



A mathematical interpretation for outbreaks of bacterial meningitis under the effect of time-dependent transmission parameters

Can Türkün · Meltem Gölgeli ·
Fatihcan M. Atay

Received: 21 February 2023 / Accepted: 8 May 2023 / Published online: 2 June 2023
© The Author(s), under exclusive licence to Springer Nature B.V. 2023

Abstract We consider a SIR-type compartmental model divided into two age classes to explain the seasonal exacerbations of bacterial meningitis, especially among children outside of the meningitis belt. We describe the seasonal forcing through time-dependent transmission parameters that may represent the outbreak of the meningitis cases after the annual pilgrimage period (Hajj) or uncontrolled inflows of irregular immigrants. We present and analyse a mathematical model with time-dependent transmission. We consider not only periodic functions in the analysis but also general non-periodic transmission processes. We show that the long-time average values of transmission functions can be used as a stability marker of the equilibrium. Furthermore, we interpret the basic reproduction number in case of time-dependent transmission functions. Numerical simulations support and help visualize the theoretical results.

Keywords Bacterial meningitis · Epidemic models · Seasonal outbreaks · Non-autonomous systems · Stability

1 Introduction

Bacterial meningitis is a severe infection that occurs as an explosive epidemic every 5–10 years in the sub-Saharan African meningitis belt, as well as seasonal outbreaks in different parts of the world [1]. The bacterium *Neisseria meningitidis* is known to be the main cause of bacterial meningitis. It has been reported that the infection has high rates of fatality and may leave serious sequelae in survivors [2]. Six (A, B, C, W, X , and Y) of the twelve serogroups are responsible for nearly all cases of invasive meningococcal disease (IMD), with a large variation of serogroups in different age groups and geographic regions [3]. IMD is transmitted through respiratory droplets by a close contact, and the asymptomatic carriers play a major role in the spread of the disease, although only less than 1% of them develop meningococcal disease [4]. The seasonal as well as irregular outbreak patterns of IMD have been discussed by various researchers in the concept of dry season (from December to May) along the meningitis belt [5–7]. IMD displays seasonal exacerbations outside of the meningitis belt, too. In 1987, an outbreak was caused by a strain of *N. meningitidis* serogroup A associated with the Hajj pilgrimage [8], which is one of the religious duties of Islam that consists of visiting the

C. Türkün · M. Gölgeli (✉)
Department of Mathematics, TOBB University of Economics and Technology, Ankara, Turkey
e-mail: mgolgeli@etu.edu.tr

F. M. Atay
Department of Mathematics, Bilkent University, Ankara, Turkey
e-mail: f.atay@bilkent.edu.tr

Present Address:

C. Türkün
Department of Industrial Engineering, Altınbaş University, Istanbul, Turkey
e-mail: turkuncn@gmail.com

Kaaba in Mecca at least for a week and participating in communal worship processions. According to the data of the General Authority for Statistics (GASTAT) of the Kingdom of Saudi Arabia, 2.4 million Muslims from different parts of the world joined to pilgrimage in 2019, of which 634 thousand were domestic pilgrims [9]. The geographic and ethnic diversity of the people promote the transmission of respiratory infections during the Hajj [10]. Furthermore, pilgrims from hyper-endemic areas, including the African meningitis belt, carry different *N. meningitidis* strains to this community that will soon transfer the disease to their home country, and thus, seasonal outbreaks all over the world come forward [4, 8, 11–14].

The Saudi authorities have required all Hajj pilgrims to receive the quadrivalent (serogroups A, C, W, and Y) meningococcal (MenACWY) polysaccharide vaccine prior to their arrival in Saudi Arabia since 2002 [15]. However, there is no vaccine available to protect people against all serogroups today [16]. In addition, meningococcal polysaccharide vaccination does not prevent the acquisition of carriage, whereas a quadrivalent conjugate vaccine may prevent acquisition of new carriage. Nevertheless, no vaccine can remove an existing carriage that may take two months or more [13]. In some studies, researchers have noticed the seasonal spikes of IMD among the household contacts of returning pilgrims [4, 17–19].

Pilgrimage and Umrah (a voluntary pilgrimage to Mecca) were temporarily suspended in 2020 because of the COVID-19 pandemic, and Hajj pilgrimage was limited to just 60,000 citizens and residents in 2021 by the Saudi Arabian authorities. However, as of August 2021 it was announced that the requests of two million Muslim pilgrims who want to perform Umrah from abroad will be accepted every month. As one can predict heuristically, the number of pilgrims may increase in the coming years with the decrease in the effect of the COVID-19 pandemic. Taking into account the spread dynamics of infectious diseases, preventive measures may also be increased and new regulations may be put into effect during the worship process [20, 21].

Since Daniel Bernoulli's publication on an early mathematical model for smallpox [22], mathematical epidemiology has largely been devoted to explaining the dynamics of the spread of contagious diseases and suggesting control strategies. There are various modelling approaches for the spread of bacterial meningitis, but only a few of them deal with the seasonal trans-

mission dynamics of the disease [23–27]. On the other hand, there exist modelling studies on the seasonality of several other infectious diseases (influenza, measles, chickenpox, pertussis, malaria, etc.) or epidemiological models with a generic aspect [28–34].

In this paper, we consider a mathematical model motivated by explaining possible seasonal outbreaks of IMD that are caused by the returning pilgrims from Hajj, who transmit the disease to their close contacts, or other mass movements such as uncontrolled migration. We draw attention to the fact that the time-dependent transmission rates do not have to be periodic functions. Consequently, we present a mathematical analysis of the model under time-dependent transmission parameters in the most general sense. We include various examples for seasonal exacerbation of IMD in the simulations.

This paper is organized as follows. The main modelling ideas are given in Sect. 2. Basic properties of the nonlinear model are derived in Sect. 3, and a linear stability analysis of the disease-free equilibrium is presented in Sect. 4. The concept of the basic reproduction number is discussed in Sect. 5. The analytical results are numerically verified in Sect. 6. A brief conclusion in Sect. 7 ends the paper.

2 Modelling ideas

Our starting point is the autonomous model given in [35], which describes the transmission dynamics of a contagious disease between children and adults. While presenting a general approach that could be applied to different childhood diseases, the authors also mention there the specific example of IMD carried by Hajj pilgrims. Since IMD displays temporary outbreaks rather than stable epidemics all over the world except the meningitis belt, a non-autonomous system may better explain the seasonal exacerbation of the disease. Inspired by this idea, an age-structured model driven by a seasonal forcing function was introduced in [34] that takes into account the variability of the climate describing the transmission dynamics between children and adults, where the authors obtained sufficient conditions that assure the existence and global attractivity of a positive periodic solution. In the present paper, we concentrate on the stability of the disease-free state in the time-dependent transmission case and show that the

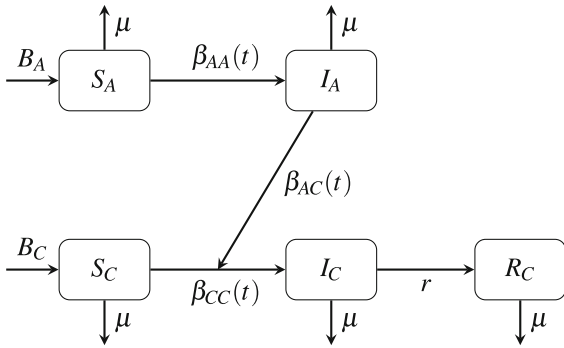


Fig. 1 Flowchart of model (1)

mean values of transmission functions enable to define the exacerbation of IMD as an outbreak.

The basic structure of the model and the transmission routes are shown in Fig. 1. Our aim is to investigate the seasonal spikes of IMD among the household contacts of returning pilgrims. Although people of any age can develop IMD, children are at increased risk of the disease [36]. The incidence of IMD in infants and young children (aged less than 5 years) occupies 75% of all cases of meningococcal meningitis and meningococemia in children. Further, the second peak of incidence according to age scale appears in adolescents and young adults [14]. In this sense, the population is divided into two age groups: adults and children, indicated by the subscripts A and C in this paper. The key assumption here is that these close contacts are households and that children largely constitute the target group. However, in the absence of a large dataset on the prevalence of the IMD in sub-age groups of childhood, the childhood is limited to a single age group. As a result of this assumption, the interpretation of the transmission parameters of the disease is limited to two age groups. As usual, S , I , and R represent the susceptible, infectious, and recovered individuals, respectively.

We assume that all adults are vaccinated and they may carry IMD to the children with a time-dependent transmission rate. While the vaccines for IMD offer protection against some most common serogroups of the disease, the rarer serogroups of disease may cause novel outbreaks. The available literature claims that the majority of pilgrims receive the polysaccharide MenACWY vaccine and that this does not affect carriage and onward transmission. A more complete compliance and transition to a conjugate MenACWY vaccine could provide more robust and broader protection for

pilgrims, and additional immunization options could be considered [37]. Because of not displaying any symptoms of the disease, the recovery process for adults is neglected. Although the prevalence of the disease varies in age subgroups of children, we do not define an age threshold between adult and child classes clearly, as we do not analyse any other age subgroup of children. We assume that all surviving children are recovered, although some of them are effected by neurologic sequelae [38]. Certainly, children continuing their lives with severe sequelae cannot be considered as a complete recovery, but since our study focuses on the spread of the disease rather than recovery, leaving sequelae is not considered as a distinct class.

The time-dependent parameters $\beta_{AA}(t)$, $\beta_{CC}(t)$ and $\beta_{AC}(t)$ represent the transmission rate among adults, among children, and between adults and children, respectively. We ignore the transmission from children to adults since biological literature indicates that children (< 18 years) are drastically more likely to contract IMD than adults. The parameter B_C is the number of daily births in the households of pilgrims, and B_A represents the daily entrance of adult people to the system. Further, μ represents the natural death rate and r denotes the recovery rate from the disease. The parameters B_A , B_C , μ , and r are positive and the time-dependent transmission rates $\beta_{AA}(t)$, $\beta_{AC}(t)$ and $\beta_{CC}(t)$ are taken to be non-negative bounded functions.

Based on the foregoing considerations, we arrive at the following non-autonomous model, which is an extension of the autonomous model studied in [35].

$$\begin{aligned}
 \frac{dS_A}{dt} &= B_A - \beta_{AA}(t)I_A S_A - \mu S_A \\
 \frac{dS_C}{dt} &= B_C - (\beta_{CC}(t)I_C + \beta_{AC}(t)I_A)S_C - \mu S_C \\
 \frac{dI_A}{dt} &= \beta_{AA}(t)I_A S_A - \mu I_A \\
 \frac{dI_C}{dt} &= (\beta_{CC}(t)I_C + \beta_{AC}(t)I_A)S_C - \mu I_C - r I_C \\
 \frac{dR_C}{dt} &= r I_C - \mu R_C.
 \end{aligned}
 \tag{1}$$

3 Basic properties of the nonlinear system

We first show the positivity and boundedness of the solutions of the model (1).

