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Optimal Strategies for Controlling the MERS Coronavirus During a Mass Gathering

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Abstract

A two-group model for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is designed and used to assess the impact of quarantine of susceptible individuals and a hypothetical anti-MERS-CoV vaccine on the transmission dynamics of MERS-CoV within the two groups. The model undergoes a backward bifurcation, which is shown to arise due to the assumption that the hypothetical vaccine offers incomplete protection against infection. The model can have one or more endemic equilibria when the associated reproduction number exceeds unity. Uncertainty and sensitivity analyses are carried out to determine the effect of uncertainties in the parameter estimates of the model, as well as to determine the main parameters that drive the disease transmission process. The model is re-formulated as an optimal control problem, and the resulting model is used to evaluate the impact of various control strategies. Numerical simulations of the optimal control model suggest that if the cost of implementing quarantine and vaccination strategies are high, the two strategies can be administered optimally by using their maximum feasible (coverage) levels for a relatively shorter period of time (i.e., "hit-hard and hit-early"), and the coverage level then continuously decreased the next few days afterwards. Furthermore, a universal strategy, based on the combined use of quarantine and vaccination strategies, is shown to be more effective than the singular implementation of either the vaccination or quarantine strategy.

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1. Introduction

Middle East Respiratory Syndrome (MERS), caused by the MERS-CoV *coronavirus*, is a viral respiratory disease first reported in Saudi Arabia in 2012 [1, 6, 12, 22, 39]. It has also been reported to have been transported to a number of countries, including Algeria, Austria, China, Egypt, France, Germany, Greece, Iran, Italy, Jordan, Korea, Kuwait, Lebanon, Malaysia, Netherlands, Oman, Philippines, Qatar, Thailand, Tunisia, Turkey, UAE, UK, USA and Yemen [39]. Since 2012, a total of 1368 laboratory-confirmed MERS-CoV cases have been reported to WHO, with 487 deaths [39]. Overall, 63.5% of reported cases are male. The median age is 47 years, old (range 9 months to 94 years old) [39].

The virus, which apparently evolved from a coronavirus that existed in bats and camels [22], is not the same coronavirus that caused the severe acute respiratory syndrome (such as SARS) in 2003 [6, 22]. However, MERS-CoV is most similar to coronaviruses found in bats [6]. It is very efficiently transmitted during close person-to-person contact, presumably through droplets of respiratory secretions, or through contaminated surfaces, such as pillows and duvets [6, 22, 39]. Transmission from infected patients to healthcare personnel has also been observed [6, 12]. The incubation period of MERS-CoV is not yet known, but is assumed to follow the pattern (of a week) observed in most coronaviruses [22]. Moreover, PRC (polymerase chain reaction) tests are now available to detect MERS-CoV [6]. The common symptoms of the disease include severe acute respiratory illness with fever, cough, and shortness of breath [1, 6, 22, 39].

There is currently no effective and safe vaccine against the virus, but efforts are underway to develop one [6, 22, 23, 30, 39]. In particular, two candidate vaccines (by *Novavax* and *Greffex* Inc.) are currently awaiting clinical trials [24, 26]. Basic control measure (quarantine and isolation) have been suggested to combat the spread of the disease [6, 39]. Furthermore, medical care (support) is administered to help relieve symptoms in patients [6, 22, 39]. Public health organizations generally advise people to adopt the same measures for protection from flu to help prevent MERS-CoV illnesses [1, 6, 22, 30, 39]. The risk-factors for MERS-COV are chronic diseases, weakened immune system, cancer or terminal illnesses [6, 22].

MERS-CoV threatens the lives of millions of pilgrims who go to Mecca for the Hajj and Umrah (owing to the associated mass gatherings) [1, 6, 12, 22, 39]. For these reasons, the Saudi Arabian Ministry of Health [22] urged the elderly and chronically ill to refrain from performing the Hajj and issued set of conditions (aimed at minimizing cases of MERS-CoV) for travellers to Hajj and Umrah in 2013 [6, 12, 22]. It is known that, in Saudi Arabia, cases of MERS-CoV is more common in males than in females (perhaps because of the face coverings some females use) [22, 30].

The purpose of this paper is to design and analyse a new model for the transmission dynamics of MERS-CoV during Hajj and Umrah, and to use the model to evaluate optimal control strategies. The paper is organized as follows. The two-group model is formulated in Section 2, and its basic feature is also analysed. In Section 3, the model is qualitatively analysed for steady states and their stability properties. Optimal control analysis and numerical simulations are reported in Sections 4 and 5, respectively.

2. Model Formulation

The model is constructed based on the transmission dynamics of MERS-CoV in a population composed of two groups, hereafter named Group 1 (for example the local residents of Mecca) and Group 2 (for example pilgrims visiting Mecca from other countries or other parts of Saudi Arabia). The model allows for travel in either direction between the two groups. Two control strategies to combat MERS-CoV, namely quarantine of susceptible individuals and a potential vaccine, are considered. It is worth mentioning that in practice quarantine involves removing a big number of individuals suspected of being exposed to MERS-CoV. For example as of June 2015 about 6,700 people are quarantined in South Korea [36], the country that has seen the highest number of MERS cases after Saudi Arabia (this includes an entire village of 105). The model thus accounts for the significant number of people in quarantine who turn out to be susceptible at the end of the quarantine period. Mathematical models incorporating quarantining of susceptible individuals have been proposed in the literature (see, for example, [28], and the references therein). In other words, quarantine in this model means the temporary removal of susceptible individuals (feared to have been exposed to the MERS-CoV) from the general population and assumes that (i) quarantined susceptible individuals do not acquire infection during quarantine and (ii) no new asymptomatic cases are detected during quarantine.

The total population of Group 1 at time t, denoted by $N_1(t)$, is sub-divided into seven mutually-exclusive compartments of unvaccinated non-quarantined susceptible ($S_1(t)$), unvaccinated quarantined susceptible ($S_{1Q}(t)$), vaccinated susceptible ($S_{1V}(t)$), non-quarantined exposed (i.e., latently-infected, and showing no clinical symptoms of MERS-CoV) ($E_1(t)$), non-quarantined symptomatic (i.e., infected with clinical symptoms of MERS-CoV) ($I_1(t)$), non-quarantined hospitalized (isolated) ($H_1(t)$) and recovered ($R_1(t)$) individuals.

Similarly, the total population of Group 2 at time t, denoted by $N_2(t)$, is sub-divided into unvaccinated non-quarantined susceptible ($S_2(t)$), unvaccinated quarantined susceptible ($S_{2Q}(t)$), vaccinated susceptible ($S_{2V}(t)$), exposed ($E_2(t)$), symptomatic ($I_2(t)$), hospitalized ($H_2(t)$) and recovered ($R_2(t)$) individuals. Thus, the total population at