

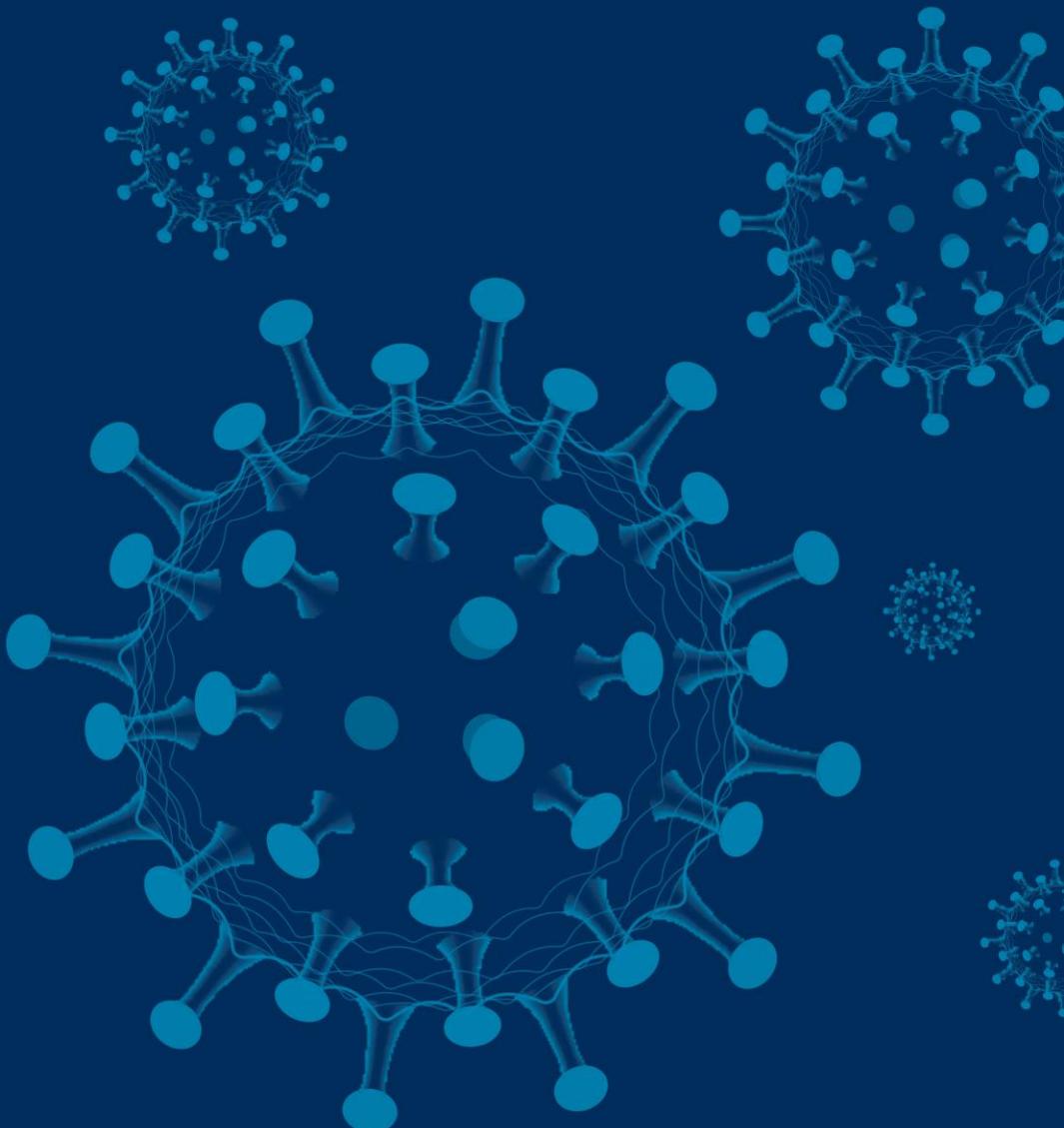


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COVID-19

Review of the Hottest COVID-19 Science: Catching You Before the Fall

September 3, 2020



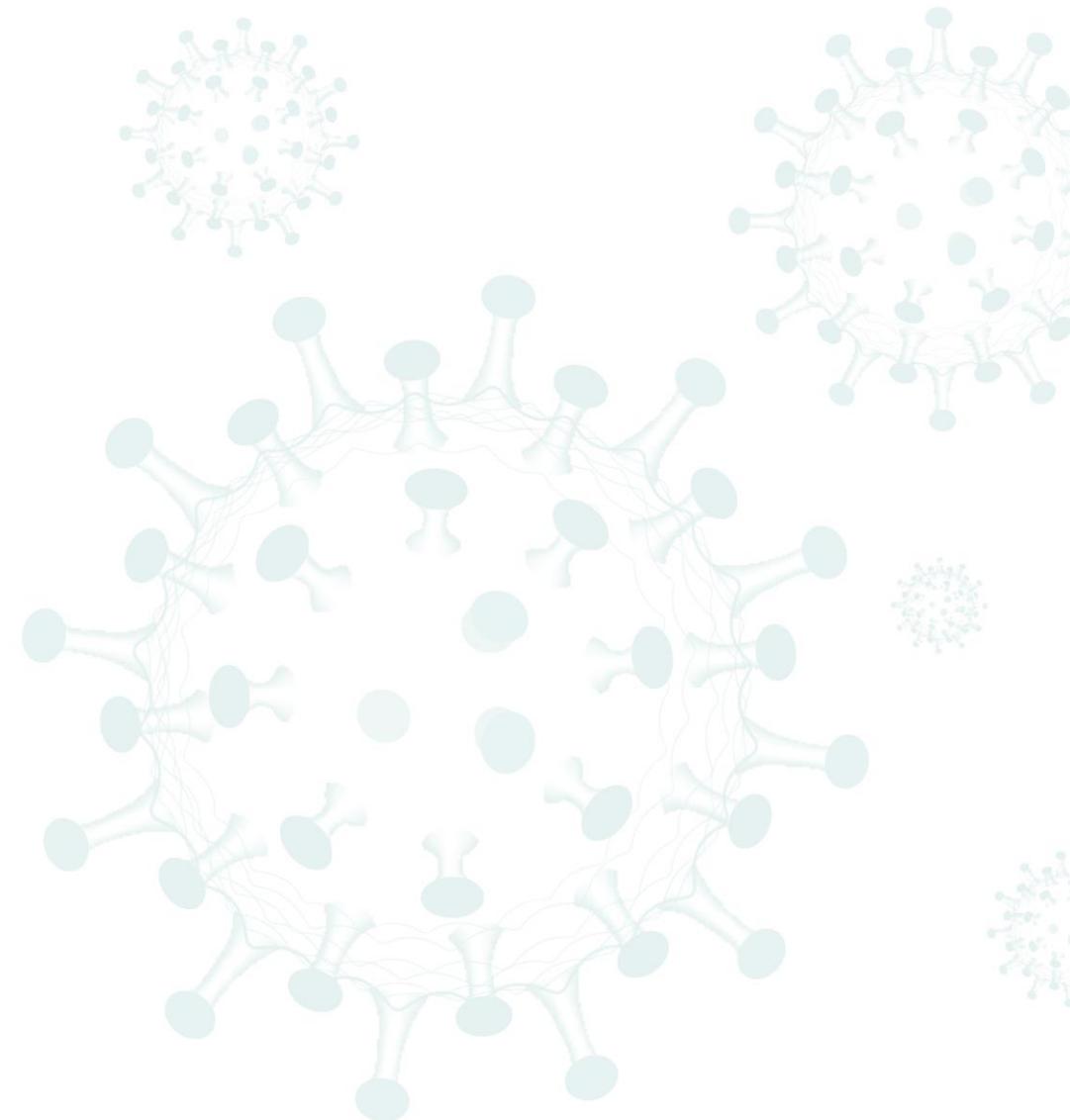


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Speakers

- Kim Eagle, MD, FACC, Moderator
- Bina Ahmed, MD, FACC
- Geoffrey D. Barnes, MD, MSc, FACC
- Nicole Bhave, MD, FACC
- Shashank S. Sinha, MD, MSc, FACC



Presenter Disclosure Information

- Kim Eagle, MD, FACC, Moderator
 - Nothing to disclose
- Bina Ahmed, MD, FACC
 - Nothing to disclose
- Geoffrey D. Barnes, MD, MSc, FACC
 - Consulting for Pfizer/Bristol-Myers Squibb, Janssen, Acelis Connected Health.
- Nicole Bhave, MD, FACC
 - Nothing to disclose
- Shashank S. Sinha, MD, MSc, FACC
 - Nothing to disclose

