Mandated Bacillus Calmette-Guérin (BCG) vaccination predicts flattened curves for the spread of COVID-19

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The current analysis is based on data through June 10, 2020. This is the fifth biweekly update to our paper, which originally included data through April 1, 2020. Address correspondence to Martha Berg or Shinobu Kitayama at Department of Psychology, University of Michigan, Ann Arbor, MI 48109 USA. Emails: bergmk@umich.edu and kitayama@umich.edu.

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Supplementary Materials:

Supplementary Materials document includes all supplementary results, tables, and figures.

Teaser

National policies for universal BCG vaccination are associated with flattened growth of country-wise COVID-19 cases and deaths.

Abstract

BCG vaccination may reduce the risk of a range of infectious diseases, and if so, it could serve as a protective factor against COVID-19. Here, we compared countries that mandated BCG vaccination at least until 2000 with countries that did not. To minimize any systematic effects of reporting biases, we analyzed the rate of the day-by-day increase in both confirmed cases (135 countries) and deaths (134 countries) in the first 30-day period of country-wise outbreaks. The 30-day window was adjusted to begin at the country-wise onset of the pandemic. Linear mixed models revealed a significant effect of mandated BCG policies on the growth rate of both cases and deaths after controlling for median age, gross domestic product per capita, population density, population size, net migration rate, and various cultural dimensions (e.g., individualism). Our analysis suggests that mandated BCG vaccination can be effective in the fight against COVID-19.

Introduction

The current pandemic of COVID-19 began in December 2019 in Wuhan, China. Since then, it has rapidly spread across the globe. Currently, there is no end in sight. The present work is motivated by prior evidence that Bacillus Calmette-Guérin (BCG) vaccination (typically given at birth and/or during childhood) offers a long-lasting protective effect not only against tuberculosis (the intended target of BCG), but also against various other infectious diseases (1–3). Recent suggestions abound that BCG could be an effective tool in fighting against COVID-19. However, existing cross-national analyses are hampered by methodological weaknesses. For the most part, no effort has been made to exclude potential effects of reporting biases. The potential benefit of universal BCG policies requires careful assessment. To address this gap, we focused on the *rate of the increase* in both confirmed cases and deaths during an early period of country-wise outbreaks, and tested whether this rate might be slower in countries that mandated BCG vaccination at least until 2000, compared to those that did not.

The BCG vaccine is used against tuberculosis (4). One review has found that BCG vaccination reduces the risk of tuberculosis by 50% (5). A follow-up of an earlier BCG clinical trial performed on native Americans show that BCG protects people from both tuberculosis and lung cancer for up to several decades, throughout each person's life (2, 3). A more recent meta-analysis of a broader range of observational studies and clinical trials (1) suggests that the effectiveness of BCG could extend to all-cause mortality. Several controlled trials provide consistent results, showing that the reduced mortality is attributable to protection against respiratory infections, as well as neonatal sepsis (6–8). Altogether, the available evidence suggests that BCG has beneficial effects on immunity against a range of lung-related infections that go beyond tuberculosis, which makes it a promising candidate for defending against COVID-19. As for mechanisms, recent experimental work (9) finds that BCG vaccination causes genome-wide epigenetic reprogramming of human monocytes, which in turn predicts protection against experimental viral infection.

Over the last century, many countries adopted universal policies of mandatory BCG vaccination to fight against tuberculosis, which was then a major threat. Since then, many countries maintained such a policy at least until very recently (e.g., China, Ireland, Finland, and France). Some other countries terminated the policies as tuberculosis ceased to be a threat (e.g., Australia, Spain, Ecuador). Of note, some countries never mandated BCG vaccination (e.g., U.S., Italy, and Lebanon). Therefore, there is sufficient variability in the presence or absence of such policies distributed across different regions of the world, which makes it possible to draw a systematic comparison.

We examined the day-by-day increase of both confirmed cases and deaths and compared the rate of increase between countries that had mandated BCG policies at least until recently and those that did not. The start of the growth curves was set to be equal across countries, thereby controlling for the varying onset of the pandemic in different countries. Specifically, we focused on a time period either after the first 100 confirmed cases (as in 10) or after one confirmed COVID-caused death. We then tested the initial, exponential spread of the virus. To exclude any systematic influences of cross-national variation in reporting biases, we focused on the rate of increase of both cases and deaths. These rates are uncontaminated by reporting biases as long as the biases are stable during the period tested. Thus, to avoid any systematic variations in reporting biases, it is important to examine a short initial period of growth. At the same time, it is necessary to test a sufficiently long period to obtain reliable estimates of the growth rate. To simultaneously meet these two competing demands, we chose to examine the first 30 days of the onset of country-wise outbreaks in the main analysis, which was followed by a robustness check testing an even shorter 15-day period. In addition, in a subsequent analysis, we adopted a measure of country-wise reporting biases and weighted the data accordingly. Further, we also controlled for test availability.

We first tested whether the growth rate would be significantly slower in countries that have continued to mandate BCG vaccination at least until the year 2000, as compared to countries that do not currently require it. This year (2000) was chosen since vaccination may become effective at the population level only when a vast majority (70-80% according to a simulation reported in 11) is made resistant against a target virus, a phenomenon known as "herd immunity" (12). In the countries that had mandated BCG at birth at least until the year 2000, a vast majority of adults must have been made resistant against lung-related viral infections. We also explored whether there might be any difference between those that never had such a policy and those that had one during the 20th century but have since terminated the policy for at least a few decades. As a final robustness check, we tested whether the groups of countries that vary in BCG policy status might also vary on various cultural dimensions, such as individualism vs. collectivism (14).

