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The trade-off between deaths by infection and socio-economic costs in the emerging infectious disease

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COVID-19, caused by the novel coronavirus (SARS-CoV-2), is an emerging infectious disease (EID) with a relatively high infectivity and mortality rate. During the state of emergency announced by the Japanese government in the spring of 2020, citizens were requested to stay home, the number of infected people was drastically reduced without a legally-binding lockdown. It is well-acknowledged that there is a trade-off between maintaining economic activity and preventing the spread of infectious diseases. We aimed to reduce the total loss caused by the epidemic of an EID like COVID-19 in the present study. We focused on early and late stages of the epidemic and proposed a framework to reduce the total loss resulted from the damage by infection and the cost for the countermeasure. Mathematical epidemic models were used to estimate the effect of interventions on the number of deaths by infection. The total loss was converted into the monetary base and different policies were compared. In the early stage, we calculated the damage by infection when behavioral restrictions were implemented. The favorable intensity of the intervention depended on the basic reproduction number, infection fatality rate, and the economic impact. In the late stage, we calculated indicators and showed it depended on the ratio of the cost to maintain the hospitalization system to the monetary loss per deaths by infection which strategies should be adopted.

KEYWORDS
COVID-19, Decision making, Emerging Infectious Disease, Epidemic model, Total loss

1 | INTRODUCTION

We're facing the risk of emerging infectious diseases (EIDs) due to the increase on the movement between different regions. The COVID-19, caused by the novel coronavirus (SARS-CoV-2), is an infectious disease with a relatively high infectivity and mortality rate. The number of persons around the world infected with the COVID-19 had grown at an alarming rate since the beginning of 2020. The world health organization (WHO) first declared COVID-19 a public health emergency of international concern (PHEIC) on January 30, 2020 (WHO, 2020) . Although the virus was not eliminated and had been changing, the WHO announced an end to PHEIC of COVID-19 on May 5, 2023 (WHO, 2023). Since even asymptomatically infected person can be infectious, it is difficult to take measures against the spread of the COVID-19 infection. Some argued that it is difficult to eliminate the SARS-CoV-2 due to its property (Thompson et al., 2020; Furuse and Oshitani, 2020). The elimination, as an ideal ending, is achieved when the transboundary cooperation is established and the vaccine is fairly distributed (Fontanet et al., 2021; Metcalf et al., 2021). However, if not so, we should choose the cohabitation option with the virus (Kofman et al., 2021).

From lessons of the previous pandemic, we should pay attention to EIDs in the future as well as the new variant of the SARS-CoV-2. The important index to consider preventing the spread of the virus is the effective reproduction number, which is defined as the average number of people infected by an infectious person by the time for his or her recovery or death. Reducing this number is essential to contain the epidemic (Ferguson et al., 2005). One of challenges for policy making against the outbreak of an EID is preparedness to enable prompt and effective actions to control outbreaks (Hadley et al., 2021; Petersen et al., 2020). In addition, it is well-acknowledged that there is a trade-off between maintaining economic activity and the prevention of an outbreak of disease. Dangerfield et al. (2022) discussed the key challenges when merging of epidemiology and economics, such as evaluating the trade-off between saving lives and economic costs. Kretzschmar et al. (2022) emphasized the interdisciplinary collaboration of different fields including mathematics, biology, and medical economics for EIDs in the future. Their review also argued that it is necessary to find models reflecting the realistic system.

In the present study, we took an EID like COVID-19 for example and examined three types of interventions: behavioral restrictions, tests for detecting exposed people, and the hospitalization of infected people. For example, lockdowns are considered behavioral restrictions: the short-term effect of suppression measures tends to involve urban lockdowns and the huge economic impact of such lockdowns. We explored the trade-off between the damage by infection and the cost of countermeasures, and demonstrated a framework of investigating the total damage of the EID. We investigated the negative impact on the economy and the reduction of deaths as a result of executing such interventions in the early stage and the late stage of an epidemic. Mathematical epidemic models are important tools in an epidemic since they are reference tools for policymakers in deciding which policy should be adopted. Calculation was done to determine the mortality rate from infection cases and the socio-economic cost.

When an EID breaks out, like in the early stage of the COVID-19 (Anderson et al., 2020), little information is available. The behavioral restriction is then one of realistic options in the absence of the mass testing and pharmaceutical interventions. A mathematical epidemic model known as the Susceptible-Infected-Recovered (SIR) has been used to estimate the effect of interventions on the number of deaths by infection. During the state of emergency announced by the Japanese government in the spring of 2020, citizens were requested to stay home, which resulted in a drastic reduction in the number of infected people without a legally-binding lockdown. However, some research implied that people cannot follow this restriction for a long time and may change their behaviors (Nakanishi et al., 2021; Pan et al., 2020).

In the late stage, when the mass testing and pharmaceutical interventions are available, the detection and isolation of infected persons become a continuous policy. Infected persons are detected by conducting tests based on the reverse transcriptase polymerase chain reaction (RT-PCR) and the antibody test. The Susceptible-Infected-Recovered (SIR) model does not consider the isolation of confirmed infections in health care facilities, even though this measure is known to be successful in that isolation prevents new infections. In this stage, we developed another model to incorporate the detection and isolation of infected people. It helps determine the appropriate isolation measures to be taken for those who test positive. The model assumptions used in our analysis were simplistic, the parameter values were provisional, and we were not aiming for quantitative comparative verification.

2 | METHODS

2.1 | General approach

We can define the loss caused by the epidemic as the sum of the damage by infection and the cost for the countermeasure. The objective of this research is reducing the total loss consisting of the death by infection and the socio-economic cost. In order to finding out an effective solution, we need to understand population dynamics under the epidemic. Converting the total loss and the cost into a monetary base helps us compare the trade-off and countermeasure plans.

