A practical review of ‘containment’ during the influenza A (H1N1): an audit of the flu response centre in Yorkshire and the Humber

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ABSTRACT

Background During the ‘containment’ phase of the influenza A (H1N1) pandemic 2009, antivirals were used for treatment and prophylaxis. This audit aimed to review the speed of the process involved in delivering antivirals and to assess whether this was likely to have occurred fast enough to be in keeping with the aims of reducing transmission.

Methods Flu Response Centres in each region were tasked with co-ordinating local delivery and all case data were entered into Fluzone (an electronic case management system). All data between 1 June and 2 July in the Yorkshire and Humber region were reviewed. Forty-eight hours from the onset of illness to treatment and prophylaxis were used as reference standards.

Results The median estimate for the earliest point cases could have received treatment was 2 days (95% CI 2–3 days) and the earliest point contacts of cases could have received prophylaxis was 4 days (95% CI 4–5 days).

Conclusions The logistical difficulties of delivering ‘containment’ according to the national algorithms meant there were significant time delays involved and that this was likely to have reduced the effectiveness of the strategy. This would be important to consider if a ‘containment’ strategy was to be employed in any future emergency.

Keywords communicable diseases, population-based and preventative services, management and policy

Introduction

At the time of the emergence of the influenza A (H1N1) pandemic 2009, there was considerable concern about the severity and the potential impact of the illness associated with it. The objective of the UK response in the early stages was to slow the spread of the virus within the UK in order to buy time for a vaccine and other counter measures to be developed. This period was called the ‘containment’ phase and lasted from 24 April to 2 July 2009. In addition to the self-isolation of cases and a greater emphasis on good respiratory hygiene, a fundamental part of containment was the use of antiviral medicines. Cases were offered treatment on suspicion of pandemic influenza once they had presented to a doctor. Following confirmation with a positive virology result, their close contacts were then offered prophylaxis according to national algorithms.

The UK approach to the use of antivirals during containment was based on the assumption that the pandemic strain would behave in a similar way to seasonal influenza in terms of its transmission and response to antivirals. It was therefore assumed that:

- people are most infectious soon after they develop symptoms, though they can continue to shed virus for usually up to 5 days after the onset of symptoms (7 days in children).¹

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• the duration of symptoms and the complication rate could be reduced provided that treatment could be started within 48 h of the onset of symptoms.3–5
• treatment may also reduce an individual’s infectivity to others.4,6
• post-exposure prophylaxis might be effective in reducing the spread of a pandemic.4
• post-exposure prophylaxis was most effective when started within 48 h of exposure to an index case.4,5,7,8

It had been acknowledged in the UK guidance that seasonal influenza may not be a good model for pandemic strains and that the latter may be associated with higher viral loads and infectivity.4 This would, however, increase the urgency to treat promptly and that prophylaxis of household contacts could have a more marked impact on reducing spread. At the onset of the influenza A (H1N1) pandemic 2009, the incubation period of the new strain was unknown and antivirals were advised for symptomatic cases and identified close contacts of confirmed cases without limitation of use within 48 h of onset in the index, but with the aim of starting as soon as possible.9,10

In England, regionally based Flu Response Centres were established. These were tasked with co-ordinating the process of testing and treating suspected cases and prophylaxing close contacts. This was done using antivirals from the national stockpile in accordance with national algorithms. Flu Response Centres, therefore, were involved in establishing many new mechanisms for the distribution of antivirals from the national stockpile, the testing of suspected cases and the communication of results both locally and centrally.

This resulted in processes that involved multiple steps and were often complex and varied by primary care trusts (PCTs) (Some PCTs in urban areas were able to resource-specific response teams for some of the steps). From the point of notification to the Flu Response Centre (usually by a General Practitioner), the process often involved several potential bottlenecks. It was not common at the time the influenza A (H1N1) pandemic 2009 began for a General Practice to maintain a stock of the specific swabs and viral transport media required for testing suspected cases. The transport of a swab kit from a central location had first to be arranged. The swab then had to be taken by a clinician and transport then arranged to take this back to a laboratory to be tested. Testing could only be carried out by Health Protection Agency regional laboratories and once analysed the result had to be communicated back to the Flu Response Centre.9,10 As antivirals were not available through routine pharmacy routes, a separate process also had to be devised to enable access for the treatment of cases and the prophylaxis of contacts. Bottlenecks did also occur in many of these processes due to weight of demand at various times. The algorithms also changed frequently in accordance with the epidemiology and risk assessment.

**Purpose of the audit**

This audit aimed to review the speed of the process involved in delivering treatment and prophylaxis during the containment phase of the influenza A (H1N1) pandemic 2009 and to assess whether this was likely to have been in keeping with the aims of reducing transmission.

