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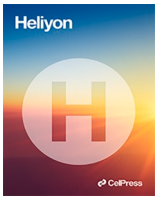

Research article

The strategy to control the outbreak of an emerging respiratory infectious disease in a simulated Chinese megacity

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ABSTRACTS

Objectives: The emergence of respiratory infectious diseases (ERID) poses a significant threat to global public health. However, effectively managing ERID outbreaks in large cities remains a challenge.
Methods: An age-structured Susceptible-Exposed-Infectious-Removed (SEIR) model was developed to predict the effectiveness of non-pharmaceutical interventions (NPIs) in controlling ERID outbreaks. Four ERID outbreak scenarios were created based on varying levels of infectivity and pathogenicity. Based on the World Health Organization's (WHO) categorization for responding to the influenza pandemic, the combinations of NPIs were classified into five levels: base, any, moderate, high, and extraordinary levels (from mild to severe). The simulated progression of ERID outbreaks in a megacity were compared across different levels of NPI.
Results: Our findings indicate that the response strategies should be formulated based on the epidemiological characteristics of ERID. In the low transmission scenarios, the mandatory NPIs were unnecessary to control ERID outbreaks regardless of their pathogenicity. However, even with low pathogenicity, severe NPIs are required to control the spread of ERID and minimize harm to the public in high transmission scenarios.
Conclusion: The NPIs for the EIRD outbreak in a city should be tailored to the epidemiological characteristics to control its impact and protect public health.

1. Introduction

Over the past two decades, the pandemic of several emerging respiratory infectious diseases (ERIDs), such as SARS-CoV I, MERS, and SARS-CoV II (COVID-19) have posed significant challenges to global public health and economic development. The severe acute respiratory syndrome coronavirus (SARS-CoV, 2003), a newly emerging respiratory disease, resulted in over 8000 cases and 900 deaths across 32 countries or regions in 2003 [1]. Similarly, the newly discovered H1N1 influenza virus led to 18,449

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laboratory-confirmed deaths from April 2009 to August 2010 [2]. In particular, the COVID-19 pandemic triggered a global crisis, threatening the health of billions and disrupting economic growth in all countries from 2019 to 2022 [3]. More than 772 million infections and over 6.9 million deaths have been caused by COVID-19 by the time the WHO declared the end of COVID-19 in 2023 [4]. To combat these ERIDs, various control measures have been proposed to control the pandemic of these diseases, including vaccines, drugs, and NPIs. However, the appropriate response to the initial outbreak of ERIDs remains highly debated.

Countries have implemented various interventions to control ERID outbreaks based on the epidemiological characteristics of diseases. For instance, most countries included medication and treatments in response to the H1N1 pandemic, considering its low fatality rate (about 0.2 %) and limited transmissibility (R_0 is 1.4) [5]. In contrast, early COVID-19 was characterized by a high fatality rate of 5.73%–6.09 % and a quick spread speed (R_0 is over 2.2) in Wuhan 2020, China [6]. As a result, the control strategy for the COVID-19 outbreak shifted to strict non-pharmaceutical interventions (NPIs), including internal travel restrictions, reactive school closures, proactive school closures, reactive workplace closures, home working, and reducing meetings in many countries. So, when we face the outbreak of future ERIDs, it is urgent to identify its epidemiology parameters and implement proper responses quickly. Our study hypothesizes that tailoring NPIs to the specific epidemiological characteristics of an ERID, such as transmission rates and age-specific vulnerabilities, will enhance the ability to control disease spread and reduce the burden on healthcare systems [7].

Mathematical modelling can be used to simulate the effectiveness of potential interventions in the battle against the outbreak of ERID. In particular, the epidemic model could estimate and predict the demand for hospital beds and intensive care units (ICUs) [8,9]. Several studies utilize models to assess the effectiveness of NPIs in controlling outbreaks, such as social distancing, mask-wearing policies, etc. [10]. Mathematical modelling has also been crucial in guiding policy decisions during ERID outbreaks, particularly in the COVID-19 pandemic, where it has informed strategies to balance health protection and minimize socio-economic disruptions [11]. By simulating detailed projections of infection spread, healthcare resource needs, and the potential effectiveness of various public health interventions, the models enable informed and timely decision-making during the outbreak of ERID [12].

In this study, we developed an age-structured mathematical model to assessed the effectiveness of employing various interventions in different scenarios during the outbreak of an ERID in a simulated megacity based on Chinese population data. We estimated the demand for hospital beds and ICUs and evaluated the impact of NPIs to reduce the potential ERID burden and preventing the collapse of the local healthcare system. Our findings offer guidelines for future interventions to control new ERID outbreaks.

2. Methods

2.1. A dynamic model for emerging respiratory infectious disease outbreak

We developed an expanded age-structured Susceptible-Exposed-Infectious-Removed (SEIR) model to simulate ERID transmission in a hypothetical megacity based on Chinese population data. This model includes the susceptible, exposed, infectious, and removed populations, further groups infectious individuals into asymptomatic, symptomatic, and unquarantined symptomatic categories (Fig. 1). Our model simulates the transition of susceptible individuals (S) to the exposed (E) compartment upon infection using a stochastic chain binomial process. This process calculates the new exposures using binomial sampling at each time step, reflecting the inherent stochasticity in disease transmission. We conducted 200 simulations with 95 % confidence intervals to capture the stochastic variability. We applied a Gamma distribution to represent the variability in incubation periods to model the transition from latent (E) to infectious states (I). The average duration of the latent period ($1/\gamma_E$) was 4.1 (range: 3.4–5.0) days. The likelihood of progressing to either asymptomatic or symptomatic states is determined by the symptomatic probability ($P_s = 81.2$ %) [13]. Asymptomatic and symptomatic individuals are assumed to remain infectious for an average of $1/\gamma_I = 7$ (range: 7–10) days before moving to the removed compartment. Both asymptomatic and symptomatic individuals were assumed to be equally infectious [14]. The model assumes that 2.5 % of the population has pre-existing immunity due on cross-immunity from other respiratory diseases [15]. We also conducted sensitivity analyses with 5 % and 10 % immunity levels.

