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An investigation of the combined effect of an annual mass gathering event and seasonal infectiousness on disease outbreak

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ABSTRACT

In this paper, we investigate the effects of recurring mass gathering event on the spread of an epidemic. Mass gatherings take place when a large number of people from different locations visit a particular region during a short time period. Such activity plays a crucial role in the epidemic spread as traveling facilitates the spread of an epidemic between disparate locations and crowded conditions can accelerate the disease transmission.

An additional component that affects disease spread is the seasonality in transmission. In this paper, we study the interplay between the periodic natures of seasonal transmission and of an annual mass gathering event. We find that the timing of the gathering relative to the peak in transmissibility can have a profound impact on the likelihood of an outbreak.

1. Introduction

A mass gathering event is an occasion where a very large number of people from various locations gather at a single location for a short period before returning again to their places of origin when the event ends. Examples include sporting events such as the Olympics and religious events such as the Hajj.

In this work, we are interested in a recurring mass gathering event, with the Hajj being the key motivating example. In 2014, the Hajj in Saudi Arabia had approximately 2 million attendees, with 700,000 coming from Saudi Arabia [7] and 1.3 million visitors from outside the country. Visitors perform the Hajj over a period of five or six days, staying in a tent city outside of Mecca. The timing of the Hajj follows a lunar calendar, occurring 10 or 11 days earlier each year according to the Gregorian calendar. From 2011 to 2018, it has moved from early November to mid-August. In this work, we will not take this drift into account.

Due to the large number of visitors living in close proximity, there is the possibility of an infectious disease such as influenza or MERS (Middle East respiratory syndrome) spreading within the mass gathering and then being transported to many locations when attendees return home. In fact, mass gatherings have the potential to facilitate or amplify disease outbreaks. Influenza season in Saudi Arabia typically runs from September to March [3]. A detailed discussion of the Hajj with regard to H1N1 influenza can be found in [5].

An additional focus of this paper is to see how the periodicity of a mass gathering event interacts with seasonality in disease transmission. In particular, how does the timing of the mass gathering in relation to the peak in the seasonal disease transmissibility affect the basic reproduction number \( R_0 \) (often seen as an indicator of the likelihood of an outbreak)? Can an adjustment in this relative timing affect the likelihood of an outbreak?

The paper is organized as follows. In Section 2, we present our model. Section 3 presents a brief summary of the model. In Section 4, we study the (periodic) dynamics within the disease-free space finding a periodic orbit as the attractor. In Section 5, we use the monodromy matrix methods discussed in [11] to calculate \( R_0 \), which serves as a threshold parameter for the stability of the disease-free attractor. In Section 6, we perform simulations that explore how \( R_0 \) depends on various system parameters. Finally, Section 7 presents a discussion of the results, as well as a brief analysis of the impact that latency would have on the system.

2. The epidemic model

In this section, we construct a mathematical model to study the spatial spread of an epidemic in the presence of an annual mass gathering event. We suppose that there are \( M \geq 2 \) locations or patches, between which individuals may move. Following [4], the population in location \( j \) is subdivided into susceptibles \( S_j \), infectives \( I_j \), recovered

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individuals with full immunity $R_0$ and recovered individuals with partial immunity $P_j$. Within these locations, we make no distinction between inhabitants and visitors.

Following [4], the travel rate from location $j$ to location $i$ is denoted by $h_{ij}$. To determine the rate at which the various epidemiological groups in location $j$ travel to location $i$, we multiply by the fraction of the local population that is in that epidemiological group. For instance, the rate that susceptibles travel from location $j$ to location $i$ is $h_{ij}S_j / N_j$, where $N_j = S_j + I_j + R_j + P_j$. Thus, the total rate at which susceptibles leave location $j$ for other patches is $\sum_{i=1}^{M} h_{ij}S_j / N_j$ and the total rate at which susceptibles arrive in location $j$ from other patches is $\sum_{i=1}^{M} h_{ji}S_i / N_i$. Similar terms apply to the recovered and the partially immune groups. For the corresponding term for infectious groups, we allow that the individuals may be less likely to travel and we replace $h_{ij}$ with $h_{ij}k_j$, where $k_j$ is typically in the interval [0,1]. If $k_j = 0$, then infectious individuals in location $j$ do not travel. If $k_j = 1$, then infectious individuals travel at the same rate as the rest of the population of that patch.

We note that if $k_j < 1$ and $N_j > 0$, then the total travel rate from $j$ to $i$ is less than $h_{ij}$. We interpret $h_{ij}k_j$ as the travel capacity from $j$ to $i$, perhaps measured in airplane seats. If infected individuals choose not to travel (i.e. $k_j < 1$), then the travel rate $h_{ij}$ will be reduced, resulting in empty seats on the planes.

The per capita death rate is $\mu$, affecting all subgroups equally. The recruitment rate for location $j$ is $\mu S_j$ for some $S_j > 0$ with all new individuals entering into the susceptible group. Thus, in the absence of travel between the regions, the total population in location $j$ will tend to $S_j$.

The average time spent in an infectious group before recovering with immunity is $\frac{1}{\alpha}$. After an average time of $\frac{1}{\alpha}$ spent in a recovered group, an individual’s immunity wanes losing some of its effectiveness so that they become susceptible, but at a reduced rate. After a duration of $\frac{1}{k_r}$, this partial immunity passes, and the individual becomes susceptible.

Within location $j$, the rate at which susceptibles are infected is given by $r_S S_j I_j / N_j$, where $r$ denotes the average number of contacts per individual per unit time, $r_S$ represents the probability of transmitting the disease in a contact. The constant $q \in [0,1]$ allows for mass action incidence ($q = 0$), standard incidence ($q = 1$) or something in between. Individuals with partial immunity are infected at a rate $r^p S_j I_j / N_j$, where $r^p \leq r_S$.