The reference parameters were:

• Onset to treatment should be < 48 h
• Onset to prophylaxis of close contacts should be < 48 h after exposure to an index case.

**Method**

Containment in the UK began on 24 April and ended on 2 July. The Flu Response Centre in the Yorkshire and Humber region opened on 12 May and Fluzone, an electronic web-based case management system, became available from 20 May onwards. Retrospective data entry occurred of cases notified prior to 20 May so that data were available on all cases reported to the Flu Response Centre in Yorkshire and the Humber during the whole of the containment phase.

All data fields on all cases entered into Fluzone for the period 1 June to 2 July (the end of the containment phase in the UK) were downloaded and patient identifiers removed.

Collation and analysis were carried out for three parameters: the date of onset, the date of entry onto Fluzone and the date of a test result becoming available to the Flu Response Centre. All suspected cases entered onto Fluzone were included in this audit (including both confirmed and negative cases, which were the majority), as the aim was to carry out a review of the process undertaken and all of the actions reviewed here had to be carried out before the outcome of the test was known.

Results entered for the month of May were not used in the audit as many of these were entered retrospectively from paper notes and the time of data entry did not correspond to the time of notification of the Flu Response Centre. Data entered after 2 July were also not used as this marked the end of the containment phase.

The date of entry onto Fluzone was used as a proxy for the date of presentation. It was observed that, in general, this proxy was valid as clinicians did contact the Flu Response Centre soon after a consultation in order to get
swabs and treatment carried out and had no other means of doing this. Data were entered onto Fluzone at the time the call was received, and a time and date automatically recorded by the system. From the 12 June onwards, the algorithms for treatment of cases allowed the clinician to test and treat without first notifying the Flu Response Centre. As the proxy value does not hold for these cases, they have been excluded although they represent only a small proportion (Table 1). Test results were entered onto Fluzone as they arrived and a time and date automatically recorded. This was used as a proxy to estimate the earliest point contacts could have been offered prophylaxis as this step depended on this result being known.

Whole number differences between calendar dates entered for each suspected case were calculated. Some manual checking was required to verify exclusions (Table 1). It was not attempted to measure differences in hours as the ‘onset of illness’ was not collected and recorded to the nearest hour. This audit only provides an estimate of the time differences and an assumption was made that exposure in the contacts also occurred from the onset of symptoms in the index case. A measurement difference of ‘2 calendar days’ will contain some data that are within the 48 h parameter and some that are over the 48 h parameter. A measurement of ‘3 calendar days’ difference will always be greater than the 48 h parameter.

Kaplan Meier estimates were performed. Medians and confidence intervals were calculated in STATA for all data (Table 1).

**Results**

No data were missing for the date of onset or the date of notification to the Flu Response Centre; however, 205 records did not contain an influenza A (H1N1) pandemic 2009 test result, and two records contained data entered incorrectly (Table 1).

The median time to the earliest point treatment could have been commenced in suspected cases was estimated at 2 days (95% confidence interval 2–3 days) (Table 2). The median time to the earliest point prophylaxis could have been started in the contacts was estimated at 4 days (95% confidence interval 4–5 days) (Table 2). This is in keeping with the analysis of the detailed national surveillance data from the ‘First Few Hundred’ cases (FF100 surveillance system). This showed a median time to receipt of treatment with antivirals of 3 days and median time to receipt of prophylaxis in household contacts of 4 days.12

Table 3 shows the number and the percentage of cases who could not have received treatment earlier than 3 days after onset. It also shows the number and the percentage of cases whose contacts could not have received prophylaxis earlier than 3 days after onset in the index. All of these cases and contacts could not have received antivirals inside the 48 h standard.

Figures 1–3 demonstrate the spread of the data for all of the time differences between the events of interest. The shape of each distribution is important in the interpretation of the aims of the audit. Figure 2 shows the spread of time intervals for completing all the tasks in the algorithm up to the receipt of a virology result. This is an indication of the contribution to the time delays from the processes involved in responding to cases.

Further time delays may also have accrued after the time events measured here. This includes multiple other steps in the process after notification in order to sanction and arrange access to antivirals followed by travel times to collect in many cases.