2.2 | Population dynamics

2.2.1 | Early stage

In the early stage of an epidemic, there would not be much information available. We used one of the simplest models and assumed the population dynamics of an EID are given as follows:

$$\begin{cases} \dfrac{dS}{dt} = -(1-f)\beta S I \\[2ex] \dfrac{dI}{dt} = (1-f)\beta S I - \gamma I \\[2ex] \dfrac{dR}{dt} = \gamma I \end{cases} \tag{1}$$

where S, I, and R represent the density of susceptible, infected, recovered people, respectively. The total population density, including the number of deaths, $S(t) + I(t) + R(t) = 1$ for any time. β is the infection rate, while γ is the recovery rate. The basic reproduction number, denoted by $\mathfrak{R}_0$, is defined by β/γ. f is a control parameter and represents the degree of the behavioral restrictions. While $f = 0$ represents the absence of behavioral restrictions (usual state), $f > 0$ means that some policies, such as the restriction of movement, are implemented. We defined f_{max} as the maximum value of f and assume $f_{max} = 0.6$. We also defined f_c as the threshold of f such that satisfies $dI/dt \leq 0$ at any time t. We can obtain $f_c = 1 - \gamma/\beta$ from the second equation of Eq.1.

2.2.2 | Late stage

In the late stage, we assumed that some information of the EID is available to make a decision. We developed a new epidemic model by adding two new compartments: E and H. E stands for "Exposed" and represents the density of those who are exposed to the virus. On the other hand, H stands for facilities for isolation such as "Home", "Hotel", and "Hospital" and represents the density of isolated people including those who are detected by testing and hospitalized by onset of the symptom. The population dynamics of our SEIHRS model are given as follows:

$$\begin{cases} \dfrac{dS}{dt} = -\beta S I + \epsilon R \\[2ex] \dfrac{dE}{dt} = \beta S I - \eta E - \theta E \\[2ex] \dfrac{dI}{dt} = \eta E - \lambda I - \gamma I \\[2ex] \dfrac{dH}{dt} = \theta E + \lambda I - \gamma_h H \\[2ex] \dfrac{dR}{dt} = \gamma I + \gamma_h H - \epsilon R \end{cases} \tag{2}$$

where η is the reciprocal of the incubation period; θ is the detection rate of the exposed people. λ is the hospitalization rate of the infected people and the reciprocal of the time from onset to hospitalization. ϵ is the waning rate of the immunity; γ is the recovery rate of infected people, while γ_h is that of isolated people. We denoted vector state (S, E, I, H, R) by $\mathbf{X}$. The total population $S(t)+E(t)+I(t)+H(t)+R(t) = 1$ is constant for any time t. Infection mortality would reduce the total population; however we assume that it can be negligible. θ and λ are control parameters in this system. When $\epsilon > 0$, this system has two equilibrium points, $\mathbf{X}_1$ and $\mathbf{X}_2$.

$$\begin{aligned} \mathbf{X}_1 &= (S_1, E_1, I_1, H_1, R_1) \\ &= (1, 0, 0, 0, 0) \end{aligned} \tag{3}$$

$$\begin{aligned} \mathbf{X}_2 &= (S_2, E_2, I_2, H_2, R_2) \\ &= \left(\frac{(\eta+\theta)(\lambda+\gamma)}{\beta\eta}, \frac{\lambda+\gamma}{\eta} I^*, I^*, \frac{\theta(\lambda+\gamma)+\eta\lambda}{\eta\gamma_h} I^*, \frac{(\lambda+\gamma)(\theta+\eta)}{\eta\epsilon} I^* \right) \end{aligned} \tag{4}$$

where

$$I^* = \left(1 - \frac{(\eta+\theta)(\lambda+\gamma)}{\beta\eta}\right)\left(1 + \frac{\lambda+\gamma}{\eta} + \frac{\theta(\lambda+\gamma)+\eta\lambda}{\eta\gamma_h} + \frac{(\lambda+\gamma)(\theta+\eta)}{\eta\epsilon}\right)^{-1} \tag{5}$$

2.3 | Trade-off between the mortality rate and the socio-economic cost

2.3.1 | Early stage

In the early stage, we assumed that the period of interest was 180 days ($T = 180$). The mass testing in this stage is not prepared well and pharmaceutical interventions such as vaccination are not available yet. We calculated the mortality rate, the density of susceptible and recovered people at day T ($S(T)$ and $R(T)$), the maximum value of $I(t)$, and the day when $I(t)$ is maximized. Since the total population is assumed to be one in this paper, these indicators are per capita values.

It is assumed that those who get sick die of infection at a rate. Let $D(t)$ be the mortality rate by COVID-19 in those who are newly confirmed cases from time 0 to t. we calculated it as follows:

$$D(T) = \delta \times \int_0^T (1-f)\beta S(t)I(t)dt \tag{6}$$

where δ is the infection fatality rate, defined as the ratio of deaths to the number of infected cases. Nishiura et al. (2020) estimated that $\delta = 0.3\%$ to 0.6%, and we assumed $\delta = 0.5\%$. There is a time lag between infection and recovery or death, but the lag is assumed to be negligible.

In the absence of acquired herd immunity, the realistic option is to continue with behavioral restrictions until a medical resolution is found. There are suppression and mitigation strategies (Ferguson et al., 2020). We also defined the socio-economic cost resulted from behavioral restrictions as an indicator depending on the intensity of implemented behavioral restrictions and the management period. It is denoted by C_f and is calculated as follows:

$$C_f(T) = \int_0^T m_f(f)dt \tag{7}$$

where $m_f(f)$ is the cost to maintain the behavioral restriction on a daily basis and is assumed $m_f(f) = M_f \cdot f/f_{max}$. $m_f(0) = 0$ means that the usual state is maintained, and $m_f(f_{max}) = M_f$ is the cost per day required to execute a state of emergency.

