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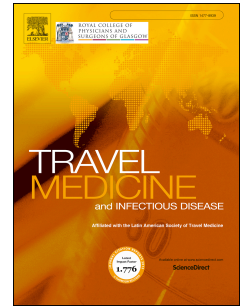
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COVID-19 –the role of Mass Gatherings

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Table: 1

Box:1

Figure: 1

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Mass gathering (MG) medicine emerged against the backdrop of the 2009 *pdm H1N1* Public Health Emergency of International Concern (PHEIC) when the Kingdom of Saudi Arabia (KSA) hosted the largest annual mass gathering of over 3 million pilgrims from 180 plus countries.(1) Recognizing the contribution of mass gatherings to the development of travel and International Health Regulations (IHR) guidelines on polio and meningitis and highlighting the potential bi-directional synergy between MG and emerging diseases (Box 1), a Lancet conference on the theme in 2010 formulated the scope of the newly named discipline.(2) The establishment of a WHO collaborating center on mass gatherings institutionalized the various ad-hoc research activities with expert recommendations on the utility and scope of MGs to inform emerging disease and transmission dynamics and response strategies. MGs may be planned such as the Hajj and Olympics or may occur spontaneously such as mass evacuation during a natural disaster (Table 1). The 2013 MERS outbreak originating in the middle east, notably KSA, that coincided with the 2012 Hajj, cemented the interest in mass gatherings.(3) However, MGs did not show a significant impact on the continued transmission of 2009 *pdm H1N1* or MERS-CoV nor did they lead to outbreaks among Hajj pilgrims. Thus, while scientific output on MGs have grown significantly, their impact on emerging diseases has not been fully acknowledged.

However, the events in the context of the latest threat to global health, the PHEIC COVID-19, may be sufficient to highlight the role of mass gatherings, mass migration, and other forms of dense gatherings of people in congested spaces such as cruise ships on the emergence, sustainability and transmission of novel pathogens (4). In early December 2019, the first pneumonia cases of unknown origin were identified in Wuhan, city with a population of 11 million. By the time the causative agent was recognized (now named SARS-CoV-2), and the

epidemiology was being studied, the spring festival in China, the largest mass migration of people in the world had already begun.(5) By February 2020, the now named SARS-COV-2 had reached all populated areas of China. Mathematical models had revealed that as early as January 23, 2020, most Chinese cities had already received considerable number of infected cases, even with domestic train travel: before travel bans were enforced. (6) Our knowledge of recorded history of pandemics is limited. No epidemic or pandemics have a predictable course, and all possible routes and methods of exponential spread should be anticipated.

Sporadic outbreaks of SARS-COV-2 occurred in multiple countries outside China since the beginning of the outbreak in Wuhan. But none reached the magnitude seen in Iran, now considered the second epicenter of COVID-19. (5) The Iran outbreak was unanticipated and global efforts were focused on containing the spread along the most common transport routes from China. Iran reports of COVID-19 first emerged on February 19, 2020 sending fear of a pandemic across the globe. The epidemic in Iran began in Qom, a city of 1.2 million residents, but one that attracts 20 million annual pilgrims from neighboring countries with Shiite Muslim populations mostly from the middle eastern region including Afghanistan, Iraq, Lebanon, Syria, Pakistan. The outbreak did not slow down as was seen in any of the countries earlier, and by the time national authorities were aware, the virus has taken foothold nationwide mostly spread via returning pilgrims and fellow travelers, and to neighboring countries, it was too late for containment efforts and mitigation would remain the only hope. As of March 1, case count in Iran was 593 cases and 43 deaths.

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Huge cruise ships scenario also fit the description of mass gatherings as the density of people occupying the limited space exceeds what is normally observed in other living areas in the land. Large cruise ships, including the Diamond Princess, that was quarantined in Japan due to COVID-19 outbreak, carry 2,000 to 4,000 persons, circumstances where social distancing is almost unachievable. Confining passengers inside the ship, a misjudged containment strategy, lead to 17% of the 3,700 passengers and crew being infected with SARS-CoV-2 virus. The cruise ship condition enabled a highly transmissible disease to sustain an outbreak. (3,7)

The significance of mass gatherings to disease transmission is directly linked to the efficiency of transmission expressed in epidemiologic terms as the basic reproduction number or R_0 . The most recent analysis of 425 cases at the epicenter of COVID-19 crisis in Wuhan indicate an R_0 of 2.2. This indirectly means that the number affected will double within the incubation period. Subsumed in the calculation of R_0 are both the incubation period of the illness and the viral shedding that enables excretion of the virus from the infected to non-infected. Such high rates of transmission are made possible by high titers of virus in the oropharynx early in the course of the disease at a time of minimal symptoms. (8). As with other other coronaviruses, asymptomatic infected persons may also transmit the infection. (9-10)

