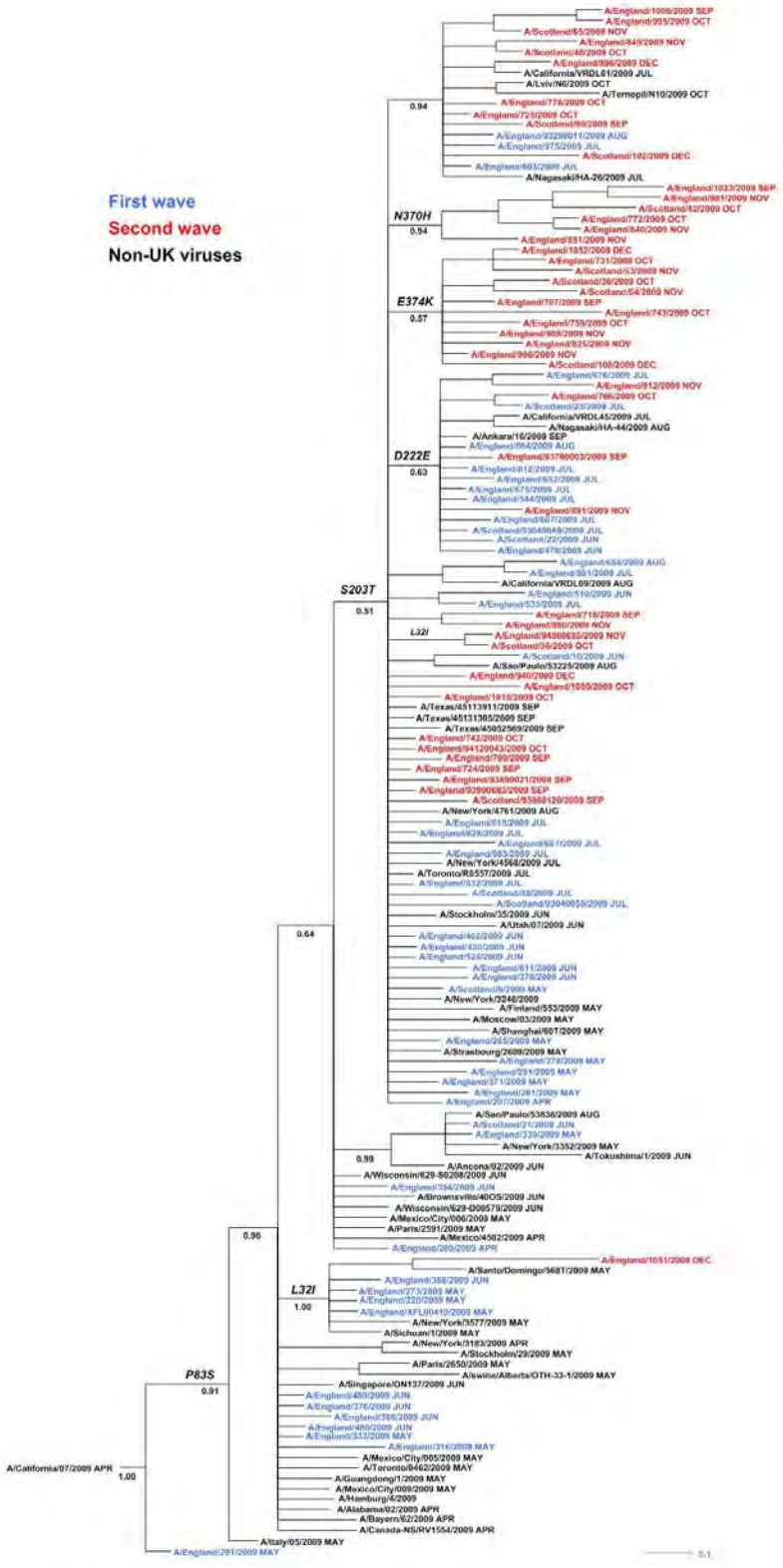
Appendix 2

PCT maps from HPA/QSurveillance system displaying GP incidence rates for ILI per 100,000. The maps illustrate the initial spread in the West Midlands and London regions during week 26, the widespread ILI activity during the peak of the first wave (week 29) and the cessation of activity following the first wave (week 34).



Appendix 3

Phylogenetic tree for pandemic (H1N1) 2009 HA sequences, April – December 2009.



References

(1) Health Protection Agency (2009). National weekly influenza report. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1246433639498.

(2) Centers for Disease Control and Prevention (2009). Swine influenza A (H1N1) infection in two children--Southern California, March-April 2009. MMWR Morbidity and Mortality Weekly Report 58: 400-402. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0421a1.htm.

(3) Centers for Disease Control and Prevention (2009). Outbreak of swine-origin influenza A (H1N1) virus infection - Mexico, March-April 2009. MMWR Morbidity and Mortality Weekly Report 58: 467-470. Available online: http://www.cdc.gov/mmwR/preview/mmwrhtml/mm58d0430a2.htm.

(4) World Health Organization (2009). Transcript of statement by Margaret Chan, Director-General of the World Health Organization, 11 June 2009. Available online: http://www.who.int/mediacentre/influenzaAH1N1_presstranscript_20090611.pdf.

(5) Health Protection Agency (2009). Pandemic (H1N1) 2009 in England: an overview of initial epidemiological findings and implications for the second wave. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1258560552857.

(6) Health Protection Agency (2009). The First Few Hundred (FF100) Project: Epidemiological Protocols for Comprehensive Assessment of Early Swine Influenza Cases in the United Kingdom. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1257260453727.

(7) Miller E, Hoschler K, Hardelid P et al (2010). Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet 375: 1100-1108. Available online: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)62126-7/abstract.

(8) Adamson WE, Maddi S, Robertson C et al (2010). 2009 pandemic influenza A(H1N1) virus in Scotland: geographically variable immunity in Spring 2010, following the winter outbreak. Euro Surveill 15: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19590.

(9) Goddard NL, Kyncl J, Watson JM (2003). Appropriateness of thresholds currently used to describe influenza activity in England. Commun Dis Public Health 6: 238-245.

(10) Cooper DL, Verlander NQ, Elliot AJ et al (2009). Can syndromic thresholds provide early warning of national influenza outbreaks? J Public Health (Oxf) 31: 17-25. Available online: http://jpubhealth.oxfordjournals.org/cgi/content/full/31/1/17?view=long&pmid=18032426.

(11) Ellis J, Iturriza M, Allen R et al (2009). Evaluation of four real-time PCR assays for detection of influenza A(H1N1)v viruses. Eurosurveillance 14: pii: 19230. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19230.

(12) Elliot AJ, Powers C, Thornton A et al (2009). Monitoring the emergence of community transmission of influenza A/H1N1 2009 in England: a cross sectional opportunistic survey of self sampled telephone callers to NHS Direct. BMJ 339: b3403. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2733951/?tool=pubmed.

(13) Health Protection Agency (2009). Method used to estimate new pandemic (H1N1) 2009 influenza cases in England in the week 3 August to 9 August 2009. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1250150839845.

(14) Nguyen-Van-Tam JS, Openshaw PJ, Hashim A et al (2010). Risk factors for hospitalisation and poor outcome with pandemic A/H1N1 influenza: United Kingdom first wave (May-September 2009). Thorax 65: 645-651. Available online: http://thorax.bmj.com/content/65/7/645.long.

(15) Serfling RE (1963). Methods for current statistical analysis of excess pneumonia-influenza deaths. Public Health Rep 78: 494-506.

(16) Office of National Statistics (2009). Population estimates for UK, England and Wales, Scotland and Northern Ireland. Available online: http://www.statistics.gov.uk/hub/release-calendar/index.html?newquery=*&uday=0&umonth=0&uyear=0&title=Population+Estimates+for+UK%2C+England+and+Wales%2C+Scotland+and+Northern+Ireland&pagetype=calendar-entry.

(17) Office of National Statistics (2009). Birth Statistics. Available online: http://www.statistics.gov.uk/downloads/theme_population/FM1-37/FM1_37_2008.pdf.

(18) Ghani AC, Baguelin M, Griffin J et al (2009). The Early Transmission Dynamics of H1N1pdm Influenza in the United Kingdom. PLoS Curr Influenza RRN1130. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2780827/?tool=pubmed.

(19) Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales et al (2009). Epidemiology of new influenza A (H1N1) virus infection, United Kingdom, April-June 2009. Eurosurveillance 14: pii:19232. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19232.

(20) Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales et al (2009). Epidemiology of new influenza A(H1N1) in the United Kingdom, April-May 2009. Eurosurveillance 14: pii: 19213. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19213.

(21) McLean E, Pebody RG, Campbell C et al (2010). Pandemic (H1N1) 2009 influenza in the UK: Clinical and epidemiological findings from the First Few Hundred (FF100) cases in the United Kingdom. Epidemiol Infect doi:10.1017/S0950268810001366.

Available online: http://journals.cambridge.org/action/displayFulltext?type=6&fid=7828773&jid=&volumeId=&issueId=-1&aid=7828772&bodyId=&membershipNumber=&societyETOCSession=&fulltextType=RA&fileId=S0950268810001366.

(22) Carrat F, Vergu E, Ferguson NM et al (2008). Time lines of infection and disease in human influenza: a review of volunteer challenge studies. Am J Epidemiol 167: 775-785. Available online: http://aje.oxfordjournals.org/cgi/content/full/167/7/775?view=long&pmid=18230677.

(23) Ihekweazu C (2010). Clinical spectrum of disease caused by novel Pandemic (H1N1) 2209 in a closed population setting: a sero-epidemiological study. Slide session at the International Conference on Emerging Infectious Diseases, Atlanta 2010.

(24) Calatayud L, Kurkela S, Neave PE et al (2009). Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. Epidemiology and Infection 138: 183-191. Available online: http://journals.cambridge.org/action/displayFulltext?type=6&fid=6879892&jid=&volumeId=&issueId=02&aid=6879888&bodyId=&membershipNumber=&societyETOCSession=&fulltextType=RA&fileId=S0950268809991191.

(25) Health Protection Agency West Midlands H1N1v Investigation Team (2009). Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. Eurosurveillance 14: pii: 19264. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19264.

(26) Smith A, Coles S, Johnson S et al (2009). An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. Euro Surveill 14: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19263.

(27) Pebody RG, Collaborative UK FF100 Group (2010). Effectiveness of anti-virals in reducing household transmission of Pandemic Influenza A (h1N1) 2009 in the United Kingdom during the"Containment" phase. Poster presented at the International Conference on Emerging Infectious Diseases, Atlanta 2010.

(28) Calatayud L (2010). Oseltamivir resistant pandemic (H1N1) 2009 virus infection in England and Scotland, 2009- 2010. Presentation at Health Protection Conference 2010.

(29) Gulland A (2009). First cases of spread of oseltamivir resistant swine flu between patients are reported in Wales. BMJ 339: b4975. Available online: http://www.bmj.com/cgi/content/full/339/nov23_2/b4975?view=long&pmid=19933735.

(30) Degail M (2010). Concurrent invasive bacterial infections in confirmed Pandemic (H1N1) 2009 influenza cases in England, 2009- 2010. Presentation at Health Protection Conference 2010 Available online: http://www.healthprotectionconference.org.uk/.

(31) Evans B, Charlett A, McLean E et al (2010). H1N1 case number estimates for England - first and second waves 2009. Poster presentation at 'H1N1: The world responds to a 21st century pandemic conference', London 2010.

(32) Campbell C, Mytton OT, McLean E (2010). Two waves of hospitalisation with pandemic influenza in England. Submitted for publication.

(33) Sfetcu O (2010). Hospitalised patients with 2009 H1N1 influenza in Northern Ireland (NI), June 2009-February 2010. Poster presentation at 'H1N1: The world responds to a 21st century pandemic conference', London 2010.

(34) Pebody RG, McLean E, Zhao H et al (2010). Pandemic Influenza A (H1N1) 2009 and mortality in the United Kingdom: risk factors for death, April 2009 to March 2010. Euro Surveill 15: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19571.

(35) Sethi M, Begum F, Gates P et al (2010). National pandemic H1N1 influenza vaccine uptake in clinical risk groups in England – winter season 2009/10. Poster presentation at Health Protection Conference 2010.

(36) Pebody RG (2010). Epidemiology of the 2009 H1N1 pandemic. Presentation at Health Protection Conference 2010 Available online: http://www.healthprotectionconference.org.uk/.

(37) Baguelin M, van Hoek AJ, Jit M et al (2010). Vaccination against pandemic influenza A/H1N1v in England: a real-time economic evaluation. Vaccine 28: 2370-2384. Available online: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD4-4Y6V99S-1&_user=8810565&_coverDate=03%2F11%2F2010&_rdoc=1&_fmt=high&_orig=search&_sort=d&_docanchor=&view=c&_acct=C000046143&_version=1&_urlVersion=0&_userid=8810565&md5=d2880d48d4e4cb6977d5a4983f258d19 .

(38) Begum F, Pebody RG on behalf of the Health Protection Agency and Department of Health (2010). Seasonal influenza vaccine uptake among the 65 years and over and under 65 years at risk in England, Winter season 2009-10. Available online: http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_118542.pdf.

(39) Hardelid P, Fleming D, McMenamin J et al (2010). Effectiveness of pandemic and seasonal influenza vaccine in preventing pandemic influenza A (H1N1) 2009 infection in England and Scotland 2009-2010. Submitted for publication.

(40) Pebody RG, Andrews N, Waight P et al (2010). No effect of 2008/09 seasonal influenza vaccination on the risk of pandemic H1N1 2009 influenza infection in the UK. Submitted for publication.

(41) World Health Organization (2010). Recommended viruses for influenza vaccines for use in the 2010-2011 northern hemisphere influenza season. Available online: http://www.who.int/csr/disease/influenza/recommendations2010_11north/en/index.html.

(42) Davies S, Beasley C, Ridge K (2010). The influenza immunisation programme 2010/11. Professional letter, Department of Health website. Available online: http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Professionalletters/Chiefmedicalofficerletters/DH_116507.

(43) World Health Organization (2009). Pandemic (H1N1) 2009: Countries, territories and areas with lab confirmed cases and number of deaths as reported to WHO as of 27 May 2009. WHO website. Available online: http://gamapserver.who.int/mapLibrary/Files/Maps/GlobalSubnationalMasterGradcolour_weekly_20090527.png.

(44) European Centre for Disease Prevention and Control (2009). Weekly electronic bulletin Week 32: 03 August 2009 - 09 August 2009. ECDC website. Available online: http://ecdc.europa.eu/en/activities/surveillance/EISN/Newsletter/SUN_EISN_INFL_Bulletin_2009week32.pdf.

(45) European Centre for Disease Prevention and Control (2009). Weekly influenza surveillance overview: week 40. ECDC website. Available online: http://ecdc.europa.eu/en/publications/Publications/091016_EISN_Weekly_Influenza_Surveillance_Overview.pdf.

(46) Dawood FS, Jain S, Finelli L et al (2009). Emergence of a novel swine-origin influenza A (H1N1) virus in humans. New England Journal of Medicine 360: 2605-2615. Available online: http://www.nejm.org/doi/full/10.1056/NEJMoa0903810.

(47) Centers for Disease Control and Prevention (2009). Serum cross-reactive antibody response to a novel influenza A (H1N1) virus after vaccination with seasonal influenza vaccine. MMWR Morbidity and Mortality Weekly Report 58: 521-524. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5819a1.htm.

(48) Centers for Disease Control and Prevention (2009). Novel influenza A (H1N1) virus infections in three pregnant women - United States, April-May 2009. MMWR Morb Mortal Wkly Rep 58: 497-500. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5818a3.htm.

(49) World Health Organization (2010). H1N1 in post-pandemic period. Director-General's opening statement at virtual press conference. Available online: http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html.

(50) World Health Organization (2010). WHO recommendations for the post-pandemic period. Available online: http://www.who.int/csr/disease/swineflu/notes/briefing_20100810/en/index.html.

Health Protection Agency

Epidemiological report of pandemic (H1N1) 2009 in the UK

April 2009 – May 2010

HSC Public Health Agency

Health Protection Scotland

GIG CYMRU NHS WALES

RCGP Royal College of General Practitioners

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Summary

Following the emergence of the novel pandemic (H1N1) 2009 influenza virus in North America in April 2009, the first UK cases were reported on 27 April 2009. Several existing and new surveillance systems were used to investigate the first cases, to monitor the unfolding pandemic and to measure the impact and effectiveness of the various counter-measures that were implemented in the UK.

Most confirmed cases appeared to have experienced a largely typical influenza-like illness. A minority suffered serious disease. Children were most affected; adults aged over 50 years had evidence of some pre-existing immunity, with much lower clinical attack rates.

Two waves of pandemic activity, separated by the closure of schools over the summer, were observed. The first wave peaked in mid/late-July 2009. The regions most affected initially were the West Midlands, London and central Scotland, mainly due to several early large school-based outbreaks in the former two areas. England and Wales experienced higher activity levels in the first wave compared to Scotland and Northern Ireland, which may be due to earlier closure of Scottish and Northern Irish schools for summer holidays. The second wave started with the return to school in the autumn with a peak in mid-October 2009.

All viruses characterised were similar to the California/07/2009 strain. The pandemic (H1N1) 2009 virus was the main circulating strain: from week 20 2009 to week 20 2010, of 3059 influenza viruses detected by the HPA Respiratory Virus Unit, only 78 (2.5%) were non-pandemic viruses. Through GP sentinel surveillance, the highest weekly proportion of ILI cases positive for pandemic influenza was in Northern Ireland, where it reached 83% in week 44 (ending 1 November 2009). In England, the highest rate was 43% (week 43 2009), in Scotland 47% (week 45 2009) and in Wales 57% (week 42 2009).

The first reported UK death due to pandemic influenza occurred on 14 June 2009. The majority of hospitalisations and deaths were in people aged less than 65 years. The symptomatic case-fatality ratio was estimated to be 0.04%. People with an underlying medical condition, for which influenza vaccination is recommended by the Department of Health, did not seem to be at a greater risk of acquiring the infection, but were estimated to be 10 times more likely to be hospitalised and 18 times more likely to die than those without any underlying condition. In England, Wales and Scotland, no excess all-cause mortality was observed over the summer of 2009. In the 2009/10 winter season excess mortality was observed in weeks 52 and 53; influenza is unlikely to be the main explanation as all other influenza indicators showed low activity at the time and these deaths were concentrated in the elderly.

Antiviral drugs were offered to those presenting with clinical symptoms of influenza during the treatment phase in the UK. In England and Scotland the number of courses collected during the treatment phase covered about 2% of the population and in Northern Ireland enough were prescribed through primary and secondary care to cover 1.4% of the population. Of 6,379 viruses tested, only 45 (0.7%) were found to carry a mutation known to confer resistance to the antiviral drug oseltamivir. Most cases of resistance were thought to be treatment-induced. Antiviral drugs as treatment significantly reduced the median duration of illness and, as prophylaxis and treatment, reduced the household secondary attack rate.

Some side-effects attributed to the antiviral drugs were reported; mainly gastrointestinal symptoms.

There was no evidence that the 2008/09 seasonal influenza vaccine significantly affected risk of acquisition of pandemic (H1N1) 2009 infection. The UK 2009/10 seasonal influenza vaccination programme went ahead as normal. For all people aged over 65 years uptake ranged from 64% in Wales to 77% in Northern Ireland, and for those under 65 years in an underlying clinical risk group uptake ranging from 49% in Wales to 80% in Northern Ireland. The monovalent pandemic vaccine programme was initiated in October 2009, initially recommended for front-line health care workers and people of all ages with underlying medical conditions, including pregnancy. These recommendations were extended to all healthy children aged from 6 months to under 5 years in December 2009. The uptake of pandemic influenza vaccine in people at risk (including pregnant women) was 38% in England, 52-55% in Scotland and 42% in Wales. In Northern Ireland the uptake in this group (excluding pregnant women who had a 57% uptake) was 87%. Preliminary data from routine GP sentinel influenza surveillance in England and Scotland shows that pandemic influenza vaccine was effective in preventing confirmed influenza infection.

The post-pandemic phase was declared by WHO on 10 August, 2010. For the forthcoming 2010/11 season, the virus is expected to behave as a normal seasonal influenza virus, though vigilance for changes in the virus, the disease caused, or groups affected should be maintained.

Contents

Introduction

In the United Kingdom (UK), surveillance of influenza and other respiratory viruses is undertaken by the Health Protection Agency (HPA), Health Protection Scotland (HPS), Public Health Agency Northern Ireland and Public Health Wales. Data are collated from a variety of surveillance systems to provide timely information on which influenza strains are circulating, to ascertain which have epidemic potential, and to contribute towards the decision on influenza vaccine composition for the following season. Surveillance activities also produce timely reports[1] for health professionals, the media and the public on influenza activity and spread, burden of disease and the uptake and effectiveness of the main clinical counter-measures (in particular vaccination and antivirals).

Surveillance occurs throughout the year with a focus on the winter season between October (week 40) and May (week 20). Following the identification of the first cases of a novel swine influenza virus in April 2009 in Mexico and the United States[2;3], the UK embarked on an initial "containment" strategy during May and June (see Box 1). In an effort to mitigate the impact of the pandemic, during the containment phase all symptomatic cases were ascertained through enhanced surveillance, and those who met the clinical and epidemiological case definition, were followed up, laboratory confirmed and their close household and non-household contacts traced. *Antiviral drugs were recommended for early treatment of all confirmed cases and post-exposure p*rophylaxis offered to identified close contacts. Selective school closures were also recommended during the containment phase.

Box 1: Key actions during the containment and treatment only phases in the UK, adapted from[5]

Containment phase

- Diagnosis by laboratory confirmatory testing
- Suspected cases treated with antivirals and requested to self-isolate at home
- Household/close contacts of suspected cases traced
- Close contacts offered antiviral prophylaxis if index case laboratory confirmed; contacts advised to self-isolate only if they became clinically ill
- Risk assessment dependent closure of schools for 7 days if confirmed case(s) identified; treatment of clinically ill patients with antivirals
- Close contacts of confirmed/suspected cases in confirmed school outbreaks offered anti-viral prophylaxis

Treatment-only phase

- Diagnosis by clinical illness; laboratory testing not required
- Clinical cases offered antiviral treatment through consultation with healthcare professional or National Pandemic Flu Service (NPFS); emphasis on treatment for persons in higher risk groups
- Contacts of cases not offered prophylaxis apart from special circumstances (e.g. household member with serious underlying health problem)

In June 2009, WHO declared a global influenza pandemic[4], the first for over four decades.

