

Journal of Epidemiology and Global Health

ISSN (Online): 2210-6014

ISSN (Print): 2210-6006

Journal Home Page: <https://www.atlantis-press.com/journals/jegh>

Could influenza transmission be reduced by restricting mass gatherings? Towards an evidence-based policy framework

David A. Ishola, Nick Phin

To cite this article: David A. Ishola, Nick Phin (2011) Could influenza transmission be reduced by restricting mass gatherings? Towards an evidence-based policy framework, Journal of Epidemiology and Global Health 1:1, 33–60, DOI:

<https://doi.org/10.1016/j.jegh.2011.06.004>

To link to this article: <https://doi.org/10.1016/j.jegh.2011.06.004>

Published online: 13 April 2019



ELSEVIER



<http://www.elsevier.com/locate/jegh>

REVIEW

Could influenza transmission be reduced by restricting mass gatherings? Towards an evidence-based policy framework

David A. Ishola ^{a,b}, Nick Phin ^{a,c,*}

^a *Pandemic Influenza and Legionnaires' Disease Section, Health Protection Services, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ, United Kingdom*

^b *Centre for Infectious Disease Epidemiology, Department of Infection and Population Health, University College London, Royal Free Campus, Rowland Hill Street, London NW3 2PF, United Kingdom*

^c *Faculty of Health and Social Care, University of Chester, Riverside Campus, Castle Drive, Chester CH1 1SL, United Kingdom*

Received 28 March 2011; received in revised form 20 June 2011; accepted 20 June 2011

Available online 17 August 2011

KEYWORDS

Influenza;
Mass gathering;
Transmission;
Evidence;
Policy

Abstract *Introduction:* Mass gatherings (MG) may provide ideal conditions for influenza transmission. The evidence for an association between MG and influenza transmission is reviewed to assess whether restricting MG may reduce transmission.

Methods: Major databases were searched (Pubmed, EMBASE, Scopus, CINAHL), producing 1706 articles that were sifted by title, abstract, and full-text. A narrative approach was adopted for data synthesis.

Results: Twenty-four papers met the inclusion criteria, covering MG of varying sizes and settings, and including 9 observational studies, 10 outbreak reports, 4 event reports, and a quasi-experimental study. There is some evidence that certain types of MG may be associated with increased risk of influenza transmission. MG may also "seed" new strains into an area, and may instigate community transmission in a pandemic. Restricting MGs, in combination with other social distancing interventions, may help reduce transmission, but it was not possible to identify conclusive evidence on the individual effect of MG restriction alone. Evidence suggests that event duration and crowdedness may be the key factors that determine the risk of influenza transmission, and possibly the type of venue (indoor/outdoor).

Conclusion: These factors potentially represent a basis for a policy-making framework for MG restrictions in the event of a severe pandemic.

© 2011 Ministry of Health, Saudi Arabia. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author at: Pandemic Influenza and Legionnaires' Disease Section, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ, United Kingdom. Tel.: +44 2083276661; fax: +44 2082007868.

E-mail addresses: david.ishola@hpa.org.uk (D.A. Ishola), nick.phin@hpa.org.uk (N. Phin).

Contents

1. Introduction	34
2. Methods	35
2.1. Inclusion criteria	35
2.2. Search strategy	35
2.3. Other sources	36
2.4. Study selection and data extraction	37
2.5. Temporal and situational context of the review	37
2.6. Quality assessment	37
2.7. Data synthesis	38
3. Results	38
3.1. Quasi-experimental study	38
3.2. Observational studies	38
3.3. Outbreak reports	47
3.4. Historical outbreak analyses	53
3.5. Event surveillance reports	53
3.6. Systematic review	53
4. Discussion	53
4.1. What is a mass gathering?	55
4.2. What does the evidence say about mass gatherings and the risk of influenza transmission?	55
4.2.1. Are mass gatherings associated with influenza transmission?	55
4.2.2. Does the type of mass gathering influence the association with influenza transmission?	56
4.2.3. Can influenza transmission be reduced by restriction of mass gatherings?	56
4.3. Practical implications of the findings of the review	57
4.4. The need for further evidence.	58
4.5. Strengths and weaknesses of the review	58
5. Conclusion	59
6. Conflict of interest statement	59
Acknowledgements	59
References	59

1. Introduction

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 are still unclear, but is believed to involve multiple routes, including respiratory droplets and direct/indirect contact [1] with secretions or fomites. Aerosol transmission may also occur, but controversy surrounds this [2] and some further evidence of aerosol transmission has recently been put forward [3]. This is an important issue as 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.

Whilst there is not a “standard” definition of what constitutes a mass gathering, there is an understanding that these are events that involve large numbers of people (suggested minimum of 1000 people) [4–6] 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.

Therefore for those infectious diseases such as influenza, where close contact is the main determinant of transmission, it appears self-evident that mass gathering events could lead to the rapid transmission of a new causative agent.

In the event of an influenza pandemic, minimizing transmission of influenza has been a priority for public health action. A variety of non-pharmaceutical public health interventions to reduce close contact between infected and susceptible individuals,

or the opportunities for the virus to be picked up by susceptible people such as self-isolation of patients, respiratory etiquette and hand washing have been advocated. 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 gatherings could have on society.

There have been other systematic reviews undertaken in recent years on the broader subject of non-pharmaceutical interventions aimed at reducing transmission of respiratory viral infections [7,8]. These reviews considered a range of such interventions, and they explicitly recognized that there is a paucity of primary evidence regarding restriction of mass gatherings (and other “social distancing” measures); thus they did not primarily focus on this specific area.

The aim of this review, therefore, was to attempt to reduce this evidence gap by assessing the available evidence base relating to the utility of restrictions on mass gatherings 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 findings of the review may be able to help inform policy statements on the effectiveness of mass gathering restriction interventions that may be deployed to help reduce influenza virus spread during a pandemic.

2. Methods

The study protocol was largely based on the University of York’s Centre for Reviews and Dissemination guidance for undertaking reviews in healthcare [9]. Work commenced in mid-July 2010 and the main part of it was completed in mid-October 2010. Further work was carried out in June 2011 to bring the literature coverage up to date.

The following specific questions were developed to capture the objectives of the review:

- 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)?

2.1. Inclusion criteria

The following types of studies were included in the review:

- Randomized controlled trial
- Quasi-experimental study
 - Non-randomized 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 [9], but with the addition of outbreak and surveillance reports, not traditionally included in such lists, important to the topic of this review. To cover the other “non-standard” study design encountered, the term “quasi-experimental” is employed to describe controlled but non-randomized studies [10,11].

Only studies published in English were included. Relevant systematic and narrative reviews and operational description papers were utilized for useful background information. The reference lists of the systematic reviews were scanned to identify potentially relevant primary studies that could be considered for inclusion. Case reports, mathematical modelling and human/non-human experimental laboratory studies were excluded from the review.

