RESEARCH ARTICLE

Effect of mortality from COVID-19 on inpatient outcomes

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Abstract
When hospitals first encountered coronavirus disease 2019 (COVID-19), there was a
dearth of therapeutic options and nearly 1 in 3 patients died from the disease. By the
summer of 2020, as deaths from the disease declined nationally, multiple single-
center studies began to report declining mortality of patients with COVID-19. To
evaluate the effect of COVID-19 on hospital-based mortality, we searched the
Vizient Clinical Data Base for outcomes data from approximately 600 participating
hospitals, including 130 academic medical centers, from January 2017 through
December 2020. More than 32 million hospital admissions were included in the
analysis. After an initial spike, mortality from COVID-19 declined in all regions of the
country to under 10% by June 2020 and remained constant for the remainder of the
year. Despite this, inpatient, all-cause mortality has increased since the beginning of
the pandemic, even those without respiratory failure. Inpatient mortality has parti-
cularly increased in elderly patients and in those requiring intubation for respiratory
failure. Since June 2020, COVID-19 kills one in every 10 patients admitted to the
hospital with this diagnosis. The addition of this new disease has raised overall
hospital mortality especially those who require intubation for respiratory failure.

KEYWORDS
COVID-19, hospital, mortality, SARS-CoV-2, United States

1 | INTRODUCTION

On New Year's Eve 2019, the Chinese government announced a
cluster of pneumonia-like illnesses in the City of Wuhan. Over the
following year, coronavirus disease 2019 (COVID-19) became the
third leading cause of death in the United States in 2020 and was
responsible for lowering the average life expectancy of Americans to
an extent not seen since World War II.[1] When US hospitals first
encountered COVID-19, in March and April of 2020, clinicians were
confronted with a disease that killed one out of every three patients
admitted to the hospital, primarily from septic organ failure, pneu-
monia, respiratory insufficiency, and right ventricular heart failure.[2,3]
Mortality was highest among the elderly and those with comorbid
conditions, especially metabolic and cardiovascular diseases.[4] Non-
respiratory complications further drove mortality with patients who

developed kidney injury, myocarditis, and thromboembolism having
significantly worse outcomes.[5]

Within a few months, however, the mortality of COVID-19 be-
gan to fall. In England, utilizing data from a nationalized electronic
medical records system, it was reported that the 30-day unadjusted
mortality for patients with COVID-19 went from 28.4% in late March
to 7.3% in mid-June.[6] In the United States, multiple single-center
studies have also reported that the mortality of COVID-19 was de-
clining, specifically in the intensive care unit (ICU) setting and for
patients who were mechanically ventilated.[2,7,8] On a national level
though, there has been little analysis of the inpatient outcomes of
COVID-19 in the United States. More broadly, there is a dearth of
knowledge about how the changing outcomes of COVID-19, as a
new disease encountered in hospitals, have changed inpatient out-
comes overall.

Utilizing data compiled from over 600 hospitals across the United States, we evaluate temporal shifts in the number of cases, deaths, and mortality of COVID-19. We then put this new disease in the context of hospital outcomes over the past 4 years. By exploring this data longitudinally, we sought to gain a greater understanding of the changing outcomes of COVID-19 and how this new disease has changed inpatient hospital outcomes nationally.

2 | METHODS

We searched for mortality, diagnostic, and age information regarding all admission to hospitals participating in the Vizient Clinical Data Base (CDB) from January 2017 through December 2020. Vizient is a health care performance improvement company that manages a database for retrospective performance improvement and research purposes compiled from member health systems, academic medical centers, and community hospitals geographically dispersed throughout the United States.[9] This database currently consists of outcomes data from all admissions at over 600 hospitals, which include 130 participating academic medical centers, across all geographical regions in the United States. General database searches were conducted for observed mortality for all inpatient admissions reported by the participating hospitals. Data were analyzed as percentages and rates to avoid variation from increased participation in the CBD database over the 4-year study period. Subset searches focused on patients who did or did not have a discharge diagnosis of acute respiratory failure (ICD10 codes J960, J9600, and J9601) or COVID-19 (U071), with or without intubation (ICD10 code 0BH17EZ). Both principal and secondary diagnoses were included in the search. Respiratory failure was chosen given the near-ubiquity of this pathology in COVID-19-related deaths and hospitalizations.[3,10,11] Mortality data from affiliated hospitals and their patients were also analyzed by geographic regions: Mid-Atlantic (DE, DC, MD, NJ, NY, PA, VA, WV), Mid-Continent (CO, KS, NE, NM, ND, OK, SD, TX, WY), Midwest (IL, IN, IA, MI, MN, MO, OH, WI), New England (CT, MA, ME, NH, RI, VT), Southeast (AL, AR, FL, GA, KY, LA, MS, NC, SC, TN), and West (AK, AZ, CA, HI, ID, MT, NV, OR, UT, WA).