In June, significant community transmission developed in a number of UK regions, in particular in London, the West Midlands and central Scotland. At the beginning of July 2009, with evidence of community transmission, the UK moved to a 'treatment-only phase' of cases to manage the pandemic. This phase focussed on provision of antivirals to people presenting with clinical respiratory illness (without the need for confirmatory testing) through primary and secondary care and the telephone and web-based National Pandemic flu Service (in England). Surveillance continued throughout this period to monitor trends, burden of disease and changes in the characteristics of the virus and the uptake and effectiveness of the pandemic influenza vaccine programme that was implemented in autumn 2010.

This report describes influenza activity in the UK from the beginning of the pandemic (end of April 2009) to week 20 2010 (ending 23 May 2010).

Methods

SOURCES OF DATA

A number of different data sources are traditionally used to monitor influenza activity in the UK. In response to the pandemic, some systems were enhanced and new ones were created to strengthen pandemic surveillance. Systems evolved as the UK moved through the different stages of the pandemic. Traditional seasonal influenza surveillance systems, along with several new influenza surveillance schemes, were utilised throughout the pandemic in the UK to provide a comprehensive assessment of this novel virus, to monitor its activity, to estimate impact and to measure the uptake, safety and effectiveness of the various counter-measures.

FIRST FEW 100 (FF100) SURVEILLANCE SYSTEM (NEW)

The FF100 system collected detailed demographic, exposure, clinical, treatment and outcome data for 392 of the first UK cases of laboratory confirmed pandemic (H1N1) 2009 and their close household and non-household contacts during the early part of the summer pandemic wave. Information was obtained through interviews and record reviews. Virological swabbing was undertaken when possible from symptomatic cases and blood samples for serological testing were sought from cases and their contacts[6].

The secondary household attack rate was calculated as the proportion of household contacts who became cases at two weeks. Uni- and multi-variable analyses were undertaken.

FLUZONE (NEW)

Fluzone was a case management system created by the HPA based on the generic clinical assessment information system HPZone. It was rapidly developed and rolled out to all English Health Protection Units and Flu Response Centres in summer 2009 during the containment phase. It was used in case management and follow-up of contacts, and also provided data on English cases by local area during this period.

FIELD EPIDEMIOLOGY STUDIES

A number of ad hoc field epidemiology investigations were undertaken by local Health Protection Units and their equivalents across the UK. These investigations occurred in various closed settings including schools and other venues.

SERO-EPIDEMIOLOGY STUDIES (NEW)

Serological analysis of serum samples was performed by the application of two assays – microneutralisation (MN) and haemagglutination inhibition (HI). These were designed and validated at the HPA Centre for Infections (CfI).

Serological assays were performed using NIBRG122, a reverse genetics version of a virus isolated from a human case (confirmed and isolated end of April 2009; A/England/195/2009) and antigenically representative for the pandemic viruses circulating

in the UK at that time. Recent infection was confirmed on the basis of 4-fold titre increase between an acute and convalescent serum sample by HI or MN. For unpaired sera (single convalescent serum samples from field studies or samples for sero-incidence study), the probability of recent infection was calculated based on the achievement of HI titres ≥32 (which correlates to a four-fold titre rise from a baseline titre of <8).

Serological samples for field epidemiological studies were collected as serum pairs where possible (acute and convalescent, separated by at least 14 days). In most cases, a single convalescent sample was obtained.

Population pre- and post-pandemic sero-prevalence and sero-incidence studies were undertaken. The HPA sero-epidemiology unit (SEU) and NHS chemical pathology laboratories in England provided the principal source of sera – using anonymised residual samples with information on age and month of sample. The SEU serum bank was examined from before the pandemic and at monthly intervals until the end of the pandemic[7].

A sero-prevalence study was also carried out in Scotland, using anonymised sera from residual diagnostic samples taken in March 2010[8].

CONSULTATION RATES FOR ILI WITH GPS

Clinical data are obtained from networks of general practitioner (GP) surgeries in the UK. Data reported are the weekly consultations for influenza-like illness (ILI) and other acute respiratory illnesses. These schemes use the number of patients registered with the participating GP as the denominator. In the UK, each country runs a national scheme. In addition, there is also a system (HPA/QSurveillance®) which includes practices from England, Northern Ireland and Wales, although the majority are from England. To aid interpretation of the consultation rates and comparison with previous years, thresholds have been defined for most GP-based schemes to indicate expected rates when influenza is not circulating widely (baseline levels), when normal seasonal levels of influenza are circulating in the winter season and when higher than expected or epidemic activity is occurring (see table 1). These thresholds have been set based on experience with several years of data.

Table 1: GP influenza surveillance system in the UK (click links in left-hand column for further information on the schemes from external websites)

Scheme (Country)	Baseline	Normal	Above Average	Case definition
RCGP (England)**	30	200	-	ILI
Public Health Wales	25	100	100-400	Influenza
PIPeR (Scotland)	50	-	-	ILI/ARI
PHA (Northern Ireland)	70	500	-	ILI/ influenza
HPA/QSurveillance® (UK*)	20	70	130	ILI

**** QSurveillance® is based on data from 43% of England's population, 11% of the population in Wales, 17% in Northern Ireland and 0% in Scotland; ** The thresholds for RCGP clinical data were lowered in 2004[8]***

COMMUNITY SYNDROMIC SURVEILLANCE

NHS Direct is a 24/7 nurse-led telephone health advice and information service in England and Wales. The NHS Direct/HPA surveillance scheme analyses data from this service. Key respiratory indicators are the proportion of callers reporting colds/flu and fever by age group and region[10]. In Scotland a similar system (NHS-24) operates.

In Northern Ireland there is no equivalent of NHS Direct/NHS-24. Data are collected from out-of-hours centres. During the 08/09 influenza season a pilot was undertaken with two of the seven primary care out-of-hours (OOH) centres. Data on total consultations and those for influenza/ILI, stratified by age, were extracted daily for the previous 24 hours and compared with sentinel consultation rates. This involved an auto-extraction process, with data being imported into a central repository. This process has now been extended to the remaining five centres.

On 23 July 2009 the National Pandemic Flu Service (NPFS) became operational in England only. Patients with uncomplicated ILI were asked to telephone or access the NPFS website rather than go to their GP. The service authorised antiviral drugs to people aged over one year, with ILI, who did not fall into a specified risk group. If they fell into one of these groups the individual was referred to the health service. NPFS replaced NHS Direct as the data source for community ILI syndromic surveillance. Data from NPFS provided information on the number of antiviral authorisations and collections.

In Northern Ireland, the number of antiviral courses, prescribed through primary and secondary care, was collated regionally on a weekly basis. In Scotland, the rate of antiviral prescriptions was analysed weekly.

MICROBIOLOGICAL SURVEILLANCE (ENHANCED)

Following development of a sensitive and specific H1N1 RT-PCR assay[11], all testing for pandemic (H1N1) 2009 was initially carried out at CfI. HPA regional laboratories forwarded all untypeable influenza A viruses to CfI for confirmation until a validated test had been developed and rolled out to them. Results of all tests from HPA laboratories for the novel virus (positive or negative) in England were reported to CfI, initially through standardised emailed spreadsheets. Reporting was later undertaken through the automated Datamart system for influenza and other respiratory viruses.

In addition, the National Laboratory Reporting Scheme (LabBase) comprises approximately 230 NHS, HPA and independent sector microbiology laboratories throughout England and Wales. This system reports positive results for human samples (from community and hospital settings) testing positive for pathogens. Trends in respiratory viruses including influenza, respiratory syncytial virus, rhinovirus and parainfluenza are examined.

A subset of ~50 general practices in the Royal College of General Practitioners (RCGP) Weekly Returns Service submit respiratory samples for virological testing from patients presenting with influenza-like illness in participating practices. Respiratory specimens, along with key demographic and epidemiological information about the patient and illness (e.g. use of antivirals and vaccination history), are submitted to the HPA CfI. A complementary sentinel primary care scheme of sampling is carried out by the HPA whereby respiratory specimens from patients presenting to their GP with an acute respiratory infection are

submitted to the local HPA Regional Microbiology Network (RMN) laboratory together with epidemiological information from the patient. Specimens are evaluated by PCR for influenza and other respiratory virus infections. Similar sentinel swabbing schemes through primary care operate in Scotland, Wales and Northern Ireland. Data from these schemes allow the calculation of the proportion of ILI cases consulting in primary care testing positive for influenza each week.

Beginning on 28 May 2009, a systematic sample of symptomatic callers to NHS Direct were asked to participate in a virological surveillance scheme. This involved self-sampling with nasal swabs. Swabs were then posted to HPA CfI for virological testing[12]. Virological self-sampling from NHS Direct stopped after week 30 and started through NPFS in week 32, until February 2010, when NHS Direct was used again.

HPA CfI undertakes antigenic and genetic characterisation of influenza isolates submitted for testing by HPA and NHS laboratories. Antigenic characterization of pandemic (H1N1) 2009 viruses circulating in the UK during 2009 was performed by haemagglutination inhibition (HI) assay using post-infection ferret antisera to A/California/07/2009 (vaccine strain), A/England/195/2009 (UK reference strain) and A/Brisbane/59/2007 (previous seasonal H1N1 vaccine strain). An isolate with a 4-fold or less change in reactivity to the reference strain is classed as being like the reference strain.

CfI also monitors the occurrence of anti-viral resistance in influenza isolates using a molecular marker for oseltamivir resistance (H275Y) and subsequent full phenotypic susceptibility testing. Cases found to be resistant were followed up through clinicians and microbiologists using a standard questionnaire.

To identify the role played by concurrent bacterial infections during the pandemic, an attempt was made to identify English pandemic (H1N1) 2009 cases who has also tested positive for a bacterial infection through record linkage.

ESTIMATED CASE NUMBERS (NEW)

The estimated number of symptomatic cases with ILI due to pandemic influenza, by English region and age group, was calculated each week using a statistical model. This used data from several surveillance sources including GP and NPFS age-specific consultation rates, age-specific positivity rates through sentinel virological schemes and estimated proportions consulting health care. The parameters altered over the pandemic period to take into account changes in policy (e.g. the introduction of NPFS and impact on proportion consulting health care) and changes in data[13]. An estimate of the total number of new symptomatic cases was given each week with the previous week estimates recalculated with updated data. There was uncertainty around the proportion of people with ILI symptoms who contacted their GP (or NPFS). To take this uncertainty into account a range of values were used resulting in a range of estimated symptomatic case numbers surrounding the central estimate.

HOSPITALISATION DATA (NEW)

During the initial part of the first wave, detailed information was collected for all laboratory confirmed cases as part of the FF100 project. Information collected included details of contact with the health care service and, where appropriate, of hospitalisation.

In England, after the closure of FF100, information on cases including possible hospitalisation was collected by Health Protection Units through the Fluzone system. Once the treatment phase started, not all suspected cases were tested for influenza infection, Acute Trusts reported to the Department of Health (DH) the number of confirmed or clinically suspected cases of pandemic (H1N1) 2009 admitted to local NHS hospitals. In October 2009, a web based reporting system was introduced by HPA and the Chief Medical Officer (CMO) across England to collect demographic, clinical and epidemiological information on all laboratory confirmed pandemic (H1N1) 2009 cases admitted to NHS trusts. In addition to collecting information prospectively, this system was used to collect information retrospectively on all laboratory confirmed cases admitted to hospital since the beginning of the pandemic. Information was collected on clinical details, underlying risk factors, use of antivirals and outcome of admission.

In Northern Ireland similar information on virologically confirmed hospitalised cases was forwarded, initially daily and subsequently weekly, by the hospital trusts to the Public Health Agency throughout the pandemic period.

In Scotland data on virologically confirmed hospitalised cases were collated by Health Protection Scotland.

In Wales similar data were collated by Public Health Wales Health Protection.

In addition, a detailed case note-based investigation was carried out in 55 hospitals across the UK. The Influenza Clinical Information Network (FLU-CIN) study collection in-dept clinical and demographic information on patients admitted to hospital with confirmed pandemic (H1N1) 2009 infection[14].

MORTALITY MONITORING (ENHANCED)

The Office for National Statistics (ONS) collates and reports to HPA estimated total all-cause death registrations on a weekly basis. This information is used to estimate excess all-cause all-age death registrations in England and Wales as compared to previous seasons each week. A statistical model is used based on the Serfling method, to establish a baseline of the expected weekly number of registered deaths[15]. If the observed number is above the upper limit of a 90% confidence interval around this expected number for at least one week, an excess is said to have occurred.

In addition to the ONS data, during the pandemic, the General Registry Office of England and Wales reported daily individual death registrations by age and registration district. This information was used to estimate excess all-cause mortality by age-group in England and Wales.

In Scotland the weekly total number of death registrations (overall and by age group) is compared to the expected number calculated using two methods; a Serfling cyclical model and a Gam model based upon previous winters.

The CMO undertook a confidential enquiry of confirmed pandemic (H1N1) 2009 deaths in England with reporting from all NHS trusts. In addition, individual pandemic (H1N1) 2009 deaths were ascertained through the various enhanced surveillance systems operated by

the HPA and reconciled. Similar information was gathered by health protection equivalents in Scotland, Wales and Northern Ireland. Information on cause of death, complications and underlying conditions was collected.

VACCINE UPTAKE MONITORING

Priority groups for pandemic (H1N1) 2009 vaccination were defined by the Joint Committee for Vaccination and Immunisation as those aged six months and up to 65 years in the current seasonal influenza vaccine clinical at-risk groups, all pregnant women, household contacts of immunocompromised individuals, and those aged 65 years and over in the current seasonal influenza vaccine clinical at-risk groups. These priority groups were offered pandemic vaccine from late October 2009. Following the DH announcement on phase two of the vaccination programme, healthy children aged six months and up to 5 years were offered pandemic vaccine from December 2009.

The DH recommended that all those aged 65 years and over and those aged 6 months to under 65 years falling in a clinical at risk group, be offered the seasonal 09/10 trivalent influenza vaccine. Clinical at risk groups include individuals with one of the following underlying medical condition: chronic respiratory disease, chronic heart disease, chronic renal disease, chronic liver disease, chronic neurological disease, diabetes or immunosuppression.

Uptake of both vaccines in the different eligible groups was monitored in England by the HPA through the DH web-portal ‘Immform’. Data on the eligible populations and the number of patients/health-care workers vaccinated were automatically extracted or manually outputted from GP and acute trust information systems and uploaded.

In Scotland, Wales and Northern Ireland similar data were collected using automated and manual methods.

VACCINE EFFECTIVENESS MONITORING

Estimates of vaccine effectiveness were made using data from GP sentinel virological schemes in England and Scotland. A swab negative case-control study of individuals with influenza-like-illness was undertaken. Those testing PCR positive for pandemic (H1N1) 2009 were cases and those testing negative were controls. Vaccine effectiveness was estimated as (1-OR).

DENOMINATOR DATA and MODELLING

Where population rates are presented, the population figures are from the ONS mid-2008 estimates, which are available by age and region[16].

In the case of rates by underlying medical condition, the population denominators are derived from the HPA-DH vaccine uptake surveys. These data provide information on the number of patients registered in primary care by specific underlying condition for people aged between six months and 65 years and for the 65-year or older group the overall number in a risk group is available. The estimate of the number of pregnant women is

derived from the annual maternities and number of miscarriages/abortions provided by ONS[17].

Where case-based rates are presented, the denominator used is the HPA estimated number of symptomatic cases (see above). To take into account the range of values used due to uncertainty around the case numbers, the case-rates are presented with a range; the upper and lower limits of 95% confidence intervals around the rates obtained using the low and high estimate of cases.

Follow-up of confirmed cases and their close household contacts in the FF100 project allowed an estimation of the overall household secondary attack rate (SAR), and of the impact of containment measures on the reproduction number (*R*)[18]. *R* is a measure of the transmissibility of the virus and sustained transmission requires $R>1$. Real-time modelling work also examined vaccination policy options for the Joint Committee of Vaccination and Immunisation.

Results

ENHANCED CASE FINDING AND EPIDEMIOLOGY STUDIES (CONTAINMENT PHASE to 1 JULY 2009)

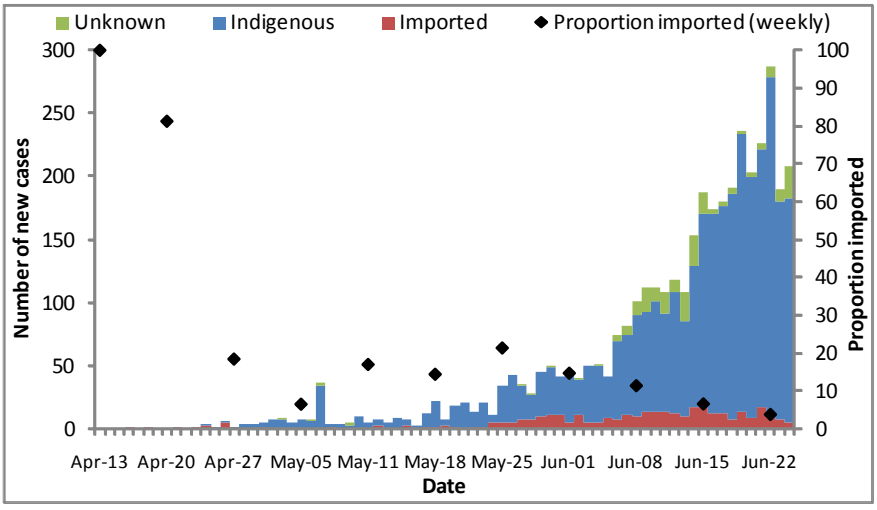
TIMING

The first cases of pandemic (H1N1) 2009 infection in the UK were reported on 27 April 2009, in a Scottish couple returning from a trip to Mexico[19;20]. Two days later, the first English case was reported in a person who had travelled on the same flight from Mexico.

In the first four weeks of the outbreak in the UK, transmission of the virus was sporadic and generally linked to travellers returning from affected areas (Mexico and the US) or to indigenous transmission to close contacts in school and household settings[5].

Sustained community transmission became established initially in Scotland (South Glasgow), the West Midlands and then London. In England, much of the transmission was linked to school outbreaks. By the end of the containment phase (1 July 2009), 7447 confirmed cases had been reported in the UK; 6162 (83%) in England, 1217 (16%) in Scotland and 34 (0.5%) each in Northern Ireland and Wales. Case numbers were doubling approximately every week at this stage. The proportion of cases who were imported (as opposed to infection acquired indigenously in the UK) decreased over the initial weeks to less than 5% by the end of June (figure 1).

Figure 1: Cases of pandemic (H1N1) 2009 by onset date and route of acquisition of infection and weekly proportion imported, UK (to 1 July 2009)



Datasources: Fluzone in England and equivalants in Scotland, Wales and Northern Ireland

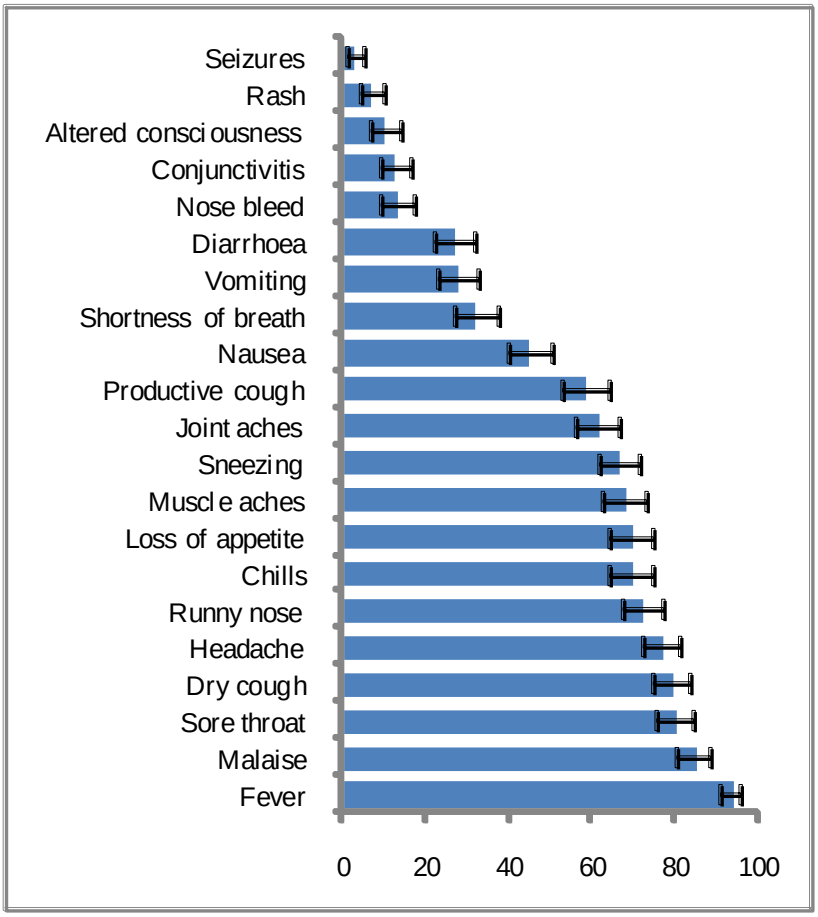
CLINICAL PRESENTATION

Most cases appear to have experienced an illness fairly typical for influenza.

Detailed investigation of 392 early laboratory-confirmed cases as part of the FF100 surveillance project found fever, malaise, dry cough, sore throat and headache to be the commonest (>70% of respondents) reported symptoms (figure 2). However, a greater proportion of cases reported gastrointestinal (diarrhoea and vomiting) than is usually seen with seasonal influenza. The median reported duration of illness was seven days (range 1-29 days)[21].

Asymptomatic infection is a well-recognised feature of seasonal influenza[22]. Serological studies of a boarding school outbreak of pandemic (H1N1) 2009 showed that sub-clinical infection occurred in about one third of those with serological evidence of infection [23].

