Exhibit 4

COVID-19 Pandemic Planning Scenarios Coronavirus Disease 2019 (COVID-19) <u>Infection Fatality Ratios</u> Page 6

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COVID-19 Pandemic Planning Scenarios COVID-19 Pandemic Planning Scenarios Coronavirus Disease 2019 (COVID-19)

Summary of Recent Changes

Updated September 10, 2020:

- The Infection Fatality Ratio parameter has been updated to include age-specific estimates
- The parameter for Number of Days from Symptom Onset to Seeking Outpatient Care—which was based on influenza care seeking data—has been replaced with the Median Number of Days from Symptom Onset to SARS-CoV-2 Test among SARS-CoV-2 Positive Patients
- A new parameter for the likelihood of an infection being reported has been added: The Ratio of Estimated Infections to Reported Case Counts

CDC and the Office of the Assistant Secretary for Preparedness and Response 🗹 (ASPR) have developed five COVID-19 Pandemic Planning Scenarios that are designed to help inform decisions by public health officials who use mathematical modeling, and by mathematical modelers throughout the federal government. Models developed using the data provided in the planning scenario tables can help evaluate the potential effects of different community mitigation strategies (e.g., social distancing). The planning scenarios may also be useful to hospital administrators in assessing resource needs and can be used in conjunction with the COVID-19Surge Tool.

Each scenario is based on a set of numerical values for biological and epidemiological characteristics of COVID-19 illness, which is caused by the SARS-CoV-2 virus. These values—called *parameter values*—can be used in models to estimate the possible effects of COVID-19 in U.S. states and localities. This document was first posted on May 20, 2020, with the understanding that the parameter values in each scenario would be updated and augmented over time, as we learn more about the epidemiology of COVID-19. The September 10 update is based on data received by CDC through August 8, 2020.

In this update, age-specific estimates of Infection Fatality Ratios have been updated, one parameter measuring healthcare usage has been replaced with the median number of days from symptom onset to positive SARS-CoV-2 test, and a new parameter has been included: Ratio of Estimated Infections to Reported Case Counts, which is based on recent serological data from a commercial laboratory survey in the U.S.¹

New data on COVID-19 are available daily, yet information about the biological aspects of SARS-CoV-2 and epidemiological characteristics of COVID-19 remain limited, and uncertainty remains around nearly all parameter values. For example, current estimates of infection-fatality ratios do not account for time-varying changes in hospital capacity (e.g., in bed capacity, ventilator capacity, or workforce capacity) or for differences in case ascertainment in congregate and community settings or in rates of underlying health conditions that may contribute to a higher frequency of severe illness in those settings. A nursing home, for example, may have a high incidence of infection (due to close contacts among many individuals) and severe disease (due to a high rate of underlying conditions) that does not reflect the frequency or severity of disease in the broader population of older adults. In addition, the practices for testing nursing home residents for SARS-CoV-2 upon identification of a positive resident may be different than testing practices for

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contacts of confirmed cases in the community. Observed parameter values may also change over time (e.g., the percentage of transmission occurring prior to symptom onset will be influenced by how quickly and effectively both symptomatic people and the contacts of known cases are quarantined).

The parameters in the scenarios:

- Are estimates intended to support public health preparedness and planning.
- Are **not** predictions of the expected effects of COVID-19.
- Do not reflect the impact of any behavioral changes, social distancing, or other interventions.

The five COVID-19 Pandemic Planning Scenarios (Box 1) represent a range of possible parameters for COVID-19 in the United States. All parameter values are based on current COVID-19 surveillance data and scientific knowledge.

- Scenarios 1 through 4 are based on parameter values that represent the lower and upper bounds of disease severity and viral transmissibility (moderate to very high severity and transmissibility). The parameter values used in these scenarios are likely to change as we obtain additional data about the upper and lower bounds of disease severity and the transmissibility of SARS-CoV-2, the virus that causes COVID-19.
- Scenario 5 represents a current best estimate about viral transmission and disease severity in the United States, with the same caveat: the parameter values will change as more data become available.

