Original Manuscript

Perfusion

Perfusion
2022, Vol. 0(0) 1–9
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/02676591221114959
journals.sagepub.com/home/prf
SAGE

Early trends in ECMO mortality during the first quarters of 2019 and 2020: Could we have predicted the onset of the pandemic?

J.W. Awori Hayanga, Jahnavi Kakuturu, Alper Toker, Fatima Asad, Anthony Siler, Heather Hayanga and Vinay Badhwar

Abstract

Objective: To compare mortality trends in patients requiring Extracorporeal Membrane Oxygenation (ECMO) support between the first quarters of 2019 and 2020 and determine whether these trends might have predicted the severe acute respiratory syndrome coronavirus-2 (SARS)-Cov-2 pandemic in the United States.

Methods: We analyzed 5% Medicare claims data at aggregate, state, hospital, and encounter levels using MS-DRG (Medicare Severity-Diagnosis Related Group) codes for ECMO, combining state-level data with national census data. Necessity and sufficiency relations associated with change in mortality between the 2 years were modeled using qualitative comparative analysis (QCA). Multilevel, generalized linear modeling was used to evaluate mortality trends.

Results: Based on state-level data, there was a 3.36% increase in mortality between 2019 and 2020. Necessity and sufficiency evaluation of aggregate data at state and institutional levels did not identify any association or combinations of risk factors associated with this increase in mortality. However, multilevel and generalized linear models using disaggregated patient-level data to evaluate institution mortality and patient death, identified statistically significant differences between the first ($p = .019$) and second ($p = .02$) months of the 2 years, the first and second quarters ($p < .001$ and $p = .042$, respectively), and the first 6 months ($p < .001$) of 2019 and 2020.

Conclusion: Mortality in ECMO patients increased significantly during the first quarter of 2020 and may have served as an early warning of the SARS-Cov-2 pandemic. Granular data shared in real-time may be used to better predict public health threats.

Keywords

mortality, trends, data, extracorporeal membrane oxygenation, pandemic

Introduction

Data can be used to elucidate patterns that proffer a predictive health advantage.[1] The very impetus for data collection rests on a foundation of quality and safety that underpins the efforts behind rapid response teams and failure-to-rescue algorithms.[2–4] The ability to recognize trends in real-time allows clinical teams the opportunity to craft timely interventions in response to stereotypical sequences of events that can be used to protect public health.[4] Indeed, a well-informed and well-executed preventive measure can play a pivotal role in saving lives in the face of a national disaster. The onset of a pandemic constitutes a significant public health concern and threat to the economy that can escalate exponentially in the absence of thoughtful, proactive mitigation efforts. The ability to identify, in real-time, any potential triggers or populations-at risk may be of tremendous importance in proffering public protection, particularly

Department of Cardiovascular and Thoracic Surgery, WVU Heart and Vascular Institute, West Virginia University, Morgantown, WV, USA

Corresponding author:
J W A Hayanga, Department of Cardiovascular and Thoracic Surgery, West Virginia University, 1 Medical Center Drive, Morgantown, WV 26506, USA.
Email: jeremiah.hayanga@wvumedicine.org

among those who bear a disproportionate burden of susceptibility.

Real-time trend surveillance is commonplace in the aviation industry as well as in the military, where early warnings are used to change strategic command.[5,6] Data shared in real-time by a communion of stakeholders permits expeditious modifications to occur in operational planning which minimizes casualties.[5] The ability to share and compare data improves decision making and prevents further loss of life.[7,8] Past pandemics of influenza A H1N1 highlighted the role of extracorporeal membrane oxygenation (ECMO) as a viable option when conventional therapy fails. In this vein, ECMO has become an accepted last line of defense and any sharp rise in ECMO mortality warrants attention.[9,10]

Mortality trends in ECMO are a particularly sensitive index because ECMO mortality has been falling for over a decade, most consistently in the patients with respiratory illnesses.[11] In a non-war civilian context, therefore, a sudden uptick in mortality trends in patients on ECMO is a potential signal as to the entrant of novel viral respiratory threat into the clinical landscape. We hypothesized, therefore, that the patterns of ECMO mortality drawn from publicly available data in the first quarter of the year 2020 might have been used to accurately predict the onset of the severe acute respiratory syndrome (SARS) coronavirus-2 pandemic and the growing public health threat that then ensued. In other words, during the first quarter of 2020, when awareness and testing for COVID-19 were still emerging,[12] a sudden, unusual, increase in mortality among patients with severe respiratory illnesses requiring VV-ECMO could have indicated the upcoming COVID-19 pandemic. Thus, the availability of this information through real-time tracking of ECMO mortality, such as using interoperable prospective registry data, might have proffered an earlier warning of an impending pandemic, improving the response time to the pandemic.