Five epidemiological indicators were considered as outcomes of this model: infections, symptomatic cases, hospitalizations, ICUs, and deaths in different scenarios. Symptomatic cases require hospital beds and ICUs. In contrast, the remaining symptomatic cases and all asymptomatic infections recover naturally. The average time from symptom onset to hospital admission was $1/\gamma_{sh} = 4$ or 12.5 days. It is assumed that hospitalized patients do not transmit the virus. Based on the corresponding mortality risk, patients in the ICUs (or

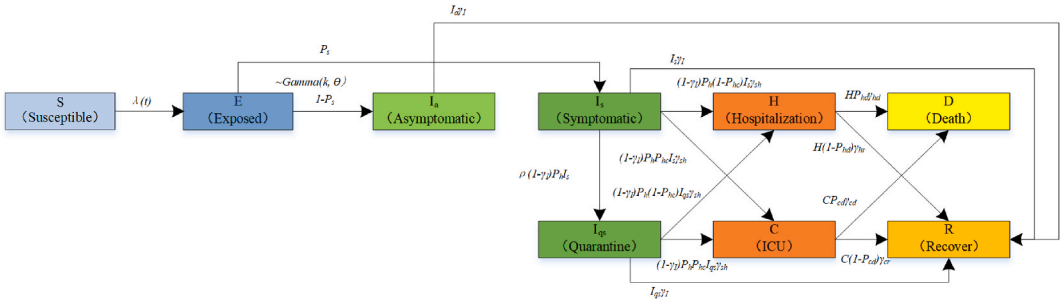

Fig. 1. Flowchart of the proposed extended SEIR transmission model. All states and parameters are defined in Table 1.

hospital beds) could stay there until they recover or die. It's assumed that all deaths occur among hospitalized patients.

We ranked the interventions in descending order according to their outcome: lower infections, symptomatic cases, hospitalizations, ICUs, and deaths. We tested different levels of NPIs by adjusting their intensity, and performed sensitivity analyses on varying initial infection levels (5, 15, 20, 50, and 100). Simultaneously, we explore mitigation interventions to reduce the ERID burden to prevent the local healthcare system from being overwhelmed.

All compartments and parameters are listed in Table 1. A stochastic chain binomial process simulates the transitions between compartments [16]. For example, susceptible individuals move to the exposed compartment at a rate of $\Delta t \sim$ Binomial (S(t), 1-$e^{-\lambda(t)}$), where $\lambda(t)$ is the force of infection at time t. The next-generation matrix method was used to calculate β from the R_0, representing the infectivity of carriers [17]. We used a contact matrix from a study conducted in Shanghai, China, aggregated into three age groups: 0–17 years, 18–59 years, and 60+ years. The total population was set at 10 million, based on the age distribution from the 2022 China Statistical Yearbook [18]. The expanded SEIR set of equations for ERID is as follows:

$$\frac{dS}{dt} = \frac{-\beta(\Theta I_a + I_s)S}{N} \tag{1}$$

$$\frac{dE}{dt} = \frac{\beta(\Theta I_a + I_s)S}{N} - \gamma_E P_s E - \gamma_E(1 - P_s)E \tag{2}$$

$$\frac{dI_a}{dt} = \gamma_E(1 - P_s)E - \gamma_I I_a \tag{3}$$

Table 1
| Summary of parameter values in the mathematical model.

Parameter	Description	Value	rang	Source
R_0	Basic reproduction number	1.5 (low) 9.5 (high)	1.3–1.7 5.5–24	2009 pandemic H1N1 influenza [1] Coronavirus disease 2019 [2]
K	Fatality rate	0.2 % (low) 34.5 % (high)	0.2%–1.3 % Worldwide: 34.5 % and South Korea: 20.4 %	2009 pandemic H1N1 influenza [3] Middle Eastern respiratory syndrome coronavirus [4]
n	Initial number of infections	20	/	Assumed value (5, 15, and 50 as sensitivity analysis)
$\lambda(t)$	Force of infection at time t	/	/	The next-generation matrix method [5]
β	Transmission rate in the absence of NPIs, inferred from the value of R_0	/	/	Inferred from the value of the reproduction number R_0
φ	Reduction of the transmission rate due to NPIs	20 %, 50 %, 80 %	/	Assumed value
P_s	Proportion of infections who developed symptoms	81.2 %	74.9%–87.5 %	Middle Eastern respiratory syndrome [6]
Θ	Infectivity of an asymptomatic individual relative to a symptomatic individual	100 %	/	Assumed value (35 % as sensitivity analysis)
ρ	Proportion of infections quarantined per day	10 %, 20 %	/	Reference [7]
P_h	Proportion of symptomatic infections requiring hospitalizations	15.4 % (high) 2.672 % (low)	2.672%–15.465 % 2.672%–15.465 %	Reference [8] Reference [8]
P_{hd}	Fatality rate among hospitalized (non-ICU) patients	39.1 % (high) 3 % (low)	37.2%–41.1 % 3%–15 %	Reference [9] Reference [10]
P_{hc}	The proportion of hospitalized patients requiring ICU	44.71 % (high) 5 % (low)	5%–44.71 % 5%–44.71 %	Reference [8] Reference [8]
P_{cd}	Fatality rate among ICU patients	30 % (high) 15 % (low)	/ /	Calibrated against the COVID-2019 outbreak in China Calibrated against the COVID-2019 outbreak in China
$1/\gamma_E$	Average duration of latent period (days)	4.1 (3.4–5.0)	3.4–5.0	Reference [11]
$1/\gamma_I$	Average infectious periods (days)	7 (7–10)	7–10	Calibrated against the COVID-2019 outbreak in China
$1/\gamma_{sh}$	Average time from symptom onset to hospitalization (days)	12.5 (high) 4 (low)	10.3–14.8 /	Reference [12] Reference [13]
$1/\gamma_{hd}$	Average time from hospital (non-ICU) admission to death (days)	7.5	/	Reference [12]
$1/\gamma_{hr}$	Length of hospital stay before recovery (days)	14	/	Calibrated against the COVID-2019 outbreak in China
$1/\gamma_{cd}$	Average time from ICU admission to death (days)	7	/	Calibrated against the COVID-2019 outbreak in China
$1/\gamma_{cr}$	Length of hospital stay before recovery (days)	8	/	Calibrated against the COVID-2019 outbreak in China