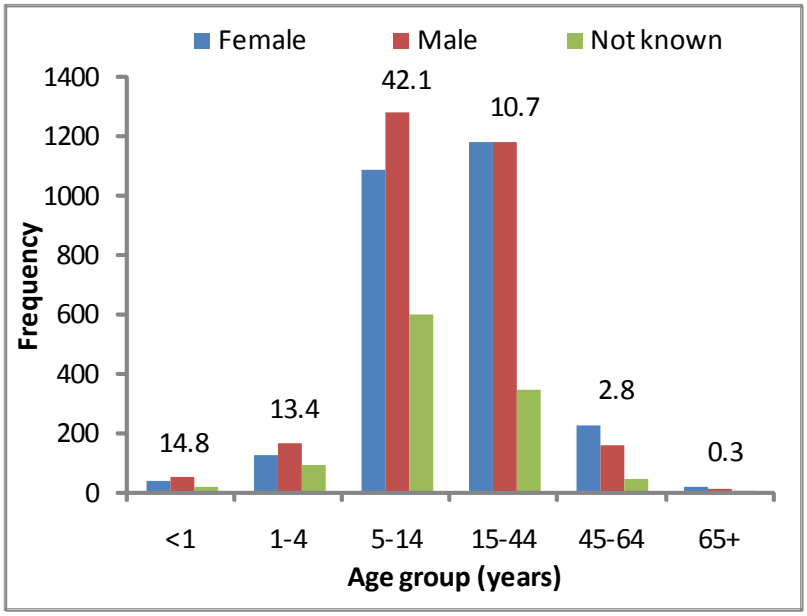
Figure 2: Proportion (%) of all UK FF100 cases of pandemic (H1N1) 2009 influenza reporting symptoms at any stage of illness, with binomial exact 95% confidence interval (adapted from[21])



GROUPS AFFECTED

During the containment phase, pandemic (H1N1) 2009 cases were identified aged from 0 to 90 years; the median age for confirmed cases up to 1 July 2009 was 14 years (IQR: 9 – 25 years). The 5-14 year age group had the highest cumulative population incidence rate (42.1 per 100,000) by 1 July 2009 (figure 3). The older age groups (aged over 45 years) had the lowest cumulative population incidence rates. At this stage, the median age varied by region; in London and the West Midlands, where there had been several large school-based outbreaks[24-26], it was 12 years while in other UK regions it ranged from 17 years (Scotland) to 25.5 years (North West England). There was an approximately equal distribution by gender (48% female).

Figure 3: Age and sex distribution of pandemic (H1N1) 2009 cases, UK with crude cumulative population rate per 100,000 (to 1 July 2009)



Cases of pandemic (H1N1) 2009 were not dispersed homogenously throughout England during the containment phase. Parts of London and the West Midlands region experienced high numbers of cases with rapid rates of increase in new cases from week to week early in the summer wave (figure 4, appendix 2). Both these areas showed the first increases in ILI reported through daily GP consultation rates before the end of the containment phase; about two weeks earlier than other areas of the country (figure 5).

Figure 4: location of UK cases of pandemic (H1N1) 2009 by week of report, June 2009

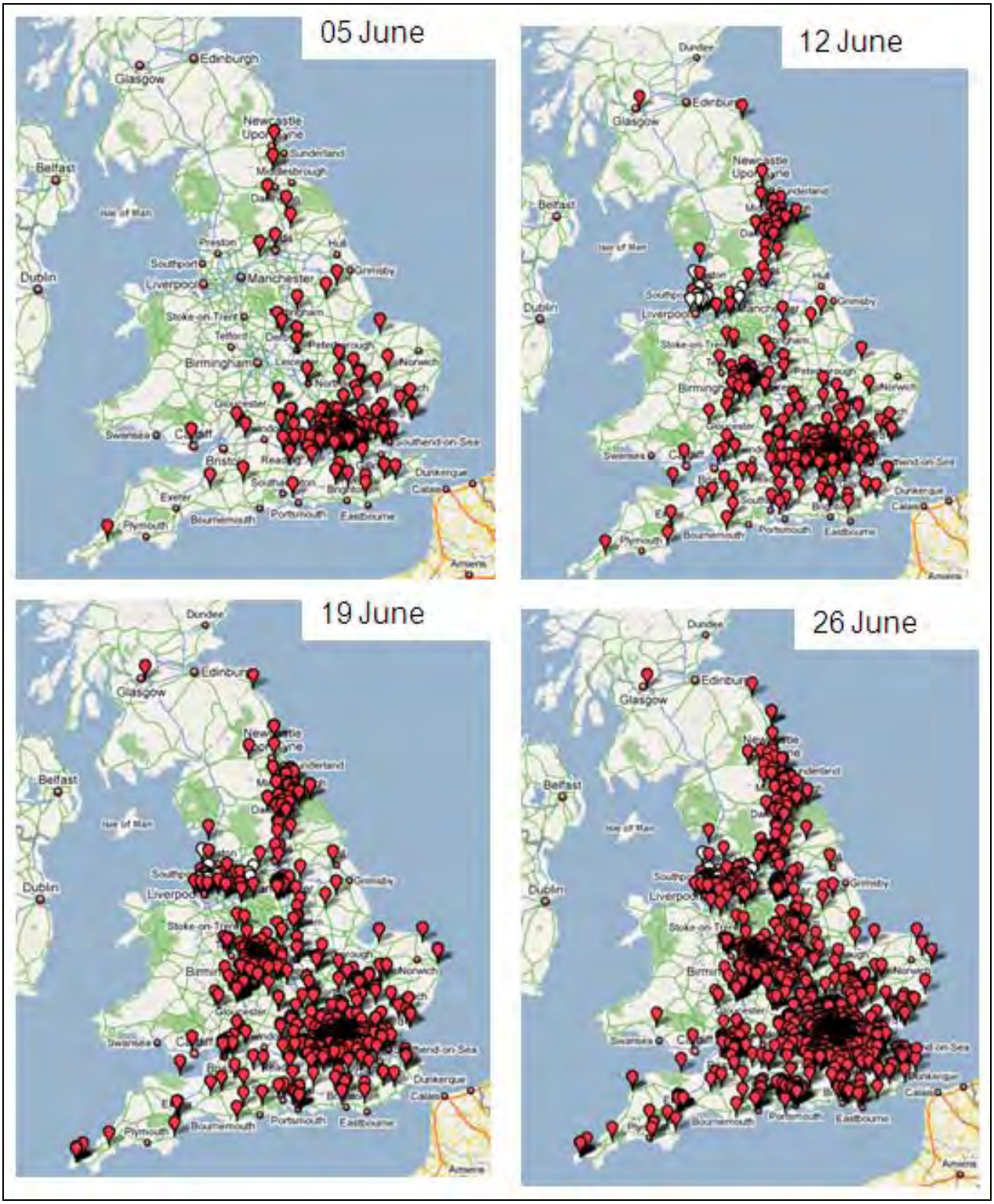
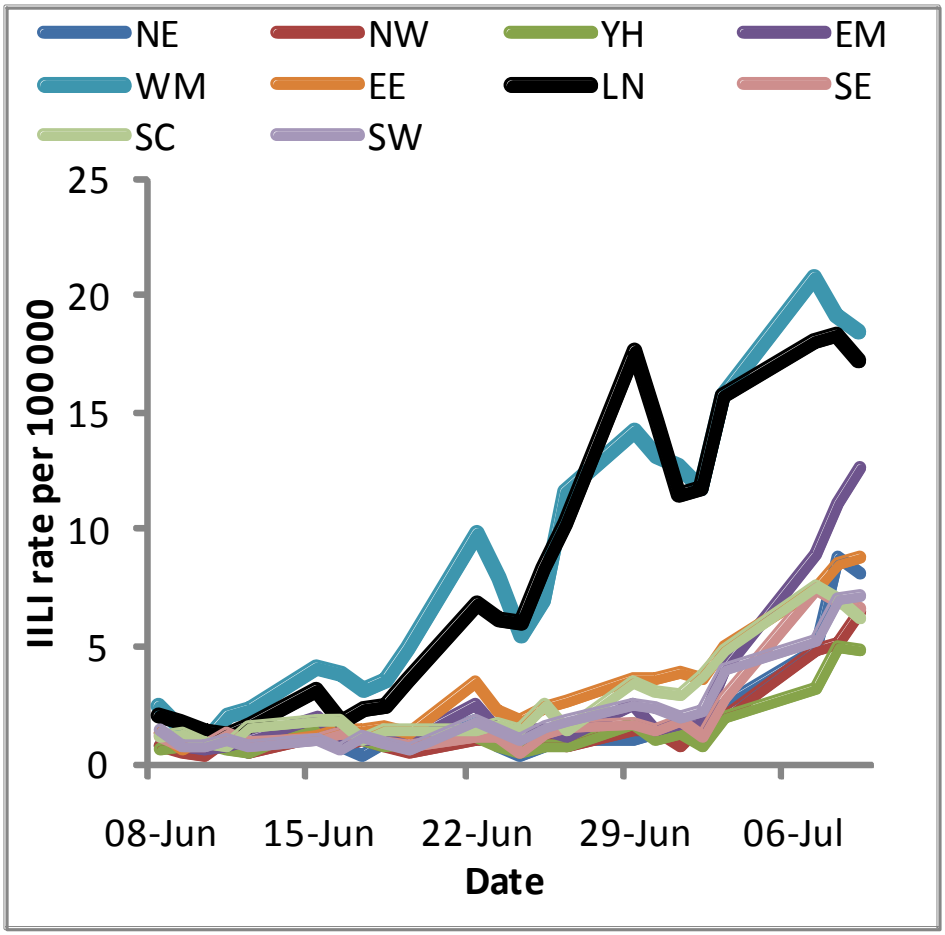


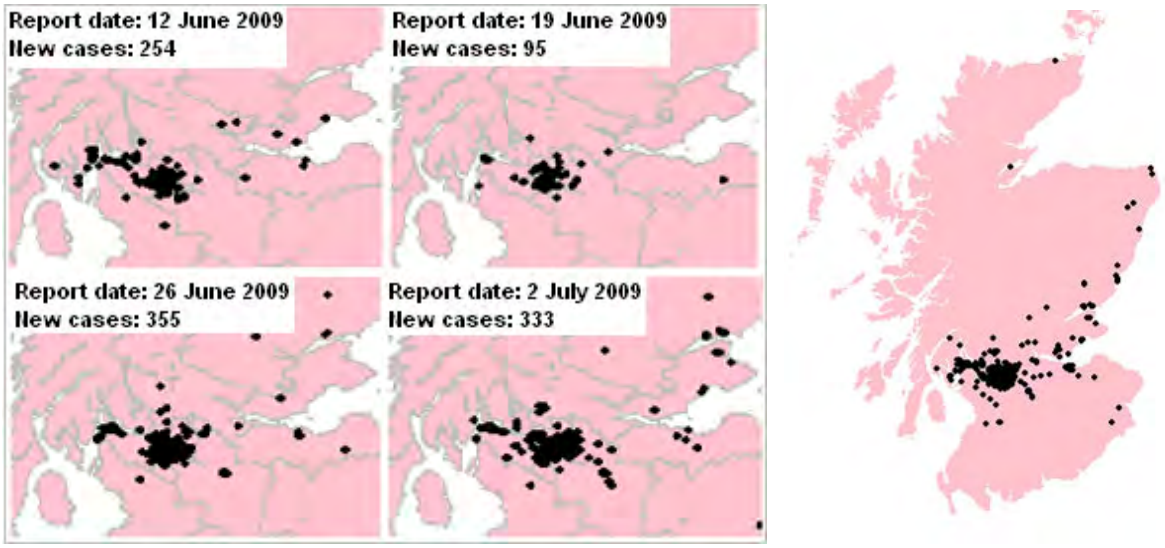
Figure 5: daily GP consultation rate for ILI through the HPA/QSurveillance system, by region*, June – July 2009



**EM: East Midlands, EE: East of England, LN: London, NE: North East, NW: North West, SC: South Central, SEC: South East Coast, SW: South West, WM: West Midlands, YH: Yorkshire and Humberside.*

In Scotland pandemic (H1N1) 2009 cases were initially clustered in the 'hotspot' areas of Greater Glasgow & Clyde in the West of the Central area of the country. Up to 2 July 2009 (after which point not all suspected cases were tested) the majority of cases were almost exclusively restricted to the Central Belt of Scotland although there was the start of gradual spread to beyond these limits (figure 6).

Figure 6: Maps of Scotland showing new laboratory confirmed cases reported to HPS by week of report and the total to 2 July 2009 (n=1238)



FIELD INVESTIGATIONS

Health protection teams across the UK initiated a number of field investigations of outbreaks in closed settings. In one early school outbreak in England, 91 symptomatic cases were identified between 15 April and 15 May 2009 of which 33 were confirmed to be positive for pandemic (H1N1) 2009. In this outbreak an overall virologically confirmed attack rate in the school pupils of 2% was observed, though in the most affected age group this increased to 15%. Transmission was documented in several households of the pupils with a 17% virologically confirmed secondary attack rate in household contacts[24].

A large, late-recognised, outbreak of pandemic (H1N1) 2009 infection in an English primary school had a 30% clinical attack rate in the pupils, with a virologically confirmed attack rate of 13% overall (ranging from 5.1% to 23% in different age groups). The symptoms reported were generally mild: predominantly fever, nasal congestion and sore throat[25].

TRANSMISSION

The overall household secondary attack rate (SAR) (for virologically confirmed pandemic (H1N1) 2009) in the FF100 was estimated as 8.2% (95% CI 6.4 – 10.3%) during the containment phase. This was significantly affected by the use of antivirals to treat index cases and as prophylaxis for close household contacts. There was also evidence of a differing SAR by age group; with the rates in children and young adults significantly higher than the rate in adults aged over 50 years (table 2)[27].

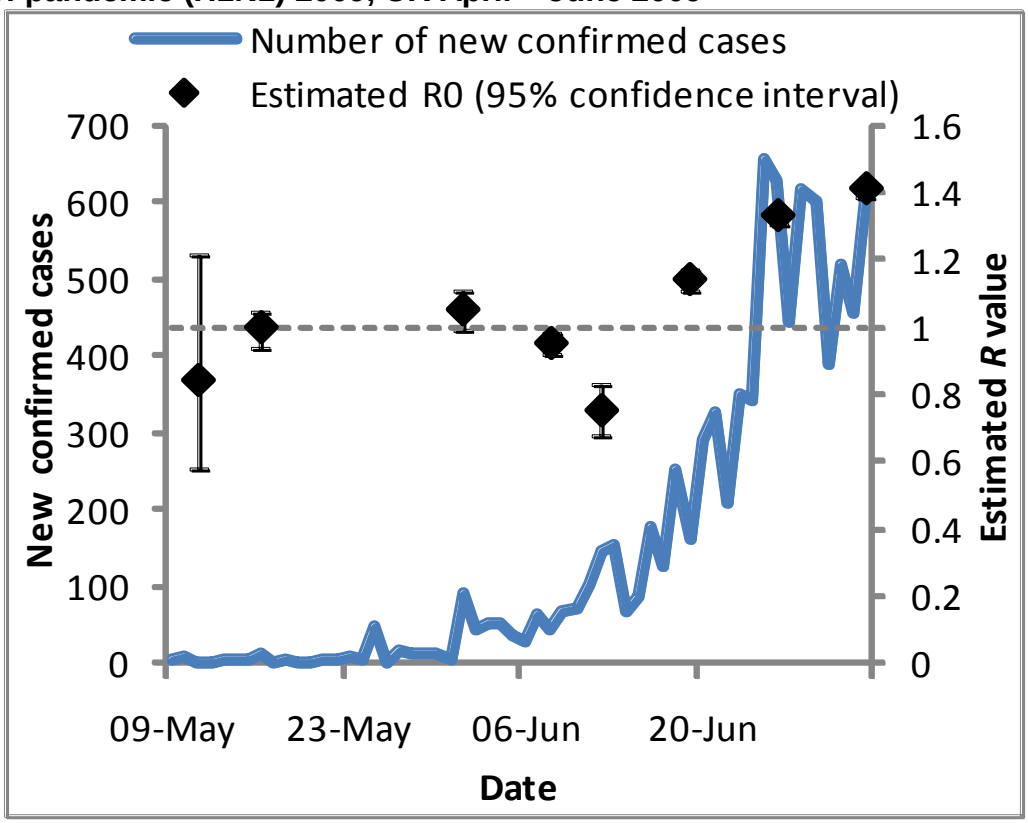
R was estimated to be close to 1 but with considerable uncertainty from early May until mid June, after which it was consistently above 1 (figure 7). This fluctuation in the estimate is to be expected due to stochastic effects (randomness) being significant when numbers of infected individuals are low.

Table 2: Uni- and multi-variable analysis of SAR by gender, age group and prophylaxis and treatment for virologically-confirmed cases (adapted from[27])

Variable level	Crude (uni-variable) SAR	Adjusted (multi-variable) OR (95% CI)	p-value
Male	37/364 (10.2%)	Baseline	0.94%
Female	25/381 (6.6%)	1.0 (0.5 - 2.0)	
<16 year	40/212 (18.9%)	14.2 (3.0 - 67.1)	<0.001
16-49 years	20/378 (5.3%)	2.8 (0.6 - 13.4)	
50+ years	2/171 (1.2%)	Baseline	
No prophylaxis	45/132 (34.1%)	Baseline	<0.001
AV prophylaxis	8/455 (1.8%)	0.03 (0.02 - 0.09)	
>48 hours*	48/453 (10.6%)	Baseline	0.004
≤48 hours*	14/308 (4.5%)	0.3 (0.13 - 0.68)	
Total	62/761 (8.1%)		

** Index case treated with antiviral drugs*

Figure 7: Estimated R by date of estimation with the number of new confirmed cases of pandemic (H1N1) 2009, UK April – June 2009



ROUTINE AND ENHANCED INFLUENZA SURVEILLANCE SYSTEMS (April 2009 – May 2010)

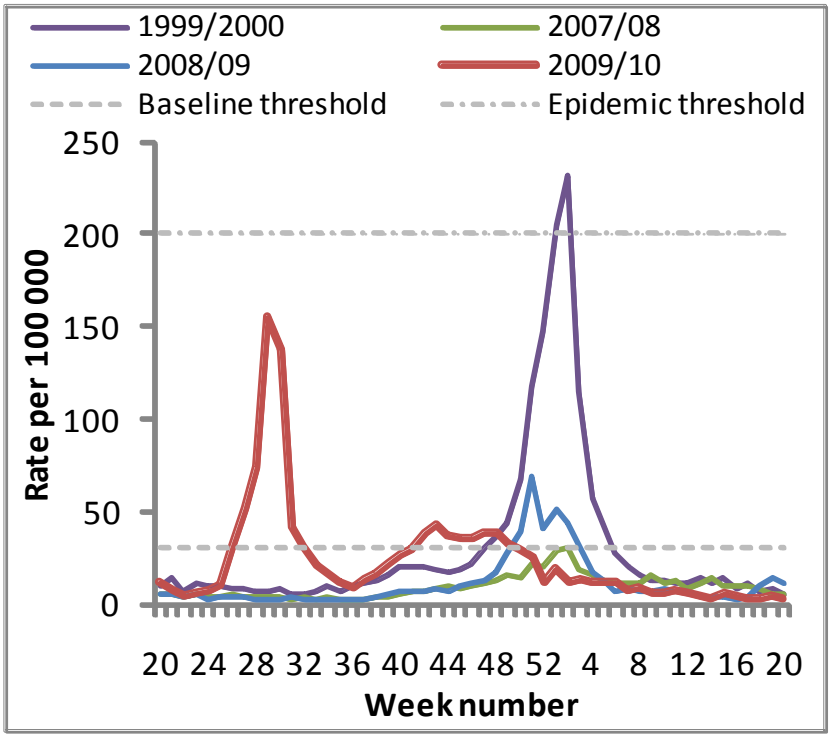
CLINICAL

Weekly GP clinical surveillance schemes in England, Scotland, Wales and Northern Ireland:

With the onset of widespread community transmission, the RCGP weekly ILI rate in England exceeded the baseline level of 30 consultations per 100,000 in week 27 (ending 5 July 2009) when it increased from 29.6 to 51.9 per 100,000. It peaked in week 29 (ending 19 July 2009) at 155.3 per 100 000 and remained above the baseline level until week 33 (ending 16 August 2009) when it decreased from 30.9 to 21.2 per 100,000. It decreased until week 36 (reaching 8.6 per 100,000 at the lowest point) after which it began to increase again, exceeding the baseline in week 42 (ending 18 October 2009) when it increased from 29.1 to 42.8 per 100,000. This was the highest rate observed in the autumn, though the rate remained above the baseline for several weeks. It finally fell below this level in weeks 50 (29.7 per 100,000) and 51 (24.7 per 100,000) (figure 8).

Observed trends in primary care consultations were likely affected by the NPFS which operated in England between 23 July 2009 (the RCGP peak week) and 11 February 2010. In addition, most state schools in England started their summer holidays in the week ending 26 July.

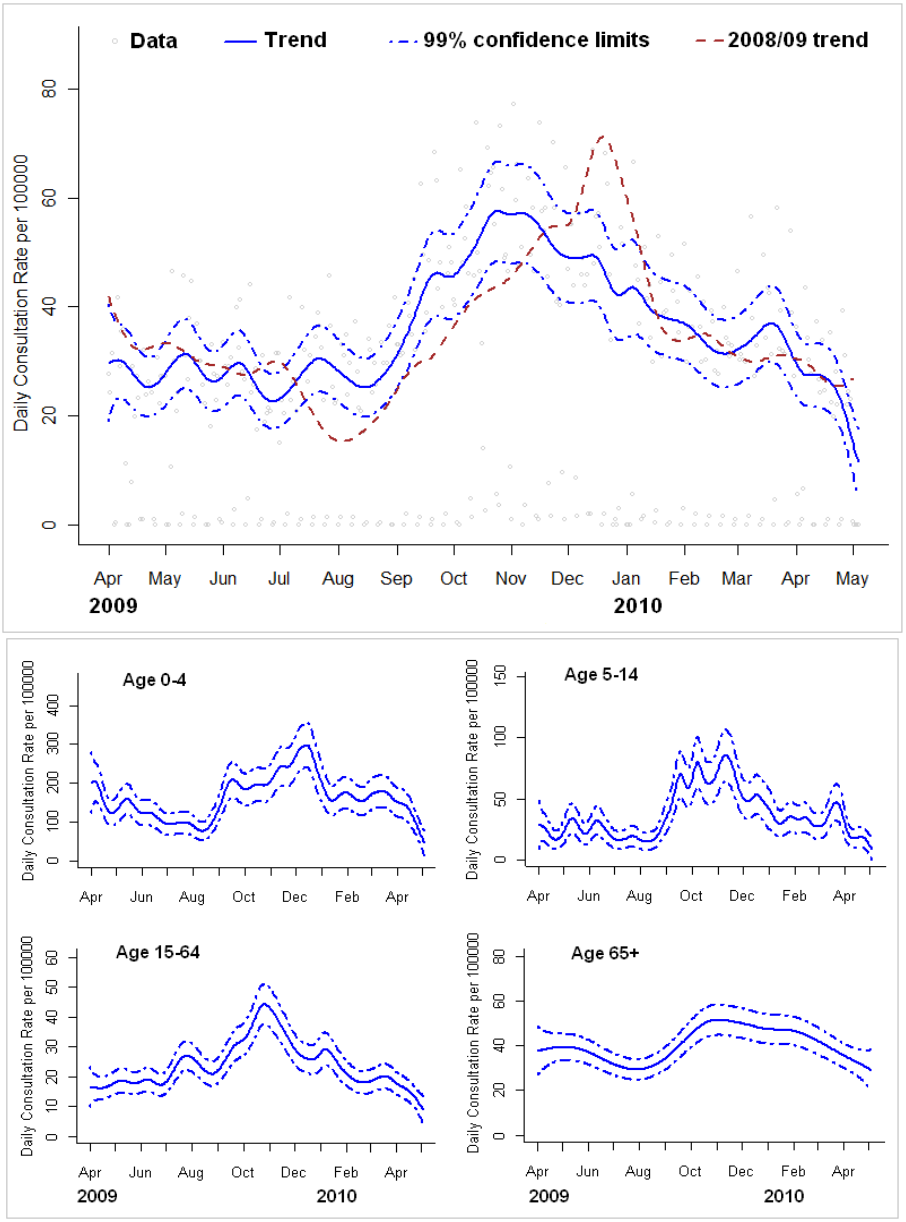
Figure 8: Royal College of General Practitioners weekly influenza-like illness rate per 100,000, May 2009 – May 2010



A summer peak has not been observed since the start of the RCGP weekly returns service in 1966. The 2009 summer peak ILI consultation rate was lower than that observed during the 1999/2000 winter season (231.1 per 100,000) but higher than the peak seen in the 2008/09 winter season (68.5 per 100,000) which was associated with moderately high activity mainly due to circulation of influenza A (H3).

