Original Research

Effect of government-issued state of emergency and reopening orders on cardiovascular hospitalizations during the COVID-19 pandemic

Sameer Arora a,⁎, Michael J Hendrickson b,⁎, Anthony J Mazzella a, Muthiah Vaduganathan a, Patricia P Chang a, Joseph S Rossi a, Arman Qamar a, Ambarish Pandey a, John P Vavalle a, Thelsa T Weickert a, Paula D Strassle a, Michael Yeung a,⁎, George A Stouffer a,⁎

a Division of Cardiology, University of North Carolina School of Medicine, Chapel Hill, NC
b Division of Cardiovascular Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA
c Section of Interventional Cardiology and Vascular Medicine, NorthShore University Health System, University of Chicago Pritzker School of Medicine, Evanston, IL
d Division of Cardiology, University of Texas Southwestern Medical Center, Dallas, TX
Division of Intramural Research, National Institute on Minority Health and Health Disparities, National Institutes of Health, Bethesda, MD

Abstract

Objective: Little is known about the effect of government-issued State of Emergency (SOE) and Reopening orders on health care behaviors. We aimed to determine the effect of SOE and Phase 1 of Reopening orders on hospitalizations for acute myocardial infarction (AMI) or acute decompensated heart failure (ADHF).

Methods: Hospitalizations for AMI and ADHF in the UNC Health system, which includes 10 hospitals in both urban and rural counties, were identified. An interrupted time series design was used to compare weekly hospitalization rates for eight weeks before the March 10th SOE declaration, eight weeks between the SOE order and Phase 1 of Reopening order, and the subsequent eight weeks.

Results: Overall, 3,792 hospitalizations for AMI and 7,223 for ADHF were identified. Rates before March 10th were stable. AMI/ADHF hospitalizations declined about 6% per week in both urban and rural hospitals from March 11th to May 5th. Larger declines in hospitalizations were seen in adults ≥65 years old (-8% per week), women (-7% per week), and White individuals (-6% per week). After the Reopening order, AMI/ADHF hospitalizations increased by 8% per week in urban centers and 9% per week in rural centers, including a significant increase in each demographic group. The decline and rebound in acute CV hospitalizations were most pronounced in the two weeks following the government orders.

Conclusions: AMI and ADHF hospitalization rates closely correlated to SOE and Reopening orders. These data highlight the impact of public health measures on individuals seeking care for essential services; future policies may benefit from clarity regarding when individuals should present for care.

1. Introduction

An unexpected decline in rates of hospitalizations for a broad range of cardiovascular conditions has been observed worldwide during the coronavirus disease-2019 (COVID-19) pandemic [1–8]. The etiology for this remains unclear with proposed etiologies including patient fears of developing COVID-19 in the hospital setting, decreased air pollution, increased sleep duration, and less work-related stress. Government-is-
non-urgent surgeries and procedures were suspended by order of the Department of Health and Human Services as of March 23. On March 27, the Governor ordered NC residents to stay at home for 30 days. On that day, there were 232 confirmed cases of COVID-19 in NC. On May 8, the Governor announced that NC would enter Phase 1 of Reopening which would permit the reopening of ‘nonessential’ businesses (e.g. clothing and hardware stores), worship centers, parks and childcare facilities and allow people to leave their homes for commercial purposes.

While much remains unknown about COVID-19, older adults and certain racial/ethnic populations disproportionately account for more severe COVID-19 illnesses and deaths [12–14]. It is also apparent that the disease has disproportionately impacted urban areas [15,16]. Therefore, there may be variation in perception of exposure risk to Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-COV-2) which may have a differential effect on the trends in hospitalizations in urban versus rural hospitals and across demographic groups. The University of North Carolina (UNC) Health system spans the state of NC and includes 11 hospitals equitably distributed throughout urban and rural areas; it serves the diverse population of NC, which is 28% rural and 22% Black [17]. Each of these hospitals is well equipped to provide care for patients who may need acute CV care such as acute myocardial infarction (AMI) or acute decompensated heart failure (ADHF). The unique geography of the state of NC and the distribution of UNC hospitals throughout the state provided an opportunity to examine the effect of government issued orders in NC.