WHO – World Health Organization.

$$\frac{dI_s}{dt} = \gamma_E P_s E - \gamma_I I_s - \rho(1-\gamma_I)P_h I_s - (1-\gamma_I)P_h(1-P_{hc})I_s\gamma_{sh} - (1-\gamma_I)P_h P_{hc} I_s \gamma_{sh} \quad (4)$$

$$\frac{dI_{qs}}{dt} = \rho(1-\gamma_I)P_h I_s - I_{qs}\gamma_I - P_h(1-P_{hc})(1-\gamma_I)I_{qs}\gamma_{sh} - (1-\gamma_I)P_h P_{hc} I_{qs}\gamma_{sh} \quad (5)$$

$$\frac{dH}{dt} = (1-\gamma_I)P_h(1-P_{hc})I_s\gamma_{sh} + (1-\gamma_I)P_h(1-P_{hc})I_{qs}\gamma_{sh} - HP_{hd}\gamma_{hd} - H(1-P_{hd})\gamma_{hr} \quad (6)$$

$$\frac{dC}{dt} = (1-\gamma_I)P_h P_{hc} I_s \gamma_{sh} + (1-\gamma_I)P_h P_{hc} I_{qs}\gamma_{sh} - CP_{cd}\gamma_{cd} - C(1-P_{cd})\gamma_{cr} \quad (7)$$

$$\frac{dD}{dt} = HP_{hd}\gamma_{hd} + CP_{cd}\gamma_{cd} \quad (8)$$

$$\frac{dR}{dt} = H(1-P_{hd})\gamma_{hr} + C(1-P_{cd})\gamma_{cr} + \gamma_I I_a + \gamma_I I_s + \gamma_I I_{qs} \quad (9)$$

The meanings of the parameters in the equations above are listed in in Table 1. Based on previous research, we hypothesize that the first 100 days are crucial for controlling the epidemic [19]. The modelling simulations were initialized with 20 imported infections and ran forward for 100 days. Sensitivity analyses were performed with 5, 15, 50, and 100 initial infections to evaluate the robustness of the results under various conditions.

2.2. The emerging respiratory infectious disease scenarios

We have summarized the transmissibility and pathogenicity of several emerging respiratory infectious diseases, including SARS, H1N1, MERS, and COVID-19 (in Table 1). The transmissibility of ERID was defined by the basic reproduction number (R_0). An R_0 value of 1.5 (1.3–1.7) from H1N1 was selected as low transmissibility, and an R_0 value of 9.5 (5.5–24) from the Omicron (B.1.351) has been selected as high transmissibility [6]. The pathogenicity of ERID was defined by the case fatality rate while also considering factors such as hospitalization and ICUs rates post-infection. A case fatality rate of 0.2 % (0.2%–1.3 %) from H1N1 was selected as indicative of low pathogenicity, and a case fatality rate of 34.5 % from MERS was selected as indicative of high pathogenicity [20]. Four scenarios were constructed to evaluate the coping strategy for ERID based on the potential transmissibility and fatality of ERID, including Scenario 1 (high transmission, high fatality), Scenario 2 (high transmission, low fatality), Scenario 3 (low transmission, high fatality) and Scenario 4 (low transmission, low fatality) [21](Supplementary Fig. 1).

2.3. Interventions for the outbreak of ERID

We referred to the WHO's NPIs for influenza outbreaks, categorized into four types: personal, community, environmental measures, and travel-related measures. We also do not consider adopting NPIs that the WHO does not recommend at any time, such as ultraviolet light, modifying humidity, contact tracing, quarantine of exposed individuals, entry and exit screening, and border closure [22].

2.4. Personal

In this classification, we considered five interventions: hand hygiene, respiratory etiquette, face masks for symptomatic individuals, isolation of sick individuals, and face masks for the public. During the pandemic, face masks were proven effective means to reduce transmission. Studies have shown that face masks for symptomatic individuals can reduce transmission by 22 %, and face masks for the public can reduce it by 25 % [23,24]. Isolation of sick individuals is also an effective measure, with studies indicating an 11 % reduction in transmission [23]. Experimental research targeting influenza has shown that hand hygiene effectively reduces influenza virus on hands and theoretically reduces transmission, though sufficient quantitative evidence is still lacking. Similarly, studies on the influenza virus show no evidence that adhering to respiratory etiquette reduces transmission, though its potential effectiveness is mechanistically plausible [22].

2.5. Community

In this category, we considered four types of interventions: school measures and closures, workplace measures and closures, avoiding crowding, and internal travel restrictions. Research has shown that school closures and measures can reduce transmission by 14 %, while workplace closures and measures can decrease it by 11 %. Avoiding crowding can lower transmission by 2 %, and Internal travel restrictions can reduce it by 3 % [23].

2.6. Environmental measures

In this category, we considered two types of interventions: cleaning of surface and object cleaning and increased ventilation. While

there is no evidence of these interventions reducing transmission in influenza, their potential effectiveness is mechanistically plausible.

2.7. Travel related measures

In this category, we considered the measure of travel advice. Research on influenza has found no scientific evidence supporting the effectiveness of travel advice during a pandemic. However, providing information to travellers is simple, feasible, and acceptable.