The inherent difference between impacts of $D(T)$ and $C_f(T)$ makes it difficult to compare them directly. To summarize the total loss of the damage by infection and the cost of countermeasures, we converted the $D(T)$ into a monetary base. In this paper, all costs are presented in Japanese yen. We then calculated the mortality rate converted into the monetary base, denoted by C_M.

$$C_M(T) = D(T) \times M_D \tag{8}$$

where M_D is the monetary loss per deaths by infection. The total loss per capita, denoted by Z, is given as:

$$Z = C_M(T) + C_f(T) \tag{9}$$

This allows these different ideas to be directly compared. To plot the result of the simulation, we define $\bar{z} = Z/M_D$ and $M_{f/D} = M_f/M_D$.

$$\bar{z} = \frac{Z}{M_D} = D(T) + \bar{f} \cdot M_{f/D} \tag{10}$$

where

$$\bar{f} = \int_0^T \frac{f}{f_{max}} dt \tag{11}$$

We conducted simulations for three basic reproduction number ($\Re_0 = 1.5, 2.5, 3.0$) and the initial state that $I(0) = 1.0 \times 10^{-3}$, $S(0) = 1 - I(0)$, and $R(0) = 0$. We examined non-intervention ($f = 0$) and three types of degree of behavioral restrictions: weak ($f = 0.2$), middle ($f = 0.4$), , and strong ($f = 0.6$). Variables and parameters are shown in Table .

2.3.2 | Late stage

We examined the late stage strategy in which we could reduce the total loss by the epidemic without behavioral restrictions in the late stage. We assumed changes in the parameter values in the early and late stages (Table 2). We also assumed that some acquired the immunity against the virus through infection and vaccination . The main intervention is the detection and isolation of exposed people and the hospitalization of infected people instead of behavioral restrictions, and their socio-economic costs were calculated in the late stage. We assumed that the immunity acquired by natural infection and vaccination would wane and the new strategy started from $t = T_0$ in the simulation. We did not consider infection dynamics from the end of the early stage T to the beginning of the late stage T_0. Therefore, the specific date of T_0 is not specified here, and the state at $t = T_0$ is also given as an initial value of the late stage.

Firstly, we explored the situation from T_0 to T_1 and investigated the sensitivity of $R(T_0)$ and calculated the death by infection, the cumulative rate of detected cases and the cumulative rate of hospitalized cases. T_1 is one year after T_0, and that is, $T_1 = T_0 + 365$. It is assumed that those who get sick die of infection at a rate. Let $D(t)$ be the mortality rate by COVID-19 in those who are newly confirmed cases from time T_0 to t. We calculated it as follows:

$$D(t) = \delta \times \int_{T_0}^{t} \beta S(t) I(t) dt \tag{12}$$

We used the cumulative rate of detected cases, denoted by c_1, as an indicator of detection and isolation:

$$c_1(t) = \int_{T_0}^{t} \theta E(t) dt \tag{13}$$

We also used the cumulative rate of hospitalized cases denoted by c_2, as an indicator of hospitalization:

$$c_2(t) = \int_{T_0}^{t} \lambda I(t) dt \tag{14}$$

Next, we examined reasonable policies to reduce the total loss in a long run under parameters in Table 2. The total loss per capita, Z, is given as:

$$Z(t) = C_M(t) + C_\theta(t) + C_\lambda(t) \tag{15}$$

where C_M, C_θ, and C_λ are the monetary loss of death by infection, the socio-economic cost relating the detection and isolation, and that of the hospitalization, respectively.

C_M is given as:

$$C_M(t) = D(t) \times M_D \tag{16}$$

C_θ consists of the cost to maintain the detection and isolation system, $m_\theta(\theta)$, and the cost resulted from the detection.

$$C_\theta(t) = \int_{T_0}^{t} m_\theta(\theta)\,dt + \frac{m_1}{\pi} c_1(t) \tag{17}$$

where m_1 is the unit cost for the detection per day per person and π is the positive rate.

C_λ consists of the cost to maintain the hospitalization system, $m_\lambda(\lambda)$, and the cost resulted from the hospitalization.

$$C_\lambda(t) = \int_{T_0}^{t} m_\lambda(\lambda)\,dt + m_2 c_2(t) \tag{18}$$

where m_2 is the mean unit cost for the hospitalization per day per person.

In a long run, we explored how the total loss increases on a daily basis. we took a time derivative of Z at $\mathbf{X} = \mathbf{X}_2$.

$$\begin{aligned} \frac{d}{dt} Z(t)\Big|_{\mathbf{X}=\mathbf{X}_2} &= \frac{d}{dt} C_M(t)\Big|_{\mathbf{X}=\mathbf{X}_2} + \frac{d}{dt} C_\theta(t)\Big|_{\mathbf{X}=\mathbf{X}_2} + \frac{d}{dt} C_\lambda(t)\Big|_{\mathbf{X}=\mathbf{X}_2} \\ &= \delta\beta S_2 I_2 M_D + M(\theta) + \frac{m_1}{\pi}\theta E_2 + M(\lambda) + m_2\lambda I_2 \end{aligned} \tag{19}$$

