Impact of non-pharmaceutical interventions on the control of COVID-19 in Iran: A mathematical modeling study

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Abstract

Background

During the first months of the COVID-19 pandemic, Iran reported high numbers of infections and deaths in the Middle East region. In the following months, the burden of this infection decreased significantly, possibly due to the impact of a package of interventions. We modeled the dynamics of COVID-19 infection in Iran to quantify the impacts of these interventions.

Methods

We used a modified susceptible–exposed–infected–recovered (SEIR) model to model the COVID-19 epidemic in Iran, from 21 January to 21 September 2020, using Markov chain Monte Carlo simulation to calculate 95% uncertainty intervals (UI). We used the model to assess the effectiveness of physical distancing measures and self-isolation under different scenarios. We also estimated the control reproductive number (R_c), using our mathematical model and epidemiologic data.

Results

If no non-pharmaceutical interventions (NPIs) were applied, there could have been a cumulative number of 51,800,000 (95% UI: 19,100,000–77,600,000) COVID-19 infections and 266,000 (95% UI: 119,000–476,000) deaths by September 21 2020. If physical distancing interventions, such as school/border closures and self-isolation interventions, had been introduced a week earlier than they were actually launched, a 30% reduction in the number of infections and deaths could have been achieved by September 21 2020. The observed daily number of deaths showed that the R_c was one or more than one almost every day during the analysis period.

Conclusions

Our models suggest that the NPIs implemented in Iran between 21 January and 21 September 2020 had significant effects on the spread of the COVID-19 epidemic. Therefore, we recommend that these interventions are considered when designing future control programs, while simultaneously considering innovative approaches that can minimize harmful economic impacts on the community and the state. Our study also showed that the timely implementation of NPIs showed a profound effect on further reductions in the numbers of infections and deaths. This highlights the importance of forecasting and early detection of future waves of infection and of the need for effective preparedness and response capabilities.

Background

The COVID-19 pandemic began in China on 26 December 2019, and the disease is now a major threat to global health, with 216 countries having reported at least one case [1]. As of September 21 2020, there have been 31,606,824 confirmed cases reported and 977,977 deaths worldwide. The first cases of COVID-19 in Iran were reported in Qom city (central Iran) on February 19 2020 [2]. Currently, the disease is being reported in all provinces throughout the country [3]. During the first months of the COVID-19 pandemic, Iran reported high numbers of infections and deaths due to COVID-19. The numbers of reported cases and deaths in Iran are the highest among the countries in the Middle East region. However, in the following months, the burden of this infection decreased significantly, possibly due to the impact of a package of interventions. By 18 September 2020, the numbers of reported cases and deaths in Iran were 419,043 and 24,118, respectively [4]. Based on COVID-19 infection rates (the number of reported cases per million population), Iran ranks seventh in the region, after Qatar, Bahrain, Kuwait, United Arab Emirates, Turkey, and Occupied Palestinian Territory [5].

Non-pharmaceutical interventions (NPIs) have been implemented in Iran since the early stage of the epidemic. These NPIs have included major physical distancing interventions, including school and university closures; closure of holy shrines in Mashhad, Qom, and other cities; cancelation of mass gatherings, such as sporting events and congregational prayers; travel bans; and strict economic and social lockdown. On April 19 2020, Iran gradually implemented the termination of most of these physical distancing measures due to the economic problems they were causing. In mid-March 2020, health authorities began promoting the self-isolation of confirmed cases at home. Also, post-discharge isolation units were developed in almost all cities in Iran [6, 7].

Mathematical models can be used to assess the impact of intervention strategies and to understand the epidemic mechanisms of infectious diseases. This study aimed to evaluate the impact of NPIs introduced in Iran, using a mathematical model. We also aimed to estimate the time-varying reproductive number and assess the impact of the NPIs on this number.