Results

Confirmed Cases

All countries that had reported at least 15 days of at least 100 total confirmed cases, and that had available data on BCG policy and covariates (median age, gross domestic product per capita, population density, population size, and net migration rate) were included (134 countries in total). For each country, day 1 was set to be the first day of at least 100 confirmed cases. See Column 2 of Table S1 for the date of day 1 for each included country.

To model the exponential growth of confirmed cases, we estimated a linear mixed model of the natural log-transformed number of confirmed cases. We entered two contrasts designating BCG policy status (current vs. [past and none] combined and past vs. none). The effect of BCG policy status on growth rate is reflected by the interactions between day and each BCG policy status contrast.

As shown in Table 1-A, we found a significant main effect of day, b = 0.114, p < .001, reflecting an exponential increase in cases over time. This increase was qualified by a significant interaction between day and BCG policy status. Specifically, the growth rate of COVID-19 cases was significantly slower in countries with mandated BCG vaccinations, compared to countries without mandated BCG vaccinations, b = -0.039, p < .001 (see Fig. 1-A and B). Fig. 2-A shows the distribution of the country-wise regression coefficients.

Countries that once had such policies but terminated them before 2000 were not significantly different in growth rate from those that never instituted mandatory BCG vaccinations, b = -0.009, p = .610. In terms of control variables, larger population size predicted a faster growth rate of confirmed cases. See Table S2 for a correlation table of all predictor variables.

The effect of BCG policy status on COVID-19 cases remained unchanged when countries were weighted by reporting quality (Supplementary analysis 1) and when controlling for the total number of tests (Supplementary analysis 2). Hence, biases in testing and reporting, demonstrably pervasive across countries, had little or no effect on the effect of universal BCG policies on the growth rate. Moreover, this effect also did not change when a 15-day time window was used (Supplementary analysis 3), adding further evidence that the main analysis is unlikely to be due to any systematic variations in reporting biases during the 30-day period. In addition, the BCG effect had little to do with the cultural dimensions of individualism vs. collectivism or power distance (Supplementary analysis 4).

Deaths

All countries that had reported at least 15 days of at least one death from COVID-19, and that had available data on BCG policy and covariates (135 countries in total) were included in this analysis. For each country, day 1 was set to be the first day of at least 1 confirmed death. See column 3 of Table S1 for the date of day 1 for each included country.

We estimated a linear mixed model of the natural log-transformed number of deaths, controlling for the same control variables as above. As in the analysis on confirmed cases, we

found a significant main effect of day, b = 0.139, p < .001, reflecting an exponential increase in deaths over time (Table 1-B). This increase was qualified by a significant interaction between day and BCG policy status. Specifically, the growth rate of COVID-19 related deaths was significantly less in countries with mandated BCG vaccinations, compared to countries without mandated BCG vaccinations, b = -0.059, p < .001 (Fig. 1-C and D). Fig. 2-B shows the distribution of the country-wise regression coefficients.

Countries that once had such policies but terminated them before 2000 were no different in growth rate from those that never instituted mandatory BCG, b = -0.007, p = .772. In terms of control variables, larger population size and higher median age predicted a faster growth rate of COVID-19 deaths.

The effect of BCG policy status on COVID-19 related deaths remained unchanged when a 15-day time window was used (Supplementary analysis 3), showing the robustness of the main analysis. In addition, the BCG effect was unrelated to the cultural dimensions mentioned above (Supplementary analysis 4).

Discussion

Our analysis shows that mandatory BCG vaccination is associated with a flattening of the curve in the spread of COVID-19. The effect we demonstrate is quite substantial. For example, our model estimates that the total number of COVID-19 related deaths in the US as of March 29, 2020 would have been 468—19% of the actual figure (2467)—if the US had instituted the mandatory BCG vaccination several decades earlier (see Supplementary Analysis 5).

Our study is not the first to test the hypothesis that the country-wise spread of COVID-19 might depend on each country's BCG policy status. However, existing analyses are hampered by their focus on the cumulative totals of confirmed cases and deaths (13–27). These tallies depend on how earlier or sooner the onset of the pandemic was in each country. Moreover, they are massively influenced by reporting biases (including the availability of diagnostic testing), which can be both sizable and variable across countries. The same reservation applies to fatality rate (total deaths/total cases) (16, 24, 26–30) since the reporting biases are far more likely and cross-nationally variable for the confirmed cases than for the deaths. We circumvented these problems in three ways. First, we focused on the rate of growth of both cases and deaths, which should be uninfluenced by reporting biases as long as these biases are stable during the period of study. To meet this requirement, we focused on a short period (either the first 30 days or 15 days). Second, we used the best available estimate of country-wise reporting biases and used this as a weight in our analysis. Third, we controlled for testing availability.

Notably, the growth curves were as steep in countries that mandated BCG policies only during the 20_{th} century as in those that never mandated the vaccine. BCG vaccination may become effective only when a substantial proportion of the population is made resistant to a virus. That is to say, the spread of the virus may be slowed only when there is "herd immunity" that prevents the virus from spreading easily across the population (see a simulation in (11)). Note that as long as others receive vaccination, any single individual will be protected without vaccination, leading to a temptation for free-riding (i.e., not getting vaccinated). Hence, in the absence of state-imposed mandatory vaccination, cultural norms emphasizing prosocial interdependent orientations (31, 32) may prove to be crucial for the success of BCG in preventing future outbreaks of COVID-19 (11, 33). While the current analysis provided no evidence, this possibility must be addressed in future work.