Theorem 3.1 *Solutions of the system (1) are non-negative and bounded for all $t > 0$ whenever the initial values are non-negative.*

Proof Treating the right-hand side of each equation in the system (1) as a linear equation of the variable on the left, the solutions can be written as

$$\begin{aligned}
 S_A(t) &= \phi_{AA}(t) \left(S_A(0) + B_A \int_0^t \phi_{AA}^{-1}(\tau) d\tau \right) \\
 S_C(t) &= \phi_{AC}(t) \left(S_C(0) + B_C \int_0^t \phi_{AC}^{-1}(\tau) d\tau \right) \\
 I_A(t) &= I_A(0) \cdot \exp \left\{ \int_0^t (\beta_{AA}(\tau) S_A(\tau) - \mu) d\tau \right\} \\
 I_C(t) &= \phi_{CC}(t) \left(I_C(0) \right. \\
 &\quad \left. + \int_0^t \beta_{AC}(\tau) I_A(\tau) S_C(\tau) \phi_{CC}^{-1}(\tau) d\tau \right) \\
 R_C(t) &= e^{-\mu t} \left(R_C(0) + r \int_0^t I_C(\tau) e^{\mu \tau} d\tau \right). \tag{2}
 \end{aligned}$$

where

$$\begin{aligned}
 \phi_{AA}(t) &= \exp \left\{ - \int_0^t [\beta_{AA}(\tau) I_A(\tau) + \mu] d\tau \right\} \\
 \phi_{AC}(t) &= \exp \left\{ - \int_0^t [\beta_{CC}(\tau) I_C(\tau) \right. \\
 &\quad \left. + \beta_{AC}(\tau) I_A(\tau) + \mu] d\tau \right\} \\
 \phi_{CC}(t) &= \exp \left\{ \int_0^t [\beta_{CC}(\tau) S_C(\tau) - \mu - r] d\tau \right\}
 \end{aligned}$$

The non-negativity of S_A , S_C , and I_A are immediate from the first three equations in (2) since the ϕ are positive functions, and the non-negativity of I_C and R_C follows from the last two equations due to integration of non-negative functions. To show boundedness, consider the equations for the adult and children population sizes, $N_A = S_A + I_A$ and $N_C = S_C + I_C + R_C$, as well as the total population size $N = N_A + N_C$, obtained by adding appropriate equations from the model (1):

$$\begin{aligned}
 \frac{dN_A}{dt} &= B_A - \mu N_A \\
 \frac{dN_C}{dt} &= B_C - \mu N_C \\
 \frac{dN}{dt} &= B_A + B_C - \mu N. \tag{3}
 \end{aligned}$$

The system (3) has solutions

$$\begin{aligned}
 N_A(t) &= S_A(t) + I_A(t) \\
 &= \frac{B_A}{\mu} + \left(N_A(0) - \frac{B_A}{\mu} \right) e^{-\mu t} \tag{4a}
 \end{aligned}$$

$$\begin{aligned}
 N_C(t) &= S_C(t) + I_C(t) + R_C(t) \\
 &= \frac{B_C}{\mu} + \left(N_C(0) - \frac{B_C}{\mu} \right) e^{-\mu t} \tag{4b}
 \end{aligned}$$

$$N(t) = \frac{B_A + B_C}{\mu} + \left(N(0) - \frac{B_A + B_C}{\mu} \right) e^{-\mu t}, \tag{4c}$$

which show that the non-negative solutions of (1) are bounded for $t > 0$. \square

Remark 3.2 Note that only the non-negativity of $\beta_{AC}(t)$ is needed to show the non-negativity and hence the boundedness of the solutions.

On the basis of (4), a reduction is possible in the equation (1), which yields an exact solution for the adult subpopulations. Solving for S_A from (4a) as

$$S_A(t) = \frac{B_A}{\mu} + (S_A(0) + I_A(0) - \frac{B_A}{\mu}) e^{-\mu t} - I_A(t) \tag{5}$$

and substituting into the equation for I_A in (1), we obtain

$$\frac{dI_A}{dt} = \left(\lambda_3(t) + k_1 \beta_{AA}(t) e^{-\mu t} \right) I_A - \beta_{AA}(t) I_A^2, \tag{6}$$

where $k_1 = (S_A(0) + I_A(0) - \frac{B_A}{\mu})$ is a constant that depends on the initial conditions and

$$\lambda_3(t) = \beta_{AA}(t) \frac{B_A}{\mu} - \mu. \tag{7}$$

(The reason for the choice of notation will become clear in the next section, where we will see that $\lambda_3(t)$ appears as one of the time-dependent eigenvalues of the system's Jacobian.) Equation (6) is a Bernoulli differential equation and can be solved after reduction to a linear equation via the well-known substitution $u = I_A^{-1}$. This gives an exact solution for $I_A(t)$ as

$$I_A(t) = \frac{I_A(0) \eta(t)}{1 + I_A(0) \int_0^t \beta_{AA}(\tau) \eta(\tau) d\tau}, \tag{8}$$

where

$$\eta(t) = \exp \left\{ \int_0^t [\lambda_3(\tau) + k_1 \beta_{AA}(\tau) e^{-\mu \tau}] d\tau \right\}.$$

Furthermore, substituting (8) into (5) gives the exact solution for $S_A(t)$. Therefore, the dynamics of the adult subgroups are explicitly determined.

One can follow a similar procedure for the young age groups. Although in this case it is not possible to obtain explicit formulas for the solutions, one can reduce the problem essentially to a knowledge of I_C . Indeed, if I_C is known, then R_C can be found from the last equation in (1) as

$$R_C(t) = e^{-\mu t} \left(R_C(0) + r \int_0^t I_C(\tau) e^{\mu \tau} d\tau \right), \tag{9}$$

following which, S_C can be determined from (4b) as

$$S_C(t) = \frac{B_C}{\mu} + k_2 e^{-\mu t} - I_C(t) - R_C(t), \tag{10}$$

where $k_2 = (S_C(0) + I_C(0) + R_C(0) - \frac{B_C}{\mu})$. Substituting (10) into the equation for I_C in (1), we obtain

$$\begin{aligned} \frac{dI_C}{dt} = & \beta_{AC}(t) I_A(t) \left(\frac{B_C}{\mu} + k_2 e^{-\mu t} - R_C(t) \right) \\ & + \left(\lambda_4(t) + \beta_{CC}(t) (k_2 e^{-\mu t} - R_C(t)) - \beta_{AC}(t) I_A(t) \right) I_C \\ & - \beta_{CC}(t) I_C^2 \end{aligned} \tag{11}$$

where

$$\lambda_4(t) = \beta_{CC}(t) \frac{B_C}{\mu} - \mu - r. \tag{12}$$

Thus, the solution of the system (1) is in principle reduced to solving (11). With $I_A(t)$ being a known function given by (8), equation (11) is a Riccati-like differential equation for I_C , except that the expression for R_C that must be substituted from (9) further contains an integral of I_C .

Although finding the exact solution of (11) is difficult, the foregoing derivation already identifies the key quantities that will prove to be important for the dynamical behaviour of the model (1), namely λ_3 and λ_4 , as defined in (7) and (12). In the next section, we will see that these are the two time-dependent eigenvalues of the system’s Jacobian matrix and thus play a decisive role in the stability of the equilibrium (as the remaining eigenvalues are constant and negative).

4 Disease-free equilibrium and linear stability analysis

With time-dependent transmission rates, the system (1) turns out to have a single equilibrium point, which is the disease-free state.

Theorem 4.1 *If $\beta_{AA}(t)$ and $\beta_{CC}(t)$ are non-constant functions, then the system (1) has a unique equilibrium $(S_A^*, S_C^*, I_A^*, I_C^*, R_C^*) = (\frac{B_A}{\mu}, \frac{B_C}{\mu}, 0, 0, 0)$, which corresponds to the disease-free state.*

Proof Let $(S_A^*, S_C^*, I_A^*, I_C^*, R_C^*)$ denote an equilibrium point of the system (1). Thus, we have

$$\begin{aligned} 0 &= B_A - \beta_{AA}(t) I_A^* S_A^* - \mu S_A^* \\ 0 &= B_C - (\beta_{CC}(t) I_C^* + \beta_{AC}(t) I_A^*) S_C^* - \mu S_C^* \\ 0 &= I_A^* (\beta_{AA}(t) S_A^* - \mu) \\ 0 &= (\beta_{CC}(t) I_C^* + \beta_{AC}(t) I_A^*) S_C^* - \mu I_C^* - r I_C^* \\ 0 &= r I_C^* - \mu R_C^*. \end{aligned}$$

By the third equation, either $I_A^* = 0$ or $\beta_{AA}(t) S_A^* = \mu > 0$. The latter cannot hold since it implies $S_A^* \neq 0$ and thus $\beta_{AA}(t) = \mu / S_A^*$, which is not possible if $\beta_{AA}(t)$ is non-constant. Therefore, $I_A^* = 0$. Substituting this value in the fourth equation and following a similar reasoning, we find $I_C^* = 0$. Substituting these in the remaining equations, we obtain $(S_A^*, S_C^*, I_A^*, I_C^*, R_C^*) = (B_A/\mu, B_C/\mu, 0, 0, 0)$. \square

We associate the outbreaks of the disease as deviations from the disease-free state, and to analyse them we consider the linear variational equation for (1) around the unique equilibrium point $(S_A^*, S_C^*, I_A^*, I_C^*, R_C^*) = (B_A/\mu, B_C/\mu, 0, 0, 0)$. To this end, we denote deviations from the equilibrium values by $\Delta S_A = S_A - S_A^*$, $\Delta S_C = S_C - S_C^*$, $\Delta I_A = I_A - I_A^*$, $\Delta I_C = I_C - I_C^*$, and $\Delta R_C = R_C - R_C^*$. Then the linear variational equations are

$$\begin{aligned} \frac{d \Delta S_A}{dt} &= -\mu \Delta S_A - \beta_{AA}(t) \frac{B_A}{\mu} \Delta I_A \\ \frac{d \Delta S_C}{dt} &= -\mu \Delta S_C - \beta_{AC}(t) \frac{B_C}{\mu} \Delta I_A - \beta_{CC}(t) \frac{B_C}{\mu} \Delta I_C \\ \frac{d \Delta I_A}{dt} &= \left(\beta_{AA}(t) \frac{B_A}{\mu} - \mu \right) \Delta I_A \\ \frac{d \Delta I_C}{dt} &= \beta_{AC}(t) \frac{B_C}{\mu} \Delta I_A + \left(\beta_{CC}(t) \frac{B_C}{\mu} - \mu - r \right) \Delta I_C \\ \frac{d \Delta R_C}{dt} &= r \Delta I_C - \mu \Delta R_C, \end{aligned} \tag{13}$$

or, equivalently, in matrix form

$$\frac{d}{dt} \Delta = J^*(t) \Delta,$$

where $\Delta = [\Delta S_A \ \Delta S_C \ \Delta I_A \ \Delta I_C \ \Delta R_C]^\top$ and

$$J^*(t) = \begin{bmatrix} -\mu & 0 & -\beta_{AA}(t) \frac{B_A}{\mu} & 0 & 0 \\ 0 & -\mu & -\beta_{AC}(t) \frac{B_C}{\mu} & -\beta_{CC}(t) \frac{B_C}{\mu} & 0 \\ 0 & 0 & \beta_{AA}(t) \frac{B_A}{\mu} - \mu & 0 & 0 \\ 0 & 0 & \beta_{AC}(t) \frac{B_C}{\mu} & \beta_{CC}(t) \frac{B_C}{\mu} - \mu - r & 0 \\ 0 & 0 & 0 & r & -\mu \end{bmatrix}.$$

We note that the eigenvalues of J^* are $\lambda_{1,2,5} = -\mu$, $\lambda_3(t) = \beta_{AA}(t) \frac{B_A}{\mu} - \mu$, and $\lambda_4(t) = \beta_{CC}(t) \frac{B_C}{\mu} - \mu - r$. The time-dependent eigenvalues $\lambda_3(t)$ and $\lambda_4(t)$ are precisely the quantities defined in (7) and (12), and they play an important role in the stability of the equilibrium, as we will see below.