Methods

Mathematical model

We implemented a generalized susceptible–exposed–infected–recovered (SEIR) compartmental model. The model framework was introduced in previous work [8]. In brief, our model divides individuals into susceptible (S), latent (E), infected (I), isolated (IS), dead (D), hospitalized (H), temporarily isolated in isolation units (T), and recovered (R) states (Fig. 1). Susceptible individuals acquire infection with a force of infection β , where β is the transmission probability, $C(t)$ is the contact rate, and I is the total number of infected people who could transmit the infection ($I + (0.1 \times \text{temporarily isolated in isolation units}) + (0.02 \times \text{hospitalized})$). We considered a seasonality effect using a sinus function for transmission probability. The transmission probability was considered 0.02 at the minimum (in June) of the infection wave in the summer and 0.045 at the maximum of the infection wave (in January). Also, the contact rate changed across different time periods, based on the specific interventions introduced in the population at a given time (Table 3). Individuals who are exposed become infected after days τ , is the latent period of the disease. We assumed that the incubation period is equal to the latent period and that infected people transmit the infection after the incubation period ends [10]. Infected individuals are divided into four groups:

- Cases with asymptomatic or mild infection. It is assumed that a proportion ϕ of these individuals do not self-isolate and recover at a rate of γ after days τ [11].
- The remaining cases with asymptomatic or mild infection $(1 - \phi)$ self-isolate days τ after demonstrating clinical symptoms.
- Cases with severe disease. These individuals are assumed to be referred to the hospital days τ after the onset of symptoms at a rate of δ .
- Cases who die of COVID-19 days τ after the onset of symptoms and before going to the hospital (0.02).

A proportion θ of individuals who go to the hospital die after days τ ; in addition, a proportion θ of patients who go to hospital proceed to the temporary isolation unit class after days τ . A proportion θ of individuals who go to temporary isolation units proceed into the recovered class after days τ . The remaining individuals who go to the temporary isolation units $(1 - \theta)$ die after days τ . Individuals who are in the isolation class proceed to the recovered class after days τ . The ordinary differential equations for each of the compartments are shown in the Appendix.

Model parameters, assumptions, and calibrations

Parameters were obtained and calibrated from the literature, national empirical data, and expert opinion. Our model was also calibrated based on the death toll in Iran to 21 September 2020 (Fig. 2). Due to a lack of sufficient tests and misdiagnosis with other acute respiratory disease, the number of deaths was underreported at the beginning of the epidemic; therefore, death toll underreporting was considered. Parameter descriptions, sources, values, and distributions are presented in the “Mathematical Model” section. Several assumptions were also considered, including:

- Susceptibility of the entire population
- Homogeneity of susceptible and infectious individuals
- No physical distancing interventions implemented during the early stages of the COVID-19 epidemic
- Only 10% self-isolation of infected individuals during the early stages of the COVID-19 epidemic
- Negligible migration rates between cities

Markov chain Monte Carlo (MCMC) simulation was performed to calculate the 95% uncertainty intervals (UI) as plausible bounds around model estimates. These uncertainties were parametrized as probability distributions, based on expert opinion and the existing evidence, and 10,000 simulations were undertaken using random sample approach. The 95% UIs were taken as the 2.5th and 97.5th percentiles of the outputs. Data were analyzed using Vensim DSS version 6.4E software.

Scenarios for the impact of NPIs

Following the official announcement of the COVID-19 epidemic in Iran, several NPIs were implemented to reduce contact rates among members of the public, as well as to increase self-isolation. In our model, seven scenarios were considered, in which the impacts of changes in contact rates and self-isolation rates were examined. The total number of COVID-19 cases, deaths, and hospitalizations, and number of the existing hospitalized cases at the peak of the epidemic were estimated under each scenario.

Scenario A: We assumed that physical distancing interventions and isolation were not implemented. Physical distancing measures included a ban on flights from Wuhan in China, closure of schools and universities, suspension of mass gatherings for religious events, suspension of conferences and social mass gatherings, travel restrictions, cancelation of sporting competitions, closure of some business units in disease epicenters, closure of religious shrines and holy places, and the closure of subways in all cities. We assumed a 50% decrease in contact rates due to behavior changes among the community. Also, we assumed that without any preventive effort the proportion of self-isolation was 10%. (Table 1).

Scenario B: Physical distancing measures were assumed to be implemented. However, the proportion of individuals self-isolating was assumed to be 10%.

Scenario C: We assumed that physical distancing interventions were not implemented. Self-isolation rates were based on the results of the calibrated model.

Scenario D: The impact of physical distancing interventions and self-isolation was evaluated in the context of what would have happened had the health system detected the epidemic in Iran one week earlier, and hence the interventions had started sooner. We also considered three optimistic scenarios if NPIs were increased in Iran.