In Scotland there was little distinction between the summer and autumn pandemic waves according to the GP ILI/ARI rate. A gradual increase was observed over the summer but the baseline of 50 per 100,000 was only exceeded in week 39 (ending 27 September 2009) when it increased from 48.6 to 51.8 per 100,000. Note that schools in Scotland finished earlier than England in week 27 (ending 5 July 2009). The highest rate observed was 66.1 per 100,000 in week 43 (ending 25 October 2009). The rate decreased to below the baseline level in week 2 (ending 17 January) when it decreased from 51.8 to 39.5 per 100,000 (figure 9). The Scottish ILI/ARI rate did not exceed the 2008/09 peak rate of 92 per 100,000. The younger age groups had the highest rates.

Figure 9: Health Protection Scotland: PIPeR daily ILI rate per 100,000 overall and by age group*, April 2009 – May 2010

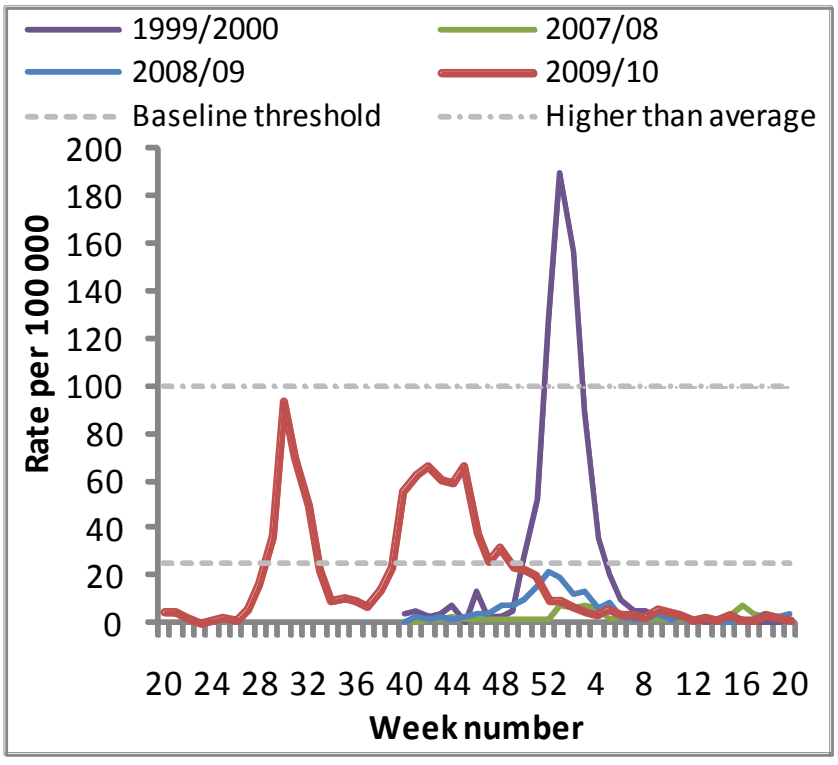


**Note differing scales on age break-down figures.*

In Wales, the influenza primary care consultation rate showed a similar pattern to the RCGP ILI rate in England. The baseline level of 25 per 100,000 was exceeded for the first time in nine years in week 29 (ending 19 July 2009) when it increased from 15.8 to 36 per 100,000. The rate climbed to a peak of 92.8 per 100,000 in week 30 and rapidly declined to below the baseline by week 33 (ending 16 August 2009). For most Welsh schools, the summer term ended in week 29 (ending 19 July 2009).

After week 37 (ending 13 September 2009), the rate began to increase again exceeding the baseline once more in week 40 (ending 4 October 2009) when it increased from 22.8 to 54.8 per 100,000. A second peak of 66.2 per 100,000 was observed in week 42 (ending 18 October 2009), after which the rate declined to below the baseline level by week 49 (ending 6 December 2009) (figure 10). The highest Welsh ILI consultation rate exceeded the level seen in the 2008/09 winter (21.5 per 100,000), but was half as high as the level observed in 1999/2000 (189.5 per 100,000).

Figure 10: Wales: weekly influenza rate per 100,000, May 2009 – May 2010

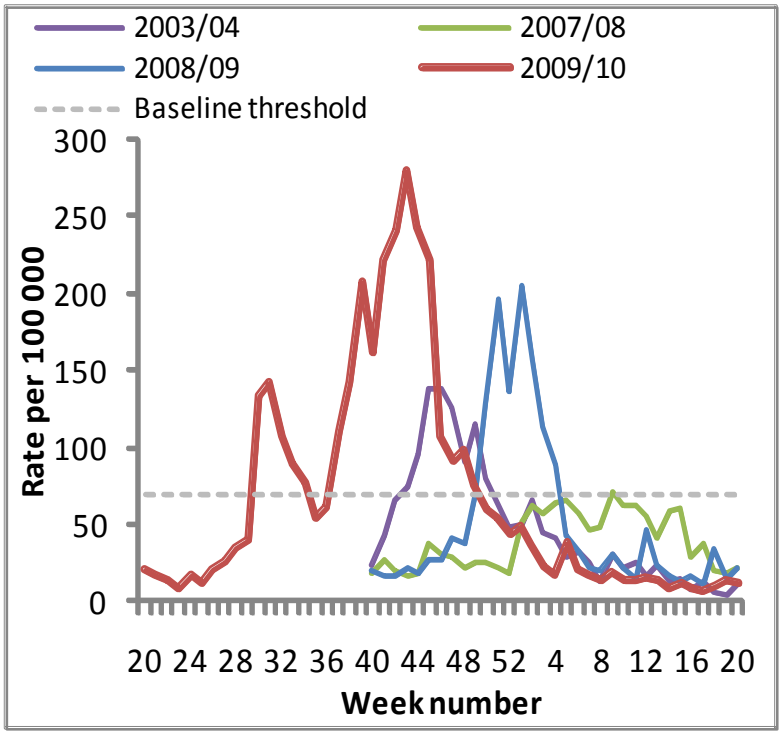


In Northern Ireland, the combined influenza/ILI rate peaked in the summer at 142.5 per 100,000 in week 31 (ending 2 August 2009). A provisional threshold of 70 per 100,000 was set for the 2009/10 influenza season and the rate was above this level for five weeks over the summer wave. The Northern Ireland school year ended in week 27 (ending 5 July 2009).

The threshold was also exceeded in the autumn in week 37 (ending 13 September 2009) when it increased from 61.9 to 113.8 per 100,000. A second peak of 280.6 per 100,000 was observed in week 43 (ending 25 October 2009) at a higher level than the summer. The rate declined to below the new baseline level by week 50 (ending 13 December 2009) (figure

11). The rate exceeded the level observed in previous years; 204.9 per 100,000 in 2008/09, though it should be noted that this system was not operational during the last large UK epidemic in 1999/2000.

Figure 11: Northern Ireland: weekly influenza/ILI rate per 100,000, May 2009 – May 2010



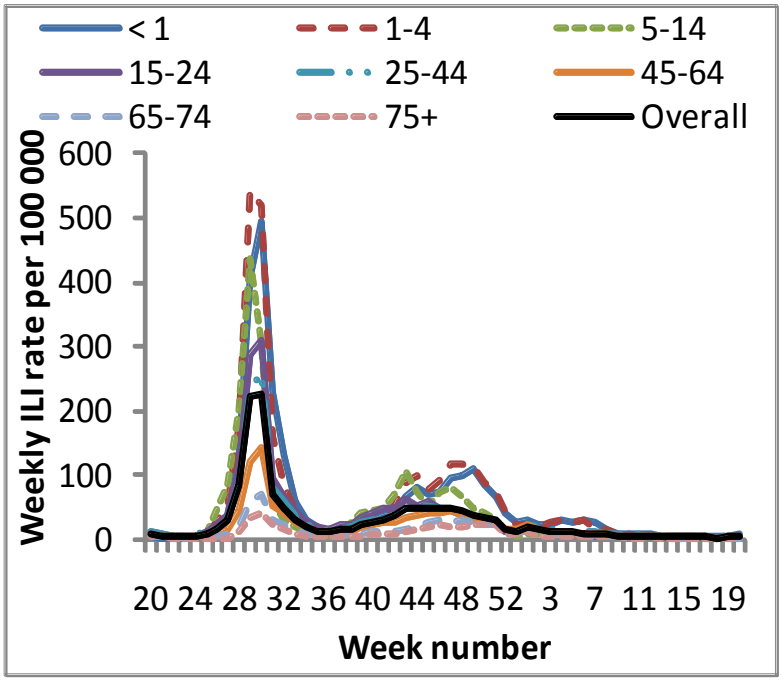
Weekly GP clinical surveillance through the HPA/QSurveillance system (England, Wales and Northern Ireland)

The weekly ILI rate for England, Wales and Northern Ireland (no Scottish data are available) through the HPA/QSurveillance system showed a similar pattern to the RCGP ILI rate. A peak of 226 per 100,000 was observed in week 30 (ending 26 July 2009), after which the rates decreased until week 36 then increased to a second peak of 50.5 per 100,000 in week 47 (ending 22 November 2009). Similar to the RCGP scheme, the autumn wave was much lower and flatter; the rate was around 50 per 100,000 from week 43 to week 48 (figure 12). This GP consultation rate was also affected by the use of the NPFS from 23 July 2009 to 11 February 2010.

By age group, the highest rate was seen in the 1-4 year group in week 29 (ending 12 July) at 541.2 per 100,000, followed by 493 per 100,000 in the under one year group in week 30 and 437.1 per 100,000 in the 5-14 year olds in week 29 (the week before English school summer holidays). All age groups peaked in week 29 or 30 in the summer wave; however a different pattern was seen in the autumn wave. The 5-14 year group peaked earliest at 105.2 per 100,000 in week 43 (ending 25 October 2009 – which was the week before the English school half-term holiday), followed by the 1-4 year group at 118.2 per 100,000 in week 47 (ending 22 November) and the under one year group at 108.9 per 100,000 in week

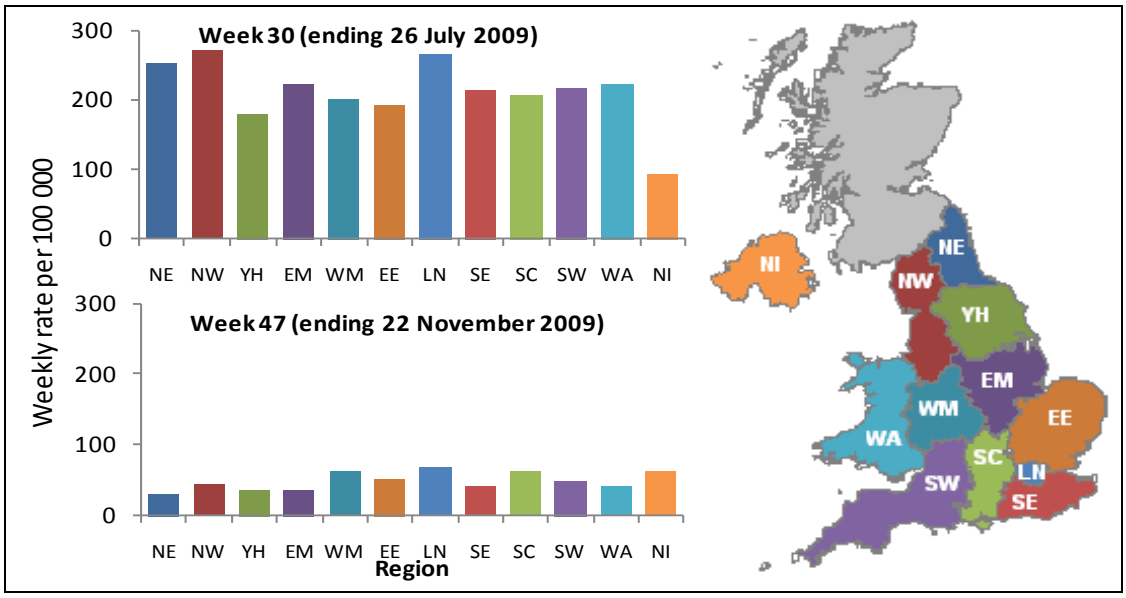
49 (ending 6 December). The lowest rates in both waves were in the older age groups over 45 years of age (figure 12)

Figure 12: Weekly ILI consultation rate through the HPA/QSurveillance system, by age group, E, W NI, May 2009 – May 2010



The London and West Midlands Strategic Health Authorities (SHA) were the first to show increases in the ILI rate, but most regions peaked in week 29 or 30 in the summer wave (appendix 2). The highest regional rate was observed in London at 310 per 100,000. In the autumn wave, the rates peaked in the Northern regions in week 43 (ending 25 October 2009), with the highest in the North East (67.3 per 100,000). Most of the central and southern regions peaked later in week 47 (ending 22 November 2009) with the highest in London at 67.3 per 100,000 (figure 13).

Figure 13: GP ILI rates through HPA/QSurveillance system by region in the peak weeks (peak of overall rate), E, W, NI

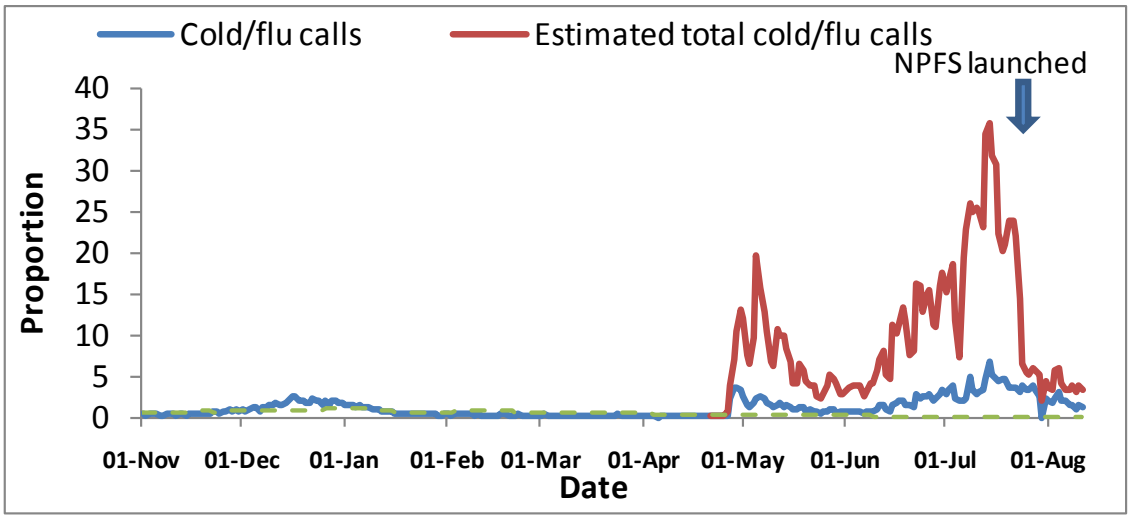


Syndromic Surveillance in the community through call/out-of-hours centres

Following the initial reports of the pandemic and the first confirmed cases in the UK at the beginning of May 2009, an early increase in cold/flu calls to NHS Direct in England and Wales was observed with a peak on 5 May 2009. This is thought to be in part due to media coverage (figure 14)

There was a further rise in cold-flu calls from early July, commensurate with evidence of community transmission. The proportion of cold/flu calls rose to a peak of 35.9% on 14 July 2009. A marked decline was then observed coinciding with the launch of the NPFS on 23 July 2009. NPFS, rather than NHS Direct, handled the majority of calls from people with an ILI in England (figure 14).

Figure 14: Daily proportion of calls due to colds/flu through NHS Direct, England and Wales, November 2008 – August 2009



From the launch of NPFS in July 2009 to February 2010, when it ceased operation, a total of 2,401,043 assessments were carried out. As a result, 1,635,948 authorisations for antivirals were issued, and 1,079,179 courses of antiviral treatment were collected in England. Assessments, authorisations and collections peaked when the service was first launched in July 2009 followed by a steady decline. In the autumn wave the peak occurred in week 43 (ending 25 October 2009) when 137,739 assessments were completed, 98,590 antiviral authorisations were issued and 66,218 antiviral courses were collected (figure 15).

In Scotland, similar to what was seen in England and Wales; there was an increase in the proportion of cold/flu calls to NHS24 during early May 2009 at a time when there was considerable media attention. A similar pattern was evident in June that may reflect the increased publicity following outbreaks in schools and the first UK death reported from Scotland, rather than evidence of widespread community transmission. Call volumes for cold/flu then increased again during July in Scotland and peaked in early August, about two weeks before the return of the schools from the summer holiday. The proportion of calls due to colds/flu increased in the beginning of October followed by a fall in early November, probably resulting from the effect of the school half-term holiday in October, before increasing once more and peaking at the end of November (figure 16).

Figure 15: Number of assessments completed, antivirals authorised and collected through the National Pandemic Flu Service, England July 2009 – February 2010

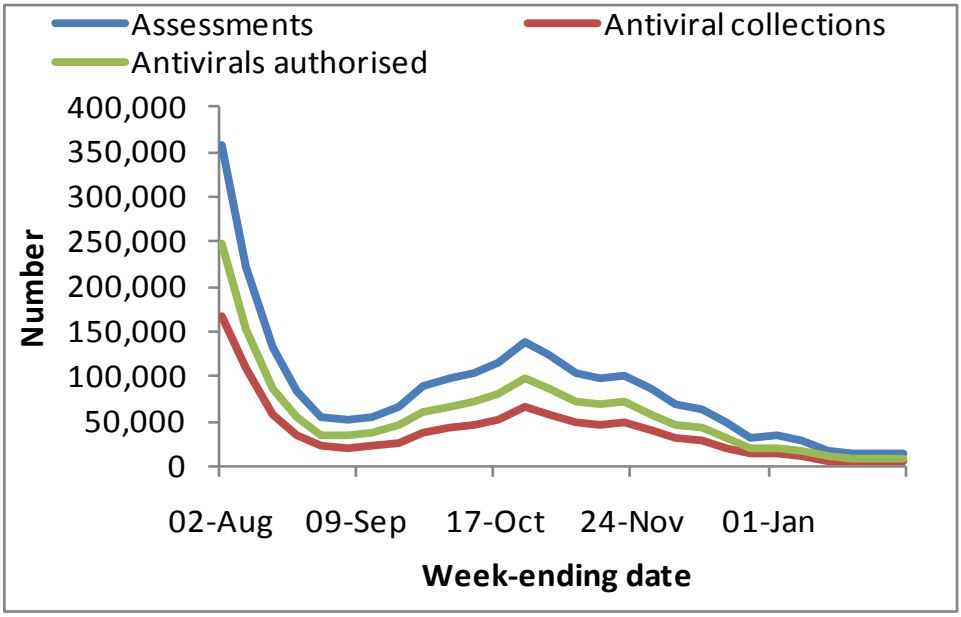
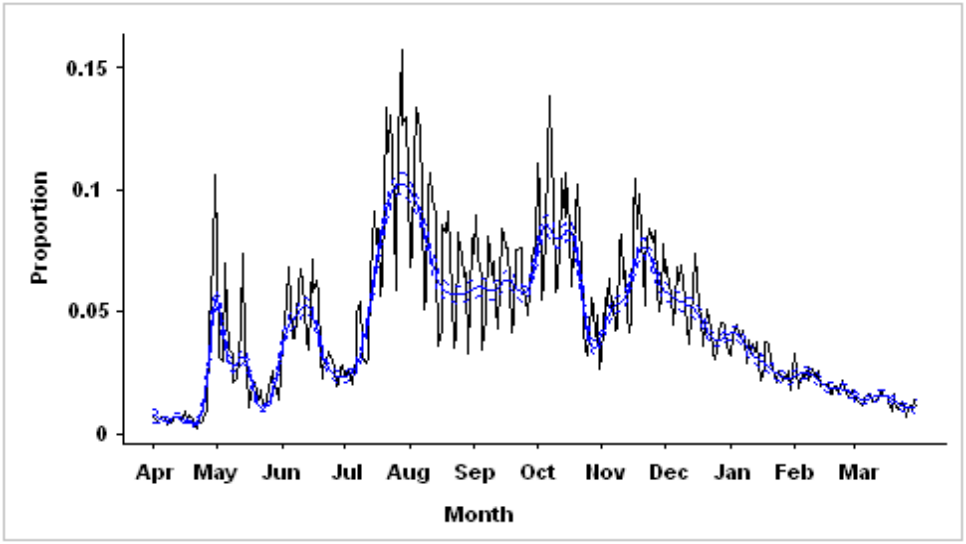


Figure 16: Daily proportion of calls due to colds/flu through NHS 24, Scotland, April 2009 – April 2010

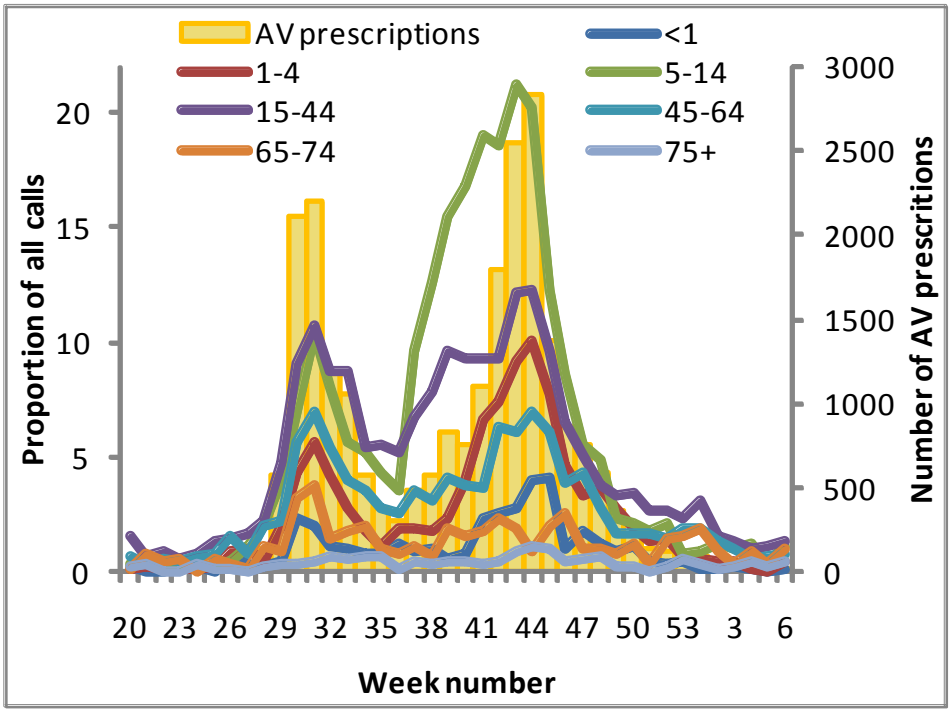


In Scotland antiviral prescribing was restricted to general practice in the treatment phase. A total of 98,000 courses of antivirals were issued across the entire pandemic. Antiviral prescribing patterns were broadly consistent with the increasing trends seen in General Practice consultations and hospital admissions. The rate of antiviral prescribing corresponded to the peak of Scotland's GP consultation rate in week 46.

