



Department  
of Health

# Impact of Mass Gatherings on an Influenza Pandemic

*Scientific Evidence Base Review*

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## Executive summary

**Background:** Influenza and other respiratory viruses may be transmitted from person to person by the inhalation of droplets or aerosols containing virus particles and by direct/indirect contact with the virus. Although the complete details of factors that affect transmissibility of influenza are not yet fully understood, close contact is a consistent finding associated with the transmission and spread of the virus and while the relative contributions of each of these routes of transmission are not known, droplet spread is considered to be the most important. Mass gatherings involve large numbers of people gathered together in small geographical areas for a period of time. Based on this understanding of how influenza is spread and the conditions that characterise mass gatherings, from first principles, these events would seem to provide a good opportunity for the rapid transmission of influenza to large numbers of people and its subsequent dissemination. By extension, it would seem plausible that banning or regulating such gatherings could reduce influenza transmission. However, the implications of banning or restricting mass gatherings may be far reaching and coherent policy making in this area has been hampered by a lack of scientific evidence in this area.

Restricting mass gatherings is one of a number of social distancing measures that has been put suggested should be considered in the event of an influenza pandemic occurring, in 2010 the Health Protection Agency (HPA) undertook a scientific review of the evidence to determine whether:

- (a) mass gatherings contribute to the transmission of influenza
- (b) restrictions on mass gatherings are effective at reducing or preventing transmission.

The methodology and results of the review were peer reviewed by the XXXX and published on the Department of Health website on 22 March 2011.

In light of the large number of publications and the operational experience that have emerged since the 2009 pandemic (H1N1 pdm09), the Department of Health commissioned the HPA to update this review and several other pandemic influenza topic areas.

**Methods:** An updated systematic review of the published literature to 31 November 2012 was undertaken (with a restricted time frame of 19 April 2010 to 31 November 2012). The same inclusion criteria were used and this included randomised controlled trials, quasi-experimental studies, observational studies, outbreak reports, and published in English, with an outcome of laboratory-confirmed or clinically diagnosed influenza or other viral respiratory infections. The search strategy incorporated a wide range of terms to reflect the different types of mass gatherings and for this update, the search terms were expanded to include maritime mass gathering settings, including civilian and military ships. Since terms for ships was not included in the last review, there was no restricted timeframe for studies including outbreaks or transmission on ships (through to 31 November 2012). The list of papers generated by the search was sifted for relevance by title, then by abstract and finally by reading the full text to determine whether each article fulfilled the inclusion criteria. Each of the selected papers was summarised and a narrative approach was adopted for data synthesis. As in the previous review, the

selected papers underwent a quality assessment process before being included in the final review.

**Results:** The updated search identified an additional 320 papers (combined total of 1990 papers) of which 17 new papers or 35 combined papers met the inclusion criteria. The papers included one quasi-experimental study, 14 observational studies (9 new), 12 outbreak reports (6 new), 4 historical outbreak reports (1 new) , and 4 event surveillance reports (1 new). There were no relevant randomised controlled trials.

The selected papers covered mass gatherings of varying sizes and settings, including events as diverse as an academic conference, games and sports meetings, musical festivals, maritime settings and associated with global events such as the Hajj pilgrimage highlighting the variation in the way that the term mass gathering is used.

The observational studies and the quasi-experimental study together provided evidence that mass gatherings are associated with a risk of influenza transmission, particularly within the specialised setting of Hajj. New evidence supports the findings that respiratory viruses (including influenza) are transmitted at specialised events such as the Hajj; however specific evidence for pandemic influenza does not suggest widespread transmission occurs.

Four strands of evidence emerged from the outbreak reports. First, they provided further evidence linking mass gatherings with influenza transmission. Second, the evidence suggests that crowd density and event duration may be the key characteristics of a mass gathering that determine the risk of influenza transmission. There is some new evidence that ships provide an example of a specialised setting that may be a risk factor for influenza outbreaks, particularly out of season. It is therefore argued that the mass gathering definition should be expanded to include civilian and military ships. Third, some evidence suggests that mass gatherings can be “seeding” events leading to the introduction of new strains of influenza into the host geographical area, or instigating community transmission in the early stages of a pandemic. Finally, evidence from the historical outbreak analyses suggests that, when implemented in combination with other social distancing interventions such as isolation measures and school closures, restriction of mass gatherings may significantly help to reduce influenza transmission. It was not possible to tease out from the data available any conclusive evidence on the individual effect of restriction of mass gatherings. However there was no new evidence to support hypotheses that restrictions can be effective at reducing influenza transmission in these settings

Surveillance reports from multi-location sports championships (including World Cup tournaments, the Winter Olympiad and the Asian Youth Games) provided no evidence of significant influenza transmission at such events, and one new study supported this view.

**Conclusion:** The evidence to help address important public health questions around mass gatherings and influenza transmission is sparse, especially in the context of an influenza pandemic. This remains the case following the recent update. However, it is possible to draw three principal conclusions from the review. Firstly, mass gatherings are very varied and the type, size, duration and setting of such events may play a role in the risk of influenza transmission. Secondly, there is some evidence that influenza may be transmitted at certain kinds of mass gatherings. Thirdly, limited - and mainly historical - evidence indicates that restrictions of mass gatherings can reduce transmission when

part of a package of other public health interventions including isolation and school closures.

In terms of policy implications, it is clear that mass gatherings should not be considered as a homogenous group of events; the adoption of a common terminology for describing mass gatherings and the development of a hierarchy based on factors such as event size, duration, and crowd density may be helpful towards risk assessment and policy decision making. The inclusion of updated evidence to support a new type of setting, ships strengthens this argument that certain type of settings should be more carefully analysed. While there is little, if any direct evidence, to support banning mass gatherings, voluntary rather than legislated restrictions may, if implemented as part of a package of other public health measures, be a pragmatic and beneficial approach should the severity of a future pandemic warrant extraordinary measures. In addition, the practical implications of potential policies aimed at mass gathering restrictions should be carefully assessed, including economic and logistical ramifications.

More studies of appropriate design and power are required to generate an improved evidence base to support policy making on this subject. It remains the case that studies with improved study design are required, especially ensuring that a comparison group such as non-exposed individuals are factored into studies to enhance the validity of findings.



## Background

It is generally considered by policy makers, planners and emergency services that mass gatherings can be the cause of outbreaks or an increased incidence of various infectious diseases. These views are based on an understanding of the ways that certain infectious diseases can be spread and the conditions that are observed at mass gathering events and sites.

It is well established that influenza is transmitted from person to person through close contact with an infected, symptomatic individual. The exact mechanisms by which transmission occurs have not been fully elucidated, but is believed to involve multiple routes including large respiratory droplets and direct/indirect contact (1) with secretions or fomites. Aerosol transmission may also occur, but there is considerable controversy about this. A body of evidence supporting an important role for aerosol transmission (2) was called into question by other investigators holding that aerosols do not play a major role (3). This is an ongoing debate and some further evidence of aerosol transmission has recently been put forward (4). This is an important dialogue because the mechanism of transmission is always a key factor in infection control planning.

While uncertainty persists regarding aerosols, droplet and contact transmission remain largely regarded as the most important and likely routes. Transmission through these routes clearly requires physical nearness to infected persons, via either direct touch or the propulsion of large droplets across a relatively short distance. This requirement makes the consideration of mass gatherings a crucial issue. Mass gathering events involve large numbers of people congregating in finite geographical areas to share an event or experience. Individuals can be in very close proximity for variable periods of time and, if the event is over a number of days, may even share over-crowded and/or temporary accommodation.

For those infectious diseases, like influenza, where close contact is the main determinant of transmission it therefore appears self evident that mass gathering events could lead to the rapid transmission of a new influenza virus.

In the event of an influenza pandemic, minimising transmission of influenza has been a priority for public health action. A variety of non-pharmaceutical public health interventions such as quarantine, self isolation of patients, respiratory etiquette and hand washing have been advocated to reduce the opportunities for close contact between infected and susceptible individuals or the opportunities for the virus to be picked up by susceptible people. Banning or restricting mass gatherings has been seen as a logical extension of this policy, however, it is a particular concern of policy makers that the scientific evidence upon which to base guidance for mass gatherings is lacking. This is particularly important given the need to weigh any potential benefits against the economic and social disruption that banning or restricting mass gathering could have on society.

The Department of Health (DH) commissioned the Health Protection Agency (HPA) to undertake an update of the previous systematic review of the evidence base relating to the effect or impact that mass gathering restrictions may have during an influenza pandemic. This is an important policy area not only because of the impact such restrictions could have on public confidence and morale but also because of the

economic and liability issues that such action might generate. The primary purpose of the review was to assess the impact of new evidence and to a) identify whether mass gathering events facilitate transmission during a pandemic and b) inform statements on the effectiveness of interventions that may be deployed to reduce spread of a new influenza virus at mass gathering events during a pandemic. The previous DH review examined the scientific literature published up until the end of June 2010 and provided the evidence base to underpin policies on mass gatherings in the 2011 UK Influenza Pandemic Preparedness Strategy. Evidence in this update therefore examines, alongside the previous findings, new studies published since June 2010 through to Nov 2012.

## Methods

Guidance developed by the HPA, largely based on the University of York's Centre for Reviews and Dissemination guidance for undertaking reviews in healthcare, was followed (5). A scientist (MD) with general knowledge in systematic review techniques and influenza epidemiology undertook the primary review work with support from the original team (consultant epidemiologist (NP) and a Specialist Registrar in Public Health (DI)). Initial scoping was based on a review written by MZ in 2009 (unpublished). The work for the original review commenced in mid-July 2010 and was completed in mid-October 2010. The work of updating the review started mid-Nov 2012 and a draft was available by the end of February 2013 for review by members of the SAGE. The final document was submitted to the Department of Health XXXX

Both MD and DI reviewed the previous questions and agreed they would be suitable for the update. Consequently there was no change to the questions addressed:

- Is there an association between mass gatherings and influenza outbreaks or spread?
- Are there any particular characteristics (such as size or duration) of mass gatherings that influence transmission of influenza?
- Does the restriction of mass gatherings reduce the spread of influenza within the community (compared with no restriction or with other interventions)?

### **Inclusion criteria** (Figure 1)

The following types of studies were included in the review:

- Randomised controlled trial
- Quasi-experimental study
  - Non-randomised controlled study
  - Before-and-after study
- Observational study
  - Cohort study
  - Case-control study
- Outbreak reports
  - Outbreak/cluster reports
  - Historical archival outbreak analyses
- Surveillance reports
  - Major event infection surveillance reports

The list above is largely in hierarchical order of study design quality (5), but with an added element as outbreak and surveillance reports are not traditionally included in such lists, but these two types of studies are important for the particular topic of this review.

Only studies published in English and which had an abstract were included, but WHO papers or Eurosurveillance articles with relevant titles were also considered even if they had no abstracts. Only studies in humans were considered directly relevant for the review. Relevant systematic and narrative reviews and operational description papers were utilised for useful background information. The reference lists of the systematic reviews and other key review papers were scanned to identify potentially relevant primary studies that could be considered for inclusion in the review. Case reports, mathematical modelling and human/non-human experimental laboratory studies were excluded from the review.

Outcome measures were the development of laboratory-confirmed influenza infection (i.e. documented by virus isolation, molecular testing such as polymerase chain reaction and serological studies). Clinical influenza-like illness as defined by the investigators was also included although these are less specific.

### **Figure 1. Summary of criteria for the review**

#### **Inclusion criteria**

- Type of study: observational studies, cross-sectional studies, outbreak/cluster reports, surveillance reports, quasi-experimental, RCT
- Participants: humans
- Setting: community
- Language: English only
- Abstract: available
- Outcome: laboratory-confirmed or clinically diagnosed influenza, influenza-like illness (ILI), or other viral respiratory infections in individuals; or population levels of influenza, ILI, or other viral respiratory infections

#### **Exclusion criteria**

- Type of study: case report, mathematical modelling and human/non-human experimental laboratory studies
- Participants: animals
- Setting: laboratory
- Language: non-English
- Abstract: not available
- Outcome: bacterial infections

### **Search strategy**

The search strategy focused on primary studies taking into account the issues detailed above. The term 'influenza' rather than 'pandemic influenza' was used to reflect the entire spectrum of influenza (i.e. zoonotic, seasonal and pandemic) for which guidance would be relevant. The transmission of respiratory viruses other than influenza was also included because of the similarity of transmission and therefore the potential applicability of any results to influenza.

The term mass gathering on its own proved inadequate as a search term as there is no clearly accepted definition of what constitutes a mass gathering. Therefore a range of additional terms were used, such as public gatherings, social gatherings, large crowds, mass events, festival, Olympics, Hajj, sport championships etc. As a key part of this update, civilian ships (both cruise and cargo) and military ships were included in the search strategy. To define a ship under the mass gathering definition, the population on-board (both combined passengers and crew for cruise/cargo ships or crew for military ships) needed to be above 1000 and the cruise duration exceeding one day. The full updated list of search terms is shown in appendix 2.

A PubMed search was conducted on 07 December 2012 with no time period restrictions. This was an update of the previous review; therefore new literature between the period 19 April 2010 (*original review conducted on 19 July 2010 - this allowed a 3 month overlap*) to 31 November 2012 was assessed. For cruise ships, any previous literature to 31 November 2012 was included. All previous and updated literature has been included in this review. Appendix 1 details the global search terms used for searching the PubMed database. In addition, the following databases were searched: Scopus, Excerpta Medica Database (EMBASE), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). Appendix 2 details the terms used for these searches.

### **Other sources**

In addition to the search results, the reference lists of papers identified from the search were scanned for other potentially relevant studies. Efforts were also made to identify studies other than those published in the peer-reviewed literature (including any relevant systematic reviews or key review articles) and relevant literature findings from the parallel Pandemic Influenza reviews updates (*Routes of Transmission of the Influenza Virus and the use of facemasks and respirators during a pandemic*).