Based on the WHO's recommendations for responding to an influenza pandemic, we categorized response strategies into five levels: base, any, moderate, high, and extraordinary levels of NPI [22]. Each level includes the aforementioned different interventions, and the intensity of the same intervention varies across levels. We have hypothesized different effects for each level of intervention. We assume that implementing interventions at the levels of daily, any, moderate, high, and extraordinary, can reduce transmission by 0 %, 10 %, 25 %, 50 %, and 70 %, respectively. By isolating symptomatic patients at home, their transmission can be reduced by 0 %, 15 %, 25 %, 50 %, and 75 % respectively (Table 2). In addition to formal NPIs, we also account for natural human adaptive behaviours, such as voluntary social distancing, hygiene improvements, and avoidance of crowded places. Based on the literature, we assumed that such behaviours could reduce transmission rates by 10 % [25,26]. Sensitivity analyses were conducted with reductions in the transmission of 0 %, 10 %, 20 %, and 40 % to reflect different levels of adaptive behaviour.

We evaluated the effects of different intervention strategies by varying the reduction values of transmission in the extended SEIR equations, Eqs. (1)–(9), making the parameters time-dependent.

2.8. Model calibration using the MCMC algorithm

Based on the comprehensive epidemiological data from Wuhan in JAN 2020 [27], we estimated the parameters β, Θ, γ_E using a Markov Chain monte Carlo (MCMC) method. Data of COVID-19 cases in Wuhan in January 2020 were used to calibrate the model parameters using MCMC [28,29]. Calculate the correlation between the estimated cases and the reported number from January 1 to January 22, 2020 (because few interventions were implemented before January 23). We assumed that the transmission and ascertainment rates did not change.

2.9. Sensitivity analyses

To evaluate the use of interventions at the different times of effect, five, 15, 50, and 100 seeds of infections are considered sensitivity analyses [30] (Supplementary Figs. 6–8). The main analysis assumes that the infectiousness of asymptomatic and symptomatic cases are identical. Here, it's assumed that the asymptomatic individuals were considered to be 65 % less infectious than symptomatic ones as a sensitivity analysis (Supplementary Figs. 9–11). Natural immunity levels (0 %, 5 %, and 10 %) and human adaptive behaviours (with transmission reductions of 0 %, 10 %, 20 %, and 40 %) were both evaluated through sensitivity analyses (Supplementary Figs. 12–17).

Table 2
| Summary of different levels of NPI used in the simulations under four scenarios over the simulated 100-day period.

Category	Specific intervention	Reduction	Severity[a]				
			Base	Any	Moderate	High	Extraordinary
Personal							
personal protective measures for everyday use	(1)Hand hygiene	/		+	+	+	+
	(2)Respiratory etiquette	/		+	+	+	+
	(3)Face masks for symptomatic individuals	22 % [14]		+	+	+	+
personal protective measures Reserved for Pandemics	(4)Isolation of sick individuals	11 % [15]		+	+	+	+
	(5)Face masks for public	25 % [16]				+	+
Community							
School closures and dismissals	(6)School measures and closures	14 % [15]				+	+
social distancing measures	(7)Workplace measures and closures	11 % [15]					
	(8)Avoiding crowding	2 % [15]			+	+	+
	(9)Internal travel restrictions	3 % [15]					+
Environmental measures							
Environmental Surface Cleaning Measures	(10) Surface and object cleaning	/		+	+	+	+
Other environmental measures	(11)Increased ventilation	/		+	+	+	+
Travel related measures							
	(12)Travel advise	/		+	+	+	+
Reduction on translation (all)			0 %	10 %	25 %	50 %	70 %
Isolation rate of symptomatic			0 %	15 %	25 %	50 %	75 %

[a] Recommendations on the use of NPIs by severity level based on the World Health Organization in 2019 [14].

2.10. Data analysis

For each scenario, 200 stochastic model realizations were performed. The number of model simulations used in the analysis was empirically determined to guarantee the stability of the results. We defined 95 % credible intervals as quantiles 0.025 and 0.975 of the estimated distributions. Microsoft Visual Studio Enterprise 2019 (.NET Framework 4.5) was used to build the model code. The model output was analyzed in R (version 4.3.2).

3. Results

This model fits the data well (Supplementary Fig. 18). The overall correlation between the estimated cases and the reported cases from January 1 to January 22, 2020, was also significant ($P < 0.001$, $R^2 = 0.966$). In each scenario, we quantify the effects of different NPI levels on infections, symptomatic cases, hospitalizations, ICU admissions, and deaths. Below, we present the results for each scenario, categorized into three age groups: 0–17 years, 18–59 years, and 60+ years.

3.1. Scenario 1 (high transmission, high fatality)

For the 0–17 age group, under the base NPI level, infections are 21,895.95 (95 % CI, 21,895.51–21,896.41), symptomatic cases are 17,779.51 (95 % CI, 17,779.15–17,779.88), hospitalizations are 676.64 (95 % CI, 676.62–676.65), ICU cases are 547.16 (95 % CI, 547.15–547.17), and deaths are 548.23 (95 % CI, 548.20–548.25). Any NPI level reduces infections by 1.08 %, and at the extraordinary level, infections, hospitalizations, ICU cases, and deaths are reduced by 99.99 %. For the 18–59 age group, the base NPI level results in 43,725.98 (95 % CI, 43,725.97–43,725.98) infections, 35,505.50 (95 % CI, 35,505.49–35,505.50) symptomatic cases, 1351.24 (95 % CI, 1351.24) hospitalizations, 1092.67 (95 % CI, 1092.67) ICU cases, and 1095.02 (95 % CI, 1094.97–1095.05) deaths. NPI measures at any level reduce infections and deaths by 0.10 % and, at the extraordinary level, by 99.99 %. For the 60+ age group, the base NPI level results in 23,601.45 (95 % CI, 23,601.40–23,601.48) infections, 19,164.38 (95 % CI, 19,164.33–19,164.40) symptomatic cases, 729.34 (95 % CI, 729.34) hospitalizations, 589.78 (95 % CI, 589.78) ICU cases, and 591.04 (95 % CI, 591.02–591.06) deaths. The extraordinary NPI level reduces all outcomes by over 99.99 %.

With high-level NPI measures, hospital bed demand is below the national capacity for the age group (0–17 years) and the age group (60+ years). Only at the extraordinary NPI level dose the demand for hospital and ICU beds below the average capacity in China (218.5 beds/100,000 and 4.51 ICU beds/100,000) [31].