The mass gathering event takes place at (or near) location $j$, so that individuals at the mass gathering may interact with individuals at location $i$. Depending on the specific details and logistics of the mass gathering, inhabitants of location 1 may or may not travel to join the mass gathering. In later sections, we consider the example of the Hajj, with location 1 being Saudi Arabia; in this case individuals from location 1 travel to the site of the mass gathering, staying in the same style of accommodation as other visitors.

At the mass gathering, we distinguish between individuals from different regions, denoting the groups from location $j$ by $S_j^m$, $I_j^m$, $R_j^m$ and $P_j^m$ (where the superscript $m$ stands for mass gathering).

The travel rate from location $j$ to the mass gathering is $\phi_{ij}$, representing a fixed number of travellers per day as would be the case if there were a set number of flights available. Thus, susceptibles in location $j$ leave for the mass gathering at rate $\phi_{ij} S_j / N_j$. Similar terms apply to the recovered and partially immune groups. The rate at which infectious individuals in location $j$ leave for the mass gathering is $\phi_{ij} I_j / N_j$.

Once the mass gathering ends, all individuals (healthy or not) must return home, and so we assume per capita travel rates giving a rapid exponential decay in the number of visitors. For all epidemiological statuses, individuals return from the mass gathering site to location $j$ with per capita rate $\theta_j$ (with no reduction for the infectious groups). As discussed later, $\phi_j$ and $\theta_j$ are periodic functions.

We note that the form of the travel rates for individuals going to and returning from the mass gathering are different. This is because the nature of those movements are different. Travel to the gathering from location $j$ is limited by availability (of flights or accommodation, for example), while travel back to location $j$ is set so that a fixed fraction of the remaining travellers will return home in a given time-period (similar to half-life dynamics).

For $j = 2, \ldots, n$ the groups in location $j$ are described by the following differential equations.

\begin{align*}
S_j &= \mu(S_j - S_i) - r_S S_j I_j / N_j + \eta_{ij} P_j + \sum_{i=1}^{M} h_{ji} S_i - \phi_{ij} S_j / N_j - \theta_j S_j^m, \\
I_j &= r_S S_j I_j / N_j + r^p S_j I_j / N_j - (\alpha + \mu)I_j + \sum_{i=1}^{M} h_{ji} k_j I_i - \phi_{ij} k_j I_j / N_j - \theta_j I_j^m, \\
R_j &= \alpha I_j - (\eta_{ij} + \mu)R_j + \sum_{i=1}^{M} h_{ji} R_i - \phi_{ij} R_j / N_j + \theta_j R_j^m, \\
P_j &= \eta_{ij} R_j - (\eta_{ij} + \mu)P_j - r^p S_j I_j / N_j + \sum_{i=1}^{M} h_{ji} P_i - \phi_{ij} P_j / N_j + \theta_j P_j^m.
\end{align*}

(1)

Since the mass gathering takes place at or near location $j = 1$, it is possible for susceptibles in location 1 to be infected by infectious individuals at the mass gathering, with mass action incidence rate of $r_S^m S_1 I_1^m$.

\begin{align*}
S_1 &= \mu(S_1 - S_i) - r_S S_1 I_1 / N_1 + \sum_{i=1}^{M} h_{1i} S_i - \phi_{1i} S_1 / N_1 - \theta_1 S_1^m, \\
I_1 &= r_S S_1 I_1 / N_1 + r^p S_1 I_1 / N_1 + \sum_{i=1}^{M} S_i I_1^m + r^p S_1 I_1^m - (\alpha + \mu)I_1 + \sum_{i=1}^{M} h_{1i} k_i I_i - \phi_{1i} k_i I_1 / N_1 + \theta_1 I_1^m, \\
R_1 &= \alpha I_1 - (\eta_{1i} + \mu)R_1 + \sum_{i=1}^{M} h_{1i} R_i - \phi_{1i} R_1 / N_1 + \theta_1 R_1^m, \\
P_1 &= \eta_{1i} R_1 - (\eta_{1i} + \mu)P_1 - r_S S_1 I_1 / N_1 + r^p S_1 I_1^m + \sum_{i=1}^{M} h_{1i} P_i - \phi_{1i} P_1 / N_1 + \theta_1 P_1^m.
\end{align*}

(2)

Next we consider the individuals attending the mass gathering event. Amongst attendees, we assume mass action transmission with coefficients $r_S^a$ for susceptibles and $r^p_a$ for individuals with partial immunity, giving rates $r_S^a S_1^m I_1^m$ and $r^p_a S_1^m I_1^m$, respectively, for attendees from patch $j$. Susceptibles and individuals with partial immunity from patch $j$ that are attending the mass gathering are infected by individuals in patch 1 at rates $r_S^a S_1 I_1^m$ and $r^p_a I_1^m$, respectively. The epidemic spread is described by the following differential equation system.
beginning of the year. An alternate interpretation is that we are simply shifting time so that \( t \) obtains an integer value at the beginning of each mass gathering event.

The travel rate from location \( j \) to the mass gathering is \( \phi_j \). During the long periods between mass gatherings, \( \phi_j = 0 \). We assume there is a short period of duration \( \alpha_1 > 0 \), during which individuals begin travelling to the mass gathering site. During this period, \( \phi_j \) increases linearly from 0 to its maximum value \( \phi^\max \) before decreasing linearly to 0 again by \( t = \alpha_2 \in (\alpha_1, \omega) \). We write

\[
\phi_j(t) = \tilde{\phi}_j(t),
\]

where \( \phi(t) \) is the \( \omega \)-periodic function satisfying

\[
\tilde{\phi}_j(t) = \tilde{\phi}_j(t) \tilde{\theta}(t),
\]

for \( i = 1, \ldots, M \).