We defined z as $dZ(t)/dt|_{\mathbf{X}=\mathbf{X}_2}$. This problem can be interpreted as a minimization problem:

$$\text{Minimize} \quad z \tag{20}$$

$$\begin{aligned} \text{constraint to} \quad \theta &\geq 0 & (21) \\ \lambda &\geq 0 & (22) \\ 0 \leq S_2 &\leq 1 & (23) \end{aligned}$$

However, it is hard to solve this problem analytically and some parameters are uncertain. We define $\bar{z} = z/M_D$ and assume $m_\theta(\theta) = \theta \cdot M_\theta$ and $m_\lambda(\lambda) = \lambda \cdot M_\lambda$.

$$\bar{z} = \delta\beta S_2 I_2 + \theta M_{\theta/D} + \frac{m_{1/D}}{\pi}\theta E_2 + \lambda M_{\lambda/D} + m_{2/D}\lambda I_2 \tag{24}$$

where $M_{\theta/D} = M_\theta/M_D$, $M_{\lambda/D} = M_\lambda/M_D$, $m_{1/D} = m_1/M_D$, and $m_{2/D} = m_2/M_D$. We aimed to minimize this $\bar{z}$ and prepared candidate policies based on two strategies: elimination and cohabitation. We referred to a policy in which $\mathbf{X}_2$ (Eq.4) did not exist as the "intensive (intervention) policy”. The parameter set (λ, θ) satisfies $\lambda \geq \beta\eta/(\eta+\theta) - \gamma$. On the other hand, the policy with the cohabitation strategy in which $\mathbf{X}_2$ exists is called “moderate (intervention) policy”. Of the latter, a policy that does not intervene at all $(\lambda = \theta = 0)$ is called a “non-intervention policy”. Table 3 shows policy cases and their combinations of θ and λ. We assumed four combination cases of $m_{1/D}$ and $m_{2/D}$: $(m_{1/D}, m_{2/D}) = (10^{-5}, 10^{-3})$, $(10^{-5}, 10^{-4})$, $(10^{-4}, 10^{-3})$, and $(10^{-4}, 10^{-4})$.

3 | RESULTS

3.1 | Early stage

We conducted simulations and calculated the mortality rate $D(T)$, $S(T)$, $R(T)$, the maximum value of $I(t)$ during the management period, and the day when $I(t)$ is maximized. Table 4 shows results of the simulations. A larger $\mathfrak{R}_0$ and a lower f increased $D(T)$ and the maximum value of $I(t)$. When $f \geq f_c$, the mortality can be greatly reduced but few people were immunized. On the other hand, the peak of $I(t)$ was delayed when $f < f_c$.

We examined the total loss during the first 180 days of the epidemic. Figure 1 demonstrates the reasonable policy to reduce the total loss during the early stage with different $M_{f/D}$. When $M_{f/D}$ was small, the total loss by the epidemic was relatively small and the strong behavioral restriction ($f = 0.6$) was recommended with any $\mathfrak{R}_0$ (Figure 1 (a), (b), and (c)). As $M_{f/D}$ became larger, the strong behavioral restriction was not effective in reducing the total loss and middle or weak behavioral restriction became a better solution. The total loss under non-intervention ($f = 0$) was constant and could be a better strategy when $M_{f/D}$ was large. These intermediate interventions are only supported in a narrow region, and either non-intervention or strong behavioral restrictions are effective. The non-intervention is favored when the economic loss of behavioral restrictions is more important than the economic value of life. In the case of a larger $\mathfrak{R}_0$, the domain in which the middle and weak behavioral restrictions were favorable decreased. When $\mathfrak{R}_0 = 3.0$, the non-intervention or the strong intervention was effective (Figure 1 (c)).

3.2 | Late stage

We conducted simulations in the late stage from T_0 to T_1 and calculated the mortality rate by infection $D(T_1)$, the cumulative rate of detected cases $c_1(T_1)$, and the cumulative rate of hospitalized cases $c_2(T_1)$. Figure 2 shows the sensitivity of indicators with increasing the detection rate θ and the hospitalization rate λ. Results of indicators with different densities of those who has recovered by the late stage $R(T_0)$ were similar, and they became lower as $R(T_0)$ got higher. $D(T_1)$ was monotonically decreasing with increasing θ or λ (Figure 2 (a) and (b)). The shape of lines of $c_1(T_1)$ seemed convex with increasing θ (Figure 2 (c)). The curves reached their peaks at a higher θ as $R(T_0)$ got higher. The similar behaviors were obtained in $c_2(T_1)$ with increasing λ (Figure 2 (f)). $c_1(T_1)$ with increasing λ and $c_2(T_1)$ with increasing θ were monotonically decreasing (Figure 2 (d) and (e)).

Figure 3 shows the reasonable policy with different $M_{\theta/D}$ and $M_{\lambda/D}$. It depended on $M_{\lambda/D}$ which policy should be implemented. Intensive policies were reasonable in $M_{\lambda/D} < 3 \times 10^{-5}$, the non-intervention policy was in $M_{\lambda/D} < 2 \times 10^{-4}$. When $m_{1/D} = 10^{-5}$, the total loss was minimized with a moderate policy in a limited area (Figure 3 (a) and (b)). The area in which policy G was reasonable was around $M_{\theta/D} < 9 \times 10^{-6}$ and $7 \times 10^{-5} \leq M_{\lambda/D} < 2 \times 10^{-4}$. When $m_{1/D} = 10^{-4}$, most of the area was replaced by policy F (Figure 3 (c) and (d)). Other moderate policies (H-K) were not favored in any region. As $M_{\theta/D}$ was increasing, the policy with a lower θ became more effective.