Parameter values that vary among the Pandemic Planning Scenarios are listed in Table 1, while parameter values common to all five scenarios are listed in Table 2. Definitions of the parameters are provided below, and the source of each parameter value is indicated in the Tables.

Parameter values that vary across the five COVID-19 Pandemic Planning Scenarios (Table 1) include measures of viral transmissibility, disease severity, and pre-symptomatic and asymptomatic disease transmission. Age-stratified estimates are provided, where sufficient data are available.

Viral Transmissibility

• **Basic reproduction number (R₀):** The average number of people that one person with SARS-CoV-2 is likely to infect in a population without any immunity (from previous infection) or any interventions. R₀ is an estimate of how transmissible a pathogen is in a population. R₀ estimates vary across populations and are a function of the duration of contagiousness, the likelihood of infection per contact between a susceptible person and an infectious person, and the contact rate.²

Disease Severity

• Infection Fatality Ratio (IFR): The number of individuals who die of the disease among all infected individuals (symptomatic and asymptomatic). This parameter is not necessarily equivalent to the number of reported deaths per reported case because many cases and deaths are never confirmed to be COVID-19, and there is a lag in time between when people are infected and when they die. This parameter also reflects the existing standard of care, which may vary by location and may be affected by the introduction of new therapeutics.

Pre-symptomatic and Asymptomatic Contribution to Disease Transmission

A **pre-symptomatic case** of COVID-19 is an individual infected with SARS-CoV-2, who has not exhibited symptoms at the time of testing, but who later exhibits symptoms during the course of the infection. An **asymptomatic case** is an individual infected with SARS-CoV-2, who does not exhibit symptoms during the course of infection. Parameter values that measure the pre-symptomatic and asymptomatic contribution to disease transmission include:

• Percentage of infections that are asymptomatic: The percentage of persons who are infected with SARS-CoV-2 but never show symptoms of disease. Asymptomatic cases are challenging to identify because individuals do not know

they are infected unless they are tested over the course of their infection, which is typically only done systematically as a part of a scientific study.

- Infectiousness of asymptomatic individuals relative to symptomatic individuals: The contribution to transmission of SARS-CoV-2 from asymptomatic individuals compared to the contribution to transmission of SARS-CoV-2 from symptomatic individuals. For example, a parameter value of 50% means that an asymptomatic individual is half as infectious as a symptomatic individual, whereas a parameter value of 100% means that an asymptomatic individual is just as likely to transmit infection as a symptomatic individual.
- Percentage of transmission occurring prior to symptom onset: Among symptomatic cases, the percentage of new cases of COVID-19 due to transmission from a person with COVID-19 who infects others before exhibiting symptoms (pre-symptomatic).

Parameter values that do not vary across the five Pandemic Planning Scenarios (Table 2) are:

- Level of pre-existing immunity to COVID-19 in the community: The percentage of the U.S. population that had existing immunity to COVID-19 prior to the start of the pandemic beginning in 2019.
- Ratio of estimated infections to reported case counts: The estimated number of infections divided by the number of reported cases. The level of case detection likely varies by the age distribution of cases, location, and over time.
- **Time from exposure to symptom onset:** The number of days from the time a person has contact with an infected person that results in COVID-19 infection and the first appearance of symptoms.
- Time from symptom onset in an individual and symptom onset of a second person infected by that individual: The number of days from the time a person becomes symptomatic and when the person who they infect becomes symptomatic.

Additional parameter values common to the five COVID-19 Pandemic Planning Scenarios are these ten measures of healthcare usage:

- Median number of days from symptom onset to SARS-CoV-2 test among SARS-CoV-2 positive patients
- Median number of days from symptom onset to hospitalization
- Median number of days of hospitalization among those not admitted to the ICU
- Median number of days of hospitalization among those admitted to the ICU
- Percentage of patients admitted to the ICU among those hospitalized
- Percentage of patients on mechanical ventilation among those hospitalized (includes both non-ICU and ICU admissions)
- Percentage of patients who die among those hospitalized (includes both non-ICU and ICU admissions)
- Median number of days on mechanical ventilation
- Median number of days from symptom onset to death
- · Median number of days from death to reporting of that death

These healthcare-related parameters (Table 2) are included to assist in assessment of resource needs as the pandemic progresses.