The solution to the linear variational system (13) can be written as

$$\begin{aligned} \Delta S_A(t) &= \Delta S_A(0) e^{-\mu t} \\ &\quad - \frac{B_A}{\mu} \int_0^t e^{-\mu(t-\tau)} \beta_{AA}(\tau) \Delta I_A(\tau) d\tau \end{aligned} \tag{14a}$$

$$\begin{aligned} \Delta S_C(t) &= \Delta S_C(0) e^{-\mu t} \\ &\quad - \frac{B_C}{\mu} \int_0^t e^{-\mu(t-\tau)} \left(\beta_{AC}(\tau) \Delta I_A(\tau) \right. \\ &\quad \left. + \beta_{CC}(\tau) \Delta I_C(\tau) \right) d\tau \end{aligned} \tag{14b}$$

$$\Delta I_A(t) = \Delta I_A(0) \cdot \eta_3(t) \tag{14c}$$

$$\begin{aligned} \Delta I_C(t) &= \Delta I_C(0) \cdot \eta_4(t) \\ &\quad + \frac{B_C}{\mu} \int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{\eta_4(t)}{\eta_4(\tau)} d\tau \end{aligned} \tag{14d}$$

$$\begin{aligned} \Delta R_C(t) &= \Delta R_C(0) e^{-\mu t} \\ &\quad + r \int_0^t e^{-\mu(t-\tau)} \Delta I_A(\tau) d\tau. \end{aligned} \tag{14e}$$

where the positive functions η_3 and η_4 are defined by

$$\eta_3(t) = \exp \left\{ \int_0^t \lambda_3(\tau) d\tau \right\}$$

$$\eta_4(t) = \exp \left\{ \int_0^t \lambda_4(\omega) d\omega \right\}.$$

We investigate the conditions under which the perturbations Δ around the equilibrium go to zero. The next lemma shows that the question can be reduced to a consideration of only the pair $(\Delta I_A, \Delta I_C)$.

Lemma 4.2 $\lim_{t \rightarrow \infty} \Delta(t) = \mathbf{0}$ if and only if $\lim_{t \rightarrow \infty} \Delta I_A(t) = \lim_{t \rightarrow \infty} \Delta I_C(t) = 0$.

Proof If $\Delta \rightarrow \mathbf{0}$, then ΔI_A and ΔI_C clearly go to zero, being components of Δ . To prove the other direction, let $\Delta N_A(t) = \Delta S_A(t) + \Delta I_A(t)$, $\Delta N_C(t) = \Delta S_C(t) + \Delta I_C(t) + \Delta R_C(t)$, and $\Delta N(t) = \Delta N_A(t) + \Delta N_C(t)$. Then from (13),

$$\begin{aligned} \frac{d \Delta N_A}{dt} &= -\mu \Delta N_A, & \frac{d \Delta N_C}{dt} &= -\mu \Delta N_C, \\ \frac{d \Delta N}{dt} &= -\mu \Delta N, \end{aligned}$$

yielding

$$\begin{aligned} \Delta N_A(t) &= \Delta N_A(0) e^{-\mu t}, & \Delta N_C(t) &= \Delta N_C(0) e^{-\mu t}, \\ \Delta N(t) &= \Delta N(0) e^{-\mu t}. \end{aligned}$$

Thus, $\Delta N_A(t)$, $\Delta N_C(t)$, and $\Delta N(t)$ go to zero as $t \rightarrow \infty$.

Now assume that both ΔI_A and ΔI_C go to 0 as $t \rightarrow \infty$. Then $\Delta S_A \rightarrow 0$ since $\Delta S_A = \Delta N_A - \Delta I_A$ and both terms on the right go to zero. Similarly, $\Delta S_C \rightarrow 0$ since $\Delta S_C = \Delta N_C - \Delta I_C - \Delta R_C$ and each term on the right goes to zero. To show that $\Delta R_C \rightarrow 0$ as $t \rightarrow \infty$, we compute the limit from (14e) using L'Hospital's rule:

$$\begin{aligned} \lim_{t \rightarrow \infty} \Delta R_C(t) &= \lim_{t \rightarrow \infty} \left[\Delta R_C(0) e^{-\mu t} \right. \\ &\quad \left. + e^{-\mu t} \int_0^t r e^{\mu \tau} \Delta I_A(\tau) d\tau \right] \\ &= \lim_{t \rightarrow \infty} \frac{\int_0^t r e^{\mu \tau} \Delta I_A(\tau) d\tau}{e^{\mu t}} \\ &= \lim_{t \rightarrow \infty} \frac{r e^{\mu t} \Delta I_A(t)}{\mu e^{\mu t}} \\ &= \lim_{t \rightarrow \infty} \frac{r}{\mu} \Delta I_A(t) = 0. \end{aligned}$$

Hence, $\Delta \rightarrow \mathbf{0}$ since all of its components go to zero. □

On the basis of the above lemma, we focus on the conditions that yield $\lim_{t \rightarrow \infty} \Delta I_A(t) = 0$ and

$\lim_{t \rightarrow \infty} \Delta I_C(t) = 0$. The first limit is straightforward, as (14c) implies that a necessary and sufficient condition for $\Delta I_A(t) \rightarrow 0$ is that $\int_0^\infty \lambda_3(t) dt = -\infty$. The case for $\Delta I_C(t) \rightarrow 0$ is more involved: by (14d) it can be seen that a similar condition $\int_0^\infty \lambda_4(t) dt = -\infty$ is only a necessary condition for $\Delta I_C(t) \rightarrow 0$ but not a sufficient one. A full characterization of stability therefore requires consideration of additional conditions. Below we list several relevant conditions and investigate their implications for stability.

- (C1) $\int_0^\infty \lambda_3(t) dt = \int_0^\infty (\beta_{AA}(t) \frac{B_A}{\mu} - \mu) dt = -\infty$.
- (C2) $\int_0^\infty \lambda_4(t) dt = \int_0^\infty (\beta_{CC}(t) \frac{B_C}{\mu} - \mu - r) dt = -\infty$.
- (C3) There exists $M > 0$ such that $\lambda_4(t) = \beta_{CC}(t) \frac{B_C}{\mu} - \mu - r \leq -M$ for $t \geq 0$.
- (C4) There exists $a > 0$ such that $a\beta_{AC}(t) \leq \beta_{AA}(t) \frac{B_A}{\mu} - \beta_{CC}(t) \frac{B_C}{\mu} + r$ for $t \geq 0$, or equivalently $a\beta_{AC}(t) \leq \lambda_3(t) - \lambda_4(t)$ for $t \geq 0$.

As noted above, the first two conditions (C1)–(C2) are necessary for the stability of equilibrium solution, which we state as a theorem.

Theorem 4.3 *The disease-free equilibrium of the non-autonomous system (1) is unstable if either (C1) or (C2) fails to hold.*

Proof If either (C1) or (C2) does not hold, then the variations $\Delta I_A(t) \not\rightarrow 0$ or $\Delta I_C(t) \not\rightarrow 0$ since the exponential terms in (14c) or (14d) do not tend to zero, and the result follows from Lemma 4.2. \square

For the remainder of this section, we focus on the local stability of the unique equilibrium solution of (1), in the sense of stability of the zero solution of the linear variational equation (13).

Theorem 4.4 *Suppose the condition (C1) holds. Then all solutions of the variational equation (13) decay to zero if either of the conditions (C3) or (C4) holds.*

Proof Condition (C1) guarantees that $\Delta I_A(t) \rightarrow 0$ by (14c). By Lemma 4.2, it suffices to show $\Delta I_C(t) \rightarrow 0$. We consider the limit under each of the conditions (C3) and (C4) separately.

i) If (C3) holds, then $\int_0^\infty \lambda_4(t) dt \leq \int_0^\infty -M dt = -\infty$, so the first term on the right-hand side of (14d) goes to zero. For the remaining term, the limit is cal-

culated using L’Hôpital’s rule as

$$\begin{aligned} & \lim_{t \rightarrow \infty} \frac{\int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} d\tau}{\exp \left\{ -\int_0^t \lambda_4(\tau) d\tau \right\}} \\ &= \lim_{t \rightarrow \infty} \frac{\beta_{AC}(t) \Delta I_A(t) \frac{B_C}{\mu} e^{-\int_0^t \lambda_4(w) dw}}{-\lambda_4(t) \cdot \exp \left\{ -\int_0^t \lambda_4(\tau) d\tau \right\}} \\ &= \lim_{t \rightarrow \infty} \frac{\beta_{AC}(t) \Delta I_A(t) \frac{B_C}{\mu}}{-\lambda_4(t)} = 0, \end{aligned}$$

showing that $\Delta I_C(t) \rightarrow 0$.

ii) If (C4) holds, then $\lambda_3(t) - \lambda_4(t) \geq 0$ since a is positive and β_{AC} is non-negative. Therefore, $\int_0^\infty \lambda_4(t) dt \leq \int_0^\infty \lambda_3(t) dt = -\infty$ by (C1). This yields $\int_0^\infty \lambda_4(t) dt = -\infty$, i.e. the condition (C2). Thus, the first term on the right-hand side of (14d) goes to zero. Now, using (14c) and (C4), we write the integral in the second term of (14d) as

$$\begin{aligned} & \int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} \\ &= \Delta I_A(0) \frac{B_C}{\mu} \int_0^t \beta_{AC}(\tau) e^{\int_0^\tau [\lambda_3(w) - \lambda_4(w)] dw} d\tau \\ &\leq \frac{\Delta I_A(0) B_C}{a\mu} \int_0^t (\lambda_3(\tau) - \lambda_4(\tau)) e^{\int_0^\tau [\lambda_3(w) - \lambda_4(w)] dw} d\tau \\ &= \frac{\Delta I_A(0) B_C}{a\mu} \left(e^{\int_0^t [\lambda_3(w) - \lambda_4(w)] dw} - 1 \right). \end{aligned}$$

Hence, the second term on the right-hand side of (14d) is bounded above by

$$\frac{\Delta I_A(0) B_C}{a\mu} \left(\exp \left\{ \int_0^t \lambda_3(\tau) d\tau \right\} - \exp \left\{ \int_0^t \lambda_4(\tau) d\tau \right\} \right),$$

which goes to zero as $t \rightarrow \infty$ since (C1) and (C2) hold. Hence, $\Delta I_C(t) \rightarrow 0$. \square

We now establish stability criteria in terms of average quantities. Recall that if $f : [0, \infty) \rightarrow \mathbb{R}$ is integrable on $[0, t]$ for all $t > 0$, then the average of f is the (extended) real number defined by

$$\bar{f} := \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f(\tau) d\tau. \tag{15}$$

If f is a T -periodic function, then its average (15) can be calculated over one period:

$$\bar{f} = \frac{1}{T} \int_0^T f(t) dt. \tag{16}$$

Useful results about averages are summarized in Appendix.

We list further conditions in terms of averages that play a role in stability.

- (C5) $\bar{\beta}_{AA} < \frac{\mu^2}{B_A}$ and $\bar{\beta}_{CC} < \frac{\mu(\mu+r)}{B_C}$, or equivalently, $\bar{\lambda}_3 < 0$ and $\bar{\lambda}_4 < 0$.
- (C6) $\int_0^t (\beta_{CC}(\tau) - \bar{\beta}_{CC}) d\tau$, or equivalently $\int_0^t (\lambda_4(\tau) - \bar{\lambda}_4) d\tau$, is bounded for $t \geq 0$.
- (C7) $\bar{\beta}_{AA} \frac{B_A}{\mu} < \bar{\beta}_{CC} \frac{B_C}{\mu} - r < \mu$, or equivalently, $\bar{\lambda}_3 < \bar{\lambda}_4 < 0$.