Outcome measures included laboratory-confirmed influenza infection (i.e., documented by virus isolation, molecular testing such as polymerase chain reaction, and serological studies) and clinical influenza-like illness as defined by the investigators, whilst recognizing that this is less specific.

2.2. 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 for which guidance would be relevant. The transmission of other respiratory viruses was also included because of the similarity of transmission and therefore the potential applicability of any results to influenza.

An initial “scoping” search was followed by further discussions and consultation on the work plan and search strategy. 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, festivals, Olympics, Hajj, championship, and others listed in Table 1. Transit settings such as long-distance flights and cruise ships were not included, as it was decided that these settings would fit better in a separate review of evidence for influenza transmission through transport. The final search with revised terms and refined using the “advanced search” tool on PubMed was carried out as described in Table 1, with no time period

restrictions. The initial searches included the literature up till July 2010. A further search was conducted on 31 May 2011 to bring the literature coverage up to date as part of an editorial process.

In addition, secondary searches were also initially carried out in the following databases: Scopus, Excerpta Medica Database (EMBASE), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). These are described in Table 2.

2.3. 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; the authors’

Table 1 Details of PubMed database search.

#41	Search #22) AND #40)
#40	Search #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) OR #37) OR #38) OR #39)
#39	Search “world cup”
#38	Search games
#37	Search festival
#36	Search championships
#35	Search Hajj
#34	Search olympics
#33	Search “big event”
#32	Search “mass event”
#31	Search “large event”
#30	Search crowd
#29	Search “large crowd”
#28	Search “public event”
#27	Search “social event”
#26	Search “social gathering”
#25	Search distancing
#24	Search “public gathering”
#23	Search “mass gathering”
#22	Search #1) OR #2) OR #4) OR #5) OR #7) OR #8) OR #11) OR #12) OR #14) OR #15) OR #16) OR #17) OR #18) OR #19) OR #20) OR #21)
#21	Search “respiratory syncytial virus”
#20	Search “parainfluenza virus”
#19	Search “ILI”
#18	Search “flu like”
#17	Search flu-like
#16	Search tuberculosis
#15	Search “acute respiratory tract infection”
#14	Search “acute respiratory infection*”
#12	Search sars
#11	Search “severe acute respiratory syndrome”
#8	Search coronavirus*
#7	Search adenovirus*
#5	Search rhinovirus*
#4	Search “common cold”
#2	Search flu
#1	Search influenza*

Table 2 Searches of additional databases.

Database	Outcome
SCOPUS	16 Hits; 2 excluded as had been found on PubMed. The remaining 14 were added to the list of titles considered for review
Excerpta medica database (EMBASE)	27 Hits; 24 were excluded as had been found on PubMed. The remaining 3 were added to the list of titles considered for review
The cumulative index to nursing and allied health literature (CINAHL)	6 Hits; 5 were excluded as had been found on PubMed, The last one was also excluded as had been found on EMBASE

Search terms: flu or influenza or “respiratory infection” or flu-like or “respiratory viruses” AND “mass gatherings” or crowd or “major event” or “large crowd” or “large event” or “big event” or “mass event.”

hardcopy literature files were hand-searched to identify additional published articles or other documents of relevance.

2.4. Study selection and data extraction

Study selection was conducted in stages. At all stages, scanning and reviews were done independently by the authors, who then harmonized their selections. Papers identified by the searches were scanned and some excluded on the basis of the ‘title’ for relevance to the review. The abstracts of the remaining papers were then reviewed to identify studies that appeared to meet the inclusion criteria. The full text versions of all these articles were then sought and read in full. For papers that had relevant titles but no abstracts, the full text articles were also obtained, scanned for relevance, and if relevant they were read in full. 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.

Data from the selected full text papers were extracted using a pre-designed form. Data elements included publication information, study characteristics, participant characteristics, the intervention (if any) and setting, outcome and results. The data extracted were used to determine the eligibility of each paper for inclusion in the review. This process resulted in a final selection of eligible articles that were then included in the review.

2.5. Temporal and situational context of the review

The main body of this work was undertaken in 2010 by the UK Health Protection Agency as part of a

comprehensive influenza scientific evidence review informing the UK National Pandemic Influenza Strategy. Within this context, the work was carried out within a very tight three-month timeframe and with significantly limited resources. As a result, some of the most comprehensive steps required of a full systematic review could not be realistically accommodated. Therefore, a modified process was adopted in conducting this “rapid evidence assessment” rather than a full, formal systematic review. Rapid evidence assessments are well recognized as a pragmatic approach to include all the major elements of a full systematic review, ensuring an outcome that is as comprehensive as possible while accepting limited compromises in order to meet stipulated deadlines for feeding into the policy process [9].

Due to the time constraints, it was not practical to pursue time-intensive contacts with authors or to seek translations for non-English articles, which were therefore excluded. Articles lacking abstracts were largely excluded, and there was a limited search for unpublished studies. However, to try to mitigate these limitations, full draft versions of the review were submitted to national experts at the UK Health Protection Agency and the Scientific Pandemic Influenza committee of the UK Department of Health, seeking their comments and advice on any papers or documents that may have been omitted. Some further work was carried out in May to June 2011 to update the literature.

2.6. 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 [12]. However, after completion of the literature search, it was clear that the types of studies and the study design types

identified were not suitable for assessment by the CASP tools. Similarly for the outbreak reports included in the review, no suitable existing framework could be readily identified for quality assessment. The ORION tool was not strictly applicable as it is specific to outbreaks of nosocomial infection [13,14]. Therefore, a modified approach was adopted, whereby each paper was categorized as having low risk, some risk, or high risk for bias with respect to the relevant review question addressed by that study. The grading was assessed based on the presence of significant methodological limitations. A high risk of bias was attributed to papers with at least three significant methodological issues as identified by the review authors, while papers with at least two issues were classified as having some risk. This approach was adapted from a system previously used by Jefferson et al. [7].

The quality of the review itself was tested against checklists based on the MOOSE [15] and PRISMA [16,17] standards. Within the restrictions of the time constraints already described, key gaps and issues identified by the checklists were addressed as appropriate and/or acknowledged in Sections 2.5 (explaining the review context including time constraints) and 4.4 (recognizing the study limitations).

2.7. 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 [9]. In addition, the synthesis considered the implications for policy and guidance development as well as future research.

3. Results

The search identified a total of 1706 papers after accounting for overlaps between the different databases. These were reviewed on the basis of 'title' for relevance to the review (Fig. 1), and on this basis 1593 papers were excluded. Abstracts for the remaining 113 papers were reviewed and a further 54 were eliminated.