Box 1 Description of the Five COVID-19 Pandemic Planning Scenarios

For each Pandemic Planning Scenario:

- Parameter value for viral transmissibility is the Basic Reproduction Number (R₀)
- Parameter value for disease severity is the Infection Fatality Ratio (IFR)
- Parameter values for the pre-symptomatic and asymptomatic contribution to disease transmission are:
 Percentage of transmission occurring prior to symptom onset (from pre-symptomatic individuals)
 - Percentage of infections that are asymptomatic
 - o Infectiousness of asymptomatic individuals relative to symptomatic individuals

For Pandemic Scenarios 1-4:

• These scenarios are based on parameter values that represent the lower and upper bounds of disease severity and viral transmissibility (moderate to very high severity and transmissibility). The parameter values used in these scenarios are likely to change as we obtain additional data about the upper and lower bounds of disease severity and viral transmissibility of COVID-19.

For Pandemic Scenario 5:

• This scenario represents a current best estimate about viral transmission and disease severity in the United States, with the same caveat: that the parameter values will change as more data become available.

Scenario 1:

- Lower-bound values for virus transmissibility and disease severity
- Lower percentage of transmission prior to onset of symptoms
- · Lower percentage of infections that never have symptoms and lower contribution of those cases to transmission

Scenario 2:

- Lower-bound values for virus transmissibility and disease severity
- Higher percentage of transmission prior to onset of symptoms
- Higher percentage of infections that never have symptoms and higher contribution of those cases to transmission

Scenario 3:

- Upper-bound values for virus transmissibility and disease severity
- Lower percentage of transmission prior to onset of symptoms
- Lower percentage of infections that never have symptoms and lower contribution of those cases to transmission

Scenario 4:

- Upper-bound values for virus transmissibility and disease severity
- · Higher percentage of transmission prior to onset of symptoms
- Higher percentage of infections that never have symptoms and higher contribution of those cases to transmission

Scenario 5:

• Parameter values for disease severity, viral transmissibility, and pre-symptomatic and asymptomatic disease transmission that represent the best estimate, based on the latest surveillance data and scientific knowledge. Parameter values are based on data received by CDC through August 8, 2020.

Table 1. Parameter Values that vary among the five COVID-19 Pandemic Planning Scenarios. The scenarios are intended to advance public health preparedness and planning. They are **not** predictions or estimates of the expected impact of COVID-19. The parameter values in each scenario will be updated and augmented over time, as we learn more about the epidemiology of COVID-19. Additional parameter values might be added in the future (e.g., population density, household transmission, and/or race and ethnicity).

Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5: Current Best Estimate
Ro*	2.0		4.0		2.5

Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5: Current Best Estimate
Infection Fatality Ratio [†]	0-19 years: 0.00002 20-49 years: 0.00007 50-69 years: 0.0025 70+ years: 0.028		0-19 years: 0.0001 20-49 years: 0.0003 50-69 years: 0.010 70+ years: 0.093		0-19 years: 0.00003 20-49 years: 0.0002 50-69 years: 0.005 70+ years: 0.054
Percent of infections that are asymptomatic [§]	10%	70%	10%	70%	40%
Infectiousness of asymptomatic individuals relative to symptomatic [¶]	25%	100%	25%	100%	75%
Percentage of transmission occurring prior to symptom onset**	30%	70%	30%	70%	50%

*The best estimate representative of the point estimates of R₀ from the following sources:

Chinazzi M, Davis JT, Ajelli M, et al. The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science*. 2020;368(6489):395-400; Imai N., Cori, A., Dorigatti, I., Baguelin, M., Donnelly, C. A., Riley, S., Ferguson, N.M. (2020). Report 3: Transmissibility of 2019-nCoV. *Online report*

Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med*. 2020;382(13):1199-1207

Munayco CV, Tariq A, Rothenberg R, et al. Early transmission dynamics of COVID-19 in a southern hemisphere setting: Lima-Peru: February 29th-March 30th, 2020 [published online ahead of print, 2020 May 12]. *Infect Dis Model*. 2020; 5:338-345

Salje H, Tran Kiem C, Lefrancq N, et al. Estimating the burden of SARS-CoV-2 in France [published online ahead of print, 2020 May 13] [published correction appears in Science. 2020 Jun 26;368(6498):]. *Science*. 2020;eabc3517.

