



## PREDICTION OF INFLUENZA TRANSMISSION IN MASS GATHERING: A SYSTEMATIC REVIEW

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### Abstract

**Introduction:** The annual Hajj pilgrimage in Mecca, Saudi Arabia, uniquely attracts over 3 million participants from more than 180 countries, who gather for several days. Although Saudi authorities have effectively managed these vast numbers, the risk of epidemics poses a continuous challenge. An early warning system capable of forecasting epidemic outbreaks could significantly enhance preparedness and containment efforts. This review aims to assess the existing literature on influenza prediction models, focusing on their application to the Hajj pilgrimage setting.

**Methods:** We collected data on influenza's infectivity, the susceptibility and immunity levels among Hajj pilgrims from health authorities, and contact rates and patterns from previous surveys. Crowd modeling techniques were employed to simulate the pilgrims' movements in terms of time and location. A close contact was defined as any individual within a 2-meter radius of an infected person, with further categorizations based on the pilgrims' countries of origin and ages to reflect the impact on transmission patterns.

**Results:** The compilation of epidemiological parameters and crowd movement simulations offers a foundation for predicting the spread of the influenza virus among Hajj pilgrims. These models consider various factors, including contact rates and pilgrim demographics, to forecast potential outbreaks.

**Conclusion:** Effective prediction models for influenza transmission during the Hajj can guide and enhance preventive measures. By understanding the dynamics of pilgrim interactions and the disease's infectivity, health authorities can better prepare for and potentially mitigate the impact of epidemics.

**Keywords:** Mass Gatherings, Transmission Dynamics, Hajj Pilgrimage

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## Introduction

A mass gathering (MG) is typically characterized by the assembly of 1,000 or more individuals, though some definitions set the threshold at 25,000 participants to qualify as an MG [1]. The likelihood of respiratory infection transmission within such gatherings is influenced by several factors, including the crowd's density, duration of stay, susceptibility to infections, the infectivity of the disease, and the response capability of medical facilities [2]. The Hajj pilgrimage stands out among other mass gatherings due to its annual congregation of approximately 3 million pilgrims from over 180 countries, lasting several days in Mecca, Saudi Arabia [3]. Respiratory diseases have been identified as the culprits in 14 out of 21 events impacting MG attendees [4]. Notable recent respiratory outbreaks linked to MGs include a measles outbreak among German participants at a religious event in France [5], a mumps outbreak at a youth gathering in Australia, and another outbreak during a village celebration in Spain [6, 7]. Influenza outbreaks have also been reported during various MGs, such as the 2002 Winter Olympics [8], Youth Day in 2008 [9], and the Hajj pilgrimage in 2009 [10]. The dense and close proximity of individuals at MGs creates an ideal environment for the rapid spread of diseases. The nature of disease transmission is largely dependent on the contact networks among individuals, which can be studied through surveys or, more recently, with electronic devices [11, 12]. The combination of infectious and susceptible individuals in close quarters during events like pilgrimages can facilitate swift transmission of airborne and droplet-borne respiratory infections. Under favorable conditions, this rapid spread can escalate to epidemics or pandemics, such as the 2009 H1N1 influenza pandemic during the Hajj, which saw a high mortality rate among pilgrims [10]. Disease transmission modeling represents the spread of diseases through mathematical equations. There are two main approaches to mathematical modeling of disease transmission [13]. The first is the assumption of homogeneous mixing models, dating back to 1927 with the simple SIR model by Kermack and McKendrick, comprising susceptible (S), infected (I), and recovered (R) compartments and assuming a uniform mixing of the population [14]. The second approach is agent-based modeling (ABM), which assumes heterogeneous mixing and has gained popularity over the past two decades. ABM introduces variability in contact characteristics among hosts,

significantly affecting disease dynamics at the individual level by considering social contact networks, movement patterns, and demographic structures of the population [15]. Effective crowd management aims to gather people while maintaining spatial and temporal separation. Agent-based models incorporate essential aspects of crowd dynamics and epidemic parameters [16]. The primary aim of this review is to assess the literature on influenza prediction models.