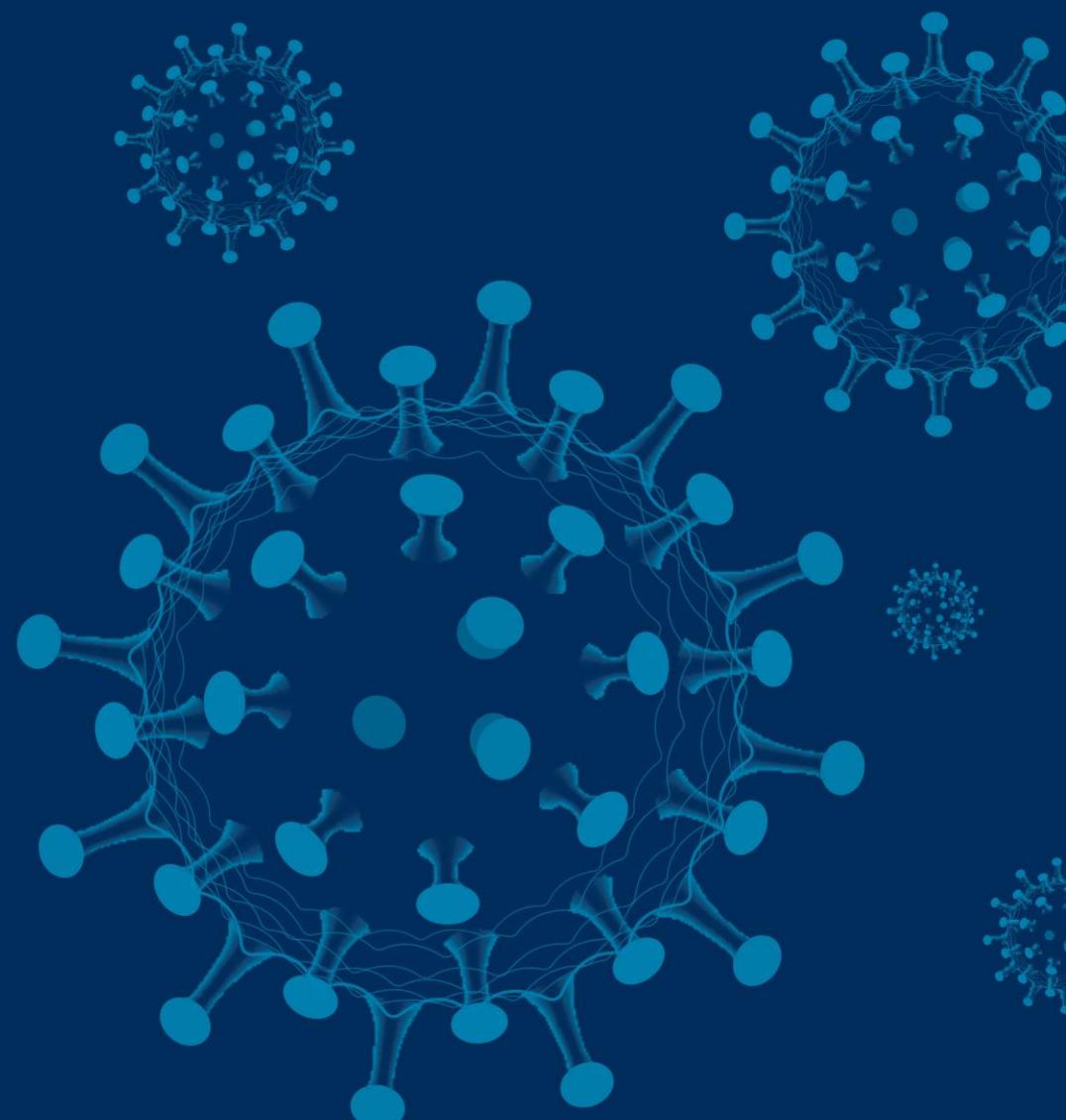


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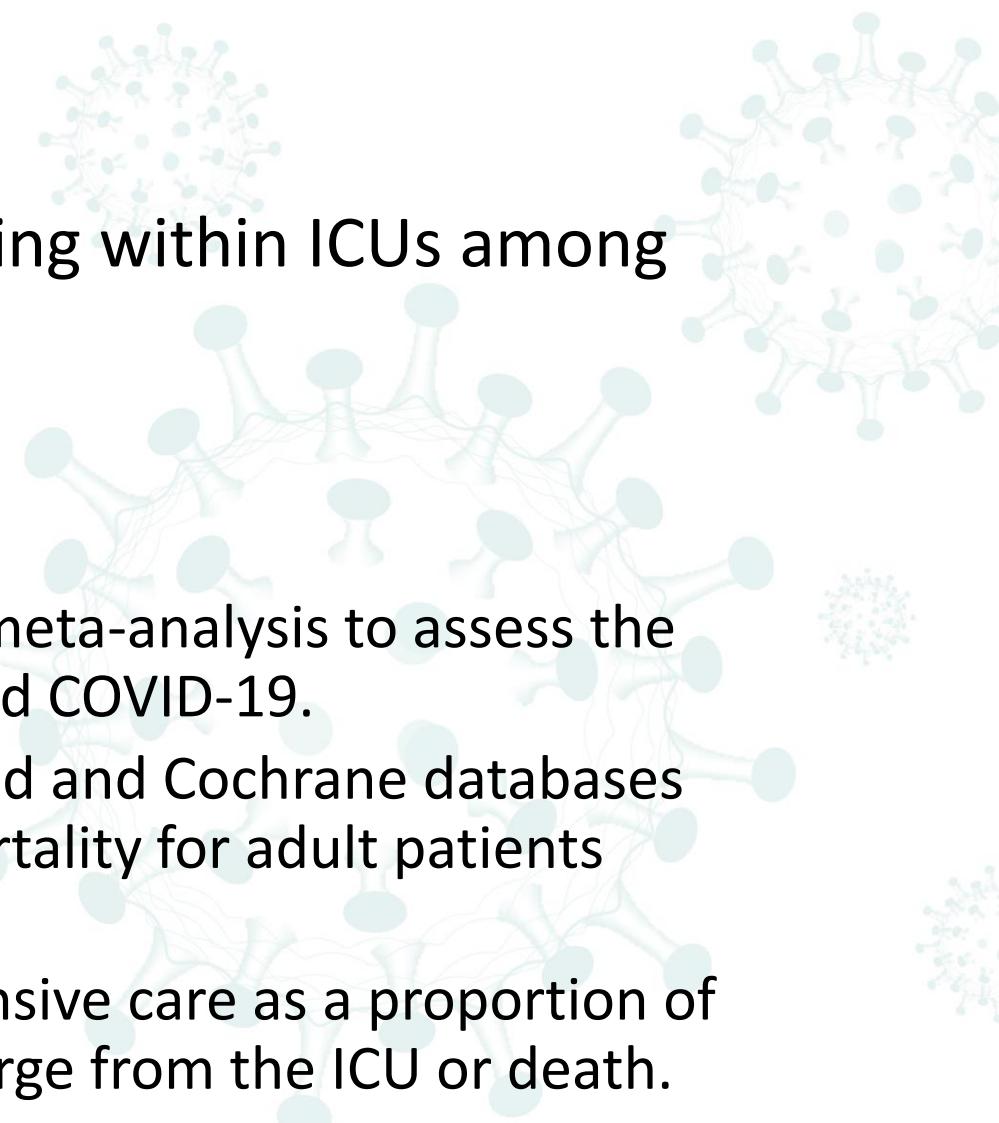
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Outcomes from Intensive Care in Patients with COVID-19: A Systematic Review and Meta- analysis of Observational Studies

Armstrong et al *Anaesthesia* 2020 June 30

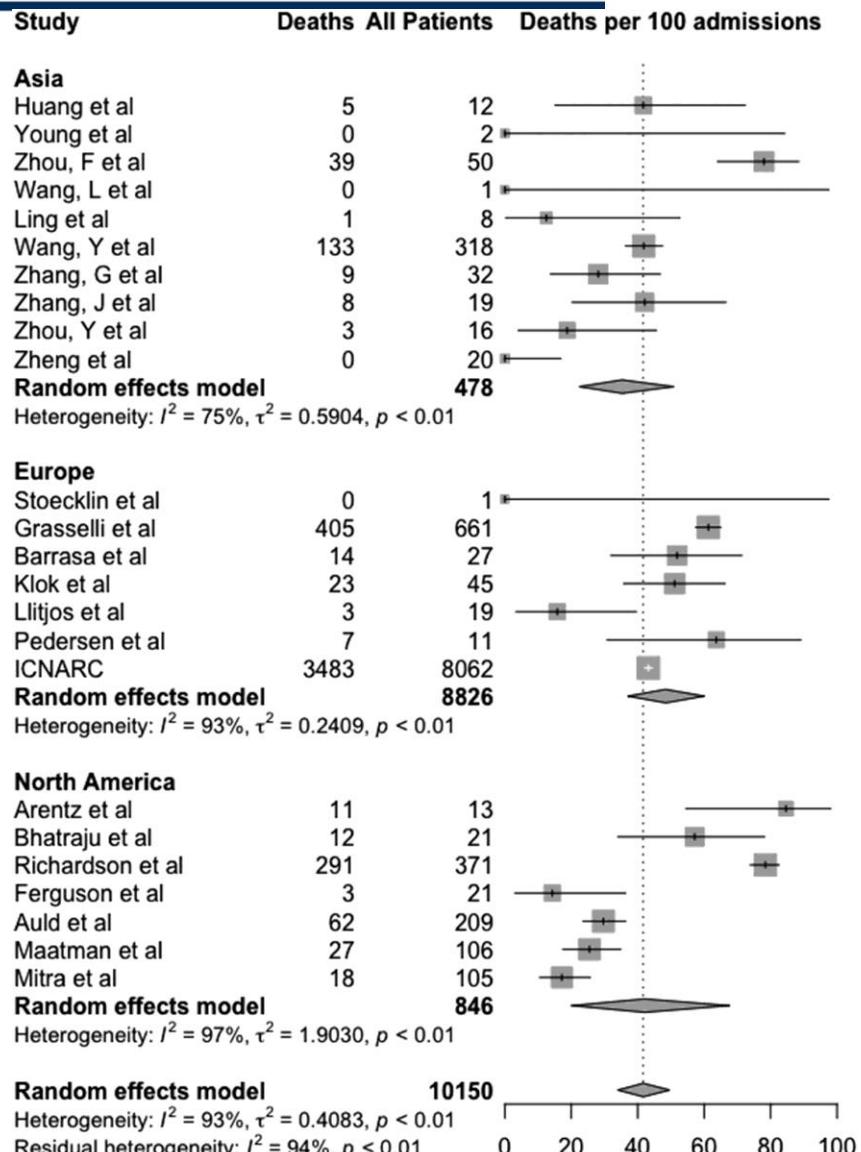


- **Study Question:** What is the mortality occurring within ICUs among patients admitted with COVID-19?
- **Methods:**
 - The authors performed a systematic review and meta-analysis to assess the reported ICU mortality for patients with confirmed COVID-19.
 - The authors searched MEDLINE, EMBASE, PubMed and Cochrane databases up to May 31, 2020, for studies reporting ICU mortality for adult patients admitted with COVID-19.
 - The primary outcome measure was death in intensive care as a proportion of completed ICU admissions, either through discharge from the ICU or death.





COVID-19 Hub



41.67 [15.17-72.33]
0.00 [0.00-84.19]
78.00 [64.04-88.47]
0.00 [0.00-97.50]
12.50 [0.32-52.65]
41.82 [36.34-47.46]
28.12 [13.75-46.75]
42.11 [20.25-66.50]
18.75 [4.05-45.65]
0.00 [0.00-16.84]
35.31 [22.32-50.92]

0.00 [0.00-97.50]
61.27 [57.44-65.00]
51.85 [31.95-71.33]
51.11 [35.77-66.30]
15.79 [3.38-39.58]
63.64 [30.79-89.07]
43.20 [42.12-44.29]
48.44 [36.96-60.09]

84.62 [54.55-98.08]
57.14 [34.02-78.18]
78.44 [73.90-82.51]
14.29 [3.05-36.34]
29.67 [23.56-36.36]
25.47 [17.51-34.86]
17.14 [10.49-25.73]
42.02 [19.96-67.81]

41.65 [34.01-49.70]



- **Results:**

- In-ICU mortality in reported studies ranged from 0 to 84.6%. Only seven studies reported outcome data for all patients.
- In the remaining 17 studies, the proportion of patients discharged from the ICU at the point of reporting varied from 24.5% to 97.2%.