Full copies of the remaining 59 papers plus 6 papers identified from scanning the reference lists of review papers, and 3 papers retrieved from the authors' hardcopy files, were reviewed and summarized. Table 3 provides a classification of the 68 papers that were read in full text.

After full text review, 24 papers were classified as meeting the inclusion criteria. These included a

quasi-experimental study (a non-randomized trial) [18], nine observational studies [19–27], seven outbreak reports [28–34], three historical outbreak archive analyses [35–37], and four event surveillance reports [38–41]. Details for each of these studies are summarized in Table 4. The 44 papers that were read but not included in the review are listed in Table 5.

3.1. Quasi-experimental study

One quasi-experimental study by Qureshi et al. [18] 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 usually involving 2 to 3 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 rates of influenza-like illness reported in vaccinated pilgrims were 36% compared with 62% in non-vaccinated pilgrims. However, these results were based on clinical endpoints without microbiologic confirmation; a non-randomized design was used, and the study was not designed to address the primary question of this review.

3.2. Observational studies

Nine observational studies estimated the risk of acute respiratory illness and/or influenza-like illness associated with the Hajj pilgrimage by attempting to measure its occurrence in pilgrims. Four [23–25,27] of these studies confirmed the cause of illness by laboratory testing, while the other five relied on specified symptom complexes as surrogate indicators.

Among the nine observational studies were four cross-sectional studies. Balkhy and colleagues [24] tested 500 Hajj pilgrims in 2003 who presented with symptoms of upper respiratory tract infection in the second week of the event; 30 (6%) of the 500 pilgrims tested positive for influenza. Rashid et al. [23] assessed the burden of laboratory-confirmed influenza and respiratory syncytial virus (RSV) infections in symptomatic British Hajj pilgrims in the 2005 event. Of 202 symptomatic pilgrims who underwent nasal swab testing, 28 (about 14%) had confirmed influenza (mostly A type), while only 9 (4%) had RSV infection. In the 2006 Hajj, the same investigators [27] found comparable levels of laboratory confirmed influenza (10–11%) in both UK and

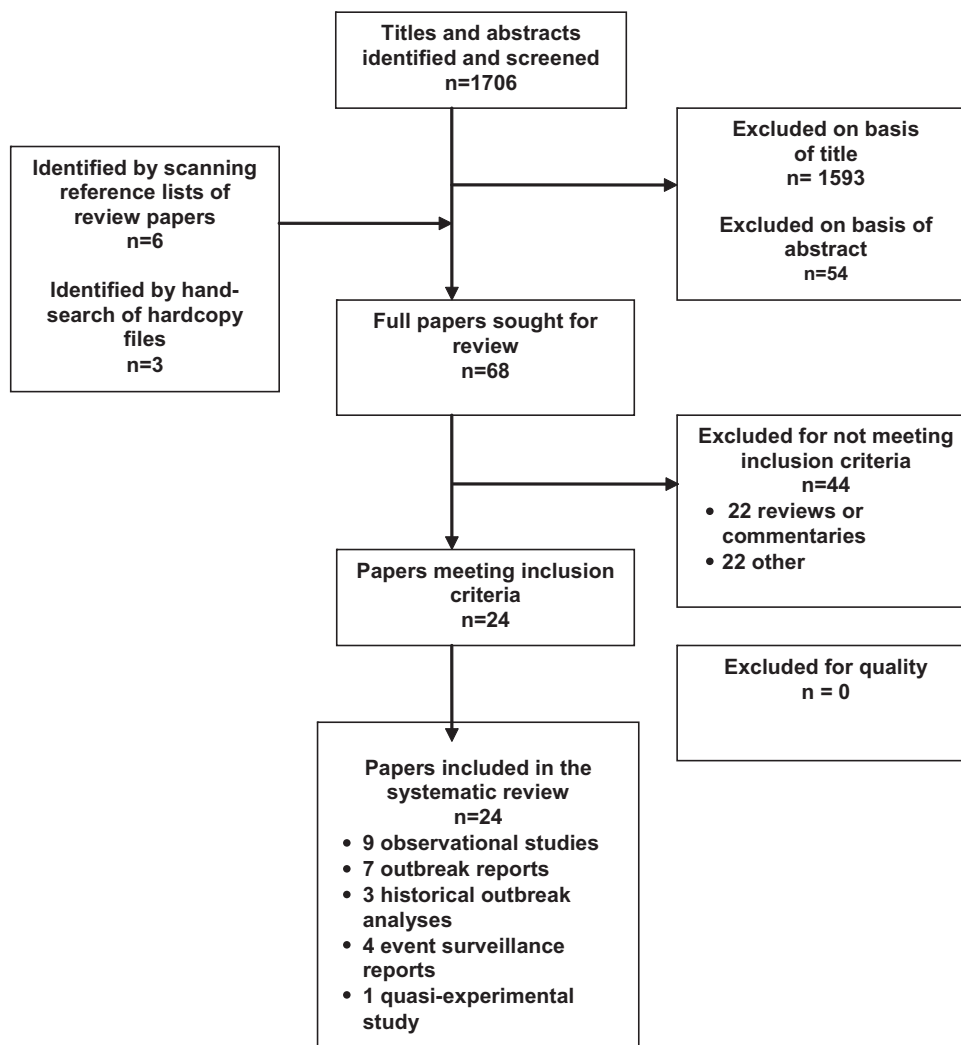


Figure 1 Diagram of search strategy results and article selection.

Table 3 Classification of 68 papers read in full, by type of paper.

Type	Total number of papers	Number included in the review
Quasi-experimental study (non-randomized trial)	2	1
Observational study	13	9
Outbreak report	8	7
Historical outbreak archival data study	7	3
Event surveillance report	7	4
Systematic review	3	0
Narrative review	6	0
Editorial/commentary/statement/opinion	13	0
Background/operational/supplemental information	9	0
Total	68	24

Saudi pilgrims. These relatively low levels of infection contrasted with the findings in the cross-sectional study by Deris et al. [20] who based their assessment on syndromic influenza-like illness rather than laboratory-confirmed infection. They found an influenza-like illness prevalence of 40%

in Malaysian pilgrims who had just completed the Hajj.

The other five observational studies were similarly designed, involving groups of intending Hajj pilgrims who were recruited in their home regions or countries prior to the event, and then re-assessed

Table 4 Synopsis of studies included in the final review.