To analyze these trends, we plotted data using control charts. We looked at both mortality, as a percent, and deaths per 1000 discharges for all discharges, discharges with acute respiratory failure (both intubated and nonintubated), and discharges without acute respiratory failure (to establish a baseline for non-COVID-19 related outcomes) using p Laney charts and u Laney charts, respectively. The data were subgrouped by month, beginning January 2017, and analyzed using QI Macros® Version 2019.01.[12] P charts were selected for this classification data, and the p' or Laney charts were used to address overdispersion seen in control charts with large denominators.[13] Control chart limits were calculated separately for the pre-COVID period of January 2017 to February 2020 and the COVID period of March 2020 to December 2020. The IHI Healthcare rules were used to determine special cause variations. Similarly, p' Laney charts were used to analyze data for mortality in the different age categories. Microsoft Excel, XL STAT (Addinsoft USA) was used for Pearson correlations and Student's T tests.

Per 45 Code of Federal Regulations Part 46, this study does not constitute human subjects research as there was no intervention or interaction with patients and no information was individually identifiable as no patient records were accessed.

3 | RESULTS

3.1 | COVID-19 cases and mortality

To understand the impact of COVID-19 on hospital outcomes, we first wanted to investigate how the outcomes from the disease itself had changed over time. The COVID-19 ICD10 diagnostic code began to be captured in patients admitted in March of 2020 (the effective date for the code was officially April 1, 2020). From March through December of 2020, the total number of COVID-19 cases included in this analysis was 410,231 and included 48,179 deaths. There were 6,266,097 admissions with diagnoses other than COVID-19 over this same period and 125,773 deaths in this population.

During March and April, the first 2 months in which this COVID-19 ICD10 code was captured, the number of cases and deaths both sharply rose (Figure 1A). There was a large, concurrent decrease in the total number of patients who were not diagnosed with COVID-19, dropping over 200,000 discharges between February and April (Figure 1B). During these months, mortality from COVID-19 was also the highest it would be during the study period, peaking at 22% in March and 18% in April (Figure 1A). Mortality for patients not diagnosed with COVID-19 also rose slightly during this period, corresponding to the decrease in the total number of patients (Figure 1B).

Following this initial peak, the number of cases and deaths dropped to a nadir low in the summer months. This was accompanied by a drop in inpatient mortality for patients diagnosed with COVID-19, dropping to below 10% mortality in June. Both cases and deaths began rising again in October, November, and December but the mortality remained at around 10% despite an apparent worsening of the pandemic. Interestingly, the percentage of patients with COVID-19 intubated also decreased in a similar fashion. In March, 27% of COVID-19 cases were intubated. This fell to 8% of cases by June and remained low through the winter surge, decreasing to only 4% of discharges in December (Figure S1).

We next looked at COVID-19 inpatient outcomes based on the region of the country. The number of COVID-19 cases and deaths varied widely across the United States. Initial peaks in COVID-19 cases occurred in April for New England, Mid-Atlantic, and the Midwest. In contrast, the initial peak of COVID-19 cases for the Southeast, Mid-Continent, and West occurred in July (Figure S2). Despite this temporal difference in peak cases, the inpatient mortality for COVID-19 followed the same trend across the country. In all regions, mortality dropped below 10% in June and remained within 2% of this for the remainder of the year. Using June as the inflection point, there was a significant difference ($t = 6.45$; $p < 10^{-5}$) in mortality before June (average 15.3% ± 4%) as compared to June and after (average 9.1% ± 1.7%).
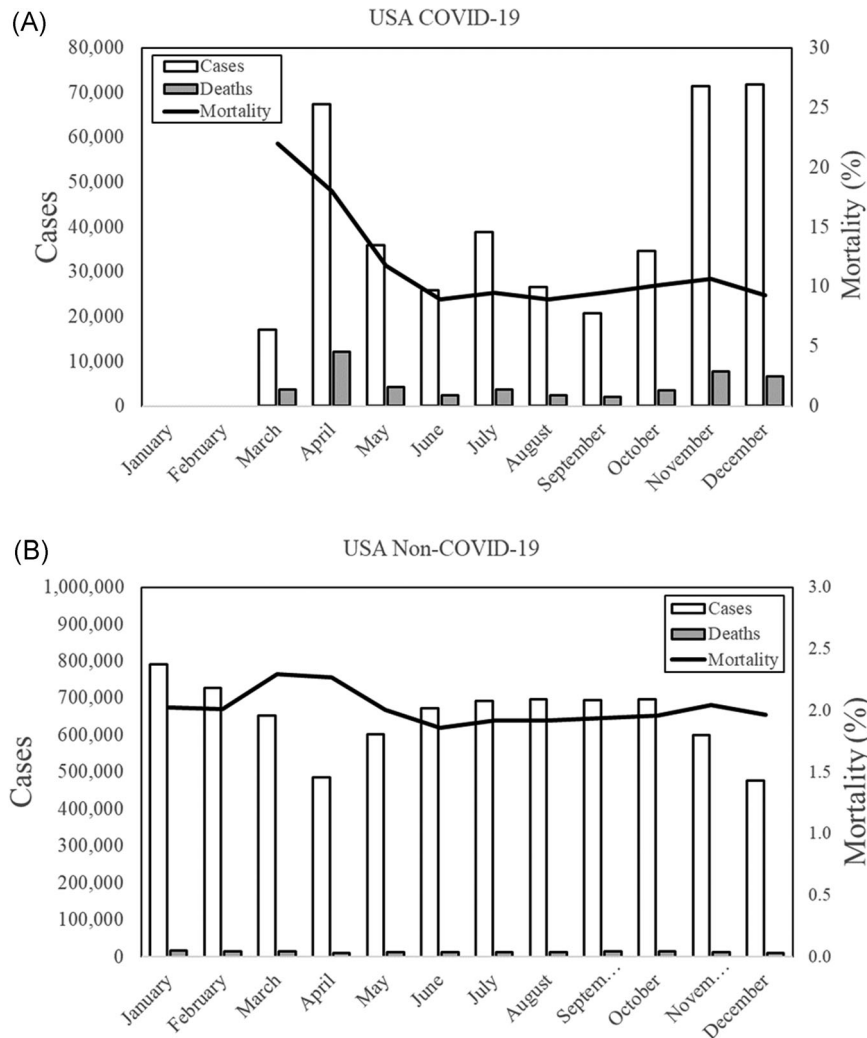
(A)