2. Methods

Hospitalizations containing a hospital billed discharge diagnosis of acute CV conditions of interest with a primary discharge date between January 15th, 2020 and June 30th, 2020 at inpatient care entities across the UNC Health system were retrospectively examined. Hospitalizations were categorized according to International Classification of Diseases, Tenth Revision (ICD-10) coding into the following categories: AMI, ADHF, and cardiac arrest using the Informatics for Integrating Biology and the Bedside Platform (i2b2) (Supplemental Table 1). UNC Health system began recording COVID-19 data in its centers on March 12th.
(Central illustration and supplemental figure 1). i2b2 is the flagship tool developed by the i2b2 Center, in the North Carolina Translational & Clinical Sciences Institute (NC TraCS) [18]. i2b2 provides a way for researchers to query the Carolina Data Warehouse for Health, a central data repository containing clinical, research, and administrative data sourced from the UNC Health System. Researchers can apply criteria for patient demographics, encounter information, ICD-9-CM and ICD-10-CM diagnoses, ICD-9-CM/ICD-10-CM/CPT/HCPCS procedure codes, vitals, laboratory results, discharge disposition, and medications. To protect patient information, i2b2 does not report frequencies <10; we used 9 as an estimate when values were suppressed. The i2b2 at the University of North Carolina is supported by the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health, through Grant Award Number UL1TR002489.

There are 100 counties in NC of which 80 counties were identified as rural, 14 as suburban, and 6 as urban based on the population densities derived from 2014 estimates of the 2010 U.S. Census population by the NC Rural Center [19]. Data were available for 10 of 11 UNC health system hospitals (Onslow Memorial Hospital was acquired in 2019 and was not reporting to i2b2 at the date of data collection); these hospitals were categorized into urban, suburban, or rural based on the county in which they were located (Fig. 1). For this study, we collapsed the urban and suburban counties into one analytic category and compared with rural counties. Urban/suburban hospitals included UNC Medical Center, UNC REX Hospital, and Pardee Hospital. Rural hospitals included Caldwell Hospital, Chatham Hospital, Johnston Hospital, Lenoir Memorial Hospital, Nash Hospital, UNC Rockingham Hospital, and Wayne Memorial Hospital (Fig. 1). This study was considered exempt from institutional review board approval as i2b2 contains only deidentified information.

Demographics and clinical characteristics including age, sex, race, diabetes mellitus, and hypertension, chronic obstructive pulmonary disease, discharge disposition, and length of stay data were collected. To account for the large daily variation in hospital volume during the pandemic, weekly rates of acute CV diagnoses of interest were calculated. Age was categorized as ≥65 years and <65 years old. To examine the impact of COVID-19 on trends in CV hospitalizations, we utilized an interrupted time series (ITS) design and segmented log-linear negative binomial regression. The ITS design is a quasi-experimental approach and considered one of the strongest methods for evaluating longitudinal effects of interventions [20,21]. Briefly, the study period is divided into pre-intervention and post-intervention segments, and separate regression analyses are built for each period. Using ITS, we then compared both the immediate impact (intercepts) and weekly trends (slopes) from the eight weeks before March 10th, 2020 (January 15th–March 10th) to the eight weeks after (March 11th–May 5th), and then the eight weeks after March 10th to the following eight weeks (May 6th–June 30th) during reopening. In-hospital mortality and cardiac arrest were also examined using similar methods. Categorical variables were compared using Chi-square tests and continuous variables were compared using Kruskal Wallis test, as appropriate. All analyses were done using SAS version 9.4 (SAS Inc, Cary, NC) and R version 4.0.0 (2020, R Core Team, Vienna, Austria).

