

Statewide Interventions and Coronavirus Disease 2019 Mortality in the United States: An Observational Study

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Background. Social distancing is encouraged to mitigate viral spreading during outbreaks. However, the association between distancing and patient-centered outcomes in coronavirus disease 2019 (COVID-19) has not been demonstrated. In the United States, social distancing orders are implemented at the state level with variable timing of onset. Emergency declarations and school closures were 2 early statewide interventions.

Methods. To determine whether later distancing interventions were associated with higher mortality, we performed a state-level analysis in 55 146 COVID-19 nonsurvivors. We tested the association between timing of emergency declarations and school closures with 28-day mortality using multivariable negative binomial regression. Day 1 for each state was set to when they recorded ≥ 10 deaths. We performed sensitivity analyses to test model assumptions.

Results. At time of analysis, 37 of 50 states had ≥ 10 deaths and 28 follow-up days. Both later emergency declaration (adjusted mortality rate ratio [aMRR] 1.05 per day delay; 95% confidence interval [CI], 1.00–1.09; $P = .040$) and later school closure (aMRR 1.05; 95% CI, 1.01–1.09; $P = .008$) were associated with more deaths. When assessing all 50 states and setting day 1 to the day a state recorded its first death, delays in declaring an emergency (aMRR 1.05; 95% CI, 1.01–1.09; $P = .020$) or closing schools (aMRR 1.06; 95% CI, 1.03–1.09; $P < .001$) were associated with more deaths. Results were unchanged when excluding New York and New Jersey.

Conclusions. Later statewide emergency declarations and school closure were associated with higher Covid-19 mortality. Each day of delay increased mortality risk 5 to 6%.

Keywords. pandemic; SARS-CoV-2; coronavirus; social distancing; nonpharmaceutical interventions.

Nonpharmaceutical interventions, such as social distancing and issuance of emergency public health warnings seeking to modify activity, are recommended to mitigate the spread of viral epidemics and pandemics [1–7], including the current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated coronavirus disease 2019 (COVID-19) disease. Historical analysis of the 1918–1919 influenza pandemic during the second wave of infections that examined 43 cities in the United States demonstrated an association between earlier school closures and bans on public gatherings with lower mortality [5]. A recent modeling study supported multilayered nonpharmaceutical interventions, including quarantine, school closures, and workplace distancing, for COVID-19 [8]. At this stage in the pandemic, the efficacy

of social distancing measures on patient-centered outcomes specifically for SARS-CoV-2 and COVID-19 have not been demonstrated.

In the United States, social distancing measures have been implemented primarily at the local and state levels, with evidence of mistrust for their efficacy or necessity. As these interventions are fundamentally political and decided upon by elected officials, real-time evidence of efficacy would be helpful for informing policy.

If social distancing measures were causal for improved outcomes, we reasoned there would be a dose-response, with states implementing distancing measures later experiencing worse outcomes. This rationale is premised on the association retrospectively seen between timing of social distancing measures and mortality during the 1918–1919 influenza pandemic [5]. Therefore, we assessed the association between the timing of emergency declarations and school closures, 2 specific statewide distancing measures, and subsequent COVID-19 mortality. We hypothesized that states with delayed emergency declarations and school closures would experience higher COVID-19 mortality.

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METHODS

Study Design

This was an ecologic study of publicly available data. The protocol was reviewed by the Children's Hospital of Philadelphia institutional review board and deemed exempt from further review or oversight (institutional review board 20-017546). COVID-19 cases and deaths were obtained from the Johns Hopkins Center for Systems Science and Engineering Coronavirus Resource Center [9], a web-based tracker that records cases and mortality in the United States starting January 21, 2020. State-level demographic characteristics for confounder selection were extracted from the 2019 American Community Survey from the Census Bureau (www.census.gov). Timing of emergency declarations and statewide school closures were determined based on official press releases by states and governors.

Population

This was a decedent-only analysis of attributed COVID-19 deaths in the Hopkins Coronavirus Resource Center between January 21, 2020, and April 29, 2020 ($n = 55\,146$ nonsurvivors). We chose to analyze decedents given the relatively low and variable rates of testing between states [10, 11], making number of cases unreliable. We reasoned that eventual COVID-19 nonsurvivors were more likely to have experienced severe infection and have undergone testing, thereby making this the most accurate of available metrics to track pandemic spread.

