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Health Protection Agency submission to the Review of the Response to the 2009 Influenza Pandemic: Call for Evidence

Contents

1. Overview of HPA submission
2. Surveillance of pandemic influenza
3. Epidemiology of pandemic influenza
4. Modelling of pandemic influenza
5. Containment
6. Vaccination
7. International intelligence and reporting
8. Press and communications
9. List of supporting papers

Supporting documents

- S Surveillance of pandemic influenza
- E Epidemiology of pandemic influenza
- M Modelling of pandemic influenza
- C Containment
- V Vaccination
- Int International intelligence and reporting
- P Press and communications

1. Overview of HPA submission

The Health Protection Agency carries out a wide range of work in preparation for, and in response to, pandemic influenza. Much of this work is to support the NHS, the Department of Health and other UK wide bodies in their response to the threat of pandemic influenza. Other aspects of the work include implementation of control measures at the local level, national surveillance of influenza, information to health professionals and the public, and international liaison.

This submission provides papers relevant to the review of the response to the 2009 influenza pandemic. The topics covered in this submission have been selected on the basis of the information provided in the call for evidence including the terms of reference and the 'Flu review areas of inquiry'.

In the light of the quantity of information potentially relevant to the review, and the limited time available to prepare or review the material, the submission is necessarily selective. Nevertheless, the quantity of submitted material is large. The HPA has therefore organised the submission so that the relevant information is as accessible as possible to the reviewers.

This overarching paper summarises the material provided in the supporting documents. The submission is organised in eight themes (see below) with an introductory section on each theme in this paper and a list of the supporting documents for each theme at the very end of this paper. The supporting documents are thereafter organised in separate portfolios and categorised so that they link to the introductory section in this paper.

Main themes

Surveillance of pandemic influenza
This section describes the aims of surveillance during a pandemic, the methods employed and the main outputs during the course of the pandemic. Supporting documents are labelled S1-39.

Epidemiology of pandemic influenza
This section describes the information on the occurrence of pandemic influenza in the UK and its impact in the population, based on information from surveillance and supplemented by the results of field investigations and research studies. Documents supporting this section, including a 'timeline', provide information on what was known about the pandemic threat at each stage of its occurrence in the UK. Supporting documents are labelled E1-10

Modelling of pandemic influenza
This section describes the application of modelling to the pandemic including the information used to inform the modelling, the methods employed, the main outputs from the HPA modelling team and the key findings. Supporting documents are labelled M1-10.

Containment

This section describes in more detail the approach taken from April to July 2009 to 'contain' the pandemic threat in the UK. It includes a description of the objectives of 'containment', the measures adopted and a preliminary assessment of the effectiveness of the containment phase (from the perspective of the HPA). Supporting documents are labelled C1-11

Vaccination
This section describes aspects of the pandemic vaccination programme in which the HPA was directly involved including vaccine development, vaccine uptake monitoring, vaccine effectiveness assessment and safety monitoring. Supporting documents are labelled V1-11

International intelligence and reporting
This section describes the role of the HPA in both monitoring the occurrence, impact and control measures for pandemic influenza in other countries and the UK role in reporting the UK experience to international partners. Supporting documents are labelled Int1-5

Press and Communications
This section describes the role of the HPA in responding to the needs of the public and media for information on pandemic influenza and arrangements for liaison with other bodies. The supporting document is labelled P1.

2. Surveillance of pandemic influenza

The Health Protection Agency conducts surveillance of influenza activity in England and, in collaboration with the health protection organisations in Scotland, Wales and Northern Ireland, collates surveillance information on influenza activity across the UK. Routine influenza surveillance is carried out during the traditional period when influenza virus activity occurs in the northern hemisphere (week 40 to week 20, early October to late May). In the event of an influenza pandemic, the routine systems in place for surveillance of seasonal influenza are augmented with further elements of surveillance in order to respond to the need for very timely and detailed information on the new threat.