3. Results

A total of 11,015 hospitalizations for AMI or ADHF were identified from January 15, 2020 to June 30, 2020 in the UNC Health system, including 3792 for AMI (34%) and 7223 for ADHF (66%). A breakdown showed that 6895 (63%) occurred at hospitals in urban counties, 5943 (54%) were men, 7099 (64%) were White, 3372 (31%) were Black, and 7064 (64%) were 65 years or older.

There were 1462 AMI and 2776 ADHF admissions in the eight weeks preceding the SOE declaration in NC (January 15th to March 10th), compared to 1089 AMI and 2088 ADHF admissions from March 11th to May 5th, and 1241 AMI and 2359 ADHF admissions from May 6th to June 30th (Table 1, Fig. 2). Incident rate ratios (IRR) representing average weekly AMI/ADHF hospitalizations during the three time intervals in our study are displayed in Table 2, stratified by hospital location and demographic group. Between January 15th and March 10th, there were an average of 512 (95% CI 457, 574) AMI or ADHF hospitalizations per week at centers in the UNC Health system, and trends were stable (IRR 1.01 95% CI 0.99, 1.03, p = 0.52). Following the March 10th SOE declaration, there was a 33.8% drop in AMI/AHDF hospitalizations from March 11th through March 24th which then stabilized. Overall admissions for AMI
or ADHF declined by about 6% per week in the 8 weeks after the SOE order (change in intercept p = 0.32, change in slope p = 0.0002). In the first three weeks during Phase 1 of Reopening, there was a substantial increase in rates of hospitalization for AMI or ADHF which then stabilized; overall rates increased by 8% per week during the 8 weeks after reopening (change in intercept p = 0.0009, change in slope p < 0.0001, Central Illustration, panel A).

In-hospital mortality among AMI/ADHF patients remained relatively unchanged at about 6% (Central Illustration, panel B). Hospital admissions for cardiac arrest remained unchanged over the entire study period (26 in the first week to 33 in the final week; change in first intercept p = 0.77, change in first slope p = 0.53; change in second intercept p = 0.49, change in second slope p = 0.77).

Before March 10th, urban centers accounted for 328 (95% CI 291, 370) and rural centers accounted for 184 (95% CI 165, 206) weekly hospitalizations for AMI or ADHF and trends for both were stable during this time (IRR 1.00, 95% CI 0.98, 1.03, p = 0.77 and IRR 1.01 95% CI 0.99, 1.04, p = 0.22, respectively). In the eight weeks after March 10th, AMI or ADHF hospitalizations declined by about 6% each week in both urban and rural centers (Urban: change in intercept p = 0.34,
change in slope $p < 0.0001$; Rural: change in intercept $p = 0.47$, change in slope $p < 0.0001$, Table 2, Central Illustration). A similarly expeditious decline in AMI or AHDF hospitalizations in the first two weeks after the SOE declaration was seen in urban (33.3%) and rural (34.6%) hospitals alike. After reopening measures were implemented in May, AMI or AHDF hospitalizations increased by 8% per week in urban centers (change in intercept $p = 0.003$, change in slope $p = 0.0001$) and 9% per week in rural centers (change in intercept $p = 0.0005$, change in slope $p < 0.0001$, Table 2), despite increases in COVID-19 cases (Supplemental Figure 1).

Compared to the same dates in 2019, there were 14% fewer AMI hospitalizations (1089 vs 1265) and 24% fewer AHDF hospitalizations (2088 vs 2741) from March 10th to May 5th, 2020. Hospitalizations at urban centers in 2020 were down 20% for AMI and 26% for AHDF compared to 2019. Rural centers had similar AMI volumes but were down 21% in AHDF hospitalizations. In 2019, admissions for AMI or AHDF were stable in the time matched eight weeks before March 10th (IRR 0.98, 95% CI 0.95, 1.02, $p = 0.33$, and IRR 0.99, 95% CI 0.97, 1.02, $p = 0.54$, respectively), in the eight weeks following March 10th (AMI: change in intercept $p = 0.83$, change in slope $p = 0.23$; AHDF: change in intercept $p = 0.98$, change in slope $p = 0.45$), and in the next eight weeks (AMI: change in intercept $p = 0.20$, change in slope $p = 0.70$; AHDF: change in intercept $p = 0.01$, change in slope $p = 0.22$).