3.2. Scenario 2 (high transmission, low fatality)

For the 0–17 age group, under the base NPI level, infections are 21,895.85 (95 % CI, 21,895.28–21,896.31), symptomatic cases are 17,779.43 (95 % CI, 17,778.97–17,779.80), hospitalizations are 650.88 (95 % CI, 650.86–650.89), ICU cases are 34.26 (95 % CI, 34.26), and deaths are 41.05 (95 % CI, 41.04–41.05). Any NPI level reduces infections by 1.08 %, and at the extraordinary level, infections, hospitalizations, ICU cases, and deaths are reduced by 99.99 %. For the 18–59 age group, the base NPI level results in 43,725.98 (95 % CI, 43,725.97–43,725.98) infections, 35,505.50 (95 % CI, 35,505.49–35,505.50) symptomatic cases, 1299.81 (95 % CI, 1299.81) hospitalizations, 68.41 (95 % CI, 68.41) ICU cases, and 82.04 (95 % CI, 82.02–82.05) deaths. NPI measures at any level reduce infections and deaths by 0.10 % and, at the extraordinary level, by 99.99 %. For the 60+ age group, the base NPI level results in 23,601.45 (95 % CI, 23,601.41–23,601.49) infections, 19,164.38 (95 % CI, 19,164.35–19,164.41) symptomatic cases, 701.58 (95 % CI, 701.58) hospitalizations, 36.93 (95 % CI, 36.93) ICU cases, and 44.28 (95 % CI, 44.27–44.29) deaths. The extraordinary NPI level reduces all outcomes by over 99.99 %.

With high-level NPI measures, hospital bed demand is below the national capacity for the age group (0–17 years) and the age group (60+ years). Only at the extraordinary NPI level dose the demand for hospital and ICU beds below the average capacity in China.

3.3. Scenario 3 (low transmission, high fatality)

For the 0–17 age group, under the base NPI level, infections are 29.95 (95 % CI, 8.70–65.58), symptomatic cases are 24.32 (95 % CI, 7.06–53.25), hospitalizations are 0.63 (95 % CI, 0.18–1.39), ICU cases are 0.51 (95 % CI, 0.15–1.12), and deaths are 0.34 (95 % CI, 0.10–0.73). The extraordinary NPI level reduces all outcomes by 99.99 %. For the 18–59 age group, the base NPI level results in 119.50 (95 % CI, 35.36–266.46) infections, 97.03 (95 % CI, 28.71–216.37) symptomatic cases, 2.53 (95 % CI, 0.76–5.67) hospitalizations, 2.04 (95 % CI, 0.62–4.59) ICU cases, and 1.35 (95 % CI, 0.42–3.00) deaths. NPI measures at the extraordinary level reduce all outcomes by over 99.99 %. For the 60+ age group, the base NPI level results in 57.16 (95 % CI, 16.80–125.79) infections, 46.41 (95 % CI, 13.64–102.14) symptomatic cases, 1.21 (95 % CI, 0.37–2.68) hospitalizations, 0.98 (95 % CI, 0.30–2.17) ICU cases, and 0.64 (95 % CI, 0.20–1.41) deaths. The extraordinary NPI level reduces all outcomes by over 99.99 %.

In all levels of NPIs, the demand for beds and ICUs is less than the existing average bed and ICU resources in China for all age groups.

3.4. Scenario 4 (low transmission, low fatality)

For the 0–17 age group, under the base NPI level, infections are 27.06 (95 % CI, 7.47–58.92), symptomatic cases are 21.97 (95 % CI,

6.07–47.84), hospitalizations are 0.56 (95 % CI, 0.15–1.20), ICU cases are 0.03 (95 % CI, 0.01–0.06), and deaths are 0.02 (95 % CI, 0.01–0.04). The extraordinary NPI level reduces all outcomes by 99.99 %. For the 18–59 age group, the base NPI level results in 111.16 (95 % CI, 29.96–236.79) infections, 90.26 (95 % CI, 24.32–192.27) symptomatic cases, 2.25 (95 % CI, 0.62–4.81) hospitalizations, 0.12 (95 % CI, 0.03–0.25) ICU cases, and 0.08 (95 % CI, 0.02–0.18) deaths. NPI measures at the extraordinary level reduce all outcomes by 99.99 %. For the 60+ age group, the base NPI level results in 52.32 (95 % CI, 14.36–112.66) infections, 42.48 (95 % CI, 11.66–91.48) symptomatic cases, 1.07 (95 % CI, 0.30–2.29) hospitalizations, 0.06 (95 % CI, 0.02–0.12) ICU cases, and 0.04 (95 % CI, 0.01–0.08) deaths. The extraordinary NPI level reduces all outcomes by over 99.99 %.

In all levels of NPIs, the demand for beds and ICUs is less than the existing average bed and ICU resources in China for all age groups.

All results are calculated as relative values based on every 100,000 people in these four scenarios. Detailed results are in Fig. 2, Supplementary Figs. 3–5, and Table 3.

4. Discussion

Our study highlights the importance of tailoring mitigation strategies to the epidemiological characteristics of a new ERID during an outbreak. For ERIDs with low transmissibility, regardless of their pathogenicity, NPIs targeting specific vulnerable populations, such as the elderly and those with chronic conditions, are still recommended. This ensures the reduction of disease burden, hospitalizations, deaths, and other social impacts, even when the overall transmission and fatality rates are low. NPIs are sufficient, and there is no need to resort to intensive NPIs to manage the outbreak. However, in the case of highly contagious ERIDs, promptly adopting NPIs with an extraordinary level of NPI is crucial to prevent the collapse of the healthcare system. Our study provides strategic options for Chinese cities during an ERID outbreak, which will help effectively respond to future ERID outbreaks in urban areas.