Methods

We conducted a retrospective observational analysis of the association between hospital ECMO volume and in-hospital mortality using Medicare 5% claims data following STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines[13] (Supplementary Table 1). The Medicare 5% sample contains all final action claims data for a random 5% sample of all claims of Medicare beneficiaries.[14] We evaluated two independent samples. First, aggregate data at the state level including information on state, United States (US) region, total claims, deaths, percentage mortality during 2019 and 2020, and the percentage change in mortality between the 2 years. This sample included data for the first quarter of 2019 and 2020, the latter corresponding to the 2020 "COVID-19" pandemic year. The second sample involved individual patient data including discharge status, age, race, gender, Diagnosis Related Group codes (DRG), Major Diagnostic Category (MDC), date, procedure, provider, city, state, as well as institution number of beds, Medicare wage index, and Medicare case-mix index (CMI). The sample included data pertaining to claims for hospitalizations between January 2017 and June 2020. We aggregated data from the second sample at the institution level and calculated ECMO mortality rates per institution. Additionally, we combined Medicare data aggregated per state from the first sample with state-level data from the US Census Bureau's American Community Survey (ACS).[15]

Claims with Medicare Severity-Diagnosis Related Group (MS-DRG) codes for ECMO, including 5A15223, 5A1522F, 5A1522G, and 5A1522H were analyzed. The outcome evaluated at the state level was percentage change in mortality between the first quarters of 2019 and 2020, calculated as the percentage difference in 2020 and 2019 divided by the percentage mortality in 2019. Outcomes for models using institution and patient-level data included patient discharge status (expired vs non-expired) and the institution mortality rate per month, quarter, and semester, calculated as the total number of deaths per institution in a given period divided by the total number of patients per institution over the same period. Predictors at the state level included total patient volume per state, as well as variables extracted from the ACS, namely, the Gini index of inequality, percentage of African Americans, percentage of individuals with a Hispanic origin, and percentage of individuals above 65 years of age. These variables were selected consistent with existing literature that has linked them to increased mortality rates.[16,17] Calendar year was used as a predictor for models using data at the institution and patient-level. We took into consideration the following confounders: patient age, gender, and race, as well as institution number of beds, and ECMO volume.

The analysis strategy is provided under Supplementary Text 1. All analyses were performed using the R language.[18] The Institutional Review Board of the West Virginia University approved the study.

Results

Sample description

This sample was drawn from 4,787,544 million beneficiaries from whom there were 2595 ECMO encounters pertaining to primary respiratory illness. Of these, 1428 were drawn from the first quarter of 2019, and 1167 from the first quarter of 2020. Because the exploratory data analysis indicated minimal missing data, we did not use any missing imputation method. We categorized age by average groups. Most patients in the sample had an average age of 33 years (32.6%), were white (75.1%), and male (64.2%). There were no significant differences observed between the 2 years. Table 1 displays a description of the non-aggregate ECMO sample and a comparison between the years 2019 and 2020.

Aggregate data evaluated through qualitative comparative analysis

We observed an overall mortality rate of 3.62 (± 0.928), and the West had the highest mortality among all US regions 3.77 (± 0.773) (Figure 1). No significant differences were observed in the number of cases or mortality in each region between the first quarter of 2019 and 2020. There was an overall increase in regional mortality of 3.36% between 2019 and 2020. The regions with the highest mean mortality rates per state were Northeast and West.

We used qualitative comparative analysis (QCA) to evaluate state-level data in keeping with the high level of aggregation and a low number of observation units, mimicking data commonly used by healthcare policy agencies.[19] We evaluated necessity relations between the change in mortality between 2019 and 2020 and five conditions (patient volume, Gini index of inequality, and percentages of the population with age above 65 years old, African Americans, and Latin Americans singly and in combination) (Supplementary Table 3). The necessary elements with the highest coverage scores in determining increased mortality were (a) the disjunction of a low patient volume or a high percentage of individuals above 65 years of age, as well as (b) the disjunction of a high rate of individuals above 65 years of age, Gini index below 0.47, or a percentage of African Americans above 25%, and (c) the disjunction among a high percentage of individuals above 65 years of age, Gini index below 0.47, or a rate of Latin Americans below 25%. However, the overall low relevance of necessity scores indicated that these necessary conditions are trivial. We provide additional details on the QCA analysis in the Supplementary Text 1 and Supplementary Figure 1.