4 | DISCUSSION

We examined early and late stages of an epidemic caused by an EID and proposed a framework to reduce the total loss caused by the epidemic. There is not much information available in the early stage of the epidemic, and the situation changes over time afterward. We converted the mortality rate and the socio-economic cost into a monetary base (Figure 1). Our result demonstrated non-intervention or the strong behavioral restriction may be effective in reducing the total loss with different $\mathfrak{R}_0$. Especially when the $\mathfrak{R}_0$ was large, middle or weak behavioral restrictions did not reduce the number of deaths by infection so much. As a result, they became less supportive. Essentially, the ratio of M_f to M_D ($M_{f/D}$) is an important criterion for making a decision. The socio-economic cost resulted from behavioral restrictions is flexibly changed depending on the purpose. Zeytoon-Nejad and Hasnain (2021) proposed and examined the trade-off relationship between saved lives and saved jobs. Instead of saved jobs, we can also adopt indices such as the reduction of individual consumption or the gross domestic product. The behavioral restriction is a countermeasure until other intervention become available. When the mass testing which detects the infected people becomes available, these interventions are combined to reduce the effective reproduction number. Holtemöller et al. (2020) conducted an economic impact assessment of the disease and its mitigation measures in a standard neoclassical growth model. He concluded that the optimal policy would be a mixture of temporary partial shutdowns and intensive testing and long-term quarantine of infected individuals.

We explored the late stage of epidemic after leaving the behavioral restriction policy. We used the SEIHRS model, assuming that some information relating the virus and countermeasures had been available. We calculated three indicators one year after leaving the behavioral restriction policy: the cumulative detected case rate, the cumulative hospitalized rate, and the mortality rate. Utilizing the positive rate, we can estimate the necessary amount of resource for testing. When the initial value of the density of immunized people was high, indicators resulted in smaller values (Figure 2). This result implies when the behavioral restriction policy should be lifted. Continued monitoring of antibody retention rates may reduce the need for repeated behavioral restrictions if the efficacy of the antibody is known when a mutant strain emerges.

We also examined the reasonable policy to reduce the total loss in a long run. Our conclusion is that the moderate intervention policy is supported only in very limited circumstances, and either the intensive intervention policy or non-intervention policy is recommended. It depended on the ratio of the cost to maintain the hospitalization system to the monetary loss per deaths by infection which policies should be adopted (Figure 3). It is desirable to develop a cost-effective hospitalization system in which infected individuals can quickly take a medical care.

There are some limitations in our research. Even though this model assumes a homogenous population, the population is actually heterogeneous. Furthermore, the difference between the infection rate and mortality rate at different age is important when looking at actual data. An indicator such as the maximum value of the density of hospitalized people in a day can be converted into the maximum amount of health care facilities. However, it is not clear whether the required medical personnel can be obtained or not. We assumed that the monetary cost was linearly increasing with the intensity of each intervention ($m_f(f)$, $m_\theta(\theta)$, and $m_\lambda(\lambda)$); however the non-linearity may change the favorable policy. The quantitative verification of this model cannot be guaranteed. We didn't consider the opportunity cost when calculating the total loss. Recession caused by behavioral restrictions increases the unemployment rate and imposes psychological stress on many people, and those factors have also been shown to result in an increase in the suicide rate (e.g. Kawohl and Nordt, 2020; Reger et al., 2020; Sher, 2020).

Many nations shifted from suppression to mitigation strategies, partly due to the widespread use of vaccination. However, the validity of this change has been insufficiently evaluated. We adopted a one-shot intervention to demonstrate the total loss in the early stage; however, it can be investigated under a cycle of behavioral restrictions and relaxation (e.g. Chowdhury et al., 2020; Watanabe and Matsuda, 2022). We examined the elimination strategy in the late stage simulation and proposed intensive intervention policies; however, the immigration of infected persons from other countries should also be considered. This paper can provide a framework to compare strategies and policies, although the quantitative results need to be improved. If the values of the parameters vary from country to country, the appropriate strategy may also differ (Khalifa et al., 2020). The knowledge provided by these models can only be understood in terms of a dynamical system. It must be stressed that there is no objective optimal solution, and that evaluation in decision-making depends on the values of policymakers. Further consideration is required with regard to the decisions, the justifications of those decisions, and their impact.

Since the outbreak, the SARS-CoV-2 has been being replaced by different variants, probably with increased reproduction number (e.g Tanaka et al., 2021; Campbell et al., 2021; Furuse, 2022). Some reported that the omicron variant has the property that reduces the effectiveness of the vaccine against the symptomatic disease and evades the immunity (Andrews et al., 2022; Tan et al., 2023). Furuse (2021) conducted numerical simulations and examined how the property of a new variant and human antibodies influenced the epidemic. Ferguson et al. (2006) recommended using the real-time data to allow interventions to be tuned to match the virus. We have to observe the property of such a new variant and EIDs to take a quick countermeasure.

Some studies measured the burden and the damage of COVID-19 and pointed out that they are unevenly distributed by a part of people (e.g. Yoshikawa and Kawachi, 2021; Silva et al., 2023). As a lesson from the epidemic of SARS-CoV-2 and previous events, Norheim et al. (2021) showed the importance to set up systems that can provide for open and inclusive decision-making in an institutionalized manner rather than as ad hoc efforts when hard policy choices and trade-offs are called for on a regular basis. Furthermore, as Grimm et al. (2020) argued, it is important to keep in mind that the responsibility for using model outputs lies with decision makers. For the epidemic in the future, it is necessary to develop a decision-making system showing who is responsible for the decision clearly.

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conflict of interest

The author declares no conflict of interest.