- **Conclusions:**

- This systematic review and meta-analysis identified 24 observational studies including 10,150 patients from centers across Asia, Europe and North America, and demonstrated an ICU mortality rate in those with a completed ICU stay of 41.6% (95% CI, 34.0%-49.7%, $I^2=93.2\%$) broadly consistent across the world.

- **Key Takeaway:** The mortality of patients with COVID-19 admitted to the intensive care unit (ICU) is reportedly high, but the current literature contains small case series and cohort studies.

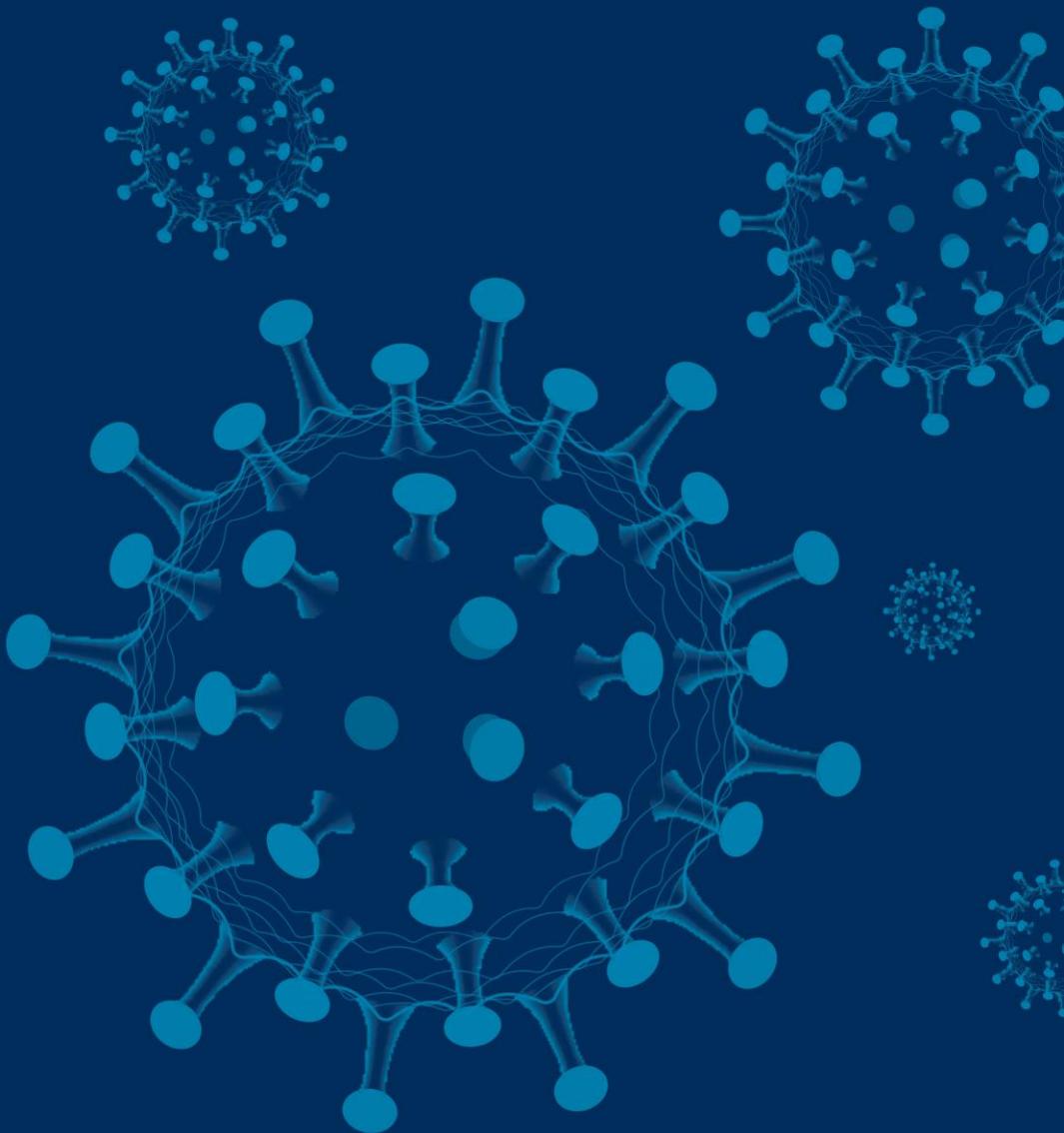


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Out-of-hospital Cardiac Arrest Response and Outcomes During the COVID-19 Pandemic

Uy-Evanado et al. *JACC Clin. Electrophysiol.*
2020; Aug. 14



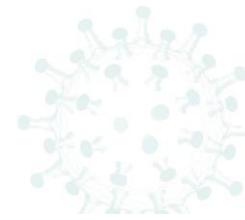
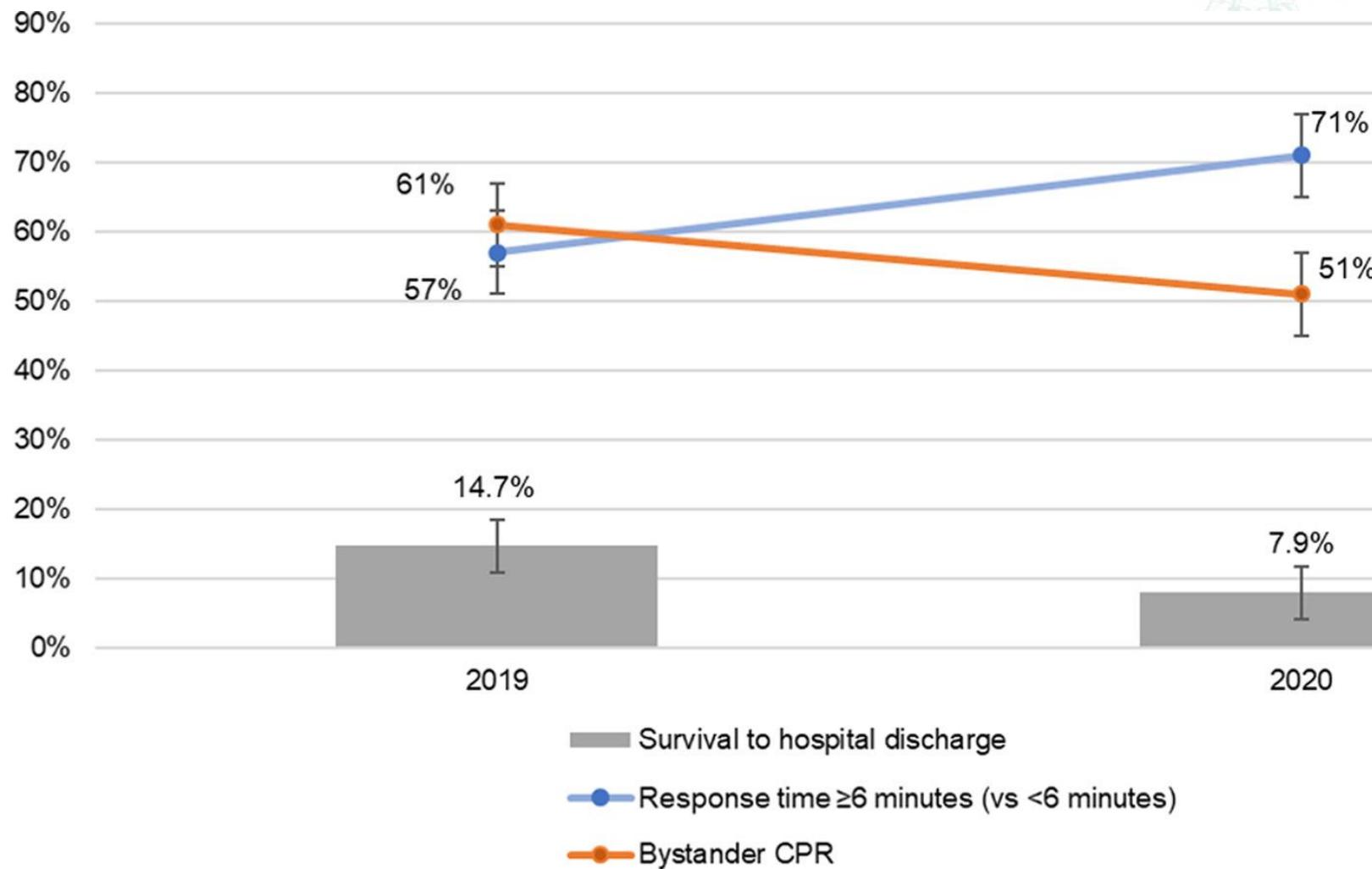
Out-of-hospital cardiac arrest during the pandemic

- Sites: Multnomah County, OR and Ventura County, CA
- Study period: March 1-May 31, 2020, compared with 2019
- OHCA incidence: 231 cases in 2019, 278 in 2020
- 3-month incidence rates
 - Multnomah: $12.2 \rightarrow 15/100,000$ ($P=0.12$)
 - Ventura: $14.2 \rightarrow 17.7/100,000$ ($P=0.07$)
- OHCA pts younger during pandemic (64.9 vs. 69.1 yr, $P=0.01$)
- More in-home OHCA during pandemic (61% vs. 51%, $P=0.01$)



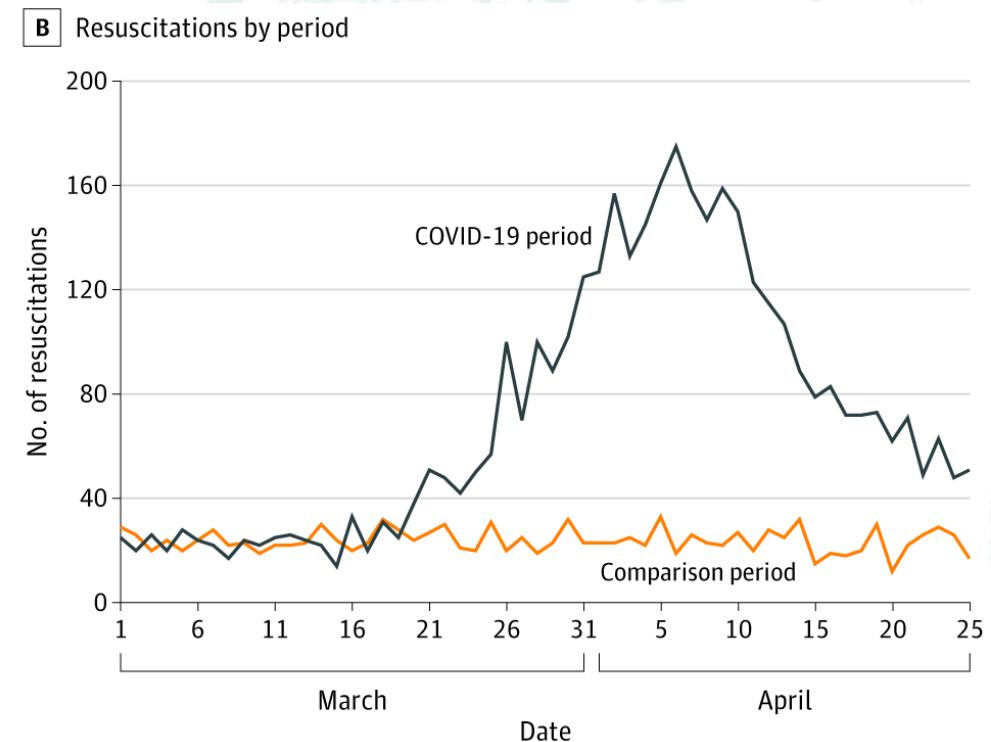
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Perspective: OHCA in US and Europe