Scenario E: Physical distancing interventions were based on the results of the calibrated model; however, the self-isolation rate was increased to 40%.

Scenario F: We considered the self-isolation rate were based on the results of the calibrated model; however, the contact rate was considered to be 8 (we assumed that only work ban interventions were canceled after 11 May 2020 while the other interventions remained).

Scenario G: We assumed that the self-isolation rate increased to 40% and the contact rate was 8 after 11 May 2020.

Table 1. Contact rates and self-isolation rates for different scenarios from 21 January to 21 September 2020

Date	Scenario															
	Calibrated model		A		B		C		D		E		F		G	
	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I
From Jan 21, 2020 to Jan 30, 2020	13	10	13	10	13	10	13	10	13	10	13	10	13	10	13	10
From Jan 31, 2020 to Feb 9, 2020	12	10	12	10	12	10	12	10	12	10	12	10	12	10	12	10
From Feb 10, 2020 to Feb 19, 2020	11	10	11	10	11	10	11	10	11	10	11	10	11	10	11	10
From Feb 20, 2020 to Feb 22, 2020	9	20	9	10	9	10	9	20	9	20	9	20	9	20	9	20
From Feb 23, 2020 to Feb 29, 2020	9	20	9	10	9	10	9	20	5	20	9	20	9	20	9	20
From Mar 1, 2020 to Mar 10, 2020	5	20	9	10	5	10	9	20	5	20	5	20	5	20	5	20
From Mar 11, 2020 to Mar 12, 2020	5.5	20	9	10	5.5	10	9	20	5.5	20	5.5	20	5.5	20	5.5	20
From Mar 13, 2020 to Mar 20, 2020	5.5	20	9	10	5.5	10	9	20	5.5	20	5.5	20	5.5	20	5.5	20
From Mar 21, 2020 to Mar 31, 2020	6	30	9	10	6	10	9	30	6	30	6	40	6	30	6	40
From Apr 1, 2020 to Apr 12, 2020	5	30	9	10	5	10	9	30	5	30	5	40	5	30	5	40
From Apr 13, 2020 to Apr 20, 2020	5.5	30	9	10	5.5	10	9	30	5.5	30	5.5	40	5.5	30	5.5	40
From Apr 21, 2020 to Apr 28, 2020	6	40	9	10	6	10	9	40	6	40	6	40	6	40	6	40
From Apr 28, 2020 to May 5, 2020	6.5	40	9	10	6.5	10	9	40	6.5	40	6.5	40	6.5	40	6.5	40
From May 6, 2020 to May 12, 2020	7	40	9	10	7	10	9	40	7	40	7	40	7	40	7	40
From May 13, 2020 to May 22, 2020	8.5	40	9	10	8.5	10	9	40	8.5	40	8.5	40	8	40	8	40
From May 23, 2020 to Jun 9, 2020	9	30	9	10	9	10	9	30	9	30	9	40	8	30	8	40
From Jun 10, 2020 to Jun 30, 2020	10	30	10	10	10	10	10	30	10	30	10	40	8	30	8	40
From Jul 1, 2020 to Jul 20, 2020	10	30	10	10	10	10	10	30	10	30	10	40	8	30	8	40
From Jul 21, 2020 to Aug 5, 2020	8	40	8	10	8	10	8	40	8	40	8	40	8	40	8	40
From Aug 6, 2020 to Aug 15, 2020	7	40	7	10	7	10	7	40	7	40	7	40	8	40	8	40
From Aug 16, 2020 to Aug 25, 2020	8	40	8	10	8	10	8	40	8	40	8	40	8	40	8	40
From Aug 26, 2020 to Sep 5, 2020	9	40	9	10	9	10	9	40	9	40	9	40	8	40	8	40
From Sep 27, 2020 to Sep 21, 2020	9	30	9	10	9	10	9	30	9	30	9	40	8	30	8	40

C = contact rate, I = percentage self-isolation rate

Control reproductive number (R_c)