(B)

Regional surges, as measured by the percentage of a region's total COVID-19 cases (between March and December 2020) encountered at CBD hospitals in a given month, did not correlate with inpatient mortality ($r = 0.19$, $p = 0.14$). On a regional level, having "experience" with COVID-19 also did not seem to have an impact on inpatient mortality. Hospitals in all regions except for New England and the Mid-Atlantic had experienced between 23% and 26% of the total COVID-19 cases captured in this data set when mortality dropped below 10% in June (Figure S3). In contrast, mortality in CDB hospitals in New England and the Mid-Atlantic dropped below 10% after having experienced 55% of their total cases. In sum, differences in the dynamics of the pandemic across CDB hospitals by region did not appear to influence the lethality of COVID-19.

3.2 | All-cause mortality

Next, we explored how the addition of COVID-19 affected overall inpatient mortality. We expanded our analysis to include all discharges and outcomes available in the Vizient Clinical Data Base between January 2017 through December 2020. The analysis encompassed 33,836,429 hospital discharges and 685,996 hospital deaths (average of 704,926 discharges and 14,292 deaths per month).

Utilizing a p' Laney control chart, there was a mean monthly mortality of 1.9% from January 2017 until February 2020 (prepandemic) with special cause variation from December 2017 to May 2018 and from December 2018 to July 2019 (these time periods display a decreasing trend of 6 or more data points). Special cause variation refers to trends that are outside what would normally be expected in a given system. Between March and December of 2020 (during the pandemic), after inpatient outcomes began capturing the diagnosis of COVID-19, the mean monthly mortality increased to 2.7%, with special cause variation seen from March to September 2020 (Figure 2). A similar pattern can be seen when deaths per 1000 admissions are plotted on a u' Laney control chart (Figure S4). The mean before March 2020 was 19.2 per thousand with similar special cause variation from December 2017 to May 2018 and again from December 2018 to July 2019. Inpatient deaths from March 2020 onward increased to 27.1 per thousand. In both mortality and death per 1000 admissions, there was special cause variation in April 2020 when deaths and mortality exceeded the upper control limit.
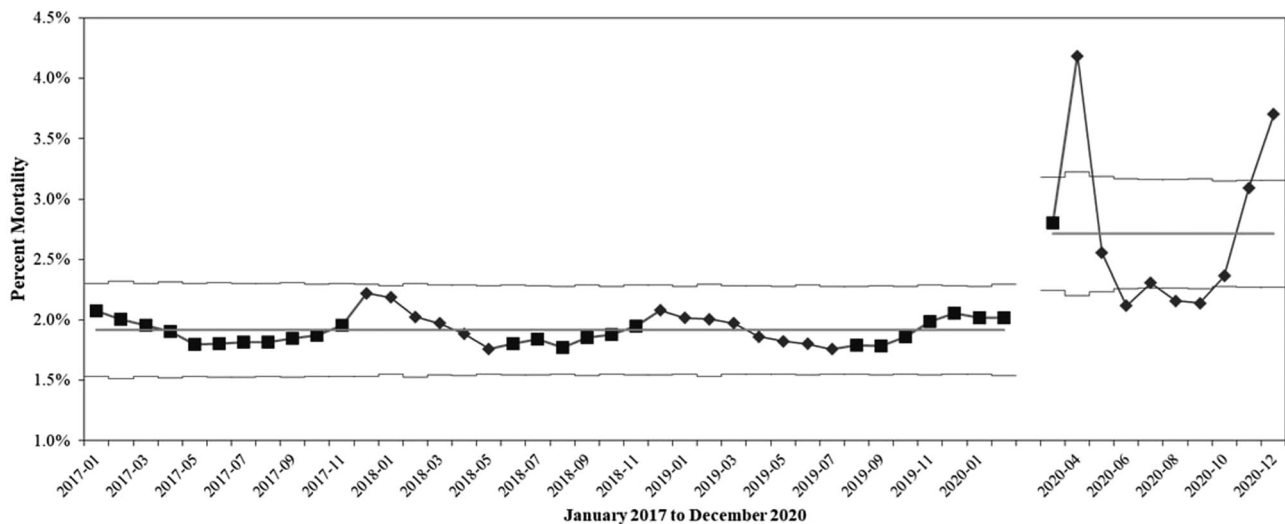
FIGURE 2 Inpatient mortality has increased since the beginning of the COVID-19 pandemic in March of 2020. The top and bottom lines represent the upper and lower control limits, respectively. Bold line in the center represents the mean. Diamond markers represent special cause variation, Square markers represent common cause variation. A p' Laney chart demonstrated an increase in mortality. Mean mortality increases from 1.9% to 2.7% after March 2020. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved