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TABLE 1 The list of variables, indicators, and parameters

Symbol	Definition
$S(t)$	Density of susceptible persons at time t
$E(t)$	Density of those who are exposed to the virus at time t
$I(t)$	Density of infected people at time t
$H(t)$	Density of isolated people at time t
$R(t)$	Density of recovered persons at time t
$D(t)$	Mortality rate by infection during the management period
λ	Hospitalized rate of infected people
θ	Detection rate of exposed people
$\mathfrak{R}_0$	Basic reproduction number
T_0	Start time of the late stage
f	Degree of behavioral restrictions, such as the restriction of movement and shortening business hours
f_{max}	The maximum degree of behavioral restrictions (assuming $f_{max} = 0.6$)
$\bar{f}$	Mean of f during the period of interest
Z	The total loss caused by the epidemic (Eqs.9, 15)
z	Differential coefficient of Z at $\mathbf{X} = \mathbf{X}_2$ (Eq.19)
$\bar{z}$	z/M_D (Eqs. 10, 24)
C_M	Monetary loss of death by infection (Eq.16)
C_f	Socio-economic cost resulted from the behavioral restrictions (Eq.7)
C_θ	Socio-economic cost caused by the detection and isolation (Eq.17)
C_λ	Socio-economic cost caused by the hospitalization (Eq.18)
M_D	Unit monetary loss per deaths by infection
M_f	Unit monetary cost to convert the degree of behavioral restrictions
M_θ	Unit monetary cost to convert the detection and isolation
M_λ	Unit monetary cost to convert the hospitalization
$M_{f/D}$	Relative cost to conduct the detection (M_f/M_D)
$M_{\theta/D}$	Relative cost to conduct the detection (M_θ/M_D)
$M_{\lambda/D}$	Relative cost to conduct the hospitalization (M_λ/M_D)
m_1	Unit monetary cost for detected people
m_2	Unit monetary cost for hospitalized people
$m_{1/D}$	Relative cost of m_1 to M_D (assuming $m_{1/D} = 1 \times 10^{-4}$ or 1×10^{-5})
$m_{2/D}$	Relative costof m_2 to M_D (assuming $m_{2/D} = 1 \times 10^{-3}$ or 1×10^{-4})
$c_1(t)$	Cumulative rate of detected cases (Eq.13)
$c_2(t)$	Cumulative rate of hospitalized cases (Eq.14)

TABLE 2 Parameter values for simulations

Parameter	Definition	Early stage	Late stage
β	Infection rate	0.75, 0.125, 0.15	0.3
γ	Recovery rate of infected people	0.05	0.1
γ_h	Recovery rate of isolated people	-	$\gamma_h \approx \gamma$
η	Reciprocal of the incubation period	-	0.3
δ	Infection fatality rate	0.005	0.001
T	Management period for the early stage	180 days	-
T_1	End time of the late stage	-	365 days after T_0

TABLE 3 Simulation cases in the late stage. Non-intervention policy (A), the intensive intervention policies (B-F), and moderate policies (G-N).

Policy	θ	λ
A	0.00	0.000
B	0.00	0.200
C	0.06	0.150
D	0.10	0.125
E	0.20	0.080
F	0.30	0.050
G	0.30	0.040
H	0.15	0.050
I	0.20	0.070
J	0.10	0.120
K	0.06	0.075
L	0.05	0.125
M	0.03	0.150
N	0.00	0.180

TABLE 4 Results of simulations in the first 180 days of the epidemic. The mortality rate $D(T)$, the density of susceptible, infected, recovered (immunized, including death) people at $t = T$, the maximum value of $I(t)$, and T_{max}, the day when $I(t)$ is maximized.

$\Re_0$	f_c	f	$D(T)$	$S(T)$	$R(T)$	$\max_{0\leq t\leq T} I(t)$	T_{max}
1.5	0.33	0	8.88×10^{-4}	0.821	0.130	4.81×10^{-2}	180
		0.2	1.41×10^{-4}	0.971	2.39×10^{-2}	5.35×10^{-3}	180
		0.4	2.63×10^{-5}	0.994	5.87×10^{-3}	1.00×10^{-3}	0
		0.6	7.26×10^{-6}	0.998	2.43×10^{-3}	1.00×10^{-3}	0
2.5	0.6	0	4.41×10^{-3}	0.118	0.856	0.234	98
		0.2	3.58×10^{-3}	0.283	0.631	0.154	136
		0.4	8.88×10^{-4}	0.821	0.130	4.81×10^{-2}	180
		0.6	4.40×10^{-5}	0.990	8.84×10^{-3}	1.00×10^{-3}	0
3.0	0.67	0	4.69×10^{-3}	6.15×10^{-2}	0.929	0.301	77
		0.2	4.31×10^{-3}	0.136	0.830	0.219	104
		0.4	2.72×10^{-3}	0.456	0.436	0.118	161
		0.6	1.41×10^{-4}	0.971	2.39×10^{-2}	5.35×10^{-3}	180