In Northern Ireland, out-of-hours (OOH) consultation rates peaked initially in week 33 (49.6/100,000) when 7.5% of OOH consultations were due to influenza/ILI and then again in week 43 (rate 77.5/100,000) when 10.2% were due to influenza/ILI. In the first wave the highest proportion of OOH consultations due to influenza/ILI by age band was in the 15-44 year age group closely followed by the 5-14 year age group. This was in contrast to the second wave, when the proportion of influenza/ILI calls was markedly higher in the 5-14 year group. In week 43, 21.2% of OOH consultations in this age group were due to influenza/ILI (figure 17).

Trends in antiviral prescriptions closely corresponded to sentinel consultation rates and OOH calls, though the early increase in calls in the 5-14 year group was not mirrored by the prescription data (figure 17).

Figure 17: Weekly proportion of calls due to influenza/ILI of total calls to out-of-hours centres by age group and total number of antiviral prescriptions, Northern Ireland, May 2009 – February 2010

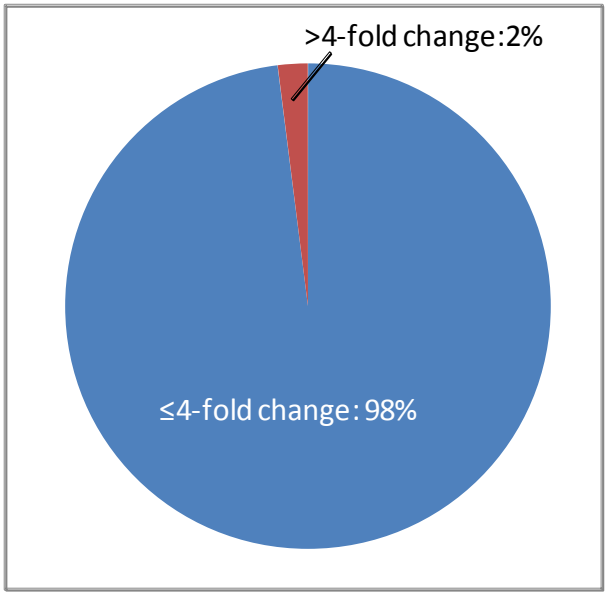


MICROBIOLOGICAL

A total of 29,228 (20,595 in England, 6,600 in Scotland, 1,369 in Northern Ireland and 664 in Wales) virologically confirmed cases of pandemic (H1N1) 2009 were reported up to 1 June 2010 (note: from July 2009 onwards, not all suspected cases were tested).

Characterisation of sentinel and non-sentinel pandemic (H1N1) 2009 viruses revealed that the majority of UK isolates were antigenically similar to the A/California/07/2009 vaccine strain. There were sporadic identifications of viruses with a greater than four-fold change in reactivity to A/California/07/2009 antiserum (2% of all isolates tested, figure 18); this change did not appear to correlate with specific amino acid substitutions in the haemagglutinin (HA) gene.

Figure 18: Antigenic reactivity with A/California/07/2009 antiserum, UK isolates, April 2009 – May 2010



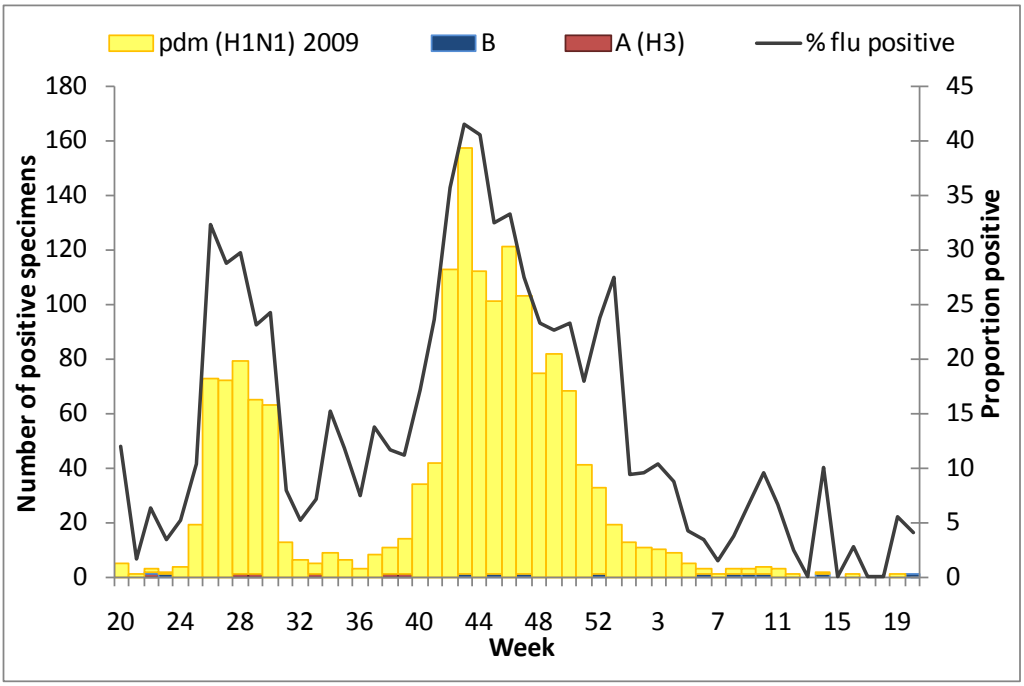
Genetic analysis of the HA gene of UK pandemic (H1N1) 2009 viruses from 2009 indicates that they are similar to the pandemic vaccine strain, A/California/07/2009. UK viruses clustered together with viruses isolated in geographically distant places, showing that there was global circulation of pandemic influenza lineages (appendix 3). The diversity seen among these viruses was less that that seen for seasonal influenza, with only 12 amino acids of difference between the two most distant viruses. All UK viruses isolated after June 2009 are characterised by substitution S203T. Other amino acid changes at residues D222E, or E374K, or N370H were also observed in the HA sequence of some UK and non-UK pandemic viruses.

From week 20 2009 to week 20 2010, an additional 78 non-pandemic influenza viruses were detected by CfI: six A (H1), four of which were detected from May to July 2009; 51 A (H3), 90% detected before October 2009 and 21 influenza B, the majority detected between January and May 2010.

Sentinel virological schemes

The proportion of samples taken by GPs in the two English sentinel schemes (RCGP/HPA and HPA/RMN schemes) positive for influenza showed two peaks corresponding to the summer and autumn waves. Unlike GP consultations, the number of positive samples and proportion positive reached higher levels in the autumn wave compared to the summer wave (figure 19). The positivity peaked at 41.2% in week 43 (ending 25 October 2009), when 156 of 379 samples were positive for pandemic (H1N1) 2009. A similar pattern was observed for the NHS Direct/NPFS schemes, with a summer and higher autumn peak (figure 19). The highest proportion positive through NHS Direct/NPFS was observed in week 44 (31.3%).

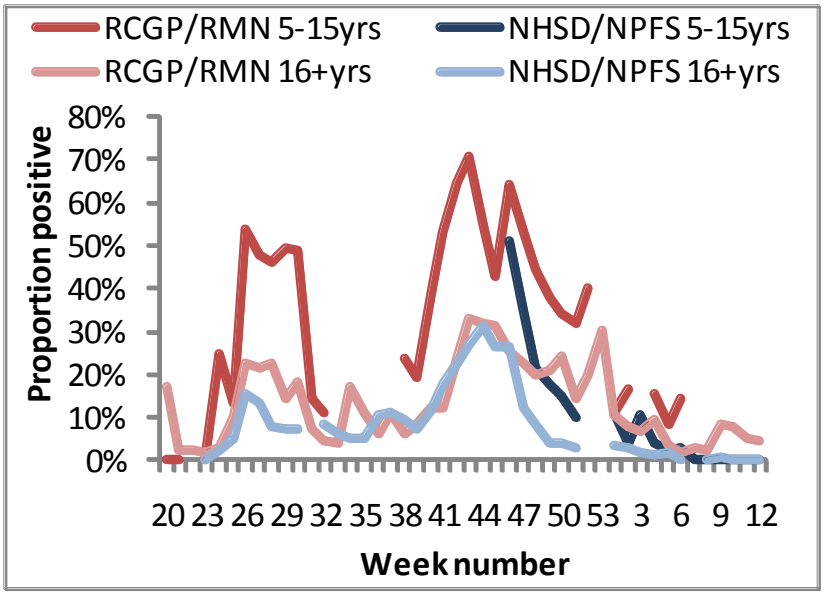
Figure 19: Samples positive for influenza through English GP sentinel virological schemes, May 2009 – May 2010



Very few specimens through the GP and self-sampling schemes tested positive for other influenza subtypes: from week 20 2009 to week 20 2010, only six influenza A (H3) and 12 influenza B viruses were detected.

The overall positivity rates through the NHS Direct and the NPFS self-sampling schemes were consistently lower than that through the GP schemes. However, children aged less than 16 years were not sampled until week 46 through NPFS; after age adjustment, the positivity rates for the GP and self-sampling schemes were largely similar (figure 20).

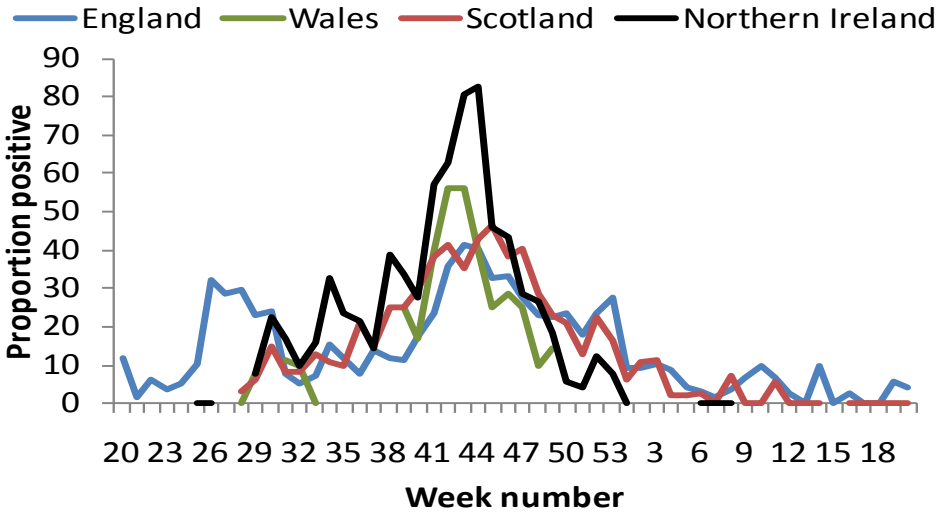
Figure 20: Samples positive for influenza through English GP and NHS Direct/NPFS sentinel virological schemes by age group, May 2009 – March 2010



NB. Sampling of children aged 5-15 years commenced through NPFS in week 46 (ending 15 November); weekly proportion positive omitted when fewer than five samples tested.

Few samples were positive for influenza through the primary care sentinel schemes in Scotland, Wales and Northern Ireland during the summer wave (figure 21). In Scotland additional sentinel swabbing centres were recruited to submit 500 samples per week across the containment phase to allow any differences within the 14 Scottish NHS boards to be identified on a weekly basis. The positivity rate increased from week 30 (ending 26 July 2009) to a peak of 46.5% positive (236/508) in week 45 (ending 8 November 2009). In Wales, a peak of 56.3% (9/16 samples positive) was observed in week 42, corresponding to the GP consultation rate peak. In Northern Ireland a peak of 82.9% (34/41 samples positive) was observed in week 44, one week after the peak in clinical activity, though the virological data from Northern Ireland is based on week of report.

Figure 21: Proportion of sentinel samples positive for influenza through GP-based schemes in the UK, by week May 2009 – May 2010



NB. All data is based on week sample was taken from the patient except in Northern Ireland, where it is the week of the reported result from the laboratory; weekly proportion positive omitted when fewer than 5 samples tested.

Antiviral resistance

From the beginning of the pandemic to 23 May 2010, a total of 6,379 pandemic (H1N1) 2009 viruses were analysed for the marker commonly associated with resistance to oseltamivir in seasonal influenza (H275Y). The viruses tested came from a cross-section of patients from all regions in the UK, age groups and from both community and hospital sources. The first two cases with viruses carrying this mutation were reported in week 38 (ending 20 September).

To date, a total of 45 (0.7%) pandemic cases have been found to carry this mutation in the UK; 15 of these 45 viruses have been tested phenotypically and confirmed to be resistant to oseltamivir while retaining sensitivity to zanamivir. Three hundred and thirty-eight of the 6,379 viruses have been fully tested for susceptibility to oseltamivir; all except the 15 described above have been found to be sensitive. Further information was available for 37 of the 45 resistant cases; 26 (70.3%) were male and 11 female, the ages ranged from 0 to 55 years with a median of 48 years. Thirty-one (83.8%) of the cases had an underlying medical condition: 23 (74.2%) were immunosuppressed and eight had another underlying

illness. Ten (22.2%) resistant cases are known to have died. In the majority (30 cases, 81%) of cases, resistance was treatment induced[28], although probable person-to- person transmission was documented in an outbreak in a hospital ward in Wales in November 2009[29].

Other respiratory viruses

The number of specimens reported to be positive for other respiratory viruses from hospital and regional laboratories across England and Wales was higher throughout the pandemic compared to the previous year (figure 22). This is likely to be due to increased collection and testing of respiratory samples during the pandemic from individuals presenting with acute respiratory illness to health services. There was a notable increase in rhinovirus detections over the autumn of 2009 and detections of parainfluenza were at higher levels in April 2010 than in the previous year. Detections of respiratory syncytial virus (RSV) were at slightly higher levels than the previous winter season. The peak of RSV detections was slightly later (1,164 in week 51) compared to the 2008/09 winter (759 in week 48). The highest number of detections was in children aged less than 5 years of age (figure 23).

Figure 22: Reports of samples positive for other respiratory viruses by week of specimen, England and Wales (LabBase), May 2008 – May 2010

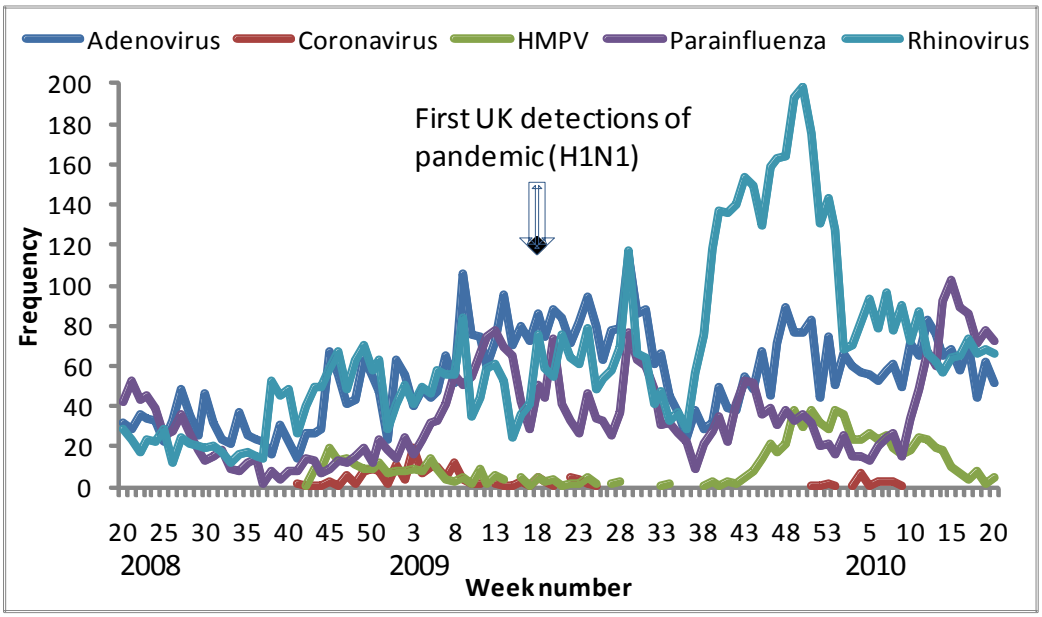
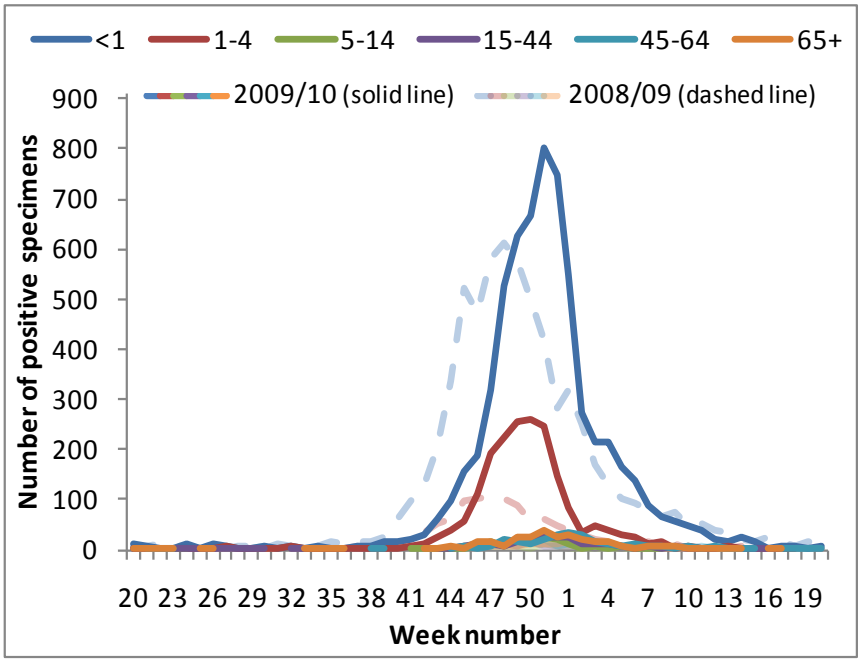
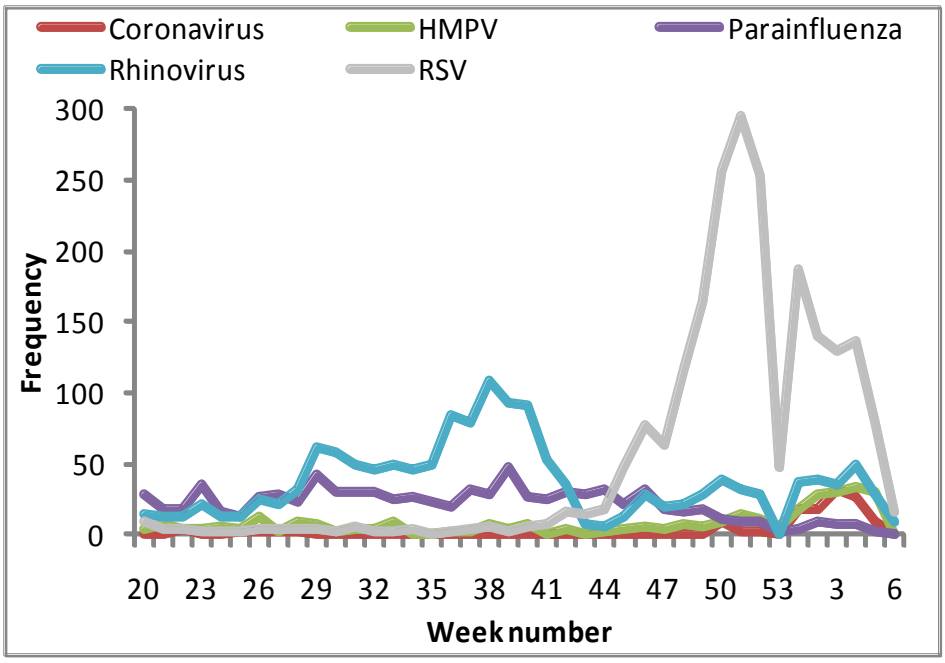


Figure 23: Reports of samples positive for respiratory syncytial virus by age group and week of specimen, England and Wales (LabBase), May 2009 – May 2010



In Scotland there was also an increase in rhinovirus detections between weeks 35 and 42 (August – October 2009). From January to March, RSV was the predominant pathogen seen, with low levels of HMPV, rhinovirus and coronavirus (figure 24).