- Marked increase in OHCA incidence in Italy, France, and NYC
- Non-shockable rhythms, failure to achieve ROSC more common
- Communities of color hardest hit
- Message to patients: if you feel sick, don't go it alone



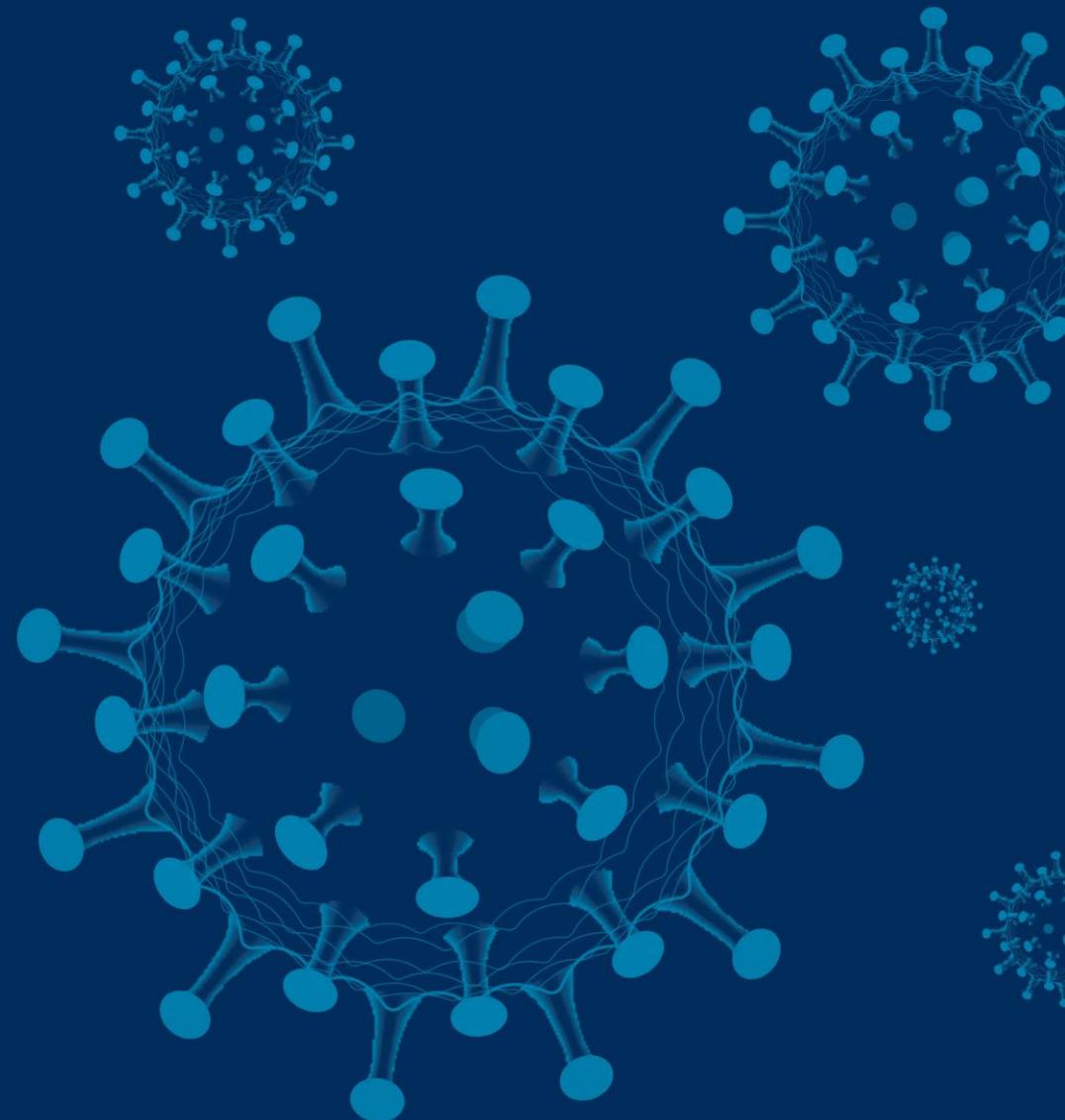


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Factors Associated with Death in Critically Ill Patients with Coronavirus Disease 2019 in the US

Gupta, et al *JAMA Internal Medicine* 2020 July 15



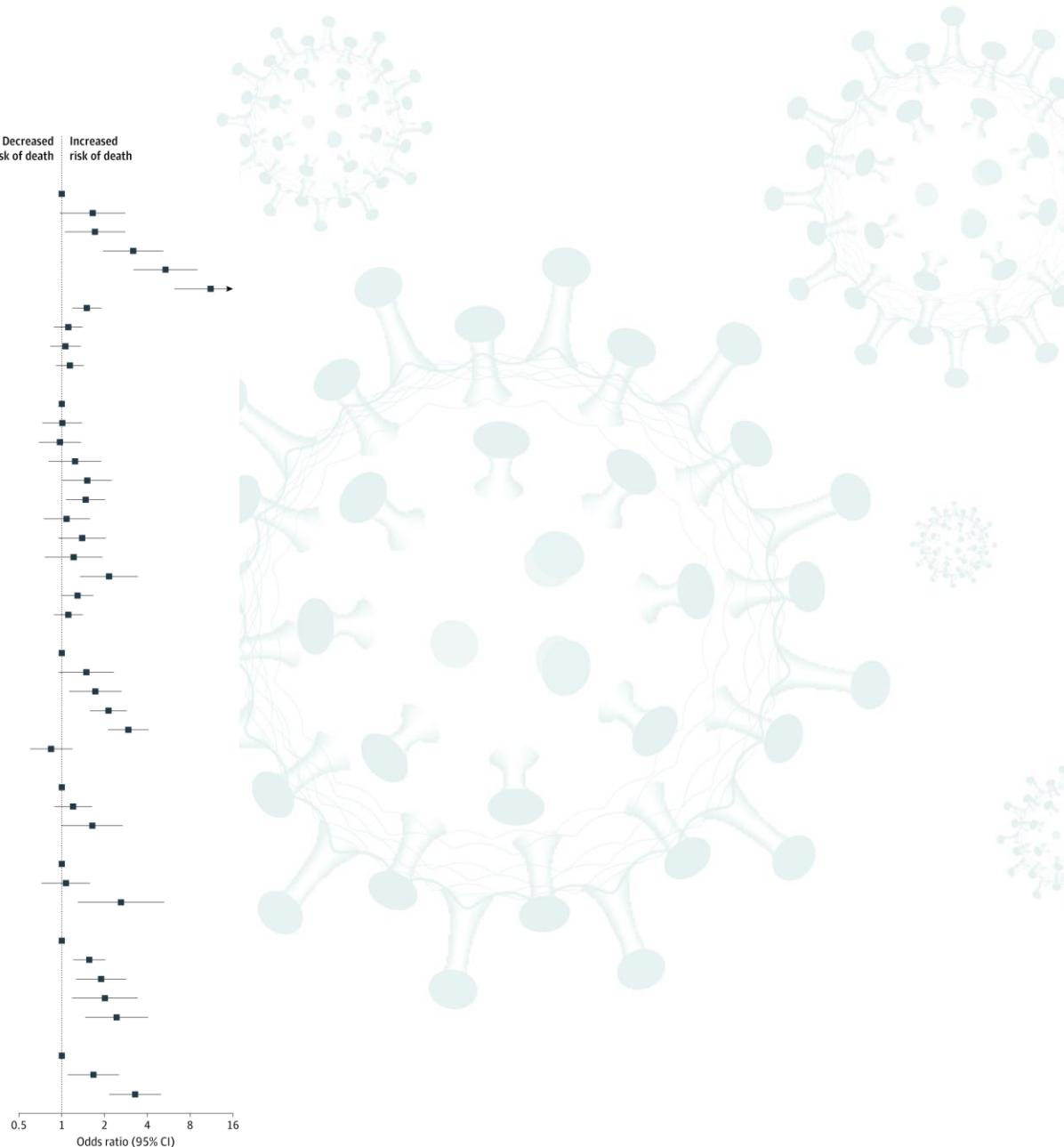
- **Study Question:** What are the characteristics, outcomes and factors associated with death among critically ill patients with coronavirus disease 2019 (COVID-19) in the US?

- **Methods:**

- This multicenter cohort study assessed 2215 adults with laboratory-confirmed COVID-19 who were admitted to ICUs at 65 hospitals across the US from March 4 to April 4, 2020.
- Patient level data, including demographics, comorbidities, and organ dysfunction, and hospital characteristics, including the number of ICU beds
- The primary outcome was 28-day in-hospital mortality.
- Multilevel logistic regression was used to evaluate factors associated with death and to examine inter-hospital variation in treatment and outcomes.