The purpose of influenza surveillance is to provide early warning of influenza virus activity, provide detailed information on the viruses circulating (such as how they relate to previously circulating strains and anti viral drug resistance), the levels of illness occurring in the community and in hospitals as a result of influenza, and risk factors for severe illness and death. This information is used to inform control and prevention policy as well as to provide health professionals and the public with an understanding of the level of current and future threat and appropriate health protection measures.

Influenza surveillance information is made available in a wide variety of forms including situation reports (SitReps) to the Department of Health, updates and bulletins on the HPA web site, ad hoc reports to external bodies such as the Joint Committee on Vaccination and Immunisation, the Scientific Advisory Group for Emergencies, the European Centre for Disease Control and the World Health Organisation.

A more detailed overview of influenza surveillance conducted by the HPA is provided as paper S1. This paper draws on a list of further documents and published papers which are listed below and included in the portfolio of supporting documents S2-39.

3. Epidemiology of pandemic influenza

Surveillance data on influenza activity, combined with information from field investigations and research studies, has enabled the HPA to provide a picture of the occurrence and impact of pandemic influenza at every stage of its occurrence in the UK.

The influenza pandemic resulted in two distinct waves of influenza activity in the population of the UK during 2009. Following the initial introduction of the virus through travellers to other affected parts of the world in April and May 2009, and subsequent spread to contacts of these cases, generalised influenza activity was apparent in the population from the end of June, rising to a peak at the end of July and reducing rapidly as school broke up for the summer holidays. The second wave began in early September as the new school term began, and continued through to early December. Levels of activity subsequently declined and have since remained low.

A detailed description of the epidemiology of the pandemic during the first wave is provided in the paper 'Pandemic H1N1 2009 in England: an overview of initial epidemiological findings and implications for the second wave' which was published on the HPA web site in November 2009 (E1).

A timeline of the key events throughout the period of pandemic influenza activity in the UK is given in the Pandemic (H1N1) 2009: timeline of descriptive epidemiological data as reported to SAGE by HPA (E2). This paper draws from the information provided in:
- weekly reports to SAGE (E3),
- situation reports (SitRep) provided by the HPA to DH, initially on a daily basis and subsequently on a weekly basis. The final SitRep, number 100, is provided as an example (E4).
- weekly updates on influenza activity published by the HPA on its web site - the update from 18th March 2010 is provided as an example (E5).

A series of graphs of key indicators of influenza activity throughout the pandemic period is provided (E6). The graphs form a standard part of the of the influenza activity surveillance published each week on the HPA web site.

A paper outlining the key epidemiological facts about the pandemic virus and its impact on the population is provided (E7). This information was derived from HPA epidemiological and virological surveillance, HPA field investigation and research studies, and from information published in peer review publications from elsewhere.

Estimates of the numbers of cases of pandemic influenza in England were developed on the basis of surveillance data on numbers of individuals seeking health care or advice for symptoms of an influenza-like illness, and the proportion of such cases positive for pandemic influenza virus infection based on sampling of subsets of such patients. The methodology for these estimates and the estimates of the numbers during the course of the pandemic are provided in paper E8.

Population based serological surveys were carried out in England before and after the first pandemic wave (E9). Comparison of the proportions found to be positive on serological testing before and after the first wave, by age group, provides the opportunity to estimate the total number of people infected during the first wave (including those with infections without any symptoms [asymptomatic infections] and those with very mild illness not seeking healthcare).

A series of papers summarising the epidemiology of the pandemic, with particular emphasis on its impact within the UK, was prepared for submission to the Joint Committee on Immunisation and Vaccination (JCVI) and are provided in paper E10.

4. Modelling of pandemic influenza

Modelling has provided a very valuable tool in the process of analysing and anticipating influenza activity and its impact on the population. The HPA modelling team has contributed substantially to this work in the UK.