The basic reproduction number (R_0) is the average number of secondary infections resulting from one infected individual in a susceptible host population. R_0 is used when there is no immunity from past exposures, vaccinations, or interventions. However, the control reproductive number (R_c)

is used when there are intervention measures. R_c can be estimated using mathematical modeling and epidemiologic data. In the current study, we estimated R_c using both methods. R_c was derived using next generation methods with the model that we introduced in previous work [8].

$$R_c = \frac{\beta(t) * C(t)}{\left(\frac{\theta}{\delta_6} + \frac{\alpha}{\delta_8} + \frac{\varepsilon}{\delta_2} + \frac{\omega}{\delta_9}\right)}$$

To estimate the basic reproductive number from data, we used the daily number of deaths reported by Iran's Ministry of Health and Medical Education from 19 February to 21 September 2020. A time-dependent method was used to estimate the trend of R_c in Iran. The mean and standard deviation of serial intervals were considered to be 4.55 and 3.3 days, respectively [12]. The generation time distribution was considered to be gamma. We analyzed the basic reproductive number using the R_0 package in R version 4.0.2 software.

Ethical issues

Ethical approval for this research was received from the Kerman University of Medical Sciences, Kerman, Iran (reference 98001239).

Results

Calibrated model

Under the calibrated model scenario, the total number of deaths up to 21 September 2020 would be 26,000 (95% UI: 3,700–91,000). The total number of infected cases predicted in this scenario would be 5,100,000 (95% UI: 680,000–18,000,000). The total number of hospitalized cases and the number of the existing hospitalized cases at the peak of the epidemic would be 420,000 (95% UI: 52,000–1,500,000) and 16,000 (95% UI: 500–70,000), respectively (Table 2).

Scenario A

Under scenario A, the death toll by 21 September 2020 would be 266,000 (95% UI: 119,000–476,000). It is estimated that the total number of infected cases under scenario A would be 51,800,000 (95% UI: 19,100,000–77,600,000). Also, the total number of hospitalized cases in this scenario would be 4,800,000 (95% UI: 1,600,000–9,500,000). At the peak of epidemic, there would be 360,000 (95% UI: 112,000–650,000) existing cases in hospital (Table 2).

Scenario B

The death toll in scenario B was expected to be 155,000 (95% UI: 24,000–360,000). The total number of infected cases would be 29,200,000 (95% UI: 4,800,000–58,700,000). It is estimated that the total number of hospitalized cases and the number of the existing hospitalized cases at the peak would be 3,000,000 (95% UI: 476,000–6,800,000) and 153,000 (95% UI: 17,000–350,000), respectively (Table 2).

Scenario C

Under this scenario, the total number of death cases up to 21 September 2020 would be 127,000 (95% UI: 26,000–282,000). It is predicted that the total number of infected cases under scenario C would be 25,400,000 (95% UI: 5,900,000–51,700,000). The total number of hospitalized cases and the number of the existing hospitalized cases at the peak would be 2,190,000 (95% UI: 424,000–5,100,000) and 114,000 (95% UI: 16,000–260,000), respectively (Table 2).

Scenario D

Under scenario D, the death toll up to 21 September 2020 would be 18,000 (95% UI: 2,600–70,000). It is estimated that the total number of infected cases under scenario D would be 3,300,000 (95% UI: 430,000–13,200,000). The total number of hospitalized cases in this scenario would be 312,000 (95% UI: 39,000–1,190,000). Also, the number of the existing hospitalized cases at the peak would be 13,000 (95% UI: 2,000–67,000) (Table 2).

Scenario E

Under this scenario, the death toll up to 21 September 2020 would be 13,000 (95% UI: 2,600–41,000). It is predicted that the total number of infected cases under scenario E would be 2,300,000 (95% UI: 400,000–7,200,000). The total number of hospitalized cases and the number of the existing hospitalized cases at the peak would be 223,000 (95% UI: 43,000–780,000) and 10,000 (95% UI: 3,500–20,000), respectively (Table 2).

Scenario F

The death toll in scenario F was expected to be 17,000 (95% UI: 3,600–55,000). It is estimated that the total number of infected cases would be 2,800,000 (95% UI: 599,000–9,500,000). The total number of hospitalized cases would be 284,000 (95% UI: 55,000–924,000). Also, the number of the existing hospitalized cases at the peak would be 13,000 (95% UI: 5,000–28,000) (Table 2).