Next, we reported the sufficient risk factors in determining the change in mortality between 2019 and 2020 (Supplementary Table 4). States with low inequality (Gini Index < 0.47) and low patient volume (below 121,408) presented the highest sufficiency scores. Supplementary Table 5 presents the truth table. Two configurations had an inclusion score value of 1. One of these configurations included two states (District of Columbia and Georgia) that had positive values for a Gini index above 0.47 and a percentage of Black/African Americans above 25. The second configuration with an inclusion score value of 1 corresponded to one state (Colorado) that had a positive value for the percentage of Hispanics above 15. Finally, we evaluated conservative solutions for these associations (Supplementary Table 6). All solutions presented low coverage values.

We also reported the change in mortality per state between the first quarters of 2019 and 2020 (Figure 2). Most areas observed an increase in mortality between these years. The areas with the highest increase in mortality between 2019 and 2020 were Virgin Islands (41.77%) and New York (19.81%). The areas with the highest mortality in 2019 were Puerto Rico (7.97%), Guam (6.12%),

Table 1. Sample characteristics.

Variable [Missing]	Total (2595)	2019 (1428)	2020 (1167)	*p*	SMD
Average age [0]					
Avg. 33	846 (32.6%)	468 (32.8%)	378 (32.4%)	*p* = .506	0.006
Avg. 67	820 (31.6%)	453 (31.7%)	367 (31.4%)		
Avg. 72	525 (20.2%)	277 (19.4%)	248 (21.3%)		
Avg. 77	269 (10.4%)	156 (10.9%)	113 (9.68%)		
Avg. 82	86 (3.31%)	43 (3.01%)	43 (3.68%)		
Avg. 90	49 (1.89%)	31 (2.17%)	18 (1.54%)		
Race [80]					
White	1948 (75.1%)	1082 (78.3%)	866 (76.4%)	*p* = .527	0.038
Black	354 (13.6%)	186 (13.5%)	168 (14.8%)		
Other	213 (8.21%)	114 (8.25%)	99 (8.74%)		
Gender [0]					
Male	1665 (64.2%)	915 (64.1%)	750 (64.3%)	*p* = .952	0.004
Female	930 (35.8%)	513 (35.9%)	417 (35.7%)		

*SMD: standardized mean difference.