Definitions

Our coprimary exposures were the number of days between a state experiencing ≥ 10 COVID-19 deaths (standardized across states as day 1) and implementation of a statewide emergency declaration (day of emergency declaration minus day 1), and separately school (kindergarten through grade 12) closure (day of school closure minus day 1). We chose emergency declarations and school closures as the primary exposures because they were unambiguous interventions. Other distancing measures, such as bans on public gatherings, closure of nonessential businesses, and shelter-in-place orders were variably implemented between states, using divergent definitions, thresholds for maximum group sizes, and carve out exemptions.

The primary outcome was COVID-19 mortality on day 28. We chose the timepoint of 28 days because we reasoned that, if a statewide emergency declarations and school closures impacted mortality, then several weeks would be required to allow for a reduction in transmission, hospitalizations, and mortality.

Potential state-level confounders considered a priori were 2019 population, population density, percent of the population < 18 years of age, percent ≥ 65 years of age, percent Black, percent Hispanic, and percent below census-designated poverty threshold. We included the country-level confounder of census-designated division, which divides the country into nine geographic regions.

Statistical Analysis

All analyses were performed in Stata SE/14.2 (StataCorp, College Station, TX, USA) on April 30, 2020 (N.Y. and M.H. separately). Summary data are presented as mean \pm standard deviation (SD) or as proportions, and analyzed for monotonic trends using a nonparametric test of trend across tertiles of states ordered based on timing of emergency declarations or school closings. For our primary analyses, we used multivariable negative binomial regression to test the association between earlier emergency declaration and (separately) school closing and number of deaths on day 28 (Supplementary Methods and Supplementary Figure 1). By setting day 1 as the day when a state had ≥ 10 COVID-19 deaths, we attempted to scale every state to a similar point in the pandemic based on a comparable number of deaths. The analysis was adjusted for the number of deaths on day 1 (as recommended) [12] and aforementioned confounders. We report mortality rate ratios (MRR) and 95% confidence intervals (CIs).

To test the dependence of our results on our assumptions, we performed a secondary analysis where we set day 1 to the day when a state recorded its first COVID-19 death. Exposures were calculated as before (day of emergency declaration or of school closures minus day 1), whereas the primary outcome was death on April 29, 2020. The negative binomial model allows for an offset to allow states to have different lengths of follow-up time. These analyses were adjusted for the same confounders as in the primary analyses. Second, because deaths per million is a common method to compare localities, we provide an analysis testing the association between deaths per million at the state level after multivariable adjustment relative to timing of emergency declarations or statewide school closures. We set day 1 to equal when a state experienced at least 1 death per million, and followed deaths until April 29, 2020, allowing different follow-up times between states. Finally, to account for the potential impact from the excess of deaths in the New York City metropolitan area, all models above were rerun excluding New York and New Jersey.

Role of the Funding Source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. The corresponding author had full access to the data and had final responsibility for the decision to submit for publication.

RESULTS

At the time of analysis on April 29, 2020, 37 of 50 states had experienced ≥ 10 deaths by April 2, 2020, thus ensuring availability of 28-day mortality. These 37 states composed the cohort for our primary analyses (Tables 1 and 2). Timing of emergency declarations and school closing were highly correlated ($r = 0.84$, $P < .001$). States declared an emergency at a median

Table 1. Characteristics of States Stratified by Tertile of When, Relative to Experiencing at Least 10 COVID-19 Deaths, Statewide Emergency Declarations Were Made