There are two infectious-disease modelling groups within HPA: the Modelling & Economics Unit of the Centre for Infections and the Microbial Risk Assessment group at Porton Down. Both groups have been involved in pandemic influenza planning and in providing real-time analysis and advice during the swine flu epidemic.

Modelling is a vital tool in the analysis of transmission patterns of infectious diseases because of their dynamic complexity. Epidemics typically have a bell shape: in the early stages there is accelerating exponential growth as spreading of infection increases the number of infectious people which in turn increases the rate of spreading; subsequently the epidemic reaches a peak and declines due to depletion of the supply of susceptible people (because people who have been infected become immune). The timing and height of the peak of the epidemic depend upon the reproduction number, the proportion of the population with prior immunity, and other factors.

Modelling is needed to analyse data because a model that takes account of transmission patterns is necessary to analyse those transmission patterns. It is necessary to monitor the reproduction number because to control an epidemic requires that the reproduction number be below one, so that the epidemic declines rather than grows.

Models are needed to quantify the impact of interventions to control the epidemic because preventing someone from passing on infection prevents the people that they would otherwise have infected from infecting more people - so benefits can accrue over time.

Modelling has a key role to play in synthesising data from multiple sources; and is vital for examining the potential impact of interventions. There is inevitably uncertainty about the trajectory of an epidemic due to our having limited information – especially at the start – and a key strength of modelling is the quantification of that uncertainty. In the absence of key data modelling can be used to guide decision making through scenario analysis.

A more detailed description of the modelling approaches employed by the HPA, and a commentary on the main findings arising from the modelling work is provided at M1. Further documents in support of the modelling work are provided at M2-10.

5. Containment

The HPA, working with the NHS and others, was responsible for implementing measures with the aim of containing the newly emergent pandemic influenza virus in the UK. An assessment of the containment phase, from the perspective of the HPA, is provided (C1) and is summarised below.

When pandemic influenza A H1N1 emerged at the end of April 2009, there was uncertainty about its severity and the impact of the illness associated with it. Some of the initial reports caused considerable concern. It was therefore considered appropriate for the UK to instigate a robust public health response. Despite extensive pandemic preparedness, countermeasures such as pandemic specific vaccine, were unlikely (and had never been likely) to be available for six months or more.

Measures to attempt to slow the spread of the pandemic in England (labelled 'containment'), and buy time for the development of countermeasures, were judged to be appropriate. With respect to possible cases, the containment measures included early identification, isolation, testing and treatment with anti-virals. Close contacts of cases were identified, offered prophylactic treatment with antivirals, asked to isolate themselves and to report any illness. Containment measures, implemented by the HPA working with the NHS, were demonstrated to be very effective in households, and have some protective effect in other settings in which they were applied. These measures were not expected; however, to prevent the possibility of transmission in the community and, during May and June, an increasing number of cases were identified with no links to other known cases. Although severe illness, and deaths, occurred in a minority of cases, especially in children and young adults and particularly in those with conditions placing them at high risk of the complications of influenza, most cases experienced a mild illness or no symptoms at all. During June, mounting evidence of sustained community transmission suggested that the benefit of containment measures was increasingly doubtful, and preparations were made to move to a treatment only approach.

There is insufficient information at present to draw firm conclusions about the effectiveness of the measures taken during the containment phase to slow the spread of infection in the population or to affect the ultimate size of the first wave of the pandemic in England which peaked in late July.

The use of prophylaxis in containment

From the end of April to 2 July 2009 the UK was in the containment phase of the pandemic. The objectives of containment were to slow the spread of the virus in order to provide more time to optimise the UK pandemic response measures that had been put in place and facilitate in-depth public health investigation of early cases.

During the containment phase antiviral prophylaxis of all close contacts was implemented as a key control measure. The Health Protection Agency made recommendations on treatment and prophylaxis at various stages during the

pandemic (C2) This policy was refined at points during the containment phase (C3) and some flexibilities introduced that allowed for an element of judgement around the contacts to be offered prophylaxis, particularly in the household setting or where there were people with serious underlying medical conditions, but the underlying principle of antiviral prophylaxis to close contacts remained in place.