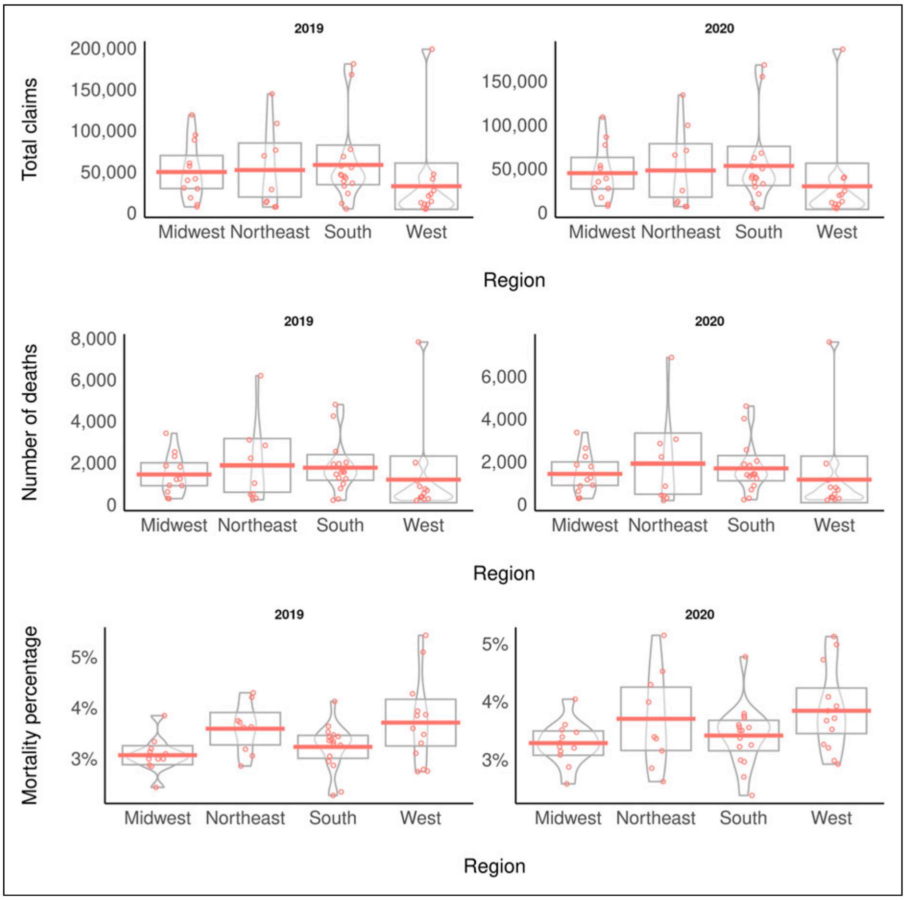

Figure 1. Number of claims, deaths, and mortality percentage for 2019 and 2020 per US region.

Alaska (5.42%), and Hawaii (5.09%). In 2020, the highest mortality rates occurred in Puerto Rico (7.83%), Virgin Islands (5.77%), Guam (5.55%), and New York (5.14%).

Change in mortality per institution

We applied multilevel modeling to aggregated data at the institution level to evaluate the mortality changes between 2019 and 2020. We adjusted these models for the number of patients and beds. There were no statistically significant differences between the years (Supplementary Table 7).

Patient-level data evaluated through multilevel modeling

Finally, we reported individual patient data using a series of multilevel and generalized linear models to evaluate the mortality changes between 2019 and 2020. We reported predicted means along with 95% confidence intervals for the comparison between 2019 and 2020 mortality per semester, quarter, and month. First, institution mortality was evaluated as the outcome (repeated for each patient in the same institution) with year as the predictor. We adjusted this model for age, race, and gender (Table 2). Compared to the first semester of 2019 (first 6 months of the year), the mortality in the first semester of 2020 was significantly higher (0.51, 0.48–0.53 vs 0.56, 0.54–0.59, $p < .001$). There was also significantly higher mortality in the first quarter of 2020 (0.474, 0.428–0.519 vs 0.518, 0.472–0.564, < 0.001), as well as in the first (0.518, 0.438–0.598 vs 0.585, 0.503–0.667, $p = .019$) and second (0.542, 0.455–0.628 vs 0.612, 0.529–0.696, 0.02) months of 2020. Next, we used a multilevel model with encounter-level and institutional-level data to report patient discharge status (expired vs non-expired) as the outcome, with year as the predictor. The model was adjusted for age, race, and gender (Table 3). Compared to the first semester of 2019, the first semester of 2020 had a statistically significantly higher proportion of deaths (1.23, 1.04–1.44, $p = .015$). Similarly, we observed a significantly higher proportion of deaths in the first quarter of 2020 (1.26, 1.01–1.58, $p = .042$) (Table 3). Figure 3 displays an exploratory smoothed time series of weekly mortality per institution. Except for 2 weeks (week 13 through 15), ECMO mortality was higher every week of 2020 compared to 2019. The most marked peak occurred between weeks 4 and 10. Supplementary Figure 3 displays the percent change between years for the first quarters of 2018 through 2020. This figure illustrates that overall mortality trends in ECMO patients had decreased for two consecutive years prior to the pandemic. This trend in reducing mortality was reversed in the first and second quarters of 2020 with the onset of the COVID-19 pandemic.