	Earliest (n = 13)	Middle (n = 15)	Late (n = 9)	PValue for Trend
States	AL, AR, DE, IN, KS, KY, MD, MN, NC, OR, PA, RI, TN	AZ, CT, IA, IL, MA, MI, MS, MO, NV, OH, OK, SC, VA, VT, WI	CA, CO, FL, GA, LA, NJ, NY, TX, WA	...
Governor party				.945
Democratic	8 (62)	6 (40)	6 (67)	
Republican	5 (38)	9 (60)	3 (33)	
Population	5 391 506 ± 3 388 379	6 101 328 ± 3 453 891	16 329 049 ± 11 970 560	.006
Population density (per square mile)	214 ± 197	183 ± 201	275 ± 299	.662
Demographics (%)				
< 18 y	22.1 ± 1.3	22 ± 1.5	22.5 ± 1.7	.796
≥ 65 y	16.7 ± 1.0	16.8 ± 1.0	15.4 ± 2.2	.032
Black	14.6 ± 8.9	13.0 ± 9.4	15.9 ± 10.7	.913
Hispanic	8.7 ± 3.6	11.0 ± 9.1	21.6 ± 12.0	.015
Poverty	13.4 ± 2.6	13.0 ± 2.6	13.0 ± 2.9	.758

of -14 (interquartile range [IQR] -18, -13) days relative to experiencing ≥ 10 COVID-19 deaths, with all 37 states declaring an emergency before recording at least 10 deaths. States implemented school closures at a median of -9 (IQR -11, -4) days relative to experiencing ≥ 10 COVID-19 deaths, with 32 of 37 states (86%) closing schools before experiencing at least 10 deaths. States declaring emergencies and closing schools earlier had a lower population, but were otherwise comparable to states closing schools later.

Association Between Emergency Declaration and Mortality

After adjusting for confounders, later emergency declaration was associated with higher mortality (Figure 1A). Assigning the day that a particular state had ≥ 10 COVID-19 deaths as day 1, every day a state delayed declaring an emergency increased 28-day mortality by 5% (MRR 1.05; 95% CI, 1.00–1.09). When assigning day 1 as the day a state experienced its first COVID-19 death and using data from all 50 states until April 29, 2020 (Figure 1B), mortality increased by 5% (MRR 1.05; 95%

CI, 1.01–1.09) for every day of delay. Results were consistent when excluding New York and New Jersey from both analyses (Figures 1C and 1D), with later declaration of emergency associated with higher mortality risk.

Association Between School Closings and Mortality

Later implementation of a statewide school closure was similarly associated with higher mortality (Figure 2A). Assigning the day that a particular state had ≥ 10 COVID-19 deaths as day 1, for every day a state delayed implementing a school closure, 28-day mortality risk increased by 5% (MRR 1.05; 95% CI, 1.01–1.09). When assigning day 1 as the day that a state experienced its first COVID-19 death and using all available data from all 50 states until April 29, 2020 (Figure 2B), for every day a state delayed implementing a school closure, final mortality increased by 6% (MRR 1.06; 95% CI, 1.03–1.09). Results were consistent when excluding New York and New Jersey from both analyses (Figures 2C and 2D), with later implementation of school closures associated with higher mortality risk.

Table 2. Characteristics of States Stratified by Tertile of When, Relative to Experiencing at Least 10 COVID-19 Deaths, Statewide School Closure was Implemented

	Earliest (n = 14)	Middle (n = 11)	Late (n = 12)	PValue for Trend
States	AL, AZ, AR, DE, KS, KY, MD, MN, NC, OK, RI, SC, TN, VA	CT, IL, MA, MI, MS, NV, OH, OR, PA, VT, WI	CA, CO, FL, GA, IN, IA, LA, MO, NJ, NY, TX, WA	...
Governor party				.975
Democratic	7 (50)	7 (64)	6 (50)	
Republican	7 (50)	4 (36)	6 (50)	
Population	5 089 825 ± 2 688 607	6 757 020 ± 4 350 053	13 582 179 ± 11 383 133	.012
Population density (per square mile)	197 ± 192	222 ± 228	234 ± 268	.730
Demographics (%)				
< 18 y	22.4 ± 1.3	21.4 ± 1.5	22.7 ± 1.5	.792
≥ 65 y	16.6 ± 1.0	17.0 ± 1.1	15.7 ± 2.0	.112
Black	16.1 ± 9.0	12.1 ± 9.6	14.0 ± 9.9	.457
Hispanic	10.2 ± 7.0	10.7 ± 8.1	17.7 ± 12.5	.129
Poverty	13.7 ± 2.7	12.7 ± 2.7	12.9 ± 2.6	.388