3.3 | Respiratory failure and intubation as drivers of mortality

The strain on the healthcare system during a pandemic and changes in human behavior both have the potential to change inpatient mortality by changing the patient population and level of care they seek out and receive. These changes can lead to increases in mortality from other diseases, as seen with acute cardiovascular mortality in England and Wales.[14] To see if this was true in our data, we next investigated whether the increased all-cause mortality was secondary to an increase in the mortality from respiratory failure, as seen in nearly all COVID-19 hospital admissions, or if the increased mortality was spread across other diseases as well.[3]

Between January 2017 and December 2020, there was a steady increase in the percentage of hospital admissions in which the ICD10 code of acute respiratory failure was captured (Figure S5). Over this same period, control charts of hospital mortality and death rate (per 1000 admissions) display special cause variation for the periods of January 2017 to April 2019. Interestingly, the mortality and death rate do not increase from the prepandemic mean after March of 2020. There is special cause variation in April 2020 on both charts (Figures 3A and S6).

We next subdivided the acute respiratory failure data into those who required intubation and those who did not. Similar to patients with respiratory failure overall, those who did not require intubation also do not increase from the prepandemic mean after March of 2020, though both also had special cause variation in April 2020 with this data point outside the upper control limit (Figures 3B and S7). In patients with respiratory failure requiring intubation there is a striking increase in mortality, increasing 6% from the pre-COVID-19 baseline, and death rate which increases from 321 to 382 deaths per 1000 admissions (Figures 3C and S8). In contrast with AHRF patients who were not

intubated, there is a dramatic increase in mortality seen during November and December of 2020 in patients requiring intubation.

Interestingly, from March 2020 to December 2020, there was a marginal increase in the mean mortality from 1.02% to 1.41% and death rate from 10 per 1000 to 14 per 1000 of patients without respiratory failure as compared to prepandemic means, from January 2017 to February 2020 (Figures 3D and S9). There is again a special cause variation in April 2020, November 2020, and December 2020 on both charts with mortality and death rate exceeding the upper control limit, reflecting a spring and winter surge as seen with AHRF patients who required intubation.