Some limitations of our effort must be acknowledged. In all national policies, BCG is given early in life, typically at birth. It remains unclear whether BCG vaccination might be effective when given to adults. Nor is it known how long BCG vaccination might provide immunity to COVID-19 although it is effective against tuberculosis and lung cancer for several decades (2, 3). Moreover, it is uncertain whether BCG might have any adverse effects when

given to those already infected with COVID-19. There is an urgent need for randomized clinical trials. Lastly, the rates of exponential growth showed substantial variability across countries that have mandated BCG vaccination (Fig. 2-A and B). Hence, BCG is by no means a magic bullet that assures safety against COVID-19. In all likelihood, there are some societal variables that moderate this effect. This variation must be addressed in future work.

All these limitations notwithstanding, the current evidence is the first to show a significant advantage of universal BCG policies in reducing the spread of COVID-19, thereby justifying a thorough investigation of the merit of the mandatory BCG vaccination in the fight against COVID-19.

Methods

Data

Main variables. We retrieved data on daily confirmed COVID-19 cases and deaths by country from a public repository updated daily by the Johns Hopkins University Center for Systems Science and Engineering (https://github.com/CSSEGISandData/COVID-19). Our current results are based on data through June 10, 2020. For confirmed cases, we included countries with at least 15 days of data, starting with at least 100 reported cases as 'day 1'. For deaths, we included countries with at least 15 days of data, starting with at least 1 reported death as 'day 1.'

BCG vaccination policy data for each country were compiled from the BCG World Atlas (http://www.bcgatlas.org/index.php) (34). Countries were excluded if policy information was unavailable. Data included BCG policy status (vaccination never mandated, vaccination mandated in the past but terminated before 2000, vaccination mandated either currently or up until at least 2000). We defined this variable based on data from the year 2000, so that 'vaccination currently mandated' refers to any country that continued to mandate the BCG vaccination into the 21st century. We created 2 contrast-coded variables to capture BCG policy. The first was a contrast between countries that currently mandate BCG (including those that maintained mandated BCG until at least 2000) and countries that do not currently mandate BCG (including those that terminated mandated BCG before 2000). The second was a contrast between countries that previously mandated BCG that terminated it before 2000 and countries that never mandated BCG.

The 129 included countries are listed in Table S1, which shows the date of the first 100 confirmed cases, the date of the first confirmed death, and the BCG policy status for each of the countries.

Demographics. Total population (in thousands) was included since the number of both confirmed cases and deaths should be larger for more populous countries. It was compiled from the United Nations Department of Economic and Social Affairs World Urbanization Prospects 2018 (*35*). Population was natural log-transformed to reduce skewness. Median age of the total population (in years) was included since older adults are more susceptible to viral threats. Population density (in persons per square kilometer) was used because it is likely to foster greater social contact, resulting in greater chances of infection. Net migration (persons entering country minus persons exiting country, per 1000 population) was included so as to control for population movement. These statistics were compiled from the United Nations Department of Economic and Social Affairs World Population Prospects 2019 (*36*). Gross domestic product (at purchasing power parity) per capita (GDP per capita), compiled from the World Bank International Comparison Program database (*37*), was included to control for economic development.

Underreporting of cases. Countries may vary in underreporting of COVID-19 cases due to governmental information suppression, a lack of tests, or both. As noted, this variable is likely relatively stable over the 30-day period under study, and therefore, it is unlikely to have systematic influences on the slope of the growth curves in the present analysis. Nevertheless, underreporting may decrease data quality and therefore may cause more subtle biases in the

estimation of the slopes. To account for this, we ran the same models and weighted each country based on the accuracy of their reporting.

We used an index of underreporting devised by Russell and colleagues (*38*), who first computed a case fatality ratio (CFR) for each country that is adjusted for the delay between admission to the hospital and death. They then computed a ratio comparing each country's adjusted CFR to the best empirical estimate of CFR (1.4%). Thus, if the ratio is smaller than one, it indicates some degree of underreporting. Some countries, such as Italy, Spain, and Morocco, show substantial underreporting (index < 10%), whereas some others, such as Norway, Israel, and South Korea, show less underreporting (index > 50%). These country-wise underreporting scores are publicly available at https://github.com/thimotei/CFR_calculation. Since only daily estimates are available, rather than averages over time, we used estimates from April 15, 2020, which is included in the majority of countries' 30-day period of data. Due to the lack of available data for some nations, the number of countries included in the analysis of cases dropped from 118 to 77. This analysis was performed only on the number of cases.

Number of tests. Countries may vary in the number of COVID-19 tests that are available, which may influence the number of cases and deaths that are reported. As noted, this variable is likely relatively stable over the 30-day period under study, and therefore, it is unlikely to have systematic influences on the slope of the growth curves in the present analysis. Nevertheless, to account for the possibility that our results are explained by differences in testing availability, we ran the same models and controlled for the total number of tests in each country.

We used country-wise numbers of total COVID-19 tests (https://github.com/owid/covid-19-data/tree/master/public/data/) (10). Consistent with our underreporting analysis, we used estimates from April 15, 2020. Due to the lack of available data for some nations, the number of countries included in the analysis of cases dropped from 118 to 77. This analysis was performed only on the number of cases.

Cultural dimensions. Two cultural dimensions were tested as potential confounding variables. We included individualism vs. collectivism (39) and power distance (40) since Western individualistic and/or more egalitarian societies tend to have no current mandated BCG policies. The culture scores for the two dimensions were obtained from (40).

Statistical Analysis

All analyses were conducted on up to 30 days of data from each eligible country. Linear mixed effect models with restricted maximum likelihood estimation were used to analyze both the number of cases and deaths. We first natural log-transformed both cases and deaths in order to account for the exponential nature of the increase of both (41). Each model estimated a random intercept, and a random slope across days for each country, to allow for heterogeneity in growth curves between countries. We used a second random effect to account for countries being nested in geographic regions, as defined by the World Bank (37). Since our maximal model did not converge, we dropped the slope-intercept covariance from all models. When this model failed to converge, we additionally dropped random intercept from the model (Supplementary analysis 2). Day was centered so that main effects could be interpreted as differences at the mean day of the growth curve. Models included day, BCG status (with 2 contrasts), and the interaction between day and BCG contrasts. All demographic variables were included along with their interactions with day: median age, population density, net migration, total population and GDP per capita. Total population was natural log-transformed to reduce skewness. All demographic and cultural variables were standardized. All code is available on OSF (https://osf.io/39mfj/?view_only=9d967767d8f040329e6063c286798eca).