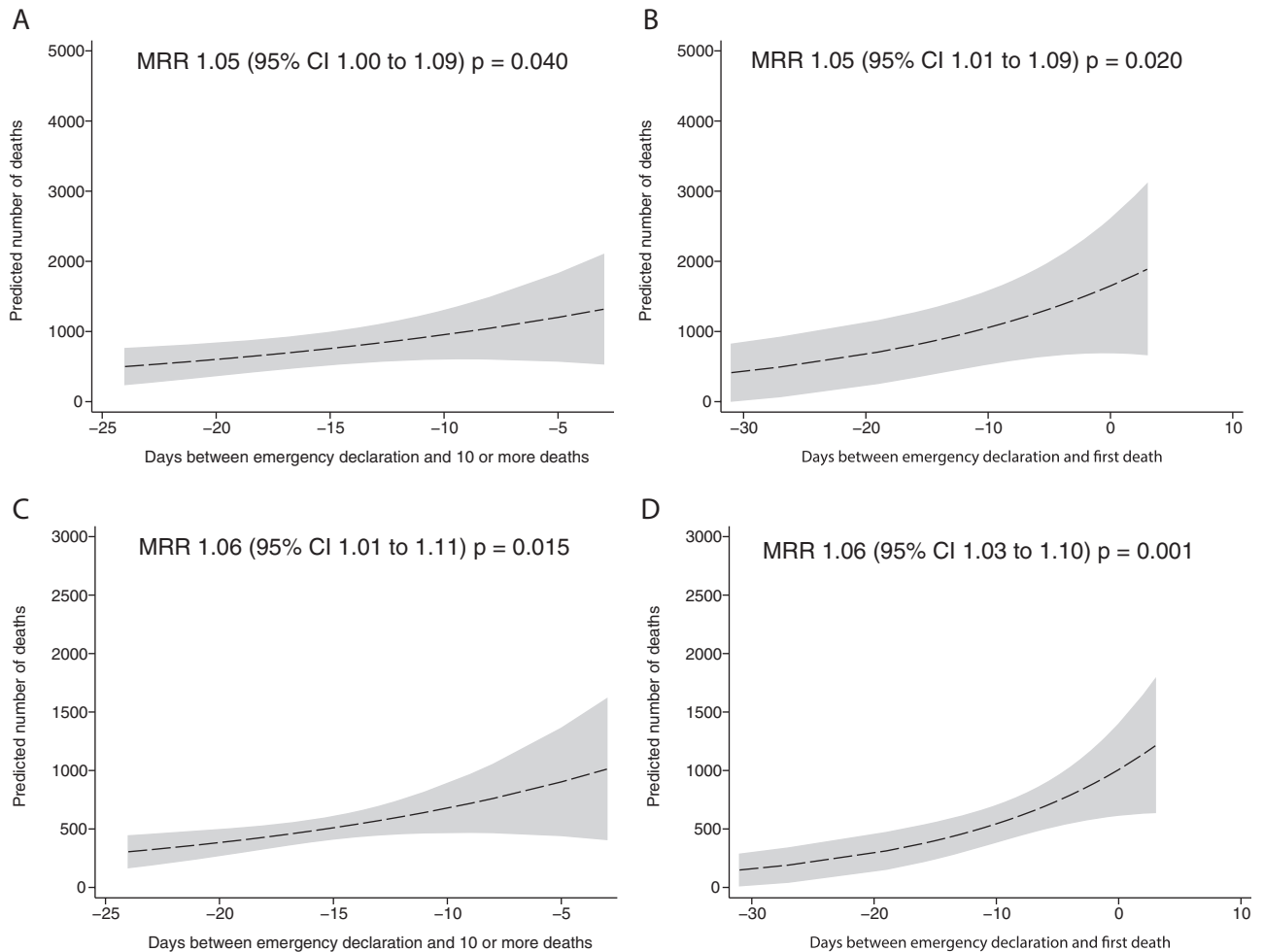


Figure 1. Predicted number of deaths at the state level after multivariable adjustment relative to timing of statewide emergency declaration. (A) Predicted number of deaths 28 days after a state experienced ≥ 10 deaths ($n = 37$ states). (B) Predicted number of deaths on April 29, 2020, with all states included and day 1 set to the day a state experienced its first death and accounting for differential follow-up times between states ($n = 50$ states). (C) Predicted number of deaths 28 days after a state experienced ≥ 10 deaths ($n = 35$ states, excluding New York and New Jersey). (D) Predicted number of deaths on April 29, 2020, with all states included and day 1 set to the day a state experienced its first death and accounting for differential follow-up times between states ($n = 48$ states, excluding New York and New Jersey). All mortality rate ratios (MRRs) are adjusted for confounders (see Methods for details).