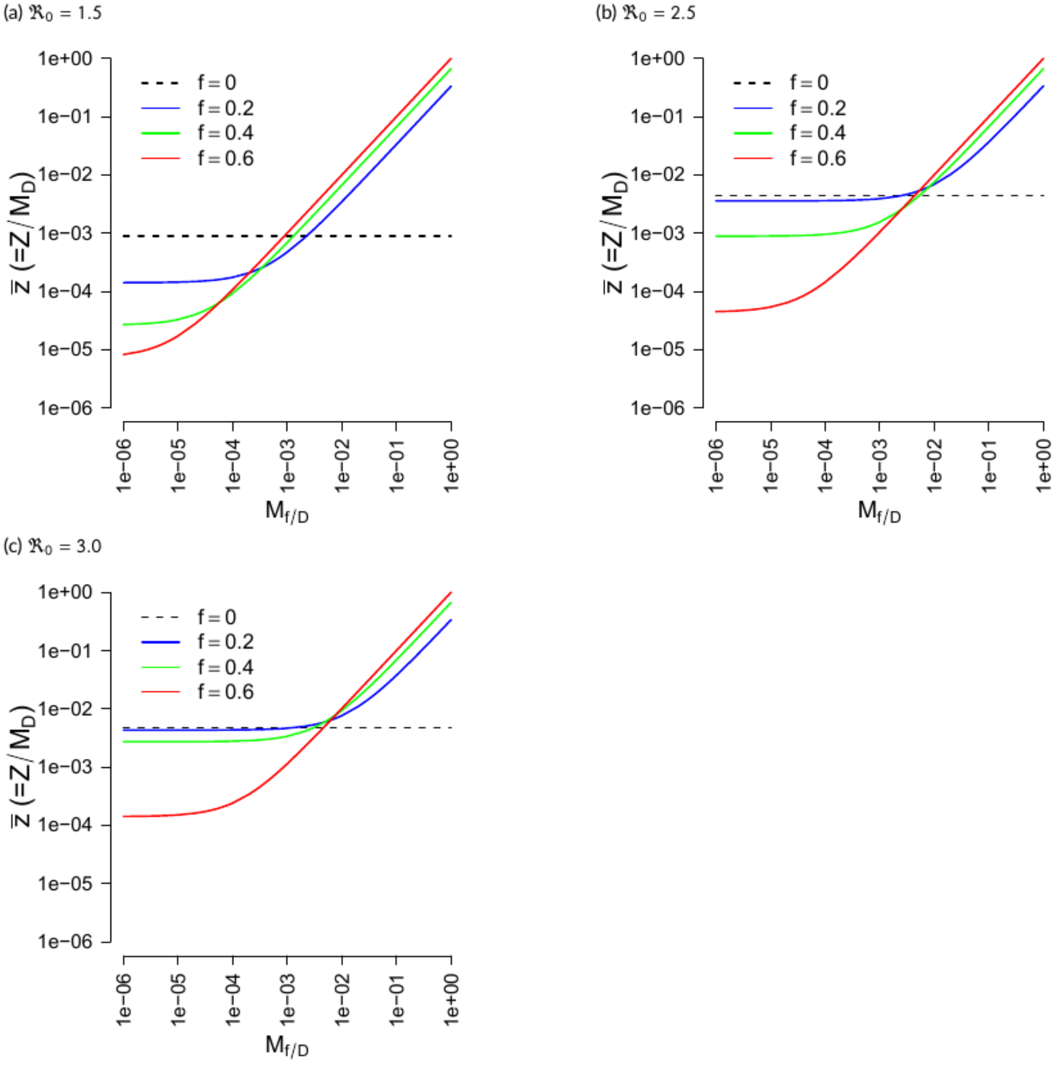

FIGURE 1 The total loss caused by deaths by infection and the cost of countermeasures against the infection under four different degrees of behavioral restrictions f = 0, 0.2, 0.4, and 0.6.