Theorem 4.5 *All solutions of the variational equation (13) decay to zero if either (C7) holds, or else both (C5) and (C6) hold together.*

Proof In both cases $\Delta I_A(t) \rightarrow 0$, so by Lemma 4.2 it suffices to show that $\Delta I_C(t) \rightarrow 0$. Now the first term on the right-hand side of (14d) goes to zero by Lemma A.3. It remains to show that the second term

$$\exp \left\{ \int_0^t \lambda_4(\tau) d\tau \right\} \cdot \int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} d\tau \quad (17)$$

goes to zero as well, which we will establish under each of the given assumptions.

i) Suppose both (C5) and (C6) hold. Multiplying and dividing the expression (17) by $e^{-\bar{\lambda}_4 t}$ gives

$$\frac{\underbrace{\exp \left\{ \int_0^t (\lambda_4(\tau) - \bar{\lambda}_4) d\tau \right\}}_{\text{bounded by (C6)}} \cdot \int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} d\tau}{e^{-\bar{\lambda}_4 t}}$$

Taking the limit for the fraction using L'Hospital's rule yields

$$\begin{aligned} & \lim_{t \rightarrow \infty} \frac{\int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} d\tau}{e^{-\bar{\lambda}_4 t}} \\ &= \lim_{t \rightarrow \infty} \frac{\beta_{AC}(t) \Delta I_A(t) \frac{B_C}{\mu} e^{-\int_0^t \lambda_4(w) dw}}{-\bar{\lambda}_4 \cdot e^{-\bar{\lambda}_4 t}} \\ &= \lim_{t \rightarrow \infty} \underbrace{e^{\int_0^t \bar{\lambda}_4 - \lambda_4(\tau) d\tau}}_{\text{bounded by (C6)}} \frac{1}{-\bar{\lambda}_4} \frac{B_C}{\mu} \beta_{AC}(t) \Delta I_A(t) \\ &= 0, \end{aligned}$$

which shows the expression (17) goes to zero. Therefore, $\Delta I_C(t) \rightarrow 0$.

ii) Suppose (C7) holds. Note that $\beta_{AC}(t)$ is bounded. Using (14c) in expression (17) gives

$$\begin{aligned} & \int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} d\tau \\ &= \Delta I_A(0) \frac{B_C}{\mu} \int_0^t \beta_{AC}(\tau) e^{\int_0^\tau \lambda_3(w) - \lambda_4(w) dw} d\tau \\ &\leq K \int_0^t e^{\int_0^\tau \lambda_3(w) - \lambda_4(w) dw} d\tau \end{aligned}$$

for some $K > 0$. If we let $f(t) = \lambda_3(t) - \lambda_4(t)$, then $\bar{f} = \bar{\lambda}_3 - \bar{\lambda}_4 < 0$ by (C7), and using Lemma A.4 we observe boundedness of the left-hand side of the above inequality. Thus, expression (17) has the bound

$$\begin{aligned} & e^{\int_0^t \lambda_4(\tau) d\tau} \int_0^t \beta_{AC}(\tau) \Delta I_A(\tau) \frac{B_C}{\mu} e^{-\int_0^\tau \lambda_4(w) dw} d\tau \\ &\leq K N e^{\int_0^t \lambda_4(\tau) d\tau} \end{aligned}$$

for some $K, N > 0$, which goes to zero by Lemma A.3. Therefore, $\Delta I_C(t) \rightarrow 0$. \square

Finally, in case of periodic transmission functions, we can give a simple and sharp criterion for stability in terms of averages.

Theorem 4.6 *Suppose $\beta_{AA}(t)$ and $\beta_{CC}(t)$ are periodic functions. Then the origin of the variational equation (13) is asymptotically stable if and only if (C5) holds.*

Proof If $\beta_{CC}(t)$ is periodic, then (C6) is satisfied by Lemma A.5. Therefore, if (C5) holds then stability follows by Theorem 4.5. On the other hand, if (C5) does not hold, then either (C1) or (C2) does not hold by Lemmas A.3 and A.7, and instability follows by Theorem 4.3. \square

To summarize, considering outbreaks as small deviations from the disease-free equilibrium state of the system, we have constructed the linear variational Eq. (13) around the disease-free equilibrium for the model (1) and analysed the non-autonomous system. This approach is not only specific to epidemiological models but can also be used for compartmental models representing various dynamical processes in various disciplines like sociology, chemistry, finance etc.

5 Note on the basic reproduction number under time-dependent transmission

In autonomous epidemic models, the basic reproduction number \mathcal{R}_0 is commonly defined as the number of secondary infections that result from the introduction of a single infectious individual into an entirely susceptible population [39], and is typically associated with the local stability of the equilibria via the method of next-generation matrix [40]. However, this standard definition of \mathcal{R}_0 is no longer applicable in periodic environments [41]. One of the earliest works for the case of time-dependent systems is [42], where the authors approximate the basic reproduction number for a periodically transmitted disease model. This work and its followers revealed that a general explicit formula for \mathcal{R}_0 does not exist under seasonal dynamics [43–45]. Moreover, in numerical simulations large outbreaks have been observed even when \mathcal{R}_0 was below the threshold value 1 [46,47]. Since then, the computation and interpretation of an appropriate formula for \mathcal{R}_0 for non-autonomous systems have attracted much attention [34,48,49].

The derivation of the basic reproduction number is based on the linearization of the ODE model about a disease-free equilibrium, and is therefore directly related to the analysis of Sect. 4. Hence, considering only the infected compartments, let the matrices F and V denote, as usual, the rate at which secondary infections increase the compartment size and the net outflow from the compartment, respectively. Hence, for the model (1),

$$F(t) = \begin{bmatrix} \beta_{AA}(t) \frac{B_A}{\mu} & 0 \\ \beta_{AC}(t) \frac{B_C}{\mu} & \beta_{CC}(t) \frac{B_C}{\mu} \end{bmatrix}$$

and

$$V(t) = \begin{bmatrix} \mu & 0 \\ 0 & \mu + r \end{bmatrix}$$

and the next-generation matrix $M = FV^{-1}$ is given by

$$M(t) = \begin{bmatrix} \beta_{AA}(t) \frac{B_A}{\mu^2} & 0 \\ \beta_{AC}(t) \frac{B_C}{\mu^2} & \beta_{CC}(t) \frac{B_C}{\mu(\mu + r)} \end{bmatrix}.$$

In autonomous systems, the basic reproduction number is defined as the dominant eigenvalue of the next-

generation matrix M . In our case, $M(t)$ and its eigenvalues are time dependent. We denote the eigenvalues as

$$\Lambda_3(t) = \beta_{AA}(t) \frac{B_A}{\mu^2} \quad \text{and} \quad \Lambda_4(t) = \beta_{CC}(t) \frac{B_C}{\mu(\mu + r)}.$$

The reason for the notation is that these eigenvalues are directly related to the two eigenvalues (7) and (12) that are responsible for the stability of the disease-free equilibrium, namely

$$\lambda_3(t) = \mu(\Lambda_3(t) - 1) \quad \text{and} \quad \lambda_4(t) = (\mu + r)(\Lambda_4(t) - 1).$$

Therefore, $\lambda_3 < 0$ (resp., $\lambda_4 < 0$) if and only if $\Lambda_3 < 1$ (resp., $\Lambda_4 < 1$), and conditions (C1)–(C4) can be readily expressed in terms of the eigenvalues Λ_3, Λ_4 of the next-generation matrix.

To obtain a single quantity that can play the role of the basic reproduction number, it is thus natural to consider time averages, in the sense of (15). Hence, the mean next-generation matrix is $\bar{M} = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t M(\tau) d\tau$ and has eigenvalues

$$\bar{\Lambda}_3 = \bar{\beta}_{AA} \frac{B_A}{\mu^2} \quad \text{and} \quad \bar{\Lambda}_4 = \bar{\beta}_{CC} \frac{B_C}{\mu(\mu + r)},$$

which are related to the time averages of the Jacobian eigenvalues by

$$\bar{\lambda}_3 = \mu(\bar{\Lambda}_3 - 1) \quad \text{and} \quad \bar{\lambda}_4 = (\mu + r)(\bar{\Lambda}_4 - 1). \quad (18)$$

The conditions (C5)–(C7) for the stability of the disease-free equilibrium are then immediately available in terms of $\bar{\Lambda}_{3,4}$. A mean basic reproduction number $\bar{\mathcal{R}}_0$ can be defined as the spectral radius of \bar{M} , that is,

$$\begin{aligned} \bar{\mathcal{R}}_0 &= \max\{|\bar{\Lambda}_3|, |\bar{\Lambda}_4|\} \\ &= \max \left\{ \bar{\beta}_{AA} \frac{B_A}{\mu^2}, \bar{\beta}_{CC} \frac{B_C}{\mu(\mu + r)} \right\}. \end{aligned} \quad (19)$$

For periodic transmission functions, the relation of $\bar{\mathcal{R}}_0$ to stability is sharp by Theorem 4.6, which we state as a corollary.

Corollary 5.1 *Suppose $\beta_{AA}(t)$ and $\beta_{CC}(t)$ are periodic functions. Then the disease-free equilibrium is locally asymptotically stable if and only if $\bar{\mathcal{R}}_0 < 1$.*

The situation is less clear-cut for non-periodic transmission functions. As Theorem 4.5 indicates, condition (C5), i.e. $\bar{\mathcal{R}}_0$ being less than 1, may not be enough for the stability of the disease-free state, unless condition

(C6) holds as well. Indeed, the sufficient condition (C7) shows that both eigenvalues, and not just the dominant eigenvalue, may have a role in stability. More precisely, using (18), condition (C7) can be expressed as

$$\frac{\bar{\Lambda}_4 - \bar{\Lambda}_3}{1 - \bar{\Lambda}_4} > \frac{r}{\mu}$$

when $\bar{\mathcal{R}}_0 < 1$, which is the condition that $\bar{\Lambda}_4$ be larger than $\bar{\Lambda}_3$ by an amount that depends on the ratio r/μ . Hence, there may be subtler cases when the condition $\bar{\mathcal{R}}_0 < 1$ by itself does not suffice to guarantee the stability of the disease-free equilibrium. On the other hand, $\bar{\mathcal{R}}_0 > 1$ is always a marker of instability.

Corollary 5.2 *If $\bar{\mathcal{R}}_0 > 1$, then the disease-free equilibrium is unstable.*

Proof If $\bar{\mathcal{R}}_0 > 1$, then either $\bar{\lambda}_3$ or $\bar{\lambda}_4$ is positive by (18), in which case Lemma A.3 implies that either $\int_0^\infty \lambda_3(t) dt = \infty$ or $\int_0^\infty \lambda_4(t) dt = \infty$. The result then follows by Theorem 4.3. \square

6 Numerical simulations

To visualize the dynamical behaviour of the mathematical model (1) in the light of the theoretical results obtained from mathematical analysis, we perform numerical simulations using the standard Matlab routines for solving systems of differential equations [50]. Although local and international outbreaks of IMD have been strictly associated with Umrah/Hajj travel in different studies, data on IMD are still sparse or lacking in the Eastern Mediterranean and North Africa regions [14,51,52]. For this reason, we cannot fit the model (1) to a particular data set, but we use the findings from different studies when choosing the model parameters. While there are gaps in the available statistical data, the reality is that Hajj, one of the world's largest mass movements and gatherings of people, is directly related to a variety of health problems, including the seasonal outbreaks of infectious diseases. The World Bank classifies the countries in the African meningitis belt as low-middle income countries. Since we have noted seasonal outbreaks of IMD outside the meningitis belt, we perform our simulations for a hypothetical upper-middle income country.