Investigator (Reference number)	Study design and participants	Reported results	Comments
<i>(A) Quasi-experimental study</i>			
Qureshi et al. [18]	Controlled, non-randomized, 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). 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% Vaccine efficacy 38% Vaccine preventable ILI incidence of 22/100 control participants	Limitations include: - The non-randomized design. - Underpowered as recruitment fell slightly short of estimated sample size. - Difficult presentation style; lack of flow-chart to clearly show the progression of participants through the trial process
<i>(B) Observational studies</i>			
Deris et al. [20]	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 center 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: - Small study – uncertain how representative of the Malaysian pilgrims. - Participant recruitment site was not ideal. - Influenza diagnosis was subjective. - There was no unexposed suitable control group for prevalence comparison. - It is unclear whether the study attempted to measure point prevalence of ILI at the time of study, or ILI incidence during the Hajj period
Rashid et al. [27]	A cross-sectional comparison of viral respiratory infections between UK and Saudi pilgrims at Hajj 2006. Pilgrims with symptoms of URTI were recruited from a dedicated UK pilgrims’ walk-in clinic service at the event; and a Saudi clinic which mainly served Saudi pilgrims but was open to everyone A total of 260 pilgrims were recruited, having presented with URTI several days after the start of Hajj (infection presumed acquired during the event). They completed questionnaires, and provided nasal swabs for testing by both on-site rapid diagnostic screening (to guide antiviral therapy) and later analysis by real-time RT-PCR	UK pilgrims: $n = 150$. 38 (25%) had at least one virus; 17 (11%) had influenza. Saudi pilgrims: $n = 110$. 14 (13%) had at least 1 virus; 11 (10%) had influenza. There were similar influenza proportions between the two, despite differences in vaccination rates. A risk-group analysis was done to compare those “at-risk” for influenza with those who were not	Laboratory confirmation was a strength of the study Limitations include: - The sample size was rather small for comparing the two populations, especially as the Saudi Hajj population was apparently much larger than the UK delegation. - Lack of non-exposed (non-Hajj) control groups

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
Balkhy et al. [24]	A cross-sectional study of pilgrims from different parts of the world attending the Hajj 2003 event. Participants were pilgrims or event workers presenting at dedicated walk-in clinics with URTI on days 10, 11 and 12 of the Hajj (making it likely that infection was acquired during the event). 500 URTI patients who completed questionnaires and had throat swabs were included. 52.8% were males and most participants were in the 20–40 year age group. Swab samples were subjected to viral studies to detect a range of respiratory viruses (inoculation into designated cell lines, followed by immunofluorescence studies)	54 (10.8%) of the 500 URTI patients tested positive for at least one virus, and a number had multiple infections. Influenza was the most common virus, found in 30 individuals (representing 6% of the total 500 URTI patients). By simple extrapolation of these findings to the total event population of approximately 2 million, it was estimated that at least 400,000 pilgrims would develop URTI, of which 24,000 would have influenza	A notable strength of the study was that influenza infection was confirmed by viral studies Limitations include: - No data on the local prevailing influenza activity. - Selection by convenience sampling rather than a discernible strategy; probably not representative of the event population. It is difficult to extrapolate based on these data, - Any extrapolation to the whole event population should require complex modelling to account for a variety of factors
Rashid et al. [23]	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; and (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. Nine 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 Limitations include: - Sampling was restricted to only a small proportion of pilgrims; may not be representative of the 25,000 British Hajj pilgrims for that year. - Lack of a suitable (non-Hajj attending) control group to compare influenza occurrence
Choudhry et al. [19]	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 two 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: - Lack of control group to compare ARI in people not exposed to Hajj event. - Lack of information on the background influenza or ILI activity in Saudi Arabia at the time

(continued on next page)

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
Gautret et al. [26]	An observational study of French pilgrims in the 2009 Hajj. The study primarily focused on the influence of preventive measures on the occurrence of influenza in these pilgrims 405 intending French pilgrims were recruited from pre-Hajj mandatory meningococcal vaccination clinics; 247 people who completed a post-Hajj telephone questionnaire were included in the study. The mean age was 58 years and the male:female ratio was 1:1. The use of a range of preventive measures was recorded	22 participants (8% of 247) had ILI, defined as a triad of cough, sore throat and fever. Cough was the most common respiratory symptom found (48.5% of participants) The use of preventive measures including vaccination and face masks did not significantly reduce symptoms	Limitations include: - Dependence on clinical outcomes rather than laboratory confirmation of influenza. - No information on the 131 people (33% of initial recruitment)
El Bashir et al. [25]	Influenza serological study of a cohort of UK pilgrims attending the 2003 Hajj. Participants were recruited among worshippers at a single mosque in East London who intended to attend the Hajj. Venous blood samples and questionnaires were completed before and within 2–3 weeks after the Hajj; 115 participants were enrolled Haemagglutination inhibition tests were used for laboratory assessment, with influenza diagnosis based on seroconversion defined as at least fourfold antibody titre rise	44 (38%) of the pilgrims developed influenza (based on seroconversion). A total of 93 (81%) had symptoms of respiratory infection. Vaccination did not seem to be significantly protective	A small but useful study that was strengthened by laboratory testing for influenza Limitations include: - The analysis would have been strengthened by having a non-exposed (non-Hajj) control group. - Recruitment from a single London mosque means that the sample is unlikely to be representative of UK pilgrims
Gautret et al. [22]	Prospective cohort study of French pilgrims attending 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 hypercholesterol; 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: - Lack of control group to compare ARI in people not exposed to Hajj event. - Lack of information on the background influenza or ILI activity. - Actual Hajj dates not given, reducing the utility of the provided "epidemic curve" of fever and cough
Gautret, et al. [21]	Prospective cohort study of travel-associated health problems in French pilgrims attending 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	Limitations: - A fairly small number of subjects. - All recruited from a single clinic. - Lack of a control group to compare ARI in people not exposed to Hajj event

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
<i>(C) Outbreak reports</i>			
Pang et al. [32]	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. [33]	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 1968, but had not been found in Teheran prior to this congress. 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	304 of 844 respondents fulfilled criteria for influenza, with a final attack rate of 36%. Illness was mostly mild; more marked and prolonged in those aged >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	This was a well-reported outbreak. Surprisingly, serological test results were not reported even though samples were said to have been taken. Also, information on the numbers of cases in contacts of participants was not provided
Gutierrez et al. [30]	Influenza outbreak report at the “Rock Werchter” musical festival in Belgium, July 2–5, 2009, during the 2009 A(H1N1) pandemic. The event involved 113,000 participants	30 event-linked ILI cases, with 12 confirmed A(H1N1). 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	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

(continued on next page)