3.4 | Demographic outcome changes during COVID-19

Finally, we wanted to see if differences in outcomes by age contributed to the changing inpatient, all-cause mortality. Throughout 2020, even after the pandemic, the percentage of elderly patients over the age of 75 did not change compared to the previous 3 years (Figure 4A). The total number of admissions for patients over the age of 50 did not increase over the course of the pandemic either (Figure S10). This age group did however have a more dramatic increase in mortality after March of 2020 and the onset of the COVID-19 pandemic leading to a relative increase in the number of elderly inpatient deaths (Figure 4B). Analyzing this data using p' Laney control charts, we find that the mean mortality for ages 18–30 increased marginally from 0.4% to 0.5%; without any special cause variation (Figure 5A). However, in the remaining age groups, the mean mortality increased from 0.9% to 1.2% for the 31–50 group with a special cause in April 2020, for ages 51–75, the mean mortality jumps from 2.5% to 3.4% with a similar special cause in April (Figure 5B,C). For the over
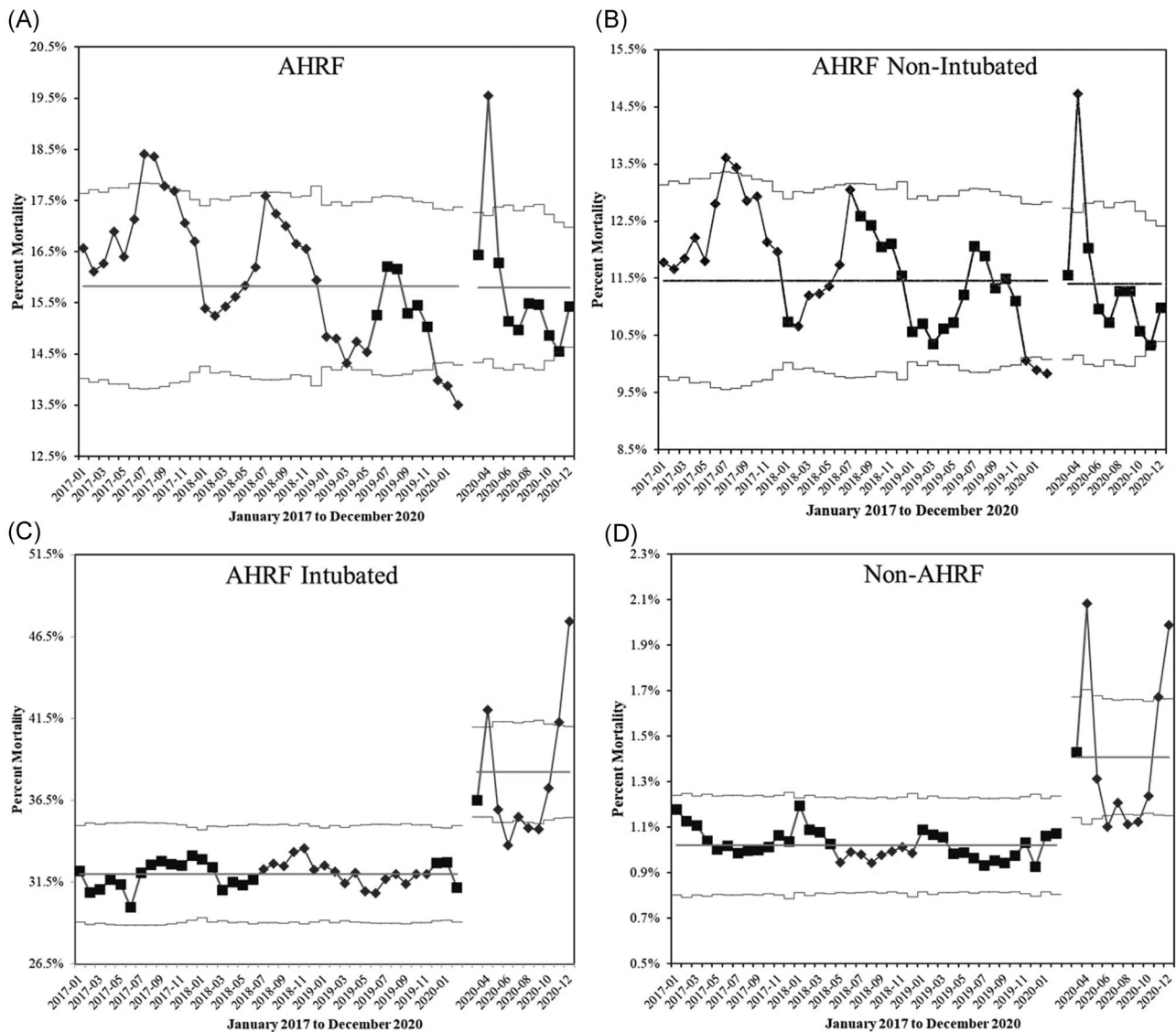
(A)

(B)

(C)

(D)

FIGURE 3 Changes in mortality and death rate for patients based on respiratory failure and intubation status. The top and bottom lines represent the upper and lower control limits, respectively. The bold line in the center represents mean mortality. Diamond markers represent special cause variation, Square markers represent common cause variation. (A) Patients with AHRF as a whole and those who were not intubated (B) did not have meaningful changes in mortality before and after March 2020. (C) Patients who were intubated with AHRF and those without AHRF (D) have increased inpatient mortality since March 2020. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved. AHRF, Acute Hypoxic Respiratory Failure

75 age group, the mean mortality increases from 4.0% to 5.8%, with special cause variation seen in April 2020 and again in November and December 2020 (Figure 5D).

4 | DISCUSSION

An evaluation of more than 30 million hospital discharges from over 600 participating hospitals shows that while the mortality of COVID-19 in 2020 has decreased, the uncontrolled spread of this novel disease in the United States has had profound effects on the American hospital ecosystem.