Dogu et al. [14] presented a recent review of available IMD data by scanning the literature between January 2000–February 2021. Based on 11 different studies, they report that the rates of asymptomatic carriage

Table 1 Parameters of the model (1)

Parameters	Value	Units	Source
B_A	1	year ⁻¹	Assumed
B_C	13.1	year ⁻¹	[60]
μ	0.0132	year ⁻¹	[58]
r	26.06	year ⁻¹	[59]

in the pilgrim risk group range from 0.0% [53,54] to 27.4% [18]. The IMD incidence in the general population ranges from 0 to 20.5/100,000 in children aged under 5 years [14]. The most recent study among them refers to a data set from Turkey and indicates an incidence of 0.9/100,000 [55]. Another recent study from Morocco points out an incidence of 3.75/100,000 for children aged under 18 years [56]. From the perspective of mathematical models, the transmission rate β of IMD among the whole population is estimated between 0.137–0.548 per day [24,57]. As a matter of fact, it is statistically difficult to assign a transmission rate specific to age groups. We assume that the average values of transmission parameters (β_{AA} , β_{AC} , β_{CC}) remain in the interval [0.00005,0.05]. To estimate the natural death rate μ , we use the World Bank data, according to which the average life expectancy at birth varies from 64 years in low-income countries to 81 years in high-income countries. Therefore, in the numerical simulations, we take the life expectancy for an upper-middle income country [58] as $\mu = \frac{1}{76} \frac{1}{\text{year}}$. For the recovery rate r , we use the value $26.06 \frac{1}{\text{year}}$, based on the fact that recovery from bacterial meningitis in infants and children takes approximately 14 days [59].

The Saudi government has established a Hajj visa quota of 1 pilgrim per 1000 people for each Muslim country since 1987 [61]. Let us assume a hypothetical upper-middle income country with a total population number of 1000. Only 1 person per year from this country would go to Hajj and come back home; therefore, we take $B_A = 1$. For the remaining parameters, we use the available data set of a specific upper-middle income country (Turkey) in order to have more precise values. Thus, the number of yearly births is chosen to be 13.1 in a population of 1000 people and the initial population $S_A(0) = 734$ and $S_C(0) = 265$ according to the percentage of young people aged under 18 in Turkey [60].

To visualize the results of Sect. 4, we create three different scenarios for various choice of the transmission functions where we mainly focus on their average values. We study the short-and long-term behaviour of outbreaks by taking the average values of transmission functions $\beta_{AA}(t)$, $\beta_{CC}(t)$ and $\beta_{AC}(t)$ equal and in the range $[0.00005, 0.05]$ for different types of transmission functions.

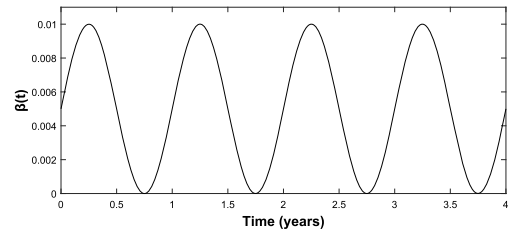
The choices of transmission functions represent the model in three possible scenarios, see Fig. 2. In scenario 1, we employ periodic transmission functions $\beta_{AA}(t)$, $\beta_{CC}(t)$, and $\beta_{AC}(t)$ with a sinusoidal shape (Fig. 2a) that may represent a yearly outbreak caused by the seasonal transmission after the annual Hajj pilgrimage. In scenario 2, we choose a discontinuous periodic transmission function in the form of $\beta(t) = 2\bar{\beta}H(1/2 - t + \lfloor t \rfloor)$, where $H(t)$ is the Heaviside function with $H(0) = 1$ and $\lfloor t \rfloor$ is the floor function (Fig. 2b), that may correspond to the behaviour of an outbreak after an Umrah-like intermittent movement of people. In scenario 3, we consider more general non-periodic transmission functions (Fig. 2c) that may describe irregular mass movements such as migration.

In the following simulations, we manipulate the average values of $\bar{\beta}_{AA}$, $\bar{\beta}_{CC}$, and $\bar{\beta}_{AC}$ in the interval $[0.00005, 0.05]$ to get different signs of $\bar{\lambda}_3$ and $\bar{\lambda}_4$, which are markers of stability according to theorems 4.4–4.3. Table 2 summarizes the organization of the simulations.

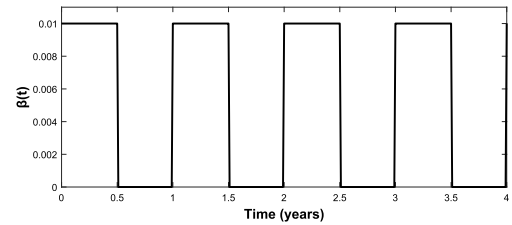
7 Conclusion

Bacterial meningitis shows various seasonal patterns outside of the African meningitis belt, which consists of a group of countries in sub-Saharan Africa where major epidemics occur every few years [62, 63]. Increased incidences in Europe, Middle East, Australia, and America are often associated with Hajj, Umrah, or other mass gatherings [64]. Indeed, over two million Muslims visit Mecca every year in the Hajj season where all pilgrims stay in close contact for a long time period [13]. Furthermore, the role of migrants and refugees in the spread of bacterial meningitis has been highlighted under current global conditions [65]. Based on the seriousness of the issue, the World Health Organization (WHO) has put forward a roadmap to defeat meningitis by 2030.

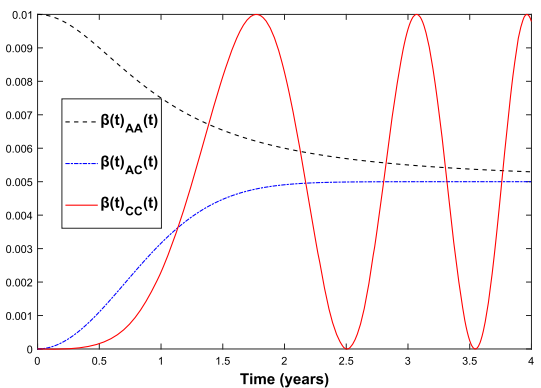
In this paper, we have presented and analysed a mathematical model (1) to understand the seasonal out-



(a) $\beta(t) = \bar{\beta}(1 + \sin(2\pi t))$ is a sinusoidal periodic function with period $T = 1$.



(b) $\beta(t) = 2\bar{\beta}H(1/2 - t + \lfloor t \rfloor)$ where H is the Heaviside function and $\lfloor t \rfloor$ is the floor function.



(c) $\beta_{AA}(t) = \bar{\beta}_{AA}(1 + \cos(t^2))$, $\beta_{AC}(t) = \bar{\beta}_{AC}(1 - \sin(t \sin(t)))$, and $\beta_{CC}(t) = \bar{\beta}_{CC}(1 - 1/(1+t))$.

Fig. 2 The three categories of transmission functions used in the simulations

breaks of meningitis among adults and children by taking account the time-dependent transmission processes of IMD. Outbreaks are identified with deviations from the disease-free equilibrium state. Mathematical analysis of the model (1) shows that the long-time average values $\bar{\lambda}_3$ and $\bar{\lambda}_4$ of the time-dependent eigenvalues of the Jacobian matrix (4) determine the stability of the disease-free equilibrium. Thus, we are able to establish the average values $\bar{\lambda}_3$ and $\bar{\lambda}_4$ as “markers of stability.” Furthermore, stability is connected to a time-averaged basic reproduction number. In this

Table 2 Summary of the presentation of simulation results

Type of transmission function	$\bar{\lambda}_3$	$\bar{\lambda}_4$	Implications	Figure
Periodic sinusoidal transmission	+	-	Short-term and long-term existence of outbreak	Fig. 3
	-	-	Short-term periodic increase and long-term quenching of outbreak	Fig. 4
	+	+	Short-term periodic increase and long-term existence of outbreak	Fig. 5
	+	-	Short-term and long-term periodic existence of outbreak	Fig. 6
Periodic discontinuous transmission	-	-	Short-term periodic increase and long-term quenching of outbreak	Fig. 7
	+	+	Short-term periodic increase and long-term existence of outbreak	Fig. 8
	+	-	Short-term and long-term periodic existence of outbreak	Fig. 9
	-	-	Short-term periodic increase and long-term quenching of outbreak	Fig. 10
Non-periodic transmission	-	-	Short-term periodic increase and long-term quenching of outbreak	Fig. 10
	+	+	Short-term periodic increase and long-term existence of outbreak	Fig. 11

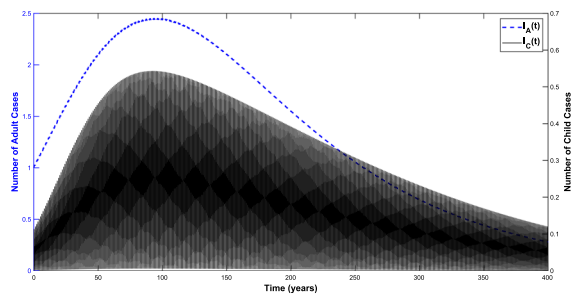
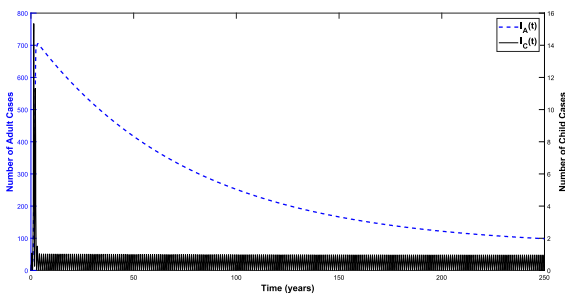
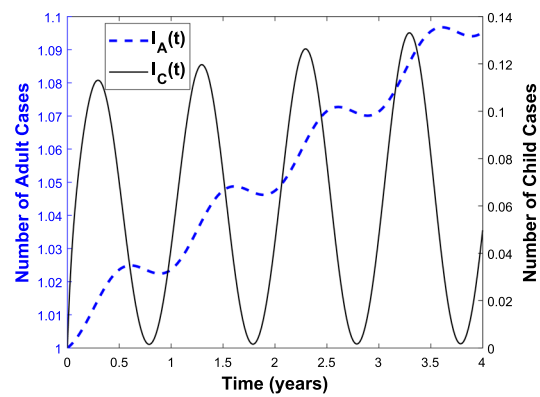
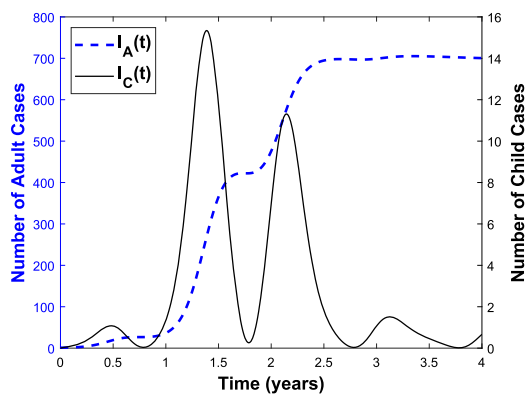


Fig. 3 $\bar{\beta}_{AA} = \bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.005$ ($\bar{\lambda}_3 = 0.3668$, $\bar{\lambda}_4 = -21.1066$)

Fig. 4 $\bar{\beta}_{AA} = 0.00005$, $\bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.005$ ($\bar{\lambda}_3 = -0.0094$, $\bar{\lambda}_4 = -21.1066$)

study, the time-dependent transmission rates $\beta_{AA}(t)$, $\beta_{AC}(t)$ and $\beta_{CC}(t)$ are taken as non-negative bounded functions in the most general sense. Thus, an advantageous model setup is presented which can also address the case where the transmission rates are non-periodic. However, in real-life problems, it may not be possible to determine the functions $\beta_{AA}(t)$, $\beta_{AC}(t)$ and $\beta_{CC}(t)$ in some cases. Being aware of this limitation, we have extracted the parameter values used in the numerical

simulations from real statistical data. Since the irregular migration process has a very complicated structure, and the data are not available, we have used some hypothetical functions to describe them. We hope that our results motivate more detailed research in this area to determine more realistic functional forms.