Scenario G

Under scenario D, the death toll up to 21 September 2020 was expected to be 10,000 (95% UI: 3,000–26,000). The total number of infected cases under scenario G would be 1,700,000 (95% UI: 511,000–4,800,000). It is predicted that the total number of hospitalized cases and the number of the existing hospitalized cases at the peak would be 163,000 (95% UI: 44,000–463,000) and 11,000 (95% UI: 4,000–24,000), respectively (Table 2).

The estimated death tolls, numbers of infected cases per day, and numbers of existing hospitalized cases under the different scenarios from 21 January to 21 September 2020 are shown in Fig. 4, 5, and 6.

Table 2. Comparison of the total numbers of infected and hospitalized cases, deaths, and the number of the existing hospitalized cases at the peak, under different scenarios, up to September 21 2020

	Scenarios								
	Calibrated model	Reported data	A	B	C	D	E	F	G
Number of deaths (95% UI)	26,000 (3,700–91,000)	24,478	266,000 (119,000–476,000)	155,000 (24,000–360,000)	127,000 (26,000–282,000)	18,000 (2,600–70,000)	13,000 (2,600–41,000)	17,000 (3,600–55,000)	10,000 (3,000–26,000)
Number of infected cases (95% UI)	5,100,000 (680,000–18,000,000)	-	51,800,000 (19,100,000–77,600,000)	29,200,000 (4,800,000–58,700,000)	25,400,000 (5,900,000–51,700,000)	3,300,000 (430,000–13,200,000)	2,300,000 (400,000–7,200,000)	2,800,000 (599,000–9,500,000)	1,700,000 (511,000–4,800,000)
Number of hospitalized cases (95% UI)	420,000 (52,000–1,500,000)	425,481	4,800,000 (1,600,000–9,500,000)	3,000,000 (476,000–6,800,000)	2,190,000 (424,000–5,100,000)	312,000 (39,000–1,190,000)	223,000 (43,000–780,000)	284,000 (55,000–924,000)	163,000 (44,000–463,000)
Number of the existing hospitalized cases at the peak (95% UI)	16,000 (500–70,000)	-	360,000 (112,000–650,000)	153,000 (17,000–350,000)	114,000 (16,000–260,000)	13,000 (2,000–67,000)	10,000 (3,500–20,000)	13,000 (5,000–28,000)	11,000 (4,000–24,000)
Scenario A: no physical distancing or self-isolation interventions; Scenario B: physical distancing interventions only implemented; Scenario C: self-isolation interventions only implemented; Scenario D: physical distancing and self-isolation interventions started a week earlier; Scenario E: self-isolation rate increased to 40%; Scenario F: contact rate decreased to 8 after 11 May 2020; Scenario G: self-isolation rate increased to 40% and contact rate decreased to 8 after 11 May 2020									

3.9. Impact of interventions on reproductive numbers

At the beginning of the epidemic, the R_c in Iran was estimated to be more than 3. After the implementation of various interventions, R_c decreased to less than one from April 5 to May 10 2020. Unfortunately, after May 11, the R_c increased again, to more than one. The R_c was more than 1.26 from 6 June to 15 June 2020 (Figure 6). The R_c decreased to near 1 in July then increased to more than one from mid-August to 21 September 2020.

Discussion

Iran is in a challenging position, having a population with a relatively high average age and therefore a relatively large proportion of the population at risk of severe COVID-19 disease. Limits to the health system capacity mean that there is a continuous risk of breaching this capacity. Given the economic constraints and the abundance of multigenerational households, shielding of the elderly is not a viable component of any scenario for Iran. Economic constraints also limit the feasible levels of self-isolation of infected individuals to a range of between 10% and 40%. This means that neither containment nor shielding approaches are realistic strategy options in Iran. Maintaining a balance between deaths caused by COVID-19, as explored with this modeling approach, and deaths caused through economic hardship resulting from COVID-19 interventions (which are beyond the scope of this article), while avoiding breaches in health system capacity, is therefore a continuing challenge for the Iranian government, until a vaccine or other health technologies become available.

As the COVID-19 pandemic progressed, countries increasingly implemented a broad range of responses. Our results demonstrate that the multiple interventions performed in Iran have had a profound effect in mitigating the epidemic. Our results also showed that the interventions resulted in an average self-isolation rate of 30% of the population.