The range of estimates for Scenarios 1-4 represent the upper and lower bound of the widest confidence interval estimates reported in: Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med.* 2020;382(13):1199-1207.

Substantial uncertainty remains around the R₀ estimate. Notably, Sanche S, Lin YT, Xu C, Romero-Severson E, Hengartner N, Ke R. High Contagiousness and Rapid Spread of Severe Acute Respiratory Syndrome Coronavirus 2. *Emerg Infect Dis.* 2020;26(7):1470-1477 (https://dx.doi.org/10.3201/eid2607.200282 ^[]) estimated a median R₀ value of 5.7 in Wuhan, China. In an analysis of 8 Europe countries and the US, the same group estimated R₀ of between 4.0 and 7.1 in the pre-print manuscript: Ke R., Sanche S., Romero-Severson, & E., Hengartner, N. (2020). Fast spread of COVID-19 in Europe and the US suggests the necessity of early, strong and comprehensive interventions. *medRxiv*.

† These estimates are based on age-specific estimates of infection fatality ratios from Hauser, A., Counotte, M.J., Margossian, C.C., Konstantinoudis, G., Low, N., Althaus, C.L. and Riou, J., 2020. Estimation of SARS-CoV-2 mortality during the early stages of an epidemic: a modeling study in Hubei, China, and six regions in Europe. *PLoS medicine*, *17*(7), p.e1003189. Hauser et al. produced estimates of IFR for 10-year age bands from 0 to 80+ year old for 6 regions in Europe. Estimates exclude infection fatality ratios from Hubei, China, because we assumed infection and case ascertainment from the 6 European regions are more likely to reflect ascertainment in the U.S. To obtain the best estimate values, the point estimates of IFR by age were averaged to broader age groups for each of the 6 European regions using weights based on the age distribution of reported cases from COVID-19 Case Surveillance Public Use Data (https://data.cdc.gov/Case-Surveillance/COVID-19-Case-Surveillance-Public-Use-Data/vbim-akqf). The estimates for persons ≥70 years old presented here do not include persons ≥80 years old as IFR estimates from Hauser et al., assumed that 100% of infections among persons ≥80 years old were reported. The consolidated age estimates were then averaged across the 6 European regions. The lower bound estimate is the lowest, non-zero point estimate across the six regions, while the upper bound is the highest point estimate across the six regions.

§ The percent of cases that are asymptomatic, i.e. never experience symptoms, remains uncertain. Longitudinal testing of individuals is required to accurately detect the absence of symptoms for the full period of infectiousness. Current peer-reviewed and preprint studies vary widely in follow-up times for re-testing, or do not include re-testing of cases. Additionally, studies vary in the definition of a symptomatic case, which makes it difficult to make direct comparisons between estimates. Furthermore, the percent of cases that are asymptomatic may vary by age, and the age groups reported in studies vary. Given these limitations, the range of estimates for Scenarios 1-4 is wide. The lower bound estimate approximates the lower 95% confidence interval bound estimated from: Byambasuren, O., Cardona,

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M., Bell, K., Clark, J., McLaws, M. L., & Glasziou, P. (2020). Estimating the extent of true asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *Available at SSRN 3586675*. The upper bound estimate approximates the upper 95% confidence interval bound estimated from: Poletti, P., Tirani, M., Cereda, D., Trentini, F., Guzzetta, G., Sabatino, G., Marziano, V., Castrofino, A., Grosso, F., Del Castillo, G. and Piccarreta, R. (2020). Probability of symptoms and critical disease after SARS-CoV-2 infection. *arXiv preprint arXiv:2006.08471*. The best estimate is the midpoint of this range and aligns with estimates from: Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review [published online ahead of print, 2020 Jun 3]. *Ann Intern Med*. 2020; M20-3012.