We have carried out numerical simulations to support our analysis via three different scenarios of time-varying transmission: periodic sinusoidal functions,

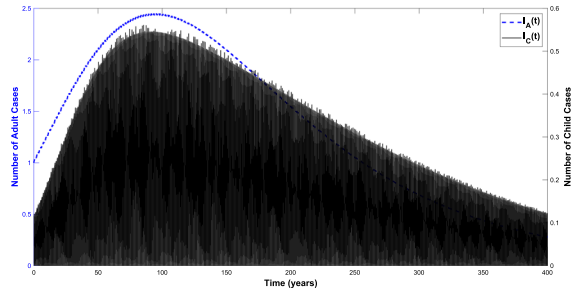
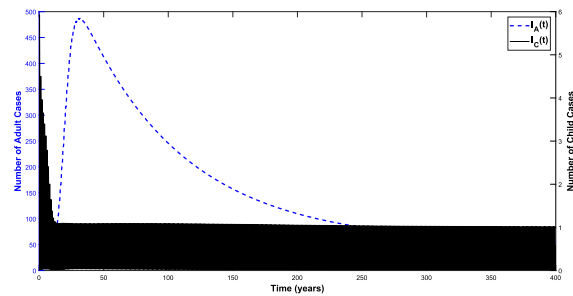
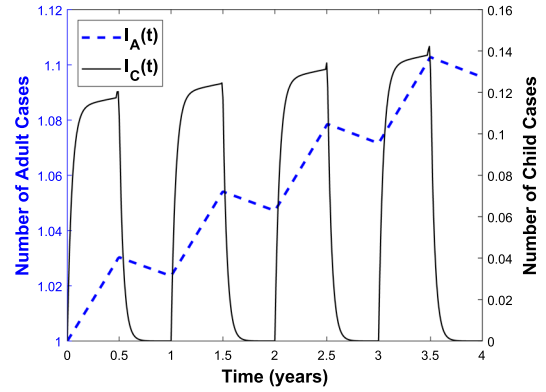
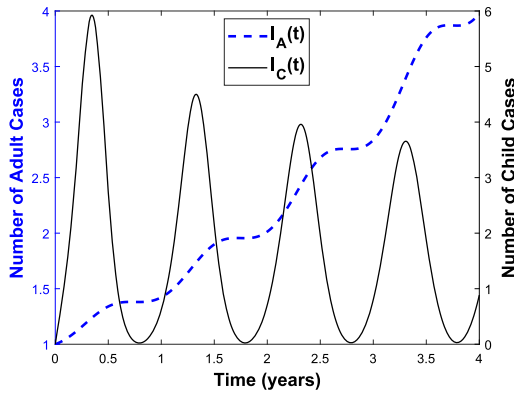


Fig. 5 $\bar{\beta}_{AA} = 0.0005, \bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.05$ ($\bar{\lambda}_3 = 0.0248, \bar{\lambda}_4 = 23.6954$)

Fig. 7 $\bar{\beta}_{AA} = 0.00005, \bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.005$ ($\bar{\lambda}_3 = -0.0094, \bar{\lambda}_4 = -21.1066$)

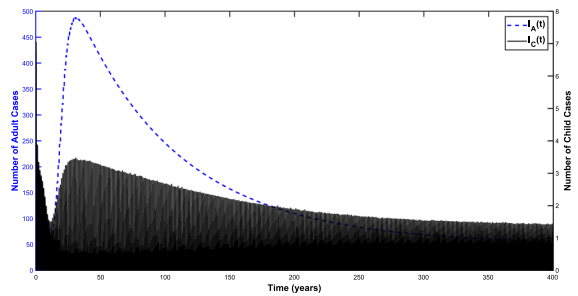
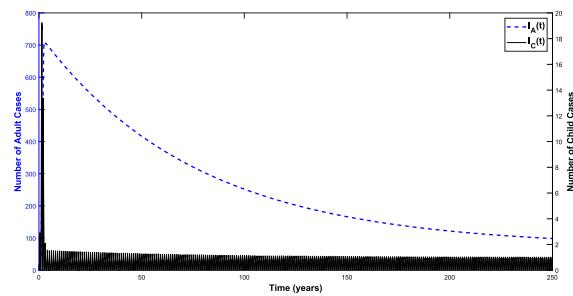
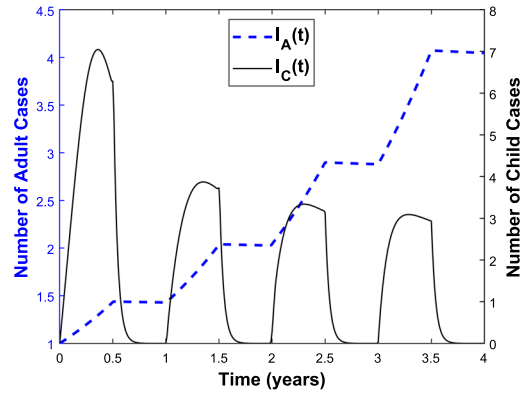
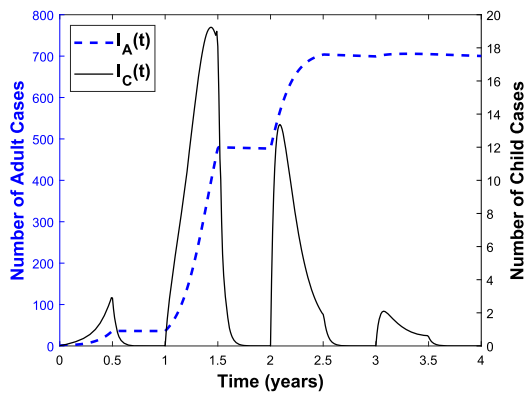


Fig. 6 $\bar{\beta}_{AA} = \bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.005$ ($\bar{\lambda}_3 = 0.3668, \bar{\lambda}_4 = -21.1066$)

Fig. 8 $\bar{\beta}_{AA} = 0.0005, \bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.05$ ($\bar{\lambda}_3 = 0.0248, \bar{\lambda}_4 = 23.6954$)

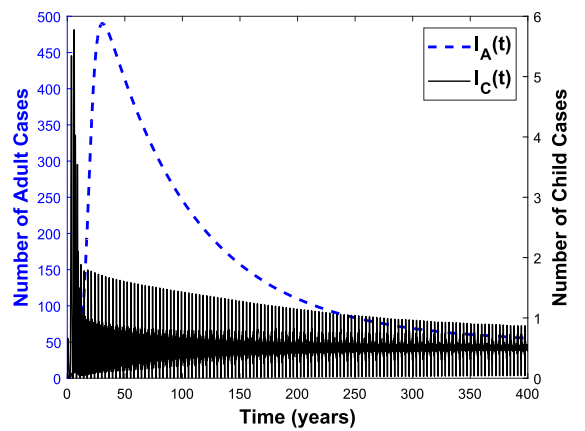
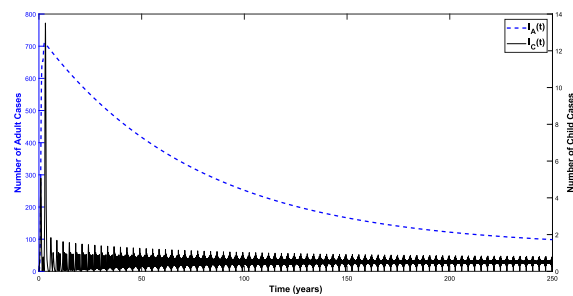
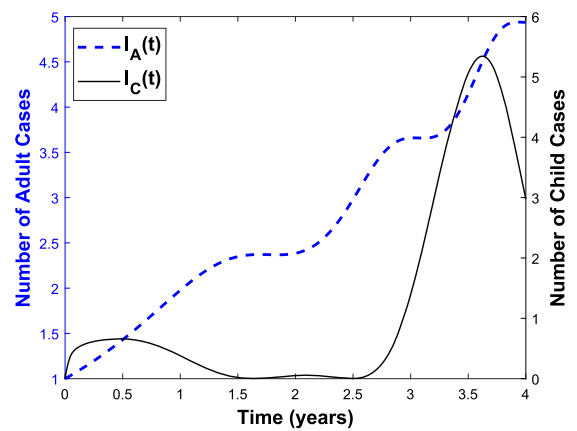
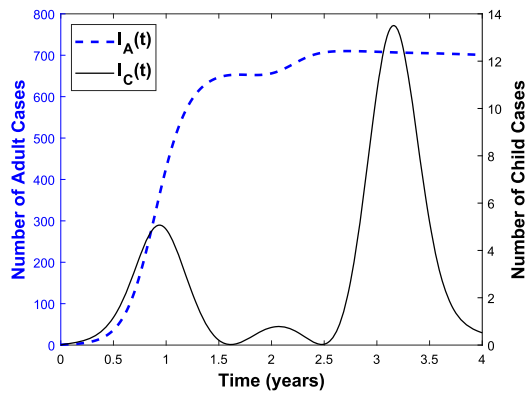


Fig. 9 $\bar{\beta}_{AA} = \bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.005$ ($\bar{\lambda}_3 = 0.3668$, $\bar{\lambda}_4 = -21.1066$)

Fig. 11 $\bar{\beta}_{AA} = 0.0005$, $\bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.05$ ($\bar{\lambda}_3 = 0.0248$, $\bar{\lambda}_4 = 23.6954$)

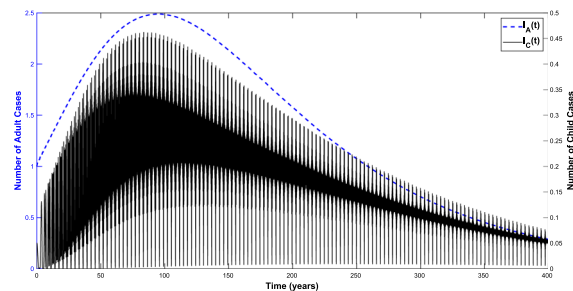
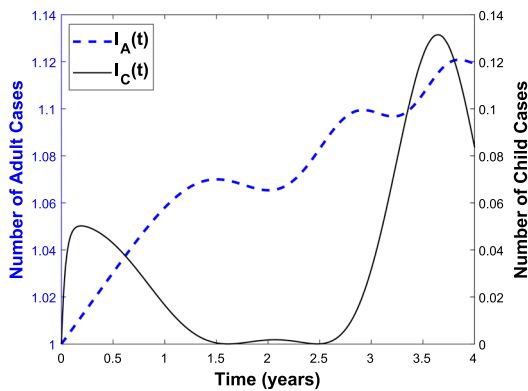


Fig. 10 $\bar{\beta}_{AA} = 0.00005$, $\bar{\beta}_{CC} = \bar{\beta}_{AC} = 0.005$ ($\bar{\lambda}_3 = -0.0094$, $\bar{\lambda}_4 = -21.1066$)

periodic discontinuous step functions, and arbitrary non-periodic functions. Periodic sinusoidal functions represent a seasonal transmission of the disease once a year as in the Hajj season, periodic step function represents the transmission rate during Umrah mass movement, and non-periodic functions represent irregular migration. Our methodology can also be applied to similar epidemiological and social processes that involve adult/children age groups and time-dependent transmission between them.

Author contributions All authors read and approved the final manuscript, and the authors contributed equally to this work.

Funding This research is supported by The Scientific and Technological Research Council of Turkey (TUBITAK) within the scope of the 1001-Scientific and Technological Research Project (119F162).