### **Study selection and data extraction**

As with the previous review the study selection was conducted in stages. Primary screening and decisions on inclusion of papers was conducted by MD based on a global search in databases and screened on the basis of relevance of the title. . The abstracts of the remaining papers were then reviewed to identify studies that appeared to meet the inclusion criteria. In addition, some papers that did not meet the inclusion criteria (e.g. operational descriptions of interventions, commentaries, or editorial reviews of influenza transmission or pandemic influenza) were selected to provide relevant background or supplemental information. The full text of all these articles was then sought.

Data from the selected papers was extracted using a pre-designed form (Appendix 3). Data elements included publication information, study characteristics, participant characteristics, the intervention (if any) and setting and outcome measures. The data extracted was used to determine the eligibility of each paper for inclusion in the review. At this stage DI performed a secondary examination of the completed form with extracted data to independently assess whether papers met the inclusion criteria. MD and DI then agreed a final list of papers for inclusion into the systematic review. Once papers had been identified as meeting the inclusion criteria, data extraction focussed on capturing results and statistical precisions of the results from each study at the full paper review stage. The results section describes the number of papers identified at each stage.

### **Quality assessment**

At the outset, a strategy was developed to assess the quality of eligible studies using the Critical Appraisal Skills Programme (CASP) tools as appropriate for each type of study (6). However, after completion of the literature search, it was clear that the types of studies (i.e. cross sectional studies, outbreak and surveillance reports) identified were not suitable for assessment by the CASP tools. Therefore as utilised in the previous DH report, a modified approach was adopted, as detailed in Table 3. Each paper was categorised into low or high risk for bias. The grading was assessed based on the presence of significant methodological limitations. A high risk of bias was attributed to papers with at least two significant methodological problems as identified by the review authors.

### **Data synthesis**

The data synthesis was restricted to a narrative approach that included an analysis of the relationships within and between studies and an overall assessment of the robustness of the evidence and limitations of both the studies and the evidence review (5). In addition, the synthesis considered the implications for policy and guidance development as well as future research.

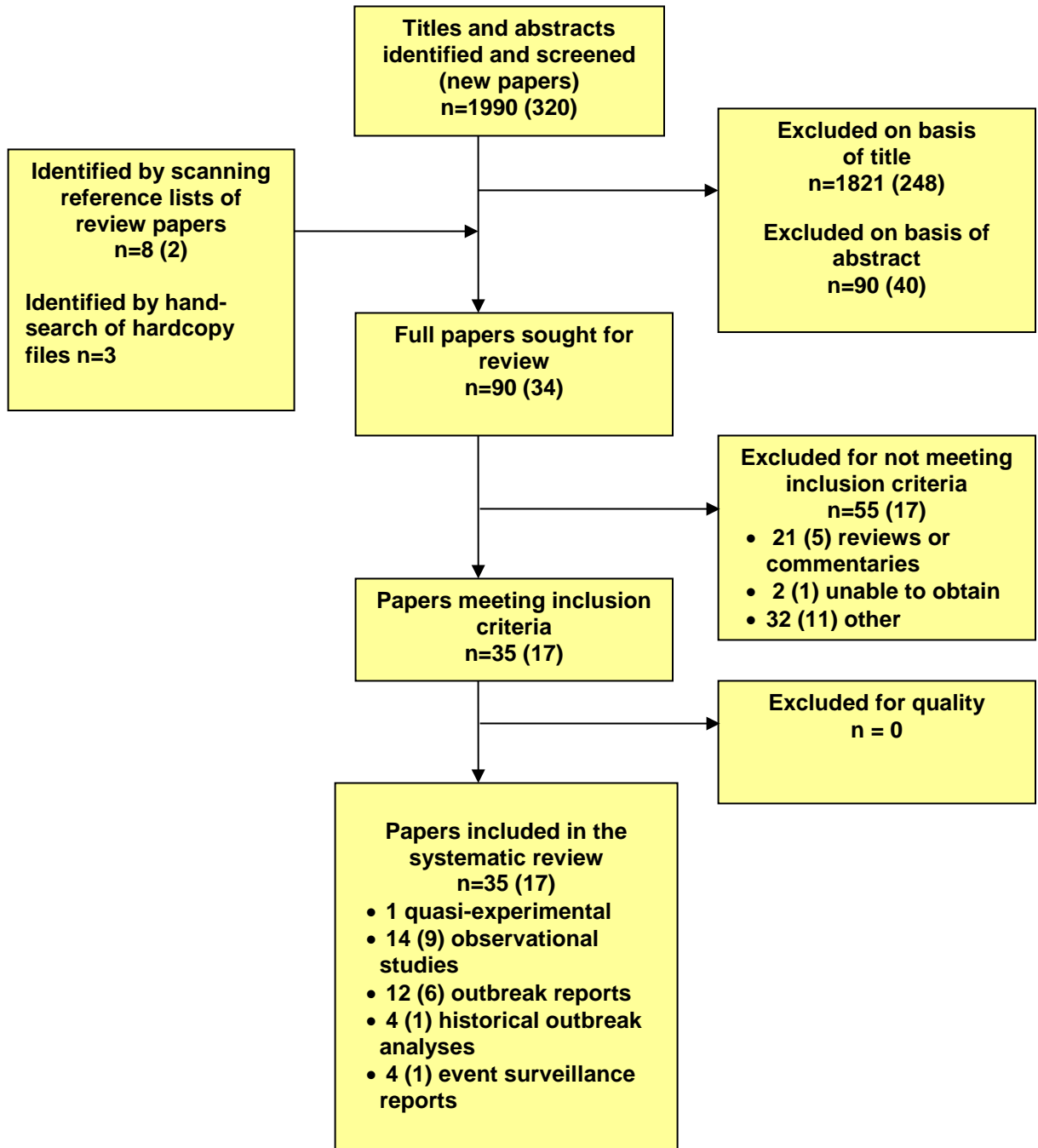
## **Results**

The previous DH review identified 1670 papers to June 2010. The updated search with the restricted timeframe, identified an extra 320 papers, yielding a combined total of 1990 papers (Figure 2). On the basis of title relevance 1821 papers (248 new papers) were excluded. Abstracts for the remaining 169 papers (72 new abstracts) were reviewed and a further 90 (40 new abstracts) were eliminated. 8 papers (2 new papers) were identified from scanning the reference list of review papers and 3 papers retrieved from MZ and NP's hardcopy files.

A total of 90 full papers were reviewed and summarised, including 34 new papers. Table 1 provides a classification of the 90 papers that were read in full text.

After full text review, 35 papers were classified as meeting the inclusion criteria (including 17 new papers). These included a quasi-experimental study (a non-randomised trial) (7), fourteen observational studies (8-21) including 6 new papers (8-11, 14, 15, 19-21), twelve outbreak reports (22-33) including 6 new papers (28-33), four historical outbreak archive analyses (34-37) including 1 new paper (37), and four event surveillance reports (38-41) including 1 new paper (41). Details for each of these studies are summarised in Table 2.

Figure 2. Diagram of search strategy results and article selection (new papers)



**Table 1. Results for 90 papers read in full, by type of paper**

| <b>Classification</b>                           | <b>Total number of papers (new papers)</b> | <b>Number included in the review (new papers)</b> |
|---|--|---|
| Quasi-experimental study (non-randomised trial) | 2  | 1   |
| Observational study                             | 21 (11)                                    | 14 (9)  |
| Outbreak report                                 | 17 (10)                                    | 12 (6)  |
| Historical outbreak archival data study         | 8 (1)                                      | 4 (1)   |
| Event surveillance report                       | 13 (7)                                     | 4 (1)   |
| Systematic review                               | 4 (1)                                      | 0   |
| Narrative review                                | 10 (4)                                     | 0   |
| Editorial/commentary/statement/opinion          | 7  | 0   |
| Background/operational/supplemental information | 8  | 0   |
| <b>Total</b>                                    | <b>90 (34)</b>                             | <b>35 (17)</b>                                    |

The following section breaks down the evidence base by type of study (new studies are indicated by \*). A full analysis of the new findings and impact on the pre-existing evidence base is detailed in the discussion section.

#### **Quasi-experimental study**

One quasi-experimental study by Qureshi et al 2000 (7) attempted to investigate the incidence of vaccine preventable influenza-like illness among Pakistani pilgrims to the Hajj religious gathering in 1999. The Hajj is an annual religious event that takes place over a number of days in a very small geographic area of Saudi Arabia. It usually involves two to three million pilgrims from all over the world. Accommodation is at a premium during this event and many pilgrims stay in tents specifically erected for the event and that are often over-crowded. Although primarily a vaccine efficacy study the study reported rates of influenza-like illness in vaccinated pilgrims of 36% compared to 62% in non-vaccinated pilgrims. However, these results were based on clinical endpoints without microbiologic confirmation, a non-randomised design was used and the study was not designed to address the primary question of this review.

#### **Observational studies**

Thirteen observational studies (8-20) attempted to estimate the risk of acute respiratory illness and/or influenza-like illness associated with the Hajj pilgrimage by attempting to measure its occurrence in pilgrims, while one observational study assessed influenza prevalence and risk-factors within a maritime setting (21\*). Seven of these studies confirmed the cause of illness by laboratory testing (8-11, 13-15), while the other seven relied on specified symptom complexes as surrogate indicators (12, 16-21).

There were eight relatively small cross-sectional studies. Ziyaeyan et al (8\*) examined returning pilgrims in Southern Iran during the 2009 Hajj and documented 10.5% of cases with fever, sore throat and cough (meeting the criteria for ILI). 1.6% cases had a positive RT-PCR result for 2009 pandemic influenza (H1N1 pdm09) while a further 2.6% cases had other influenza A viruses. A Similarly low prevalence of lab-confirmed influenza was

detected in returning Egyptian pilgrims at both airport and passenger ship port sites following the 2009 Hajj - only 1.0% tested positive for influenza A H3N2 (9\*).

In two cross-sectional studies conducted by Memish et al (10\*, 11\*) during the 2009 Hajj, influenza was either detected in very low numbers amongst pilgrims (0.2%) (10) or not detected at all amongst health-care workers (11) where 52.4% of respondents reported respiratory symptoms. Both of these studies used multiplex PCR to examine the distribution of a range of viruses; in (10) Memish et al examined the distribution of respiratory viruses both before and after in different pilgrim samples, demonstrating that the prevalence of viruses did not significantly alter after the pilgrimage. Both studies (10, 11) identified rhinovirus as the most prevalent virus, accounting for 12.9% (10) and 12.6% (11).

This relatively low level of infection contrasts with the findings of the cross-sectional study by Deris et al (12) that used syndromic influenza-like illness rather than laboratory-confirmed infection. They found an influenza-like illness prevalence of 40.1% in Malaysian pilgrims completing the Hajj. Several studies utilizing lab-confirmed infection also indicated higher influenza prevalence's during the Hajj. Rashid et al (13) assessed the burden of laboratory-confirmed influenza and respiratory syncytial virus (RSV) infections in symptomatic British Hajj pilgrims. Of 202 pilgrims who underwent nasal swab testing, 28 (about 14%) had confirmed influenza (mostly type A), while only 9 (4%) had RSV infection. In a further study conducted by Rashid et al (14\*), lab-confirmed influenza A prevalence in UK pilgrims followed at two consecutive Hajj events (2004 and 2005) reported an overall prevalence of 10.6% across the two events. Alborzi et al (15\*) also identifies influenza (combined types A & B) prevalence of 9.8% amongst returning Iranian pilgrims. This study also highlighted that 76.5% of pilgrims developed acute respiratory illness within the first two weeks of Hajj.

Five of the observational studies were described by their respective authors as "prospective cohort" studies- all with a similar study design. However, none of them had an unexposed (non-Hajj attending) group for comparison, indicating that they should be more accurately regarded as "before and after" studies. Choudhry et al (16) assessed Saudi residents (attending the Hajj from a different part of the country) and found an incidence of influenza-like illness at approximately 40%. Two studies of French pilgrims by Gautret et al (17, 18) found rates of acute respiratory illness of 25.9% and 51% respectively. In a third study by Gautret (19\*) at Hajj taking place during the 2009 influenza pandemic, influenza-like-illness incidence was reported at 8.0% in a cohort of French pilgrims. Balaban et al (20\*) similarly followed US pilgrims during the pandemic to the 2009 Hajj; identifying 23.7% self-reported ILI incidence and 41.3% respiratory illness incidence.

As part of this update, we also included military or civilian ships with a population exceeding 1000 on a multi-day cruise. One observational study by Brotherton et al (21\*) captured a dual outbreak of influenza A and B. As part of the outbreak investigation, the team conducted both a case-control study with suspected cases (later to be lab-confirmed) attending the ships infirmary and a cohort study to cover the entire cruise population; with possible or probable cases based on clinical definitions. A total of 40 lab-confirmed influenza A and 7 Influenza B cases were captured; in the case control study it was recognised that the age groups 40-64 were most likely to have influenza, a significant association, and the cohort analysis highlighted that amongst returned questionnaires, 37% of passengers met the criteria for influenza-like-illness.



## **Outbreak reports**

There were four types of outbreaks in the reports that we reviewed. The first of those was a paper by Pang et al (22) that described the experience of dealing with the SARS outbreak of 2003 in Beijing and attempted to evaluate the control measures that were deployed. However, there was no reliable indication of the impact of mass gatherings restrictions on controlling the outbreak as mass gatherings was grouped together with a number of measures loosely described as social distancing.

The next group consists of four reports of influenza outbreaks occurring at a religious event in Australia and at three large open-air music festivals in Europe. All of the events lasted several days and involved crowds ranging from 100,000 to 400,000 people. It is particularly relevant that all of the music festivals occurred during the 2009 influenza pandemic – two at the beginning and one later in the pandemic.

