The cross-scale correlations between individuals and nations in COVID-19 mortality

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Research Article

Keywords: COVID-19, mortality, cross-scale, dynamical model, scale law

Posted Date: December 15th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1133246/v1>

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The cross-scale correlations between individuals and nations in COVID-19 mortality

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Abstract

It is challenging to quantitatively clarify the determining medical and social factors of COVID-19 mortality, which varied by 2-3 orders of magnitude across countries. Here, we present evidence that the whole-cycle patterns of mortality follow a logistic law for 52 countries. A universal linear law is found between the ICU time in the early stage and the most important quantity regarding the epidemic: its duration. Saturation mortality is found to have a power law relationship with median age and bed occupancy, which quantitatively explains the great variation in mortality based on the two key thresholds of median age (=38) and bed occupancy (=15%). We predict that deaths will be reduced by 36% when the number of beds is doubled for countries with older populations. Facing the next wave of the epidemic, this model can make early predictions on the epidemic duration and medical supply reservation.

Since COVID-19 was declared a pandemic by the World Health Organization (WHO) on March 11, 2020, approximately 5 million deaths have been reported across 184 countries or regions as of October 1, 2021. Therefore, lessons learned from the first wave, such as quantitative assessment of the severity of the epidemic and clarification of the determining medical and social factors, are urgently needed to help policy-makers prevent more deaths in the next wave. Reliable death statistics and quantitative modelling are essential for understanding the pandemic¹. However, it is a great challenge to quantitatively interpret observational data presenting a high variation in mortality evolution across countries, which reaches two to three orders of magnitude for the difference in case fatality rate (deaths per confirmed case) and crude death rate (deaths per 100,000 population). We attempt to propose a reliable understanding of this observation.

Previous studies have not yet reached a conclusion regarding this issue because they focused only on the individual scale or the national scale and ignored the cross-scale correlation. Specifically, patient-level studies have shown that older patients, men and patients with underlying diseases have a greater risk of death and require respiratory assistance in the intensive care unit (ICU)^{2, 3, 4, 5, 6, 7}. However, the demographics of confirmed cases are changing over time, with more young people being infected in the later stages than in the early stages of the outbreak. On the other hand, country-level studies have suggested that healthcare resource availability, infection scale, etc., are associated with mortality^{8, 9, 10, 11}. However, countries' capacity to prevent, detect, and respond to the outbreak varies widely over time¹², so COVID-19 mortality presents great heterogeneity in space (across countries) and time¹³. Therefore, the commonly used method of a cross-sectional study, in which the mortality data for a given day are selected, yields misleading representation by comparing the mortality data at different evolutionary stages. For example, two studies concluded differently on whether there was a correlation between the case fatality rate and the number of tests^{8, 9}. Moreover, these various factors analysed at different levels must form a coherent view to offer effective guidance for fighting against the pandemic.

56

57 In sharp contrast to the above-mentioned studies, we adopt a dynamic study with a
 58 complete description of the whole-cycle evolution of mortality to better uncover robust
 59 features and explain the underlying mechanisms, which yields a quantitative prediction
 60 about future epidemic evolution. Considering that almost all countries have already
 61 experienced the first wave of the epidemic, it is time to derive a law governing the
 62 dynamics of COVID-19 mortality based on the data. Here, we present a logistic model
 63 that accurately describes the whole-cycle evolutionary patterns of COVID-19 mortality
 64 (deaths per 100,000 population, $S(t)$) across 52 countries, quantitatively explaining
 65 the great variation in mortality based on two key thresholds from exact scales of the
 66 median age (=38) and bed occupancy (=15%), finding the cross-scale correlations
 67 between ICU time and epidemic duration with a dimensionless coefficient k . As a result,
 68 cross-scale correlation analysis between individual and national scales is achieved in
 69 the first wave of COVID-19 mortality (see **Fig. 1**).