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Table 1. Regression tables predicting growth in (A) cases and (B) deaths. Day is mean centered, and BCG policy variables are both contrast-coded. Population is natural log-transformed, and all covariates are standardized. This analysis is based on 134 and 135 countries for cases and deaths, respectively.

	A. Cases			B. Deaths		
Predictor	b	t	р	b	t	р
Intercept	6.793	42.165	<.001	2.445	8.284	<.001
Day	0.114	12.218	<.001	0.139	9.236	<.001
Median age	0.219	2.164	0.034	0.224	1.363	0.176
GDP per capita	0.163	1.586	0.115	0.145	0.930	0.354
Population density	-0.099	-1.715	0.089	-0.012	-0.135	0.893
Net migration rate	0.111	1.242	0.217	0.050	0.368	0.713
Population	0.518	8.533	<.001	0.679	7.281	<.001
BCG past vs. never	0.136	0.415	0.679	-0.164	-0.322	0.748
BCG current vs. not current	-0.633	-3.388	0.001	-0.993	-3.437	0.001
Day x median age	0.008	1.442	0.153	0.020	2.631	0.010
Day x GDP per capita	0.010	1.951	0.053	0.011	1.515	0.132
Day x population density	-0.001	-0.390	0.697	-0.003	-0.674	0.502
Day x net migration rate	0.005	1.051	0.295	0.003	0.492	0.623
Day x population	0.030	9.617	<.001	0.037	8.860	<.001
Day x BCG past vs. never	-0.009	-0.511	0.610	-0.007	-0.291	0.772
Day x BCG current vs. not current	-0.039	-3.978	<.001	-0.059	-4.530	<.001

Figure 1. Growth curves by country BCG policy for (A-B) cases and (C-D) deaths, presented on linear (A & C) and logarithmic (B & D) scales.

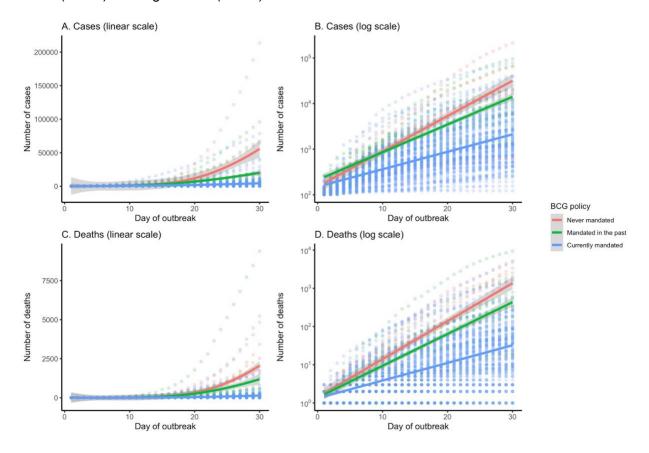
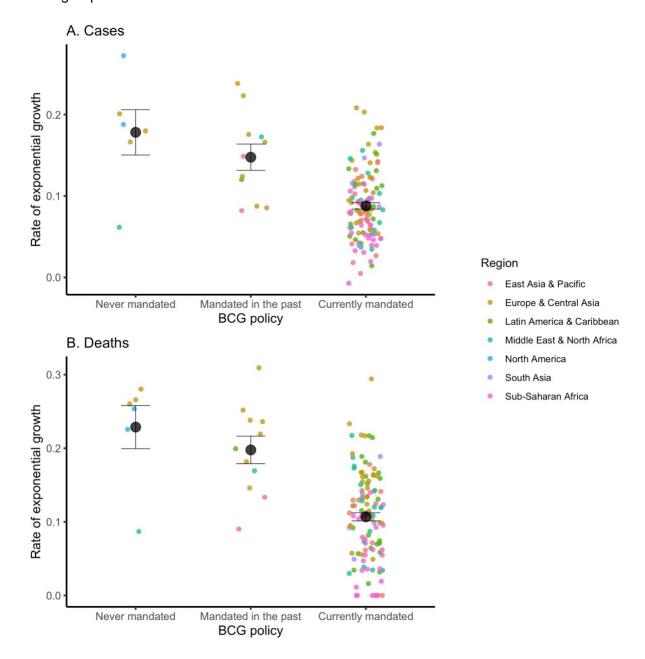


Figure 2. Growth rate of (A) cases and (B) deaths for each country, plotted by BCG policy and region. Growth rate is adjusted by median age, GDP per capita, population density, total population (log-transformed), and net migration rate. Means and standard error are plotted for each group.



Mandated Bacillus Calmette-Guérin (BCG) vaccination predicts flattened curves for the spread of COVID-19

Supplementary Materials

Supplementary analysis 1. Weighting country data based on underreporting index

We estimated a linear mixed model that was identical to that used in our main analysis, except that reporting index was included as a weighting factor in the model predicting the number of cases. Results were consistent with our main analysis, demonstrating that our effects are robust against differences in reporting quality across countries (see Table S3).