The report by Blyth et al (23) described an outbreak of influenza at a large, five day, religious event in Australia during July 2008 and attended by over 400,000 participants from 170 countries. Over 100,000 of the pilgrims were accommodated in a variety of make-shift, over-crowded venues such as sports halls, community centres and schools. One hundred laboratory confirmed cases of influenza were identified in attendees. Seven different strains of influenza were identified (four influenza A and three influenza B); highlighting the potential for the introduction of novel influenza strains.

Loncarevic et al (24) described an outbreak of influenza at a four day, music festival in Serbia during July 2009 involving over 190,000 participants, with a number coming from other European countries. Many of the participants stayed at a large campsite where over-crowding was an issue. Sixty two laboratory confirmed cases of H1N1pdm09 were identified; some of these were in secondary cases. Although the virus was already present in Serbia at the time of the festival, the sudden increase in cases, in particular the secondary cases associated with the festival, suggests possible local spread. The authors also reported on a small outbreak of influenza at an international sporting event held in Serbia in July over 12 days and attended by over 500,000 spectators. Seven confirmed cases of H1N1 pdm09 were identified in six athletes and a volunteer helping at the Games. Although a much larger event the numbers affected are considerably smaller and seem to be restricted to participants rather than those attending.

Gutierrez et al (25) described a four day, music festival in Belgium during early July 2009 attended by an estimated 120,000 people from all over Europe. Twelve laboratory confirmed cases of H1N1 pdm09 were identified. Although sporadic cases of H1N1 (2009) had been detected in Belgium prior to the festival, an increase in cases was observed after the event and the decision to shift to mitigation was taken almost a week after the first festival associated cases were identified. The authors suggest that this festival highlights the potential seeding role for these events in the early stages of a pandemic.

Botelho-Nevers et al (26) depict an outbreak of influenza at a seven day music festival in Hungary during August 2009 attended by 390,000 people from all over Europe. Many of the participants were located on a campsite set up for the festival. Eight laboratory, confirmed cases of H1N1 pdm09 were identified. Cases of pandemic influenza had already been identified in Hungary and at the time the community influenza-like illness rate was 7.8 per 100,000 against an estimated 3.6 per 100,000 at the music festival.

The third type of outbreak report was that described by Saenz et al (27) of a large, international medical conference held in Iran during September 1968 at the early stages of the 1968/69 pandemic. The conference was over seven days and was attended by over a thousand participants from all over the world. It was estimated that about a third of the participants developed an influenza-like illness with an overall attack rate of 36%. Where virus was isolated from throat and nasal washings this was found to be the A/Hong Kong/68 virus. There was evidence that close contacts of those returning from home were also affected but none of the episodes led to a rapidly expanding focus of infection. The high attack rate raises the question of whether the indoor setting may represent a particularly high risk.

The final type of outbreak report included six studies within maritime settings in either civilian or military ships. Miller et al (28\*) described an outbreak of lab-confirmed influenza on three consecutive North American cruises between 31st August and 30 September 1997. 17% of passengers and 19% of crew developed self-reported acute respiratory illness during the second cruise (following self-administered surveys to all crew and passengers). The authors also noted a higher proportion of elderly individuals on board the ship during each cruise.

An outbreak of influenza B Christensen et al (29\*) on a Northern European cruise reported acute respiratory illness in 13% of crew members (through active surveillance) and 4% of passengers (through medical visitation to the ships infirmary) with an overall influenza-like-illness calculated as 3.85%.

Ward et al (30\*) conducted a complex outbreak investigation onboard two Australian cruises during May 2009 and reported results from the initial ten day cruise. All symptomatic cases were tested which in turn identified 3.0% of the ships population infected with H1N1 pdm09, 3.6% with H3N2 and 0.1% with both, and a more focused epidemiological investigation in the ships childcare centre (where it was believed the outbreak originated) showed that the risk for pandemic influenza was significantly higher (19 cases from 344 sessions attended by susceptible children with a 95% CI 0.033-0.086) against the risk of seasonal influenza (3 cases from 279 sessions with a 95% CI 0.002-0.031), with children also identified as the most susceptible age group for H1N1 pdm09. Four subsequent cases were discovered as epidemiologically linked to passengers but there was no evidence of sustained community transmission.

Another outbreak investigation onboard a trans-Tasman cruise (31\*) reported that 8.0% of passengers and 4.1% of crew attended for upper-respiratory tract infection (utilizing data from the end-of-cruise medical log), and influenza A was identified in a small subset of samples analysed later.

The final passenger-ship outbreak report detailed an investigation on a summer-time Mediterranean cruise (32\*), reporting 5.5% of loosely defined 'respiratory symptoms' amongst passengers (later confirmed as H3N2 influenza A in 20/29 lab-analyzed samples).

One military ship study Dill & Fevata (33\*) captured an outbreak on-board a ship with 1100 crew following identification of 3 index cases at the 2009 fleet-week demonstrations in New York City. During the subsequent 17 day military tour, 135 new influenza-like-illness cases were reported, with a secondary infectivity rate of 12%.

### **Historical outbreak analyses**

Inevitably for a subject of research such as mass gathering restrictions, where prospective studies present serious practical challenges, researchers have sought to utilise historical data to try to draw out major lessons for current impact. This updated review included four historical analyses which all focus on the non-pharmaceutical responses to the 1918-1919 influenza pandemic, an additional report of pandemic influenza on a military ship was identified.

Markel et al (34) examined the way that a variety of non pharmaceutical interventions were deployed in 43 cities across the US during the 1918-19 influenza pandemic. The combination of school closure and concurrent public gathering bans was implemented in 34 (79%) of the 43 cities and was the commonest combination of measures deployed. This combination applied early in the pandemic was significantly associated with reductions in the weekly excess death rates. Hatchett et al (35) undertook a similar analysis on a smaller number of cities in the US where the timing of 19 different types of non-pharmaceutical interventions was available. They found that the early application of multiple interventions showed a trend towards lower cumulative excess mortality but that no single intervention showed an association with improved aggregate outcomes for the pandemic. Both studies suggested that for non-pharmaceutical interventions to be beneficial they should be applied early and in a sustained manner.

A further review of the US public health response to the 1918 pandemic by Aimone (36) gave conflicting results. This review examined the public health response in New York City. In New York during the 1918 pandemic mass gatherings were not prohibited nor were schools closed, instead the city opted for a policy of staggered business hours to avoid rush hour crowding, enhanced surveillance so that cases were quickly identified and isolated and an intensive programme of health education. The reported outcome measures for New York City were comparable to those seen in other US cities and New York City experienced one of the lowest excess death rates on the eastern seaboard of the United States.

Summers et al (37\*) analysed historical data from an outbreak of 1918 pandemic influenza on-board a military transport ship (the HMNZT Tahiti) during August and September 1918. The ship was sailing between Sierra Leone and the UK when the outbreak occurred. Using multiple data sources, the authors estimated that over 1000 of the on board population of 1217 were symptomatic, with an overall mortality rate of almost 7% and estimated cumulative incidence of over 90%. An analysis of risk factors indicated that a higher mortality rate was associated with persons in cabins with bunks (with poor ventilation and severe over-crowding) in comparison to less crowded areas where hammocks were used for sleeping.

### **Event surveillance reports**

Surveillance reports from four major sporting events within the last decade were considered suitable for review (38-41), an additional paper related to the 1998 World Cup event in France was identified. The study by Gundlapalli et al (38) reported the experience of influenza surveillance during the Winter Olympiad at Salt Lake City in 2002. No indication of the numbers attending was given but it is assumed that the numbers were large. Twenty eight cases of confirmed influenza from three clusters of

influenza-like illness were identified and these were restricted to either participants in the Games or support staff for the Games. The clusters consisted of 12 members of a national team who trained and lived together, eight participants of a sport and 13 law enforcement officers who worked and lived in close proximity.

Lim et al (39) reported on the experience of managing the Asian Youth Games at Singapore in June, 2009. These games involved over 2,000 athletes and officials from 43 countries. Although numbers of spectators are not given it is assumed that the crowds would have been large. At the start of the Games Singapore had already reported 600 confirmed cases of H1N1 pdm09. Six laboratory confirmed cases of H1N1 pdm09 were identified during the eight days of the event – four in one football team. No information on the numbers of confirmed H1N1 pdm09 in the population after the Games was available.

Schenkel et al (40) reporting on the experience of syndromic surveillance during the FIFA World Cup in Germany during June/July 2006. At this time Germany was experiencing a very large outbreak of measles. Measles is essentially spread by the respiratory route and is highly infectious. However, despite enhanced daily surveillance, no outbreaks of respiratory disease or measles associated with the World Cup were detected.

A final surveillance study by Hanslik et al (41\*) examined general community health in host cities during the 1998 World Cup held in France. Over the total 66 day period, which included a reference period of two-weeks prior to the World Cup, physicians reported 558,829 medical encounters registered on the surveillance network. Influenza-like-illness was a syndrome captured on the system and did not exceed epidemic threshold levels nor exceed incidence during the event in comparison to the reference period.

**Table 2. Synopsis of studies included in the final review (new studies indicated by\*)**

**A. Quasi-experimental study**

| Investigator (Reference no.) | Study design and participants  | Reported results   | Comments   |
|------------------------------|--|--|--|
| Qureshi et al. 2000 (7)      | Controlled, non-randomised, open-label (non-blinded) influenza vaccine trial. <i>Vaxigrip</i> (Aventis –Pasteur) was used as a “vaccine probe” to investigate the incidence of vaccine-preventable influenza-like illness (ILI) among Pakistani pilgrims to the Hajj religious gathering in 1999. There were 2070 participants spread across five groups of pilgrims (1120 vaccine group; 950 control group)<br><br>Participants followed up to record ILI symptoms using daily health status report forms and clinic report forms for those referred to local hospitals during Hajj | ILI attack rate: Vaccine group 36%; control 62%.<br><br>Vaccine efficacy 38%<br><br>Vaccine preventable ILI incidence of 22/100 control participants | Limitations include<br>- the non-randomised design<br>- underpowered as recruitment fell slightly short of estimated sample size<br>- difficult presentation style; lack of flow-chart to clearly show the progression of participants through the trial process |

**B. Observational studies**

| Investigator (Reference no.) | Study design and participants  | Reported results   | Comments  |
|------------------------------|--|--|---|
| Deris et al 2010 (12)        | A relatively small (n = 387) cross-sectional study of Malaysian pilgrims who had just completed the Hajj. Participants were recruited at the post-Hajj transit centre for returning pilgrims. Occurrence of respiratory symptoms was elicited by questionnaire | Almost all participants had at least one respiratory symptom (cough 91.5%). The prevalence of ILI was 40.1%, even though 72% received influenza vaccination before the trip. | Limitations include:<br>- Small study – uncertain how representative of the Malaysian pilgrims.<br>- Participant recruitment site was not ideal.<br>- Influenza diagnosis was subjective.<br>- There was no unexposed suitable control group for prevalence comparison.<br>- It is unclear whether the study attempted to measure |

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|                                 |   |   | point prevalence of ILI at the time of study, or ILI incidence during the Hajj period.   |
| Rashid et al (13)               | A cross-sectional study estimating the incidence of laboratory confirmed influenza and RSV infection in British Hajj 2005 pilgrims who developed URTI symptoms. The study also compared a rapid point-of-care diagnostic technique with definitive PCR testing. Participants were recruited (a) among pilgrims presenting at designated British Hajj clinics with URTI symptoms (b) by visiting several groups of pilgrims in their camps and inviting those with symptoms to participate. Symptoms were documented by questionnaire and clinical examination; and nasal swabs taken. | 202 URTI symptomatic persons were tested. 28 (14%) had PCR confirmed influenza (20 with AH3 strain; 7 with B strain, and 1 with AH1). All presented 4 days or more after reaching the Hajj, suggesting infection during the event. Influenza vaccination was not significantly protective. 9 other persons had RSV infection. There were no complications found on follow-up checks 12 weeks after the Hajj | The use of laboratory confirmation was a strength of the study.<br>Limitations include: <ul style="list-style-type: none"> <li>- sampling was restricted to only a small proportion of pilgrims; may not be representative of the 25,000 British Hajj pilgrims for that year</li> <li>- Lack of a suitable (non-Hajj attending) control group to compare influenza occurrence</li> </ul> |
| Choudhry et al, 2006 (16)       | Prospective cohort study of ARI incidence among Riyadh residents attending the 2002 Hajj in Mecca, Saudi Arabia. Pre-Hajj questionnaire administered at recruitment at travel vaccine clinics. Post-Hajj telephone interviews were used to collect data on ARI incidence  | Of 1027 participants, 39.8% developed ARI during or within 2 weeks of Hajj. Older subjects and those with underlying disease (diabetes) were more at risk. Stay at Hajj area for 5 days or more was associated with increased risk of ARI.  | Limitations include: <ul style="list-style-type: none"> <li>- Lack of control group to compare ARI in people not exposed to Hajj event</li> <li>- Lack of information on the background influenza or ILI activity in Saudi Arabia at the time</li> </ul>   |
| Gautret, Yong, et al, 2009 (17) | Prospective cohort study of French pilgrims to 2006 Hajj, assessing influence of statin on febrile cough incidence. 580 subjects were recruited at pre-travel clinic facility. 10.3% were taking statin for hypercholesterolaemia. 34.3% had influenza vaccine. 43% had an underlying chronic disease. A post-Hajj questionnaire was used to collect data on health problems faced during the trip.   | 447 participants responded. High attack rate of cough episodes (60.6% overall). In all, 13.9% had both cough and fever. Neither influenza vaccine nor statin use were protective.   | Limitations include: <ul style="list-style-type: none"> <li>- Lack of control group to compare ARI in people not exposed to Hajj event</li> <li>- Lack of information on the background influenza or ILI activity</li> <li>- Actual Hajj dates not given,</li> </ul>   |