Per Capita Analysis

When analyzing deaths per million as the primary outcome (Supplementary Figure 2), later implementation of emergency declarations was associated with higher mortality (MRR 1.03; 95% CI, 1.00–1.07), although this did not reach a traditional threshold for statistical significance ($P = .077$). Later implementation of statewide school closure was similarly associated with higher mortality (MRR 1.04; 95% CI, 1.01–1.07), which attained statistical significance ($P = .014$). Results were similar when excluding New York and New Jersey (Supplementary Figure 2B and 2D).

Regional Analysis

Because different regions of the United States experienced local epidemics, we assessed the cumulative death curves for each census-designated division (Supplementary Figure 3). Curves grew in all divisions, without evidence for plateauing. Census

divisions 2 and 3 were among the latest of the 9 divisions to implement statewide emergency declarations, whereas divisions 4 and 8, which showed the slowest increase in deaths, were the 2 earliest.

DISCUSSION

States implementing emergency declarations or school closures later in the course of the pandemic experienced higher COVID-19 mortality, with each day of delay increasing mortality risk 5%–6%. This effect size was attenuated when measured as deaths per million, but still consistent with lower mortality with earlier statewide declarations. To our knowledge, this is the first demonstration of an association between statewide social distancing orders and mortality during COVID-19. Our results support early social distancing as a nonpharmaceutical intervention for reducing mortality.