77 countries were included in this analysis. We found a significant main effect of day, b = 0.112, p < .001, reflecting an exponential increase in cases over time. This increase was qualified by a significant interaction between day and the contrast between current and non-current BCG policy. Specifically, the growth rate of COVID-19 cases was significantly slower in countries with mandated BCG vaccinations, compared to countries without mandated BCG vaccinations, b = -0.030, p = .006. Countries that once had such policies but terminated them before 2000 were not significantly different in growth rate from those that never instituted mandatory BCG vaccinations, b = -0.006, p = .716. In sum, our focal effect was no different with reporting index added as a weighting factor. See Table S3 for full regression table.

Supplementary analysis 2. Controlling for the total number of tests

We estimated linear mixed models that were identical to those used in our main analysis, except that the total number of tests for each country was included as a covariate in the model predicting the number of cases. Results were consistent with our main analysis, demonstrating that our effects are robust against differences in testing availability across countries (see Table S4).

64 countries were included in this analysis. We found a significant main effect of day, b = 0.112, p < .001, reflecting an exponential increase in cases over time. This increase was qualified by a significant interaction between day and the contrast between current and non-current BCG policy. Specifically, the growth rate of COVID-19 cases was significantly slower in countries with mandated BCG vaccinations, compared to countries without mandated BCG vaccinations, b = -0.039, p = .004. Countries that once had such policies but terminated them before 2000 were not significantly different in growth rate from those that never instituted mandatory BCG vaccinations, b = -0.009, p = .702. In sum, our focal effect was no different with total tests added as a covariate. See Table S4 for full regression table.

Supplementary analysis 3. Robustness check with 15-day time window

To test the robustness of our models, we conducted a set of analyses only using the first 15 days of data (rather than the first 30). The 15-day cutoff allowed us to examine more exclusively than the 30-day cutoff the very first phase of the outbreak in each country. Because our primary analysis included only countries that reported at least 15 days of eligible data, the same set of countries was included here (see Table S1 for full list for each analysis). All patterns were identical to the primary analyses.

A. Confirmed cases

We found a significant main effect of day, b = 0.157, p < .001, reflecting an exponential increase in cases over time. This increase was qualified by a significant interaction between day and BCG policy. Specifically, the growth rate of COVID-19 cases was significantly slower in countries with mandated BCG vaccinations, compared to countries without mandated BCG vaccinations, b = -0.052, p = .001. Countries that once had such policies but terminated them before 2000 were not significantly different in growth rate from those that never instituted mandatory BCG vaccinations, b = 0.016, p = .521. In sum, our focal effect was no different with

a shorter time window. See Table S5-A for full regression table and Figure S1-A and B for growth curves.

B. Deaths

Similarly, we found a significant main effect of day, b = 0.174, p < .001, reflecting an exponential increase in deaths over time. This increase was qualified by a significant interaction between day and BCG policy. Specifically, the growth rate of COVID-19 deaths was significantly slower in countries with mandated BCG vaccinations, compared to countries without mandated BCG vaccinations, b = -0.070, p = .004. Countries that once had such policies but terminated them before 2000 were not significantly different in growth rate from those that never instituted mandatory BCG vaccinations, b = 0.018, p = .671. In sum, our focal effect was no different with a shorter time window. See Table S5-B for full regression table and Figure S1-C and D for growth curves.

Supplementary analysis 4. Testing cultural dimensions

We first dummy-coded BCG status (BCG currently mandated vs. BCG not currently mandated). We then tested each variable that varied significantly as a function of BCG policy status as an additional covariate in our primary models, to test our key finding (the interaction between day and the primary BCG contrast) would be observed after controlling for the cultural dimension. Since the cultural indices were not available for all the countries included in the main analyses, and moreover, different indices were available for different sets of countries, each cultural dimension was analyzed separately so as to preserve the maximal number of countries.

A series of t-tests revealed that countries that currently mandate BCG (compared to all others) were significantly lower in individualism, whereas they were higher in power distance (Table S6).

A. Confirmed cases

To test whether the cultural dimensions shown to vary between the countries that differed in the BCG policy status might explain the effect of BCG policy status, we repeated the analyses reported in the main text with each of the cultural dimensions included as a covariate (see Tables S7-A and S8-A). 65 countries were included in each analysis. The key interaction between day and BCG policy status (contrasting countries that currently mandate BCG with those that do not) remained statistically significant when either individualism or power distance was added as a covariate.

B. Deaths

We conducted the same two analyses to test whether individualism and power distance qualified the effect of BCG on the increase in deaths over time (see Tables S7-B and S8-B). 64 countries were included in each analysis. The key interaction between day and BCG policy status (contrasting countries that currently mandate BCG with those that do not) remained statistically significant when either individualism or power distance was added as a covariate.

Supplementary analysis 5. Predicting US cases and deaths if BCG were mandated

We estimated the numbers of confirmed cases and deaths estimated for the U.S. if it had instituted a mandatory BCG vaccination policy decades ago. To do this, we used the "predict" function in R. In particular, we plugged the value of each predictor for the U.S. into the regression equation. The value for day was set at 14.5, corresponding to the centered value of day 30, the final U.S. data point (on April 1 and March 29, 2020, for the analysis of confirmed cases and deaths, respectively). The BCG vaccination policy status was set to be equal to the countries that currently have mandatory BCG vaccination policies. The values for all other predictors were taken from available current U.S. values. The output gives the predicted number of cases (using the confirmed cases model) and deaths (using the deaths model) after natural log transformation. We thus calculated the numbers on their original scale by exponentiating our

predicted value. This analysis applied to the number of cases yielded a predicted value of 11.621, which translates to 111403.711 cases (compared to the actual 213372 cases reported in the US by April 1). This analysis applied to the number of deaths yielded a predicted value of 6.149, which translates to 468.038 deaths (compared to the actual 2467 deaths reported in the US by March 29).

Table S1. List of all countries included in analysis of cases and deaths, with the date set as day 1 in each country. Countries with dates entered in columns 2 and 3 are those included in our analysis of cases and deaths, respectively.