Our results showed that without strict social distancing and self-isolation measures there would have been a considerably higher number of infections and deaths, as much as ten-times higher than currently. It is widely understood that suppression of the epidemic will require the use of more intensive and socially disruptive measures. Suppression may not be a feasible target in all countries, as the choice of interventions and their intensity ultimately depends on the infrastructure required and the relative feasibility of these measures in different social contexts.

It should be noted that self-isolation, social distancing, and travel restrictions will have a profound effect, reducing the workforce across many economic sectors and causing many jobs to be lost. However, the effect of opening low-risk jobs that have minimum interference with the above control measures seems to have little effect on the number of infections and deaths. Economic anxiety and economic crisis are currently considered to be two major side effects of the COVID-19 pandemic. This economic crisis and anxiety will be more disruptive in resource-limited countries [13]. Iran, as a developing country, needs resilient and strong leadership in healthcare, business, government, and wider society to manage the financial challenges presented by the COVID-19 pandemic. Immediate relief measures may need to be adjusted for workers who may otherwise fall through the cracks. Medium- and longer-term strategies to re-balance the economy will also be needed following this crisis [14].

Our study found that the number of infections and deaths would not decrease significantly if the self-isolation rates were increased or contact rates were decreased from those achieved by the measures actually implemented in Iran. This suggests the interventions already implemented in the country were effective.

Our results also demonstrated that if the control measures in Iran had been started just 7 days earlier, the total number of deaths and infections would have decreased by 30%. This would also have resulted in a reduction in the number of hospitalizations at the peak by 20%. These findings have important implications for any second and third waves of the epidemic, either in Iran or other countries, and highlight the necessity for countries to develop early-warning systems as soon as possible. The use of triggers based on hospital admissions might be a more efficient early-warning system in settings where extended and ongoing community-based testing is not in place. In countries where testing coverage and consistency is not homogenous across the country, local early-warning triggers based on community-testing results might be an efficient method in localities where there are comprehensive and ongoing community-testing activities. Local time-series analyses that provide correlations and time-lags between infections and hospitalizations would also help in warning hospitals to be prepared.

To avoid any rebound in transmission, these policies will need to be maintained until large stocks of vaccine are available to immunize the population. When this might be remains unclear. Until then, early-warning systems can be used as a guide for policymakers, helping them to adjust their control measures in the population.

Our model indicated that if minimum (i.e., only school closures, border closures, work bans, or event bans) or no interventions were implemented, the number of hospitalizations with COVID-19 would exceed hospital bed capacity. As of April 2020, public hospitals in Iran, which are mainly responsible for the COVID-19 response, had around 150,000 beds, 9,000 of which were in intensive care units (ICU). As of April 2020, there were 0.41 physicians and 1.14 nurses per public hospital bed in Iran. This implies that a shortage of healthcare workers would be challenging in this scenario and even in scenarios with more interventions. Given that a proportion of healthcare workers would be infected, isolated, and even die due to complications of COVID-19, the shortage of healthcare workers would become even worse, especially under scenarios where no intervention or minimum intervention is considered.

Our projections suggest that the measures introduced by the government of Iran resulted in large (around 60%) reductions in the total number of contacts. The observed reduction appears unlikely to have been due to chance, given the large difference in the average R_c . This is consistent with recent studies conducted in Wuhan, China, as well as in the UK, that respectively estimated an 85% and 74% reduction in the average number of daily contacts under physical distancing interventions [15, 16]. This is also in line with the results of Khosravi et al. and Aghaali et al., who reported a gradual decrease in R_c over time in Shohroud and Qom (central Iran) [12, 17]. The gradual decrease in R_c observed in our study is promising and further highlights the possible effectiveness of NPIs implemented in Iran. Some of these measures included public education to promote social distancing and self-isolation at home.

There are some limitations to this study. Many of the properties of the virus that causes COVID-19 remain unknown, thus some of the data we used may have uncertainties. However, to address these uncertainties, we used the MCMC method and reported the uncertainty intervals. We also made several assumptions; these were mentioned in the Methods section.