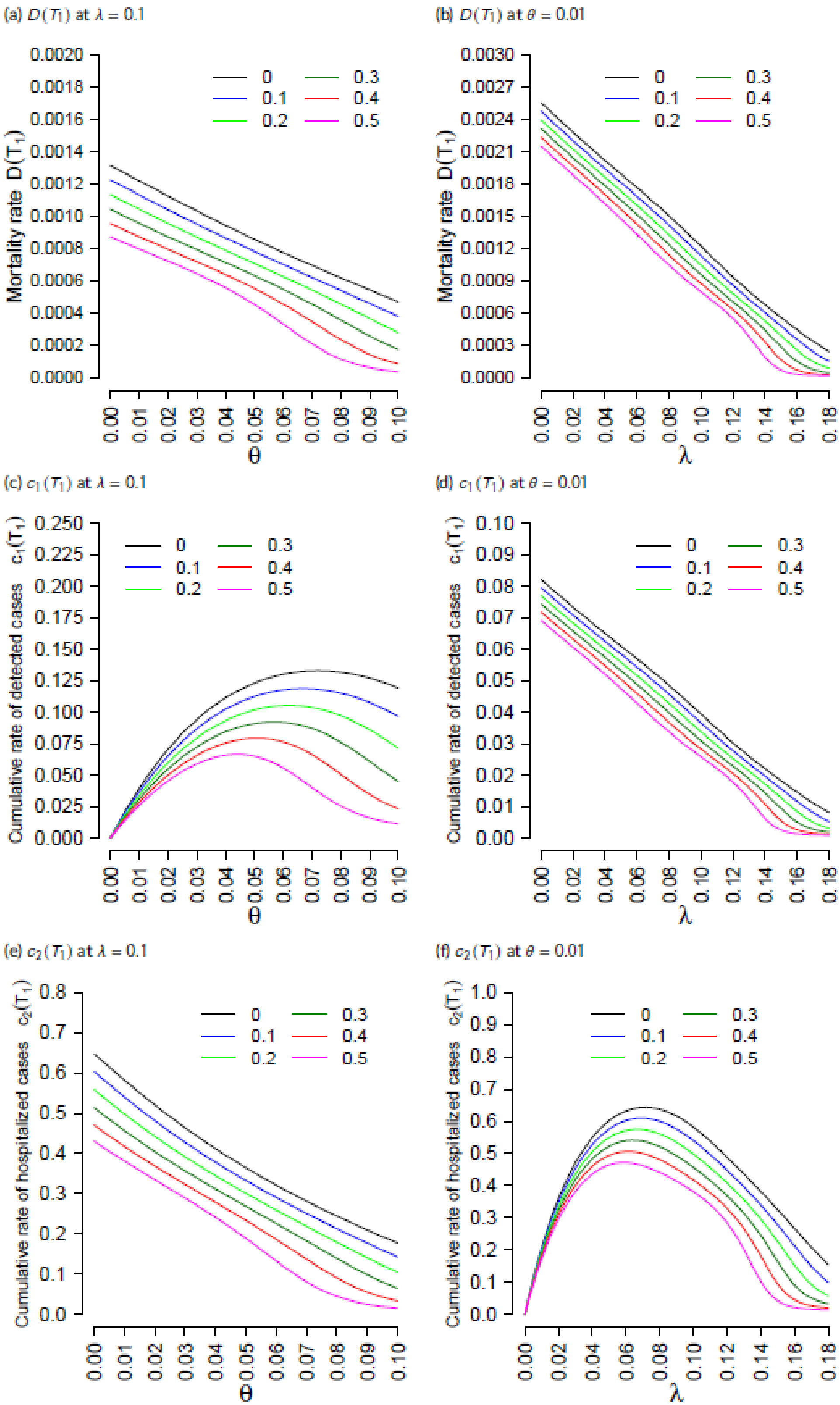

FIGURE 2 Sensitivity of indicators with the detection rate θ and the hospitalization rate λ. Lines demonstrate results of different $R(T_0) = 0, 0.1, 0.2, 0.3, 0.4, 0.5$.

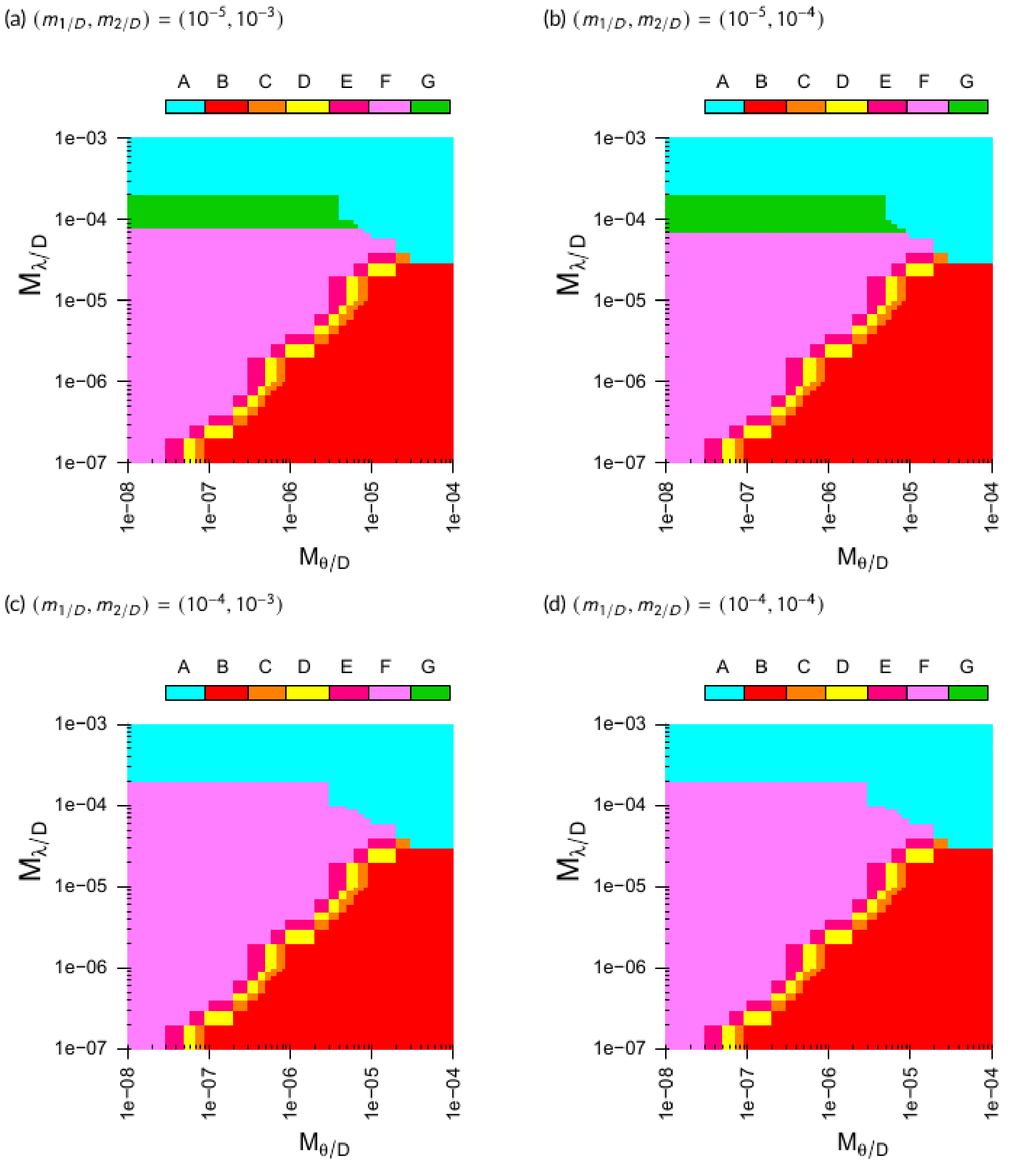

FIGURE 3 Reasonable policies with different $M_{\theta/D}$ and $M_{\lambda/D}$. The numbers in brackets in panels a to d indicate the values of $(m_{1/D}, m_{2/D})$. Domain A represents the non-intervention policy, domains B to F represent intensive intervention policies, and domain G is one of moderate policies (Refer to Table 3).