71 **Fig. 1 The cross-scale correlation between the individual scale and the national**
 72 **scale in this paper.**

73

74 Specifically, the data show that, for all countries, the temporal evolution of mortality
 75 during the first pandemic wave well fits a logistic pattern with just two parameters (see

“Methods” for details), which allows decoupling the complex evolutionary behaviour into two independent processes with close medical and social correspondences. One is saturation mortality (s_0) in the late stage of the epidemic, which is positively correlated with the state’s median age and bed occupancy (see **Fig. 2**). This finding allows us to derive, from data, a law that yields a prediction of practical interest, namely, how many medical supplies need to be reserved in the continuing fight against the next wave of the epidemic if the aim is to cut the number of deaths by half (see **Fig. 4**). The other is a characteristic survival time (τ), which is closely related to the ICU time in the early stage and shows a universal linear correlation with epidemic duration across different countries (see **Fig. 3**). If this is further confirmed, it would be possible to predict the epidemic duration from collected data at the early stage of the outbreak (see **Table. 1**). Thus, we highly recommend testing the current model, which, if successful, would greatly enhance our ability to understand and control the current epidemic.

Results

Two key thresholds associated with age, beds, and saturation mortality (s_0)

When the epidemic ends, the mortality $S(t)$ evolves to s_0 , so the saturation mortality parameter s_0 quantifies the epidemic. Previous published cross-sectional studies did show a correlation between age, hospital beds, and mortality, but it is not clear which role these factors play in different countries and at different stages of the outbreak. In **Fig. 2**, we plot s_0 as a function of the nation’s median age and available hospital beds, which immediately reveals some remarkable features. First, the high-mortality patterns ($s_0 > \overline{s_0} = 12.0$) were all found in countries with a median age over 38 years old, which suggests that median age is one of the key factors influencing mortality, consistent with previous studies^{3, 4, 5, 6, 7}. The current finding is more quantitative: it presents a scaling between the saturation mortality and median age, with a power law exponent of 2.1 (see **Fig. 2a**).

On the other hand, the deviation from this scaling is quite substantial for countries of

high median age (most pink dots are outside of the confidence interval, see **Fig. 2a**). The strong scattering suggests that there must be other important factors causing high mortality. Indeed, we found that there exists a nice scaling between saturation mortality and bed occupancy at the peak of the first wave (confirmed cases at peak time over bed number, see “Methods” for details) for countries with a median population age above 38 years old (see **Fig. 2b**). The saturation mortality increases with the peak bed occupancy, following a power law of exponent 0.6, which attributes the large variation in the mortality of older countries to the great variation in peak bed occupancy (almost by two orders of magnitude) across countries.

For example, Wuhan City (Hubei Province, China) is comparable in population size and pandemic scale to some countries. The bed occupancy (at the peak) based on the number of beds before the outbreak was 39.2%, and the saturation mortality (s_0) was predicted to be 24.8. However, after the construction of Fang Cang Hospital, the number of beds increased by 15,000¹⁴, and s_0 reduced to 22.6, which is very close to the actual saturation mortality of 22.0. Thus, the power law could explain 76.7% (248 deaths) of the decline in the number of deaths, as shown in **Fig. 4b**.

The peak bed occupancy reflects the degree of countries’ medical support during the pandemic. It would be interesting to discover a critical value of the peak bed occupancy to separate low and high mortality. Shown in **Fig. 2b**, a value between 10% to 20%, e.g., 15%, may be a reference. It would be intriguing to examine the second wave of data to determine whether a universal threshold can be found.

In summary, the high variation in mortality across countries can be explained quantitatively. First, two key quantities of median age and bed occupancy can classify all countries into three typical patterns (see **Fig. 2c**). Older countries (>38) with high bed occupancy (>15%) have far greater mortality than the other two low-mortality groups, which include younger groups (<38), without exception, and the group with low bed occupancy (abundant medical supplies). What is interesting is that some older

countries (>38) can evolve into a low-mortality pattern if they have a low bed occupancy (<15%). This indicates that bed occupancy is an essential indicator to evaluate the effectiveness of national anti-COVID-19 measures.

Fig. 2 The great mortality variation is explained by the median age and bed occupancy. a The scaling between saturation mortality and the median age for all countries ($N = 52$). **b** The scaling between saturation mortality and peak bed

occupancy for countries aged over 38 years old ($N = 24$). **a** and **b** take the double logarithmic coordinates for a better display of the data. The orange, blue and pink dots correspond to the low-mortality pattern-1, low-mortality pattern-2, and high-mortality pattern, respectively. The black lines are the fitting predictions by power functions. The grey areas are the 95% confidence intervals. Note that the red circle furthest from the confidence interval in **Fig. 2b** represents Belgium, probably because it uses a broader inclusion criterion for COVID-19 deaths¹⁵. **c** The flow of COVID-19 mortality patterns between the region, median age, and bed occupancy. The orange, blue and pink connecting lines correspond to the low-mortality pattern-1, low-mortality pattern-2, and high-mortality pattern, respectively. The width of each line is proportional to the number of countries.