For \( i, j = 1, \ldots, M \), with \( i \neq j \), the constant parameters \( h_{kj} \) and \( k_j \) are non-negative and \( S_j, \mu, \eta_p, \eta_R, \) and \( \alpha \) are positive. As stated earlier, the constant \( q \) lies in the interval \([0,1]\).

The parameters \( \phi_p, \theta_p \), and the products \( \rho^S_{pi}, \rho^P_{pi}, \rho^S_{pi}, \rho^P_{pi}, \rho^p_{mi}, \rho^m_{pp}, \) and \( \rho^p_{mm} \) are variable in time, non-negative and not identically zero.

For \( i = 1, \ldots, M \), with \( i \neq j \), we assume that \( h_{ij} = h_{ji} \), guaranteeing that \( S_j + S_m \) tends to the constant \( S_j \) in the absence of disease \([4]\). (This is discussed in Section 4.)

The case for using different incidence functions from those that are used here can be easily made. However, in the work that follows, we focus on the dependence of the basic reproduction number \( R_0 \) on various parameters. In doing so, we study a time-varying linear problem (see Section 5). In our numerical work (see Section 6) we use parameter values so that the different incidence terms are of similar size - regardless of whether the term comes from mass action or from a different incidence function. Thus, any non-linear dependence that the incidence may have on the group sizes has no impact on our analysis.

### 2.1. Time dependence of \( \phi \), \( \theta \) and \( \rho^p \)

In this work, we are particularly interested in the interplay between the periodic nature of a mass gathering and the seasonal fluctuation in the transmissibility of a disease.

We assume that the mass gathering event is held periodically, always at the same time of year. Thus, \( \phi_j = \phi_j(t) \) and \( \tilde{\phi}_j = \tilde{\phi}_j(t) \) are both periodic functions of time \( t \) with a period \( \omega \) corresponding to an integer number of years. (For an annual event, \( \omega = 365 \).) In the years that the mass gathering event takes place, we assume that it takes place at the beginning of the year. An alternate interpretation is that we are simply shifting time so that \( t \) obtains an integer value at the beginning of each mass gathering event.

The travel rate from location \( j \) to the mass gathering is \( \phi_j \). During the long periods between mass gatherings, \( \phi_j = 0 \). We assume there is a short period of duration \( \alpha_1 > 0 \), during which individuals begin travelling to the mass gathering site. During this period, \( \phi_j \) increases linearly from 0 to its maximum value \( \phi^\max \) before decreasing linearly to 0 again by \( t = \alpha_2 \in (\alpha_1, \omega) \). We write

\[
\phi_j(t) = \tilde{\phi}_j(t),
\]

where \( \phi(t) \) is the \( \omega \)-periodic function satisfying

\[
\tilde{\phi}_j(t) = \tilde{\phi}_j(t) \tilde{\theta}(t),
\]

for \( i = 1, \ldots, M \).

For \( i, j = 1, \ldots, M \), with \( i \neq j \), the constant parameters \( h_{kj} \) and \( k_j \) are non-negative and \( S_j, \mu, \eta_p, \eta_R \) and \( \alpha \) are positive. As stated earlier, the constant \( q \) lies in the interval \([0,1]\).

The parameters \( \phi, \theta, \) and the products \( \rho^S_{pi}, \rho^P_{pi}, \rho^S_{pi}, \rho^P_{pi}, \rho^p_{mi}, \rho^m_{pp}, \) and \( \rho^p_{mm} \) are variable in time, non-negative and not identically zero.

For \( i = 1, \ldots, M \), with \( i \neq j \), we assume that \( h_{ij} = h_{ji} \), guaranteeing that \( S_j + S_m \) tends to the constant \( S_j \) in the absence of disease \([4]\). (This is discussed in Section 4.)

The case for using different incidence functions from those that are used here can be easily made. However, in the work that follows, we focus on the dependence of the basic reproduction number \( R_0 \) on various parameters. In doing so, we study a time-varying linear problem (see Section 5). In our numerical work (see Section 6) we use parameter values so that the different incidence terms are of similar size - regardless of whether the term comes from mass action or from a different incidence function. Thus, any non-linear dependence that the incidence may have on the group sizes has no impact on our analysis.

**Fig. 1.** (a) \( \phi_j(t) \) with \( \tilde{\phi}_j = 0.03 \), (b) \( \phi_j(t) \) with \( \tilde{\phi}_j = 0.0186 \) for \( j = 2, 3, 4 \), and (c) \( \theta_j(t) \) with \( \tilde{\theta}_j = 0.3 \) for \( j = 1, 2, 3, 4 \). These functions are plotted using parameters \( a_1 = 20, a_2 = 33, a_3 = 34, b_1 = 42, b_1 = 44, b_2 = 363 \) and \( b_1 = \omega = 365 \).
gathering may become negligible while t is still much smaller than $b_2$ or $b_3$. The seasonality in transmissibility may be due to changes in the survivability of the pathogen as the temperature varies or due to changes in individuals’ behaviour that alter the likelihood of transmission. Although the fluctuation may be manifested in both the contact rate r and in the transmission probability $\beta$, we take each of the $\beta$’s to be a positive constant and encapsulate all of the variation in r, setting

$$r = R \left[ 1 + \cos \left( \frac{2\pi}{365} (t - \tau) \right) \right],$$

(6)

where $R > 0$ is the average contact rate, $\epsilon \in [0, 1)$ determines the amplitude of oscillation in the contact rate and $\tau$ gives the offset between the time of the peak in disease transmissibility and the time that travel to the mass gathering begins. The denominator 365 shows that we are taking time to be measured in days (and also shows that we are ignoring leap years).

This choice of r has the effect of making all of the transmission rates periodic with the same period. The choice also keeps the ratio between different transmission rates constant, which is not necessarily accurate, but is used as an approximation for the purposes of this study.