## Methods

To obtain papers on the effectiveness of combination strategies, data for this review were identified by the authors through searches of the PubMed search engine for English language articles and articles translated into the English language. The authors used the following search terms to focus on modeling studies, and those which had a focus on pandemic preparedness and strategies -influenza and pandemic and (preparedness or strateg\* or model\*); influenza and modeling or modelling. The search included all published articles listed on PubMed from 1990 to September 2019 there were few articles on influenza pandemic planning or modeling before this period. Abstracts were reviewed where available to determine if a study met the inclusion criteria and the full manuscript was obtained for further scrutiny. Snowball searches by hand were performed on the reference lists of articles meeting the inclusion criteria to find additional studies. The inclusion criteria were primary mathematical modeling papers that compared and reported the quantitative effectiveness of that large combination strategies (two or more strategies used together) versus individual strategies for human pandemic influenza. Mathematical modeling papers were those which used quantitative predictive methods to determine the likely impact of strategies, and had descriptions of these methods which could be reproduced or verified. Mathematical modeling articles that described the effectiveness of multiple singular strategies but did not analyze the quantitative effect of combination strategies were excluded. Articles that referred to general pandemic preparedness without quantitative evidence, or provided only qualitative discussion were also excluded. Reviews without primary data, articles in abstracts without full publication, and unpublished studies were excluded as their methodology and results could not be verified. Results and discussion The search yielded a total of 920 papers including overlaps. Of

these, 72 used mathematical modeling techniques and on closer review, 60 were excluded based on the exclusion criteria listed in Methods. The remaining 12 studies were included for analysis, together with one additional study identified from the snowball searches. Recent studies have showed more accurate results of diseases modeling that uses ABM with contact network modeling [17, 18]. Other important parameters in epidemic modeling are the demographic characteristics of this crowd include age, sex, immunity, and country of origin [15, 19]. Another potential factor is the initial number of source cases and their contact pattern and points of entrance [20]. Studies have found the increase in epidemic size associated with increase in number of initial cases [2]. Agent-based models that incorporating detailed data on individual level have been used to model dissemination of rapidly transmitted infections such influenza [21-24]. The modeling of epidemic spread in MGs should not ignore the interaction with the local community where the event is scheduled, thus studies have highlighted the use of large-scale models with network of surrounded community [2]. These large scales models can incorporate the air-travelling data with many seasonal and immunization parameters to predicted the international transmission of emergent pandemics [25-27]. They predicted the influenza pandemic of 2009 depend on simulation results. Several modeling studies found that reduction of air-traffic could delay the progression of influenza pandemic [28, 29]. These large-scale ABM have become an important tool to understand the dynamics of epidemic transmission in a city, country and the globe. The health authorities in KSA recommended use of preventive measures of respiratory infection such as use of facemasks and influenza vaccine [30]. Despite the successful efforts of the authorities in Saudi Arabia in the management of this huge crowd of Hajj and Umrah pilgrims, the epidemic have been an emerging concern. The presence of early warning system that can predict the occurrence of epidemics will guide the preparedness plans and strengthen the ability to contain the problem. The modeling is a powerful tool for prediction of the epidemics dissemination among Hajj pilgrims, which can guide and improve the preventive interventions. The epidemic forecasting will provide early warning system for protection of pilgrims and population of Saudi Arabia from contiguous dangerous epidemics and pandemics. It can build an early warning system for an epidemic transmission among the Hajj pilgrims making health authorities proactive rather than

only responsive for any epidemic threats. In the last two decades, the modeling of infectious diseases has been developed rapidly, which is mainly attributed to the great improvement of the computation capacity associated with the recent advancement in the computer industry [31]. Agent based modeling especially requires high computational capacity, which sometimes needs Cyber-systems to run the simulation of these models [32]. Many studies have focused on the modeling of infectious diseases conducted in virtual environments based on empirical data that collected from surveys and censuses [33-36]. Del Valle et al. have conducted a simulation study supported by the data obtained from national surveys and censuses in the United States [33]. A wealth of data about contact patterns, population movement cycles, and social interactions were introduced into the simulation software called EpiSimS. This software can simulate the movement and social behavior of an individual interacting in the virtual environment. Activities for each individual were determined according to data collected by household surveys, and then locations were linked to each activity. For example, studying were assigned to the available schools and universities, shopping activity was assigned to the surrounded commercial centers and supermarkets. Similarly, creational activities were assigned to the available restaurants bars, and cinemas. The researchers concluded that contact patterns and social interactions had an essential role in the dissemination of infectious diseases. The infection usually occurs by the contact between infectious and susceptible populations. The recommended use of the empirical data to model the transmission of infectious diseases and it will result in predictions that are more accurate [33]. In another study conducted by Bansal et al., they compared the homogeneous mixing of the populations versus the heterogeneous mixing. In the heterogeneous mixing, they incorporated the contact patterns in the simulation process based on the concepts of social networking. They found similar results to that found by Del Valle et al. where the simulations based in the empirical data would result in predictions that are more realistic. They also found that homogenous mixing simulations are suitable only for homogenous populations, which interact in semi-random pattern [34]. In influenza H1N1 pandemic, that started in primary schools and then disseminate to the local community in 2009, the type of contact pattern showed a significant effect on the disease transmission. Cauchemez et al. found that an assertive mixing has affected the