Characteristic	Odds ratio (95% CI) for death
Age group, y	
18-39	1 [Reference]
40-49	1.65 (0.97-2.80)
50-59	1.71 (1.05-2.80)
60-69	3.18 (1.95-5.18)
70-79	5.36 (3.20-9.00)
≥80	11.15 (6.19-20.06)
Male sex	1.50 (1.19-1.90)
Race other than White	1.11 (0.88-1.40)
Hypertension	1.06 (0.83-1.36)
Diabetes	1.14 (0.91-1.43)
BMI	
<25	1 [Reference]
25-29.9	1.01 (0.73-1.39)
30-34.9	0.97 (0.69-1.37)
35-39.9	1.24 (0.81-1.89)
≥40	1.51 (1.01-2.25)
Coronary artery disease	1.47 (1.07-2.02)
Congestive heart failure	1.08 (0.75-1.58)
Chronic obstructive pulmonary disease	1.39 (0.95-2.04)
Current smoker	1.21 (0.76-1.93)
Active cancer	2.15 (1.35-3.43)
≤3 d From symptom onset to ICU day 1	1.29 (0.99-1.67)
Lymphocyte count <1000/µL on ICU day 1	1.11 (0.88-1.41)
PaO ₂ :FiO ₂ on ICU day 1	
Not receiving IMV support	1 [Reference]
≥300	1.49 (0.95-2.33)
200-299	1.72 (1.13-2.63)
100-199	2.13 (1.58-2.87)
<100	2.94 (2.11-4.08)
Shock on ICU day 1	0.84 (0.60-1.19)
Coagulation component of SOFA score	
0	1 [Reference]
1	1.20 (0.89-1.63)
2	1.64 (1.00-2.69)
Liver component of SOFA score	
0	1 [Reference]
1	1.07 (0.72-1.58)
2	2.61 (1.30-5.25)
Renal component of SOFA score	
0	1 [Reference]
1	1.56 (1.20-2.02)
2	1.89 (1.26-2.84)
3	2.01 (1.18-3.42)
4	2.43 (1.46-4.05)
No. of ICU beds	
High (≥100)	1 [Reference]
Medium (50-99)	1.67 (1.10-2.53)
Low (<50)	3.28 (2.16-4.99)



- **Results:**

- A total of 2215 patients were included. At 28 days after ICU admission, 35.4% had died, 37.2% had been discharged, and 27.4% remained hospitalized.
- Factors independently associated with death included older age, male sex, higher body mass index, coronary artery disease, active cancer, presence of hypoxemia, liver dysfunction and kidney dysfunction at ICU admission.
- Patients admitted to hospitals with fewer ICU beds had a higher risk of death (< 50 vs > 100 ICU beds: OR, 3.28; 95% CI, 2.16-4.99).

- **Conclusions:**

- In this multicenter cohort study of critically ill adults with COVID-19 in the US, more than 1 in 3 died within 28 days after ICU admission.
- **Key Takeaway:** In a cohort of > 2200 patients with COVID-19 who were admitted to intensive care units (ICUs) at 65 geographically diverse sites in the US, 35% died within 28 days, with wide variation observed among hospitals.

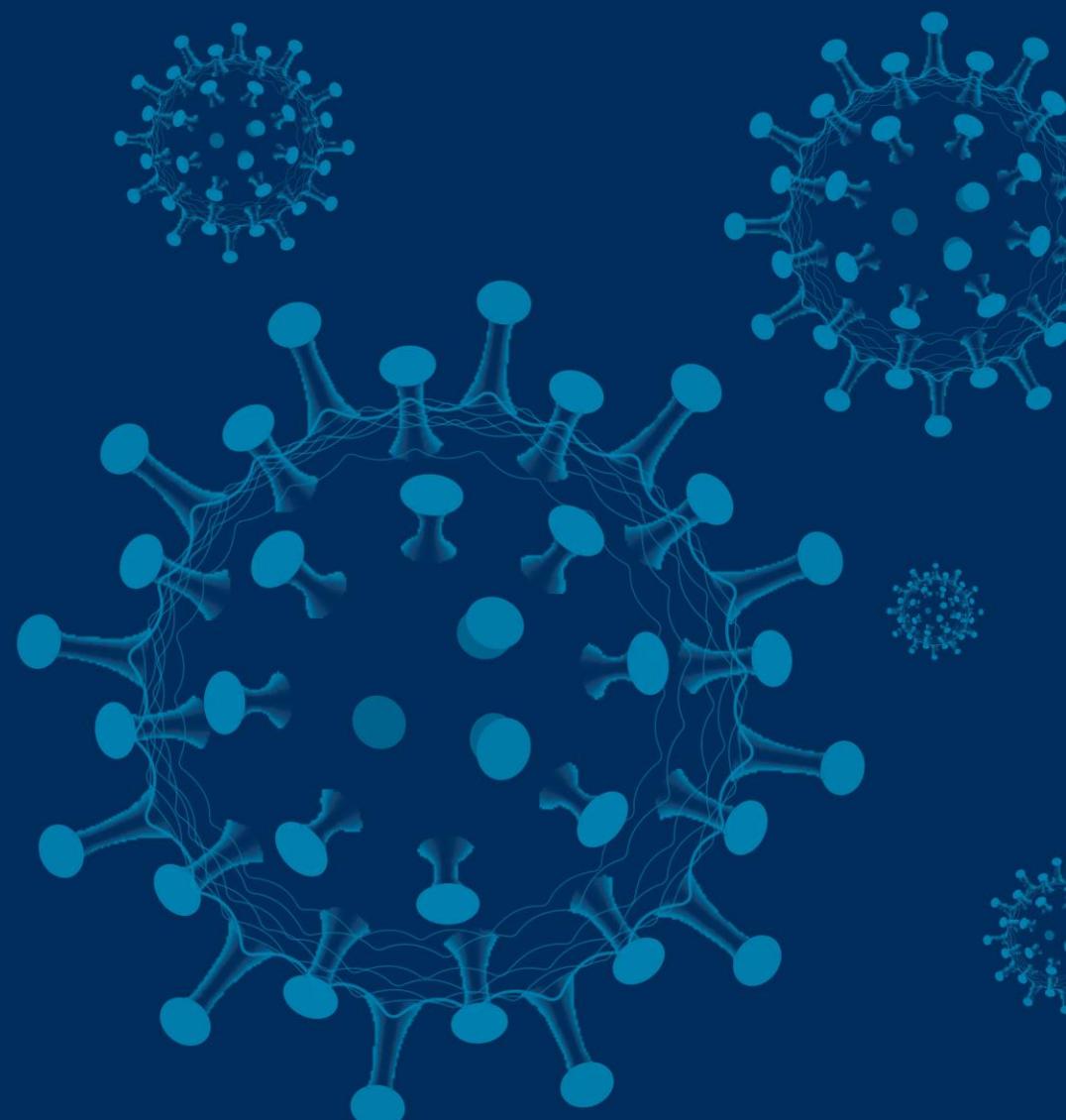


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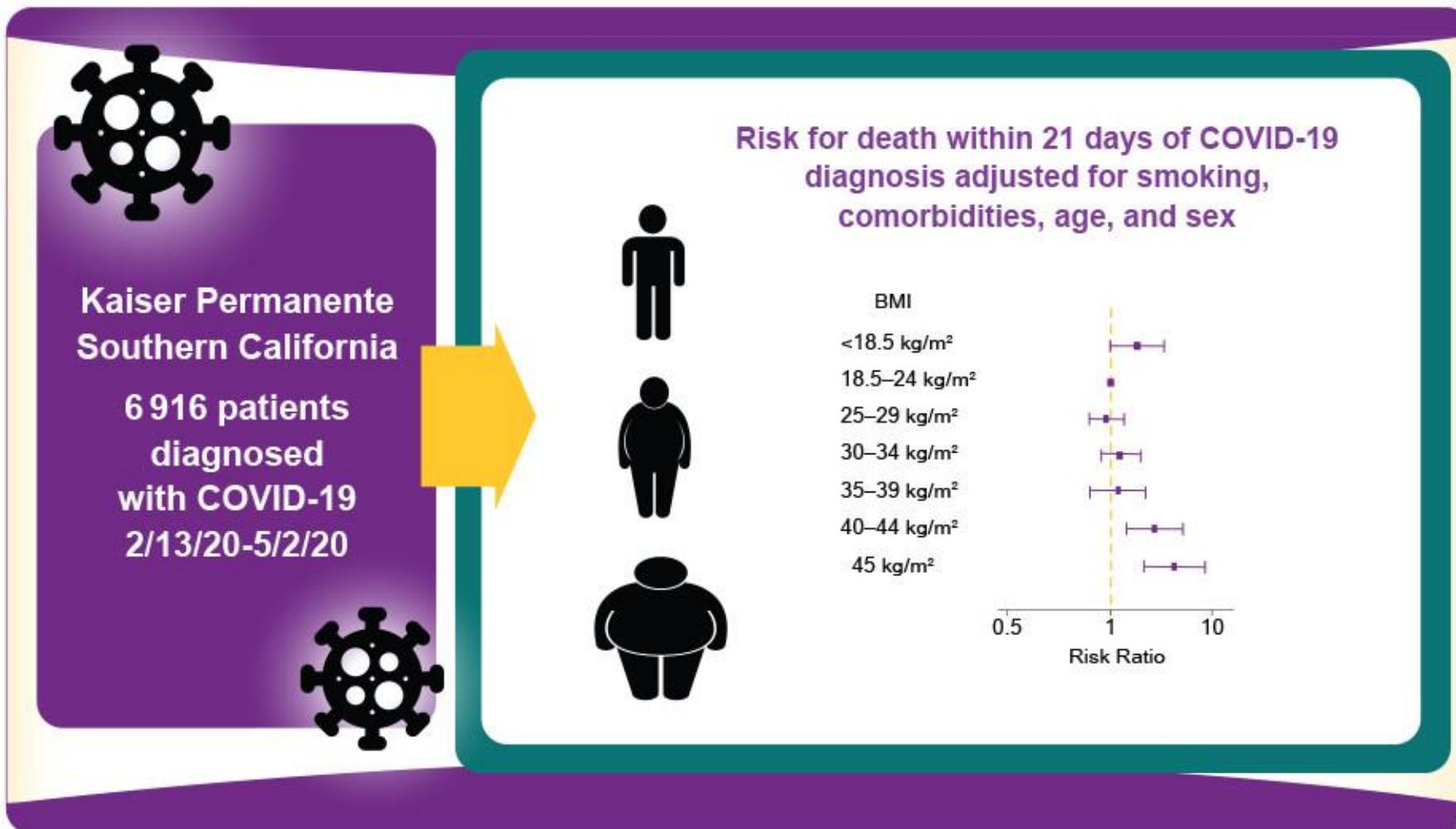
Obesity and Mortality Among Patients Diagnosed with COVID- 19: Results from an Integrated Healthcare Organization

Tartoff et al. *Annals of Internal Medicine* 2020 Aug 12



- **Study Question:** How is body mass index (BMI) associated with death due to coronavirus disease 2019 (COVID-19)?
- **Methods:**
 - The authors conducted a retrospective cohort study of all Kaiser Permanente Southern California members diagnosed with COVID-19 from February 13 to May 2, 2020, identified through ICD-10 codes or laboratory testing.
 - They examined the association between BMI and death within 21 days after diagnosis with COVID-19, stratified by whether or not they were hospitalized or intubated, and adjusting for individual-level factors such as race, sex, and clinical risk factors, in addition to neighborhood level factors such as population density and median income.
 - The authors also explored the interaction between BMI, age, and sex.