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|                                  |   |  | reducing the utility of the provided “epidemic curve” of fever and cough   |
| Gautret, Soula, et al, 2009 (18) | Prospective cohort study of travel-associated health problems in French pilgrims to 2007 Hajj. 545 subjects were recruited at pre-travel clinic facility. All had influenza vaccine. A post-Hajj questionnaire was used to collect data on health problems faced during the trip.   | 462 participants responded. 58.9% had at least one health problem. 2.8% were hospitalized. Cough was the commonest symptom overall (51%) – about a fifth of these (overall 9%) had fever and cough; the risk of this increased with age.       | <p>Limitations:</p> <ul style="list-style-type: none"> <li>- A fairly small number of subjects</li> <li>- All recruited from a single clinic</li> <li>- Lack of a control group to compare ARI in people not exposed to Hajj event</li> </ul>  |
| Ziyaeyan et al, 2012 (8)*        | Cross-sectional study of pilgrims arriving back at an airport in southern Iran following the 2009 Hajj. 305 subjects were recruited at airport arrival terminal from 8-11 December 2009. A post-Hajj questionnaire was administered to collect data on health problems and throat and nose samples were collected for PCR analysis. | 10.5% of cases had a fever, sore throat and cough (matching ILI definition). 97.7% had 2009-10 seasonal influenza vaccination. Following lab analysis, 1.6% of cases had a positive result for H1N1 pdm09 and 2.6% for other influenza A virus | <p>The use of laboratory confirmation was a strength of the study.</p> <p>Limitations:</p> <ul style="list-style-type: none"> <li>- May have missed individuals that were infected and recovered during 30 day Hajj period through RT-PCR (active infection)</li> <li>- Small sample size</li> <li>- Lack of a suitable (non-Hajj attending) control group to compare influenza occurrence</li> <li>- Only sampled pilgrims arriving by air- different to pilgrims arriving by other transport means?</li> </ul> |
| Memish et al, 2011 (10)*         | Two separate cross sectional surveys were conducted at King Abdulaziz airport in Saudi Arabia (main airport used during the 2009 Hajj. A random sample was selected each time- a total of 519 arriving pilgrims and 2768 departing pilgrims completed a survey and provided samples for lab analysis.                               | Overall prevalence of any respiratory virus detected was 14.5% with 12.5% in arriving pilgrims and 14.8% in departing pilgrims. The main virus detected in both arriving and departing   | <p>The use of laboratory confirmation was a strength of the study.</p> <p>Limitations:</p> <ul style="list-style-type: none"> <li>- Recruitment methodology not clearly defined at airport-</li> </ul>   |

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|                          |  | <p>pilgrims was rhinovirus. Influenza A virus was only detected in 8 samples including 3 positive for H1N1 pdm09. The prevalence of any respiratory virus was significantly lower among those receiving pandemic vaccine in comparison to those not receiving the vaccine.</p>              | <p>thermal pre-screening upon arrival may have affected selection</p> <ul style="list-style-type: none"> <li>- Small sample size for arriving pilgrims in particular</li> <li>- Two individual cross-sectional studies for before and after with different subject- ideally would have followed same subjects before/after</li> </ul>   |
| Rashid et al, 2008 (14)* | <p>This was primarily a vaccine efficacy study conducted through multiple cross sectional surveys. Over two Hajj events (2004 and 2005), participants were sampled in December-Jan after each Hajj and were recruited either while attending Hajj or from UK mosques after returning from the event. Nasal swabs were analysed and immunization histories checked. A combined total of 567 pilgrims were included for the two Hajj events. Participants were grouped into either 'at risk' or 'not at risk' sub-groups. Of 555 pilgrims who underwent virological surveillance, 27% received seasonal influenza vaccination.</p> | <p>11 % of pilgrims in 2004 and 10% of pilgrims in 2005 had PCR confirmed influenza- a mixture of influenza A (78%) and B (22%) was identified. The proportion of influenza among vaccinated individuals was 8% in comparison to 12% among unvaccinated pilgrims across the two events.</p> | <p>The use of laboratory confirmation was a strength of the study.</p> <p>Limitations:</p> <ul style="list-style-type: none"> <li>- Small sample size and sampling was restricted to only a small proportion of pilgrims; may not be representative of the 25,000 British Hajj pilgrims for that year</li> <li>- Lack of a suitable (non-Hajj attending) control group to compare influenza occurrence</li> <li>- No detailed evidence on recruitment methodologies although this study was preceded by similar studies with more detailed methodologies</li> </ul> |
| Kandeel et al, 2011 (9)* | <p>Conducted a cross-sectional study of arriving pilgrims at Port Tawfiq and Cairo International airport in Egypt (2009 Hajj) - convenience sampling utilised for</p>  | <p>6 (1%) of pilgrims tested positive for influenza A- all had subtype H3N2 and no pilgrims tested</p>  | <p>Laboratory confirmation and sampling from multiple entry sites (port and airport) is a</p>   |



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|                                  | <p>selection of individuals. A total of 551 pilgrims were sampled- swabs taken for analysis by PCR and pilgrims asked about H1N1 pdm09 vaccination status. 98.1% of pilgrims reported receiving pre-departure H1N1 pdm09 vaccination</p>   | <p>positive for H1N1 pdm09.</p>   | <p>strength<br/>Limitations:</p> <ul style="list-style-type: none"> <li>- Small sample size probably not representative of all Egyptian pilgrims (certain areas of Egypt under-represented in analysis)</li> <li>- Convenience sampling weak method for participant selection</li> <li>- Potential responder bias- Authors believe unvaccinated pilgrims possibly reluctant to tell interviewers not vaccinated since vaccination mandatory</li> </ul> |
| <p>Alborzi et al, 2009 (15)*</p> | <p>Cross-sectional study of returning Iranian pilgrims into a Southern Iran airport (between Dec 2006 and Jan 2007) following the 2006 Hajj. Questionnaires were distributed to returning pilgrims by physicians- identified individuals with ARI were selected. 255 pilgrims were enrolled and provided samples for laboratory analysis (to detect multiple viral agents). Inactivated influenza vaccine was received in 85.5% before departing for Hajj.</p> | <p>From this sample, 75.6% of participant had developed ARI within the first two weeks of Hajj with viral pathogens identified in 32.5% of those with ARI. Influenza was the most prevalent virus identified (9.8%). Influenza virus was identified in more unvaccinated than vaccinated individuals but this was not a significant result.</p> | <p>Limitations:</p> <ul style="list-style-type: none"> <li>- Although laboratory confirmation is a strength, the use of culture is not the most sensitive approach.</li> <li>- Very small sample size (in comparison to an estimated 100,000 pilgrims from Iran each year)</li> <li>- Sampling, selection and data collection methodologies unclear</li> </ul>   |
| <p>Gautret et al, 2011 (19)*</p> | <p>Prospective cohort study of 405 geographically defined French pilgrims. Recruited individuals presenting at a travel clinic in France for compulsory meningococcal vaccination. A pre-travel questionnaire and post-travel questionnaire was completed with a total of 274 completing both (67% response rate). 97.4% vaccinated against seasonal</p>   | <p>8% reported influenza-like illness in this sample. Influenza vaccine and face mask use did not significantly reduce respiratory symptoms</p>   | <p>Limitations:</p> <ul style="list-style-type: none"> <li>- Small sample size (cannot be extrapolated to all French pilgrims- only one clinic in southern France used as recruiting site)</li> <li>- Self-reported data collection</li> </ul>   |

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|                              | influenza but only 5.8% vaccinated against H1N1 pdm09.  |  | (in person for pre-travel and via telephone for post-travel)<br>- Significant number loss to follow up (paper suggests these individuals similar but no details of analysis)   |
| Memish et al, 2012 (11)*     | Two separate cross sectional surveys were conducted in healthcare workers working at the 2009 Hajj. 184 health care workers were included with 161 answering the initial questionnaire and 104 answering the follow-up questionnaire. 120 combined samples for laboratory analysis were collected to determine the incidence of a range of respiratory viruses. 51% reported receiving seasonal influenza and 22% H1N1 pdm09 vaccination prior to Hajj. | 61% of health care workers reported being within 1 metre of an individual with ILI symptoms during Hajj. Respiratory symptoms were reported in 52% of participants- only 2 viruses were detected in lab analysis (rhinovirus-13% and coronavirus 1%). Rhinovirus was more prevalent after Hajj (12%) than before (8%). | Limitations:<br>- Small sample size (cannot be extrapolated to all French pilgrims- only one clinic in southern France used as recruiting site)<br>- Ideally would have designed cohort analysis to sample same participants before and after<br>- No p-value given for differences between pre-/post-Hajj distributions |
| Balaban et al, 2012 (20)*    | A prospective cohort following 186 recruited US pilgrims to the 2009 Hajj. Participants completed both a pre and post travel questionnaire and were recruited from a) a weekly clinic for Hajj travelers in Minnesota and b) multiple sites across Michigan. Seasonal influenza vaccination reported in 63% and 39% H1N1 pdm09 vaccination pre-departure.   | Respiratory illness was reported in 41.3% respondents with 23.7% meeting criteria for self reported ILI. Reduced risk of respiratory illness was reported practicing social distancing, contact avoidance and hand-hygiene.  | Limitations:<br>- Very small sample size (cannot be extrapolated to all US pilgrims- only two areas studied across US)<br>- Self-reported data collection<br>- No unexposed suitable control group   |
| Brotherton et al, 2003 (21)* | Case-control and cohort studies were conducted as part of an outbreak investigation to examine a possible influenza outbreak on board an Australian Cruise (September 2000). A total of 1100 passengers and 400 crew were on-board. Laboratory confirmation identified Influenza A and B were circulating during the cruise. The case-control study recruited   | 37% reported suffering from ILI. The case-control study showed that there the age group 40-65 was the highest risk group for influenza infection. Influenza vaccination was not protective.  | Limitations:<br>- May have over-estimated lab-confirmed influenza because lab technique utilized (serology) may have captured recently vaccinated individuals in addition  |

suspected cases (lab-confirmed influenza post-cruise) and 55 controls obtained from the ship's population to provide an acute sample and a follow-up sample 4-6 weeks post-cruise (serological laboratory analysis conducted). For the cohort analysis all passengers were asked to complete a questionnaire 3 weeks after the cruise- achieved 75% response rate. 37% of passengers reported receiving influenza vaccination.

- Selection bias- recruitment of cases- these individuals had a higher likelihood of pre-existing medical conditions and were therefore more likely to use medical services
- Small number of healthy controls
- Possible recall bias in cohort study
- Relatively low response rate- no analysis on difference with non-responders
- No unexposed group for comparison in cohort study

### C. Outbreak reports

| Investigator (Reference no.) | Study design and participants  | Reported results   | Comments  |
|------------------------------|--|--|---|
| Pang et al 2003 (22)         | An overview report of the 2003 SARS outbreak in Beijing, China, with 2521 probable cases reported over a 3-month period from March to May, and 7.6% case fatality rate. The authors also reported the control measures taken by health authorities against the outbreak. They analysed the timeline of response measures against the epidemiological progression of the outbreak, attempting to identify which control measures were the most effective. | A range of medical, physical and social control measures were taken at different time points. Among these was the closure of public entertainment sites such as theatres and indoor sports facilities. Authors concluded that control of the outbreak was achieved through a combination of factors. | As mass gatherings restriction was only part of a battery of interventions, it is hard to make out the individual effect of restrictions. |
| Saenz et al, 1969 (27)       | Influenza outbreak report from a medical congress held in Teheran on September 7-15, 1968. Background: The A2/Hong Kong/68 virus caused a series of outbreaks across several Asian countries in  | 304 of 844 respondents fulfilled criteria for influenza, with a final attack rate of 36%. Illness was mostly mild; more marked and   | This was a well reported outbreak. Surprisingly, serological test results were not reported even though samples                           |

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|                                    | <p>1968 but had not been found in Teheran prior to this congress.</p> <p>Description: during the congress, many participants developed symptoms and one of them started an investigation. Questionnaires were later sent to all 1036 participants from 82 countries on all continents. 844 responded,</p>  | <p>prolonged in those aged &gt;55 years. 50 respondents returned to their home countries with fever, of which 36% were believed to have spread infection to contacts, but no large local foci developed.</p>  | <p>were said to have been taken. Also, information on the numbers of cases in contacts of participants was not provided.</p>   |
| <p>Gutierrez et al, 2009 (25)</p>  | <p>Influenza outbreak report at the "Rock Werchter" musical festival in Belgium, July 2-5, 2009, during the 2009 influenza pandemic. The event involved 113,000 participants.</p>  | <p>30 event-linked ILI cases, with 12 confirmed H1N1 pdm09. There were no hospital admissions; mean age 23 (range 18-45) years. The index case was identified as an Israeli participant who arrived in Belgium via London, became ill on July 3 (day after arrival) and presented to festival clinic on July 5. The median generation interval for secondary cases was estimated to be 4 (range 3-7) days. Later, two further event-linked confirmed cases were found in the Netherlands and Luxembourg. The outbreak prompted a national shift to a mitigation strategy in Belgium as it was assessed that community transmission had started.</p> | <p>There was likely under-reporting as there was no active case-finding at the festival site. However there was considerable national mass media and Internet publicity about the cases.</p> |
| <p>Loncarevic et al, 2009 (24)</p> | <p>Influenza outbreak reports at two large events held in Serbia in July 2009, during the 2009 pandemic. Prior to the events 20 cases of H1N1 pdm09 influenza had been reported. The events were: (i) The 25th Universiade - world university Games, July 1-12, involving 8600 athletes, 15000 volunteers and staff, and 500,000 spectators; on 53 sites in 9 locations. (ii) The 10th EXIT music festival, July 9-12; involving 190,000</p> | <p>(i) Universiade: 7 confirmed cases (4 believed linked to the Games).<br/> (ii) EXIT festival: 62 confirmed cases (47 linked to event); mostly aged 16-30 years, and all mild. A further 32 probable cases linked to the festival occurred after the festival ended, but not confirmed due to a</p>   | <p>Cases may have been under-reported due to asymptomatic cases or non-presenters.</p>   |