The dimensionless coefficient k between ICU time and epidemic duration

The present two-parameter model not only explained the large variations in mortality across countries but also discovered a cross-scale correlation between ICU time and epidemic duration, which provides new insights regarding the spread and evolution of COVID-19. First, a dimensionless coefficient k can be derived from our model (see “Methods” for details), which is the ratio of the epidemic duration to the model parameter τ (which coincides with the ICU time of non-survivors in the early stage of the epidemic). Importantly, we find that the k values are nearly constant across different continents, and the average is 7.0 (IQR, 6.3-7.7), as shown in **Fig. 3**. This linear law is better obeyed for countries with shorter ICU times ($\tau < 20$), while the data are more diffused for countries with longer ICU times ($\tau > 20$) (see **Fig. 3a**). This suggests that ICU time is a good indicator of the “strength” of the epidemic, or how long it may last. The longer the ICU time is, the longer the epidemic will last. Note that the ICU time is related to an individual’s antiviral ability, while the duration of the epidemic is a social scale property. Thus, this linear law reveals an important property of COVID-19, which might be very important and needs further investigation. Knowing the value of k , one may then predict the duration of the outbreak from the data of the ICU time (τ) in the early stage. It would be intriguing to test this finding

with data and make predictions for the duration of the second wave.

Fig. 3 The cross-scale correlation between τ (ICU time) and epidemic duration.

a-e are the correlations with different but similar correlation coefficients k for all countries, Europe, Africa, Asia, and America, respectively. The abscissa variable is the model fitting parameter τ , which represents the ICU time of non-survivors in the early stage of the epidemic. The ordinate variable is the duration of the epidemic. The blue dots are the data across countries. The black lines are the fitting predictions by linear functions. The grey areas are the 95% confidence intervals.

Quantitative evaluation of national interventions and the prediction of epidemic duration

The above discussion on the cross-scale correlations in the first wave of COVID-19 mortality yields a method for the quantitative evaluation of the efficacy of interventions and the prediction of epidemic duration. First, a good fit is shown with the scaling between bed occupancy and saturation mortality (see **Fig. 2b**) for countries with low

mortality, such as Austria ($s_0 = 7.02$) and Germany ($s_0 = 9.95$), and for countries with high mortality, such as Canada ($s_0 = 22.85$) and Sweden ($s_0 = 54.54$). Interestingly, this power law predicts that the deaths will be reduced by approximately 36% when the number of beds is doubled (see **Fig. 4a**). In other words, increasing the number of beds is very effective for preventing deaths in older countries. Specifically, if Canada could double the number of beds, approximately 3,500 deaths could be prevented in the first wave, and similarly, approximately 2,200 deaths could be prevented for Sweden, as shown in **Fig. 4a**.

The other remarkable prediction of the present model is the duration of the whole epidemic by using the dimensionless coefficient k and the ICU time in the early stage of the outbreak. As shown in Table 1, the durations predicted by using a range of $k = 7 - 8$ and the reported ICU time are very close to the actual values. As a result, policymakers can more accurately anticipate the difficulties of the fight against the pandemic and better optimize the load on the health system to minimize the number of deaths.

Fig. 4 Changes in mortality as bed numbers increase. a Reduction in saturation mortality when changing the number of beds. The black and orange lines represent Sweden and Canada, respectively. **b** Contribution of the construction of Fang Cang

hospital to the reduction in mortality in Wuhan City (Hubei Province, China). The grey circles are the official reported data. The red line represents the simulation of mortality evolution without Fang Cang hospital, while the blue line represents the simulation of mortality evolution with Fang Cang hospital.

Table 1. The prediction of epidemic duration by using the $k = 7 - 8$

Country/Region	ICU time* (days)	Actual duration (days)	Predicted duration (days)
Wuhan	7	51	49-56
Germany	9	73	63-72
Italy	10	87	70-80

* Data are expressed as the median in references^{16, 17, 18}.