3. Model summary

We have modelled the spatial spread of an infectious disease for which there is seasonality in the transmission, while also including a periodic mass gathering event such as the Hajj. We consider $M \geq 2$ locations or regions, along with a single mass gathering location that may or may not be adjacent to one of the patches. Along with periodic movement to and from the mass gathering, there is also movement between the patches.

At the mass gathering, we assume mass action incidence in order to account for crowding. In the individual patches, we assume incidence of the form $\beta S_i^m R_i^m$ for some $q \in [0, 1)$, allowing for both standard and mass action incidence. In principle, the equations can easily be rewritten to allow for more general incidence functions.

While the equations are valid for longer events, our intention is to consider mass gathering events that last for a few weeks or less. During a short period leading up to the mass gathering, individuals travel from the patches to the gathering site, and return home after the gathering. This gives a periodicity in the travelling dynamics.

The contact rate of the disease may depend on the season or temperature and thus is modeled by a periodic function of time $t$. Here, we are particularly interested in how the timing of the peak in the contact rate relative to the timing of the mass gathering event affects the basic reproduction number of the model.

4. The disease-free subspace

In order to determine the basic reproduction number $R_0$ in Section 5, it is necessary to determine the attractor of the disease-free subspace. Thus, in this section we assume that $I_j = I_j^m = 0$ for $j = 1, \ldots, M$, and determine the attractor within this set.

Let $R^* = \sum_{j=1}^M R_j + R_j^m$. Then in the disease-free subspace

$$\frac{dR^*}{dt} = -(\gamma_k + \mu) R^*.$$ Thus, $R^*$ tends to 0. Thus, the disease-free attractor satisfies $R^* = 0$ and so $R_j = R_j^m = 0$ for $j = 1, \ldots, M$.

Similarly, letting $P^* = \sum_{j=1}^M P_j + P_j^m$, we find that

$$\frac{dP^*}{dt} = -(\eta_k + \mu) P^*.$$ Within the disease-free attractor, this simplifies to

$$\frac{dP^*}{dt} = -(\eta_k + \mu) P^*$$ and so, within the disease-free attractor, $P^* = 0$ and $P_j = P_j^m = 0$ for $j = 1, \ldots, M$.

Now, we calculate that

$$\frac{d(S_j + S_j^m)}{dt} = \mu (S_j - (S_j + S_j^m)),$$

(7)

and so $\lim_{t \to \infty} (S_j + S_j^m) = S_j$. Thus, in the disease-free attractor we must have $S_j + S_j^m = S_j$. Using this to replace $S_j^m$, we find

$$\frac{dS_j}{dt} = \mu (S_j - S_j) - \phi_j (S_j - S_j) = (\mu + \theta_j) S_j - \phi_j - (\mu + \theta_j) S_j.$$ (8)

Since this system is $\omega$-periodic, with $\phi_j$ and $\theta_j$ varying over time, we don’t expect an equilibrium. Instead, we show that the function $\varphi_\omega$, which maps points forward in time by $\omega$ along solutions, has a unique fixed point; this will correspond to a unique $\omega$-periodic solution.

Since $\theta_j$ is non-negative and $\omega$-periodic, the coefficient $\mu + \theta_j$ is bounded above and below by positive numbers. Similarly, the term $(\mu + \theta_j) S_j - \phi_j$ is bounded above and below. Thus, there exists a sufficiently small initial condition $x_1$ (possibly negative), such that the corresponding solution to (8) is monotonically increasing for $t \in [0, \omega]$. Similarly, there exists a sufficiently large initial condition $x_2$ such that the corresponding solution is monotonically decreasing for $t \in [0, \omega]$. This implies that $\varphi_\omega$ maps the interval $[x_1, x_2]$ into itself. By the Brouwer Fixed Point Theorem (see [10, Theorem 4.8], for example), $\varphi_\omega$ has a fixed point.

If $x$ and $y$ are any two solutions to (8), then $\frac{d}{dt} (x - y) = - (\mu + \theta_j) (x - y).$ Thus, $x - y$ tends to 0 exponentially and the flow is contractive. Thus, by the Contraction Mapping Theorem, $\varphi_\omega$ has at most one fixed point. Furthermore, this fixed point is globally attracting under $\varphi_\omega$. Therefore, Eq. (8) has a globally attracting $\omega$-periodic orbit. We have now proven the following result.

Theorem 1. Amongst disease-free states, there is a globally attracting $\omega$-periodic orbit $x(t)$ for System (1)–(3).

We denote the coordinates of the unique disease-free periodic orbit by

$$S_j(t) = S_j^*(t) \quad \text{and} \quad S_j^m(t) = S_j - S_j^*(t),$$ (9)

with $I_j^*, R_j^*, I_j^{m*}, R_j^{m*} \equiv 0$ for $j = 1, \ldots, M$.

5. The basic reproduction number

In this section we consider the basic reproduction number $R_0$, using the monodromy matrix method described in [11]. The symbols $\mathcal{F}, V, F$ and $V$ that we use here denote periodic functions, but are analogous to the same symbols used by van den Driessche and Watmough in [9] to calculate $R_0$ for non-autonomous systems. $\mathcal{F}(t)$ includes the appearance of newly infected individuals in each infected compartment and $V(t)$ includes all other terms. Differentiating gives $F(t)$ and $V(t)$. Then, $R_0$ is given by performing a spectral radius calculation according to Lemma 1 below. As with the non-autonomous case, the sign of $R_0$ determines whether or not the disease should be expected to survive.