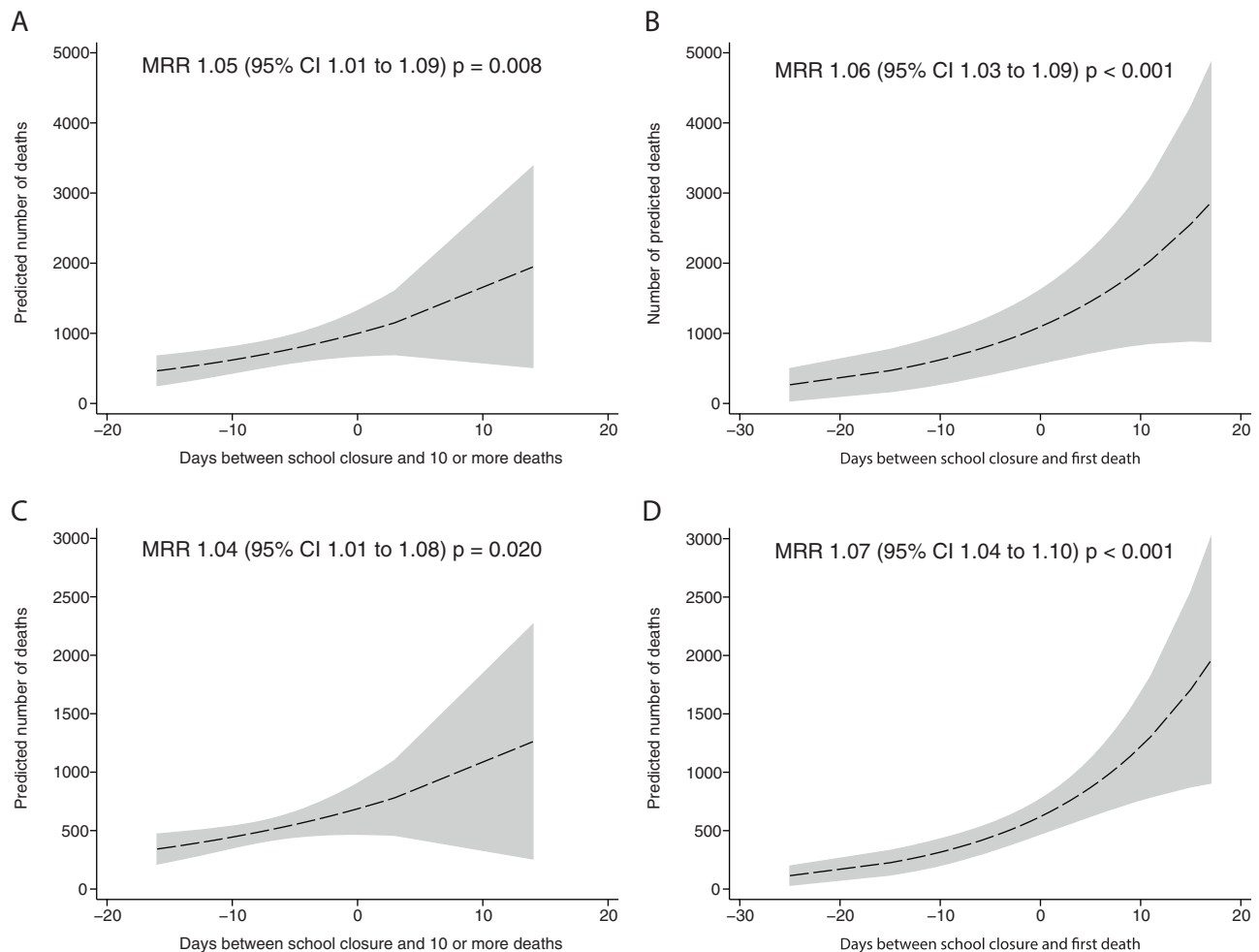


Figure 2. Predicted number of deaths at the state level after multivariable adjustment relative to timing of statewide school closures. (A) Predicted number of deaths 28 days after a state experienced ≥ 10 deaths ($n = 37$ states). (B) Predicted number of deaths on April 29, 2020, with all states included and day 1 set to the day a state experienced its first death and accounting for differential follow-up times between states ($n = 50$ states). (C) Predicted number of deaths 28 days after a state experienced ≥ 10 deaths ($n = 35$ states, excluding New York and New Jersey). (D) Predicted number of deaths on April 29, 2020, with all states included and day 1 set to the day a state experienced its first death and accounting for differential follow-up times between states ($n = 48$ states, excluding New York and New Jersey). All mortality rate ratios (MRRs) are adjusted for confounders (see Methods for details).

Our study design and results do not directly implicate timing of either emergency declarations or school closings specifically as causal for reduced mortality, although causality is plausible. Emergency declarations, for example, have been shown to reduce social contacts. In a time-series analysis conducted by the National Bureau of Economic Research during the early weeks of COVID-19, state-level emergency declarations had the largest reduction in within-state mixing [13]. Thus, early state-level social distancing measures, including declaration of an emergency, may have contributed to reducing the spread of COVID-19, and by extension lower mortality.

The causality of timing of school closures on COVID-19 mortality is even less certain. Although SARS-CoV-2 appears not to cause as severe a disease in children [14, 15], children are potential asymptomatic carriers. In an analysis of laboratory-confirmed cases in the United States up to April 2, 2020, 27% of

patients < 18 years of age were completely asymptomatic, compared with 7% of patients 18–64 years of age [16]. Modeling of influenza and a review of nonpharmaceutical interventions for 2003 SARS suggested that school closings are effective at reducing transmission between children, but only modestly affected transmission in the larger population, particularly if children were not disproportionately affected by the virus [17, 18]. However, school closings also prompt additional social distancing measures as caretakers reduce their workplace presence and travel, causing indirect social distancing and improving overall population transmission rates [19–23]. In the aforementioned National Bureau of Economic Research time-series analysis, school closing orders had negligible impact on within-state mixing, but reduced interstate travel by 10% [13]. Thus, school closings may directly reduce SARS-CoV-2 transmission rates by reducing contact among asymptomatic

pediatric carriers, and indirectly via changing contact patterns between adults. Last, because this study is occurring early in COVID-19, it is possible that the efficacy of both emergency declarations and school closings are not in reducing total eventual COVID-19 mortality, but in reducing peak infection rates and improving hospital surge capacity [24].