Data Availability Data sharing is not applicable to this article as no new dataset was created or analysed in this study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Appendix A: The average of a function

Let $f : [0, \infty) \rightarrow \mathbb{R}$ be integrable on $[0, t]$ for all $t > 0$. The average of f is the number defined by $\bar{f} := \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f(\tau) d\tau$, whenever the limit exists as an extended real number. We provide some properties about the average of a function.

Lemma A.1 *If $\int_0^t (f(\tau) - \alpha) d\tau$ is bounded for $t > 0$, then $\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f(\tau) d\tau = \alpha$.*

Proof Suppose $|\int_0^t f(\tau) - \alpha d\tau| \leq M$ for $t > 0$. Then $|\frac{1}{t} \int_0^t f(\tau) d\tau - \alpha| \leq M/t$ and letting $t \rightarrow \infty$ proves the result. \square

The converse of Lemma A.1 is not always true, that is, the existence of \bar{f} does not imply the boundedness of $\int_0^t (f(\tau) - \bar{f}) d\tau$. An example is provided by the function $f(x) = (x + 2)/(x + 1)$.

Lemma A.2 *If $\lim_{t \rightarrow \infty} f(t) = \alpha$ and $\int_0^t f(\tau) d\tau$ exists for $t > 0$, then $\bar{f} = \alpha$.*

Proof For a given $\epsilon > 0$, there is a $t_0 > 0$ such that $|f(x) - \alpha| < \epsilon/2$ for $t \geq t_0$. Let $I_\epsilon = \int_0^{t_0} |f(\tau) - \alpha| d\tau$ and $t_1 = 2I_\epsilon/\epsilon$. Then for all $t > \max\{t_0, t_1\}$,

$$\begin{aligned} \left| \frac{1}{t} \int_0^t f(\tau) d\tau - \alpha \right| &= \left| \frac{1}{t} \int_0^t (f(\tau) - \alpha) d\tau \right| \\ &\leq \frac{1}{t} \int_0^t |f(\tau) - \alpha| d\tau \\ &= \frac{1}{t} \int_0^{t_0} |f(\tau) - \alpha| d\tau + \frac{1}{t} \int_{t_0}^t |f(\tau) - \alpha| d\tau \\ &< \frac{1}{t} I_\epsilon + \frac{1}{t} \int_{t_0}^t \frac{\epsilon}{2} d\tau < \frac{\epsilon}{2} + \frac{t - t_0}{t} \frac{\epsilon}{2} < \epsilon, \end{aligned}$$

which completes the proof. \square

The converse of Lemma A.2 is not true, as the existence of \bar{f} does not necessarily imply that $f(t)$ has a limit as $t \rightarrow \infty$. (As an example, consider $f(t) = \sin t$.)

Lemma A.3 *If $\bar{f} > 0$ (resp., < 0), then $\int_0^\infty f(t) dt = \infty$ (resp., $-\infty$).*

Proof $\int_0^\infty f(t) dt = \lim_{t \rightarrow \infty} \int_0^t f(\tau) d\tau = \lim_{t \rightarrow \infty} t \left(\frac{1}{t} \int_0^t f(\tau) d\tau \right)$. \square

Here $\bar{f} = \pm\infty$ are also included, as the proof suggests.

Lemma A.4 *If $\bar{f} > 0$, then $\int_0^\infty \exp\{\int_0^t f(\tau) d\tau\} dt = \infty$. If $\bar{f} < 0$, then $\int_0^\infty \exp\{\int_0^t f(\tau) d\tau\} dt$ exists as a positive real number.*

Proof Limit comparison with the integral of $\exp(\bar{f}t/2)$ gives the result. \square

Here $\bar{f} = \pm\infty$ are also included, because in this case there exists $t_0 > 0$ such that for $t \geq t_0$, $\int_0^t f(\tau) d\tau > t$ or $\int_0^t f(\tau) d\tau < -t$, and the result follows from comparison with e^t or e^{-t} , respectively.

Lemma A.5 *If there is a $T > 0$ such that $f(t + T) = f(t)$ for $t \geq 0$ and $\frac{1}{T} \int_0^T f(t) dt = \alpha$, then the function defined by $g(t) := \int_0^t f(\tau) d\tau - \alpha t$ is continuous, T -periodic, and hence bounded on $[0, \infty)$.*

Proof Since f is integrable, $\int_0^t f(\tau) d\tau$ is continuous, and so is αt . Thus, g is continuous and

$$\begin{aligned} g(t + T) &= \int_0^{t+T} f(\tau) d\tau - \alpha(t + T) \\ &= \underbrace{\int_0^t f(\tau) d\tau - \alpha t}_{g(t)} + \underbrace{\int_t^{t+T} f(\tau) d\tau - \alpha T}_0 \\ &= g(t) \end{aligned}$$

so g is T -periodic. Hence, g is bounded on $[0, \infty)$, being continuous on $[0, T]$. \square

Corollary A.6 *If f is T -periodic and $\frac{1}{T} \int_0^T f(t) dt = \alpha$ then $\bar{f} = \alpha$.*

Proof $\int_0^t (f(\tau) - \alpha) d\tau$ is bounded by Lemma A.5 and the result follows by Lemma A.1. \square

In case f is a periodic function, we can be more precise when $\bar{f} = 0$ in Lemmas A.3 and A.4.

Lemma A.7 *Let f be T -periodic and $\int_0^T f(t) dt = 0$. Then $\int_0^\infty f(t) dt$ does not exist unless f is the zero function. Furthermore, $\int_0^\infty \exp\left\{\int_0^t f(\tau) d\tau\right\} dt = \infty$.*

Proof $g(t) := \int_0^t f(\tau) d\tau$ and $h(t) := \exp(g(t))$ are periodic by Lemma A.5 thus $g(t)$ cannot have a limit as $t \rightarrow \infty$ unless it is constant. Also, $\int_0^\infty h(t) dt = \lim_{n \rightarrow \infty} n \int_0^T h(t) dt = \infty$ since $h(t) > 0$ and T -periodic. \square

References

- Soeters, H.M., Diallo, A.O., Bicaba, B.W., et al.: Bacterial meningitis epidemiology in five countries in the meningitis belt of sub-Saharan Africa, 2015–2017. *J. Inf. Dis.* **220**(Supplement–4), 165–174 (2019). <https://doi.org/10.1093/infdis/jiz358>
- Parikh, S.R., Campbell, H., Bettinger, J.A., et al.: The ever-changing epidemiology of meningococcal disease worldwide and the potential for prevention through vaccination. *J. Infect.* **81**(4), 483–498 (2020). <https://doi.org/10.1016/j.jinf.2020.05.079>
- Berti, F., Romano, M.R., Micoli, F., Adamo, R.: Carbohydrate based meningococcal vaccines: past and present overview. *Glycoconj. J.* (2021). <https://doi.org/10.1007/s10719-021-09990-y>
- Yezli, S.: The threat of meningococcal disease during the Hajj and Umrah mass gatherings: a comprehensive review. *Travel Med. Infect. Dis.* **24**, 51–58 (2018). <https://doi.org/10.1016/j.tmaid.2018.05.003>
- Traore, Y., Tameklo, T.A., Njanpop-Lafourcade, B.-M., et al.: Incidence, seasonality, age distribution, and mortality of pneumococcal meningitis in Burkina Faso and Togo. *Clin. Infect. Dis.* **48**(s2), 181–189 (2009). <https://doi.org/10.1086/596498>
- Agier, L., Deroubaix, A., Martiny, N., et al.: Seasonality of meningitis in Africa and climate forcing: aerosols stand out. *J. R. Soc. Interface* **10**(79), 20120814 (2013). <https://doi.org/10.1098/rsif.2012.0814>
- Mazamay, S., Broutin, H., Bompangue, D., et al.: The environmental drivers of bacterial meningitis epidemics in the Democratic Republic of Congo, Central Africa. *PLOS Negl. Trop. Dis.* **14**(10), 0008634 (2020). <https://doi.org/10.1371/journal.pntd.0008634>
- Lingappa, J.R., Al-Rabeah, A.M., Hajjeh, R., et al.: Serogroup W-135 meningococcal disease during the Hajj, 2000. *Emerg. Infect. Dis.* **9**(6), 665–671 (2003). <https://doi.org/10.3201/eid0906.020565>
- GASTAT, K.o.S.A.: Hajj statistics 2019. Technical report, General Authority for Statistics (2020). <https://www.stats.gov.sa/en/28>
- Gautret, P., Benkouiten, S., Griffiths, K., Sridhar, S.: The inevitable Hajj cough: surveillance data in French pilgrims, 2012–2014. *Travel Med. Infect. Dis.* **13**(6), 485–489 (2015). <https://doi.org/10.1016/j.tmaid.2015.09.008>
- Wilder-Smith, A., Goh, K.T., Barkham, T., Paton, N.I.: Hajj-associated outbreak strain of *Neisseria meningitidis* Serogroup W135: estimates of the attack rate in a defined population and the risk of invasive disease developing in carriers. *Clin. Infect. Dis.* **36**(6), 679–683 (2003). <https://doi.org/10.1086/367858>
- Ceyhan, M., Anis, S., Htun-Myint, L., et al.: Meningococcal disease in the Middle East and North Africa: an important public health consideration that requires further attention. *Int. J. Infect. Dis.* **16**(8), 574–582 (2012). <https://doi.org/10.1016/j.ijid.2012.03.011>
- Alasmari, A., Houghton, J., Greenwood, B., et al.: Meningococcal carriage among Hajj pilgrims, risk factors for carriage and records of vaccination: a study of pilgrims to Mecca. *Trop. Med. Int. Health* (2021). <https://doi.org/10.1111/tmi.13546>
- Dogu, A.G., Oordt-Speets, A.M., Kessel-de Bruijn, F., et al.: Systematic review of invasive meningococcal disease epidemiology in the Eastern Mediterranean and North Africa region. *BMC Infect. Dis.* (2021). <https://doi.org/10.1186/s12879-021-06781-6>
- Badahdah, A.-M., Alghabban, F., Falemban, W., et al.: Meningococcal vaccine for Hajj pilgrims: compliance, predictors, and barriers. *Trop. Med. Infect. Dis.* **4**(4), 127 (2019). <https://doi.org/10.3390/tropicalmed4040127>
- Al-Tawfiq, J.A., Memish, Z.A.: The Hajj 2019 vaccine requirements and possible new challenges. *J. Epidemiol. Global Health* (2019). <https://doi.org/10.2991/jegh.k.190705.001>
- Wilder-Smith, A., Chow, A., Goh, K.T.: Emergence and disappearance of W135 meningococcal disease. *Epidemiol. Infect.* **138**(7), 976–978 (2009). <https://doi.org/10.1017/S095026880999104x>
- Ceyhan, M., Celik, M., Demir, E.T., et al.: Acquisition of meningococcal serogroup W-135 carriage in Turkish Hajj pilgrims who had received the quadrivalent meningococcal polysaccharide vaccine. *Clin. Vaccine Immunol.* **20**(1), 66–68 (2013). <https://doi.org/10.1128/cvi.00314-12>
- Tezer, H., Gülhan, B., Gişi, A.S., et al.: The impact of meningococcal conjugate vaccine (MenACWY-TT) on meningococcal carriage in Hajj pilgrims returning to Turkey. *Human Vaccines Immunother.* **16**(6), 1268–1271 (2019). <https://doi.org/10.1080/21645515.2019.1680084>
- Al-Shaery, A.M., Hejase, B., Tridane, A., et al.: Agent-based modeling of the Hajj rituals with the possible spread of COVID-19. *Sustainability* **13**(12), 6923 (2021). <https://doi.org/10.3390/su13126923>
- Shambour, M.K., Gutub, A.: Progress of IoT research technologies and applications serving Hajj and Umrah. *Arab. J. Sci. Eng.* (2021). <https://doi.org/10.1007/s13369-021-05838-7>
- Bernoulli, D., Blower, S.: An attempt at a new analysis of the mortality caused by smallpox and of the advantages of inoculation to prevent it. *Rev. Med. Virol.* **14**(5), 275–288 (2004). <https://doi.org/10.1002/rmv.443>
- Broutin, H., Philippon, S., Magny, G.C., et al.: Comparative study of meningitis dynamics across nine African countries: a global perspective. *Int. J. Health Geogr.* **6**(1), 29 (2007). <https://doi.org/10.1186/1476-072x-6-29>
- Irving, T.J., Blyuss, K.B., Colijn, C., Trotter, C.L.: Modelling meningococcal meningitis in the African meningitis belt. *Epidemiol. Infect.* **140**(5), 897–905 (2011). <https://doi.org/10.1017/S0950268811001385>
- Martínez, M.J.F., Merino, E.G., Sánchez, E.G., et al.: A mathematical model to study the meningococcal meningitis. *Procedia Comput. Sci.* **18**, 2492–2495 (2013). <https://doi.org/10.1016/j.procs.2013.05.426>