¶ The current best estimate is based on multiple assumptions. The relative infectiousness of asymptomatic cases to symptomatic cases remains highly uncertain, as asymptomatic cases are difficult to identify, and transmission is difficult to observe and quantify. The estimates for relative infectiousness are assumptions based on studies of viral shedding dynamics. The upper bound of this estimate reflects studies that have shown similar durations and amounts of viral shedding between symptomatic and asymptomatic cases: Lee, S., Kim, T., Lee, E., Lee, C., Kim, H., Rhee, H., Park, S.Y., Son, H.J., Yu, S., Park, J.W. and Choo, E.J., Clinical Course and Molecular Viral Shedding Among Asymptomatic and Symptomatic Patients With SARS-CoV-2 Infection in a Community Treatment Center in the Republic of Korea. *JAMA Internal Medicine*; Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med*. 2020;382(12):1177-1179; and Zhou R, Li F, Chen F, et al. Viral dynamics in asymptomatic patients with COVID-19. *Int J Infect Dis*. 2020; 96:288-290. The lower bound of this estimate reflects data indicating that viral loads are higher in severe cases relative to mild cases (Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infect Dis*. 2020;20(6):656-657) and data showing that viral loads and shedding durations are higher among symptomatic cases relative to asymptomatic cases (Noh JY, Yoon JG, Seong H, et al. Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration [published online ahead of print, 2020 May 21]. *J Infect*. 2020; S0163-4453(20)30310-8).

** The lower bound of this parameter is approximated from the lower 95% confidence interval bound from: He, X., Lau, E.H., Wu, P., Deng, X., Wang, J., Hao, X., Lau, Y.C., Wong, J.Y., Guan, Y., Tan, X. and Mo, X. (2020). Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature medicine*, *26*(5), pp.672-675. The upper bound of this parameter is approximated from the higher estimates of individual studies included in: Casey, M., Griffin, J., McAloon, C.G., Byrne, A.W., Madden, J.M., McEvoy, D., Collins, A.B., Hunt, K., Barber, A., Butler, F. and Lane, E.A. (2020). Estimating pre-symptomatic transmission of COVID-19: a secondary analysis using published data. *medRxiv*.The best estimate is the geometric mean of the point estimates from these two studies.

Table 2. Parameter Values Common to the Five COVID-19 Pandemic Planning Scenarios. The parameter values are likely to change as we obtain additional data about disease severity and viral transmissibility of COVID-19.

Parameter values are based on data received by CDC through August 8, 2020, including COVID-19 Case Surveillance Public Use Data (https://data.cdc.gov/Case-Surveillance/COVID-19-Case-Surveillance-Public-Use-Data/vbim-akqf); data from the Hospitalization Surveillance Network (COVID-NET) (through August 1); and data from Data Collation and Integration for Public Health Event Response (*DCIPHER*).

Pre-existing immunity Assumption, ASPR and CDC	No pre-existing immunity before the pandemic began in 2019. It is assumed that all members of the U.S. population were susceptible to infection prior to the pandemic.
Time from exposure to symptom onset*	~6 days (mean)
Time from symptom onset in an individual and symptom onset of a second person infected by that individual [†]	~6 days (mean)
Mean ratio of estimated infections to reported case counts, Overall (range) [§]	11 (6, 24)
Parameter Values Related to Healthcare Usage	
Median number of days from symptom onset to SARS-CoV-2 test among SARS-CoV-2 positive patients (interquartile range) [¶]	Overall: 3 (1, 6) days