The infected classes are $I_j$ and $I_j^m$ for $j = 1, \ldots, M$. In the following calculations, the order of variables is $(I_1, \ldots, I_M, I_1^m, \ldots, I_M^m)$. Using the standard notation given in [11], we have

$$\mathcal{F}(t) = \left[ \begin{array}{c}
\rho_k^1 S_1^I N_1 + \sum_{i=1}^M \rho_k^i F_i^I N_i + \sum_{i=1}^M S_i I_i^m + \sum_{i=1}^M P_i I_i^m \\
\rho_k^2 S_2^I N_2 + \sum_{i=1}^M \rho_k^i F_i^I N_i + \sum_{i=1}^M S_i I_i^m + \sum_{i=1}^M P_i I_i^m \\
\rho_k^3 S_3^I N_3 + \sum_{i=1}^M \rho_k^i F_i^I N_i + \sum_{i=1}^M S_i I_i^m + \sum_{i=1}^M P_i I_i^m \\
\vdots \\
\rho_k^M S_M^I N_M + \sum_{i=1}^M \rho_k^i F_i^I N_i + \sum_{i=1}^M S_i I_i^m + \sum_{i=1}^M P_i I_i^m \\
\end{array} \right]$$

(10)
and
\[
V(t) = \begin{pmatrix}
(\alpha + \mu)I - \sum_{i=1}^{M} \frac{h_{i}k_{i}}{N_{i}} + \frac{\phi_{i}k_{i}}{S_{i}} + \frac{\phi_{i}k_{i}}{S_{i}} - \frac{0}{I_{i}^{n}} \\
(\alpha + \mu)I + \sum_{i=1}^{M} \frac{h_{i}k_{i}}{N_{i}} + \frac{\phi_{i}k_{i}}{N_{i}} - \frac{0}{I_{i}^{n}} \\
(\alpha + \mu)I - \sum_{i=1}^{M} \frac{h_{i}k_{i}}{N_{i}} + \frac{\phi_{i}k_{i}}{N_{i}} - \frac{0}{I_{i}^{n}} \\
(\alpha + \mu)I + \sum_{i=1}^{M} \frac{h_{i}k_{i}}{N_{i}} + \frac{\phi_{i}k_{i}}{N_{i}} - \frac{0}{I_{i}^{n}}
\end{pmatrix},
\]
where we note again that \(r, \phi_{j}\) and \(\theta_{j}\) are \(\omega\)-periodic. Following [11], we obtain
\[
F(t) = \begin{pmatrix}
F_{11} & F_{12} \\
F_{21} & F_{22}
\end{pmatrix}_{2M \times 2M}
\]
where
\[
F_{11} = \operatorname{diag}(r_{1}g_{11}^{1}, \ldots, r_{M}g_{M}^{1})
\]
\[
F_{12} = r_{2}g_{21}^{1}
\]
\[
F_{21} = r_{2}g_{21}^{1}
\]
\[
F_{22} = r_{2}g_{22}^{1}
\]
and
\[
F_{31} = r_{3}g_{31}^{1}
\]
\[
F_{32} = r_{3}g_{32}^{1}
\]
Also,
\[
V(t) = \begin{pmatrix}
V_{11} & V_{12} \\
V_{21} & V_{22}
\end{pmatrix}_{2M \times 2M}
\]
where
\[
V_{11} = \begin{pmatrix}
(\alpha + \mu) + \sum_{i=1}^{M} \frac{h_{i}k_{i}}{S_{i}} + \frac{\phi_{i}k_{i}}{S_{i}} + \frac{\phi_{i}k_{i}}{S_{i}} - \frac{0}{I_{i}^{n}} \\
(\alpha + \mu) + \sum_{i=1}^{M} \frac{h_{i}k_{i}}{S_{i}} + \frac{\phi_{i}k_{i}}{S_{i}} - \frac{0}{I_{i}^{n}}
\end{pmatrix}
\]
\[
V_{12} = -\operatorname{diag}(\theta_{1}, \ldots, \theta_{M})
\]
\[
V_{12} = -\operatorname{diag}(\phi_{1}, \ldots, \phi_{M})
\]
and
\[
V_{22} = \begin{pmatrix}
(\alpha + \mu + \theta_{1}, \ldots, \alpha + \mu + \theta_{M})
\end{pmatrix}
\]
It is easy to verify that the model in Section 2 satisfies the technical conditions (A1)–(A5) listed in [11]. Theorem 1 implies (A6) of Wang and Zhao [11] is satisfied. We note that \(-V\) is diagonally dominant by columns with Gersgorin discs [2] that all lie fully to the left of \(-\sigma + \mu\). It follows that the \(i\) th Lozinskiii measure of \(-V\) is at most \(-\sigma + \mu\), and so (A7) is also satisfied (see [1, Pg. 41] or [6]).

We now present a definition and a lemma in order to calculate \(R_{0}\) according to the method described in [11].

**Definition 1.** Suppose \(U = B(t)U\) for \(t \in \mathbb{R}\), where \(B\) is an \(\omega\)-periodic matrix that is summable on every compact interval in \(\mathbb{R}\). Let \(U(t)\) be the fundamental matrix of the system satisfying \(U(0) = 1\). Let \(W = U'(\omega)\). Then \(W\) is called the monodromy matrix of the system.

For \(\lambda > 0\), let \(W(\lambda)\) be the monodromy matrix of the linear \(\omega\)-periodic system
\[
\frac{dU}{dt} = \left[ -V(t) + \frac{F(t)}{\lambda} \right] U, \quad t \in \mathbb{R},
\]
where \(F\) and \(V\) are given in (12) and (17), respectively.

Let the spectral radius of a matrix \(W\) be denoted by \(\rho(W)\). Since \(F\) is not identically zero and \(-V\) is diagonally dominant, it follows that
\[
\lim_{\lambda \to \infty} \rho(W(\lambda)) = \lambda > 0.
\]
Applying Theorem 2.1 of Wang and Zhao [11] gives the following result.

**Lemma 1.** The basic reproduction number \(R_0\) is the unique value of \(\lambda > 0\) that solves \(\rho(W(\lambda)) = 1\).