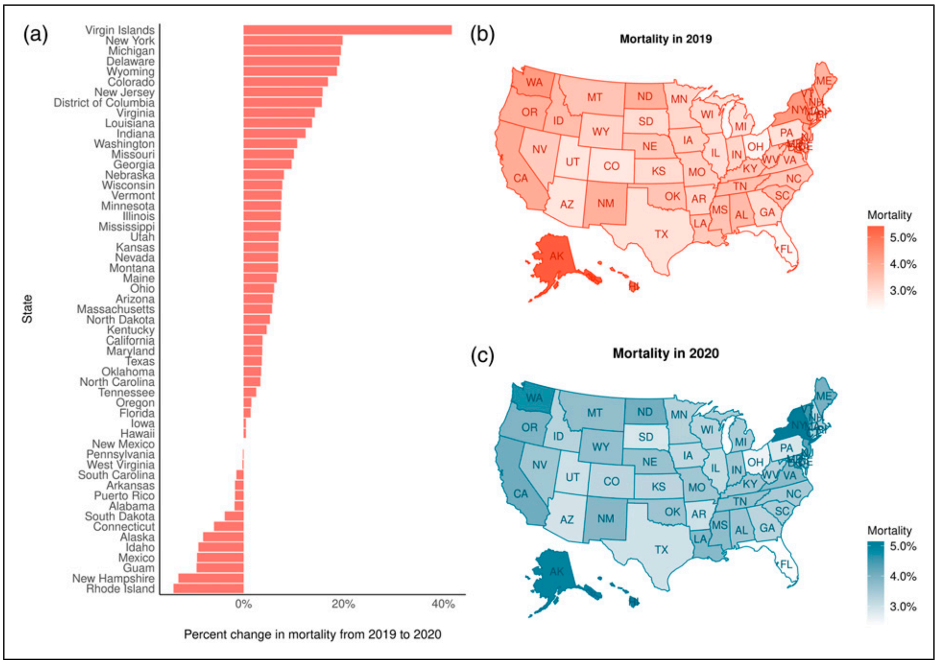

Figure 2. Percent change in mortality per US state between 2019 and 2020 (A), as well as a US map displaying mortality percentage per state during 2019 (B) and 2020 (C). We calculated the percentage change in mortality between 2019 and 2020 for each state as the difference between percentage mortality in 2020 and 2019 divided by the percentage mortality in 2019.

Table 2. Model using patient-level data, evaluating institution mortality index as the outcome and year as the predictor, grouped by quarter. We adjusted the model for age, race, and gender.

	Year 2019	Year 2020	*p*-value
First semester	0.51 (0.48–0.53)	0.56 (0.54–0.59)	<.001
Quarter 1	0.474 (0.428, 0.519)	0.518 (0.472, 0.564)	<.001
Month 1 (Jan)	0.518 (0.438, 0.598)	0.585 (0.503, 0.667)	.019
Month 2 (Feb)	0.542 (0.455, 0.628)	0.612 (0.529, 0.696)	.02
	Year 2018	**Year 2019**	
Month 12 (Dec)	0.549 (0.452, 0.646)	0.557 (0.459, 0.655)	.807

Table 3. Multilevel model using encounter-level and institutional-level data, evaluating patient discharge status (expired vs non-expired) as the outcome and year as the predictor. We adjusted the model for age, race, and gender.

	Year 2019	Year 2020	*p*-value
First semester	1 [Referent]	1.23 (1.04–1.44)	.015
Quarter 1	1 [Referent]	1.26 (1.01, 1.58)	.042
Month 1 (Jan)	1 [Referent]	1.35 (0.941, 1.95)	.104
Month 2 (Feb)	1 [Referent]	1.32 (0.874, 2.01)	.189
	Year 2018	**Year 2019**	
Month 12 (Dec)	0.52 (0.447, 0.594)	0.496 (0.422, 0.57)	.639