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
Loncarevic et al. [31]	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 influenza had been noted. The events were: (i) The 25th Universiade – World University Games, July 1–12, involving 8600 athletes, 15,000 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 visitors to an open-air, multi-stage festival. There was an enhanced daily surveillance system for both events	(i) Universiade: 7 confirmed cases (4 believed linked to the Games). (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 it ended, but not confirmed due to a change in testing policy. There were no complications or deaths	Cases may have been under-reported due to asymptomatic cases or non-presenters
Botelho-Nevers et al. [29]	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 A(H1N1) pandemic, thus a dedicated flu medical tent was set up and the local hospital placed on stand-by	14 people were hospitalized (3.6/100,000); 8 were confirmed PCR positive for A(H1N1) (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% A(H1N1) positivity Surveillance through EuroTravNet revealed no other cases in participants returning to other European nations The unusual case was a 23-year-old French male participant who had dual infection with A(H1N1) and varicella zoster virus. He was hospitalized in France and had a good outcome	ILI rates were lower at the festival than the national and continental rates; however the A(H1N1) positivity was much higher than the European population rate; together possibly suggesting that many mild cases may not have presented in clinic
Zepeda-Lopez et al. [34]	An analysis of the 2009 A(H1N1) outbreak in Mexico. The paper described the clinical features seen in a series of confirmed cases Different epidemiological resources were used to map the spread of the virus throughout the country, including the Mexican SINAVE surveillance system and official reports from the Mexican Secretariat of Health	202 of 751 suspected cases were confirmed infected with the novel 2009 pandemic A(H1N1) virus Two likely key contributory factors to influenza spread were noted: (i) high population density, and (ii) a mass gathering involving over 2 million people, held in Iztapalapa, Mexico City at an early stage of the outbreak	An innovative study using various sources of information to determine the temporal-spatial dynamics of influenza transmission

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
Blyth et al. [28]	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	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	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 the outbreak is unknown. Also, as the event was held near the onset of the usual Australian influenza season, the post-event increase in flu activity may have occurred regardless
<i>(D) Historical outbreak studies</i>			
Markel et al. [37]	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, analysing the public health responses of American cities to the pandemic; 43 American 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 U.S. Census Bureau, official public health reports, media archives, and municipal records	Three main categories of non-pharmaceutical interventions (NPI) were applied: (a) school closures; (b) isolation and quarantine; and (c) public gathering bans (which 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 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	The major strength of the study was to link archived data with modern techniques to produce research that is useful at this time The limitations are similar to those of Hatchett et al. [36] below

(continued on next page)

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
Hatchett et al. [36]	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 American cities to the pandemic; 17 American 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	19 Categories of NPIs were identified. The measures of epidemic outcome included the peak death rate, and a "normalized" peak that was standardized to facilitate inter-city comparison. Among the findings were that: - Aggressive early NPI was associated with lower peak excess mortality. - Early implementation of school, church, and theatre closures were individually associated with lower normalized peak excess weekly deaths	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 difficult to simulate as a contemporary intervention study. Limitations include: - The difficulties and drawbacks of historical record retrieval. - Heterogeneous definitions of "public gatherings". - Doubts regarding applicability of the findings to current practice as society has changed dramatically since that time
Aimone [35]	A historical examination of the response of New York City (NYC) authorities to the 1918 pandemic influenza	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 U.S. cities	
<i>(E) Event surveillance reports</i>			
Gundlapalli et al. [38]	Prospective influenza surveillance report from the Winter Olympiad, February and March 2002. Components of the surveillance program 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-organized systematic prospective influenza surveillance program, described by the authors as the first of its type at a large Games event. Limitations include: - No indication of total numbers of people at the event or in the city - No indication of the background ILI activity in the city or country; or whether this was during the local winter influenza season

Table 4 (continued)

Investigator (Reference number)	Study design and participants	Reported results	Comments
Demicheli et al. [41]	Prospective influenza surveillance report from the Winter Olympics in Torino, Italy, February and March 2006. Components of the surveillance program included: statutory notification of infectious diseases, laboratory-based surveillance of invasive diseases, sentinel surveillance of influenza-like illness, syndromic surveillance, and toxic exposure surveillance	GP-based daily reporting of ILI showed that there was no increased ILI activity throughout the period. In fact, ILI activity was less than for the corresponding period of the previous year	Well-organized systematic prospective influenza surveillance program The report was quite brief and rather short on details
Lim et al. [39]	Influenza surveillance report during the disease containment phase of the 2009 A(H1N1) pandemic. More than 600 confirmed cases had occurred in Singapore prior to the Games Asian Youth Games in Singapore, June 29 to July 7, 2009 (football preliminaries started on June 20). The Games involved 9 sports at 10 venues; 1210 athletes; and 810 officials all from 43 different countries	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 A(H1N1) transmission associated with the Games	This was a detailed operational description and surveillance report The authors stated that no transmission took place during the Games; but it is unclear how the 6 confirmed cases were infected – possibly imported cases?
Schenkel et al. [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; and (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 infections

Abbreviations used: 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.

after the pilgrimage. Even though three reports were described by their respective authors as “prospective cohort” studies [19,21,22], none of these five studies included an “unexposed” (non-Hajj attending) control group for comparison, indicating that they should be more accurately regarded as “before and after” studies. Choudhry et al. [19] assessed Saudi residents (attending the Hajj from a different part of the country) and found an incidence of influenza-like illness of about 40%. Three studies of French pilgrims by Gautret et al. [21,22,26] found rates of cough of between 48% and 61%; while in El-Bashir and colleagues’ serological study of UK pilgrims [25], respiratory symptoms occurred in more than 80%, but the seroconversion rate was 38% of 115 participants.

These variable data underline the difficulties of comparing different studies that employ contrasting measures of influenza. Interpretation needs to take account of the fact that studies using clinical outcomes suggest much higher levels of influenza-like conditions than the ones that involve laboratory confirmation. Even among the laboratory-based studies, differences in laboratory techniques may also be significant.

3.3. Outbreak reports

There were four types of outbreaks in the reports that were reviewed. The first of those was a paper by Pang et al. [32] that described the experience of dealing with the SARS (severe acute respiratory

Table 5 Excluded papers. This is a summary list of the 44 articles that were excluded after full text review as they did not meet the inclusion criteria.