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| <p>Botelho-Nevers et al, 2010 (26)</p> | <p>visitors to an open-air multi-stage festival. There was an enhanced daily surveillance system for both events.</p> <p>Influenza cluster and unusual case report, linked with the Sziget rock festival in Budapest, August 11-18 2009. The event involved 390,000 participants. This was during the 2009 influenza pandemic, thus a dedicated flu medical tent was set up and the local hospital placed on stand-by.</p>   | <p>change in testing policy. There were no complications or deaths.</p> <p>14 people were hospitalized (3.6/100,000); 8 were confirmed PCR positive for H1N1 pdm09 (57.1%). Background activity at the time in Hungary was ILI 7.8/100,000; and across Europe (ECDC) it was 34.9/100,000 with 15.3% H1N1 pdm09 positivity.</p> | <p>ILI rates were lower at the festival than the national and continental rates; however the H1N1 pdm09 positivity was much higher than the European population rate; together possibly suggesting that many mild cases may not have presented in clinic.</p>  |
|  |  | <p>Surveillance through EuroTravelNet revealed no other cases in participants returning to other European nations.</p> <p>The unusual case was a 23-year-old French male participant who had dual infection with H1N1 pdm09 and varicella zoster virus. He was hospitalized in France and had a good outcome.</p>              |  |
| <p>Blyth et al, 2010 (23)</p>          | <p>Report of influenza outbreak during the World Youth Day events in Sydney, July 15-20, 2008. This was a time of low local seasonal influenza activity but near the onset of Australian influenza season. The largest of the series of religious events was a Papal Mass with a crowd of 400,000. The first influenza case was noted on July 16 and flu clinics were rapidly set up and symptomatic people encouraged to attend. They had paired nose and throat swabs taken and detailed virological serotyping carried out.</p> | <p>100 of 227 symptomatic people who voluntarily attended clinics had laboratory confirmed influenza (a range of A and B types). Local influenza activity increased in the weeks following the event, with evidence of introduction of novel influenza viruses.</p>  | <p>The outbreak response was well organized, resourced and reported. Data collection was not standardized as numerous clinicians manned the rapidly set-up clinics. The true extent of outbreak is unknown. Also, as the event held near the onset of the usual Australian influenza season, the post-event increase in flu activity may have occurred regardless.</p> |

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| Ward et al, 2010 (30)*    | A complex outbreak investigation was conducted on-board an Australian cruise (1970 passengers and 734 crew) in May 2009. The investigation team boarding the ship obtained a list of all passengers/crew and reviewed the medical log. Laboratory testing was conducted on symptomatic isolated patients sent to hospital post-cruise, and quarantined asymptomatic passenger developing symptoms. Interviews held with case-patients at time of diagnosis and 6 weeks later to gather data on duration and severity of illness. A detailed epidemiological investigation of the on-board childcare centre was also performed.           | Identified that a dual strain outbreak had occurred- 82 (3%) were infected with H1N1 pdm09, 98 (4%) infected with influenza A H3N2 virus and 0.1% with both. The childcare investigation showed that the infection rate for H1N1 pdm09 was higher than for seasonal influenza (H3N2). Four subsequent cases were epidemiologically linked to passengers- no evidence of sustained community transmission | Limitations:<br><ul style="list-style-type: none"> <li>- Possible misclassification of cases (due to the utilized laboratory technique)</li> <li>- Recall bias in follow-up questionnaire</li> <li>- May have not identified all co-infected patients and over-estimated secondary attack rate</li> </ul> |
| Miller et al, 2000 (28)*  | An outbreak on-board three consecutive North American cruises (with the same ship) taking place between August 31 and September 30. In the initial cruise, the investigation team analysed the medical records, while on cruise two self-administered surveys were provided to all passengers. Active surveillance was conducted (crew only) for ARI symptoms on cruises two and three. Crew members were removed from next cruise if identified with ARI symptoms. Isolation and antiviral prophylaxis measures were implemented for symptomatic crew from cruise two. Influenza was laboratory confirmed on samples in cruise 1 and 2. | On cruise one, 5% and 3% of passengers presented to ships infirmary with ARI & ILI. On cruise two and three this was 3% and 1% and 2% and <1% respectively. On cruise two, 17% of passengers and 19% crew had self-reported ARI from questionnaires. The secondary attack rate for crew was 3% (cruise one), 8% (cruise two) and 1% (cruise three).  | Limitations:<br><ul style="list-style-type: none"> <li>- Likely large underestimation of cases because only very limited lab-confirmation performed &amp; passive surveillance for passengers</li> <li>- No follow-up of passengers or crew post cruise to detect cases</li> </ul>                        |
| Dill & Fevata, 1999 (33)* | Influenza, H1N1 pdm09, outbreak report related to the United States Military ship, US Iwo Jima, with 1100 servicemen. Initial index cases occurred in crew during land based <i>Fleet Week</i> celebrations in New York (May 2009). Outbreak report described resultant cases on military cruise (17-day deployment from May 27). Identification of cases during fleet week activated enhanced ship wide control measures (strict  | Using an ILI case definition, 135 new cases were detected. The secondary infectivity rate was calculated as 12%. Absolute end of outbreak matched return to home port and moving ill patients off board.   | Limitations:<br><ul style="list-style-type: none"> <li>- No controls to determine cases averted associated with control measures.</li> <li>- No laboratory testing</li> </ul>   |

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|                               | isolation, active case finding & antiviral treatment of cases).  |  |  |
| Christensen et al, 2001 (29)* | Report on respiratory illness on cruise (1311 passengers and 506 crew) occurring between June 23-July 5, 2000. Outbreak investigation conducted by ships medical department. ILI initially identified in 9 crew members- rapid diagnostic tests and later laboratory testing identified influenza B.   | Total of 64 (13%) crew members and 54 (4%) passengers were identified with ARI - of these 71% of crew and 46% of passengers had ILI. The reviewers calculated an overall 3.85% ILI rate across the total ship population. Following confirmation of Influenza B, an antiviral effective against this type was administered to symptomatic crew and passengers. | Limitations: <ul style="list-style-type: none"> <li>- Lab confirmation only used in 4 crew samples- may have missed asymptomatic cases</li> <li>- Only passive surveillance amongst passengers- likely significant underreporting</li> </ul>   |
| Ferson et al, 2000 (31)*      | Late summer outbreak reported (first two weeks of February 2000) on a Sydney-New Zealand-Sydney cruise (estimated total cruise population of 1479). Mid cruise, upper respiratory tract infection cases exceeded a notional 3% threshold. Outbreak report constructed from end-of-cruise medical report data. A sample of cases were laboratory tested which identified influenza A virus (in 2 of 7 samples). | 88 (8%) passengers and 20 (4%) crew attended a clinic with upper respiratory tract infection symptoms (identified as 7.3% of cruise total population after calculation by reviewers). Constructed epidemic curve and identified peak incidence on day 12 of cruise.  | Limitations: <ul style="list-style-type: none"> <li>- Broad definition used to determine cases (upper respiratory tract infection - URTI)- didn't define cases based on more specific definition such as ILI</li> <li>- Very limited laboratory testing to confirm causative agent</li> <li>- Passive case detection likely to under-estimate cases</li> </ul> |
| Joseph, 1999 (32)*            | Summer outbreak reported on a Mediterranean cruise in the summer of 1999. 490 crew and 590 passengers on-board. Influenza A was detected in 20 out of 29 specimens. Stated none of the crew but some of the passengers had been vaccinated against seasonal influenza.   | A total of 60 individuals or 6% (combined crew and passengers) reported respiratory symptoms (case definition matching, but not defined as ILI).   | Limitations: <ul style="list-style-type: none"> <li>- No laboratory testing</li> </ul>   |

#### D. Historical outbreak studies

| Investigator<br>(Reference no.) | Study design and participants   | Reported results   | Comments  |
|---------------------------------|---|--|---|
| Markel et al,<br>2007 (34)      | Historical archival outbreak analysis research. Setting: 1918-1919 influenza pandemic. This study examined detailed records of the period September 8, 1918 to February 22, 1919, analyzing the public health responses of US cities to the pandemic. 43 US cities (all with a population at the time exceeding 100,000) and for which the most extensive records of Public Health interventions could be found, were studied. The sources of information included the period "Weekly Health Index" of the US Census Bureau, official public health reports, media archives, and municipal records. | <p>Three main categories of non-pharmaceutical interventions (NPI) were applied: (a) school closures; (b) isolation and quarantine; and (c) public gathering bans (included closing salons, sports events, entertainment venues, and some indoor gatherings). Most cities implemented a combination of these interventions, most commonly combining public gathering bans and school closures.</p> <p>A total of 143,000 excess pneumonia and influenza deaths occurred in the 43 cities during the period studied. In general, early and sustained NPI implementation was significantly beneficial. Cities with earlier NPI reached peak mortality later and had lower peak and total mortality. Sustained and lengthier NPI implementation was associated with lower excess mortality.</p> | <p>The major strength of the study was to link archived data with modern techniques to produce research that is useful at this time.</p> <p>The limitations are similar to those of Hatchett et al above.</p> |
| Hatchett et al,<br>2007 (35)    | Historical archival outbreak analysis research. Setting: 1918 influenza pandemic. This study examined detailed records of the period September 8 to December 28, 1918, focusing on the public health responses of US cities to the  | 19 categories of NPIs were identified. The measures of epidemic outcome included the peak death rate, and a "normalized" peak that was   | A real strength of the study is that it combines archived data with modern techniques to produce potentially very valuable data. This allows an evaluation of an experimental situation that is very          |



|                           |   |  |  |
|---------------------------|---|--|--|
|                           | <p>pandemic. 17 US cities for which complete records of Public Health interventions could be found, were studied. The sources of information included newspaper archives, municipal records, and consultations with current officials.</p>  | <p>standardized to facilitate inter-city comparison. Among the findings were that:</p> <ul style="list-style-type: none"> <li>- Aggressive early NPI was associated with lower peak excess mortality</li> <li>- Early implementation of school, church, and theatre closures were individually associated with lower normalized peak excess weekly deaths</li> </ul> | <p>difficult to simulate as a contemporary intervention study.</p> <p>Limitations include:</p> <ul style="list-style-type: none"> <li>- The difficulties and drawbacks of historical record retrieval</li> <li>- Heterogeneous definitions of “public gatherings”</li> <li>- Doubts regarding applicability of the findings to current practice as society has changed dramatically since that time</li> </ul> |
| Aimone (36)               | <p>A historical examination of the response of New York City (NYC) authorities to the 1918 pandemic influenza.</p>  | <p>NYC took a number of public health actions, particularly to reduce rush-hour crowding. There were no formal closures of theatres or schools. Yet, the excess death rate due to pandemic in NYC was comparable or lower than in some other major US cities.</p>  |  |
| Summers et al, 2010 (37)* | <p>Report analyzing widespread outbreak of 1918 pandemic influenza and mortality risk factors on-board a New Zealand military transport ship (HMNZT). The ship sailed from Freetown, Sierra Leone on route to England with 1217 persons on-board when the outbreak occurred. Data was obtained from a number of sources including the official archived report, written accounts and other military databases. Modern statistical analysis constructed the epidemic curve and calculated the odds ratio's for potential mortality risk factors.</p> | <p>Estimated over 1000 symptomatic cases with an overall mortality rate of 7% and cumulative incidence of 90% on-board. Significantly higher mortality rate of persons in cabins with bunks (these cabins had extremely poor ventilation and severe over-crowding) in comparison to areas with bunks for sleeping (RR 4.28 95% CI</p>                                | <p>Limitations:</p> <ul style="list-style-type: none"> <li>- Using estimates from historical data sources</li> <li>- Conscripted men on the ship may have not been representative of general population</li> <li>- Difficult to apply findings to modern day</li> </ul>  |

2.69-6.81). Assignment to a particular military unit (field artillery- housed in cabins) significantly associated with mortality risk (adjusted OR 3.04 95% CI 1.59-5.82)