Conclusions

The effectiveness of NPIs may vary by country or community, depending on the extent of community engagement and the quality of the interventions. Our models suggest that the NPIs implemented in Iran between 21 January and 21 September 2020 had a satisfactory effect on reducing the number of COVID-19 infections and deaths in the country. Therefore, it is recommended that these interventions continue to be implemented by the government. Given the economic restrictions on Iran imposed by US sanctions, however, it is highly recommended that innovative modifications and solutions are considered that could minimize the economic impact of these NPIs on individuals and the state. Our modeling also highlighted the profound effect the timely implementation of NPIs can have on further reductions in the number of infections and deaths. This reinforces the importance of forecasting and the early detection of future waves of the epidemic through mathematical modeling

studies, as well as the development of early-warning systems. Proper preparedness and timely responses to any future waves of disease could be achieved through such systems.

Appendix

The ordinary differential equations of the compartments are as follows:

$$\frac{dS}{dt} = -\beta(t)C(t) \frac{I(t)}{N} S$$

$$\frac{dE}{dt} = \beta(t)C(t) \frac{I(t)}{N} S - \frac{1}{\delta_1} E$$

$$\frac{dI}{dt} = \frac{1}{\delta_1} E - \left(\frac{\theta}{\delta_6} + \frac{\alpha}{\delta_8} + \frac{\varepsilon}{\delta_2} + \frac{\omega}{\delta_9} \right) I$$

$$\frac{dR}{dt} = \frac{\mu}{\delta_5} T + \frac{\alpha}{\delta_8} I + \frac{1}{\delta_7} I_s$$

$$\frac{dI_s}{dt} = \frac{\theta}{\delta_6} I - \frac{1}{\delta_7} I_s$$

$$\frac{dH}{dt} = \frac{\varepsilon}{\delta_2} I - \left(\frac{\varphi}{\delta_3} + \frac{\rho}{\delta_4} \right) H$$

$$\frac{dT}{dt} = \frac{\rho}{\delta_4} H - \left(\frac{\mu}{\delta_5} + \frac{\tau}{\delta_{10}} \right) T$$

$$\frac{dD}{dt} = \frac{\varphi}{\delta_3} H + \frac{\omega}{\delta_9} I + \frac{\tau}{\delta_{10}} T$$

Abbreviations

MCMC – Markov chain Monte Carlo

NPI – non-pharmaceutical intervention

R_c – control reproductive number

R_0 – basic reproduction number

SEIR model – susceptible–exposed–infected–recovered model

UI – uncertainty interval

Declarations

Ethics approval and consent to participate

The proposal of the present study was approved by ethics committee of Kerman University of Medical Sciences, Kerman, Iran (reference 98001239).

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study will be available on request and permission of via e-mail from the corresponding author

Competing interests

The author, AAH is the Deputy Minister of Education and the Head of National Committee on COVID-19 Epidemiology. The rest of the authors declare no conflict of interest, real or perceived.

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Authors' contributions:

In this work MN, SE, and HS took the lead, were responsible for the data analysis and made substantial contributions to conception, design, and writing. YJ, and MAG made substantial contributions to conception, design, and writing. HS, LW and AAH revised the study critically, contributed substantially to conception, design, the interpretation of data, and drafting of the article.