Paper citation <i>Editorials, expert statements, and similar papers</i>	Brief notes
Anonymous. Hajj and 2009 pandemic influenza A H1N1. <i>Lancet</i> 2009;374:1724	Editorial
Anonymous. Human infection with new influenza A (H1N1) virus: WHO Consultation on suspension of classes and restriction of mass gatherings to mitigate the impact of epidemics caused by influenza A (H1N1), May 2009. <i>Wkly Epidemiol Rec</i> 2009;84(27):269–71	WHO technical consultation report
Dixon B. Mass gathering: mass effect? <i>Lancet Infect Dis</i> 2010;10:662	Expert opinion/reflection
Ebrahim SH, Memish ZA, Uyeki TM, Khoja TA, Marano N, McNabb SJ. Public health. Pandemic H1N1 and the 2009 Hajj. <i>Science</i> . 2009;13;326(5955):938–40. Epub 2009 Oct 29	Expert opinion/policy paper
Ferguson N, Nicoll A, Schwartz B. SIP 5: Social distancing during a pandemic. Not sexy, but sometimes effective: social distancing and non-pharmaceutical interventions. <i>Vaccine</i> 2009;23;27(45):6383–6	Discussion paper on social distancing
Franco-Paredes C, Carrasco P, Preciado JI. The first influenza pandemic in the new millennium: lessons learned hitherto for current control efforts and overall pandemic preparedness. <i>J Immune Based Ther Vaccines</i> 2009;7:2	Expert commentary
Gatrad AR, Shafi S, Memish ZA, Sheikh A. Hajj and the risk of influenza. <i>BMJ</i> 2006;333:1182–3	Expert opinion
Gautret P, Parola P, Brouqui P. Risk factors for H1N1 influenza complications in 2009 Hajj pilgrims. <i>Lancet</i> 2010;375:199–200	Letter and opinion
Haworth E, Rashid H, Booy R. Prevention of pandemic influenza after mass gatherings – learning from Hajj. <i>J R Soc Med</i> 2010;103(3):79–80	Editorial
Memish ZA, Ebrahim SH, Ahmed QA, Deming M, Assiri A (letter). Pandemic H1N1 influenza at the 2009 Hajj: understanding the unexpectedly low H1N1 burden. <i>J R Soc Med</i> 2010;103:386	Expert commentary
Rashid H, Haworth E, Shafi S, Memish ZA, Booy R. Pandemic influenza: mass gatherings and mass infection. <i>Lancet Infect Dis</i> . 2008;8(9):526–7. Epub 2008 Aug 4	Expert opinion/reflection
Tomes N. “Destroyer and teacher”: Managing the masses during the 1918–1919 influenza pandemic. <i>Public Health Rep</i> 2010;125 (Suppl. 3):48–62	Discussion paper on the 1918–1919 influenza pandemic
WHO. Health conditions for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj). <i>Wkly Epidemiol Rec</i> 2010;22;85(43):425–8	WHO travel recommendations
<i>Narrative reviews</i>	
Ahmed QA, Arabi YM, Memish ZA. Health risks at the Hajj. <i>Lancet</i> 2006;367(9515):1008–15	Narrative review paper
Michael JA, Barbera JA. Mass gathering medical care: a twenty-five year review. <i>Prehosp Disaster Med</i> 1997;12(4):305–12	Narrative review paper
Milsten AM, Maguire BJ, Bissell RA, Seaman KG. Mass-gathering medical care: a review of the literature. <i>Prehosp Disaster Med</i> 2002;17(3):151–62	Narrative review paper
Oshitani H. Potential benefits and limitations of various strategies to mitigate the impact of an influenza pandemic. <i>J Infect Chemother</i> 2006;12(4):167–71	Narrative review paper
World Health Organisation Writing Group. Non-pharmaceutical interventions for pandemic influenza, national and community measures. <i>Emerging Infectious Diseases</i> 2006;12:88–94	WHO recommendations on non-pharmaceutical interventions

Table 5 (continued)

Paper citation <i>Editorials, expert statements, and similar papers</i>	Brief notes
Zieliński A. Evidence for excessive incidence of infectious diseases at mass gatherings with special reference to sporting events. <i>Przegl Epidemiol</i> 2009;63(3):343–51	Narrative review paper
<i>Systematic reviews</i>	
Aledort JE, Lurie N, Wasserman J, Bozzette SA. Non-pharmaceutical public health interventions for pandemic influenza: an evaluation of the evidence base. <i>BMC Public Health</i> 2007;15(7):208	Systematic review and expert panel
Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. <i>BMJ</i> 2009;21(339):b3675. doi:10.1136/bmj.b3675	Systematic review
Jefferson T, Del Mar C, Dooley L, Ferroni E, Al-Ansary LA, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. <i>Cochrane Database Syst Rev</i> . 2010;2(1):CD006207	Systematic review (Cochrane)
<i>Observational studies</i>	
Al-Asmary S, Al-Shehri AS, Abou-Zeid A, Abdel-Fattah M, Hifnawy T, El-Said T. Acute respiratory tract infections among Hajj medical mission personnel, Saudi Arabia. <i>Int J Infect Dis</i> 2007;11(3):268–72. Epub 2006 Aug 14	Observational study of the occupational risk of influenza in healthcare facility workers at the Hajj mass gathering
Baum NM, Jacobson PD, Goold SD. “Listen to the people”: public deliberation about social distancing measures in a pandemic. <i>Am J Bioeth</i> 2009;9(11):4–14	Cross-sectional study from Michigan – focus group discussions on attitudes towards social distancing
Broderick MP, Hansen CJ, Russell KL. Exploration of the effectiveness of social distancing on respiratory pathogen transmission implicates environmental contributions. <i>J Infect Dis</i> 2008 Nov 15;198(10):1420–6	Non-randomized controlled social distancing intervention study in a community setting; not applicable to a mass gathering situation
Deris ZZ, Hasan H, Ab. Wahab MS, Sulaiman SA, Naing NN, Othman NH. The association between pre-morbid conditions and respiratory tract manifestations amongst Malaysian Hajj pilgrims. <i>Trop Biomed</i> 2010;27:294–300	This paper presents further data analysis from an observational study that is already included in this review [20]
Eastwood K, Durrheim DN, Butler M. Responses to pandemic (H1N1) 2009, Australia. <i>A. Emerg Infect Dis</i> 2010;16(8):1211–6	A follow-up cross-sectional survey on willingness to comply with potential health interventions during a pandemic
Hutton A, Roderick A, Munt R. Lessons learned at World Youth Day: collecting data and using postcards at mass gatherings. <i>Prehosp Disaster Med</i> 2010;25(3):273–7	Cross-sectional methodological study on data collection at mass gatherings
Rubin GJ, Amlôt R, Page L, Wessely S. Public perceptions, anxiety, and behaviour change in relation to the swine flu outbreak: cross-sectional telephone survey. <i>BMJ</i> 2009;2(339):b2651. doi:10.1136/bmj.b2651	Cross-sectional study of swine flu-related public perceptions
<i>Outbreak report</i>	
Witkop CT, Duffy MR, Macias EA, Gibbons TF, Escobar JD, Burwell KN, et al. Novel Influenza A (H1N1) outbreak at the U.S. Air Force Academy: epidemiology and viral shedding duration. <i>Am J Prev Med</i> 2010;38(2):121–6. Epub 2009 Oct 21	Outbreak report from a training academy

(continued on next page)

Table 5 (continued)