Our study reaffirms the critical role of NPIs in controlling new ERID outbreaks in a city. NPIs reduce the transmission of the virus by limiting contact between individuals and separating known infected individuals from those who are susceptible. In scenarios involving ERIDs with high transmissibility and high fatality rates, the significance of NPIs is further amplified, as highlighted in our findings and supported by Shengjie Lai et al. [32]. Lai's research underscored the pivotal role of NPIs in curtailing disease transmission during the COVID-19 pandemic. Our study aligns with this perspective, emphasizing the criticality of NPIs in managing high transmission risks. Similarly, for ERIDs with high transmission but lower fatality rates, our study corroborates the findings of Gao et al. [33]. Their studies demonstrated the effectiveness of NPIs in reducing influenza transmission in China and the United States. In contrast, vaccines and drugs are the main interventions for diseases with lower transmission rates but higher fatality rates, as noted by Hemachudha et al.

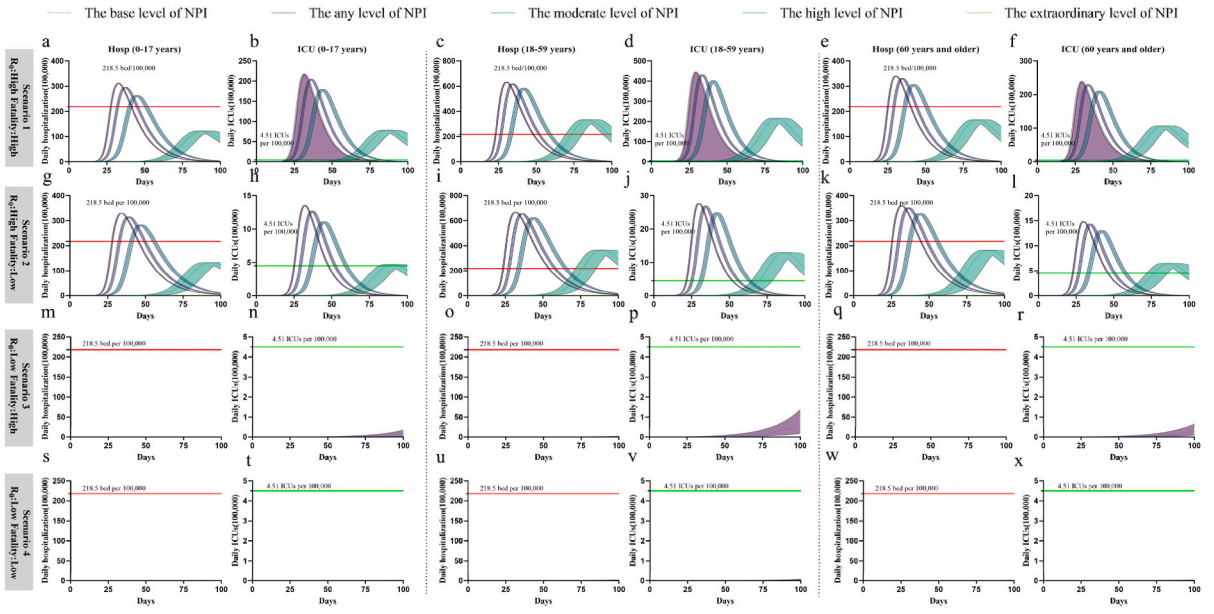

Fig. 2. Projected demand and shortage of hospital beds and ICUs when adopting the base level, any level, moderate level, high level, and extraordinary level of NPI under four scenarios over the simulated 100-day period. a, Daily demand of hospital (non-ICU) beds. **b,** Daily demand of ICUs. **In a, c, e, g, i, k, m, o, q, s, u, w,** The red dashed line indicates the number of ICUs available in China per 100,000 (China Health Statistics Yearbook 2021). **In b, d, f, h, j, l, n, p, r, t, v, x**, The green dashed line indicates the number of hospital (non-ICU) beds available in China per 100,000 (China Health Statistics Yearbook 2021). Four scenarios: scenario 1 ($R_0 = 9.5$, Fatality = 34.5 %), scenario 2 ($R_0 = 9.5$, Fatality = 0.2 %), scenario 3 ($R_0 = 1.5$, Fatality = 34.5 %), scenario 4 ($R_0 = 1.5$, Fatality = 0.2 %). Data are presented as median with 2.5 % and 97.5 % quantiles of n = 200 simulations.

Table 3
| Median and 95 % Confidence Intervals (2.5 % and 97.5 % Percentiles) of the estimated cumulative number of infections, symptomatic cases, hospitalization (non-ICU), ICU, and deaths per 100,000 individuals under four scenarios over the simulated 100-day period. Data are presented as median with 2.5 % and 97.5 % quantiles of n = 200 simulations.