Discussion

The COVID-19 pandemic has forced us to rethink the way countries prepare for public health crises. Although the end of the crisis is not nearly in sight yet, it is time to learn lessons from the first wave to improve the global capacity to respond to health crises of this magnitude. This becomes possible since, for the first time in the history of science, so much information has been collected and shared worldwide, which makes it possible to gain a deeper understanding of epidemic evolution¹⁹.

The present study demonstrates the validity of a logistic model to describe the whole-cycle evolution of COVID-19 mortality in the first wave across 52 countries. We then find, from the data, a remarkable correlation for epidemic characteristics between the individual scale (age and ICU time) and national scale (mortality and epidemic duration). This correlation quantitatively answers two crucial questions of major interest, namely, why does COVID-19 mortality vary so widely from country to country, and how long will the epidemic last?

For the first question, the power law correlation between the median age, bed occupancy, and saturation mortality yield a quantitative explanation for the large observed variation in mortality across countries (see **Fig. 2**), with two key thresholds, 38 years old for median age and 15% for bed occupancy, which classifies countries into three typical patterns (see **Fig. 2c**). Specifically, countries that are older could flatten the mortality curve by reducing bed occupancy to under 15%, offering an impressive model for other countries in reducing deaths in the next wave.

For the second question, the linear law between the two different time scales makes it possible to predict the duration of the whole epidemic wave by using the ICU time in the early stage (see **Fig. 3, Table 1**). It is well known that the long-term forecasting of outbreaks is a great challenge since there are unpredictable and complex factors that can influence epidemic evolution. Indeed, we also found that some countries with longer epidemic duration had greater fluctuations of the slope in the linear law, probably because these countries were more likely to experience those unexpected factors (see **Fig. 3**). Even so, on the national scale, there is still a nearly universal linear law across countries, which suggests that the temporal cross-scale association is an important feature of the COVID-19 pandemic. An interesting future topic is to verify and compare the values of the dimensionless coefficient k with the values in other epidemics, such as SARS or the annual flu, which may bring new insights into understanding the spread and evolution of the epidemic.

An important finding of the present study is the importance of the ICU time of non-survivors in the early stage, which is often overlooked in clinical studies. We found that Wuhan City had the smallest τ (6.3 days) among all the regions included in the study, which was very close to the 7 days of the clinical study¹⁶ (see **Fig. 7**). This result is consistent with the fact that Wuhan City was the first outbreak point and that the community knew little about the virus at the beginning of COVID-19. Moreover, the wide range of τ (ICU time) across countries (see **Fig. 3**) needs to be studied and explained in the future, and the current findings suggest collecting more accurate ICU

time data for better prediction of the next wave of the pandemic.

Our study also has several limitations. First, the data analysed here are from public databases. The limited quality, different statistical standards, and incompleteness of databases may affect the precision of our description. Second, our study does not include countries with complex evolutionary behaviours, such as repeated rebounding of the outbreak. Third, we used median age data at the national level instead of at the patient level, as such data are currently lacking in most countries. Finally, we use the number of beds before the outbreak instead of the actual data that tend to increase during the epidemic, which are currently difficult to obtain. Although these factors influence the precision of the description, they would not affect the main conclusions of the study for the first wave of COVID-19 in most countries.

In conclusion, we present dynamic modelling to decouple the complex evolution of COVID-19 mortality into two key processes: the ICU duration of non-survivors in the early stage and the saturation mortality in the late stage. This analysis uncovers three cross-correlations between the individual scale and the national scale in COVID-19 mortality, which enables us to evaluate interventions quantitatively and predict the epidemic duration. This framework also has other potential applications, such as providing country-specific suggestions for the reservation of medical supplies to fight against the next wave of COVID-19 so that more deaths can be prevented.

Methods

Study design. As of October 1, 2021, 184 countries or regions had reported COVID-19 deaths. Due to technical limitations, government interventions and multiple corrections of the data, the mortality evolution in some countries shows complex behaviours. For example, in 70 countries, the second wave breaks out before the first wave of the epidemic ends. Since the goal of this study is to analyse the whole evolution of mortality in the first wave, we propose the explicit inclusion criterion that only

countries with post-peak daily deaths falling to less than one-tenth of the peak should be considered a qualified sample. Considering the statistical stability, qualified samples should have a cumulative number of deaths of more than 100 cases. Finally, 52 countries or regions were included in this study (see Fig. 5).