The first report of COVID-19 from Latin America coincided with the Carnival, the annual mass gathering that attracts millions of Brazilians but international visitors as well. The Carnival was held during the last week of February 2020 and the first reported case had its origins in Italy. It is premature to speculate if the the first case in Brazil had sufficient contact with persons who attended the carnival or other carriers of SARS-COV-2 were present in Brazil. (11-12)

The COVID-19 spread illustrates the role of MGs in exacerbation of the scope of pandemics. Anecdotal reports from the 1957 influenza pandemic suggested that influenza first emerged in Indochina and Malaysian pilgrims travelled with it to Mecca and transmitted to fellow pilgrims from the rest of the world. Respiratory diseases are the most common infections transmitted during MGs. (Figure 1) (13) During the early phase of MG medicine, the most extensively reported epidemiological data on infectious diseases at MG emerged from the Hajj. The congestion of people during the Hajj promotes increased carrier rates of *N meningitidis* and transmission of respiratory viruses. Over the past decade, a significant number of publications from different countries based on both syndromic surveillance and PCR-based investigation of respiratory pathogen carriage at the Hajj and other MG were made available. Invasive meningococcal disease has been a Hajj-related public health concern with its last outbreaks (serogroup W-135) in the 2000s. However, since the introduction of mandatory vaccination, no case of meningococcal disease has been reported in Mecca since 2006. In November 2004, a Sudanese child was diagnosed with polio one day after arrival in Saudi Arabia. This case coincided with the diagnosis of another 104 cases in Sudan. In response, the Saudi ministry of health now stipulates requires proof of vaccination to obtain visas for entry to Saudi Arabia and supplementary vaccination is offered to pilgrims originating from (WHO determined) polio risk and endemic countries.

Cancellation or suspension of MGs would be critical to pandemic mitigation. It is unlikely that medical countermeasures are available during the early phase of pandemics. Therefore, mitigation of its impact, rather than containment and control becomes a priority during pandemics. For the first time, the U.S. Department of Homeland Security in 2007 prepared the first concept of carefully administered, layered, nonpharmaceutical interventions as a reasonable

strategy for pandemic mitigation. However, as there were no pandemic related studies on interventions other than ecologic comparisons of events during the 1918 and 1957 influenzas outbreaks, these recommendations were mostly based on assumptions and projections. This concept was revised in 2017 to accommodate evidence from the 2009 pdm H1N1 response. The strategies include a combination of social distancing, reversal of societal functions such as home-schooling, teleworking, and cancellation of public events including religious services. Pandemic mitigation is unachievable if MGs are permitted.

COVID-19 PHEIC provides an opportunity to further expand the knowledge base on implementation of nonpharmaceutical interventions and to quantify their utility in pandemic mitigation. As the most systematically studied MG-related respiratory disease data come from KSA, the cancellation of Umrah by the KSA authorities, prior to emergence of cases, provide the best opportunity to develop mathematical models to quantify event cancellations related to mitigation of COVID-19 transmission in KSA and to the home countries of pilgrims.

Mathematical models in China showed that travel ban after the onset of outbreak only delayed dispersal of SARS-COV-2 from Wuhan to other cities by 2.91 days (Tian et al). Comparative studies of outbreak in Qom, Iran (ongoing outbreak) with that of Mecca and Medina (no outbreaks at the time of writing) would also be informative. Some heterogenous international MGs provide also opportunity to study demographically diverse populations with diverse underlying risk factors under the same ecological and weather conditions and in a shorter time frame than conducting studies in multiple countries. Viral multiplication and host adaptation occur at a faster rate during an MG. Outbreaks during MGs (as in Qom, Iran), provide a one-stop opportunity to rapidly assess the natural history of disease without mitigation efforts, phylogenic studies including the timing and role of multiple reproductions on viral mutations.

In summary, MGs, both those are clearly defined and spontaneously occurring, are key determinants of epidemiologic expansion of disease outbreaks. Institutions with the mandates for outbreak monitoring and response should keep an inventory of mass gatherings and provide advance warnings and recommendations about outbreaks to the organizers including information on event cancellation, crowd size limitations, or alternatives. Not all MG organizers may have such a knowledge base or capacity. Such recommendations would be more receptive if they are based on adequate scientific data. COVID-19 has already provided examples of both clearly planned event cancellations such as the Umrah suspension in KSA, and where outbreaks and events were continued. Proactive utilization of current computing, epidemiological, laboratory capacities to fully understand the role of MGs, and that of their mitigation potential can usefully inform the future course of COVID-19.