Figure 24: Reports of samples positive for other respiratory viruses by week of specimen, Scotland May 2009 – February 2010



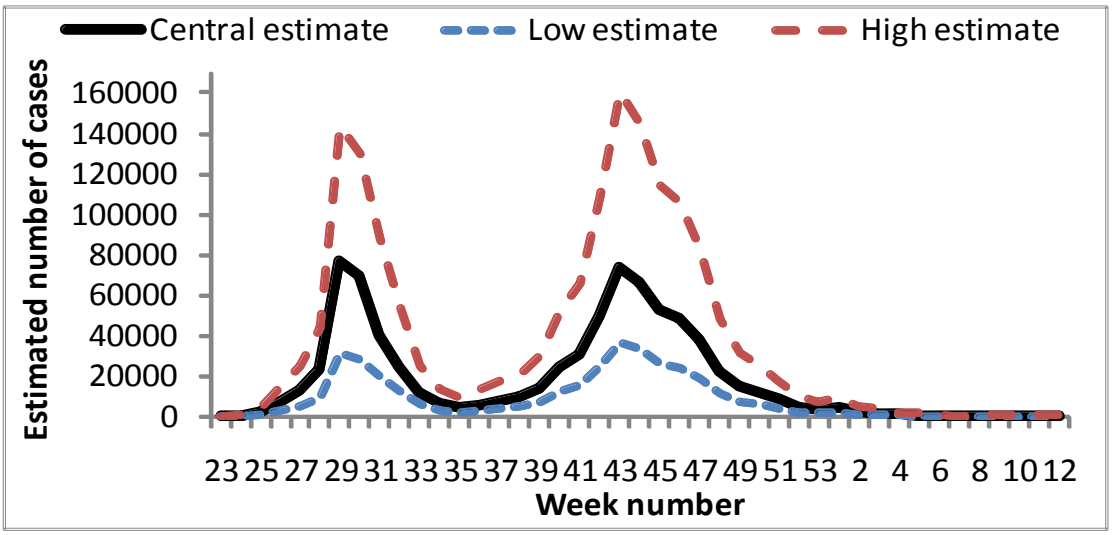
Concurrent bacterial infections

Concurrent bacterial infections (CBI) were not identified as a major feature of the pandemic. Among 20,288 confirmed English pandemic (H1N1) 2009 cases reported, a total of 76 associated CBI cases (0.4%) were identified: 39 were due to *S. pneumoniae*, 34 due to *S. aureus*, and three due to *S. pyogenes*. Twenty-four of these associated CBI cases (0.9%) were hospitalised, and 16 (4.8%) were fatal [30].

ESTIMATED CLINICAL CASES

From 7 June 2009 to 28 March 2010, a total of 784,000 (range 372,000 – 1,638,000) clinical cases of ILI due to pandemic (H1N1) 2009 were estimated to have occurred in England. The summer and autumn waves are thought to have peaked with a similar number of new cases; in week 29 (ending 19 July 2009) with an estimated 77,000 (range 31,000 – 143,000) new clinical cases and in week 43 (ending 25 October 2009) with an estimated 74,000 (range 37,000 – 160,000) clinical cases (figure 25)[31].

Figure 25: Estimated number of clinical cases in England June 2009 – March 2010



SERO-EPIDEMIOLOGY

Serological analysis of English residual population samples taken in 2008 (before the pandemic) showed that protective antibody titres increased significantly with age (*F* test $p<0{\cdot}0001$) with 31.3% (52 of 166; 24.8—38.7) of samples from adults aged 80 years or older with haemagglutination inhibition titre 1:32 or more[7]. The presence of such cross-reactive antibody in older birth cohorts explains why younger people were predominantly affected through both pandemic waves in the UK.

Comparing the proportion of English samples with haemagglutination inhibition titre equal to or above the putative threshold of 1:32 before (baseline) and after the first pandemic wave, in all regions children aged under 15 years showed a significant increase from baseline (6.3%, 1.8—12.9). In London and the West Midlands, which experienced early and intense pandemic activity compared to the rest of England, the difference between baseline and September 2009, was 21.3% (95% CI 8.8—40.3) for children younger than 5 years of age,

42.0% (26.3—58.2) for 5—14-year-olds, and 20.6% (1.6—42.4) for 15—24-year-olds. No difference between baseline and September was observed in older age groups[7]. Additional analyses for other regions and the post-second wave situation are pending.
In Scotland, serology data suggests that the proportion of people infected during the two pandemic waves varied by region, with samples from Glasgow showing a lower proportion positive than Aberdeen and Edinburgh[8].

SEVERITY INDICATORS

HOSPITALISATION

The number of people reported to be hospitalised in NHS trusts in England with suspected pandemic (H1N1) 2009 showed two peaks similar to the other surveillance indicators. The highest hospitalisation rate was consistently in children aged less than 5 years. Between July 2009 and February 2010, when this surveillance system was operational, an overall cumulative rate of 221.7 per 100,000 population (95% CI 216.4 – 227.1) was observed in children under 5 years, which was 6 times higher than in the 16-64 year group (rate ratio 5.9, 95% CI 5.7 – 6.1). The rate in the under 5 year group peaked at 17.8 (95% CI 16.3 – 19.4) per 100,000 population in week 49 when it was 10 times higher (95% CI 8.9 – 11.2) than the rate in the 16-64 year age group.

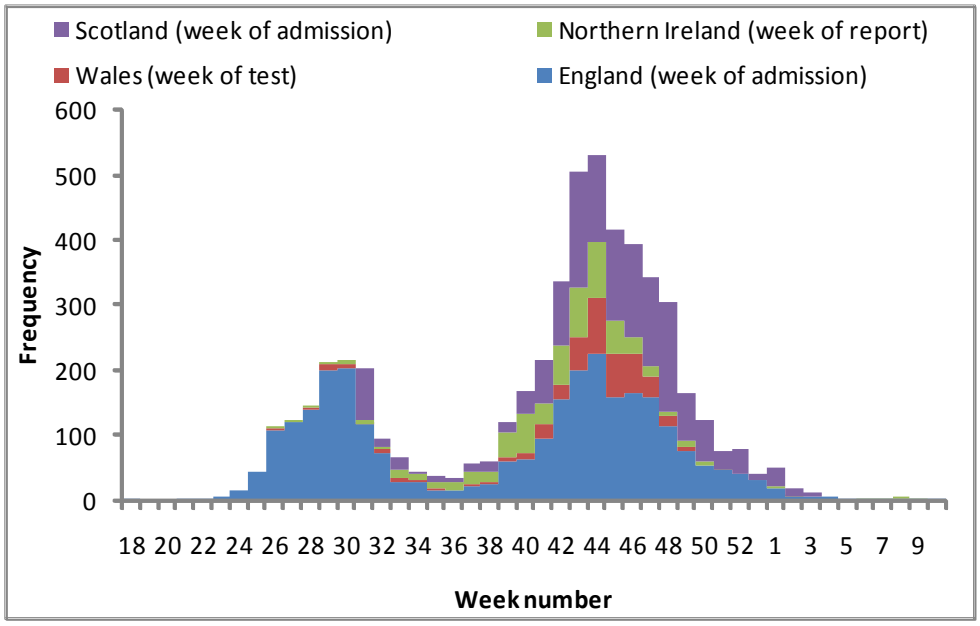
A total of 2,831 patients were reported as hospitalised with confirmed pandemic (H1N1) 2009 infection in England from the beginning of the pandemic to April 2010 through the HPA/CMO reporting system in 129 acute hospital trusts (figure 26). Thirty-eight per cent of the cases were admitted in the summer pandemic wave. In total, 55.5% of hospitalised cases with available information were reported to have an underlying risk factor for severe disease including pregnancy and obesity[32].

In Northern Ireland there were 580 hospital admissions of confirmed pandemic (H1N1) 2009 of which 51 (8.8%) occurred during the first wave (weeks 21 – 35) (figure 25), with four admissions to ICU (3.9%) The proportion of admissions of confirmed cases to ICU in the second wave was 9.1%. While the weekly hospitalisation trend closely corresponded to sentinel consultation rates in the second wave this was less so during the first wave when there were comparatively few hospitalisations. Admission rates were highest in the 0-4 year age group (109.5 per 100,000) followed by the 5-14 age group (admission rate 51.5 per 100,000)[33].

In Scotland a total of 1542 patients were hospitalised with confirmed pandemic (H1N1) 2009 infection over the period of the pandemic. The peak week for admission was week 43 (ending 25 October 2009) (figure 26).

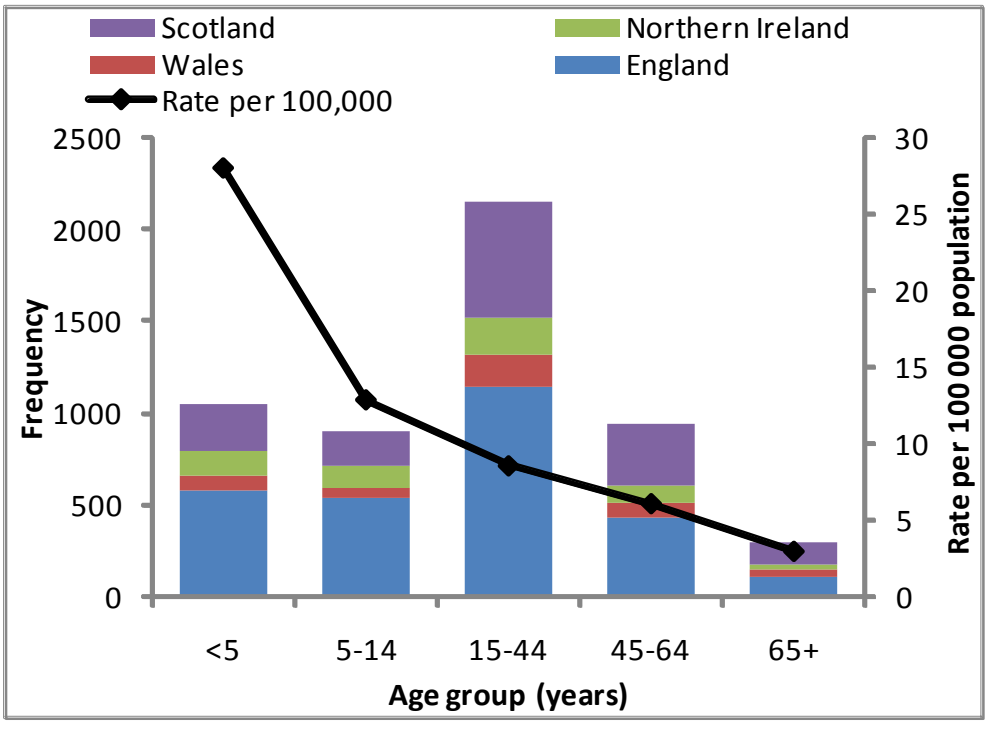
In Wales 423 patients were hospitalised with virologically confirmed pandemic (H1N1) 2009. Similar to Northern Ireland, there were few hospitalisations during the first pandemic wave; the peak of hospital admissions in Wales (by week of test) was week 44 (ending 1 November 2009) when there were 83 hospitalisations (figure 26).

Figure 26: Number of hospitalisations for confirmed pandemic (H1N1) 2009 by week and country, April 2009 – March 2010, UK



Across the UK, the hospitalisation rate decreased with age with children aged under 5 years having the highest population hospitalisation rate (28 per 100,000 for the entire UK) (figure 27).

Figure 27: Number and rate of hospitalisations with confirmed pandemic (H1N1) 2009 by age group and country, April 2009 – March 2010, UK

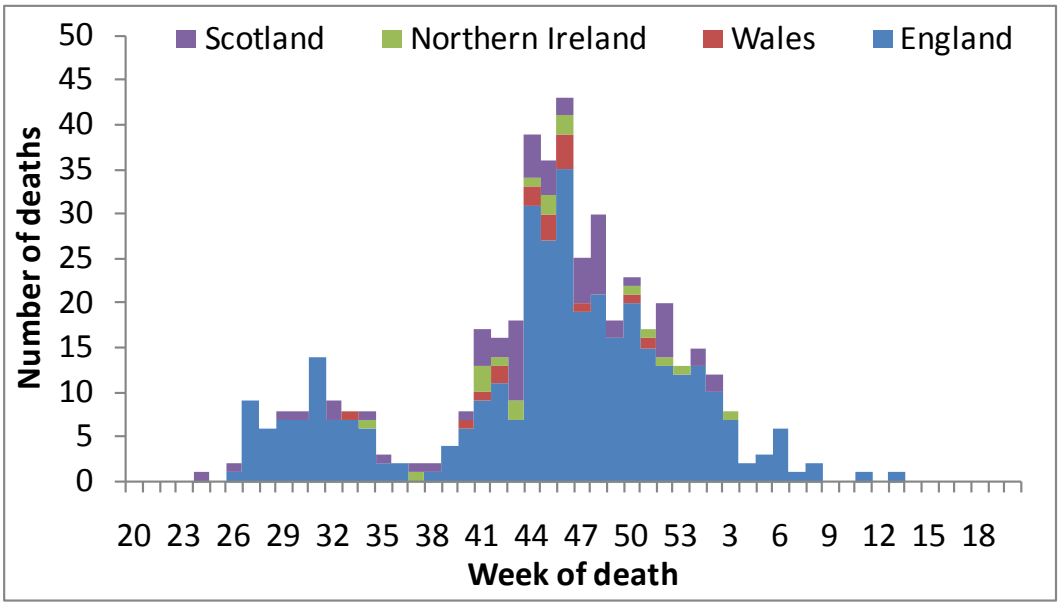


The FLU-CIN study collected information on 631 patients admitted to 55 UK hospitals with confirmed pandemic (H1N1) 2009 infection in the first wave. This in-depth study found that non-white and pregnant patients were over-represented and 45% of patients had an underlying medical condition. Of the 29 patients who died, 59% were previously healthy[14].

MORTALITY

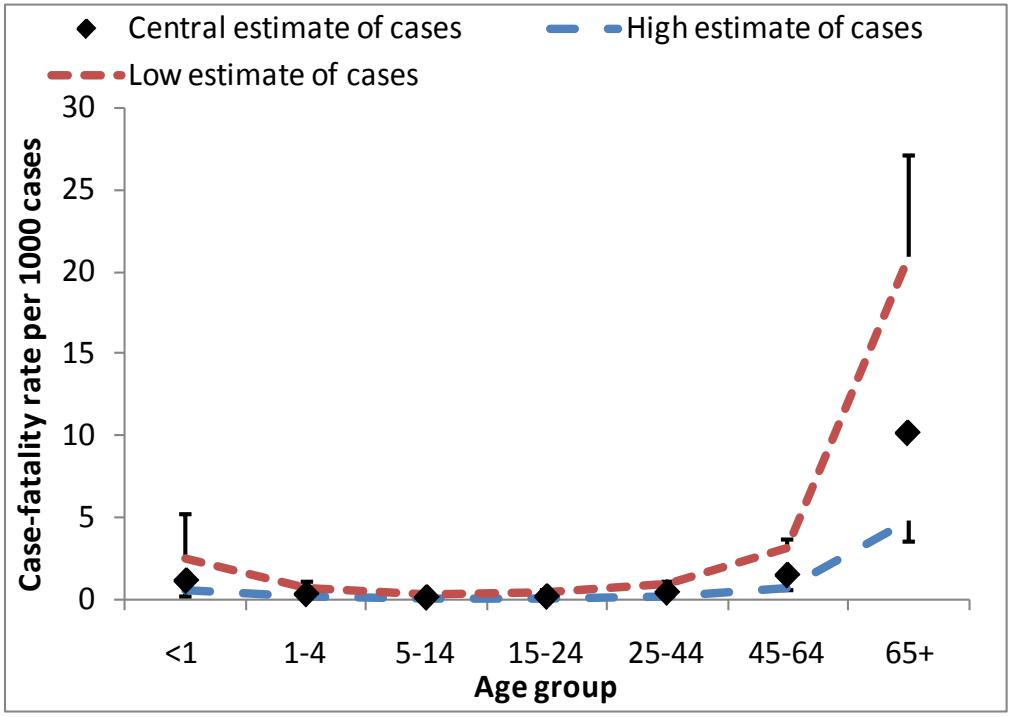
The first death due to pandemic (H1N1) 2009 in the UK occurred on 14 June 2009. A total of 474 deaths with confirmed pandemic (H1N1) 2009 (either laboratory confirmed or with mention on the death certificate) were reported in the UK up to 15 April 2010 (359 in England, 69 in Scotland, 18 in Northern Ireland and 28 in Wales). A number of deaths occurred in the spring/summer of 2009 but the majority (83%) occurred over the autumn/winter (figure 28). Seventy-two per cent of fatal cases were reported to have an underlying risk factor for severe disease[34]. [34]

Figure 28: deaths due to pandemic (H1N1) 2009 by week of death and country, UK May 2009 – May 2010 (adapted from[34])



The symptomatic case-fatality ratio was estimated to be 0.04%[34]. The majority of deaths occurred in people aged under 65 years old (85% of English deaths), though the estimated case fatality rate was much higher in older adults aged 65 years or over, in whom infection was much less common (figure 29).

Figure 29: Estimated case fatality rate by age group, England, June 2009 – April 2010



In England and Wales, no excess of weekly death registrations above the threshold was observed over the summer of 2009. In the 2009/10 winter season 3,261 (95% CI 2,993 – 3,530) excess deaths were estimated to have occurred in weeks 52 and 53 (table 3); this is unlikely to be due to influenza, as all other influenza indicators were showing low activity at that time.

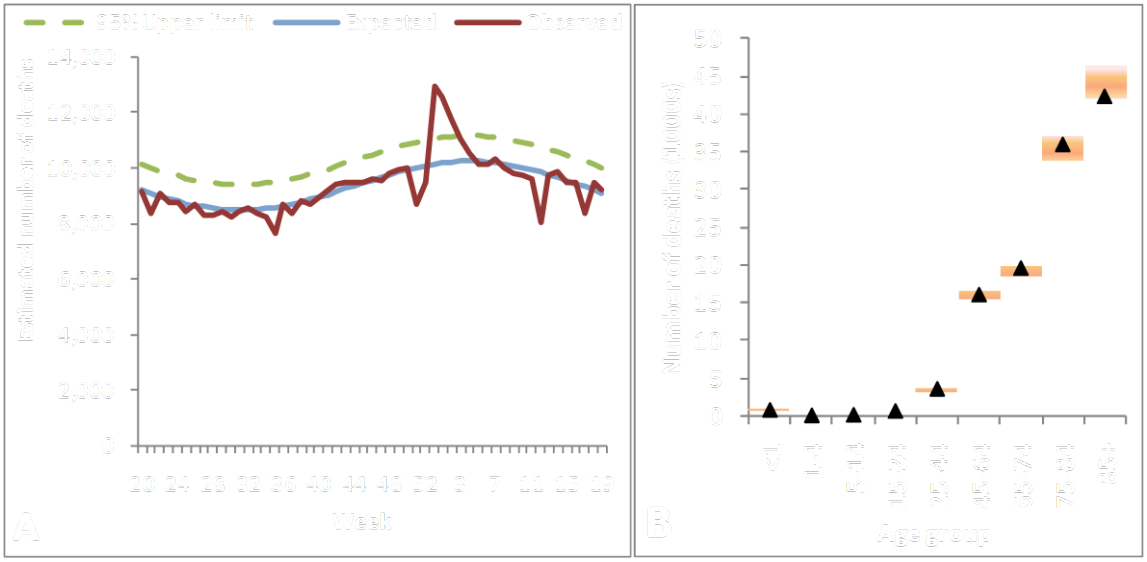
Table 3: Annual excess all-cause mortality by influenza season, 1999-2010

Season	Excess (95% CI)	Total no. of deaths	% deaths in excess
1999/2000	21227 (20690 - 21764)	395,507	5.4%
2000/2001	746 (478 - 1015)	383,805	0.2%
2001/2002	6824 (6556 - 7093)	388,552	1.8%
2002/2003	6392 (6123 - 6660)	386,946	1.7%
2003/2004	4873 (4336 - 5410)	377,242	1.3%
2004/2005	1860 (1591 - 2128)	372,259	0.5%
2005/2006	Not detected	361,910	0.0%
2006/2007	Not detected	318,775	0.0%
2007/2008	457 (0 - 994)	321,853	0.1%
2008/2009	10146 (9878 - 10588)	327,334	3.1%
Summer 2009	Not detected	170,231	0.0%
2009/2010	3261 (2992 - 3529)	315,931	1.0%

It is notable that this excess occurred in a period when the UK experienced a prolonged cold snap. Closure of registry offices over bank holidays was also temporally associated with an artefactual dip and subsequent increase at the end of December and the beginning of April (figure 30A).

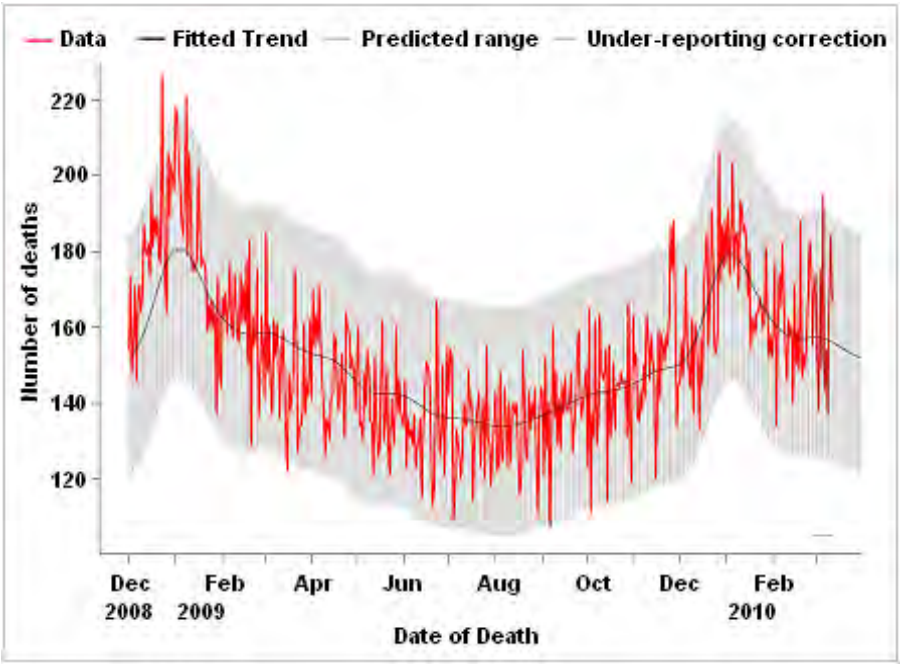
Analysis of daily mortality data made available from the General Registry Office (England and Wales) by age-group over the two pandemic waves shows that there was no evidence of any age-specific excess mortality throughout the pandemic prior to the Christmas excess (figure 30B).