### Table 1: Completeness of data

<table>
<thead>
<tr>
<th>Observations</th>
<th>Data for time between events</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Onset of illness to date of presentation (Estimate for earliest point treatment possible)</td>
<td>Presentation to date of result</td>
<td>Onset of illness to date of result (Estimate for the earliest point prophylaxis of contacts possible)</td>
</tr>
<tr>
<td>Total number of case records available</td>
<td>740</td>
<td>740</td>
<td>740</td>
</tr>
<tr>
<td>Missing data</td>
<td>0</td>
<td>205</td>
<td>205</td>
</tr>
<tr>
<td>Exclusions-General Practitioner swab without informing Flu Response Centre (algorithm 6b from 12 June)</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Exclusions-data incorrectly entered</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Case records analysed</td>
<td>713</td>
<td>508</td>
<td>508</td>
</tr>
</tbody>
</table>
Discussion

Main finding of this study

The results indicate that in the Yorkshire and Humber region only approximately half the number of suspected cases of pandemic influenza were reported early enough after the onset of illness to have been in time to allow access to antivirals during the period when antivirals were considered to be most effective. This is likely to have impacted on the effectiveness of this measure in reducing the duration of symptoms and as a way of slowing the spread of the virus. It also took on average 2 days from the reporting of a suspected case to a virology result becoming available. Since this marks the earliest point contacts could be offered prophylaxis, this is also likely to have reduced the effectiveness of this strategy in slowing the spread of the virus.

The logistical difficulties of delivering containment according to the national algorithms meant that there were significant time delays involved in the processes. Even allowing for measurement errors, the shape of the time-interval distributions suggests that any changes to the processes to

Table 2 Results for average time intervals between events (measured difference between calendar dates)

<table>
<thead>
<tr>
<th>Estimated time for the earliest point treatment of cases possible (Time from the onset of illness to date of presentation)</th>
<th>Estimated time for health organizations to confirm illness (Time from presentation to date of result)</th>
<th>Estimated time for the earliest point prophylaxis of contacts possible (Time from the onset of illness to date of result)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median duration of time interval</td>
<td>2 days</td>
<td>2 days</td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td>2–3 days</td>
<td>2–2 days</td>
</tr>
<tr>
<td>Range</td>
<td>0–13 days</td>
<td>0–11 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1–17 days</td>
</tr>
</tbody>
</table>

Table 3 Comparison of numbers and percentages of events occurring on the same day, 1 day and 2 days after the onset of illness versus events occurring 3 days after the onset of illness and beyond

<table>
<thead>
<tr>
<th>Number of cases (%)</th>
<th>Same day, 1 day or 2 days after onset</th>
<th>3 days after onset and beyond</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated time for the earliest point treatment of cases possible (Time from the onset of illness to date of presentation)</td>
<td>370 (52%)</td>
<td>343 (48%)</td>
<td>713</td>
</tr>
<tr>
<td>Estimated time for the earliest point prophylaxis of contacts possible (Time from the onset of illness to date of result)</td>
<td>99 (19%)</td>
<td>409 (81%)</td>
<td>508</td>
</tr>
</tbody>
</table>

Fig. 1 Estimated time for the earliest point treatment of cases possible (Estimated time from the onset of illness to date of presentation). 84 × 42 mm (300 × 300 DPI).
try and improve the numbers receiving antivirals closer to the 48 h standard would have had to have been substantial. The process for co-ordination of containment through regional Flu Response Centres had many steps and potential bottlenecks. Limited distribution and availability of viral swab kits, the requirement for samples to be transported to and tested at regional laboratories and limited access to antiviral medicines were also key factors in contributing to delays. Even assuming all these time intervals could have been reduced, significant delays between onset and presentation still existed which were beyond the control of the Flu Response Centres or other organizations. This was despite the high degree of media coverage that existed at the time.

What is already known on this topic
Before 2009, a national strategy of ‘containment’ had never been attempted to control the spread of an infectious disease. Evidence suggested for effective treatment and prophylaxis of cases of influenza (prior to influenza A (H1N1) pandemic 2009) that antivirals should be taken within the first 48 h.

What this study adds
This audit during a real pandemic situation shows that practical implementation of a new multi-stage process like ‘containment’ set-up at short notice during an emergency can be difficult to achieve with the speed that may be necessary to make it effective.

Limitations of this study
This paper presents the results of an audit of the processes involved in the containment phase. It used available information and estimated the times involved by measuring only the differences in calendar days between proxy markers for certain events. This has its limitations and is not able to provide an accurate measure of the times or to be able to audit exactly to the ‘48 h’ reference standard for treatment and prophylaxis. However, the proxy markers occur before the final events of interest (i.e. the exact points in time at
which patients and contacts would have been able to begin treatment and prophylaxis) which would make the estimates more conservative.

**Conclusion**

Containment may be a strategy employed in future pandemics or possible emergent infections similar to the severe acute respiratory syndrome (SARS) outbreak. Although the influenza A (H1N1) pandemic 2009 strain has been considered on the whole to cause mild illness comparable to seasonal influenza, learning the lessons of containment may be very useful in determining future strategy. If a ‘containment’ strategy were to be employed in any future emergency, decision-makers would need to consider the practicalities of delivery and likely impact of delays in any complex process on achieving the aims of reducing spread.

**References**