Paper citation <i>Editorials, expert statements, and similar papers</i>	Brief notes
<i>Historical analyses</i>	
Caley P, Philp DJ, McCracken K. Quantifying social distancing arising from pandemic influenza. <i>J R Soc Interface</i> . 2008 Jun 6;5(23):631–9	Modeling-based historical outbreak analysis of social distancing during the 1918–1919 pandemic
McSweeney K, Colman A, Fancourt N, Parnell M, Stantiall S, Rice G, et al.. Was rurality protective in the 1918 influenza pandemic in New Zealand? <i>N Z Med J</i> . 2007 Jun 15;120(1256):U2579	Historical analysis of the effect of residential location on mortality during the 1918 influenza pandemic
Nishiura H, Chowell G. Household and community transmission of the Asian influenza A (H2N2) and influenza B viruses in 1957 and 1961. <i>Southeast Asian J Trop Med Public Health</i> 2007 Nov;38(6):1075–83	Historical outbreak analysis of community setting transmission during the 1957 pandemic and the 1961 epidemic
Wallinga J, van Boven M, Lipsitch M. Optimizing infectious disease interventions during an emerging epidemic. <i>Proc Natl Acad Sci USA</i> 2010;107(2):923–8. Epub 2009 Dec 28	Vaccine-focused historical study of interventions during the 1957–1958 influenza epidemic
<i>Event surveillance</i>	
Coletta M, Dewey L, White-Russell M, Powell T, Toney D, Cheek J, et al. Surveillance for early detection of disease outbreaks at an outdoor mass gathering – Virginia, 2005. <i>MMWR Weekly</i> 2006;55:71–74	Brief description and report of surveillance for a mass gathering event in Virginia. Insufficient information regarding the syndromic surveillance system used
Giorgi Rossi P, Sangalli M, Faustini A, Forestiere F, Perucci CA. Infectious diseases in Rome during the Millennium Year. <i>Euro Surveill</i> 2003;8(9):181–5	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
Gonçalves G, Castro L, Correia AM, Queirós L. Infectious diseases surveillance activities in the north of Portugal, during the EURO 2004 football tournament. <i>Euro Surveill</i> 200;10(4):86–9	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
<i>Other types of studies</i>	
Avery JG, Chitnis JG, Daly PJ, Pollock GT. Medical planning for a major event: the Pope's visit to Coventry Airport, 30 May 1982. <i>Br Med J (Clin Res Ed)</i> . 1982 Jul 3;285(6334):51–3	Operational medical response to a mass gathering event
Barr AC, Lau RC, Ng NW, da Silva MA, Baptista M, Oliveira VF, et al. What would you do? Managing a metro network during mass crowd events. <i>J Bus Contin Emer Plan</i> 2010;4(2):174–80	Operational paper on transport issues related to mass gatherings
Fizzell J, Armstrong PK. Blessings in disguise: public health emergency preparedness for World Youth Day 2008. <i>Med J Aust</i> 2008;189(11–12):633–6	Description of planning and response to a mass gathering event
López-Cervantes M, Venado A, Moreno A, Pacheco-Domínguez RL, Ortega-Pierres G. On the spread of the novel influenza A (H1N1) virus in Mexico. <i>J Infect Dev Ctries</i> 2009;3(5):327–30	Background information on the 2009 A(H1N1) outbreak in Mexico

Table 5 (continued)	Brief notes
<p>Paper citation <i>Editorials, expert statements, and similar papers</i></p>	
<p>Markel H, Stern AM, Cetron MS, Theodore E. Woodward award: non-pharmaceutical interventions employed by major American cities during the 1918–1919 influenza pandemic. <i>Trans Am Clin Climatol Assoc</i> 2008;119:129–38; discussion 138–42</p>	<p>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 [37]</p>
<p>Memish ZA, McNabb SJ, Mahoney F, Alrabiah F, Marano N, Ahmed QA, et al. Jeddah Hajj Consultancy Group. Establishment of public health security in Saudi Arabia for the 2009 Hajj in response to pandemic influenza A H1N1. <i>Lancet</i> 2009;374(9703):1786–91. Epub 2009 Nov 14</p>	<p>Consultation and recommendations on public health planning and response for the Hajj 2009</p>
<p>Poggensee G, Gilsdorf A, Buda S, Eckmanns T, Claus H, Altmann D; RKI Working Group Pandemic Influenza, Krause G, Haas W. The first wave of pandemic influenza (H1N1) 2009 in Germany: from initiation to acceleration. <i>BMC Infect Dis</i> 2010;10:155</p>	<p>Epidemiological description – initial period of the 2009 H1N1 outbreak in Germany</p>
<p>van Hal SJ, Foo H, Blyth CC, McPhie K, Armstrong P, Sintchenko V, et al. Influenza outbreak during Sydney World Youth Day 2008: the utility of laboratory testing and case definitions on mass gathering outbreak containment. <i>PLoS One</i> 2009;3;4(9):e6620</p>	<p>An analysis of epidemic testing strategies</p>

syndrome) 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 gathering restrictions on controlling the outbreak as mass gatherings were 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 the three music festivals occurred during the 2009 influenza pandemic—two at the beginning and one later during the pandemic.

The report by Blyth et al. [28] described an outbreak of influenza at a large, 5-day religious event in Australia during July 2008 attended by over 400,000 participants from 170 countries. Over 100,000 of the pilgrims were accommodated in a variety of make-shift, overcrowded venues such as sports halls, community centers and schools. One hundred laboratory-confirmed cases of influenza were identified among 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. [31] described an outbreak of influenza at a 4-day music festival in Serbia during July 2009 involving over 190,000 participants, with

a number of them coming from other European countries. Many of the participants stayed at a large campsite where overcrowding was an issue. Sixty-two laboratory-confirmed cases of H1N1 (2009) were identified; some of which were 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 spreading. The authors also reported on a small outbreak of influenza at an international sporting event held in Serbia in July over a period of 12 days and attended by over 500,000 spectators. Seven confirmed cases of H1N1 (2009) 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. [30] described a 4-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 (2009) 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.

Table 6 Papers included in the review, assessed for risk of bias.

Study type	Author (reference number)	Risk of bias	Key assessment issues
Quasi-experimental	Qureshi [18]	High	Randomization, blinding and allocation concealment?
Observational studies: cross-sectional	Deris [20]	High	Relevant control groups?
	Rashid [23]	Some	Laboratory diagnosis?
	Balkhy [24]	Some	Appropriate follow-up?
	Rashid [27]	Some	Reliable recruitment format?
Observational studies: cohorts	Choudhry [19]	High	Unexposed control groups?
	Gautret [21]	High	Laboratory diagnosis?
	Gautret [22]	High	Appropriately classified study design?
	El Bashir [25]	Some	
	Gautret [26]	Some	
Outbreak reports	Blyth [28]	Low	Clarity of description of setting and context?
	Botelho-Nevers [29]	Low	
	Gutierrez [30]	Low	Use of laboratory diagnosis?
	Loncarevic [31]	Low	Overall data reliability?
	Pang [32]	Low	
	Saenz [33]	Low	
	Zepeda-Lopez [34]	Low	
Outbreak reports (historical studies)	Aimone [35]	Some	Reliability and multiplicity of data sources?
	Hatchett [36]	Some	In-depth methods description?
	Markel [37]	Some	Clear outcome measures? Appropriate analysis? Breadth of coverage? Applicability to contemporary setting?
Event surveillance reports	Demicheli [41]	Low	Prospectively planned surveillance?
	Gundlapalli [38]	Low	Specific focus on influenza/respiratory virus?
	Lim [39]	Low	
	Schenkel [40]	Low	Clear description of setting and context?