### E. Event surveillance reports

| Investigator (Reference no.) | Study design and participants  | Reported results   | Comments   |
|------------------------------|--|--|--|
| Gundlapalli et al, 2006 (38) | Prospective influenza surveillance report from the Winter Olympiad, February and March 2002. Components of the surveillance programme included: screening of athletes and non-athletes with respiratory symptoms; daily review of viral testing and community public health reports; and case treatment and contact prophylaxis. | 2635 medical visits reported during the Games; 12% with respiratory symptoms. Three main clusters of ILI: (a) 13-man team of security staff with 3 confirmed cases; (b) a 12-member national team with 2 confirmed; (c) 8 participants of the same sport, with 5 confirmed. Overall, 188 people were screened for influenza; 36 were positive (28 type A and 8 type B). Syndromic definition of ILI (fever and cough or sore throat) was not highly predictive of confirmed influenza (sensitivity 67% and specificity 78%). | This was a well-organised systematic prospective influenza surveillance programme, described by the authors as the first of its type at a large Games event.<br><br>Limitations include:<br>- No indication of total numbers of people at the event or in the city<br>- No indication of the background ILI activity in the city or country; or whether this was during the local Winter influenza season. |
| Lim et al, 2010 (39)         | Influenza surveillance report during the disease containment phase of the 2009 influenza pandemic. More than 600 confirmed cases had occurred in Singapore prior to the Games.<br><br>Asian Youth Games in Singapore, June 29 to July 7, 2009 (football preliminaries started on   | 66 suspected cases identified at the Games medical facility; 6 confirmed and isolated in hospital. By contact tracing, 42 persons were quarantined. There was no evidence of H1N1 pdm09 transmission   | This was a detailed operational description and surveillance report.<br><br>The authors stated that no transmission took place during the Games; but it is unclear how the 6 confirmed cases were infected – possibly imported   |

|                           |   |   |   |
|---------------------------|---|---|---|
|                           | June 20). The Games involved 9 sports at 10 venues; 1210 athletes; and 810 officials all from 43 different countries.   | associated with the Games.  | cases?  |
| Schenkel et al, 2006 (40) | Infectious disease surveillance report; World Cup 2006, Germany, June 9 – July 9, 2006. There was an extensive enhanced national surveillance system built around the event, based on existing national and local systems.  | No respiratory events of public health relevance were reported. Infection incidents reported were (a) single cases of varicella, mumps, and <i>S. enteritidis</i> (b) a suspected viral gastroenteritis outbreak (c) a confirmed norovirus outbreak | It is not specifically stated that respiratory infections were under surveillance, but the authors stated that the system was set up “to detect adverse health events of public health relevance”, - presumably including respiratory infection |
| Hanslik et al, 2001 (41)* | Reviewed effectiveness of an electronic sentinel disease surveillance system for the 1998 World Cup (held across 10 cities in France). System was active for a total period of 66 days: two weeks prior to event (reference period) and during the event (four weeks from June 10 to July 12). Medical activity and the daily number of communicable diseases (including ILI) recorded. Five sentinel networks with 553 general practitioners and a range of medical settings Included. | Compared with the reference period, ILI rates remained stable during the event period and did not exceed the epidemic threshold level. This was also true for all other communicable diseases monitored during the event.                           | Limitations include:<br>- No indication of total numbers of people at the event or in the cities  |

Abbreviations used in Table 2: ARI=Acute Respiratory tract Infection; ILI=influenza-like illness; NPI =non-pharmaceutical interventions; PCR=polymerase chain reaction; RSV=respiratory syncytial virus; URTI=upper respiratory tract infection

**Table 3. Quality assessment (risk of bias). Graded assessment of risk of bias (new studies indicated by \*)**

*This assessment format was adopted as CASP tools could not be applied (CASP resources: <http://www.sph.nhs.uk/what-we-do/public-health-workforce/resources/critical-appraisals-skills-programme> (6))*

| Study type            | Study author and reference no. |                 | Notes   | Risk of bias assessment (low or high)  |              | Author        |
|-----------------------|--------------------------------|-----------------|---|--|--------------|---------------|
|                       |                                |                 |   | Basis / key issues   | Risk of bias |               |
| Quasi-experimental    | (7)                            | Qureshi 2000    | <b>Is there an appropriate CASP tool?</b> No                            | No randomisation; no blinding<br>Thus no allocation concealment                  | High         | Qureshi 2000  |
| Observational studies | (12)                           | Deris 2009      | Cross-sectional studies<br><b>Is there an appropriate CASP tool?</b> No | No controls; subjective diagnosis; no follow-up; unreliable recruitment approach | High         | Deris 2009    |
|                       | (10)                           | Memish 2011 *   |   | No control group; unreliable recruitment approach                                | High         | Memish 2011   |
|                       | (9)                            | Kandeel 2011 *  |   | No control group; unreliable sampling approach                                   | High         | Kandeel 2011  |
|                       | (15)                           | Alborzi 2009*   |   | No control group; sampling and data collection methodology unclear               | High         | Alborzi 2009  |
|                       | (13)                           | Rashid 2008     |   | No control group   | Low          | Rashid 2008   |
|                       | (14)                           | Rashid 2008 *   |   | No control group   | Low          | Rashid 2008   |
|                       | (8)                            | Ziyaeyan 2012 * |   | No control group   | Low          | Ziyaeyan 2012 |
|                       | (11)                           | Memish 2012 *   |   | No control group   | Low          | Memish 2012   |

|                  |      |                     |   |  |  |  |             |
|------------------|------|---------------------|---|--|--|--|-------------|
|                  | (16) | Choudhry 2006       | Described as prospective cohort studies, but look more like before & after studies, which belong to the quasi-experimental category<br><br><b>Is there an appropriate CASP tool? No</b>   | No unexposed control groups<br>Subjective diagnosis<br>Studies apparently wrongly classified | High   | Choudhry 2006  |             |
|                  | (17) | Gautret 2009        |   |  | High   | Gautret 2009   |             |
|                  | (18) | Gautret 2009        |   |  | High   | Gautret 2009   |             |
|                  | (19) | Gautret 2011 *      |   |  | High   | Gautret 2011   |             |
|                  | (20) | Balaban 2012 *      |   |  | High   | Balaban 2012   |             |
|                  | (21) | Brotherton 2003 *   |   |  | Described as cohort studies, but more similar to before & after studies, which belong to the quasi-experimental category<br>Also case-control study<br><br><b>Is there an appropriate CASP tool? No for cohort/ yes for case-control</b> | No unexposed control groups; low response rate and recall bias for cohort analysis | High        |
| Outbreak reports | (23) | Blyth 2010          | <b>Is there an appropriate CASP tool? No</b><br><br>The ORION tool is also not applicable as it is specific to outbreaks of nosocomial infection - <a href="http://www.idrn.org/orion.php">http://www.idrn.org/orion.php</a> (42, 43) | Clear description of setting and context?<br>Laboratory diagnosis?<br>Data reliability?      | Low  | Blyth 2010   |             |
|                  | (26) | Botelho-Nevers 2010 |   |  | Low  | Botelho-Nevers 2010  |             |
|                  | (25) | Gutierrez 2009      |   |  | Low  | Gutierrez 2009   |             |
|                  | (24) | Loncarevic 2009     |   |  | Low  | Loncarevic 2009  |             |
|                  | (22) | Pang 2003           |   |  | Low  | Pang 2003  |             |
|                  | (27) | Saenz 1969          |   |  | Low  | Saenz 1969   |             |
|                  | (28) | Miller 2003 *       |   |  | Laboratory diagnosis?<br>Data reliability?   | Low  | Miller 2003 |
|                  | (33) | Dill 1999 *         |   |  | Significant underestimation of cases?  | Low  | Dill 1999   |

|                            |      |                    |   |   |                   |                  |
|----------------------------|------|--------------------|---|---|-------------------|------------------|
|                            | (29) | Christensen 2001 * |   |   | Low               | Christensen 2001 |
|                            | (31) | Fersen 2000 *      |   |   | Low               | Ferson 2000      |
|                            | (32) | Joseph 1999 *      |   |   | Low               | Joseph 1999      |
|                            | (30) | Ward 2010 *        |   |   | Data reliability? | Low              |
|                            | (36) | Aimone 2010        | Historical outbreak studies<br><b>Is there an appropriate CASP tool? No</b> | Reliable, multiple data sources?<br>In-depth methods description?<br>Clear outcome measures?<br>Appropriate analysis?<br>Breadth of coverage? | Low               | Aimone 2010      |
|                            | (35) | Hatchett 2007      |   |   | Low               | Hatchett 2007    |
|                            | (34) | Markel 2007        |   |   | Low               | Markel 2007      |
|                            | (37) | Summers 2010 *     |   |   | Low               | Summers 2010     |
| Event surveillance reports | (38) | Gundlapalli 2006   | <b>Is there an appropriate CASP tool? No</b>                                | Prospectively planned surveillance?<br>Specific focus on influenza/respiratory virus?<br>Clear description of setting and context?            | Low               | Gundlapalli 2006 |
|                            | (39) | Lim 2010           |   |   | Low               | Lim 2010         |
|                            | (40) | Schenkel 2006      |   |   | Low               | Schenkel 2006    |
|                            | (41) | Hanslik 2001 *     |   |   | Low               | Hanslik 2001     |

**Table 4. Papers that were abstracted but excluded from the final review (New studies indicated by \*)**

This is a summary list of the articles that were excluded (see Figure 2) after full text review as they did not meet the inclusion criteria. Full references are listed in Appendix 4.

|                            | <b>Author</b>       | <b>Notes</b>   |
|----------------------------|---------------------|--|
| <b>REVIEWS</b>             |                     |  |
| Editorials, statements etc | Anon 2009           | WHO technical consultation report  |
|                            | Ferguson 2009       | Discussion paper on social distancing  |
|                            | Rashid 2008         | Expert opinion / reflection  |
|                            | Haworth 2010        | Editorial  |
|                            | Franco-Paredes 2009 | Expert commentary  |
|                            | Ebrahim 2009        | Expert opinion / policy paper  |
|                            | Tomes 2010          | Discussion paper on the 1918-1919 influenza pandemic   |
| Narrative reviews          | Milsten 2002        | Narrative review paper   |
|                            | Zielinski 2009      | Narrative review paper   |
|                            | Michael 1997        | Narrative review paper   |
|                            | Ahmed 2006          | Narrative review paper   |
|                            | Oshitani 2006       | Narrative review paper   |
|                            | Anon 2006           | WHO recommendations on non-pharmaceutical interventions for pandemic influenza   |
|                            | Mouchtouri 2010 *   | A literature review identified 9 Influenza-confirmed outbreaks on different cruise liners between 1997-2005. Examined different epidemiological parameters such as attack rates. |
|                            | Schlaich 2009 *     | Analysis of 49 medical logs from cargo ships (average cruise size 24 persons)- distribution of ILI across log records.   |
|                            | Ferson 2005 *       | General review assessing recorded infectious disease outbreaks (including influenza) amongst cruise ships visiting the port of Sydney between 1999-2003                          |
|                            | Memish 2012 *       | Discussion on mass gathering medicine with particular reference to Hajj and policy implications.   |
| Systematic reviews         | Jefferson 2010      | Systematic review update (Cochrane)  |
|                            | Aledort 2007        | Systematic review and expert panel   |
|                            | Jefferson 2009      | Systematic review  |
|                            | Jefferson 2011 *    | Systematic review update (Cochrane)  |
| <b>OTHER</b>               |                     |  |
| Studies                    | Al-Asmary 2007      | Observational study of the occupational risk of influenza in healthcare facility workers at the Hajj mass gathering  |

|                     |                    |  |
|---------------------|--------------------|--|
|                     | Baum 2009          | Cross-sectional study from Michigan - focus group discussions on attitudes towards social distancing   |
|                     | Broderick 2008     | Non-randomised controlled social distancing intervention study in a community setting; not applicable to a mass gathering situation  |
|                     | Eastwood 2010      | A follow-up cross-sectional survey on willingness to comply with potential health interventions during a pandemic  |
|                     | Hutton 2010        | Cross-sectional methodological study on data collection at mass gatherings   |
|                     | Rubin 2009         | Cross-sectional study of swine flu-related public perceptions  |
|                     | Gautret 2012 *     | Cross-sectional study of French pilgrims attending 2010 Hajj- examined travel patterns.  |
|                     | Mandourah 2012 *   | Prospective 'cohort' study analyzing clinical data for pilgrims admitted to Intensive care in the four main hospitals serving Hajj (2009).   |
| Outbreak report     | Witkop 2010        | Outbreak report from a training academy  |
|                     | CDC/MMWR 2010 *    | Outbreak report characterizing H1N1 pdm09 influenza on a Peruvian military naval ship- 355 crew on-board.  |
|                     | Christenson 1987 * | Outbreak of respiratory illness on board a cruise ship (418 passengers) travelling round southern Europe and northern Africa- examined range of possible respiratory pathogens.          |
|                     | Tarabbo 2011 *     | H1N1 pdm09 outbreak onboard an Italian military ship in the Mediterranean- 237 servicemen on the ship.   |
|                     | Earhart 2001 *     | H3N2 outbreak on US military ship in February 1996. >500 crew on-board.  |
| Historical analysis | Caley 2008         | Modeling-based historical outbreak analysis of social distancing during the 1918-1919 pandemic   |
|                     | McSweeney 2007     | Historical analysis of the effect of residential location on mortality during the 1918 influenza pandemic.   |
|                     | Nishiura 2007      | Historical outbreak analysis of community setting transmission during the 1957 pandemic and the 1961 epidemic  |
|                     | Wallinga 2010      | Vaccine-focused historical study of interventions during the 1957-1958 influenza epidemic  |
| Event surveillance  | Coletta 2006       | Brief description and report of surveillance for a mass gathering event in Virginia. Insufficient information regarding the syndromic surveillance system used.                          |
|                     | Giorgi Rossi 2003  | Brief description and report of surveillance activities for the Millennium Year event in Rome. Respiratory virus infections were not among the target diseases for enhanced surveillance |



|       |                      |  |
|-------|----------------------|--|
|       | Goncalves 2005       | Description and report of surveillance activities for the Euro 2004 football event in Portugal. Respiratory virus infections were not among the target diseases for enhanced surveillance  |
|       | Tsui 2002 *          | Technical paper analyzing the RODS Winter Olympics Biosurveillance system in the 2002 Winter Olympics (Salt Lake city). Description of system mentioned that during deployment would detect prodrome classes- no specific mention to respiratory infections.   |
|       | Gundlapalli 2007 *   | Analysis of hospital electronic medical record based public health surveillance system- deployed in the Olympic village to monitor athletes, staff and volunteers at the 2002 Salt Lake city Winter Olympics. Detected influenza syndrome class and recorded patient level data. The data generated from this system fed into the overall surveillance data from Gundlapalli 2006. |
|       | Morimura 2007 *      | 4 day surveillance system monitoring a range of medical conditions during two separate football events in Japan. Examined levels of 'common cold' during the event.  |
|       | Boisson 2012 *       | Technical paper describing surveillance system deployed during 2007 Cricket World Cup across the West Indies.  |
|       | Jentes 2010 *        | Examined medical activity at the 2008 Beijing Olympics among foreign visitors and expatriates. Surveillance system detected level of respiratory disease   |
|       | Grissom 2006 *       | 2002 Winter Olympics (Soldiers Hollow at Salt Lake City) surveillance- examined levels of respiratory illness.   |
| Other | Avery 1982           | Operational medical response to a mass gathering event   |
|       | Barr 2010            | Operational paper on transport issues related to mass gatherings   |
|       | Fizzell 2008         | Description of planning and response to a mass gathering event   |
|       | Lopez-Cervantes 2009 | Background information on the 2009 pandemic influenza outbreak in Mexico   |
|       | Markel 2008          | Presentation and discussion paper on data from the 1918-1919 influenza pandemic. The substantial research report arising from the study was included in the study (21)   |
|       | Memish 2009          | Consultation and recommendations on public health planning and response for the Hajj 2009  |
|       | Poggensee 2010       | Epidemiological description - initial period of the 2009 pandemic influenza outbreak in Germany  |
|       | Van Hal 2009         | An analysis of epidemic testing strategies   |

## Discussion

The evidence to help address important public health questions around mass gatherings and influenza transmission is sparse, particularly in the context of an influenza pandemic. In addition, the topic does not lend itself to ease of scientific investigation and there are probably many who may feel that it is self-evident that mass gatherings facilitate the transmission of infectious diseases.