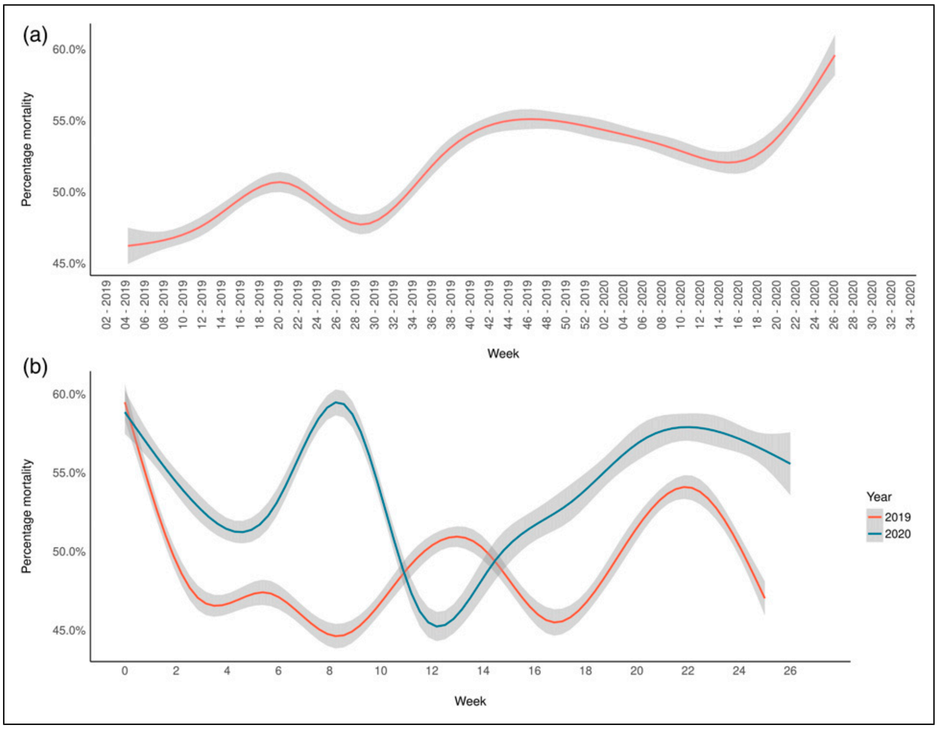

Figure 3. Exploratory time series of smoothed weekly mortality per institution. We present the entire year of 2019 and the first semester of 2020 (A), as well as a comparison between the first semesters of 2019 and 2020 (B). We used a smoothing method based on a generalized additive model with cubic splines. The shaded gray area around the lines represents the confidence intervals.

Discussion

Mortality in patients on ECMO has been steadily declining over the past two decades.[20] This is particularly true in the case of venovenous ECMO used in patients with respiratory illnesses.[21] An uptick, therefore, in mortality may serve as a potent signal of adverse trends in ECMO survival. Our results highlight that the use of Medicare claims data, linked at the aggregate, patient, and institutional levels proffers a window into trends for a resource that has become the last line of defense used when conventional therapy has failed. These trends in increased mortality were manifest by week 4 and peaked on Week 8 and might have warned of an ongoing disproportionate and uncharacteristic increase in mortality from respiratory illnesses a month before the pandemic was declared. Medicare data are broadly representative of the older adults and the infirm and thus necessarily speak to the epidemiological impact on a vulnerable population. These data therefore define a population at risk to which mitigation efforts, resource allocation, and disaster management efforts may be directed.

We derive, in this vein, a better understanding of the magnitude of threat, the demographics most acutely affected, and an estimation of the potential cost to life and economy. Our exploratory results indicated greater mortality in the Northeast and West regions, in line with the numbers of COVID-19 infections at the beginning of the pandemic.[22] Surprisingly, data aggregated by region revealed no significant insights into mortality, conveying a false sense of security despite the fact that a disproportionate number of deaths had already occurred in those jurisdictions.[23] The conditions deemed necessary contributors to the rate of change in mortality included low volume of cases, preponderance of older adult patients, environmental inequality and the varying percentage of minority populations. Each of these factors is well described in the social determinants of health literature.[24–27] The use of quantitative comparative analytics and establishment of sufficiency and necessity criteria further elucidates a granular composite of the population at risk.

The granularity in the data is a prerequisite as it permits the adjudication of multiple variables simultaneously, proffering considerable advantage over aggregated data or even publicly reported data sources such as the Johns Hopkins Resource Center datamap.[28] This latter source, though valuable in adjudicating the overarching extent of the outbreak, does not necessarily reveal much about age, gender or circumstance-specific susceptibility. No distinction is drawn, for instance, between asymptomatic infection and life-threatening illness. The interoperability of data and real time access cannot be overstated. Mortality during a pandemic is fluid and decision-making is greatly influenced by capacity, prevailing knowledge, medication efficacy and resource availability. Criteria and candidacy for cannulation may fluctuate with time, with increasing understanding, knowledge and alterations in resources and capacity. In the early stages of the pandemic, for instance, several centers accepted older patients (over 60 years of age) for cannulation. These criteria may have been supported by pre-pandemic criteria but mortality in this age group quickly proved prohibitive.[29,30] The same fate befell medications such as hydroxychloroquine, convalescent plasma and even remdesivir. Use of each of these fluctuated over the course of the pandemic. Indeed, many of the original management strategies and approaches proved to be detrimental and a more informed understanding, later in the pandemic, permitted changes in approach that decreased mortality as time ensued. This was certainly facilitated by the combination of novel vaccination initiatives, lockdown measures and non-pharmacologic initiatives.[30]

Based on our analysis, approximately 400 Medicare beneficiaries are placed on ECMO per month at a median cost of $500,000 per hospitalization, equating to $200 million per month or a staggering $2.4 billion per year.[20,31,32] A means to detect early trends in mortality would better steer decision-making in clinical and public health management in real-time and allow a re-evaluation of the indications and criteria for ECMO candidacy and address potential supply chain and resource considerations.