6. Simulations

The figures that follow are the product of numerical simulations. Except when stated otherwise in the figure caption, the parameter values used to generate the figures are the values found in Tables 1 and 2. These values are based in part on Hyman and LaForce [4] and Weber et al. [12] and are appropriate for influenza.

The simulations model the Hajj, in Saudi Arabia. We consider \(M = 4\) regions: Saudi Arabia, other parts of the Middle East, Indonesia, and India with sizes 30,380,255, 1210, measured in millions, respectively. We take \(\phi_{1} = 0.03\) million, \(\phi_{2} = \phi_{3} = \phi_{4} = 0.0186\) million, so that the mass gathering consists of approximately 2 million attendees, with 700,000 coming from Saudi Arabia, approximating the size of the Hajj in 2013 and 2014 [7]. See Fig. 2. We take \(\delta = 0.3\) in agreement with the Saudi travel restriction that all Hajj visitors leave the country within 28 days of the conclusion of the Hajj [8]. (This value gives an exponential decay in the number of Hajj visitors so that after 28 days, the number of Hajj visitors decreases from 2 million to 450.)

In studying the interplay between the timing of the peak in disease transmissibility and the timing of the Hajj, one approach is to fix the phase of the contact rate, and vary the timing of the mass gathering event. An alternative is to fix the time of mass gathering event and let the phase of the contact rate vary. The two approaches are equivalent; we adopt the second approach. As can be seen in Fig. 2, the mass gathering population is maximized approximately between day 15 and day 48 each year. Thus, the mass gathering event occurs during the height of the transmission season if \(\tau \in [15, 48]\). (We note that the Hajj itself is much shorter than this period, but disease transmission can occur before and after the religious festival, as long as people are gathered. Data that tracks the size of the Hajj gathering over time would be useful, but does not seem to be readily available.)

The solid blue curve in Fig. 3, shows \(R_0\) plotted versus \(\tau\), while the horizontal dashed red line is \(R_0 = 1\). Following the approach of Wang and Zhao [11], for each value of \(\tau\), the monodromy matrix associated with Eq. (22) was used to calculate \(R_0\) according to Lemma 1. The disease-free space is unstable when the solid blue curve lies above the dashed red line, and is stable when the solid blue curve lies below the dashed red line. Thus, Fig. 3 shows clearly that the timing of the mass gathering relative to the peak in the seasonality of the disease.
transmissibility can have a dramatic effect on the possibility of an outbreak. In the figure, \( R_0 \) varies from a minimum of approximately 0.8 to a maximum of approximately 1.2, representing an increase of about 50%.

In Fig. 4, we explore the effect of varying the relative amplitude \( \epsilon \) of the seasonality in the contact rate \( r \). We do this for four different values of \( r \) corresponding to holding the mass gathering event when the contact rate is maximized, and with phase shifts of 3, 6 and 9 months. In each case, \( \epsilon \) is varied from 0 (corresponding to no seasonality) to 0.4 (corresponding to minimums and maximums in the contact rate that are 40% lower and higher than the average value). We find that if the mass gathering occurs when the contact rate is maximized (red curve), then \( R_0 \) increases linearly with \( \epsilon \). On the other hand, if the mass gathering occurs when the contact rate is minimized (blue curve), then \( R_0 \) decreases linearly with \( \epsilon \). If the mass gathering occurs half-way between these times (green and black curves), then the effect on \( R_0 \) of varying \( \epsilon \) (even quite significantly) is negligible. This is likely due to the fact that the contact rate is near its mean during these periods, and so varying \( \epsilon \) has very little impact on the contact rate until after the gathering has concluded. (We note that all four curves show the same value of \( R_0 \) (approximately 0.9905) when \( \epsilon = 0 \), as expected since the value of \( r \) is irrelevant if there is no seasonality.) This suggests, in agreement with

### Table 1
Transmission coefficients between infectives and susceptibles in the various groups. The coefficients describing transmission from \( I_i^m \) are mass action coefficients. The interpretation of the other coefficients depends on the value of \( q \); our simulations use \( q = 1 \), making these coefficients into standard incidence transmission probabilities. The values of \( \beta^i_m \) and \( \beta^i_m \) are taken from [4]. The values of \( \beta^i_m \) and \( \beta^i_m \) are estimated so that the associated incidence rates are comparable to the other incidence rates near the disease-free equilibrium. The value of \( R_0 \) does not depend on the values of \( \beta^i_m \), \( \beta^i_m \), \( \beta^i_m \), and \( \beta^i_m \), and so no values were needed in our simulations.

| Parameter | From | To | Suitable range | Value | Source |
|-----------|------|----|----------------|-------|--------|
| \( \beta^i_m \) | \( I_i \) | \( S_j \) | \([0.0005, 0.0006]\) | 0.0005 |        |
| \( \beta^i_m \) | \( I_i \) | \( S_m^i \) for all \( i \) | \( - \) | 0.0005 |        |
| \( \beta^i_m \) | \( I_i^m \) | \( S^i \) for all \( i \) | \( - \) | \( 1.6 \times 10^{-5} \) |        |
| \( \beta^i_m \) | \( I_i^m \) | \( S^i \) for all \( i, j \) | \( - \) | 0.00575 |        |
| \( \beta^i_m \) | \( I_i \) | \( P_i \) | less than \( \beta^i_m \) | \( - \) |        |
| \( \beta^i_m \) | \( I_i^m \) | \( P_i \) for all \( i \) | less than \( \beta^i_m \) | \( - \) |        |
| \( \beta^i_m \) | \( I_i \) | \( P_m^i \) for all \( i \) | less than \( \beta^i_m \) | \( - \) |        |
| \( \beta^i_m \) | \( I_i^m \) | \( P_m^i \) for all \( i, j \) | less than \( \beta^i_m \) | \( - \) |        |