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References

1. Organization WH. Coronavirus disease (COVID-19) pandemic. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed 27 November 2020.
2. Times NY. Iran reports its first 2 cases of the new coronavirus. Available from: <https://www.timesofisrael.com/iran-reports-its-first-2-cases-of-the-new-coronavirus/>. Accessed 9 May 2020.
3. Arab-Mazar Z, Sah R, Rabaan AA, Dhama K, Rodriguez-Morales AJ. Mapping the incidence of the COVID-19 hotspot in Iran—Implications for Travellers. *Travel Medicine Infectious Disease*. 2020. <https://doi.org/10.1016/j.tmaid.2020.101630>.
4. CDC NCoC-Eal. Analysis of epidemic trend by provinces of Iran. Available from: http://corona.behdasht.gov.ir/files/site1/files/IRAN_COVID19_Factsheet_N.58_-19September_En.pdf. Accessed 19 September 2020.
5. COVID-19 Coronavirus. Available from: <https://www.worldometers.info/coronavirus/coronavirus-cases/>. Accessed 19 September 2020.
6. National Committee on COVID-19 Epidemiology and Iranian CDC - Ministry of Health and Medical Education II. Major interventions to control COVID-19 from 19 Feb. Available from: http://corona.behdasht.gov.ir/files/site1/files/1584533009223_Major_interventions_to_control_COVID-19_from.pdf. Accessed 15 March 2020.
7. Abdi M. Coronavirus disease 2019 (COVID-19) outbreak in Iran: Actions and problems. *Infection Control Hospital Epidemiology*. 2020;41(6):754–5. <https://doi.org/10.1017/ice.2020.86>.
8. Sharifi H, Jahani Y, Mirzazadeh A, Ahmadi Gohari M, Nakhaeizadeh M, Shokoohi M, et al. Estimating COVID-19-related infections, deaths, and hospitalizations in Iran under different physical distancing and isolation scenarios. *International journal of health policy management*. 2020 Aug 1. <https://doi.org/10.34172/ijhpm.2020.134>.
9. Khalili M, Karamouzian M, Nasiri N, Javadi S, Mirzazadeh A, Sharifi H. Epidemiological characteristics of COVID-19: a systematic review and meta-analysis. *Epidemiol Infect*. 2020;148:e130. <https://doi.org/10.1017/S0950268820001430>.
10. Kucharski AJ, Russell TW, Diamond C, Liu Y, Edmunds J, Funk S, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *The lancet infectious diseases*. 2020. [https://doi.org/10.1016/S1473-3099\(20\)30144-4](https://doi.org/10.1016/S1473-3099(20)30144-4).
11. You C, Deng Y, Hu W, Sun J, Lin Q, Zhou F, et al. Estimation of the time-varying reproduction number of COVID-19 outbreak in China. *Int J Hyg Environ Health*. 2020:113555. <https://doi.org/10.1016/j.ijheh.2020.113555>.
12. Aghaali M, Kolifarhood G, Nikbakht R, Mozafar Saadati H, Hashemi Nazari SS. Estimation of the Serial Interval and Basic Reproduction Number of COVID-19 in Qom, Iran, and Three Other Countries: A Data-Driven Analysis in the Early Phase of the Outbreak. *Transboundary Emerging Diseases*. 2020. <https://doi.org/10.1111/tbed.13656>.
13. COVID-19. Disrupting lives, economies and societies. Available from: <https://www.un.org/development/desa/dpad/publication/world-economic-situation-and-prospects-april-2020-briefing-no-136/>. Accessed 1 April 2020.
14. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. *Int J Surg*. 2020;78:185. <https://doi.org/10.1016/j.ijsu.2020.04.018>.
15. Zhang J, Litvinova M, Liang Y, Wang Y, Wang W, Zhao S, et al. Age profile of susceptibility, mixing, and social distancing shape the dynamics of the novel coronavirus disease 2019 outbreak in China. *medRxiv*. 2020. <https://doi.org/10.1101/2020.03.19.20039107>.
16. Jarvis CI, Van Zandvoort K, Gimma A, Prem K, Klepac P, Rubin GJ, et al. Quantifying the impact of physical distance measures on the transmission of COVID-19 in the UK. *BMC Med*. 2020;18:1–10. <https://doi.org/10.1186/s12916-020-01597-8>.

Figures

Figure 1
The SEIR conceptual model we used

Figure 1

The SEIR conceptual model we used

Figure 2

The calibrated model output based on the death toll in Iran

Figure 2

The calibrated model output based on the death toll in Iran

Figure 3

The estimated death toll in Iran under different scenarios, from 21 January to 21 September 2020

Figure 3

The estimated death toll in Iran under different scenarios, from 21 January to 21 September 2020

Figure 4

The estimated number of infected cases per day in Iran under different scenarios from 21 January to 21 September 2020

Figure 4

The estimated number of infected cases per day in Iran under different scenarios from 21 January to 21 September 2020

Figure 5

The estimated number of existing hospitalized cases in Iran under different scenarios from 21 January to 21 September 2020

Figure 5

The estimated number of existing hospitalized cases in Iran under different scenarios from 21 January to 21 September 2020

Figure 6

Comparison of the daily reproduction number using the time-dependent method and different scenarios from 21 January to 21 September 2020

Figure 6

Comparison of the daily reproduction number using the time-dependent method and different scenarios from 21 January to 21 September 2020