There are several limitations inherent in this analysis. First, the use of aggregate data bears the persistent threat of ecological fallacy, a failure in reasoning that arises when an inference is made about an individual based on aggregate data. Second, the use of administrative data poses the risk of administrative and retrospective bias. Third, any interruptions in data collection resulting from delays attributable to the pandemic itself may have compounded any prevailing bias. Fourth, despite adjustments made in the analysis, the threat of confounding could not be definitively eliminated. Fifth, the data are analyzed retrospectively and not in real-time. Lastly, the data do not include the timing of infection or duration of ventilation prior to cannulation. The use of a national claims database linked with census data, nevertheless, proffers a potent lens through which to adjudicate trends in mortality.

Our results indicate a peak in ECMO mortality by weeks 4 and 8 of 2020.[33] During this period, awareness and testing for COVID-19 had been limited if not entirely non-existent.[12] The spike could have warned of an ongoing and unusual increase in mortality from unknown respiratory illnesses which was manifest in Medicare claims data. Linking these data with concurrent CDC data and mortality statistics would have further laid ground for earlier declaration of a pandemic. Mitigation efforts might have then been instituted to save lives, particularly among the most vulnerable. We contend, therefore, that vigilant surveillance of real-time data can identify a trigger even by the mere comparison of two consecutive years' worth of data. A plausible trigger would need to be sensitive enough to identify a deviation and allow measures to be instituted to save lives. The assertion that multiple years of data accrual are required for the comparison to test specificity of the data may inadvertently perpetuate the very delay already at play and the inertia to act. Safety mechanisms should thus ostensibly be sensitive enough to occasionally trigger a false alarm but need not be so specific that they miss a true disaster altogether or delay our awareness in the process. For maximal public health benefit, the data should be assessed in real-time and disaggregated at a granular level to incorporate patient as well as the institution and state-level variables. These efforts would collectively guide resource allocation and mitigation efforts in the context of extracorporeal support and simultaneously inform vaccination, treatment, surveillance, and public health education efforts.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

J W A Hayanga https://orcid.org/0000-0001-5091-7069
Anthony Siler https://orcid.org/0000-0002-3638-5331

Supplemental Material

Supplemental material for this article is available online

References

1. Ash AS, Posner MA, Speckman J, et al. Using claims data to examine mortality trends following hospitalization for heart attack in medicare. *Health Serv Res* 2003; 38(5): 1253–1262.
2. Akinleye DD, McNutt L-A, Lazariu V, et al. Correlation between hospital finances and quality and safety of