Between January 15th and March 10th, hospitalization rates for AMI or AHDF were stable for all groups that were analyzed (Table 2). In the eight weeks after March 10th, relatively large declines in hospitalizations were seen in adults ≥65 years old (−8% per week, change in intercept $p = 0.43$, change in slope $p < 0.0001$), women (−7% per week, change in intercept $p = 0.67$, change in slope $p = 0.0004$), and White adults (−6% per week, change in intercept $p = 0.05$, change in slope $p < 0.0001$). Smaller declines were seen in men (−4% per week, change in intercept $p = 0.03$, change in slope $p = 0.007$) with non-statistically significant declines seen in Black adults (−4% per week, change in intercept $p = 0.98$, change in slope $p = 0.09$) and individuals <65 years old (−3% per week, change in intercept $p = 0.48$, change in slope $p = 0.09$). After reopening, significant increases were observed in rates of AMI or AHDF hospitalizations in all groups including White adults, Black adults, young adults, older adults, men, and women (Table 2, Fig. 3).

4. Discussion

In this analysis investigating the temporal trends in acute CV hospitalizations in a North Carolina hospital system, we found a rapid and significant decline in AMI/ADHF hospitalizations following the SOE declaration (March 10th, 2020). This affected both urban and rural hospitals in NC despite a disproportionate distribution of COVID-19 cases in urban areas [16], with older adults experiencing the most substantial declines. AMI/ADHF hospitalizations rapidly rebounded after Phase 1 Reopening was announced, even with a continued increase in COVID-19 cases. These data highlight the temporal relationship of government orders and acute CV hospitalizations in both urban and rural hospitals during the COVID-19 pandemic.

Our data are consistent with recent observational analyses from the United States that reported a significant decline in hospitalizations from CV disease [1,4,7,8]. Several potential explanations for the observed declines in AMI or AHDF hospitalizations have been proposed which can be divided into two large categories: reduction in the actual occurrence of AMI/AHDF and changes in patient behavior so that they fail to seek medical care.

Potential etiologies for reduced occurrence of AMI/AHDF include better self-care such as improved dietary compliance and adherence to medical therapy in those with heart failure with the purpose of avoiding contact with the medical system due to perceived risk of exposure to SARS-COV2 [22]. Physical isolation can also prevent exposure to infectious triggers of AHDF. Decreased fast-food intake, improved sleep hygiene and reduced exposure to air pollution may also contribute to a lower risk of AMI/AHDF [1,23–25]. While it is possible that changes in admission criteria during the pandemic also impacted hospitalization rates, various studies have documented changes in the number of patients seeking medical care, especially early during the pandemic. Outpatient visits declined by about 50% in the early period of the pandemic in the southeastern U.S. [26]. Another study that included 24 Emergency Departments in 5 health systems in 5 states found that patient visits declined between 41.5% and 63.5% in March and April of this year. Data from 5 hospitals in the UNC Health system found that the number of patients seeking Emergency Department care declined by 46.5% in March and April with the largest decline seen the week of March 11, 2020. The percentage of Emergency Department patients being admitted to the hospital were stable until COVID-19 cases increased significantly [27]. Therefore, it is likely that the decline in admissions for AHDF and AMI seen in March and April 2020 in our study was not due to changes in admission criteria but driven primarily by individuals’ perception of risk in seeking care.