Robust evidence from surveillance towards the middle of June started to show that there was sustained community transmission in some parts of the UK. On 24 June the Department of Health issued a letter about handing "hot spots" for flu around the country. In order to be classified as a "hot spot", an agreed process was undertaken in a location and if eligible then antiviral treatment was offered to cases diagnosed on clinical grounds alone, without testing, and the emphasis for prophylaxis shifted to include household contacts and contacts with serious underlying medical conditions. However, as this decision was implemented only a week before the move to treatment only phase, these recommendations did not have time to really impact on the system.

During the treatment only phase, prophylaxis continued to be primarily directed at people with serious underlying medical conditions.

Containment in schools

The objective of the approach to cases of H1N1 in school children was to prevent further spread within the school and the local community.

The interventions that were adopted for preventing further spread of H1N1 are set out in schools guidance developed for HPUs in early May (C4, C5). These included:

- Identification and isolation of children and staff with a flu like illness – initially those who had travelled from an affected country but latterly to those who were close contacts of confirmed or suspected cases of pandemic influenza
- Identification and prophylaxis with anti-viral medication of close contacts,
- Provision of information to raise awareness about swine flu so that contacts who developed symptoms of influenza like illness could be treated promptly,
- School closure, initially for a period of seven days – the incubation period of the virus considered likely at that time. School closures were instituted in order to prevent infected children mixing with susceptible children. The impact of this intervention was reduced where there were extensive informal or family networks out with the school environment

As with other public health interventions the recommended intervention depended upon an individual risk assessment taking account of the

circumstances in each school. The factors considered in each risk assessment included the nature of the illness, the type and duration of exposure in the school and the nature of the school environment. An example of a risk assessment is provided at (C6). The use of risk assessments in this way would be expected to, and did, lead to differing actions in the management of H1N1 in schools; in particular whether or not closure was recommended. If the risk assessment concluded that closure of the school would not prevent spread e.g. if a school pupil developed illness during a half term holiday and so had had no recent contact in school, then the school would not be closed. This risk assessment approach continued throughout the containment period.

Containment at ports and in air passengers

Detecting and treating influenza-like illness in returning travellers and offering antiviral prophylaxis to their close contacts from Mexico and certain areas of the United States was a key issue during the early days and weeks of the swine flu pandemic in the UK.

The HPA initially used the principles set out in the "Health Protection Agency Port Health Response to avian and pandemic influenza" (C7) that had been developed with the Department of Health and was due to be considered at a meeting of MISC 32 in the early Spring of 2009. Therefore national policy drove the response to this aspect of the pandemic. On 29 April, in a statement from the Prime Minister, the following commitments were made

- All direct flights from Mexico to be met an HPA employee who would deal with any queries relating to swine flu
- All passengers to be given an information leaflet about swine flu

Operational guidance to reflect this was issued on 30 April 2009 (C8) and continued to be refined through out the period that port health interventions were required (C 9). As the numbers of countries affected by the pandemic virus grew, the resource required to do meet the increasing number of flights also grew such that, by 19 May, the Civil Contingencies Committee (CCC) agreed that the requirement to meet all flights from Mexico should cease.

Contact tracing of passengers on flights where confirmed cases had been symptomatic was undertaken in the early stages of the pandemic. The workload associated with collating passenger lists, organising prophylaxis and follow up was significant and HPA LaRS North East established a "Flight desk arrangement" from 15 May until 18 June in order to centralise the co-ordination of flight contact tracing. At first this was only involved England but, from 24 May, the Devolved Administrations were included as well. The flight desk was stood down on 18 June following revision of recommendations on the approach to contact tracing and prophylaxis during containment. In this guidance it was recommended that routine contact tracing on flights, where cases of H1N1 had travelled, should cease.