Botelho-Nevers et al. [29] depict an outbreak of influenza at a 7-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 (2009) 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 described by Saenz et al. [33] involved a large, international medical conference held in Iran during September 1968 at the early stages of the 1968/1969 pandemic. The 7-day conference was attended by over 1000 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%. The virus was isolated from throat and nasal washings; this was found to be

the pandemic A/Hong Kong/68 virus. There was evidence that close contacts of returning attendees 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.

Lastly, there was an innovative study examining the 2009 A(H1N1) outbreak in Mexico [34]. The authors described the details of 202 cases and then used a series of epidemiological tools to map the spread of the virus throughout the country. They identified two major contributory factors to the rapid spread of influenza: one was the very high population density in parts of Mexico City; the other was the massive religious festival involving more than 2 million people, which took place in the city's Iztapalapa neighbourhood at the very early stage of the outbreak, shortly before the new virus was identified. It is suggested by the authors that this temporal association between

the mass gathering event and the subsequent increase in numbers of cases may reflect participants returning to their own neighbourhoods across the city, and from there to other parts of the country.

3.4. 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 utilize historical data to try to draw out major lessons for current impact. This review included three historical analyses of the non-pharmaceutical responses to the 1918–1919 influenza pandemic.

Markel et al. [37] examined the variety of non-pharmaceutical interventions that were deployed in 43 American cities during the 1918–1919 influenza pandemic. The combination of school closures and concurrent public gathering bans was implemented in 34 (79%) of the 43 cities and was the commonest combination of measures deployed. Applied early in the pandemic, this combination was significantly associated with reductions in the weekly excess death rates. Hatchett et al. [36] undertook a similar analysis on a smaller number of American cities 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 U.S. public health response to the 1918 pandemic by Aimone [35] 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 program of health education. The reported outcome measures for New York City were comparable with those seen in other American cities, and New York City experienced one of the lowest excess death rates on the eastern seaboard of the United States.

3.5. Event surveillance reports

Surveillance reports from four major sporting events within the last decade were considered suit-

able for review [38–41]. The study by Gundlapalli et al. [38] reported the experience of influenza surveillance during the Winter Olympics 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 (ILI) 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, 8 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 2000 athletes and officials from 43 countries. Although numbers of spectators are not given, it is assumed that the crowds were large. At the start of the Games, Singapore had already reported 600 confirmed cases of H1N1 (2009). Six laboratory-confirmed cases of H1N1 (2009) were identified during the 8 days of the event—four on one football team. No information on the numbers of confirmed H1N1 (2009) in the population after the Games was available.

There was no increase in ILI activity during the Winter Olympics in Torino in 2006 [41]. The final study by Schenkel et al. [40] reported on the experience of syndromic surveillance during the FIFA World Cup in Germany during June/July 2006. At the 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.

3.6. Systematic review

As stated in Section 2.6, the approach to quality assessment of the reviewed papers was based on a pragmatic framework for categorizing studies into low- or high-risk for bias, depending on the presence or absence 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 (Table 6).

4. Discussion

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. In addition, the

Table 7 Evidence of event characteristics that might influence an association with influenza transmission.

Numbers of participants	Duration	Example of type of event	Evidence of association with influenza?	Venue conditions		Accommodation conditions	Comment
				Indoors or outdoor	Crowded?		
1000 or more	Hours	Football matches	No – World cup [40]	Outdoor	Probably not crowded	Presumed little or no crowding	Low risk: no cases detected – outdoor, uncrowded venues
		Theatre, entertainment	No – however, closures were associated with reduction in flu transmission [36,37]	Indoor	Probably crowded	Presumed no crowding	Some risk: associated with influenza despite equivocal crowding; indoor venues may be a risk factor
	Days	Congress	Yes – outbreak report [33]	Indoor	Not crowded	Presumed no crowding	
100,000 or more	Days	Music festivals	Yes – outbreak reports [29–31]	Mostly outdoor	Crowded	Crowded	High risk: crowded venues plus crowded accommodations
		Social/religious festival	Yes – outbreak report [28,34]	Mostly outdoor	Crowded	Crowded	
500,000 or more ^a	Weeks	Hajii pilgrimage	Yes – observational and quasiexperimental studies [18–27]	Both indoor and outdoor	Crowded	Crowded	
		Major international multi-event tournaments	No/localized – event surveillance reports [31,38–41]	Mostly outdoor	Not crowded	Presumed little or no crowding	Low risk: outdoor, uncrowded venues seem ideal

^a Major multi-event gatherings like the Olympics were included in this category, even if no specific numbers of participants were given in the reports.

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.

This systematic search of the literature 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.

4.1. 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 organized events. In this setting, mass gatherings are considered to be organized events with more than 1000 people in attendance [4–6]. A recently published guidance document from the World Health Organisation (WHO) expanded the term to cover any organized or unplanned event involving enough people to “strain the planning and response resources of the (host) community, State or nation” [42].

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 1 month and involving between 2 and 3 million people), and a football match (involving several thousand spectators over a period of about 2 h).

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

4.2. 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:

4.2.1. 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-randomized 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 [18–22] 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 [43–46] that could be particularly important in a pandemic situation. 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 about 40% in some studies [19,20]. The Hajj is, however, a unique event with almost 3 million people converging on a relatively small geographic area for a period of at least 5 days, extending up to 4 weeks. Crowd density is very high and overcrowding in the living accommodation is common. Given the unusual nature of this event, the applicability of these findings to other mass gatherings is therefore limited. There is also a question regarding the fact that several of these studies are based on clinical criteria that could be due to other viral respiratory illnesses besides influenza.

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 pandemic suggest that at the beginning of a pandemic, these gatherings may act as seeding events [30]; indeed it has been suggested at the early stages of the 1999 pandemic A(H1N1), a huge Easter season mass gathering involving 2 million people may have helped in propelling the first wave of the outbreak throughout Mexico [34].

There is no compelling evidence from event surveillance reports, such as international athletic events, the World Cup and the Winter Olympics, to indicate that these major events significantly increase community transmission of influenza. Outbreaks did occur in some cases, but these always seemed restricted to the actual competitors and staff rather than the crowds attending or the wider community.