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Table 1. Characteristics of Select MG Events of Relevance to COVID-19

MG Event	Number		Interval of occurrence	Geographic scope	Type of event
	of persons (Millions)				
Arbaeen, Iraq	9-60		Annual	Regional	Religious
Carnival, Brazil	5		Annual	Regional	Cultural
Olympics	10		4 years	International	Sports
Hajj, Saudi Arabia	3-5		Annual	International	Religious
Namugongo Martyr's Day, Uganda	5-7		Annual	Regional	Religious
Expo Dubai 2020	25		Adhoc	International	Economic
Qom Shia pilgrimage, Iran	20		continuous	Regional	Religious

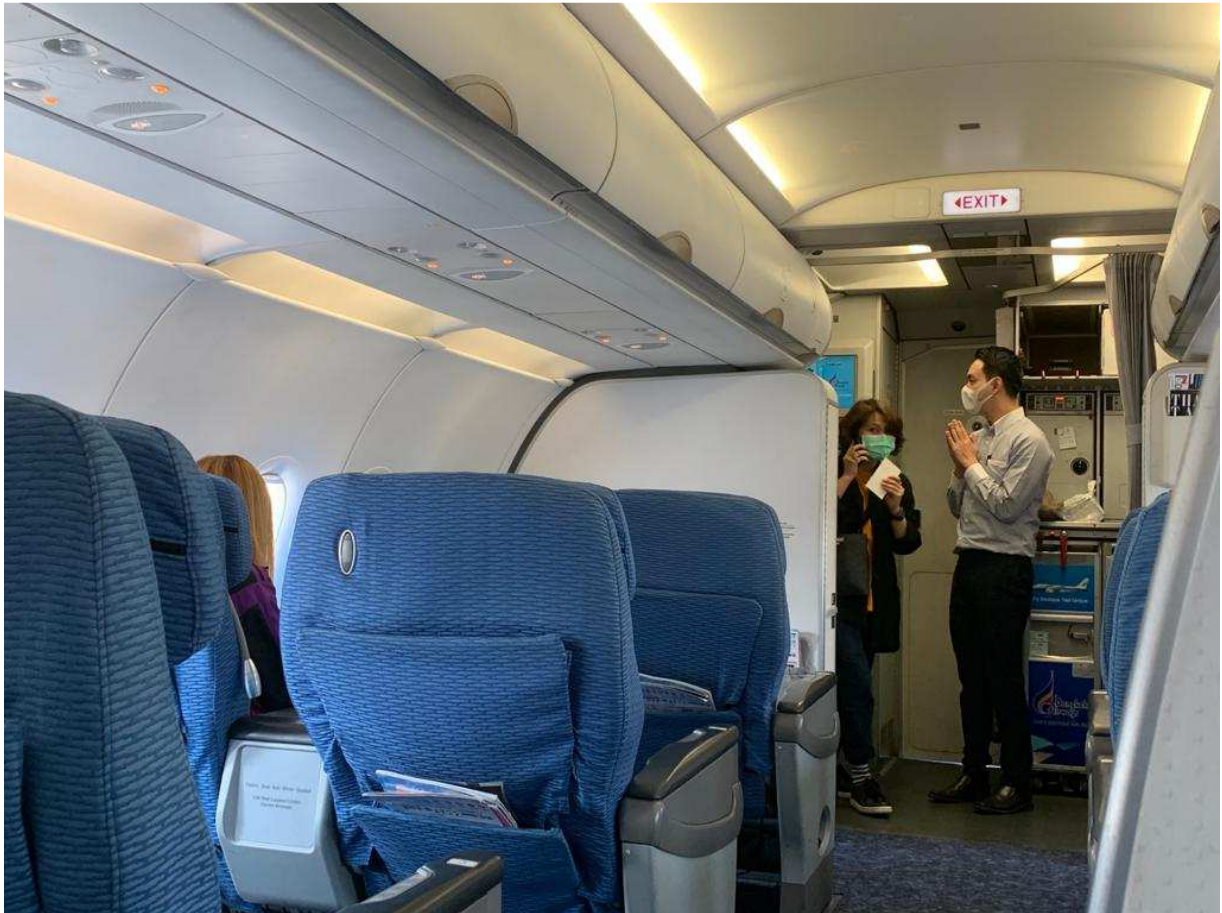


Figure 1: Mandatory mask use by flight attendants, Bangkok Airways, 22 February 2020. Photo Courtesy Shahul Ebrahim

Box 1. MG-Related Factors that Contribute to Pandemics

- Infectious diseases are the most common health problems encountered at MG
- Many MGs have disproportionately high percentage of developing country participants that are endemic to treatable infectious diseases, and emerging pathogens
- Resource poor countries with high MG participant volume may have high prevalence of self and prescription use of antibiotics
- Per-capita contact with farmed and wild animals is highest among developing countries that harbor resistant infectious agents
- Demographics of MG participants may precipitate disease transmission, as they may be elderly and with underlying chronic conditions, or younger populations emerging from countries without herd immunity from exposure to diseases.
- Suboptimal surveillance system in MG participating countries
- Suboptimal preparedness for pandemics