Scenarios	Severity	Infections	Symptomatic cases	Hospitalization	ICU	Deaths
R_0:high Fatality: high (0–17 years)	Base	21895.95 (21895.51–21896.41)	17779.51 (17779.15–17779.88)	676.64 (676.62–676.65)	547.16 (547.15–547.17)	548.23 (548.20–548.25)
	Any	21659.48 (21656.26–21662.78)	17587.49 (17584.88–17590.18)	669.32 (669.22–669.43)	541.25 (541.16–541.33)	541.99 (541.87–542.10)
	Moderate	20777.16 (20770.05–20785.67)	16871.05 (16865.28–16877.96)	642.02 (641.81–642.29)	519.17 (518.99–519.38)	518.80 (518.44–519.17)
	High	13884.15 (13174.34–14115.99)	11273.93 (10697.56–11462.18)	395.30 (347.45–412.34)	319.66 (280.97–333.44)	253.97 (195.51–279.68)
	Extraordinary	0.21(0.06–1.06)	0.17(0.05–0.86)	0.01(0.00–0.03)	0.01(0.00–0.02)	0.01(0.00–0.02)
R_0:high Fatality: low (0–17 years)	Base	21895.85 (21895.28–21896.31)	17779.43 (17778.97–17779.80)	650.88 (650.86–650.89)	34.26(34.26–34.26)	41.05(41.04–41.05)
	Any	21641.15 (21636.98–21644.04)	17572.61 (17569.23–17574.96)	643.30 (643.18–643.39)	33.86(33.85–33.86)	40.47(40.44–40.49)
	Moderate	20703.97 (20696.08–20711.48)	16811.62 (16805.21–16817.72)	615.39 (615.15–615.61)	32.39(32.38–32.40)	38.44(38.37–38.50)
	High	13209.95 (11813.56–13602.31)	10726.48 (9592.61–11045.07)	348.32 (270.65–374.68)	18.33(14.24–19.72)	14.73(9.16–17.42)
	Extraordinary	0.20(0.06–0.79)	0.16(0.05–0.64)	0.01(0.00–0.02)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:low Fatality: high (0–17 years)	Base	29.95(8.70–65.58)	24.32(7.06–53.25)	0.63(0.18–1.39)	0.51(0.15–1.12)	0.34(0.10–0.73)
	Any	0.18(0.07–0.55)	0.14(0.06–0.44)	0.01(0.00–0.02)	0.00(0.00–0.01)	0.00(0.00–0.01)
	Moderate	0.10(0.06–0.18)	0.08(0.05–0.14)	0.00(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	High	0.07(0.06–0.10)	0.06(0.05–0.08)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Extraordinary	0.06(0.06–0.09)	0.05(0.05–0.07)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:low Fatality: low (0–17 years)	Base	27.06(7.47–58.92)	21.97(6.07–47.84)	0.56(0.15–1.20)	0.03(0.01–0.06)	0.02(0.01–0.04)
	Any	0.18(0.08–0.46)	0.15(0.06–0.37)	0.01(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Moderate	0.10(0.06–0.19)	0.08(0.05–0.15)	0.00(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	High	0.07(0.06–0.10)	0.06(0.05–0.08)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Extraordinary	0.06(0.06–0.09)	0.05(0.05–0.07)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:high Fatality: high (18–59 years)	Base	43725.98 (43725.97–43725.98)	35505.50 (35505.49–35505.50)	1351.24 (1351.24–1351.24)	1092.67 (1092.67–1092.67)	1095.02 (1094.97–1095.05)
	Any	43717.08 (43716.50–43717.59)	35498.27 (35497.79–35498.68)	1350.96 (1350.94–1350.97)	1092.45 (1092.43–1092.46)	1094.38 (1094.26–1094.48)
	Moderate	43515.89 (43511.59–43518.51)	35334.90 (35331.41–35337.03)	1344.72 (1344.59–1344.80)	1087.40 (1087.29–1087.47)	1087.95 (1087.57–1088.28)
	High	36772.23 (35798.89–37062.70)	29859.05 (29068.70–30094.91)	1082.20 (997.92–1109.08)	875.11 (806.96–896.85)	737.06 (605.15–789.69)
	Extraordinary	0.67(0.14–3.27)	0.54(0.11–2.66)	0.02(0.00–0.09)	0.02(0.00–0.08)	0.02(0.00–0.07)
R_0:high Fatality: low (18–59 years)	Base	43725.98 (43725.97–43725.98)	35505.50 (35505.49–35505.50)	1299.81 (1299.81–1299.81)	68.41(68.41–68.41)	82.04(82.02–82.05)
	Any	43715.36 (43714.57–43716.13)	35496.87 (35496.23–35497.49)	1299.49 (1299.46–1299.51)	68.39(68.39–68.40)	81.88(81.83–81.91)
	Moderate	43488.26 (43485.09–43491.69)	35312.47 (35309.89–35315.25)	1292.70 (1292.61–1292.80)	68.04(68.03–68.04)	81.06(80.94–81.14)
	High	35777.36 (33636.48–36313.82)	29051.22 (27312.82–29486.82)	985.42 (830.89–1030.43)	51.86(43.73–54.23)	45.00(30.73–51.15)
	Extraordinary	0.57(0.13–2.42)	0.46(0.10–1.96)	0.02(0.00–0.07)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:low Fatality:	Base	119.50(35.36–266.46)	97.03(28.71–216.37)	2.53(0.76–5.67)	2.04(0.62–4.59)	1.35(0.42–3.00)

(*continued on next page*)

Table 3 (*continued*)