patient care. *PLoS ONE* [Internet] 2019; 14: e0219124. [cited 2021 May 17]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6697357/
3. Mehta R, Tsilimigras DI, Paredes A, et al. Assessment of hospital quality and safety standards among medicare beneficiaries undergoing surgery for cancer. *Surgery* 2021; 169(3): 573–579.
4. Sheetz KH, Dimick JB, Ghaferi AA, et al. Impact of hospital characteristics on failure to rescue following major surgery. *Ann Surg* 2016; 263(4): 692–697.
5. Shepardson D. U.S. FAA tracking all boeing 737 MAX airplanes via satellite data. *Reuters* [Internet] 2021. [cited 2021 May 17]. Available from: https://www.reuters.com/article/us-boeing-737-max-idUSKBN2AJ2FG
6. Meynard J, Chaudet H, Texier G, et al. Advantages and limits of real-time epidemiological surveillance during military deployments: the experience of the French Armed forces. *Mil Med* 2009; 174(10): 1068–1074.
7. List of accidents and incidents involving the Boeing 737. In: *Wikipedia* [Internet]. 2021 [cited 2021 May 17]. Available from: https://en.wikipedia.org/w/index.php?title=List_of_accidents_and_incidents_involving_the_Boeing_737&oldid=1021020739
8. Aireon - space-based ADS-B global air traffic surveillance and tracking [Internet]. [cited 2021 May 17]. Available from: https://aireon.com/
9. Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet* 2009; 374(9698): 1351–1363.
10. Combes A, Hajage D, Capellier G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *N Engl J Med* 2018; 378(21): 1965–1975.
11. Sanaiha Y, Bailey K, Downey P, et al. Trends in mortality and resource utilization for extracorporeal membrane oxygenation in the United States: 2008-2014. *Surgery* 2019; 165(2): 381–388.
12. Rădulescu A. Course of the first month of the COVID 19 outbreak in the New York State counties. *PloS One* 2020; 15: e0238560.
13. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147(8): 573–577.
14. Medicare C. for, Services (CMS) M. Public comment: hip knee patient-reported outcome measure public comment summary [Internet]. Available from: http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/CallforPublicComment.html
15. Bureau USC. American community survey information guide. 2017.
16. Kawachi I, Kennedy BP. The relationship of income inequality to mortality: does the choice of indicator matter? *Soc Sci Med* 1997; 45(7): 1121–1127.
17. Stewart QT, Cobb RJ, Keith VM, et al. The color of death: race, observed skin tone, and all-cause mortality in the United States. *Ethn Health* 2020; 25(7): 1018–1040.
18. Core Team RR. A language and environment for statistical computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing, 2018. Available from: https://www.R-project.org/
19. CDC. Data and statistics [Internet]. Centers for Disease Control and Prevention 2021. [cited 2021 Jul 27]. Available from: https://www.cdc.gov/datastatistics/index.html
20. McCarthy FH, McDermott KM, Kini V, et al. Trends in US extracorporeal membrane oxygenation use and outcomes: 2002-2012. In: *Seminars in thoracic and cardiovascular surgery*. New York: Elsevier, 2015, pp. 81–88.
21. *Extracorporeal life support organization - ECMO and ECLS > resources > ECMO outcome prediction scores* [Internet]. [cited 2021 May 17]. Available from: https://www.elso.org/Resources/ECMOOutcomePredictionScores.aspx
22. United States COVID-19 cases and deaths by state over time. *Centers for Disease Control and Prevention* [Internet]. [cited 2022 Apr 26]. Available from: https://data.cdc.gov/Case-Surveillance/United-States-COVID-19-Cases-and-Deaths-by-State-o/9mfq-cb36
23. CDCMMWR. Preliminary estimate of excess mortality during the COVID-19 outbreak — New York City, March 11–May 2, 2020. *MMWR Morb Mortal Wkly Rep* [Internet]; 2020; 69: 603. [cited 2021 May 17]. Available from: https://www.cdc.gov/mmwr/volumes/69/wr/mm6919e5.htm
24. Fong ZV, Hashimoto DA, Jin G, et al. Simulated volume-based regionalization of complex procedures: impact on spatial access to care. *Ann Surg* 2019; 274: 312–318.
25. Hayanga AJ, Kaiser HE, Sinha R, et al. Residential segregation and access to surgical care by minority populations in US counties. *J Am Coll Surg* 2009; 208(6): 1017–1022.
26. Hayanga AJ, Waljee AK, Kaiser HE, et al. Racial clustering and access to colorectal surgeons, gastroenterologists, and radiation oncologists by African Americans and Asian Americans in the United States: a county-level data analysis. *Arch Surg* 2009; 144(6): 532–535.
27. Tan AX, Hinman JA, Abdel Magid HS, et al. Association between income inequality and county-level COVID-19 cases and deaths in the US. [Internet]. *JAMA Netw Open* 2021; 4(5): e218799. [cited 2021 May 17]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8094008/
28. *COVID-19 Map - Johns Hopkins Coronavirus Resource Center* [Internet]. [cited 2021 May 17]. Available from: https://coronavirus.jhu.edu/map.html
29. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the extracorporeal life

support organization registry. *Lancet Lond Engl* 2020; 396(10257): 1071–1078.
30. Jacobs JP, Stammers AH, St Louis J, et al. Extracorporeal membrane oxygenation in the treatment of severe pulmonary and cardiac compromise in coronavirus disease 2019: experience with 32 patients. *ASAIO J* 2020; 66(7): 722–730.
31. Minc SD, Hayanga HK, Thibault D, et al. Vascular complications increase hospital charges and mortality in adult patients on extracorporeal membrane oxygenation in the United States. *Semin Thorac Cardiovasc Surg* 2020; 33: 397–406.
32. Hayanga JWA, Shigemura N, Aboagye JK, et al. ECMO support in lung transplantation: a contemporary analysis of hospital charges in the United States. *Ann Thorac Surg* 2017; 104(3): 1033–1039.
33. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020; 382(10): 929–936.