Several lines of evidence strongly suggest that government issued orders impact patient behaviors. First, consistent with the dramatic decrease in Emergency Department visits after the SOE [25], we found a sudden and rapid decline in acute CV hospitalizations within two weeks of the SOE declaration which is unlikely to be attributable to decreased incidence. Second, despite variance in the trends of COVID-19 cases between urban and rural areas in NC during the period of this study [16,28], both urban and rural area hospitals saw similar abrupt changes in the rates of AMI/AHDF hospitalizations following the government issued orders. The observed decrease in hospitalizations irrespective of the geographic distribution of COVID-19 suggests that the government-issued orders had a larger effect on patients’ decisions to seek emergency CV care than did the actual risk of acquiring COVID-19. Lastly, our data showed that acute CV hospitalizations rebounded following the Phase 1 of Reopening order (though not to pre-COVID levels) despite an increase in COVID-19 cases, which demonstrates that government-issued orders can both enhance and reduce fear associated with seeking medical care for acute conditions. These data emphasize the immediate impact of public health messaging on human behavior, including seeking care for potentially life-threatening cardiac conditions.

While the government orders were not designed to limit patients from seeking health services for acute CV conditions, they can be misinterpreted and perceived to be applicable to even emergency medical care. Government orders may also result in significant barriers to access to primary care physicians with one study estimating that outpatient medical visits declined approximately 50% in the southeastern part of...
The U.S. in March and April [26]. Furthermore, our data demonstrated larger declines in older adults, which is concerning as the government actions may have a disproportionate impact on groups who have increased perceived risk of contracting SARS-COV2. While the current study was not designed to determine the reasons behind patient decisions, it highlights the important implications of public health policy, which can significantly alter individuals’ behavior and response in a pandemic.

There has been discrepancy in the literature regarding inpatient mortality in HF and AMI throughout the pandemic. Most notably, while a recent study from the Danish National dataset found no changes in overall HF mortality during the initial pandemic period [22], a study from the Providence St Joseph Health System suggested increased risk-adjusted mortality in AMI in March/April 2020 [29]. It would stand to reason that mortality rates of AMI change more than ADHF, as the majority of patients with ADHF carry a diagnosis of chronic HF; therefore, HF patients are more likely medically optimized, and patient education regarding alarm symptoms that warrant seeking care is likely far superior in the population with HF as compared to those with AMI, which frequently is an acute and initial cardiovascular presentation. However, our study found significant declines in hospitalizations for both AMI and ADHF, while in-hospital mortality in AMI/ADHF hospitalizations...
remained stable and the rates of cardiac arrest did not meaningfully change. These data must be interpreted with caution as mortality and cardiac arrest data were only available for in-hospital events. This is important as reports from Italy and New York point to a surge in rates of out-of-hospital cardiac arrest during the COVID-19 pandemic as individuals attempt to avoid hospitals [30,31]. In summary, true changes in mortality from acute CV conditions such as AMI/ADHF in the initial months of the COVID-19 pandemic remain unclear. The concern for increased rates of at-home deaths remains high and must be investigated in future analyses, especially as our data demonstrated larger declines in hospitalizations for older adults who are most at risk.

Our study has important limitations. First, we did not account for changes in the population at risk during the study period; however, it is unlikely that there were significant changes over a short time span. Second, ICD-10-CM coding practices may vary across practitioners and hospitals, and it is possible patients with AMI/ADHF were coded as having an alternate diagnosis especially if there was another primary problem. This was partially mitigated by being selective in inclusion criteria and excluding all non-acute ICD-10-CM codes (Supplemental Table 1).

Third, while we were able to detect significant differences overall, some of the subgroups had relatively small sample sizes and analyses were underpowered to detect differences in these populations. Fourth, we used the county designation to classify hospitals as urban/suburban and rural; however, this likely does not fully capture or describe the patient population each hospital treats within its catchment area. Lastly, due to the functionality of i2b2, unique patients were identified within a week query, so readmissions in the same calendar week may be missed and thus hospitalizations are likely underestimated; however, we would not expect this to differ week to week.