Policy was developed around shipping and seaports but in practice during the pandemic this was not an issue (C11)

6. Vaccination

6.1 Background

The HPA has been involved for several years in vaccine-related activities for pandemic preparedness. With the emergence of influenza A (H1N1) 2009, the HPA established a series of vaccine-related strands of work:

- To contribute to the development a new monovalent pandemic strain-specific influenza vaccine;

- To undertake clinical trials to measure the immunogenicity of newly developed monovalent pandemic vaccines;

- To provide advice to JCVI on the epidemiology of pandemic influenza and a modelling and economic evaluation of a possible pandemic vaccine programme

- To monitor the uptake, effectiveness and safety of the newly implemented H1N1 pandemic influenza vaccine programme.

6.2 Pandemic vaccine development

HPA was responsible for successful work to construct a candidate vaccine seed virus in May 2009 which was supplied to laboratories around the world (V1).

Serum which is essential for the potency assay used was available from June 2009. HPA was the only one of the four Essential Regulatory Laboratories in the world to produce a serum. This was acknowledged at a recent meeting in the USA (V1).

Reference antigen materials are the other part of the potency assay and should match the strains used in production. HPA provided reference materials for all strains used from September and October 2009. Availability of the reagents was not a rate limiting step in the evaluation and granting of the licenses for the vaccines.

6.3 Pandemic vaccine clinical trials

HPA has been involved in clinical trials of novel monovalent pandemic vaccines (V2), including undertaking a head-to-head clinical trial of the GSK and Baxter vaccines (V1).

6.4 Epidemiological, modelling and economic evaluation

HPA has provided detailed reports to JCVI on the epidemiology of pandemic influenza, including risk factors for severe disease and sero-epidemiological studies to document baseline population immunity and assess age-specific attack rates (V3-4).

HPA has also provided modelling and economic evaluations to JCVI comparing the effectiveness and cost-effectiveness of alternative pandemic vaccine interventions (V5).

6.5 Pandemic and seasonal influenza vaccine uptake
The Department of Health ImmForm web-portal is an established mechanism to gather information on influenza vaccine uptake. The system has been established and run by the Department of Health, with support from HPA.

Information on seasonal and pandemic influenza vaccine uptake in high-risk groups was obtained by extracting information (either automatically or manually) from GP health information systems in England and for health care workers through information provided by NHS acute trusts. This information was reported weekly by HPA to colleagues in the Department of Health and latterly published (V6).

6.6 Pandemic and seasonal influenza vaccine effectiveness
HPA established a series of systems to provide in-season estimates of seasonal and pandemic influenza vaccine effectiveness (working with RCGP and Health Protection Scotland)

6.6.1 Primary care: RCGP and HPA-RMN sentinel spotter schemes in England and HPS spotter scheme in Scotland
RCGP and HPA-RMN are two sentinel GP networks in England (a similar scheme operates in Scotland). Each has in excess of 50 GPs who swab patients presenting with influenza-like illness during the winter season. Vaccination status is ascertained by questionnaire from persons with influenza-like illness who are swabbed by their GP. The system successfully provided an estimate of pandemic influenza vaccine effectiveness against virologically confirmed infection in primary care during the 2009/10 winter season (V7). This was reported to JCVI and the recent WHO meeting to inform composition of next season's influenza vaccine.

*6.6.2 Follow-up of cases in secondary c*are
A retrospective investigation of patients laboratory investigated for pandemic influenza in primary and secondary care was also undertaken. This demonstrated that vaccination with trivalent seasonal influenza vaccine from season 08/09 provided no protection against confirmed pandemic influenza infection (V8). This is also being used to estimate VE of pandemic vaccine in risk groups and hospitalised patients (V9).