26. Asamoah, J.K.K., Nyabadza, F., Seidu, B., et al.: Mathematical modelling of bacterial meningitis transmission dynamics with control measures. *Comput. Math. Methods Med.* (2018). <https://doi.org/10.1155/2018/2657461>
27. Blyuss, K.B.: In: Aston, P.J., Mulholland, A.J., Tant, K.M.M. (eds.) *Mathematical Modelling of the Dynamics of Meningococcal Meningitis in Africa*, pp. 221–226. Springer, Cham (2016). https://doi.org/10.1007/978-3-319-25454-8_28
28. Soper, H.E.: The interpretation of periodicity in disease prevalence. *J. Roy. Stat. Soc.* **92**(1), 34 (1929). <https://doi.org/10.2307/2341437>
29. Stone, L., Olinky, R., Huppert, A.: Seasonal dynamics of recurrent epidemics. *Nature* **446**(7135), 533–536 (2007). <https://doi.org/10.1038/nature05638>
30. Chitnis, N., Hardy, D., Smith, T.: A periodically-forced mathematical model for the seasonal dynamics of malaria in mosquitoes. *Bull. Math. Biol.* **74**(5), 1098–1124 (2012). <https://doi.org/10.1007/s11538-011-9710-0>
31. Onyango, N.O., Müller, J.: Determination of optimal vaccination strategies using an orbital stability threshold from periodically driven systems. *J. Math. Biol.* **68**(3), 763–784 (2013). <https://doi.org/10.1007/s00285-013-0648-8>
32. Doutor, P., Rodrigues, P., Céu Soares, M., Chalub, F.A.C.C.: Optimal vaccination strategies and rational behaviour in seasonal epidemics. *J. Math. Biol.* **73**(6–7), 1437–1465 (2016). <https://doi.org/10.1007/s00285-016-0997-1>
33. Greer, M., Saha, R., Gogliettino, A., et al.: Emergence of oscillations in a simple epidemic model with demographic data. *R. Soc. Open Sci.* **7**(1), 191187 (2020). <https://doi.org/10.1098/rsos.191187>
34. Arenas, A.J., González-Parra, G., Espriella, N.D.L.: Nonlinear dynamics of a new seasonal epidemiological model with age-structure and nonlinear incidence rate. *Comput. Appl. Math.* (2021). <https://doi.org/10.1007/s40314-021-01430-9>
35. Gölgeli, M., Atay, F.M.: Analysis of an epidemic model for transmitted diseases in a group of adults and an extension to two age classes. *Hacet. J. Math. Stat.* **49**(3), 921–934 (2020). <https://doi.org/10.15672/hujms.624042>
36. Oordt-Speets, A.M., Bolijn, R., Hoorn, R.C., et al.: Global etiology of bacterial meningitis: a systematic review and meta-analysis. *PLoS ONE* **13**(6), 0198772 (2018). <https://doi.org/10.1371/journal.pone.0198772>
37. Badur, S., Khalaf, M., Öztürk, S., et al.: Meningococcal disease and immunization activities in Hajj and Umrah pilgrimage: a review. *Infect. Dis. Therapy* **11**(4), 1343–1369 (2022). <https://doi.org/10.1007/s40121-022-00620-0>
38. Molesworth, A.M., Cuevas, L.E., Connor, S.J., et al.: Environmental risk and meningitis epidemics in Africa. *Emerg. Infect. Dis.* **9**(10), 1287–1293 (2003). <https://doi.org/10.3201/eid0910.030182>
39. Dietz, K.: Infectious diseases of humans: dynamics and control. *Parasitol. Today* **8**(5), 179 (1992). [https://doi.org/10.1016/0169-4758\(92\)90018-w](https://doi.org/10.1016/0169-4758(92)90018-w)
40. Driessche, P., Watmough, J.: Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Math. Biosci.* **180**(1–2), 29–48 (2002). [https://doi.org/10.1016/s0025-5564\(02\)00108-6](https://doi.org/10.1016/s0025-5564(02)00108-6)
41. Grassly, N.C., Fraser, C.: Seasonal infectious disease epidemiology. *Proc. R. Soc. B Biol. Sci.* **273**(1600), 2541–2550 (2006). <https://doi.org/10.1098/rspb.2006.3604>
42. Bacaër, N., Guernaoui, S.: The epidemic threshold of vector-borne diseases with seasonality. *J. Math. Biol.* **53**(3), 421–436 (2006). <https://doi.org/10.1007/s00285-006-0015-0>
43. Wang, W., Zhao, X.-Q.: Threshold dynamics for compartmental epidemic models in periodic environments. *J. Dyn. Diff. Equat.* **20**(3), 699–717 (2008). <https://doi.org/10.1007/s10884-008-9111-8>
44. Thieme, H.R.: Spectral bound and reproduction number for infinite-dimensional population structure and time heterogeneity. *SIAM J. Appl. Math.* **70**(1), 188–211 (2009). <https://doi.org/10.1137/080732870>
45. Griffin, J.T.: The interaction between seasonality and pulsed interventions against malaria in their effects on the reproduction number. *PLoS Comput. Biol.* **11**(1), 1004057 (2015). <https://doi.org/10.1371/journal.pcbi.1004057>
46. Heffernan, J.M., Smith, R.J., Wahl, L.M.: Perspectives on the basic reproductive ratio. *J. R. Soc. Interface* **2**(4), 281–293 (2005). <https://doi.org/10.1098/rsif.2005.0042>
47. Bacaër, N., Gomes, M.G.M.: On the final size of epidemics with seasonality. *Bull. Math. Biol.* (2009). <https://doi.org/10.1007/s11538-009-9433-7>
48. Bacaër, N.: Approximation of the basic reproduction number r_0 for vector-borne diseases with a periodic vector population. *Bull. Math. Biol.* **69**(3), 1067–1091 (2007). <https://doi.org/10.1007/s11538-006-9166-9>
49. Nakata, Y., Kuniya, T.: Global dynamics of a class of SEIRS epidemic models in a periodic environment. *J. Math. Anal. Appl.* **363**(1), 230–237 (2010). <https://doi.org/10.1016/j.jmaa.2009.08.027>
50. Inc., T.M.: MATLAB Version: 9.13.0 (R2022b). The MathWorks Inc., Natick, Massachusetts, United States (2022)
51. Dinleyici, E.C., Ceyhan, M.: The dynamic and changing epidemiology of meningococcal disease at the country-based level: the experience in Turkey. *Expert Rev. Vaccines* **11**(5), 515–518 (2012). <https://doi.org/10.1586/erv.12.29>
52. Cooper, L.V., Kristiansen, P.A., Christensen, H., et al.: Meningococcal carriage by age in the African meningitis belt: a systematic review and meta-analysis. *Epidemiol. Infect.* (2019). <https://doi.org/10.1017/s0950268819001134>
53. Metanat, M., Sharifi-Mood, B., Sanei-Moghaddam, S., Rad, N.S.: Pharyngeal carriage rate of *Neisseria meningitidis* before and after the Hajj pilgrimage, in Zahedan (southeastern Iran), 2012. *Turkish J. Med. Sci.* **45**, 1317–1320 (2015). <https://doi.org/10.3906/sag-1405-7>
54. Husain, E.H., Dashti, A.A., Electricwala, Q.Y., et al.: Absence of *neisseria meningitidis* from throat swabs of Kuwaiti pilgrims after returning from the Hajj. *Med. Princ. Pract.* **19**(4), 321–323 (2010). <https://doi.org/10.1159/000312721>
55. Ceyhan, M., Ozsurekci, Y., Basaranoglu, S.T., et al.: Multi-center hospital-based prospective surveillance study of bacterial agents causing meningitis and seroprevalence of different serogroups of *neisseria meningitidis*, *haemophilus influenzae* type b, and *streptococcus pneumoniae* during 2015 to 2018 in Turkey. *Sphere* (2020). <https://doi.org/10.1128/msphere.00060-20>

56. Loutfi, A., Hioui, M.E., Jayche, S., et al.: Epidemiological, cytochemical and bacteriological profile of meningitis among adults and children in north west of Morocco. *Pak. J. Biol. Sci.* **23**(7), 891–897 (2020). <https://doi.org/10.3923/pjbs.2020.891.897>
57. Musa, S.S., Zhao, S., Hussaini, N., et al.: Mathematical modeling and analysis of meningococcal meningitis transmission dynamics. *Int. J. Biomath.* **13**(01), 2050006 (2020). <https://doi.org/10.1142/s1793524520500060>
58. World Bank: Data, Population Website. <https://data.worldbank.org/income-level/upper-middle-income>
59. Alamarat, Z., Hasbun, R.: Management of acute bacterial meningitis in children. *Infect Drug Resist* **13**, 4077–4089 (2020). <https://doi.org/10.2147/idr.s240162>
60. TÜİK: Adrese dayalı nüfus kayıt sistemi sonuçları, 2019. Technical report, Turkish Statistical Institute (2020). <https://data.tuik.gov.tr/Kategori/GetKategori?p=Nufus-ve-Demografi-109>
61. Aleeban, M., Mackey, T.K.: Global health and visa policy reform to address dangers of Hajj during summer seasons. *Front. Public Health* (2016). <https://doi.org/10.3389/fpubh.2016.00280>
62. Kessel, F., Ende, C., Oordt-Speets, A.M., Kyaw, M.H.: Outbreaks of meningococcal meningitis in non-African countries over the last 50 years: a systematic review. *J. Global Health* (2019). <https://doi.org/10.7189/jogh.09.010411>
63. Mazamay, S., Guégan, J.-F., Diallo, N., et al.: An overview of bacterial meningitis epidemics in Africa from 1928 to 2018 with a focus on epidemics outside-the-belt. *BMC Infect. Dis.* (2021). <https://doi.org/10.1186/s12879-021-06724-1>
64. Sebastian, S., Badahdah, A.-M., Khatami, A., Rashid, H.: In: Laher, I. (ed.) *Meningococcal Disease During Hajj, Umrah, and Other Mass Gatherings*, pp. 1–22. Springer, Cham (2020). https://doi.org/10.1007/978-3-319-74365-3_52-1
65. Dinleyici, E.C., Borrow, R.: Meningococcal infections among refugees and immigrants: silent threats of past, present and future. *Hum. Vaccin. Immunother.* **16**(11), 2781–2786 (2020). <https://doi.org/10.1080/21645515.2020.1744979>

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.