	Date of first	Date of first	500 II
Country	100 cases	death	BCG policy status
Afghanistan	3.27.20	3.22.20	Currently mandated
Albania	3.23.20	3.11.20	Currently mandated
Algeria	3.21.20	3.12.20	Currently mandated
Angola		3.29.20	Currently mandated
Argentina	3.20.20	3.8.20	Currently mandated
Armenia	3.19.20	3.26.20	Currently mandated
Australia	3.10.20	3.1.20	Mandated in the past
Austria	3.8.20	3.12.20	Mandated in the past
Azerbaijan	3.26.20	3.13.20	Currently mandated
Bangladesh	4.6.20	3.18.20	Currently mandated
Belarus	3.30.20	3.31.20	Currently mandated
Belgium	3.6.20	3.11.20	Never mandated
Belize		4.6.20	Currently mandated
Benin	5.7.20	4.6.20	Currently mandated
Bolivia	3.31.20	3.29.20	Currently mandated
Bosnia and Herzegovina	3.22.20	3.21.20	Currently mandated
Botswana		3.31.20	Currently mandated
Brazil	3.13.20	3.17.20	Currently mandated
Bulgaria	3.20.20	3.11.20	Currently mandated
Burkina Faso	3.24.20	3.18.20	Currently mandated
Burundi		4.13.20	Currently mandated
Cambodia	3.29.20		Currently mandated
Cameroon	3.29.20	3.25.20	Currently mandated
Canada	3.11.20	3.9.20	Never mandated
Central African Republic	5.8.20	5.23.20	Currently mandated
Chad	5.2.20	4.28.20	Currently mandated
Chile	3.16.20	3.22.20	Currently mandated
China	1.22.20	1.23.20	Currently mandated
Colombia	3.19.20	3.22.20	Currently mandated
Costa Rica	3.21.20	3.19.20	Currently mandated
Cote d'Ivoire	3.27.20	3.29.20	Currently mandated
Croatia	3.19.20	3.19.20	Currently mandated
Cuba	3.28.20	3.18.20	Currently mandated
Czechia	3.13.20	3.22.20	Currently mandated
			•

Denmark	3.10.20	3.14.20	Mandated in the past
Dominican Republic	3.21.20	3.17.20	Currently mandated
Ecuador	3.18.20	3.14.20	Mandated in the past
Egypt	3.14.20	3.8.20	Currently mandated
El Salvador	4.9.20	3.31.20	Currently mandated
Equatorial Guinea	4.24.20	4.22.20	Currently mandated
Estonia	3.14.20	3.25.20	Currently mandated
Ethiopia	4.18.20	4.5.20	Currently mandated
Finland	3.13.20	3.21.20	Currently mandated
France	2.29.20	2.15.20	Currently mandated
Gabon	4.17.20	3.20.20	Currently mandated
Gambia		3.23.20	Currently mandated
Georgia	3.30.20	4.4.20	Currently mandated
Germany	3.1.20	3.9.20	Mandated in the past
Ghana	3.26.20	3.21.20	Currently mandated
Greece	3.13.20	3.11.20	Currently mandated
Guatemala	4.10.20	3.16.20	Currently mandated
Guinea	4.4.20	4.15.20	Currently mandated
Guinea-Bissau	4.29.20	4.26.20	Currently mandated
Guyana	5.10.20	3.12.20	Currently mandated
Haiti	5.4.20	4.5.20	Currently mandated
Honduras	3.29.20	3.26.20	Currently mandated
Hungary	3.21.20	3.15.20	Currently mandated
India	3.14.20	3.11.20	Currently mandated
Indonesia	3.15.20	3.11.20	Currently mandated
Iran	2.26.20	2.19.20	Currently mandated
Iraq	3.13.20	3.4.20	Currently mandated
Ireland	3.14.20	3.11.20	Currently mandated
Israel	3.12.20	3.21.20	Mandated in the past
Italy	2.23.20	2.21.20	Never mandated
Jamaica	4.15.20	3.19.20	Currently mandated
Japan	2.21.20	2.13.20	Currently mandated
Jordan	3.22.20	3.27.20	Currently mandated
Kazakhstan	3.26.20	3.20.20	Currently mandated
Kenya	4.2.20	3.26.20	Currently mandated
Kuwait	3.14.20	4.4.20	Currently mandated
Kyrgyzstan	3.31.20	4.3.20	Currently mandated
Latvia	3.20.20	4.3.20	Currently mandated
Lebanon	3.15.20	3.10.20	Never mandated

Liberia	4.21.20	4.4.20	Currently mandated
Libya		4.2.20	Currently mandated
Lithuania	3.22.20	3.21.20	Currently mandated
Luxembourg	3.17.20	3.14.20	Mandated in the past
Madagascar	4.11.20	5.17.20	Currently mandated
Malawi	5.25.20	4.7.20	Currently mandated
Malaysia	3.9.20	3.17.20	Currently mandated
Mali	4.12.20	3.29.20	Currently mandated
Malta	3.23.20	4.8.20	Currently mandated
Mauritania	5.19.20	3.30.20	Currently mandated
Mexico	3.18.20	3.19.20	Currently mandated
Moldova	3.23.20	3.18.20	Currently mandated
Mongolia	5.16.20		Currently mandated
Morocco	3.22.20	3.10.20	Currently mandated
Mozambique	5.11.20	5.25.20	Currently mandated
Nepal	5.7.20	5.16.20	Currently mandated
Netherlands	3.6.20	3.6.20	Never mandated
New Zealand	3.22.20	3.29.20	Mandated in the past
Nicaragua	5.19.20	3.27.20	Currently mandated
Niger	4.3.20	3.25.20	Currently mandated
Nigeria	3.29.20	3.23.20	Currently mandated
North Macedonia	3.22.20	3.22.20	Currently mandated
Norway	3.6.20	3.14.20	Currently mandated
Oman	3.26.20	3.31.20	Currently mandated
Pakistan	3.16.20	3.19.20	Currently mandated
Panama	3.19.20	3.11.20	Currently mandated
Paraguay	4.5.20	3.21.20	Currently mandated
Peru	3.17.20	3.20.20	Currently mandated
Philippines	3.14.20	2.2.20	Currently mandated
Poland	3.14.20	3.12.20	Currently mandated
Portugal	3.13.20	3.17.20	Currently mandated
Qatar	3.11.20	3.28.20	Currently mandated
Romania	3.14.20	3.22.20	Currently mandated
Russia	3.17.20	3.19.20	Currently mandated
Rwanda	4.4.20		Currently mandated
Saudi Arabia	3.14.20	3.24.20	Currently mandated
Senegal	3.26.20	4.1.20	Currently mandated
Sierra Leone	4.28.20	4.23.20	Currently mandated
Singapore	2.29.20	3.21.20	Currently mandated