5. Conclusions

In this study spanning 10 hospitals throughout NC, we observed sudden substantial declines in the weekly rates of AMI or ADHF hospitalizations within the two weeks following the SOE declaration in NC. There were similar declines in both urban and rural hospitals, despite a preponderance of COVID-19 for urban areas, and older individuals experienced the most substantial declines. In the setting of demonstrated declines in outpatient and emergency room visits over this period, these data raise concerns for patients avoiding care due to perceived risk of COVID-19 rather than a decrease in incidence of AMI or ADHF. After reopening measures were implemented, there was an abrupt rebound in AMI or ADHF hospitalizations despite a continued increase in COVID-19 cases. These data highlight the impact of government issued orders on individuals seeking care for essential services. Future measures may benefit from clarity regarding when patients should present for care.

Disclosures: Dr. Vaduganathan has received research grant support or served on advisory boards for American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, Boehringer Ingelheim, Cytokinetix, and Relypsa, and participates on clinical endpoint committees for studies sponsored by Galted, Novartis, and the NIH. Dr. Qamar is supported by Daiichi-Sankyo, the NIH T32 Program, and the AHA SFRN in Vascular Disease Grant. He is an ad hoc consultant/speaker for the American College of Cardiology, Society for Cardiovascular Angiography and Interventions, Pfizer, Medscape, and the Clinical Exercise Physiology Association. Dr. Pandey is funded by the Texas Health Resources Clinical Scholarship. Dr. Vavalle is supported by a research grant from CSI Inc. He is a principal investigator for Abbott Medical Device Company, Boston Scientific, and Cardiac Dimensions, Inc. He receives consulting fees from Edwards Lifesciences and has an Honoraria from ZOLL Medical Corporation. The remaining authors have nothing to disclose.

Funding: Dr. Paula Strassle is supported by the Division of Intramural Research, National Institute on Minority Health and Health Disparities, National Institutes of Health. The content and views in the manuscript are those of the authors and should not be construed to represent the views of the National Institutes of Health.

6. Author contributions

Sameer Arora MD MPH*: Conceptualization; Methodology; writing—original draft, review & editing; supervision.

Michael J Hendrickson BS*: Conceptualization; methodology; writing—original draft, review & editing; software; formal analysis; data curation; visualization.

Anthony J Mazzella MD: Writing—review & editing; visualization.

Muthiah Vaduganathan MD MPH: Methodology; writing—review & editing.

Patricia P Chang MD MHS: Writing—review & editing.

Joseph S Rossi MD MS: Writing—review & editing.

Arman Qamar MD MPH: Writing—review & editing.

Ambarish Pandey MD MSCR: Writing—review & editing; methodology.

John P Vavalle MD MHS: Writing—review & editing.

Theresa T Weickert MD: Writing—review & editing.

Paula D Strassle PhD MSPH: Writing—review & editing; methodology; software; formal analysis; data curation.

Michael Yeung MD: Writing—review & editing.

George A Stouffer MD: Conceptualization; visualization; writing—review & editing; supervision.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jaccp.2021.100172.

References

[1] Bhatt AS, Moscone A, McRanrh EE, et al. Declines in hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic: a multicenter tertiary care experience. J Am Coll Cardiol 2020.

[2] Colivichiv F, Di Pasco SA, Magnaniti M, et al. The impact of the Coronavirus Disease-2019 pandemic and Italian lockdown measures on clinical presentation and management of acute heart failure. J Card Fail 2020.

[3] Solomon MD, McNulty EJ, Rana JS, et al. The Covid-19 pandemic and the incidence of acute myocardial infarction. N Engl J Med 2020.

[4] Kanaga AP, Goyal MS, Hamilton S, Albers GW. Collateral effect of Covid-19 on stroke evaluation in the United States. N Engl J Med 2020.

[5] Garcia S, Albarghadi MS, Meraj PM, et al. Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. J Am Coll Cardiol 2020.

[6] De Rosa S, Spaccarotella C, Basso C, et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. Eur Heart J 2020.

[7] El-Hamammy I, Brinster DR, DeRose JJ, et al. The COVID-19 pandemic and acute aortic dissections in New York: a matter of public health. J Am Coll Cardiol 2020.

[8] Baum A, Schwartz MD. Admissions to veterans affairs hospitals for emergency conditions during the COVID-19 pandemic. JAMA 2020.