### Table 2
Parameter values and ranges for numerical simulations.

| Parameter | Description | Suitable range | Value | Source |
|-----------|-------------|----------------|-------|--------|
| \( r(t) \) | Contact rate | \([42, 625]\) | 71 | \([4]\) |
| \( R \) | Mean contact rate | \([0, 365]\) | varies | | |
| \( \tau \) | Offset between the timing of the mass gathering and the peak in infectiousness (days) | \([0.007, 0.39]\) | 0.39 | \([4, 12]\) |
| \( \omega \) | Period of the seasonal contact rate | \([0, 1]\) | 365 | \([4]\) |
| \( \eta \) | Density dependence parameter | \([0, \infty )\] | 1 | \([4]\) |
| \( \mu \) | Death rate (1/days) | \([2.7 \times 10^{-5}, 6.75 \times 10^{-5}]\) | \(3.4 \times 10^{-5}\) | \([4]\) |
| \( \alpha \) | Rate of recovery (1/days) | \([0.07, 0.5]\) | 0.07 | \([4]\) |
| \( \eta_x \) | Rate of loss of full immunity (1/days) | \([0.000137, 0.00274]\) | 0.00274 | \([4]\) |
| \( \eta_p \) | Rate of loss of partial immunity (1/days) | \([0, 5.49 \times 10^{-5}]\) | \(1.37 \times 10^{-5}\) | \([4]\) |
| \( M \) | Number of regions | \([0, 0.2]\) | 0.008 | \([4]\) |
| \( \delta_j \) | Size of region \( j \) in millions | \([0, 4]\) | 4 | \([4]\) |
| \( \delta_j \) | Total rate of travel from \( i \) to \( j \) | \([0, 0.001, 0.0025, 1210]\) | \(0.001, 0.0025, 1210\) | \([4]\) |
| \( \kappa_i \) | Relative travel rate of infectives | \([0, 1]\) | 0.4 | \([4]\) |
| \( \phi_j(t) \) | Total rate of travel from \( j \) to the mass gathering | \([0, 0.001, 0.0025, 1210]\) | \(0.001, 0.0025, 1210\) | \([4]\) |
| \( \theta_j(t) \) | Per capita rate of travel from the mass gathering to \( j \) | \([0, 0.001, 0.0025, 1210]\) | \(0.001, 0.0025, 1210\) | \([4]\) |
| \( \phi_j \) | Maximum value of \( \phi_j \) in millions per day | \([0, 0.001, 0.0025, 1210]\) | \(0.001, 0.0025, 1210\) | \([4]\) |
| \( \theta_j \) | Maximum value of \( \theta_j \) (1/days) | \([0, 0.001, 0.0025, 1210]\) | \(0.001, 0.0025, 1210\) | \([4]\) |
and on the presence of visitors from regions 2, 3 and 4. In Fig. 5(a), we let $\phi_j$ for $j = 2, 3, 4$ vary (simultaneously) between 0 and 0.02. We see that as the travel rates from the other regions are reduced, the value of $R_0$ is also reduced, reaching a positive minimum value (at the left-hand side of the plot) when no visitors from the other regions are allowed to attend ($\phi_j = \phi_1 = 0$). Overall, we see that $R_0$ varies from less than 0.7 to greater than 1.2. This shows that the potential for disease outbreak can be radically transformed by a mass gathering event that includes individuals from disparate regions. In Fig. 5(b) $\phi_1$ for $j = 1, 2, 3, 4$ are all varied from 0 to values that are shown in Table 2. Here we see that $R_0$ decreases as the travel rates (and hence the size of the gathering) are decreased, however a minimum value seems to be reached at approximately $v = 0.2$ (corresponding to a mass gathering event that is only 20% as large). At this point, $R_0$ is determined primarily by the parts of the system that do not relate directly to the mass gathering; thus, further reduction of the mass gathering has no appreciable effect on the size of $R_0$. For contrast, in Fig. 5(a), even when $\phi_2$, $\phi_3$ and $\phi_4$ are as small as 0, the mass gathering still has 700,000 visitors for disease transmission at the mass gathering.

Crowding at the event is conducive to certain types of disease transmission, allowing for a high level of infection that can be transported to visitor’s home cities. Fig. 5 shows that it can be possible to avoid an outbreak (i.e. keep $R_0$ less than 1) by dissuading individuals from travelling to the event, possibly by restricting travel.

Fig. 6(a) shows the effect of simultaneously varying $\phi_j$ for $j = 1, 2, 3, 4$ from 0.1 to 0.6. (The other simulations used a value of 0.3.) We require that $\phi_j$ be strictly greater than zero; otherwise, attendees from region $j$ would never return home. Smaller values of $\phi_j$ mean that the mass gathering attendees return home more slowly, extending the duration of the event. Thus, it is expected that $R_0$ is a decreasing function of $\phi_j$, as is apparent in Fig. 6(a). From the figure, for the parameters in Tables 1 and 2, it seems unlikely that $R_0$ can be reduced below 1 simply by increasing $\phi_j$. It should be noted, though, that the function $\Theta(t)$ only becomes non-zero when $t > h_0 = 42$; thus the effect of increasing $\phi_j$ is to prevent attendees from lingering longer after the main event has concluded. In Fig. 6(b), we see how $R_0$ depends on the mass action coefficient $\beta_{\text{min}}$ for disease transmission at the mass gathering. If disease transmissibility at the event is low, then $R_0$ does not significantly depend on $\beta_{\text{min}}$ as seen by the fact that the curve is quite flat. However, as $\beta_{\text{min}}$ grows, we enter a region where there is apparent linear growth in the basic reproduction number. This suggests that it is prudent to implement policies that reduce transmission at the mass gathering, however, at some point further effort in reducing transmission at the mass gathering has minimal impact; at this point it is likely better to put resources elsewhere.