Slovakia	3.18.20	3.18.20	Currently mandated
Slovenia	3.13.20	3.14.20	Currently mandated
South Africa	3.18.20	3.27.20	Currently mandated
South Korea	2.20.20	2.20.20	Currently mandated
Spain	3.2.20	3.3.20	Mandated in the past
Sri Lanka	3.24.20	3.28.20	Currently mandated
Sudan	4.20.20	3.13.20	Currently mandated
Sweden	3.6.20	3.11.20	Mandated in the past
Switzerland	3.5.20	3.5.20	Mandated in the past
Taiwan	3.18.20	2.16.20	Currently mandated
Tajikistan	5.3.20	5.2.20	Currently mandated
Tanzania	4.17.20	3.31.20	Currently mandated
Thailand	3.15.20	3.1.20	Currently mandated
Togo	4.29.20	3.27.20	Currently mandated
Tunisia	3.24.20	3.19.20	Currently mandated
Turkey	3.19.20	3.17.20	Currently mandated
Uganda	5.6.20		Currently mandated
Ukraine	3.25.20	3.13.20	Currently mandated
United Arab Emirates	3.18.20	3.20.20	Currently mandated
United Kingdom	3.5.20	3.6.20	Currently mandated
United States	3.3.20	2.29.20	Never mandated
Uruguay	3.20.20	3.28.20	Currently mandated
Uzbekistan	3.28.20	3.27.20	Currently mandated
Vietnam	3.22.20		Currently mandated
West Bank and Gaza	3.29.20	3.26.20	Currently mandated
Yemen	5.15.20	4.30.20	Currently mandated
Zambia	4.30.20	4.2.20	Currently mandated
Zimbabwe	5.27.20	3.23.20	Currently mandated

 Table S2. Correlation table of all predictor variables.

	1	2	3	4	5	6
1. BCG current vs. not cur	rrent					
2. BCG past vs. never						
3. GDP per capita	-0.450	0.165				
4. Median age	-0.351	-0.065	0.646			
5. Net migration rate	-0.328	0.352	0.627	0.197		
6. Population	0.029	-0.360	-0.059	0.028	-0.024	
7. Population density	0.005	-0.405	0.291	0.122	0.076	0.011

Table S3. Regression table predicting the natural log of cases, using the estimated proportion of cases that are being reported in each country as a weighting factor. Day is mean centered, and BCG policy variables are both contrast-coded. Population is natural log-transformed, and all covariates are standardized. This analysis is based on 77 countries.

	Cases				
Predictor	b	t	р		
Intercept	6.908	43.691	<.001		
Day	0.112	10.726	<.001		
Median age	0.219	1.890	0.067		
GDP per capita	0.098	0.779	0.439		
Population density	0.120	0.425	0.672		
Net migration rate	0.234	1.723	0.090		
Population	0.525	6.908	<.001		
BCG past vs. never	0.153	0.494	0.623		
BCG current vs. not current	-0.431	-2.199	0.031		
Day x median age	0.006	0.946	0.348		
Day x GDP per capita	0.011	1.691	0.096		
Day x population density	0.004	0.224	0.824		
Day x net migration rate	0.008	1.176	0.244		
Day x population	0.035	8.446	<.001		
Day x BCG past vs. never	-0.006	-0.365	0.716		
Day x BCG current vs. not current	-0.030	-2.807	0.006		

Table S4. Regression table predicting the natural log of cases, controlling for the total number of tests in each country. Day is mean centered, and BCG policy variables are both contrast-coded. Population is natural log-transformed, and all covariates are standardized. This analysis is based on 64 countries.

		Cases	
Predictor	b	t	р
Intercept	6.754	175.361	<.001
Day	0.112	8.499	<.001
Median age	0.450	16.629	<.001
GDP per capita	0.022	0.628	0.530
Population density	-0.154	-2.341	0.019
Net migration rate	0.230	6.868	<.001
Population	0.402	15.712	<.001
Total tests	0.182	7.236	<.001
BCG past vs. never	0.334	3.409	0.001
BCG current vs. not current	-0.464	-7.950	<.001
Day x median age	0.005	0.627	0.534
Day x GDP per capita	-0.004	-0.475	0.637
Day x population density	0.002	0.148	0.883
Day x net migration rate	0.012	1.710	0.093
Day x population	0.028	4.684	<.001
Day x total tests	0.012	2.183	0.033
Day x BCG past vs. never	-0.009	-0.384	0.702
Day x BCG current vs. not current	-0.039	-3.017	0.004

Table S5. Regression tables predicting the natural log of (A) cases and (B) deaths, using a 15-day window (instead of a 30-day window, as in Table 1). Day is mean centered, and BCG policy variables are both contrast-coded. Population is natural log-transformed, and all covariates are standardized. This analysis is based on 134 and 135 countries for cases and deaths, respectively.