[9] Bowman R, Crosby DL, Sharma A. Surge after the surge: anticipating the increased volume and needs of patients with head and neck cancer after the peak in COVID-19. Head and Neck 2020;42.

[10] Salenger E, Ettich EW, Ad N, et al. The surge after the surge: cardiac surgery post-COVID-19. Ann Thorac Surg. 2020.

[11] https://www.nc.gov/covid-19/covid19-orders. Accessed May 25, 2020.

[12] Armitage R, Nellums LB. COVID-19 and the consequences of isolating the elderly. Lancet Public Health 2020;5:e256.

[13] Rothen H, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmune 2020;109:102433.

[14] Yancy CW. COVID-19 and African Americans. JAMA 2020.

[15] https://coronavirus.jhu.edu/us-map. Accessed May 29, 2020.

[16] COVID-19 StatsCOVID-19 incidence, by urban-rural classification — United States, January 22–October 31, 2020. MMWR Mortal Wkly Rep 2020;69:1753. http://dx.doi.org/10.15585/mmwr.mm6946e1 external icon.

[17] https://files.nc.gov/ncohs/documents/files/2018ASCNC.pdf. Accessed May 25, 2020.

[18] https://trac.unc.edu/index.php/services/informatics-and-data-science/i2b2. Accessed May 31, 2020.

[19] https://www.sccrcalcenter.org/about-us/. Accessed May 29, 2020.

[20] Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther 2002;27(4):299–309.

[21] Bernal JL, Cumneg, S Gasprini. A interrupted time series regression for the evaluation of public health interventions: a tutorial. Int J Epidemiol 2017;46(1):348–55.

[22] Anderson C, Gerds T, Fosbol E, et al. Incidence of new-onset and worsening heart failure before and after the COVID-19 epidemic lockdown in Denmark: a nationwide cohort study. Circ Heart Fail 2020 CIRCHEARTFAILURE120007274.
23. Pranata R, Vania R, Tondas AE, Setianto B, Santoso A. A time-to-event analysis on air pollutants with the risk of cardiovascular disease and mortality: a systematic review and meta-analysis of 84 cohort studies. J Evid. Based. Med. 2020.
24. Ceriello A, Taboga C, Tonutti L, et al. Evidence for an independent and cumulative effect of postprandial hypertriglyceridemia and hyperglycemia on endothelial dysfunction and oxidative stress generation: effects of short- and long-term simvastatin treatment. Circulation 2002;106:1211–18.
25. Advani I, Gunge D, Banks S, et al. Is increased sleep responsible for reductions in myocardial infarction during the COVID-19 pandemic? Am J Cardiol 2020;131:128–30.
26. Mehrotra A, Chernew M, Linetsky D, et al. The impact of the COVID-19 pandemic on outpatient visits: a rebound emerges. The Commonwealth Fund. May 19, 2020 2020.
27. Jeffery MM, D’Onofrio G, Poek H, et al. Trends in emergency department visits and hospital admissions in health care systems in 5 states in the first months of the COVID-19 pandemic in the US. JAMA Intern Med 2020.
28. https://www.who.int/publications-detail/strengthening-preparedness-for-covid-19-in-cities-and-urban-settings. Accessed May 31, 2020.
29. Gluckman TJ, Wilson MA, Chiu ST, et al. Case Rates, Treatment Approaches, and Outcomes in Acute Myocardial Infarction During the Coronavirus Disease 2019 Pandemic. JAMA Cardiol 2020;5(12):1–6. doi:10.1001/jamacardio.2020.3629.
30. Baldi E, Sechi GM, Mare C, et al. Out-of-Hospital Cardiac Arrest during the Covid-19 Outbreak in Italy. N Engl J Med 2020.
31. Mountantonakis SE, Saleh M, Coleman K, et al. Out-of-hospital cardiac arrest and acute coronary syndrome hospitalizations during the COVID-19 surge. J. Am. Coll. Cardiol. 2020;76:1271–3.