Fig. 5 The inclusion criteria in this paper.

Data and Metrics. The data used in our study all come from open-access databases. Specifically, the COVID-19 case data are aggregated from the Johns Hopkins University database²⁰ (as of October 1, 2021), while the data of Wuhan are from the Health Commission of Hubei Province²¹. The population, median age, and hospital beds (per 1,000 population) are from the database of Our World in Data²². For China, we chose the data of Wuhan City (Hubei Province, China) instead of national data because of Wuhan’s comparable population size and pandemic scale. The population

and bed data in Wuhan are from the Wuhan Statistics Bureau²³. It is worth mentioning that the data of these state-level variables are updated to the most recent year but often not to the same year.

Bed occupancy. We propose the “**bed occupancy**” to evaluate the availability of medical resources across countries, which is calculated by dividing the number of hospitalized cases by the number of beds at the peak of the epidemic. Here, “the number of hospitalized cases” is calculated by the following relation: hospitalized cases = confirmed – recovered - deaths.

The epidemic duration. The epidemic duration is defined to prevent the long-tail effect when comparing and analysing the evolutionary time of the epidemic across countries. Using the peak of daily new deaths as a reference, we define the date when the new deaths climb to more than one-tenth of the peak as the outbreak date ($t_{outbreak}$) and the date when the new deaths fall below one-tenth of the peak as the saturation date ($t_{saturation}$) (see **Fig. 6a**). The time between the outbreak date and the saturation date is the duration of the epidemic (see **Fig. 6b**). A 10-day smoothing is carried out on the daily new deaths due to the large fluctuations.

Fig. 6 The epidemic duration of the first wave (ex. Switzerland). **a** The daily new deaths and the characteristic date. The black circles are the reported daily new deaths.

The blue line is the 10-day smoothing of the daily deaths. The square is the peak of daily new deaths. The regular triangle is the outbreak date when the new deaths climb to more than one-tenth of the peak. The inverted triangle is the saturation date when the new deaths fall below one-tenth of the peak. **b** The cumulative deaths and the duration of the first wave. The black circles are the reported cumulative deaths. The red circles are the data for the duration of the first wave.

Model and parameters. In the early stages of the outbreak, the number of deaths increased almost exponentially due to weak intervention. With the expansion of the death toll, the social system takes actions to slow down the growth of mortality, such as increasing available medical resources, controlling the spread of the epidemic, and protecting high-risk groups. Eventually, the death toll tends to be saturated in the late stages of the epidemic. Therefore, we use the logistic model to fit the COVID-19 mortality (deaths per 100,000 population, $S(t)$):

$$\frac{dS(t)}{dt} = \frac{1}{\tau} S(t) \left(1 - \frac{S(t)}{s_0} \right) \quad (1)$$

The solution to equation (1) can be written as:

$$S(t) = \frac{s_0}{1 + e^{t_c - t/\tau}} \quad (2)$$

s_0 When $t \gg 0$, $S(t) \approx s_0$. Therefore, s_0 denotes the saturation mortality in the late stage of the epidemic.

t_c When $t = t_c$, $S(t) = s_0/2$. Therefore, t_c denotes the characteristic time when mortality reaches half of the saturation mortality.

τ When $t \approx 0$, $S(t) \ll s_0$, equation (1) can be written as $\tau^{-1} \approx S(t)'/S(t)$. Therefore, τ^{-1} denotes the exponential growth rate of mortality, while τ is the characteristic time for new deaths in the early stage of the epidemic. Since almost all reported deaths of COVID-19 occur in ICU, we propose that τ denotes the time in

ICU of the non-survivors in the early stage, which is well validated by published clinical data^{16, 17, 18} (see **Fig. 7**).

Fig. 7 ICU time and the value of τ . The 45-degree black line indicates the equality of the observed and predicted data.