After an initial peak at the onset of the pandemic, mortality from COVID-19 steadily declined to below 10% by June. Mortality leveled off and remained at levels similar to June for the remainder of 2020, including during the winter surge in cases. This constant COVID-19 mortality suggests that the initial decline from March to June was likely not due to the presumed seasonality of SARS-CoV-2. The drop in mortality was seen in all regions of the country, regardless of whether that region was experiencing a local surge in cases. This may suggest that hospital crowding played a lower role in the initial high mortality, although studies with finer resolution would be required to definitively conclude hospital strain had minimal effect. Given that there was no dramatic change in the age of patients admitted with
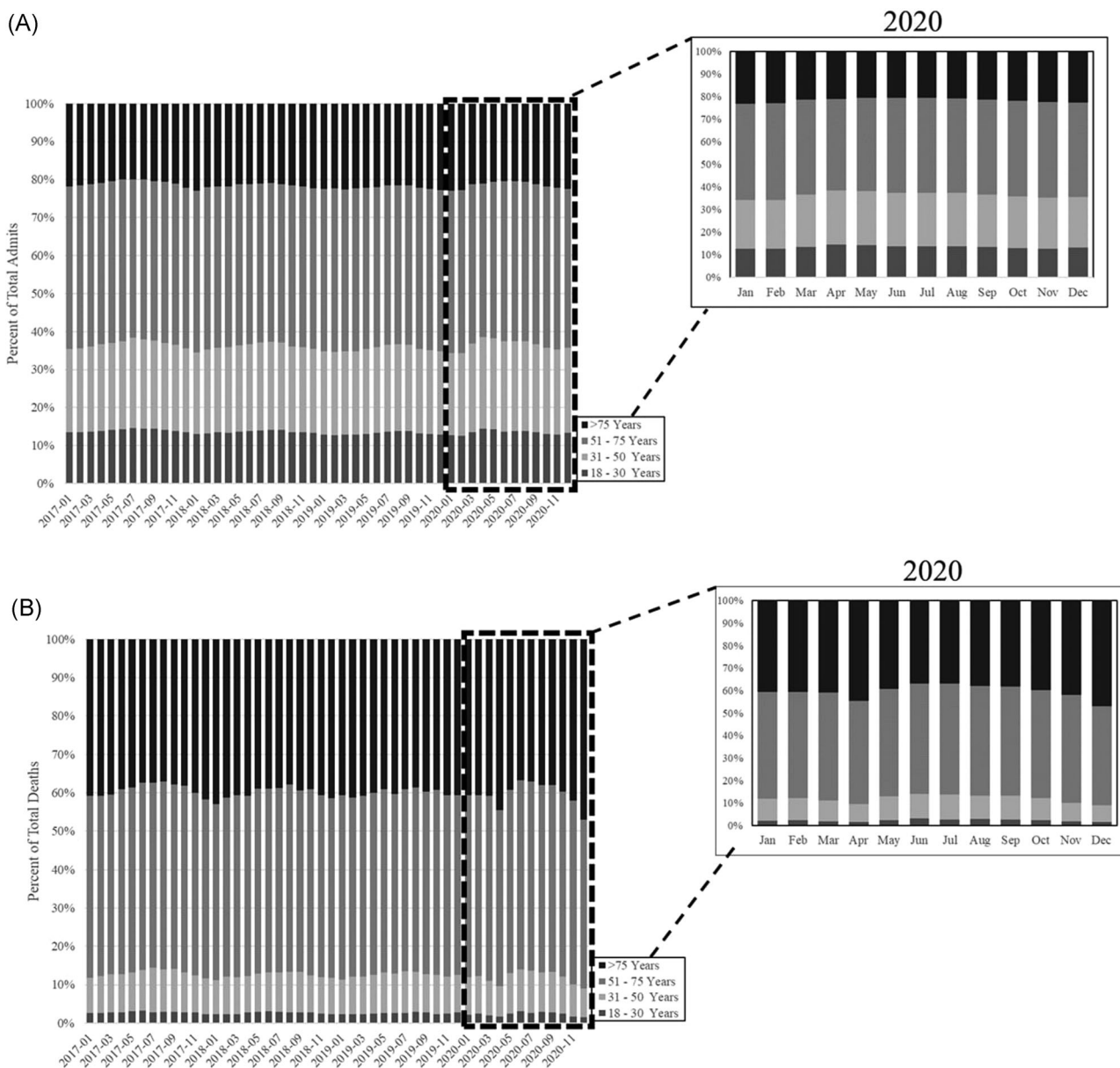
(A)

(B)

FIGURE 4 Changes in age distribution and respective outcomes during COVID-19. (A) Percent Inpatient discharges by age did not dramatically change during pandemic. (B) Percent Inpatient deaths by age. Percentage of total hospital inpatient deaths for those over 75 increased during spring and winter surges of COVID-19. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved

COVID-19, age alone also cannot fully explain changes in inpatient mortality.