What is the association of body mass index (BMI) with risk for death in patients with COVID-19?



- **Results:**

- Of a total of 6,916 patients with COVID-19 identified (45% male, 55% Hispanics, median age 49 years, and mean BMI of 30.6 kg/m^2), 206 (3.0%) died.
- High BMI ($\geq 40 \text{ kg/m}^2$) was associated with a step-wise increase in the adjusted risk of death (2.7-fold increase for BMI 40-44, and 4-fold increase for BMI $\geq 45 \text{ kg/m}^2$), compared to patients with normal BMI of 18.5-24.
- The impact of obesity on the risk of death was strongest in men and younger patients (≤ 60 years). Overall, the association was independent of whether patients were hospitalized or intubated, or of clinical risk factors.

- **Conclusions:**

- Morbid obesity is associated with an increased risk of death, notably in men and patients ≤ 60 years of age.
- **Key Takeaway:** This study expands our understanding of the association of obesity with death from COVID-19 in many ways. It: 1) confirms previous reports that younger obese patients are likely to do worse, and 2) suggests that the relationship between obesity and death from COVID-19 is not related to comorbid risk factors, or racial or neighborhood level factors.

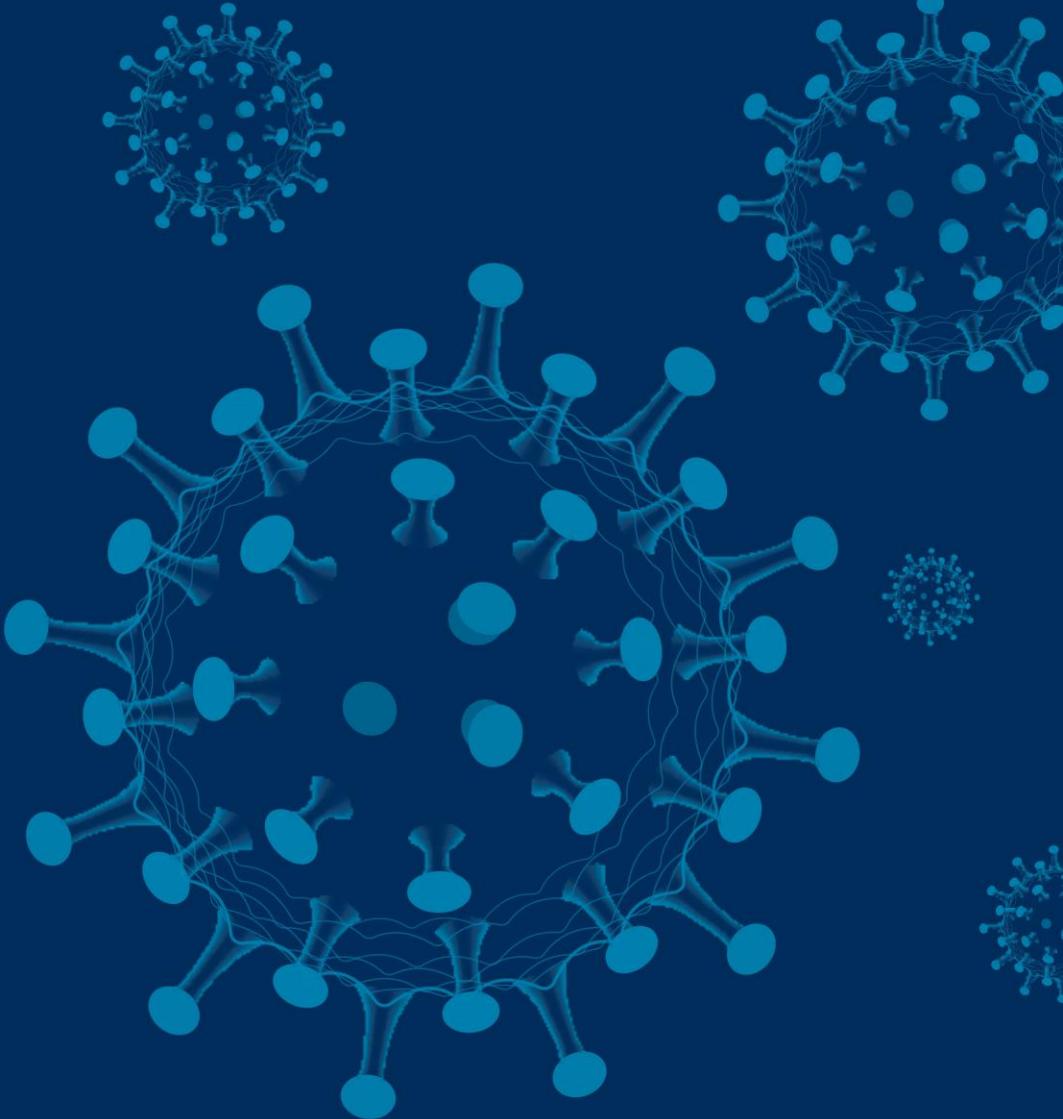


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Outcomes of STEMI Patients During the COVID-19 Pandemic in China

Xiang et al. JACC 2020 Aug 19



Management and Outcomes of Patients with STEMI During the COVID-19 Pandemic in China

Xiang et al.

- There has been concern about the impact of COVID-19 on STEMI care
- Best approach to providing timely and safe PCI during the COVID-19 pandemic has been debated.
- Retrospective analysis from the China Chest Pain Center of approximately 28,000 patients presenting with STEMI (Dec 27, 2019-Feb 20, 2020)
- STEMI protocol modified to default fibrinolytic therapy on January 23 2020 for unconfirmed COVID-19 cases



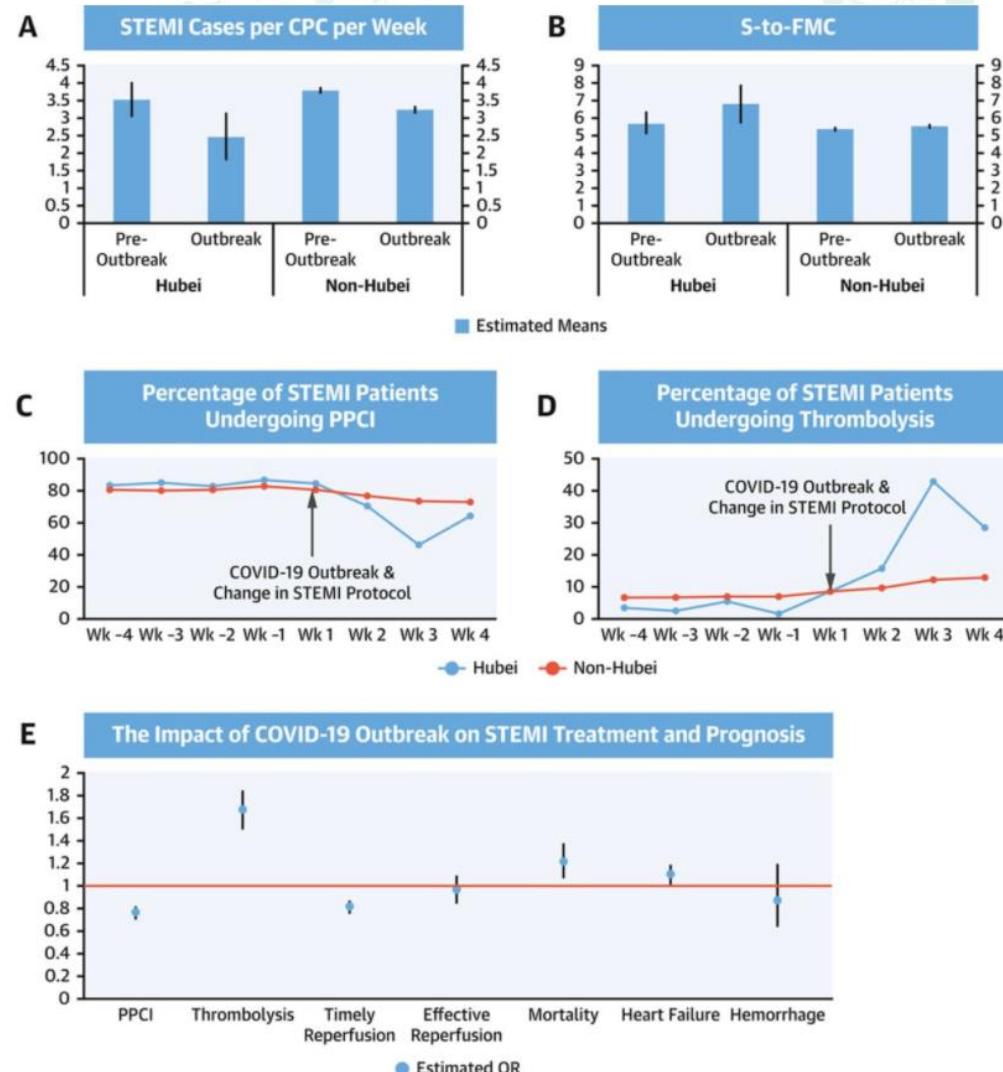
- **Key findings:**

- Total number of STEMI cases decreased (26%)
- Primary PCI dropped by 50% and fibrinolysis increased (4-fold)
- Non-significant increase in reperfusion times
- 20% increase in mortality. No significant increase in rates of bleeding

- **Conclusion:**

- STEMI care was adversely effected during the COVID-19 pandemic on mainland China.
- Reasons for increased mortality most likely multifactorial (delay in seeking care, change in reperfusion strategy, concomitant COVID-19 infection)

Management and Outcomes of Patients with STEMI During the COVID-19 Pandemic in China Xiang et al.