6.6.3 Service evaluation of pandemic vaccine programme
A clinical service evaluation is underway by HPA to monitor the immunogenicity of pandemic (H1N1) vaccine in priority groups following national introduction of the pandemic vaccine programme. Individuals from priority groups as per Department of Health recommendations have been given the opportunity to have their antibody response to vaccine checked. Immunogenicity data in priority groups will be important to inform pandemic vaccine policy.

6.7 Vaccine Safety

Vaccine safety surveillance is an integral part of the pandemic influenza vaccine programme. The MHRA has the established passive, yellow card reporting system, which provides an alerting mechanism for possible vaccine associated adverse events.

Also established baseline rates of various events of interest e.g Guillain-Barre syndrome, Bell's palsy etc. for observed and expected analyses using the GPRD (V10).

HPA has been undertaking enhanced surveillance of Guillain-Barre syndrome with the University of Cambridge through the BPSU and Association of British Neurologists on enhanced surveillance (V11).

7. International intelligence and reporting

Information on the occurrence and impact of pandemic influenza in other countries, and the measures adopted in order to control and prevent influenza, was considered essential by the HPA in order to have the best understanding of the epidemiology of the new pandemic threat and to provide advice about control and prevention measures. In addition, other countries and international organisations had a considerable interest in the occurrence of influenza in the UK and the control measures adopted here, and there are obligations within Europe and internationally to share data on disease activity in the UK.

The HPA gathered international intelligence on influenza through a range of mechanisms including;
- published reports on websites of national health ministry or health protection organisations and international bodies such as European Centre for Disease Control (ECDC) and the World Health Organisation (WHO)
- publications in peer review journals
- the news media
- teleconferences with ECDC, WHO and other international health bodies
- visits by HPA staff to Mexico and Australia

The international intelligence was synthesised by the HPA and communicated through; internal reports (Mexico Int1, Australia Int2), reports to the scientific Advisory Group on Emergencies (Int3), inclusion as a component of SitReps to the DH (Int4) and inclusion in the bulletins on influenza activity published on the HPA web site (Int5).

The HPA complied with international reporting obligations by providing information on influenza activity in the UK through the International Health Regulations Focal Point, and the European Early Warning System, and by the provision of surveillance data to ECDC and the WHO

8. Press and communications

The HPA provides a 24/7 response to the media to cover queries relating to infectious disease (through the Centre for Infections) and on other health protection issues through the Centre for Radiation, Chemicals and Environmental Hazards.

During the swine flu pandemic the Centre for Infections press office led the communications response. This included providing information on:

- the first cases of swine flu
- the treatment of the cases and prophylaxis of close contacts
- management of cases in schools
- the public health action that is taken at ports – how unwell patients are managed during flights and on disembarkation, tracing patients arriving from areas affected by swine flu
- production of the vaccine
- mass gatherings
- infection control
- virology
- modelling
- surveillance
- containment
- pregnancy

During the course of the pandemic, the CfI press office managed thousands of phone calls and enquiries across all areas of the media, both nationally and internationally.

The HPA press office liaised closely with the press office of the Department of Health. Queries relating to matters of national policy including the vaccination programme, the National Pandemic Flu Service and the response of the NHS, were dealt with by the DH press office.

Arrangements were established by the HPA to liaise, by teleconference, with colleagues in the health protection organisations of the UK devolved administrations and with relevant health professional bodies in the UK.

Further information about specific aspects of the communications work of the HPA, including responses to specific questions highlighted in the ‘Flu review areas of inquiry’ are given in the supporting paper P1.

9. Supporting documents

Surveillance

S1. Overview of HPA surveillance of pandemic influenza A (H1N1) 2009. HPA internal report, 2010. HPA internal document.

S2. Ellis J. Molecular detection of pandemic influenza A H1N1 2009 viruses in the UK . HPA Centre for Infections unpublished report . 2010. HPA website guidance and information.

S3. HPA Centre for Infections. Antiviral susceptibility testing of pandemic H1N1 2009 influenza viruses. Unpublished SAGE report . 2010. HPA internal document.