Alternatively, and equally plausibly, both emergency declarations and the timing of school closures may be a proxy for the degree to which a state began to officially and unofficially implement significant social distancing [13]. At the time of analysis, all states had declared a statewide emergency, with 43 of 50 declaring before their first recorded COVID-19 death. Similarly, all had closed schools, and 41 of 50 states had a shelter-in-place order. In all but 2 cases, school closures preceded more restrictive shelter-in-place orders, with these orders occurring simultaneously for 2 states. Emergency declarations and school closures were among the first social distancing measures implemented in the United States. Thus, our results may reflect how quickly states responded to news about the size and severity of the spreading pandemic, with emergency declarations and school closures being among the first official nonpharmaceutical interventions, rather than protective effects specific to either intervention itself.

The majority of states implemented statewide school closures, and all states declared emergencies, before experiencing 10 COVID-19 deaths. Hence, the time to declaring an emergency or implementing school closure relative to how we defined day 1 could have either a positive or a negative value. States implementing earlier were likely responding to the rapid increase in cases being reported in the early hotspot states. This is consistent with data suggesting that early intervention in an exponentially growing pandemic is more efficacious than later interventions [5]. Our choice of death as an endpoint was due to concerns about inadequate and imprecise testing, thereby making counts of cases imprecise and highly variable between states. However, death is a lagging indicator, and increased time between these early interventions and eventual nonsurvival can result in imprecise effect estimates. Reassuringly, our conclusions remained unchanged in all analyses performed.

States that implemented emergency declarations and school closings later were more populous, and included the early hotspots of Washington, California, and New York. It is likely that COVID-19 had already attained a foothold in these states, and that subsequent states had the advantage of following their lead after witnessing the exponential increase in cases. This could lead to confounding in our analyses because there were more deaths in these more populous hotspots. We attempted to control for this in three ways. First, we adjusted for state population, population density, and census-designated geographic division. Next, we designated day 1 to start at a fixed number of deaths to analyze states at the same point in the pandemic. Finally, given the 4-fold higher mortality in the New York City

metropolitan area, we performed analyses excluding New York and New Jersey. Although our analysis using deaths per capita as an outcome, rather than deaths, provided an attenuated effect size, the direction of the effect was still in favor of earlier nonpharmaceutical intervention orders.

Our study has limitations. Both of our exposures were measured at the state level, whereas local school districts also closed schools of their own accord before state orders. However, this was estimated to only affect ~16% of the population [13]. Death rates were based on publicly available data derived from inconsistent testing using assays with imperfect test characteristics and uneven state-level reporting; thus, both exposure and outcome risk being misclassified. When reliable testing and excess mortality data are available, an analysis using those data may yield more precise estimates of the efficacy of early statewide interventions on COVID-19 mortality. Additionally, we restricted analysis to the early weeks of COVID-19 because of concerns regarding accuracy of mortality data after May 1, 2020, as COVID-19 and social distancing continued to be politicized in the United States. Indeed, multiple states started reopening in the first weeks of May, and in some cases changed the method and timing of publicly reporting cases and deaths. Because of data limitations, we were unable to adjust for potentially important confounders such as outbreaks in long-term care facilities, which may have both accelerated the spread of SARS-CoV-2 and served as an impetus for physical distancing policies. State-level variation in access to healthcare and availability of hospital and intensive care unit resources were not included, which could also bias the results. Our data do not explore the association between duration of school closing orders and outcomes. However, the lesson of the 1918–1919 influenza pandemic is instructive: among 43 cities investigated, no city experienced a second peak of infections while the first set of nonpharmaceutical interventions were in effect, whereas in cities that lifted initial restrictions, death rates increased [5]. Finally, ecologic studies of group-level interventions cannot apply to individuals, and we have no metrics of either state- or individual-level adherence to social distancing in this study. However, our study satisfies several criteria for causality between timing of early interventions and mortality, including mechanistic plausibility, prior knowledge, temporal relationship, a dose-dependent effect (earlier vs later orders), and strength and consistency of the association. These results also confirm the utility and necessity of early nonpharmaceutical intervention to reduce mortality in COVID-19, and may serve to increase acceptance of social distancing measures by the lay public and by policymakers.

CONCLUSION

We provide evidence of an association between earlier statewide nonpharmaceutical interventions of social distancing and

lower mortality in the early weeks of COVID-19. Specifically, each day of delay in a state declaring an emergency or closing schools increased mortality risk by 5%–6%.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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