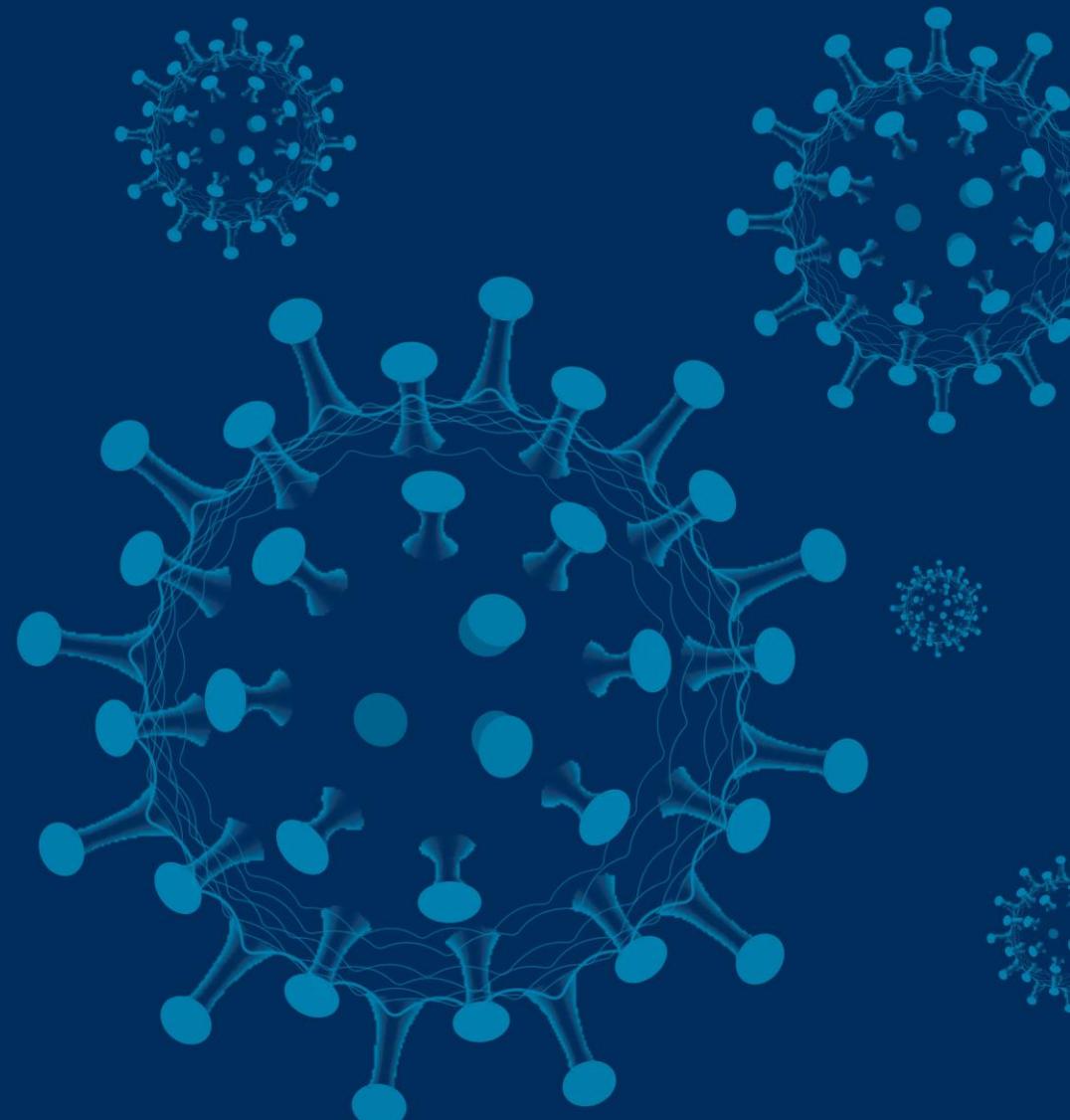




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Trends in ED Visits and Hospital Admissions in Health Care Systems in 5 States in the First Months of the COVID-19 Pandemic in the US



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

Jeffery M et al.

- Impact of COVID-19 pandemic on patients seeking timely healthcare have been evident in practices across the world.
- How did emergency department visits and hospitalizations change as Covid-19 pandemic intensified in the US?
- Cross-sectional analysis from 5 healthcare systems (Colorado, Connecticut, Massachusetts, New York and North Carolina) of ED visits and hospital admission from January to April 2020.



- **Key Findings:**

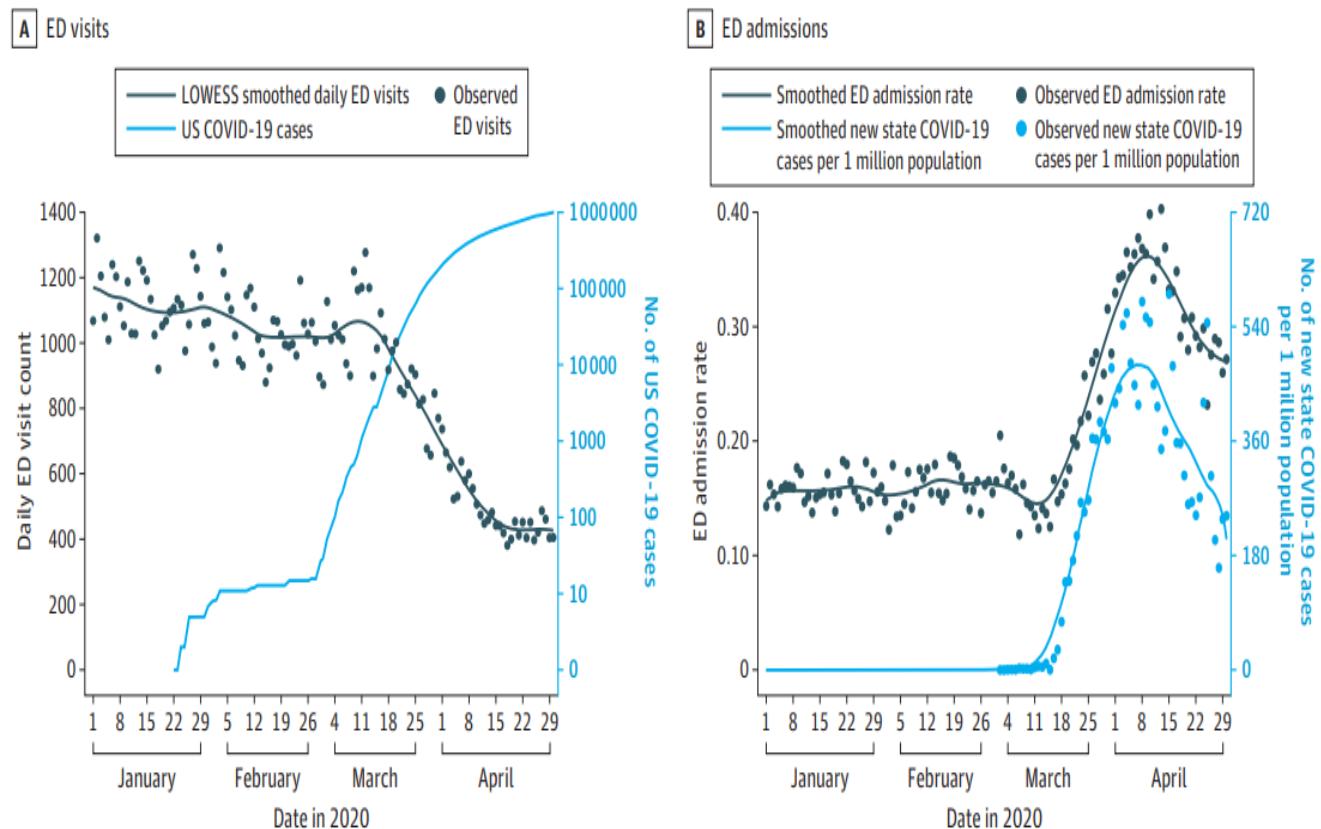
- ED visits decreased by more than 40% (up to 60% in New York)
- Hospital admission increased locally depending on COVID-19 surge (22% to 149%)
- Strong inverse temporal relationship between COVID-19 case surge and visits to ED.

- **Conclusion:**

- Stay at home orders dissuaded visits to the ED however impact of decreased ED visits on patient outcomes remains unknown.
- Increased admission rates shed light on COVID-19 burden on hospital systems

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

Jeffery M et al.



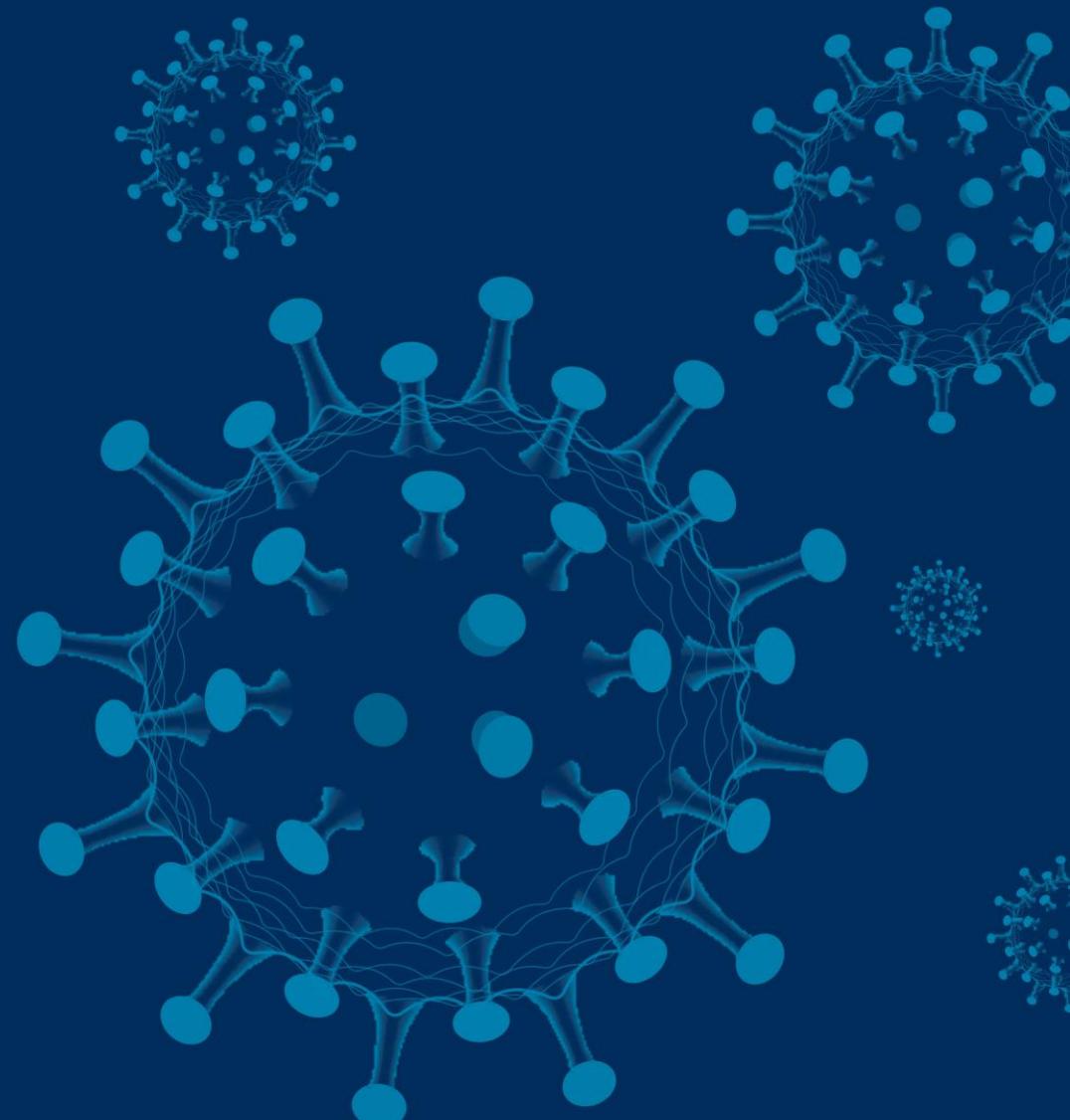


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Case Rates, Treatment Approaches, and Outcomes in Acute Myocardial Infarction During the Coronavirus Disease 2019 Pandemic

Gluckman et al *JAMA Cardiol* 2020 Aug 7





Case Rates, Treatment Approaches, and Outcomes in Acute Myocardial Infarction During the Coronavirus Disease 2019 Pandemic

Gluckman et al.