S4. HPA Centre for Infections. Virological Surveillance of H1N1v Influenza Virus. Unpublished SAGE report . 2010. HPA document for external bodies.

S5. HPA Centre for Infections. Pandemic Influenza Surveillance Framework for England. Unpublished report . 2010. HPA website guidance and information.

S6. HPA. Surveillance in the Treatment Phase of the H1N1v UK Epidemic Briefing Paper – July 2009. Unpublished SAGE report . 2010. HPA document for external bodies.

S7. HPA and DH. Overview of the Surveillance Requirements for Autumn 2009 for England. Unpublished report for SAGE . 2010. HPA document for external bodies.

S8. HPA and HPS. Swine influenza surveillance in England and Scotland. Unpublished SAGE report . 2010. HPA document for external bodies.

S9. HPA. Key epidemiological facts summary: pandemic (H1N1) 2009, England . HPA unpublished . 2010. HPA internal document.

S10. HPA Centre for Infections. Pandemic (H1N1) 2009: timeline of descriptive epidemiological data as reported to SAGE by HPA. Unpublished report . 2010. HPA internal document.

S11. HPA. Situation Report of the Influenza Pandemic (H1N1) 2009 (Swine Flu) in the United Kingdom. HPA Sit-Rep 100. 2010. HPA document for external bodies.

S12. HPA. Complete HPA key note briefings. 1-41. 2010. HPA document for external bodies.

S13. HPA. HPA weekly influenza bulletin. http://www.hpa.org.uk/web/HPAweb&Page&HPAwebAutoListName/Page/1243928258560 . 2010. HPA website guidance and information.

S14. HPA Real-time Syndromic Surveillance Team. HPA Swine-flu syndromic daily bulletin. 2010. HPA document for external bodies.

S16. HPA Real-time Syndromic Surveillance Team. Daily Real-time Syndromic Surveillance report: NPFS. 2010. HPA document for external bodies.

S16. HPA. Weekly HPA pandemic influenza international summary. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1252326269392 . 2010. HPA document for external bodies.

S17. HPA. HPA pandemic influenza JCVI papers. HPA unpublished . 2010. HPA document for external bodies.

S18. HPA. Pandemic H1N1 2009 in England: an overview of initial epidemiological findings and implications for the second wave. HPA unpublished . 2010. HPA document for external bodies.

S19. HPA. Assessment of the implementation of the 'containment' phase (24 April to 2 July), and the role of the Health Protection Agency, during the first wave of pandemic influenza in England in 2009. HPA . 2010. HPA document for external bodies.

S20. McLean E, Pebody RG, Campbell C, and Chamberland M. Pandemic (H1N1) 2009 Influenza In The Uk: Clinical And Epidemiological Findings From The First Few Hundred (FF100) Cases In The United Kingdom. Paper in preparation or submitting to peer review journal but not yet accepted for publication.

S21. Health Protection Agency., Health Protection Scotland, National Public Health Service for Wales, HPA Northern Ireland Swine infleunza investigation teams. Epidemiology of new influenza A(H1N1) in the United Kingdom, April-May 2009. Eurosurveillance 2009;14(19). Paper published in peer review journal.

S22. Health Protection Agency., Health Protection Scotland, National Public Health Service for Wales, HPA Northern Ireland Swine infleunza investigation teams. Epidemiology of new influenza A (H1N1) virus infection, United Kingdom, April-June 2009. Eurosurveillance 2009;14(22). Paper published in peer review journal.

S23. Ghani AC, Baguelin M, Griffin J, Flasche S, Pebody R, van Hoek AJ et al. The Early Transmission Dynamics of H1N1pdm Influenza in the United Kingdom. PLoS.Curr.Influenza. 2009:RRN1130. Paper published in peer review journal.