One major variable that did change between March and June of 2020 was the medical community's understanding of, and therapeutic arsenal against, COVID-19. Data on the benefits of self-proning were published by late April.[15] Multiple publications espousing the survival benefits of therapeutic anticoagulation were published in early May.[16,17] Preliminary results from the Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial were released in mid-June, establishing steroids as the standard of care.[18] Since that time, further evidence has been published solidifying these interventions as effective at reducing mortality from COVID-19.[19–21] Other promising initial therapies, such as

remdesivir, have since failed to show a significant mortality benefit and thus likely did not directly decrease inpatient mortality.[22,23] ACTT-1 did show a shorter time to discharge in the remdesivir group which potentially could have indirectly decreased overall inpatient mortality by increasing hospital resources for other patients.[22,24] Other trials such as the WHO Solidarity Trial have failed to reproduce these results however and further study would be required to definitively prove this indirect effect on inpatient mortality from remdesivir.[25]

Although no single advance would explain the dramatic fall in mortality, the sum of these separate practices and therapies likely played a dominant role in reducing the mortality of COVID-19, possibly by reducing the proportion of patients with COVID-19 who
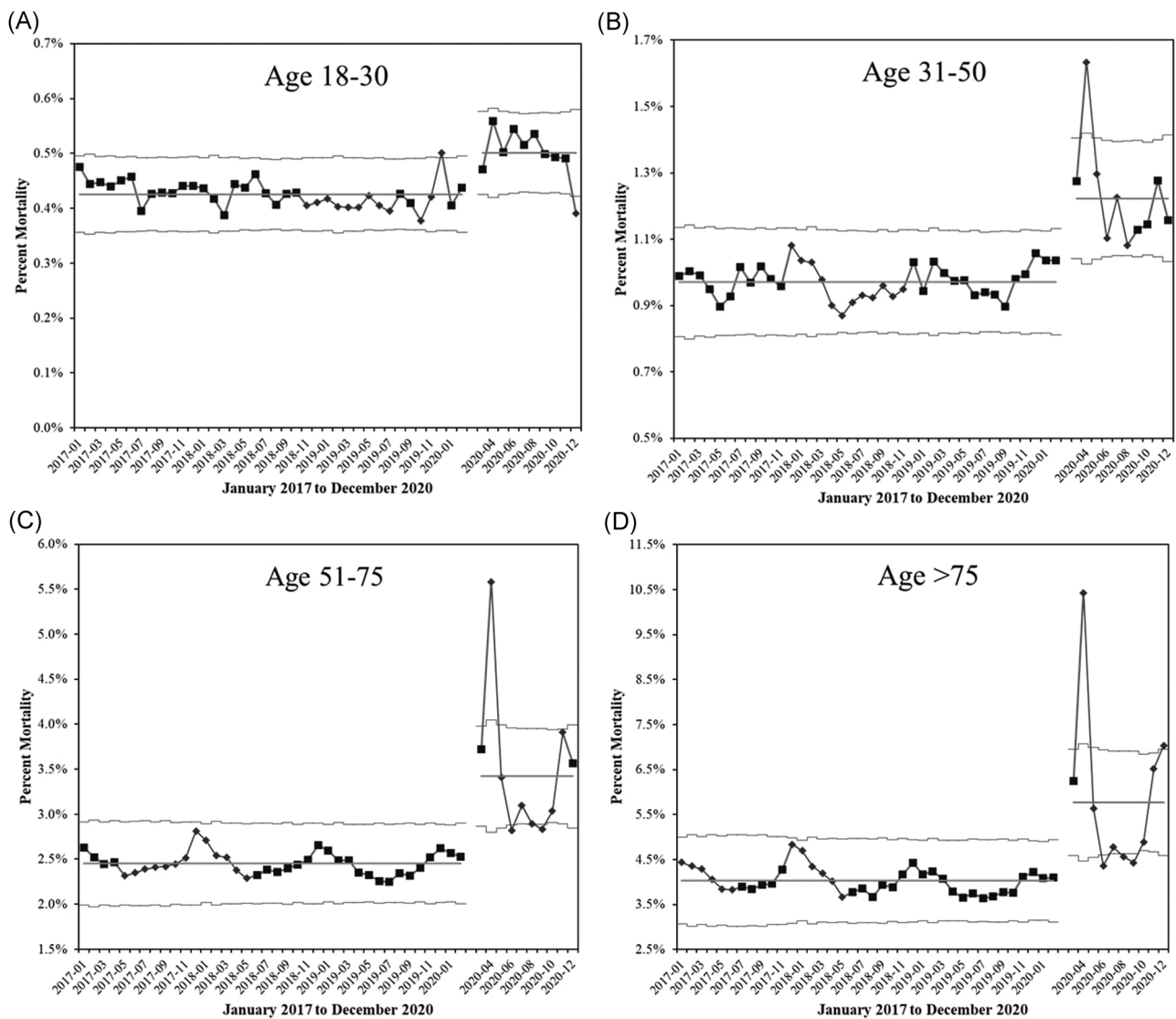
FIGURE 5 Trends in mortality by age. The top and bottom lines represent the upper and lower control limits, respectively. The bold line in the center represents mean mortality. Diamond markers represent special cause variation, Square markers represent common cause variation. (A) Percent Mortality in ages 18–30 increased from 0.4% to 0.5% after the beginning of COVID-19. (B) Mean mortality percent increases from 0.09% to 1.2 in patients age 31–50. (C) For patients age 51–75 there was increased mortality from 2.5% to 3.4%. (D) Mortality increased from 4.0% to 5.8% for patients over the age of 75. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved

required intubation and mechanical ventilation. The widespread implementation of infection prevention practices, such as isolation of affected patients, physical distancing, and mask-wearing, all could have played a role in reducing the inoculum of SARS-CoV-2, thus leading to less severe disease.[26,27]

Although mortality for COVID-19 has fallen, the addition of a new disease with a 10% mortality has changed overall inpatient outcomes when compared to the prior 3 years. Overall inpatient mortality rose 30% from its prepandemic baseline leading to an additional 8 deaths per 1000 discharges. Interestingly, outcomes of patients with acute hypoxic respiratory failure did not experience an increase in mortality. Rather, patients with respiratory failure who also were intubated had much worse outcomes since the start of the pandemic than before, with mortality increasing 6% leading to 61 excess deaths per 1000 discharges.

Outcomes of intubated patients displayed a seasonality not seen in nonintubated patients, with a spike in mortality during November and December of 2020. This divergence could represent strain in hospital resources specific to the ICU. Multiple environmental and epidemiologic studies have shown that temperature and humidity can correlate with the severity of COVID-19.[28,29] These environmental effects may manifest as worse outcomes in the most severe cases of COVID-19 although more research is needed to elucidate this potential relationship. Inpatient mortality increased for patients of all ages, but this increase was more pronounced for older patients, particularly those over the age of 75. The number of patients with respiratory failure who did not require intubation, after an initial spike, had returned to prepandemic baselines suggesting that the medical advances described above may have predominantly facilitated survival of patients not requiring intubation.

There was a small increase in deaths for patients without respiratory failure as well, with 3 excess deaths per 1000 admits. Given the dramatic decline in the total number of admissions seen at the beginning of the pandemic, it is likely that only the sickest patients were being admitted to hospitals.[30] During COVID-19-related lockdowns in Italy, this self-selection likely caused significant increases in the mortality from endocrine conditions, such as complications of diabetes, and cardiovascular disease.[30] With patients avoiding the hospital, there would also be a dramatic delay in care for patients with diseases other than COVID-19. The increase in nonrespiratory failure mortality seen during both spring and winter surges could also be evidence that human behavior is exerting a selection bias where only the sickest patients are presenting to hospitals. In a nationwide analysis of cardiovascular deaths in England, one study found not only increased mortality but also that nearly half of these deaths occurred in the community suggesting delays in seeking help, likely secondary to COVID-19.[14] Similar increases in community deaths have been reported in America and Italy.[31] Finally, this increase in mortality for patients without respiratory failure could be from the diagnosis of respiratory failure not being captured in these patients.

The primary limitations of this retrospective study include reliance on hospital-based coding data. The addition of the new diagnostic code for COVID-19 may have been underused at the beginning of the pandemic, skewing results specific for that code in March of 2020. This would not have affected data regarding respiratory failure. In addition, the analysis only included data from participating hospitals in the CBD, potentially adding a selection bias although the large number of hospitals included in the CBD likely blunted this effect.

5 | CONCLUSIONS

Mortality associated with COVID-19 declined precipitously within the first few months of the pandemic. This decline seems to have been driven by an increased understanding of the disease and the advent of multiple new therapies for treating COVID-19. Despite the medical community's successes in reducing COVID-19 mortality to below 10%, this decline stagnated in the second half of 2020. Recent studies repurposing anticytokine medications, such as tocilizumab and baricitinib, in addition to the current standards of care, could potentially further reduce inpatient mortality from COVID-19.[32-36] Additionally, the percentage of patients with COVID-19 requiring intubation has fallen and widespread vaccination efforts are underway with vaccines effective at preventing severe disease. This will ultimately decrease the number of deaths in intubated patients with COVID-19 and thus reduce overall inpatient mortality.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS
Conceptualization: Brad Spellberg. *Data collection*: Matthew C. Phillips and Brad Spellberg. *Data analysis*: Matthew C. Phillips, Josh Banerjee, Laura Sarff, and Noah Wald-Dickler. *Writing*: Matthew C. Phillips, Laura Sarff, Steve Meurer, Chase Coffey, and Brad Spellberg. *Review and wditing*: Matthew C. Phillips, Josh Banerjee, Paul Holtom, Chase Coffey, Steve Meurer, Laura Sarff, Noah Wald-Dickler, and Brad Spellberg.

DATA AVAILABILITY STATEMENT

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SUPPORTING INFORMATION

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