Scenarios	Severity	Infections	Symptomatic cases	Hospitalization	ICU	Deaths
high (18–59 years)						
	Any	0.55(0.22–1.60)	0.44(0.17–1.30)	0.02(0.01–0.05)	0.01(0.01–0.04)	0.01(0.01–0.04)
	Moderate	0.22(0.12–0.37)	0.18(0.10–0.30)	0.01(0.00–0.01)	0.01(0.00–0.01)	0.01(0.00–0.01)
	High	0.11(0.08–0.16)	0.09(0.06–0.13)	0.00(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Extraordinary	0.09(0.08–0.13)	0.07(0.06–0.11)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:low Fatality: low (18–59 years)	Base	111.16(29.96–236.79)	90.26(24.32–192.27)	2.25(0.62–4.81)	0.12(0.03–0.25)	0.08(0.02–0.18)
	Any	0.53(0.20–1.28)	0.43(0.16–1.04)	0.02(0.01–0.04)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Moderate	0.23(0.12–0.37)	0.18(0.10–0.30)	0.01(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	High	0.11(0.08–0.16)	0.09(0.06–0.13)	0.00(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Extraordinary	0.09(0.08–0.13)	0.07(0.06–0.11)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:high Fatality: high (60 years and older)	Base	23601.45 (23601.40–23601.48)	19164.38 (19164.33–19164.40)	729.34 (729.34–729.34)	589.78 (589.78–589.78)	591.04 (591.02–591.06)
	Any	23574.57 (23573.42–23575.79)	19142.55 (19141.62–19143.54)	728.51 (728.47–728.55)	589.10 (589.08–589.14)	590.14 (590.07–590.20)
	Moderate	23304.66 (23300.55–23307.54)	18923.38 (18920.04–18925.72)	720.15 (720.03–720.24)	582.35 (582.25–582.42)	582.57 (582.36–582.80)
	High	18608.01 (18052.35–18780.94)	15109.70 (14658.51–15250.12)	545.38 (500.21–560.21)	441.02 (404.49–453.01)	369.18 (301.60–396.85)
	Extraordinary	0.32(0.07–1.54)	0.26(0.06–1.25)	0.01(0.00–0.04)	0.01(0.00–0.04)	0.01(0.00–0.03)
R_0:high Fatality: low (60 years and older)	Base	23601.45 (23601.41–23601.49)	19164.38 (19164.35–19164.41)	701.58 (701.58–701.58)	36.93(36.93–36.93)	44.28(44.27–44.29)
	Any	23571.01 (23570.07–23572.42)	19139.66 (19138.89–19140.81)	700.67 (700.64–700.71)	36.88(36.88–36.88)	44.15(44.12–44.16)
	Moderate	23275.02 (23271.40–23278.73)	18899.32 (18896.38–18902.33)	691.85 (691.74–691.96)	36.41(36.41–36.42)	43.37(43.31–43.41)
	High	18023.83 (16832.02–18330.42)	14635.35 (13667.60–14884.30)	493.87 (413.04–518.19)	25.99(21.74–27.27)	22.40(15.21–25.56)
	Extraordinary	0.28(0.07–1.17)	0.23(0.06–0.95)	0.01(0.00–0.03)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:low Fatality: high (60 years and older)	Base	57.16(16.80–125.79)	46.41(13.64–102.14)	1.21(0.37–2.68)	0.98(0.30–2.17)	0.64(0.20–1.41)
	Any	0.27(0.10–0.77)	0.22(0.08–0.62)	0.01(0.00–0.02)	0.01(0.00–0.02)	0.01(0.00–0.02)
	Moderate	0.11(0.07–0.22)	0.09(0.05–0.17)	0.00(0.00–0.01)	0.00(0.00–0.01)	0.00(0.00–0.01)
	High	0.07(0.06–0.10)	0.06(0.05–0.08)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Extraordinary	0.06(0.06–0.08)	0.05(0.05–0.06)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
R_0:low Fatality: low (60 years and older)	Base	52.32(14.36–112.66)	42.48(11.66–91.48)	1.07(0.30–2.29)	0.06(0.02–0.12)	0.04(0.01–0.08)
	Any	0.26(0.10–0.66)	0.21(0.08–0.53)	0.01(0.00–0.02)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Moderate	0.12(0.07–0.21)	0.10(0.06–0.17)	0.00(0.00–0.01)	0.00(0.00–0.00)	0.00(0.00–0.00)
	High	0.07(0.06–0.10)	0.06(0.05–0.08)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)
	Extraordinary	0.06(0.06–0.08)	0.05(0.05–0.06)	0.00(0.00–0.00)	0.00(0.00–0.00)	0.00(0.00–0.00)

[34]. Overall, our study aligns with these previous findings and serves as a valuable supplement, enriching further evidence on the intervention strategic application of NPIs in various ERID scenarios.

The key to controlling a new ERID in a city is to avoid the collapse of the healthcare system during the outbreak. The differences in medical resources between cities directly affect the intensity of the interventions required in the face of the same infectious disease, especially regarding the number of beds and ICUs. For example, there are only 612 beds/100,000 in Shanghai, China, compared to 735 beds/100,000 in Chongqing, China. Regarding ICUs, Shanghai has 3.36 ICU/100,000, slightly higher than Chongqing's 3.82 ICU/100,000 [31]. Cities with fewer medical resources may need stricter NPIs to avoid overwhelming their medical resources when dealing with highly transmissible diseases. Conversely, cities with more abundant resources may take mild interventions when facing the same scenario. However, even in resource-rich cities, NPIs should still be implemented for vulnerable populations to avoid unnecessary

disease burdens. In responding to a new ERID, it is essential to consider the epidemiology characteristics of the disease and the available medical resources. Our study suggested the proper strategy against a new ERID in a city under various scenarios, which will help us respond to the outbreak of a new ERID in the future. Understanding the medical resource situation in different cities is crucial for developing effective and NPIs [35]. These measures are key to ensuring the effective control of the epidemic and maintaining the stable operation of the healthcare system.

There are several limitations to this study. Firstly, the model parameters were based on previously respiratory infectious diseases, and these parameters may change for future ERID diseases. However, the sensitivity analysis for the key parameters ensured the stability of the findings. Furthermore, our study provided a practical framework for the decision-making to control the outbreak of new ERID. Secondly, we have not discussed the specific NPIs but have categorized NPIs based on the effects of these measures, considering that the same NPI measure may have different effectiveness in different regions. Finally, the impact of NPI measures on social order and the public's acceptance of these measures were not considered. Therefore, the findings should be regarded only as a reference for decision-making. However, our analytical framework and parameters can be easily modified to be applied to the study of ERID in other places and countries.

In conclusion, it is necessary to develop and adjust intervention strategies based on the epidemiological characteristics and available interventions of ERID to address it. In the early stage of the ERID, there is not enough data and waiting time to support the model's accurate prediction ability. In uncertain prediction results, choosing the best interventions becomes a paramount concern. The present study demonstrates how to control the new ERID outbreaks in a city with proper NPIs. A comprehensive approach to NPIs will be essential for mitigating the impact of the outbreak of the new ERID and safeguarding public health.

CRediT authorship contribution statement

Zhiqun Lei: Writing – review & editing, Writing – original draft, Software, Data curation, Conceptualization. **Ziwei Shi:** Software, Data curation. **Jiao Huang:** Methodology. **Xiaolong Yan:** Data curation. **Jiayao Luo:** Software. **Meng Xu:** Data curation. **Qiuyue Wang:** Visualization. **Rui Wang:** Data curation. **Qi Wang:** Writing – original draft, Funding acquisition, Data curation. **Qu Cheng:** Writing – review & editing, Writing – original draft, Software, Data curation. **Sheng Wei:** Writing – review & editing, Writing – original draft, Validation, Supervision, Software, Data curation.

Ethical approval statement

Approval was not required.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e41383.

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