	A. Cases			B. Deaths		
Predictor	b	t	р	b	t	р
Intercept	7.125	39.257	<.001	2.717	7.577	<.001
Day	0.157	14.422	<.001	0.174	7.730	<.001
Median age	0.343	2.803	0.008	0.252	1.141	0.257
GDP per capita	0.142	1.081	0.282	0.150	0.694	0.489
Population density	-0.153	-2.096	0.038	-0.038	-0.308	0.759
Net migration rate	0.106	0.921	0.359	0.069	0.366	0.715
Population	0.583	7.605	<.001	0.720	5.639	<.001
BCG past vs. never	0.353	0.860	0.392	0.041	0.059	0.953
BCG current vs. not current	-0.716	-3.016	0.003	-1.058	-2.670	0.009
Day x median age	0.023	3.081	0.004	0.022	1.623	0.108
Day x GDP per capita	0.008	0.933	0.353	0.011	0.850	0.397
Day x population density	-0.008	-1.763	0.080	-0.005	-0.694	0.489
Day x net migration rate	0.004	0.560	0.576	0.006	0.536	0.593
Day x population	0.039	8.231	<.001	0.043	5.587	<.001
Day x BCG past vs. never	0.016	0.643	0.521	0.018	0.426	0.671
Day x BCG current vs. not current	-0.052	-3.556	0.001	-0.070	-2.915	0.004

Table S6. Results from t-tests predicting each cultural dimension from BCG status (dummy-coded; 1 = currently mandated, 0 = mandated in the past or never mandated).

Predictor	Ν	t	р	
Individualism	64	-5.127	<.001	***
Power distance	64	5.026	<.001	***

Table S7. Regression table predicting the natural log of (A) cases and (B) deaths from BCG status, controlling for individualism, as well as all covariates in our primary model. Day is mean-centered. All covariates, including individualism, are standardized. This analysis is based on 65 and 64 countries for cases and deaths, respectively.

	A. Cases			B. Deaths		
Predictor	b	t	р	b	t	р
Intercept	7.007	27.018	<.001	2.527	5.015	0.001
Day	0.120	8.514	<.001	0.146	6.333	<.001
Median age	-0.032	-0.190	0.850	0.097	0.323	0.748
GDP per capita	0.382	2.042	0.046	0.394	1.190	0.239
Population density	-0.147	-2.102	0.040	-0.049	-0.395	0.694
Net migration rate	0.096	0.664	0.509	-0.008	-0.033	0.974
Population	0.627	7.400	<.001	0.798	5.210	<.001
BCG past vs. never	-0.103	-0.284	0.777	-0.548	-0.848	0.400
BCG current vs. not current	-0.623	-2.615	0.012	-1.155	-2.744	0.008
Individualism	-0.007	-1.455	0.151	-0.012	-1.400	0.167
Day x median age	-0.004	-0.432	0.668	0.003	0.237	0.814
Day x GDP per capita	0.015	1.568	0.123	0.015	1.189	0.240
Day x population density	-0.000	-0.132	0.896	-0.002	-0.424	0.673
Day x net migration rate	0.005	0.635	0.528	0.007	0.700	0.487
Day x population	0.038	8.695	<.001	0.042	7.079	<.001
Day x BCG past vs. never	-0.012	-0.639	0.525	-0.026	-1.035	0.305
Day x BCG current vs. not current	-0.033	-2.725	0.009	-0.057	-3.487	0.001
Day x individualism	0.000	0.520	0.605	-0.000	-0.076	0.940

Table S8. Regression table predicting the natural log of (A) cases and (B) deaths from BCG status, controlling for power distance, as well as all covariates in our primary model. Day is mean-centered. All covariates, including power distance, are standardized. This analysis is based on 65 and 64 countries for cases and deaths, respectively.

	A. Cases			B. Deaths		
Predictor	b	t	р	b	t	р
Intercept	6.997	28.116	<.001	2.512	5.080	0.001
Day	0.121	8.406	<.001	0.146	6.341	<.001
Median age	-0.043	-0.249	0.804	0.057	0.182	0.856
GDP per capita	0.267	1.495	0.141	0.174	0.544	0.589
Population density	-0.113	-1.643	0.106	0.022	0.179	0.859
Net migration rate	0.142	0.976	0.334	0.078	0.309	0.759
Population	0.607	7.023	<.001	0.772	4.946	<.001
BCG past vs. never	-0.003	-0.008	0.994	-0.399	-0.608	0.545
BCG current vs. not current	-0.508	-2.144	0.037	-0.929	-2.224	0.030
Power distance	0.000	0.051	0.960	-0.002	-0.203	0.840
Day x median age	-0.002	-0.219	0.827	0.003	0.248	0.805
Day x GDP per capita	0.020	2.167	0.035	0.015	1.246	0.218
Day x population density	-0.002	-0.574	0.568	-0.002	-0.437	0.664
Day x net migration rate	0.003	0.426	0.672	0.007	0.717	0.477
Day x population	0.038	8.699	<.001	0.042	7.051	<.001
Day x BCG past vs. never	-0.011	-0.564	0.575	-0.025	-1.003	0.321
Day x BCG current vs. not current	-0.038	-3.215	0.002	-0.057	-3.577	0.001
Day x power distance	0.000	0.878	0.384	0.000	0.095	0.924

Figure S1. Growth curves by country BCG policy in the first 15 days of country-wise outbreaks for (A-B) cases and (C-D) deaths, presented on linear (A & C) and logarithmic (B & D) scales.