The previous systematic search of the literature and this update identified a limited number of studies that addressed the review questions regarding whether mass gatherings are associated with influenza transmission and whether restricting mass gatherings reduces the spread of influenza within the community.

### **What is a mass gathering?**

In attempting to understand and describe a situation or intervention a common understanding or definition is essential. There is currently no generally accepted definition of what constitutes a mass gathering. However, the literature on mass gathering medical care highlights an emerging consensus amongst those providing emergency medical care at organised events. In this setting, mass gatherings are considered to be organised events with more than a thousand people in attendance (44-46). A recently published guidance document from the World Health Organisation (WHO) expanded the term to cover any organised or unplanned event involving enough people to “strain the planning and response resources of the (host) community, state or nation” (47).

The major limitation in trying to define mass gatherings is that any single definition would inevitably be too simplistic as it would need to incorporate events as diverse as the Hajj (lasting about one month and involving between two and three million people), and a football match (involving several thousand spectators over a period of about two hours). In addition to this, mass gatherings within maritime settings including civilian and military ships should be considered, adding a further dimension to the mass gathering definition—an expansion incorporated as part of this update.

A system for classifying mass gatherings on the basis of size and duration is lacking and may be required.

### **What does the evidence say about mass gatherings and the risk of influenza transmission?**

In recognition of the difficulties of conducting hypothesis-based studies that directly implement and assess the effects of restrictions of mass gatherings in real life, an indirect approach was taken to address the review questions as follows:

#### ***I. Are mass gatherings associated with influenza transmission?***

To address whether mass gatherings are associated with influenza transmission, evidence was derived from the following:

- A quasi-experimental study that was primarily designed to quantify vaccine efficacy in the form of a non-randomised trial
- Observational studies that assessed participants before and after exposure to mass gathering events

- Reports of influenza outbreaks and other respiratory illnesses at mass gathering events
- Communicable disease surveillance reports from some major events

A number of studies (8-20) have consistently demonstrated, over a number of years, that respiratory virus transmission occurs amongst pilgrims attending the annual Hajj in Saudi Arabia, and it is recognized as an issue of international public health significance (48-52) that could be particularly important in a pandemic situation. To address this concern, this update included a number of new studies that analysed influenza in pilgrims during the 2009 Hajj (which took place during the 2009 pandemic period). Evidence from these studies suggest that for the H1N1 pdm09 pandemic virus, transmission was particularly low possibly due the relatively older age groups of pilgrims attending Hajj (individuals with a lower susceptibility) and levels of pre-departure H1N1 pdm09 vaccination coverage (although this was variable across studies).

A significant proportion of pilgrims are affected by symptoms of either an influenza-like illness or an acute respiratory illness with the proportion affected reaching between 40-77% in some studies (12, 15, 16). Results for studies with laboratory confirmed infection are variable, some indicating that influenza prevalence is low (8, 9, 10) while others suggest it is significantly higher (14, 15). The Hajj is however a unique event with almost three million people converging on a relatively small geographic area for over five days. Crowd density is very high and over-crowding in the living accommodation is common. Given the unique nature of this event the applicability of these findings to other mass gatherings is therefore limited.

The new evidence therefore supports the assertion that a mass gathering event of the nature seen at the annual Hajj exposes individuals to transmission of respiratory viruses and illness, however there is limited evidence to determine whether respiratory viral prevalence is increased when compared to background rates or unexposed groups. The new evidence also highlights that H1N1 pdm09 infection levels were very low, and in the context of the 2009 pandemic, fears regarding enhanced transmission and the Hajj acting as a seeding event for pandemic influenza were not realised.

In a small number of outbreak studies involving influenza-like illness and confirmed influenza at large music festivals, there is varying evidence about the extent to which influenza transmission occurs. Outbreaks were based on laboratory diagnosis, and transmission was confirmed in all, though they had varying infection rates ranging from roughly 3 to 25 per 100,000. Two recent studies undertaken during the 2009 influenza pandemic suggest that at the beginning of a pandemic these gatherings may act as seeding events (25) but later in the pandemic may have no appreciable impact. (26). The evidence from event surveillance reports such as international athletic events, World Cups and the Winter Olympiad suggest that influenza outbreaks can occur but these seem restricted to the actual competitors and staff rather than the crowds attending. Together, all of these reports point to the influenza outbreak and transmission potential, albeit variable, of large, multiple-day, open-air events. Only one new study, event surveillance report documented influenza-like-illness rates at a major sporting event and did not find evidence of increased incidence.

Therefore, there is no new outbreak or surveillance evidence to suggest influenza is associated with mass gatherings such as sporting events.

There is evidence in this review to suggest that Influenza outbreaks are associated with both civilian and military ships, in particular where outbreaks are out of season. A number of outbreak investigations on primarily large civilian cruise ships have occurred

in summertime in maritime locations in both Europe and around Australia (28-33). Observations for pandemic influenza spread and increased attack rates in comparison to seasonal influenza have also been identified on-board cruise ships (21). The new evidence (primarily outbreak reports) therefore identifies a new theme for ships associated with increased influenza transmission and outbreaks.

In summary, there is some evidence, including new evidence to indicate that mass gatherings may be associated with an increased risk of influenza transmission.

## ***II. Does the type of mass gathering influence the association with influenza transmission?***

The type of mass gathering event seems to be of considerable importance in terms of the risk of influenza transmission (Table 5) and this argument is strengthened by the updated findings. Most of the evidence supporting the role of mass gatherings in the transmission of influenza comes from events where there are crowds with high crowd densities (which may be theoretically estimated at >5 people per square metre), and also where the participants are likely to live close together for prolonged periods, e.g. the Hajj pilgrimage (8-20) and large musical festivals (24-26). In these events, crowded accommodation is also likely to be relatively basic, such as communal camp style living. It seems apparent that events where close contact among participants extends beyond event venues and into accommodation areas are most associated with influenza. Event size per se does not seem to be a critical factor.

There were a number of new observational studies to suggest the Hajj is associated with respiratory viral transmission, although the evidence regarding influenza specific transmission is less certain. Ideally, comparisons to background rates in the community or unexposed groups would provide a more concrete answer. For pandemic influenza (H1N1 pdm09 specific), Hajj type events do not seem to be associated with increased pandemic influenza transmission. The quality of studies also dramatically varied so care must be taken when interpreting this evidence. No new evidence to support the hypothesis that music festivals are associated with influenza transmission were identified.

In contrast, there is no convincing evidence that major organised sporting events are associated with significantly increased influenza transmission in those attending the event (38-40). An important example of this contrast comes from Serbia, where two major events of different type and scale happened to coincide in 2009, providing a “natural experimental” opportunity for comparison (24). In the larger event, only four event-linked confirmed influenza cases occurred at the World University Games held over a 12-day period and involving almost 25,000 athletes and staff with about 500,000 spectators. However, in a relatively smaller event held in the same month and within the same country, as many as 47 event-linked confirmed cases occurred at a four day music festival with around 190,000 participants.

Furthermore, in surveillance reports from recent major international sports competitions, cases or small clusters of influenza were reported, but these were mainly in the event participants rather than in the overall population of people exposed to the events (38, 39). This was true even for one major event that took place within a pandemic context (39). These events showed no clear evidence of influenza transmission, indicating that influenza may not be a significant cause for concern at modern world sports events. This view is supported by surveillance reports from the 1998 and 2006 World Cups in France and Germany (40, 41), where influenza-like-illness remained below the epidemic

threshold level or instances of transmission were not reported, meaning that they were either not detected or very low.

The single new surveillance report (41) strengthens the view that these types of events are not associated with influenza transmission.

This situation may in part be explained by the brief transitory nature of contact in the crowds in highly organized international sports festivals such as the Olympics and the World Cup, which are usually seated events with good spacing in-between seats and mostly in open-air settings with dilution of any infectious droplets that may be generated. The apparently low or absent influenza transmission at such events may also reflect the contemporary fact that many people who attend major sports championships tend to have planned their visit a long time ahead, as ticket sales usually start months or even years in advance. Spectators as well as participants tend to stay in more conventional accommodation such as hotels rather than tents or other forms of portable or camp-style quarters with highly crowded conditions. It is also important to note that contemporary major events are now deploying increasingly developed systems for infectious disease surveillance and control (54), which are crucial for early detection and containment where possible.

The London 2012 Olympic Games is a recent example of how increasingly sophisticated such surveillance systems can be. Infectious diseases, including respiratory illnesses, were closely monitored by the HPA and expedited testing arrangements were in place for conditions such as influenza. It is reassuring to note that no outbreaks of influenza were detected at any locations during the Games, providing further evidence to suggest this type of event is not associated with influenza outbreaks. A summary of the surveillance activities of the HPA during the Games has been published, and the surveillance reports (as yet unpublished in peer-reviewed journals) are available on the HPA website (53).

The other situation of note relates to indoor events such as large conferences, typified by the international medical conference held over seven days in Iran during the early stages of the 1968/69 pandemic (27). During this meeting it is estimated that about a third of the participants developed an influenza-like illness with an overall attack rate of 36%; the pandemic virus was isolated from those cases where testing had been undertaken. This potentially highlights the role that ventilation may play in the reduction of influenza transmission and is another factor worthy of consideration.

Maritime settings provide a unique situation where many people are often in relatively close contact for one to two weeks – for military ships this can be much longer. A combination of factors may facilitate the spread of influenza in passenger cruises, including the presence of proportionately more ‘at risk’ groups (older people and children), the mixing of people from different locations (both southern and northern hemispheres), the types of close-quarter living conditions and sustained/intensive contact rates. The historical outbreak investigation on board a military transport vessel in 1918 highlighted the significance of crowded accommodation on-board a ship, with poorly ventilated living quarters increasing the mortality of the 1918 pandemic strain (37).

The new evidence has identified a new type of mass gathering setting that may be associated with influenza transmission and outbreaks; the civilian cruise ship. Military vessels may also be associated with influenza transmission; however there are fewer examples of studies supporting this view. On the basis of this evidence, it should be

argued that the mass gathering definition should be expanded to include both civilian and military cruise ships if the on-board population exceeds 1000 persons.

In summary, the type of mass gathering event may exacerbate influenza transmission, key factors being the degree of crowdedness, the event duration and possibly, whether the event is in or outdoors. Multiple-day events with crowded communal accommodation and civilian or military cruise ships may be the mass gatherings most associated with influenza. The new evidence strengthens the statement that certain types of mass gatherings influence the risk of influenza transmission

**Table 5. Evidence of event characteristics that might influence an association with influenza transmission**

| Numbers of participants | Duration | Type of event                          | Evidence of association with influenza?                                     | Venue conditions    |                   | Accommodation conditions | Comment   |
|-------------------------|----------|--|---|---------------------|-------------------|--------------------------|---|
|                         |          |  |   | In or outdoor       | Crowded?          |                          |   |
| 1,000 or more           | Hours    | Football matches                       | Yes – World cup (40, 41)  | Outdoor             | Possibly crowded  | Presumed no crowding     | NO cases detected.  |
|                         |          | Theatre, entertainment                 | No – however closure associated with reduction in flu transmission (34, 35) | Indoor              | Possibly crowded  | Presumed no crowding     | Associated with influenza despite no crowding.  |
|                         | Days     | Congress                               | Yes – outbreak report (27)  | Indoor              | Not crowded       | Presumed no crowding     | Indoor venues may be a risk factor  |
|                         | Weeks    | Ships (cruise and military)            | Yes- outbreak reports (28-33 ) and observational study ( 21)                | Indoor              | Possibly crowded  | Presumed no crowding     | Cruise ships likely associated with out of season and pandemic Influenza outbreaks                        |
| 100,000 or more         | Days     | Music festivals                        | Yes – outbreak reports (24-26)  | Mostly out          | Crowded           | Very crowded             | Crowded venues PLUS crowded accommodations<br><br>Associated with influenza regardless of venue situation |
|                         |          | Social / religious festival            | Yes - outbreak report (23)  | Mostly out          | Crowded           | Very crowded             |   |
| 500,000 or more*        | Weeks    | Hajj pilgrimage                        | Yes – observational and quasi-experimental studies (7-20)                   | Both in and outdoor | Extremely crowded | Very crowded             |   |
|                         |          | Major international sports tournaments | No / limited – event surveillance reports (24, 38-40)                       | Mostly out          | Not crowded       | Presumed little crowding | Uncrowded outdoor venues seem ideal   |

\* This category also includes multi-location major events such as the Olympics, even if no specific numbers of participants are given in the reports

### **III. *Can influenza transmission be reduced by restriction of mass gatherings?***

To address whether mass gathering restriction can reduce influenza transmission, the mainly relevant papers found were archival studies of the 1918-1919 influenza pandemic (34-36) and an analysis of the 2003 SARS outbreak (22). No relevant randomised controlled trials were found, reflecting the practical difficulties that such studies would involve.