Figure 30: A: all cause mortality from ONS (England and Wales) with expected number of deaths (HPA), May 2009 – May 2010; B: Age-specific mortality monitoring (GRO), shaded areas show expected range, week 37-49 (Autumn wave) England and Wales



The number of weekly Scottish deaths remained within expected ranges over the 2009 summer. There was an increase above expected levels at the end of December/ beginning of January and a slight excess of deaths at end of November. The overall pattern was similar to what was seen in England and Wales, with the excess coinciding with low influenza activity and cold weather (figure 31).

Figure 31: all cause mortality (Scotland) with expected number of deaths through Serfling and GAM methods (HPS), April 2009 – May 2010



RISK GROUPS

Data from the FF100 surveillance project showed that people with underlying medical conditions, such as chronic respiratory, neurological or heart disease were not at significantly greater risk of clinical infection in the early stages of the pandemic[21]. In England, people aged between 6 months and less than 65 years with an underlying condition were 10 times more likely to be hospitalised with confirmed pandemic (H1N1) 2009 infection compared to people of the same age without an underlying condition, and 18 times more likely to die from the infection[32;34]. The underlying conditions with the highest risk of hospitalisation with pandemic (H1N1) 2009 infection were immunosuppression, chronic renal disease and chronic neurological disease (including stroke)[32]. For death, the risks were highest for chronic neurological disease (excluding stroke), chronic liver disease and immunosuppression[34]. Pregnant women were not at an elevated risk of becoming cases, but were 5 times more likely to be hospitalised and seven times more likely to die, once infected, compared to females of child-bearing age (15-44 years) with no underlying condition (table 4)[34].

Table 4: Rate ratios for hospitalisation and mortality by risk group, England adapted from [32] and [34]

	Hospitalisations					Deaths				
	N	Rate ratio	95% confidence interval			N	Rate ratio	95% confidence interval		
Total	2,463					361				
Total aged 65 or over	104					56				
Any risk factor (65y+)	67	2.8	1.7	–	4.5	44	6.0	2.7	–	13.4
No risk factor (65y+)	23	Baseline				7	Baseline			
Total aged 6m-65y	2,258					300				
Any risk factor (6m-65y)	1,033	10.3	9.4	–	11	190	18.7	14.5	–	24.1
No risk factor (6m-65y)	1,028	Baseline				84	Baseline			
Chronic renal disease	58	17.2	13	–	22	16	37.7	22.0	–	64.5
Chronic heart disease	85	5.9	4.7	–	7.4	26	16.7	10.8	–	25.9
Chronic respiratory disease	601	12	11	–	13	51	11.7	8.3	–	16.6
Chronic liver disease	22	8.7	5.7	–	13	23	70.8	44.4	–	112.8
Diabetes	78	4.3	3.4	–	5.4	23	9.8	6.1	–	15.6
Immunosuppression	135	18.5	15	–	22	48	56.0	39.0	–	80.4
Stroke/TIA*				–		3	7.2	2.3	–	23.0
Chronic neurological disease*	123	14.3	12	–	17	66	115.8	85.2	–	157.5
Total females of childbearing age (15-44years)	585					63				
Females of childbearing age with no risk factor	291	Baseline				22	Baseline			
Pregnant (F15-44 only)	145	5.1	4.2	–	6.1	10	7.0	3.3	–	14.8

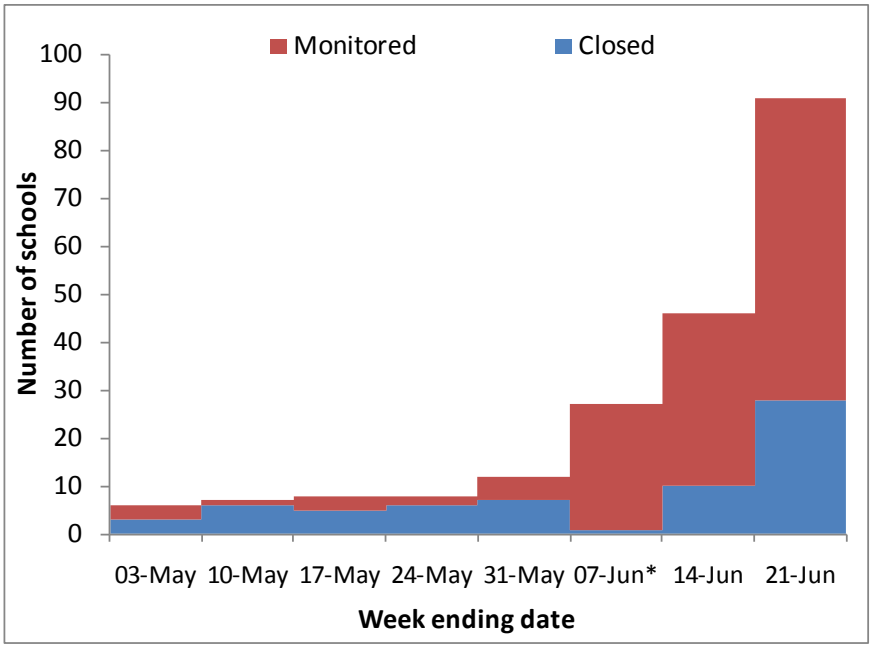
** Strokes are included under neurological disease for the hospitalisation data but are separate for mortality data*

INTERVENTIONS

SCHOOL CLOSURES

At the beginning of the pandemic, many schools were advised to temporarily close if there were confirmed cases of pandemic (H1N1) 2009 among staff or students. Antiviral prophylaxis was also given to close contacts of confirmed cases as part of the containment strategy. Up to the end of the containment phase, 74 schools in England were reported to have been closed due to pandemic (H1N1) 2009 and 417 schools reported confirmed cases to HPA. Figure 32 shows the increasing number of schools in England affected each week from the beginning of May to 21 June 2009. In Northern Ireland there were 26 school outbreaks with the last being during week 5 2010; none of these schools were closed due to the outbreak. In Scotland there were 29 school closures during the containment phase.

Figure 32: Number of schools affected by pandemic influenza, England; May – June 2009



** Half-term holiday for most schools in England; Monitored: confirmed or suspected cases in the school but remaining open, Closed: partially or total suspension of classes due to confirmed or suspected cases of pandemic influenza.*

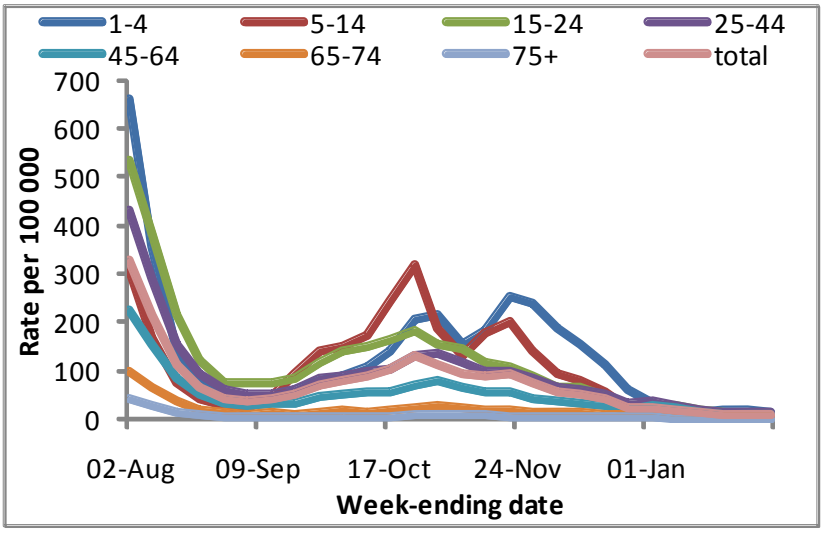
Whether individual school closures had significant effects on transmission is unclear [personal communication, H Maguire]. The closure of all UK schools for the summer holiday is likely to have played a large part in interrupting transmission over this period.

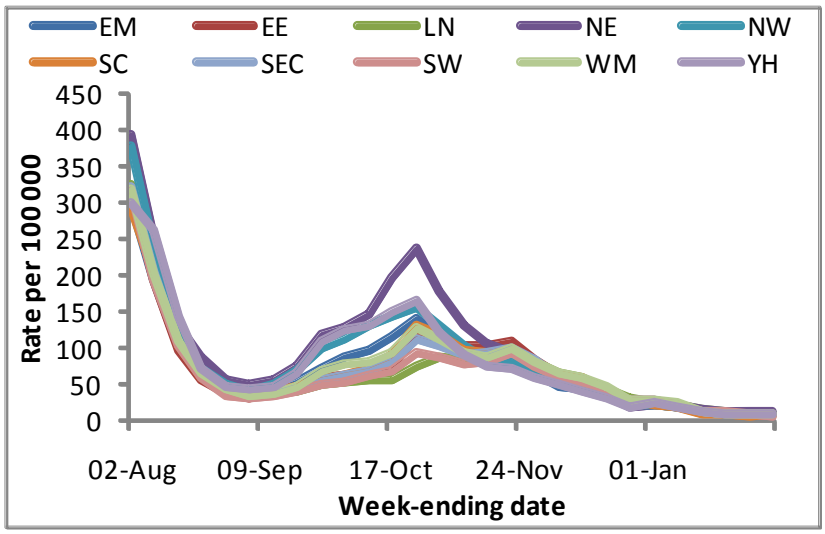
ANTIVIRALS

Uptake: Of the 365 UK FF100 cases with information available, 335 (91.8%) reported receiving treatment with antiviral drugs[21]. Of 656 contacts with available information, 595 (90.7%) reported receiving antiviral drugs[27].

Sixty-eight per cent of assessments through the NPFS (1,645,948 of 2,401,043) resulted in an authorisation for antiviral drugs being issued; of these 66% (1,079,179 [2.1% of the population]) were collected. The population rate of collection varied by region and age group. In the summer wave the rate of collection was notably higher in the North East compared to other regions and the rates were highest in children aged 1-4 and 5-14 (figure 33). Babies aged less than one year were the only age group not considered by NPFS and were always referred to their GP, as were those with underlying risk factors for severe disease.

Figure 33: weekly rate of antiviral collection, per 100,000 population through NPFS by region* and age group, August 2009 – March 2010, England





**EM: East Midlands, EE: East of England, LN: London, NE: North East, NW: North West, SC: South Central, SEC: South East Coast, SW: South West, WM: West Midlands, YH: Yorkshire and Humberside.*

A total of 24,160 courses of antivirals were issued through primary and secondary care in Northern Ireland (1.4% of the population).

In Scotland, 98,000 courses of antivirals were issued (1.9% of the population).

Effectiveness: Data from the FF100 study showed that the household secondary attack rate was significantly affected by the use of antivirals with a 92% reduction in virologically confirmed secondary attack rate at two weeks[27].

Impact: Modelling data from cases identified during the containment phase suggest that treatment of cases in association with prophylaxis of their close contacts reduced the reproduction number by an estimated 16% (95% CI 12 – 20%) in those who received the intervention; the overall population-level effect will have been smaller than this, as most affected individuals did not seek care [18].

Safety: Forty-one (12.2%) of the 335 FF100 cases who took antiviral drugs, reported side-effects which they attributed to antiviral treatment. More adults aged 16 or older (25 of 140 – 15%) than children (16 of 153 – 9.5%) reported an adverse event. Of the 17 who had specified the severity of the adverse event, 15 (88.2%) graded it as moderate and two as severe. Gastrointestinal symptoms were the most commonly reported adverse events, reported by 30 of the 41 cases reporting side-effects (11 (37.0%) children and 19 adults)[21].

VACCINATION

Pandemic vaccine uptake: In England, 37.6% of patients in clinical risk groups, including pregnant women, and 23.6% of healthy children aged six months to 5 years received the swine influenza monovalent vaccine (Pandemrix, dose 1) by 31 March 2010 [35].
In Northern Ireland and Scotland uptake was higher in all groups compared to the England data with 86.5% of people in Northern Ireland aged under 65 years in a risk group receiving the vaccine (though this does not include pregnant women of whom 57.1% received the vaccine). Welsh vaccine uptake was similar to that of England (table 5).

Table 5: Pandemic vaccine uptake, dates, by country and risk group, UK

	England*	Northern Ireland**	Scotland*	Wales***
<65 years at risk	**37.6%**	**86.5%**	**52.1% - 54.5%**	**42.1%**
Pregnant women	**Inc. above**	**57.1%**	**Inc. above**	**Inc. above**
Children <5 years	**23.6%**	**38.3%**	**44.6%**	**26.1%**
>65 years at risk	**40.4%**	**74.9%**	**56.2% - 57.4%**	**45.0%**
Health care workers	**40.3%**	**47.7%**	**55.1%**	**N/A**

** to 31 March 2010; ** to 28 February 2010, except pregnancy which is to 30 November 2009; ***to June 2010*

Pandemic vaccine effectiveness: Data from the sentinel primary care schemes in Scotland and England, gave an adjusted monovalent influenza vaccine effectiveness in excess of 70%[36].

Pandemic vaccine cost-effectiveness modelling: Modelling estimated that vaccination of high-risk groups would prevent about 45 deaths (80% credibility interval 26-67) in England, and save around 2900 quality adjusted life years (QALYs) (80% credibility interval 1600-4500). Such a vaccination programme was estimated to be cost-effective assuming the cost of the vaccine was treated as a sunk cost. Extending vaccination to school-age children was found to be the most cost-effective intervention in the model[37]. Due to the timing of the programme in relation to pandemic activity, it was unable to prevent more cases and deaths.

Seasonal vaccine uptake: In England, the uptake of the 2009/10 seasonal influenza vaccine in those aged 65 years and over reached 72.4%; a slight decrease compared to the previous season (74.1%). In those aged under 65 years falling in a clinical risk group, uptake increased from 47.1% in 2008/09 to 51.6% in 2009/10[38]. In Northern Ireland, the uptake in over 65 year-olds was similar to the previous season (77%); there was a slight decrease in Scotland (75% vs. 76.3%) and an increase in Wales (63.5% vs. 59.5%) (table 6).

Table 6: Seasonal vaccine uptake, dates, by country, UK

	England	**Northern Ireland**	**Scotland**	**Wales**
>65 years 2009/10 season	**72.4%**	**77.0%**	**75.0%**	**63.5%**
>65 years 2008/09 season	*74.1%*	*76.8%*	*76.3%*	*59.5%*
<65 years at risk 2009/10 season	**51.6%**	**80.0%**	**53.4%**	**49.1%**
<65 years at risk 2008/09 season	*47.1%*	*74.0%*	*47.8%*	*40.8%*

Seasonal vaccine effectiveness: There was no evidence that the 2008/09 nor 2009/10 seasonal influenza vaccines had any significant effect on infection with pandemic influenza[39;40].

Season vaccine 2010/11 season: The World Health Organization recommended that the 2010/11 northern hemisphere vaccine contain an A/California/7/2009 (H1N1)-like virus (pandemic), an A/Perth/16/2009 (H3N2)-like virus and a B/Brisbane/60/2008-like virus[41]. In the UK, pregnant women who have not previously received the pandemic vaccine are recommended to receive the trivalent vaccine, in addition to the normal groups (over 65 year-olds, those in risk groups, HCWs, carers etc.). There are also some groups who are recommended to receive the monovalent pandemic vaccine[42].

Discussion and conclusions

Following the emergence of pandemic (H1N1) 2009 in North America in April 2009, imported cases of this novel virus were quickly identified across the UK. The first cases were mainly travellers returning from Mexico or the United States and secondary cases linked to indigenous transmission among close contacts in households and schools. Two waves of pandemic activity were observed, separated by the closure of schools for summer holidays, which appears to have reduced transmission (appendix 1). Community transmission was initially observed in London and the West Midlands following large school outbreaks. Cases were reported from all UK regions in the summer wave, though there was a variable level of transmission; all regions of the UK were affected in a more uniform way during the autumn wave. Most cases were reported to have a mild illness consistent with influenza. Severe disease, hospitalisations and deaths were reported in a minority of cases, particularly among those with underlying clinical disease. There was an overall low case-fatality ratio, particularly compared to previous pandemics. Clinical counter-measures were employed across the UK, with evidence that antivirals were effective in reducing transmission and disease severity. Pandemic vaccine was effective, though uptake only increased in the second half of the autumn wave.

Although the first European cases of pandemic (H1N1) 2009 were confirmed in Spain on April 27 2009 and most European countries had reported cases by the end of May 2009[43], the UK and Ireland were the only European countries reporting high influenza activity during the summer of 2009[44]. In this respect there was greater similarity with other northern hemisphere countries such as the USA and Canada. Indeed, the UK has significantly more air traffic from North America compared to most European countries and thus experienced multiple introductions during spring 2009 onwards, which may be one of the explanatory factors. The main wave of pandemic influenza activity in Europe occurred in the autumn, with many countries, including the UK, reporting levels of activity higher and earlier than in recent seasons[45].

Evidence gathered from the FF100 project showed that most cases experienced a mild, typical influenza-like illness, with fever and respiratory symptoms reported most frequently[21]. A significant proportion of cases reported gastrointestinal symptoms – an observation that was also seen in other geographic settings, including those where antivirals (a potential confounding factor) were used less widely [46]. To optimise its positive predictive value, a strict case definition was used initially based on clinical (fever and respiratory symptoms) and epidemiological (recent travel to an affected area or contact with a confirmed or suspected case) criteria. This meant that people who did not fulfil these definitions, for example cases with milder clinical symptoms, may not have been tested; they would have been missed, underestimating the number of infections.

Compared to seasonal influenza, pandemic (H1N1) 2009 tended to affect younger people. Serological studies have demonstrated evidence of widespread infection in the population during the pandemic particularly in younger age-groups. People older than 50 years of age had evidence of cross-reactive H1N1 antibodies due to exposures to influenza A (H1N1) prior to 1957, explaining the lower age-specific attack rates in this group [7;8]. Other sero-epidemiology studies elsewhere have demonstrated similar findings[47].

The UK's containment approach recommended the use of antiviral drugs for all symptomatic confirmed cases and their close contacts. This may have slowed the initial spread of the virus, as suggested by transmission and modelling studies, but any impact is likely to have been small. Furthermore, use of antivirals in the early treatment of cases significantly reduced the severity of illness – in terms of duration of illness[21], risk of hospitalisation[14] and risk of ICU admission[32]. Despite this intervention, a number of patients were hospitalised and died due to pandemic influenza. Although people aged over 65 were less likely to acquire the infection, once infected they were more likely to have a more severe outcome compared to younger cases. People with underlying clinical conditions were also more likely to have a severe outcome, as would be expected with seasonal influenza. As has been found in other countries, pregnant women were also at higher risk of severe outcomes[48]. A significant minority of hospitalised and fatal cases did not have any underlying condition.

On 10 August 2010, the Director-General of the World Health Organization announced that the world had moved into the post-pandemic period[49]. For the forthcoming 2010/11 season, the pandemic (H1N1) 2009 virus is expected to behave as a normal seasonal influenza virus, continuing to circulate, perhaps along with other seasonal influenza viruses, for some years to come. The WHO has recommended vigilance regarding future activity due to the pandemic (H1N1) 2009 virus, particularly as it is likely that the virus will continue to cause serious disease in a minority of younger age groups and people in high-risk groups[50].

With the declaration of the post-pandemic phase, the focus is on normalisation of influenza surveillance. There is still, however, a requirement to monitor influenza activity for a potential resurgence and to ensure any possible increase in clinical indicators is rapidly identified and investigated. As outlined, during the pandemic a number of additional surveillance systems were developed to provide a more complete picture of influenza and broader respiratory virus activity. Several of these will be incorporated into the standard suite of influenza surveillance activities and be maintained beyond the current pandemic in particular a sentinel hospital pilot surveillance system for severe disease and the laboratory denominator surveillance system for influenza and other respiratory viruses.

In conclusion, pandemic (H1N1) 2009 caused moderate to high levels of influenza activity in the UK during summer 2009, a period when activity is usually at low levels, and in the autumn of 2009. Although the illness caused was generally mild, there were significant hospitalisations and intensive care admissions and some fatalities, particularly among younger people and those with underlying clinical risk factors. In some areas large proportions of the community are thought to have been infected, though this is likely to vary across the country. The pandemic virus was consistently the predominant influenza virus circulating and appeared to replace previously circulating A (H1N1) viruses. Experience from the 2010 winter season in the Southern Hemisphere suggests that H1N1 will continue to circulate in the coming winter season in the Northern Hemisphere, possibly with other seasonal influenza viruses. Unless there is significant antigenic drift, impact is unlikely to be as large as that observed in 2009/10.