In Fig. 7, we see how $R_0$ depends on the relative travel rate $k_j$ of

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Fig. 4. $R_0$ vs $\epsilon$ for: (Red) $\tau = 32$, (Green) $\tau = 123$, (Blue) $\tau = 215$, (Black) $\tau = 306$. The red and blue curves correspond to the mass gathering occurring when the transmission rates $\beta_j$ are maximized and minimized, respectively, resulting in a strong dependence of $R_0$ on the amplitude $\epsilon$. The green and black curves correspond to the mass gathering occurring when the transmission rates are at their mean values, resulting in a negligible dependence of $R_0$ on the amplitude $\epsilon$.

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Fig. 5. Dependence of $R_0$ on the maximum travel rates to the mass gathering, with $\tau = 32$. (a) $\phi_1 = 0.03$ is held fixed while $\phi_j$ for $j = 2, 3, 4$ are varied simultaneously from 0 to 0.02. (b) The values of $\phi_j$ for $j = 1, 2, 3, 4$ given in Table 2 are multiplied by the factor $v$, with $v$ varying from 0 to 1.
infected individuals. If \( k_j = 1 \), then infected individuals in location \( j \) are just as likely to travel as other individuals. If \( k_j = 0 \), then infected individuals in location \( j \) do not travel. We note that the reason for individuals to not travel could be based on their own choice due to how they feel or it may be due to screening of travellers for infections. We also note that \( k_j \) could be any value in the interval \([0,1]\). For the red curve, \( k_j \) varies from 0 to 0.4 for all locations \( j \). For the green curve, \( k_1 \) is held fixed at 0.4 while \( k_2, k_3 \) and \( k_4 \) are varied. It is evident that restricting travel of only the infected individuals from external locations (i.e. locations 2, 3, 4) has negligible impact on \( R_0 \) - even if the restriction is total (i.e. \( k_2 = k_3 = k_4 = 0 \)). Restricting travel from all locations, including location 1 (as shown by the red curve) is also ineffective, resulting in approximately a 1.2% reduction in \( R_0 \) (from 1.215 to 1.2) as \( k_j \) is reduced from 0.4 to 0. This is in stark contrast to the result when all travel is stopped, as seen in Fig. 5 when the parameter \( \phi_j \) is varied, which resulted in \( R_0 \) being reduced from 1.2 to near 0.6.

With the red curve in Fig. 7 when \( k_j \) is small for \( j = 1, 2, 3, 4 \), we see the effect of healthy individuals at the mass gathering interacting with infected individuals in location 1, which is adjacent to the mass gathering. This allows the disease to spread into the mass gathering, followed by transmission within the mass gathering and then exportation of the disease back to the various locations from which participants have travelled. For the blue curve in Fig. 7(c), we again let \( k_j \) for \( j = 1, 2, 3, 4 \) vary from 0 to 0.4. This time however, we set \( \phi_j \) to be 0. We see that the value of \( R_0 \) is only slightly smaller than for corresponding values on the red curve.

The blue curve of Fig. 7 (and to a lesser extent the red curve) shows a troubling subtlety in the calculation of \( R_0 \). The calculation essentially involves considering a distributed infected individual that is spread across all possible infected classes. By considering the spectrum of the monodromy matrix (or of the next generation matrix for simpler models), we detect the eigenvalue associated with the distribution of an infected individual leading to the greatest disease growth. However, at the left-hand endpoint of the blue curve, with \( k_j = 0 \) for all \( j \) and with \( \phi_j = 0 \), there is supposed to be no entry of infecteds into the mass gathering. However, if one somehow got in, the disease would spread within the gathering since \( \phi_j \) is positive. The distributed infected individual includes allowing infection at the gathering. This means that the blue curve in Fig. 7 should have a jump discontinuity at the left-hand endpoint, taking on the value that appears at the left-hand endpoint of the curve in panel (b) of Fig. 5 instead (since that corresponds to a mass gathering of size 0).

This raises an interesting mathematical question of how the method used here should be modified to detect such an issue automatically. The jump discontinuity shows that screening with even slight imperfections can have a large impact in the value of \( R_0 \); here it jumps from roughly 0.5 to roughly 1.19.

7. Discussion

We have studied a model of infectious disease transmission in the context of a major periodic mass gathering event, allowing that the transmissibility of the disease also has a seasonal variation. Due to the periodic nature of the model, it is not possible to calculate the basic reproduction number \( R_0 \) in closed form. Instead, we rely on numerical simulations to calculate \( R_0 \).

Not surprisingly, the simulations highlight the potential for various system parameters to influence whether \( R_0 \) is greater than one or less than one, a significant difference as it determines whether or not a disease outbreak should be expected or not.

In the model, the multiple locations are connected through two modes. First, there is direct travel between the locations. Furthermore, individuals from the various locations periodically meet and interact at the mass gathering event before returning home. Due to crowding effects, the mass gathering may be conducive to transmission of various diseases. In this work, we focus on the impact that the Hajj can have on influenza outbreaks.

In Fig. 5, we see that reducing travelers to the mass gathering from outside the region (panel (a)) or reducing the size of the event altogether (panel (b)) can reduce \( R_0 \) from greater than one (on the right-hand side of the figures) to less than one (on the left-hand sides). This shows that it is definitely possible that outbreaks and disease persistence can be driven by a mass gathering event. Fig. 6(b) shows that an
depends very by a factor of when the mass gathering happens at the minimum has an apparent linear dependence on the vs is highly dependent on transmission that takes place during the

200 365. Since this varies with then the inclusion of latency

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includes a period of latency that lasts an average of two days. There seems to be an approximately 30% reduction in \( R_0 \) when the mass gathering happens at peak transmissibility and an approximately 20% reduction in \( R_0 \) when the mass gathering happens at the minimum transmissibility. The difference in reduction is likely due to the difference in how much of the next generation of infections occur at the mass gathering for the different values of \( \tau \). This shows that future work should take full account of latency.

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