influenza transmission, where males were more likely to infect other males than females. They found that school closure, that was applied later to control the epidemic, had no significant effect on the influenza transmission. This was attributed to the household and neighborhood spread of the infection through the playing activity of school children [35]. These findings reflected the importance of understanding the role of contact patterns in the dissemination of infectious diseases. In another simulation study that was conducted by a university student called Laura. She has asked a community members (e.g., moms with kids, kids at school, parents who work outside the home, the elderly) a series of questions: "what are your groups, how big are they, how often do you go to them and for how long, and how many people do you interact with there." According to these information, she built a model of a virtual community consists of 10,000 persons. She run the simulation of influenza transmission and then tested the effect of influenza vaccination in this transmission. She found that immunization of 80% of school-aged students had the same effect in diseases transmission as the immunization of the whole community [36]. The incorporating of any epidemiological parameter during model building was found important to improve the accuracy of the modeling process. Helen et al, have conducted a mathematical analysis, which demonstrated the unfavorable effect of not incorporating incubation period or population growth on the model accuracy [37]. Wallinga et al. have demonstrated the importance of incorporating age-related parameters in the modeling of infectious respiratory diseases [38]. In addition, Mossong et al. have built a model of more than 100,000 people based on the contact data collected from European populations. The findings showed that, during the first wave of the epidemic, the children aged 5-19 years old were the most affected age group by the circulating infection [19]. During MGs activities, the contact patterns differ from that in the household, schools or workplaces. Hu et al. found that random contact of people at MGs could, at MGs, increase the contact rate but it would decrease in the high-density MGs [39]. Similarly, Chowell et al. highlighted the importance of estimating the mixing pattern of individuals during MGs and the development of initiative models that can mimic the transmission dynamics of infectious diseases among the MGs population [2]. Although, the field of diseases modeling has developed rapidly in the last two decades, few studies have examined the modeling of

diseases transmitted among attendants of MGs. This study will build an ABM model based on empirical data obtained from the Hajj pilgrims that simulates the spread of influenza epidemic. Conclusions The utilization of predictive modeling technology to forecast influenza transmission among Hajj pilgrims proves highly effective. It aids in identifying crucial factors that influence the magnitude and velocity of an influenza epidemic. Prediction models can evaluate the efficacy of various preventive strategies to mitigate influenza spread among Hajj attendees. The outcomes of such modeling can serve as a foundation for evidence-based planning in preparedness and containment strategies against respiratory epidemics. Computer simulations emerge as a potent tool in directing optimal preventive measures and enhancing efforts towards the preparedness and control of influenza outbreaks. Conflict of interests The authors declared no conflict of interests. References 1. Michael, J.A. and J.A. Barbera, Mass gathering medical care: a twenty-five year review. *Prehospital and disaster medicine*, 1997. 12(4): p. 72-79. 2. Chowell, G., H. Nishiura, and C. Viboud, Modeling rapidly disseminating infectious disease during mass gatherings. *BMC medicine*, 2012. 10(1): p. 159. 3. Reference, M.C., Islamic Beliefs, Practices, and Cultures. 2010: Marshall Cavendish. 4. Abubakar, I., et al., Global perspectives for prevention of infectious diseases associated with mass gatherings. *The Lancet infectious diseases*, 2012. 12(1): p. 66-74. 5. Pfaff, G., et al., Spotlight on measles 2010: Measles outbreak among travellers returning from a mass gathering, Germany, September to October 2010. 2010. 6. Schmid, D., et al., Mumps outbreak in young adults following a festival in Austria, 2006. *Euro surveillance: bulletin European sur les maladies transmissibles= European communicable disease bulletin*, 2008. 13(7): p. 1854-1861. 7. Gerstel, L., A. Lenglet, and C.M. García, Mumps outbreak in young adults following a village festival in the Navarra region, Spain, August 2006. *Euro Surveill*, 2006. 11(11): p. E061109. 8. Gundlapalli, A.V., et al., Influenza, winter olympiad, 2002. *Emerging infectious diseases*, 2006. 12(1): p. 144. 9. Chowell, G., et al., Characterizing the epidemiology of the 2009 influenza A/H1N1 pandemic in Mexico. *PLoS Med*, 2011. 8(5): p. e1000436. 10. Memish, Z.A., et al., Pandemic H1N1 influenza at the 2009 Hajj: understanding the unexpectedly low H1N1 burden. *Journal of the Royal Society of Medicine*, 2010. 103(10): p. 386-386. 11. Cattuto, C., et al.,

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