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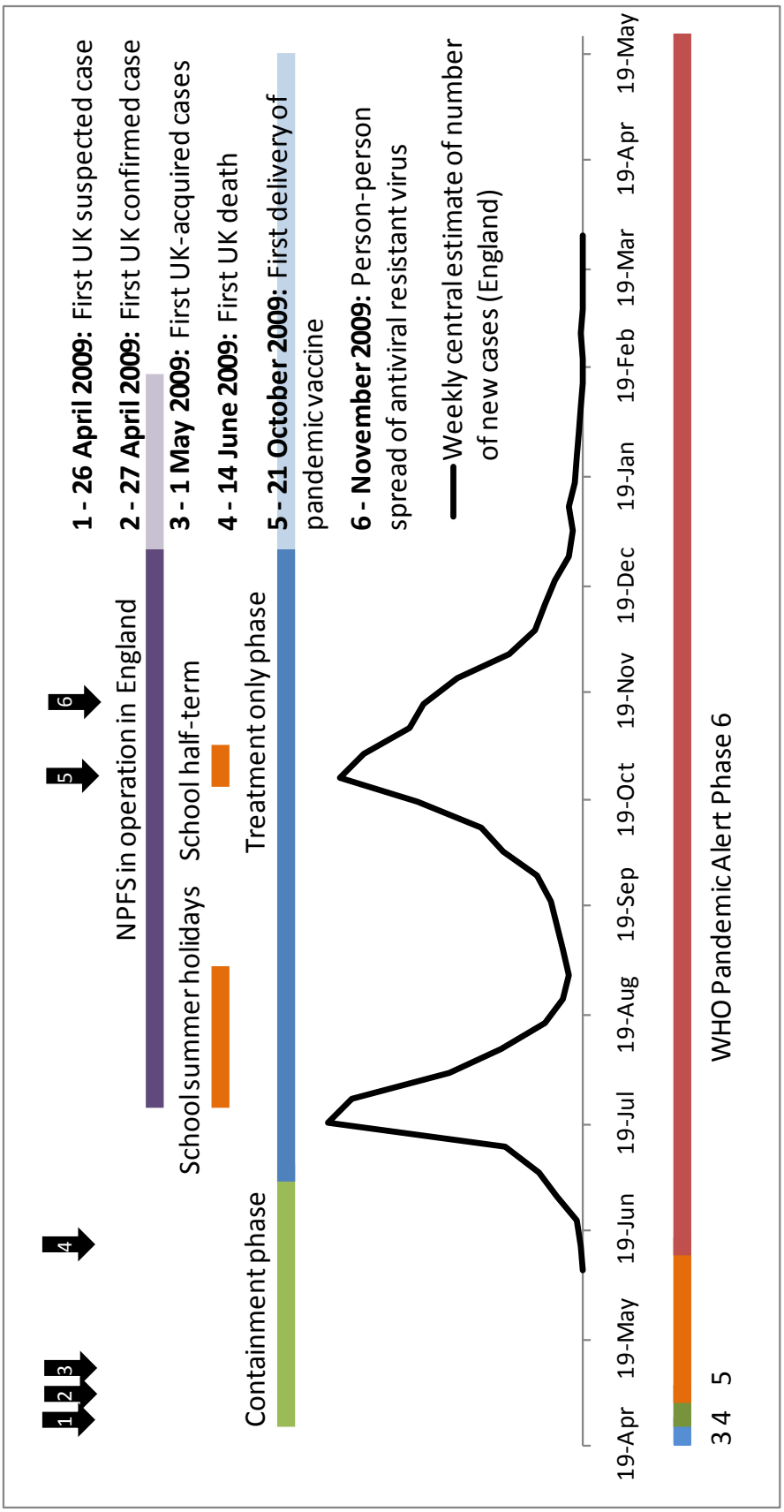
Scotland
Fiona Johnston, John Love, Louise Primrose, Ian Henton, Tricia Cassels, Cathy Hunter, Lynne Otterson, Roy Bryce, Phil Webb, Bev Wayne, Ian Watson, Billy Smyth, Oliver Blatchford, Martin Donaghy, David Goldberg, Sharon Hutchinson, Lesley Wallace, Beth Cullen, Eva Van Velsen, Amanda Weir, Alison Smith-Palmer, Katy Sinka, Shirley McLean and other HPS colleagues. Dr Bill Carman, Catherine Frew, Rory Gunson, Walt Adamson, West of Scotland Specialist Virology Centre and colleagues in each of the Scottish Virology laboratories, Adam Wagner University of Strathclyde, Dr George Crooks and colleagues in NHS 24, Gordon Munro and colleagues GRO(S), Annemarie Van Helsum and colleagues NSS PTI, Scottish General Practitioners, NHS board Health Protection and Infection Control teams.

Wales
Roland Salmon and staff at Public Health Wales CDSC; Marion Lyons, Jane Salmon in the Public Health Wales Health Protection Team; Liz McCruden, Catherine Moore at the Public Health Wales Specialist Virology Centre.

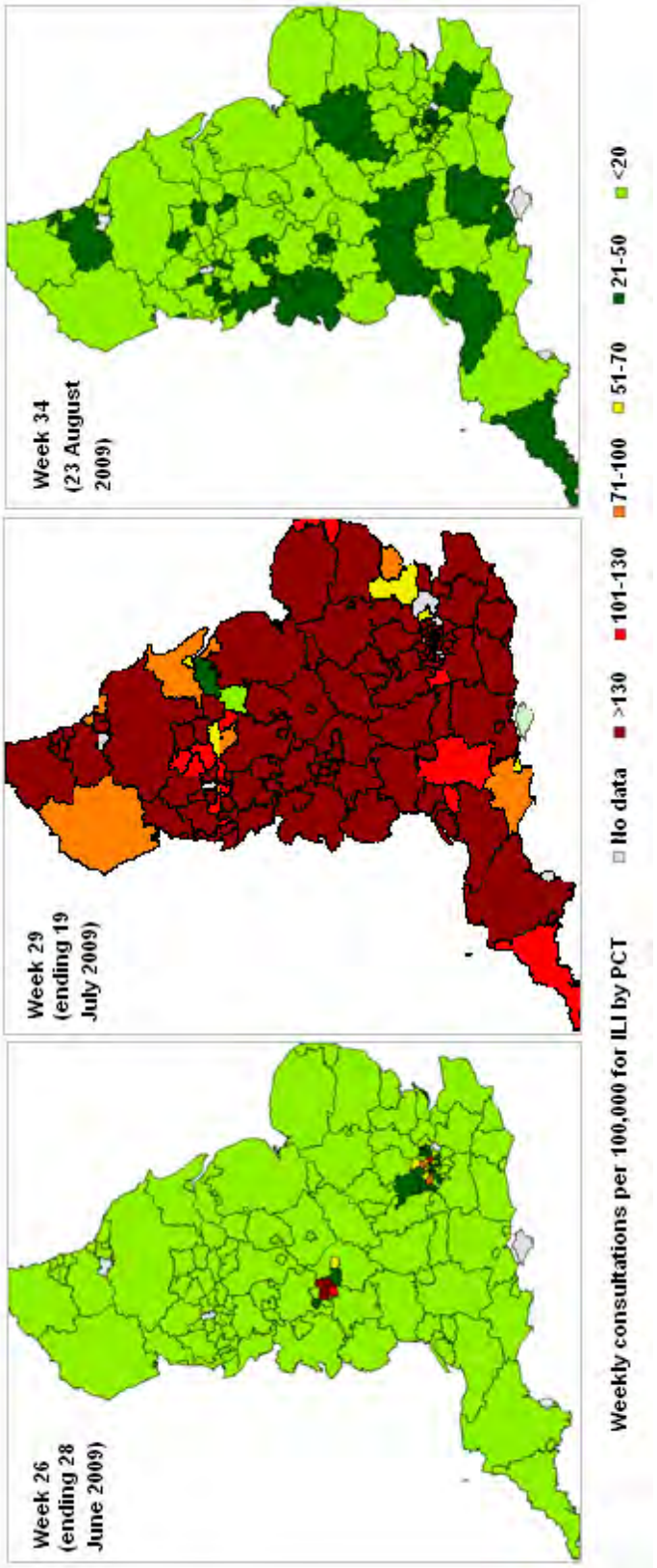
Appendix 1

Timeline of key epidemiological events of the pandemic in the UK, with HPA estimated number of clinical cases (England), April 2009 – May 2010.



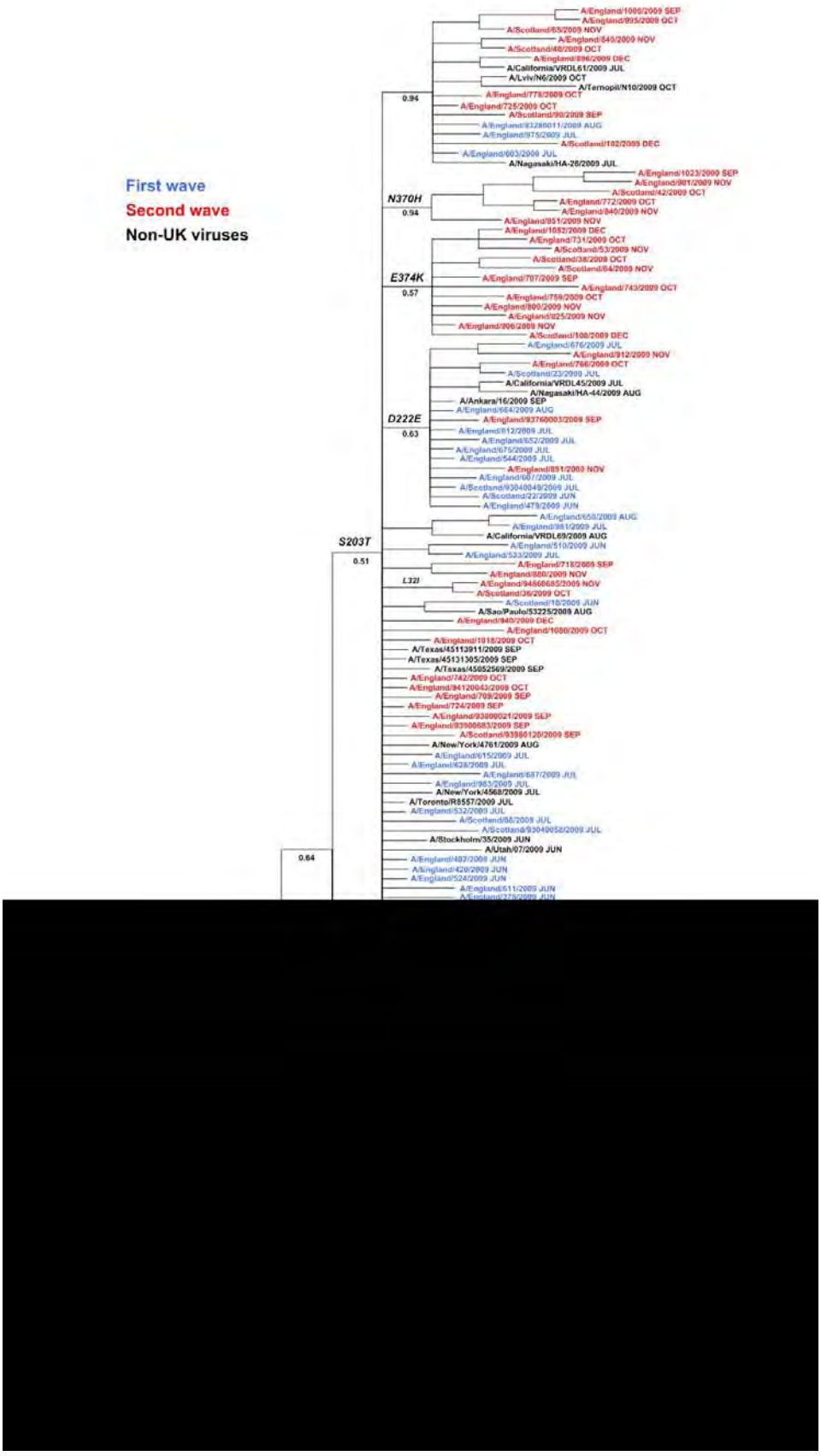
Appendix 2

PCT maps from HPA/QSurveillance system displaying GP incidence rates for ILI per 100,000. The maps illustrate the initial spread in the West Midlands and London regions during week 26, the widespread ILI activity during the peak of the first wave (week 29) and the cessation of activity following the first wave (week 34).



Appendix 3

Phylogenetic tree for pandemic (H1N1) 2009 HA sequences, April – December 2009.



References

(1) Health Protection Agency (2009). National weekly influenza report. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1246433639498.

(2) Centers for Disease Control and Prevention (2009). Swine influenza A (H1N1) infection in two children--Southern California, March-April 2009. MMWR Morbidity and Mortality Weekly Report 58: 400-402. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0421a1.htm.

(3) Centers for Disease Control and Prevention (2009). Outbreak of swine-origin influenza A (H1N1) virus infection - Mexico, March-April 2009. MMWR Morbidity and Mortality Weekly Report 58: 467-470. Available online: http://www.cdc.gov/mmwR/preview/mmwrhtml/mm58d0430a2.htm.

(4) World Health Organization (2009). Transcript of statement by Margaret Chan, Director-General of the World Health Organization, 11 June 2009. Available online: http://www.who.int/mediacentre/influenzaAH1N1_presstranscript_20090611.pdf.

(5) Health Protection Agency (2009). Pandemic (H1N1) 2009 in England: an overview of initial epidemiological findings and implications for the second wave. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1258560552857.

(6) Health Protection Agency (2009). The First Few Hundred (FF100) Project: Epidemiological Protocols for Comprehensive Assessment of Early Swine Influenza Cases in the United Kingdom. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1257260453727.

(7) Miller E, Hoschler K, Hardelid P et al (2010). Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet 375: 1100-1108. Available online: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)62126-7/abstract.

(8) Adamson WE, Maddi S, Robertson C et al (2010). 2009 pandemic influenza A(H1N1) virus in Scotland: geographically variable immunity in Spring 2010, following the winter outbreak. Euro Surveill 15: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19590.

(9) Goddard NL, Kyncl J, Watson JM (2003). Appropriateness of thresholds currently used to describe influenza activity in England. Commun Dis Public Health 6: 238-245.

(10) Cooper DL, Verlander NQ, Elliot AJ et al (2009). Can syndromic thresholds provide early warning of national influenza outbreaks? J Public Health (Oxf) 31: 17-25. Available online: http://jpubhealth.oxfordjournals.org/cgi/content/full/31/1/17?view=long&pmid=18032426.

(11) Ellis J, Iturriza M, Allen R et al (2009). Evaluation of four real-time PCR assays for detection of influenza A(H1N1)v viruses. Eurosurveillance 14: pii: 19230. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19230.

(12) Elliot AJ, Powers C, Thornton A et al (2009). Monitoring the emergence of community transmission of influenza A/H1N1 2009 in England: a cross sectional opportunistic survey of self sampled telephone callers to NHS Direct. BMJ 339: b3403. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2733951/?tool=pubmed.

(13) Health Protection Agency (2009). Method used to estimate new pandemic (H1N1) 2009 influenza cases in England in the week 3 August to 9 August 2009. Available online: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1250150839845.

(14) Nguyen-Van-Tam JS, Openshaw PJ, Hashim A et al (2010). Risk factors for hospitalisation and poor outcome with pandemic A/H1N1 influenza: United Kingdom first wave (May-September 2009). Thorax 65: 645-651. Available online: http://thorax.bmj.com/content/65/7/645.long.

(15) Serfling RE (1963). Methods for current statistical analysis of excess pneumonia-influenza deaths. Public Health Rep 78: 494-506.

(16) Office of National Statistics (2009). Population estimates for UK, England and Wales, Scotland and Northern Ireland. Available online: http://www.statistics.gov.uk/hub/release-calendar/index.html?newquery=*&uday=0&umonth=0&uyear=0&title=Population+Estimates+for+UK%2C+England+and+Wales%2C+Scotland+and+Northern+Ireland&pagetype=calendar-entry.

(17) Office of National Statistics (2009). Birth Statistics. Available online: http://www.statistics.gov.uk/downloads/theme_population/FM1-37/FM1_37_2008.pdf.

(18) Ghani AC, Baguelin M, Griffin J et al (2009). The Early Transmission Dynamics of H1N1pdm Influenza in the United Kingdom. PLoS Curr Influenza RRN1130. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2780827/?tool=pubmed.

(19) Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales et al (2009). Epidemiology of new influenza A (H1N1) virus infection, United Kingdom, April-June 2009. Eurosurveillance 14: pii:19232. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19232.

(20) Health Protection Agency, Health Protection Scotland, National Public Health Service for Wales et al (2009). Epidemiology of new influenza A(H1N1) in the United Kingdom, April-May 2009. Eurosurveillance 14: pii: 19213. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19213.

(21) McLean E, Pebody RG, Campbell C et al (2010). Pandemic (H1N1) 2009 influenza in the UK: Clinical and epidemiological findings from the First Few Hundred (FF100) cases in the United Kingdom. Epidemiol Infect doi:10.1017/S0950268810001366.

Available online: http://journals.cambridge.org/action/displayFulltext?type=6&fid=7828773&jid=&volumeId=&issueId=-1&aid=7828772&bodyId=&membershipNumber=&societyETOCSession=&fulltextType=RA&fileId=S0950268810001366.

(22) Carrat F, Vergu E, Ferguson NM et al (2008). Time lines of infection and disease in human influenza: a review of volunteer challenge studies. Am J Epidemiol 167: 775-785. Available online: http://aje.oxfordjournals.org/cgi/content/full/167/7/775?view=long&pmid=18230677.

(23) Ihekweazu C (2010). Clinical spectrum of disease caused by novel Pandemic (H1N1) 2209 in a closed population setting: a sero-epidemiological study. Slide session at the International Conference on Emerging Infectious Diseases, Atlanta 2010.

(24) Calatayud L, Kurkela S, Neave PE et al (2009). Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. Epidemiology and Infection 138: 183-191. Available online: http://journals.cambridge.org/action/displayFulltext?type=6&fid=6879892&jid=&volumeId=&issueId=02&aid=6879888&bodyId=&membershipNumber=&societyETOCSession=&fulltextType=RA&fileId=S0950268809991191 .

(25) Health Protection Agency West Midlands H1N1v Investigation Team (2009). Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. Eurosurveillance 14: pii: 19264. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19264.

(26) Smith A, Coles S, Johnson S et al (2009). An outbreak of influenza A(H1N1)v in a boarding school in South East England, May-June 2009. Euro Surveill 14: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19263.

(27) Pebody RG, Collaborative UK FF100 Group (2010). Effectiveness of anti-virals in reducing household transmission of Pandemic Influenza A (h1N1) 2009 in the United Kingdom during the"Containment" phase. Poster presented at the International Conference on Emerging Infectious Diseases, Atlanta 2010.

(28) Calatayud L (2010). Oseltamivir resistant pandemic (H1N1) 2009 virus infection in England and Scotland, 2009- 2010. Presentation at Health Protection Conference 2010.

(29) Gulland A (2009). First cases of spread of oseltamivir resistant swine flu between patients are reported in Wales. BMJ 339: b4975. Available online: http://www.bmj.com/cgi/content/full/339/nov23_2/b4975?view=long&pmid=19933735 .

(30) Degail M (2010). Concurrent invasive bacterial infections in confirmed Pandemic (H1N1) 2009 influenza cases in England, 2009- 2010. Presentation at Health Protection Conference 2010 Available online: http://www.healthprotectionconference.org.uk/.

(31) Evans B, Charlett A, McLean E et al (2010). H1N1 case number estimates for England - first and second waves 2009. Poster presentation at 'H1N1: The world responds to a 21st century pandemic conference', London 2010.

(32) Campbell C, Mytton OT, McLean E (2010). Two waves of hospitalisation with pandemic influenza in England. Submitted for publication.

(33) Sfetcu O (2010). Hospitalised patients with 2009 H1N1 influenza in Northern Ireland (NI), June 2009-February 2010. Poster presentation at 'H1N1: The world responds to a 21st century pandemic conference', London 2010.

(34) Pebody RG, McLean E, Zhao H et al (2010). Pandemic Influenza A (H1N1) 2009 and mortality in the United Kingdom: risk factors for death, April 2009 to March 2010. Euro Surveill 15: Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19571.

(35) Sethi M, Begum F, Gates P et al (2010). National pandemic H1N1 influenza vaccine uptake in clinical risk groups in England – winter season 2009/10. Poster presentation at Health Protection Conference 2010.

(36) Pebody RG (2010). Epidemiology of the 2009 H1N1 pandemic. Presentation at Health Protection Conference 2010 Available online: http://www.healthprotectionconference.org.uk/.

(37) Baguelin M, van Hoek AJ, Jit M et al (2010). Vaccination against pandemic influenza A/H1N1v in England: a real-time economic evaluation. Vaccine 28: 2370-2384. Available online: http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD4-4Y6V99S-1&_user=8810565&_coverDate=03%2F11%2F2010&_rdoc=1&_fmt=high&_orig=search&_sort=d&_docanchor=&view=c&_acct=C000046143&_version=1&_urlVersion=0&_userid=8810565&md5=d2880d48d4e4cb6977d5a4983f258d19 .

(38) Begum F, Pebody RG on behalf of the Health Protection Agency and Department of Health (2010). Seasonal influenza vaccine uptake among the 65 years and over and under 65 years at risk in England, Winter season 2009-10. Available online: http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_118542.pdf.

(39) Hardelid P, Fleming D, McMenamin J et al (2010). Effectiveness of pandemic and seasonal influenza vaccine in preventing pandemic influenza A (H1N1) 2009 infection in England and Scotland 2009-2010. Submitted for publication.

(40) Pebody RG, Andrews N, Waight P et al (2010). No effect of 2008/09 seasonal influenza vaccination on the risk of pandemic H1N1 2009 influenza infection in the UK. Submitted for publication.

(41) World Health Organization (2010). Recommended viruses for influenza vaccines for use in the 2010-2011 northern hemisphere influenza season. Available online: http://www.who.int/csr/disease/influenza/recommendations2010_11north/en/index.html.

(42) Davies S, Beasley C, Ridge K (2010). The influenza immunisation programme 2010/11. Professional letter, Department of Health website. Available online: http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Professionalletters/Chiefmedicalofficerletters/DH_116507.

(43) World Health Organization (2009). Pandemic (H1N1) 2009: Countries, territories and areas with lab confirmed cases and number of deaths as reported to WHO as of 27 May 2009. WHO website. Available online: http://gamapserver.who.int/mapLibrary/Files/Maps/GlobalSubnationalMasterGradcolour_weekly_20090527.png.

(44) European Centre for Disease Prevention and Control (2009). Weekly electronic bulletin Week 32: 03 August 2009 - 09 August 2009. ECDC website. Available online: http://ecdc.europa.eu/en/activities/surveillance/EISN/Newsletter/SUN_EISN_INFL_Bulletin_2009week32.pdf.

(45) European Centre for Disease Prevention and Control (2009). Weekly influenza surveillance overview: week 40. ECDC website. Available online: http://ecdc.europa.eu/en/publications/Publications/091016_EISN_Weekly_Influenza_Surveillance_Overview.pdf.

(46) Dawood FS, Jain S, Finelli L et al (2009). Emergence of a novel swine-origin influenza A (H1N1) virus in humans. New England Journal of Medicine 360: 2605-2615. Available online: http://www.nejm.org/doi/full/10.1056/NEJMoa0903810.

(47) Centers for Disease Control and Prevention (2009). Serum cross-reactive antibody response to a novel influenza A (H1N1) virus after vaccination with seasonal influenza vaccine. MMWR Morbidity and Mortality Weekly Report 58: 521-524. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5819a1.htm.

(48) Centers for Disease Control and Prevention (2009). Novel influenza A (H1N1) virus infections in three pregnant women - United States, April-May 2009. MMWR Morb Mortal Wkly Rep 58: 497-500. Available online: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5818a3.htm.

(49) World Health Organization (2010). H1N1 in post-pandemic period. Director-General's opening statement at virtual press conference. Available online: http://www.who.int/mediacentre/news/statements/2010/h1n1_vpc_20100810/en/index.html.

(50) World Health Organization (2010). WHO recommendations for the post-pandemic period. Available online: http://www.who.int/csr/disease/swineflu/notes/briefing_20100810/en/index.html.

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