The dimensionless coefficient k

When $t = t_{outbreak}$ or $t = t_{saturation}$, equation (2) can be written as:

$$t_{outbreak} = t_c - \ln\left(\frac{S_0}{S(t_{outbreak})} - 1\right) * \tau \quad (3.1)$$

$$t_{saturation} = t_c - \ln\left(\frac{S_0}{S(t_{saturation})} - 1\right) * \tau \quad (3.2)$$

Then, the duration can be obtained by subtracting the two equations above:

$$duration = t_{saturation} - t_{outbreak} = k * \tau \quad (4)$$

Here, k is:

$$k = \ln\left(\frac{\frac{S_0}{S(t_{outbreak})} - 1}{\frac{S_0}{S(t_{saturation})} - 1}\right) \quad (5)$$

Thus, we can see that the duration is strictly linearly related to τ by the factor k . The values of k across countries are shown in **Fig. 8**. We can see that most countries have k values between 7 and 8, although their mortality and τ values vary widely.

375

376 **Fig. 8 The k values of 52 countries.** a-d are the k values for countries in Europe,
 377 Africa, Asia, and America, respectively. The blue dots are the data across countries.
 378 The black dashed lines are the average of countries by continent. The grey areas are the
 379 interquartile range (25th–75th).

380

381 We use equation (2) to fit the mortality data of 52 countries in the first wave of COVID-
 382 19 (see Fig. 9) and obtain the values of the model parameters s_0 and τ .

383

386 **Fig. 9 Fitting of mortality using a logistic model.** The red point is the officially reported
 387 data, and the black line is the fitting result with 95% confidence intervals (blue bands).

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Figures

Figure 1

The cross-scale correlation between the individual scale and the national scale in this paper.

Figure 2

The great mortality variation is explained by the median age and bed occupancy. a The scaling between saturation mortality and the median age for all countries (N=52). b The scaling between saturation mortality and peak bed occupancy for countries aged over 38 years old (N=24). a and b take the double logarithmic coordinates for a better display of the data. The orange, blue and pink dots correspond to the low-mortality pattern-1, low-mortality pattern-2, and high-mortality pattern, respectively. The black lines

are the fitting predictions by power functions. The grey areas are the 95% confidence intervals. Note that the red circle furthest from the confidence interval in Fig. 2b represents Belgium, probably because it uses a broader inclusion criterion for COVID-19 deaths. c The flow of COVID-19 mortality patterns between the region, median age, and bed occupancy. The orange, blue and pink connecting lines correspond to the low-mortality pattern-1, low-mortality pattern-2, and high-mortality pattern, respectively. The width of each line is proportional to the number of countries.

Figure 3

The cross-scale correlation between τ (ICU time) and epidemic duration. a-e are the correlations with different but similar correlation coefficients k for all countries, Europe, Africa, Asia, and America, respectively. The abscissa variable is the model fitting parameter τ , which represents the ICU time of non-survivors in the early stage of the epidemic. The ordinate variable is the duration of the epidemic. The blue dots are the data across countries. The black lines are the fitting predictions by linear functions. The grey areas are the 95% confidence intervals.

Figure 4

Changes in mortality as bed numbers increase. a Reduction in saturation mortality when changing the number of beds. The black and orange lines represent Sweden and Canada, respectively. b Contribution of the construction of Fang Cang hospital to the reduction in mortality in Wuhan City (Hubei Province, China). The grey circles are the official reported data. The red line represents the simulation of mortality evolution without Fang Cang hospital, while the blue line represents the simulation of mortality evolution with Fang Cang hospital.

Figure 5

The inclusion criteria in this paper.

Figure 6

The epidemic duration of the first wave (ex. Switzerland). a The daily new deaths and the characteristic date. The black circles are the reported daily new deaths. The blue line is the 10-day smoothing of the daily deaths. The square is the peak of daily new deaths. The regular triangle is the outbreak date when the new deaths climb to more than one-tenth of the peak. The inverted triangle is the saturation date when the new deaths fall below one-tenth of the peak. b The cumulative deaths and the duration of the first wave. The black circles are the reported cumulative deaths. The red circles are the data for the duration of the first wave.

Figure 7

ICU time and the value of τ . The 45-degree black line indicates the equality of the observed and predicted data.

Figure 8

The k values of 52 countries. a-d are the k values for countries in Europe, Africa, Asia, and America, respectively. The blue dots are the data across countries. The black dashed lines are the average of countries by continent. The grey areas are the interquartile range (25th–75th).

Figure 9

Fitting of mortality using a logistic model. The red point is the officially reported data, and the black line is the fitting result with 95% confidence intervals (blue bands)