S24. HPA. Household transmission of new pandemic influenza A (H1N1) 2009 in the United Kingdom during the "containment" phase. Submitted for publication . 2010. Paper in preparation or submitting to peer review journal but not yet accepted for publication.

S25. Wallensten A, Oliver I, Lewis D, Harrison S. Compliance and side effects of prophylactic oseltamivir treatment in a school in South West England. Euro.Surveill 2009;14(30):19285. Paper published in peer review journal.

S26. Health Protection Agency West Midlands H1N1v Investigation Team. Preliminary descriptive epidemiology of a large school outbreak of influenza A(H1N1)v in the West Midlands, United Kingdom, May 2009. Eurosurveillance 2009;14(27). Paper published in peer review journal.

S27. Calatayud L, Kurkela S, Neave PE, Brock A, Perkins S, Zuckerman M et al. Pandemic (H1N1) 2009 virus outbreak in a school in London, April-May 2009: an observational study. Epidemiology and Infection 2009:1-9. Paper published in peer review journal.

S28. Kitching A, Roche A, Balasegaram S, Heathcock R, Maguire H. Oseltamivir adherence and side effects among children in three London schools affected by influenza A(H1N1)v, May 2. Euro.Surveill 2009;14(30):19287. Paper published in peer review journal.

S29. Elliot AJ, Powers C, Thornton A, Obi C, Hill C, Simms I et al. 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 2009;339:b3403. Paper published in peer review journal.

S30. Elliot A. Syndromic surveillance: the next phase of public health monitoring during the H1N1 influenza pandemic? Euro.Surveill 2009;14(44). Paper published in peer review journal.

S31. HPA. Has estimation of symptomatic case numbers been useful for pandemic influenza H1N1 in England in 2009? Unpublished paper . 2010. Paper in preparation or submitting to peer review journal but not yet accepted for publication.

S32. Donaldson LJ, Rutter PD, Ellis BM, Greaves FE, Mytton OT, Pebody RG et al. Mortality from pandemic A/H1N1 2009 influenza in England: public health surveillance study. BMJ 2009;339:b5213. Paper published in peer review journal.

S33. HPA. Pandemic Influenza A (H1N1) 2009 and mortality in the United Kingdom: risk factors for death, April 2009 to March 2010. Eurosurveillance - submitted for publication . 2010. Paper in preparation or submitting to peer review journal but not yet accepted for publication.

S34. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon MC. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet 2010. Paper published in peer review journal.

S35. Baguelin M, Hoek AJ, Jit M, Flasche S, White PJ, Edmunds WJ. Vaccination against pandemic influenza A/H1N1v in England: a real-time economic evaluation. Vaccine 2010;28(12):2370-84. Paper published in peer review journal.

S36. HPA. Swine flu vaccine uptake. Unpublished internal report . 2010. HPA internal document.

S37. HPA. No effect of 2008/09 seasonal influenza vaccination on the risk of pandemic H1N1 2009 influenza infection in the UK. Submitted - unpublished .

2010. Paper in preparation or submitting to peer review journal but not yet accepted for publication.

S38. HPA, HPS. Effectiveness of pandemic and seasonal influenza vaccine in preventing pandemic influenza A (H1N1) 2009 infection in England and Scotland: case-control study of laboratory confirmed cases in primary care 2009-2010. Submitted - unpublished . 2010. Paper in preparation or submitting to peer review journal but not yet accepted for publication.

S39. Black S, Eskola J, Siegrist CA, Halsey N, Macdonald N, Law B et al. Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines. Lancet 2009;374(9707):2115-22. Paper published in peer review journal.

Epidemiology

E1. HPA. Pandemic H1N1 2009 in England: an overview of initial epidemiological findings and implications for the second wave. HPA unpublished . 2010. HPA document for external bodies.

E2. HPA Centre for Infections. Pandemic (H1N1) 2009: timeline of descriptive epidemiological data as reported to SAGE by HPA. Unpublished report . 2010. HPA internal document.

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