Median number of days from symptom onset to hospitalization (interquartile range)**	18-49 years: 6 (3, 10) days		
nospitalization (interquartile fange)	50-64 years: 6 (2, 10) days		
	≥65 years: 4 (1, 9) days		
Median number of days of hospitalization among	18-49 years: 3 (2, 5) days		
those not admitted to ICU (interquartile range) ^{††}	50-64 years: 4 (2, 7) days		
	≥65 years: 6 (3, 10) days		
Median number of days of hospitalization among	18-49 years: 11 (6, 20) days		
those admitted to ICU (interquartile range) ^{††,55}	50-64 years: 14 (8, 25) days		
	≥65 years: 12 (6, 20) days		
Percent admitted to ICU among those	18-49 years: 23.8%		
hospitalized ^{††}	50-64 years: 36.1%		
	≥65 years: 35.3%		
Percent on mechanical ventilation among those	18-49 years: 12.0%		
hospitalized. Includes both non-ICU and ICU admissions ^{††}	50-64 years: 22.1%		
	≥65 years: 21.1%		
Percent that die among those hospitalized.	18-49 years: 2.4%		
Includes both non-ICU and ICU admissions ^{††}	50-64 years: 10.0%		
	≥65 years: 26.6%		
Median number of days of mechanical ventilation (interquartile range)**	Overall: 6 (2, 12) days		
ledian number of days from symptom onset to	18-49 years: 15 (9, 25) days		
death (interquartile range)**	50-64 years: 17 (10, 26) days		
	≥65 years: 13 (8, 21) days		
Median number of days from death to reporting	18-49 years: 19 (5, 45) days		
(interquartile range) ^{¶¶}	50-64 years: 21 (6, 46) days		
	≥65 years: 19 (5, 44) days		

* McAloon, C.G., Collins, A., Hunt, K., Barber, A., Byrne, A., Butler, F., Casey, M., Griffin, J.M., Lane, E., McEvoy, D. and Wall, P. (2020). The incubation period of COVID-19: A rapid systematic review and meta-analysis of observational research. *medRxiv*.

† He, X., Lau, E.H., Wu, P., Deng, X., Wang, J., Hao, X., Lau, Y.C., Wong, J.Y., Guan, Y., Tan, X. and Mo, X. (2020). Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature medicine*, *26*(5), pp.672-675.

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§ The point estimate is the geometric mean of the location specific point estimates of the ratio of estimated infections to reported cases, from Havers, F.P., Reed, C., Lim, T., Montgomery, J.M., Klena, J.D., Hall, A.J., Fry, A.M., Cannon, D.L., Chiang, C.F., Gibbons, A. and Krapiunaya, I., 2020. Seroprevalence of antibodies to SARS-CoV-2 in 10 sites in the United States, March 23-May 12, 2020. *JAMA Internal Medicine*. The lower and upper bounds for this parameter estimate are the lowest and highest point estimates of the ratio of estimated infections to reported cases, respectively, from Havers et al., 2020.

¶ Estimates only include symptom onset dates between March 1, 2020 – July 15, 2020. Estimates represent time to obtain SARS-CoV-2 tests among cases who tested positive for SARS-CoV-2. Estimates based on and data from Data Collation and Integration for Public Health Event Response (*DCIPHER*).

** Estimates only include symptom onset dates between March 1, 2020 – July 15, 2020 to ensure cases have had sufficient time to observe the outcome (hospital discharge or death). Data for 17 year olds and under are suppressed due to small sample sizes.

⁺⁺ Based on data reported to COVID-NET by Aug 1, 2020. Data for 17 year olds and under are suppressed due to small sample sizes. https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html.

§§ Cumulative length of stay for persons admitted to the ICU, inclusive of both ICU and non-ICU days.

¶ Estimates only include death dates between March 1, 2020 – July 15, 2020 to ensure sufficient time for reporting. Data for 17 year olds and under are suppressed due to small sample sizes.

References

- 1. Havers, F.P., Reed, C., Lim, T., Montgomery, J.M., Klena, J.D., Hall, A.J., Fry, A.M., Cannon, D.L., Chiang, C.F., Gibbons, A. and Krapiunaya, I., 2020. Seroprevalence of antibodies to SARS-CoV-2 in 10 sites in the United States, March 23-May 12, 2020. *JAMA Internal Medicine*.
- 2. Dietz K. The estimation of the basic reproduction number for infectious diseases. Stat Methods Med Res. 1993;2:23-41.

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