Mass gatherings of varying dimensions were restricted at a large number of US cities during the 1918-1919 period. The reports again highlighted the difficulty of interpreting what was meant by a mass gathering e.g. including schools, cinemas, theatres and other public places. In general, evidence suggests that these measures had a beneficial effect, especially where implemented early in the course of the outbreak (34, 35). However, these benefits were not universal across all the cities (36).

Restrictions were typically implemented as part of a set of interventions, e.g. combining quarantine and isolation policies with banning mass gatherings. As a result, it is extremely difficult to tease out the individual effects of mass gatherings restrictions alone. Using multivariate techniques, investigators attempted to isolate the differential effects of individual restriction measures, and found indications that certain interventions (such as closures of entertainment venues) had measurable specific impact, (20, 21) but this evidence is limited. Equally, outbreak reports from maritime settings have tentatively suggested that control measures implemented during a cruise may impact on the attack rates (28, 33), although there have been no formal investigations to identify whether on-board measures are truly associated with reducing the impact on an outbreak. There is no further evidence to confidently support the statement that a restriction on mass gathering events can reduce the transmission of influenza.

An analysis of the 2003 SARS outbreak in China attempted to probe the impact of mass gatherings restrictions that were applied in a contemporary setting (22). However, as with the historical studies, it was not possible to distinguish the specific effects of mass gatherings restrictions from amongst the broad range of other public health interventions that were applied.

In summary, there is some evidence that when applied early and in tandem with other public health measures such as isolation and quarantine and closures of educational institutions, mass gatherings restrictions may help in reducing transmission. In a pandemic like that experienced during 2009 it is unlikely that the measures described above could be justified, however, in a much more severe pandemic, the cost – benefit equation could easily shift the other way. The application of bans on mass gatherings and other related public health measures are therefore highly dependent on an early indication of the severity as measured by its impact on individuals and society.

#### **Practical implications of the review's findings**

There are two further, critical, domains of uncertainty that need to be considered in the development of evidence-based guidance and policies regarding mass gatherings. The first domain relates to issues around the current understanding about how influenza is spread, and factors that can affect transmissibility (e.g. host factors, pathogen factors, environmental factors and particle size) (5). Key questions remain in these areas, which may be important in making specific recommendations regarding particular types and scope of mass gathering restrictions.



The second domain impinging on the potential effectiveness of any public policy on mass gatherings includes the whole range of factors affecting adherence and compliance. For instance, the experience of the 2009 influenza pandemic has raised significant questions around how willing people might be to comply with bans imposed on mass gatherings restrictions (55-58). Other challenging issues include the problematic ethical and legal frameworks for implementing restrictions for public health purposes (59, 60), as well as considerable logistical and economic implications. If long-planned events were to be cancelled, who would be liable for the huge personal, corporate and national costs that such cancellations might incur? In considering policy recommendations therefore, within a pandemic context, the most practical approach for all but the more severe pandemics may be a strategy of encouraging voluntary restrictions. This would involve giving the public the best available information, and advising rather than legislating that organisations and individuals avoid non-essential events where there is at least some evidence of transmission risk. Practical implications of potential mass gathering restriction policies need careful assessment and should be an area of focus for policy-makers. Opportunities to link to other operational research assessing implications should be sought.

The new evidence does not alter the message that, in all but the most severe pandemics, compulsory restrictions offer little advantage given the delicate economic and political balance associated with mass gathering restrictions, and the continued limited evidence to suggest mass gathering events are widely associated with influenza transmission. More credence should be given to examining specific types of mass gathering events; indoor events (regardless of crowding- usually multi-day) and outdoor (with crowding and multiday events) as there appear to be specific settings associated with respiratory viral or influenza transmission. A relative paucity in evidence from other settings, including outbreak reports related to [planes, schools, universities and prisons \(with a population exceeding 1000 persons\)](#) may also reflect publication bias issues. Identifying other potential settings may also form an important part of future work.

There are other important issues to note. Although this update has focused on mass gatherings, limiting transmission of influenza clearly requires a multifaceted approach. Some studies in this review reflected such an approach; for example, in the historical outbreak investigations where restrictions on mass gatherings were combined with other non-pharmaceutical measures (22, 34, 35). It would be prudent to apply the best evidence relating to other social distancing interventions in conjunction with any specific policies on mass gatherings.

Although new evidence was identified it had limitations similar to those observed with the studies in the original DH report, particularly in relation to the lack of an unexposed group in many of the observational studies. There is therefore still a need for well-designed studies to more accurately quantify the extent of influenza transmission at mass gatherings, confirm the key parameters that influence the transmission of influenza in these settings, and to directly assess the impact of mass gathering restrictions. In the UK, mass gathering events ranging from indoor events in theatres and cinemas, to outdoor events such as football matches and major musical events like the Glastonbury festival, represent potential opportunities for carefully designed research. British people travelling abroad for mass gatherings such as the Hajj or other large events could be approached for inclusion in prospective studies for comparison with appropriately

matched non-travelling controls, with care being taken to avoid drawbacks observed in existing studies.

### **Strengths and weaknesses of the review**

As previously noted, this review has examined an intervention area in which there are a limited number of relevant studies and there is no common understanding of what constitutes a mass gathering. While a range of study designs were reviewed, there was not a single randomised controlled trial that was suitable for inclusion. This is of course not surprising, given the formidable logistical, cost and ethical hurdles that make large-scale experimental epidemiological studies of the restriction of mass gatherings impractical and probably impossible. Some of the included studies had significant design and quality issues as duly reflected in the individual paper summaries and the discussion, and highlighted in Tables 2 and 3.

The application of quantitative techniques could enhance the simple narrative approach that was adopted for the analysis. However, it is still apparent that there are insufficient studies presenting quantitative data on this subject. It is acknowledged that the inclusion of modelling studies may offer an additional dimension in order to build a fuller picture.

Within the boundaries of the inclusion criteria, this review was able to capture most of the relevant studies identified by other systematic reviews undertaken in recent years on the subject of non-pharmaceutical interventions to limit transmission of respiratory viral infections and/or specifically influenza. These reviews all considered a range of interventions (61-64) and all recognised the paucity of primary evidence regarding restriction of mass gatherings (and other “social distancing” measures). In addition to identifying the more recently published evidence, this update included maritime settings, however it is acknowledged that here are likely to be other specific “specialised” settings that may arguably be regarded as mass gatherings.

## Conclusion

In conclusion there is limited data indicating that mass gatherings are associated with influenza transmission and this theme is continued with the inclusion of new evidence for the update. Certain unique events such as the Hajj, specialised settings including civilian and military ships- a new theme for this update, indoor venues and crowded outdoor venues provide the primary evidence base to suggest mass gatherings can be associated with Influenza outbreaks. Some evidence suggests that restricting mass gatherings together with other social distancing measures may help to reduce transmission. However, the evidence is still not strong enough to warrant advocating legislated restrictions. Therefore, in a pandemic situation a cautious policy of voluntary avoidance of mass gatherings would be still the most prudent message. Operational considerations including practical implications of policy directed at restricting mass gathering events should be carefully considered.

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## Appendix 1 Search terms for PubMed database search

The following terms were combined to conduct a global search on PubMed on 07 December 2012.

| Search              | Query   | Items found            |
|---------------------|---|------------------------|
| <a href="#">#38</a> | Search <b>(#17) AND #37</b>   | <a href="#">989</a>    |
| <a href="#">#37</a> | Search <b>((((((((#18) OR #19) OR #20) OR #21) OR #22) OR #23) OR #24) OR #25) OR #26) OR #27) OR #28) OR #29) OR #30) OR #31) OR #32) OR #33) OR #34) OR #35) OR #36</b> | <a href="#">45537</a>  |
| <a href="#">#36</a> | Search <b>ship*</b>   | <a href="#">18574</a>  |
| <a href="#">#35</a> | Search <b>cruise*</b>   | <a href="#">1366</a>   |
| <a href="#">#34</a> | Search <b>"world cup"</b>   | <a href="#">290</a>    |
| <a href="#">#33</a> | Search <b>games</b>   | <a href="#">8111</a>   |
| <a href="#">#32</a> | Search <b>(festival*) OR festival</b>   | <a href="#">3810</a>   |
| <a href="#">#31</a> | Search <b>(championship*) OR championship</b>   | <a href="#">779</a>    |
| <a href="#">#30</a> | Search <b>haji</b>  | <a href="#">402</a>    |
| <a href="#">#29</a> | Search <b>olympics</b>  | <a href="#">600</a>    |
| <a href="#">#28</a> | Search <b>"big event"</b>   | <a href="#">7</a>      |
| <a href="#">#27</a> | Search <b>"mass event"</b>  | <a href="#">10</a>     |
| <a href="#">#26</a> | Search <b>"large event"</b>   | <a href="#">23</a>     |
| <a href="#">#25</a> | Search <b>(crowd) OR crowd*</b>   | <a href="#">11502</a>  |
| <a href="#">#24</a> | Search <b>"large crowd"</b>   | <a href="#">4</a>      |
| <a href="#">#23</a> | Search <b>"public event"</b>  | <a href="#">36</a>     |
| <a href="#">#22</a> | Search <b>"social event"</b>  | <a href="#">85</a>     |
| <a href="#">#21</a> | Search <b>"social gathering"</b>  | <a href="#">27</a>     |
| <a href="#">#20</a> | Search <b>distancing</b>  | <a href="#">715</a>    |
| <a href="#">#19</a> | Search <b>"public gathering"</b>  | <a href="#">14</a>     |
| <a href="#">#18</a> | Search <b>"mass gathering"</b>  | <a href="#">131</a>    |
| <a href="#">#17</a> | Search <b>((((((((#1) OR #2) OR #3) OR #4) OR #5) OR #6) OR #7) OR #8) OR #9) OR #10) OR #11) OR #12) OR #13) OR #14) OR #15) OR #16</b>                                  | <a href="#">364707</a> |
| <a href="#">#16</a> | Search <b>"respiratory syncytial virus"</b>   | <a href="#">9064</a>   |
| <a href="#">#15</a> | Search <b>((("parainfluenza") OR "parainfluenza*") OR "parainfluenza virus") OR "parainfluenza virus*"</b>  | <a href="#">6287</a>   |
| <a href="#">#14</a> | Search <b>"ILI"</b>   | <a href="#">865</a>    |
| <a href="#">#13</a> | Search <b>"flu like"</b>  | <a href="#">1961</a>   |
| <a href="#">#12</a> | Search <b>flu-like</b>  | <a href="#">1961</a>   |
| <a href="#">#11</a> | Search <b>(tuberculosis) OR tuberculosis*</b>   | <a href="#">200549</a> |
| <a href="#">#10</a> | Search <b>"acute respiratory tract infection"</b>   | <a href="#">307</a>    |
| <a href="#">#9</a>  | Search <b>"acute respiratory infection"</b>   | <a href="#">894</a>    |
| <a href="#">#8</a>  | Search <b>sars</b>  | <a href="#">6490</a>   |
| <a href="#">#7</a>  | Search <b>"severe acute respiratory syndrome"</b>   | <a href="#">5231</a>   |

| Search             | Query                                | Items found           |
|--------------------|--------------------------------------|-----------------------|
| <a href="#">#6</a> | Search (coronavirus) OR coronavirus* | <a href="#">9759</a>  |
| <a href="#">#5</a> | Search (adenovirus) OR adenovirus*   | <a href="#">44177</a> |
| <a href="#">#4</a> | Search (rhinovirus) OR rhinovirus*   | <a href="#">3877</a>  |
| <a href="#">#3</a> | Search "common cold"                 | <a href="#">4559</a>  |
| <a href="#">#2</a> | Search flu                           | <a href="#">43356</a> |
| <a href="#">#1</a> | Search Influenza*                    | <a href="#">89083</a> |

## Full global search generated on PubMed including MeSH terms

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## Appendix 2 Search terms for additional databases

### Search terms:

For SCOPUS the following search strategy was adopted: flu OR influenza OR influenza\* OR "respiratory infection" OR flu-like OR "respiratory viruses" AND "mass gathering" OR crowd OR "major event" OR "large crowd" OR "large event" OR "big event" OR "mass event" OR cruise\* OR "naval ship"

For EMBASE and CINAHL the following search strategy was adopted: flu OR influenza OR influenza\* OR "respiratory infection" OR flu-like OR "respiratory viruses") AND ("mass gathering" OR crowd OR "major event" OR "large crowd" OR "large event" OR "big event" OR "mass event" OR cruise\*)

### Details of findings:

**SCOPUS:** generated 71 articles. 2 excluded as had been found on PubMed. The remaining 69 were added to the list of titles considered for review.

**Excerpta Medica Database (EMBASE):** Generated 35 results. 24 were excluded as had been found on PubMed. The remaining 11 were added to list of titles considered for review.

**The Cumulative Index to Nursing and Allied Health Literature (CINAHL):** generated eight results. Five were excluded as had been found on PubMed, and one was also excluded as had been found on EMBASE. Three were included for review.

## Appendix 3 Data extraction elements

### Study identity

Title

Author(s)

Full reference (journal / year / page)

### Study characteristics

What type of study

Time period of study

Setting

Disease(s) studied

Population

- Participants
- Eligibility criteria for the study
- size and characteristics of groups (if any)

Intervention

- Restriction of mass gatherings?
- Other intervention(s)?

Outcome

- Did study report specific outcomes and what were they?

### Other relevant details

### Assessment on eligibility for inclusion

- Is study suitable for inclusion in the review?
- If study excluded, why?

## Appendix 4 Papers read in full but excluded from the final review

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