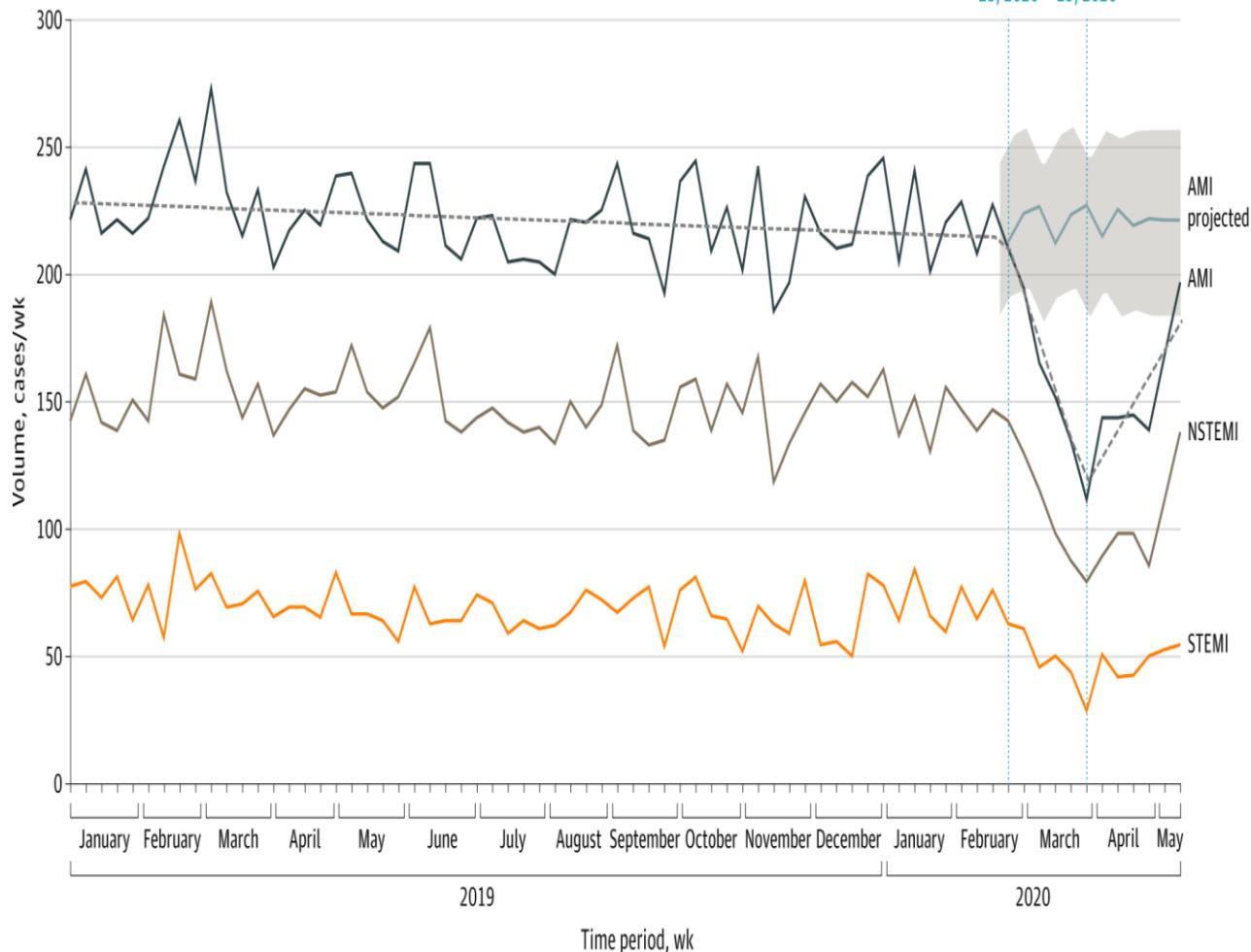
- How did COVID-19 effect management of and outcomes among patients with acute myocardial infarction in the United States?
- Retrospective analysis from a large hospital system across 6 US states (Alaska, Washington, Montana, Oregon, California and Texas)
- Data from 15,244 AMI patients (33% with STEMI and 67% with NSTEMI) hospitalized between Dec 30th 2019 to May 16th 2020 was retrospectively analyzed.



- Key Findings:
 - Appreciable decrease in AMI rates beginning February 23rd followed by slow correction
 - Observed/expected mortality ratios were significantly higher during the COVID-19 period among STEMI patients but not among the NSTEMI patients
 - Reperfusion strategies did not change over study period
- Conclusions:
 - AMI rates decreased sharply at the start of the pandemic but STEMI related mortality increased.
 - Delay in time to reperfusion and symptoms to first medical contact are speculated to play a role.

Case Rates, Treatment Approaches, and Outcomes in Acute Myocardial Infarction During the Coronavirus Disease 2019 Pandemic

Jeffery et al.





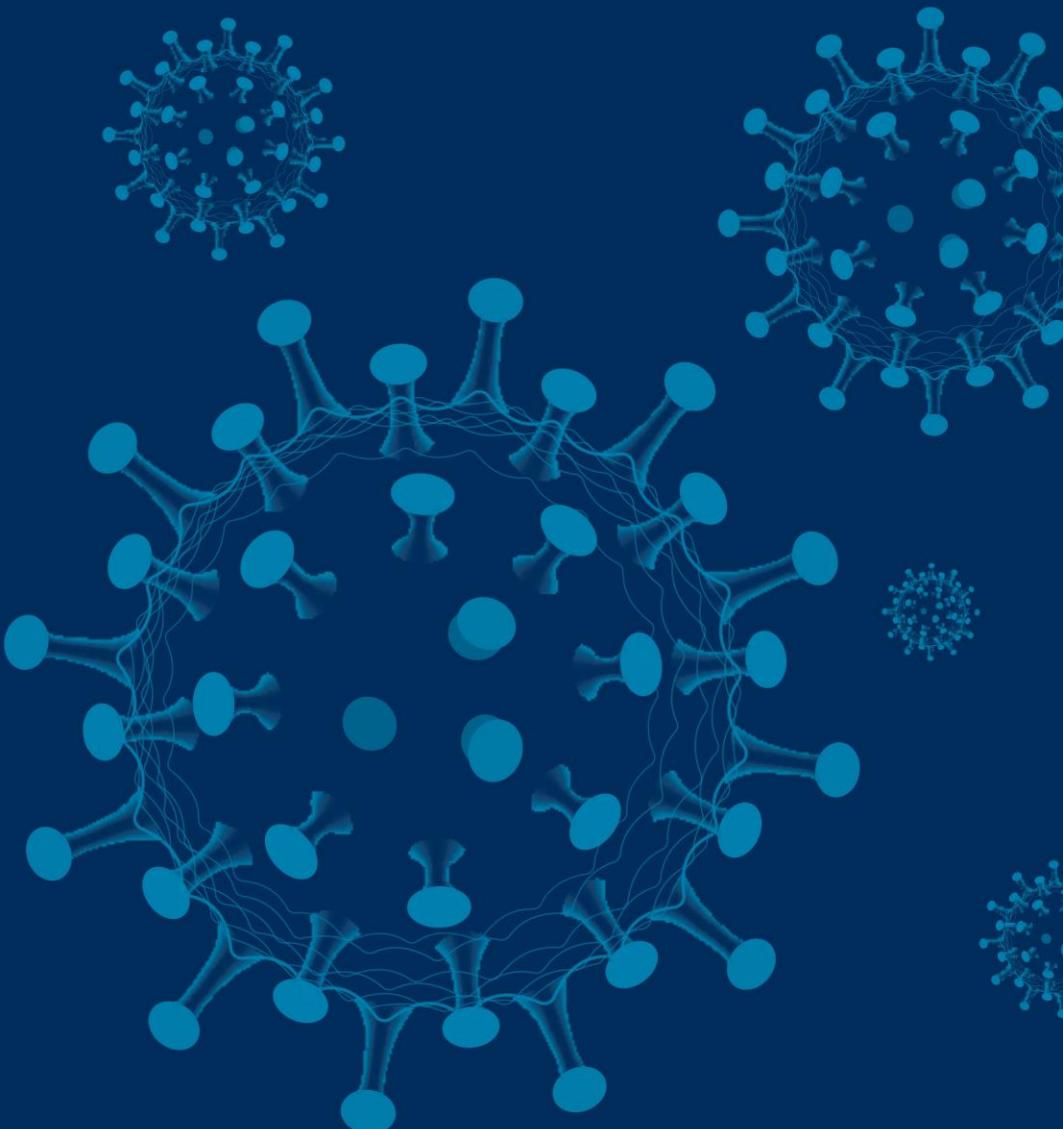
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Anticoagulation Among Patients Hospitalized With COVID-19 and; Post-discharge Venous Thromboembolism Following Hospital Admission with COVID-19

Nadkarni et al *JAMA* 2020, Aug 26

Roberts et al *Blood* 2020 Aug 3



COVID-19 and Thrombosis Risk

- Variable risk estimates for venous thromboembolism
 - 4%-46% in hospitalized patients
 - Unknown post-hospital risk
- How best to prevent thrombosis?
 - What dose of anticoagulation?
 - Should it continue post-hospital?



Study Design

Inclusion

- Adult patients hospitalized with COVID-19 March-April, 2020
- 5 Hospitals in New York City

Research Question

Therapeutic vs. Prophylactic vs. No anticoagulation and in-hospital mortality, intubation, or bleeding?

Just Accepted

Anticoagulation, Mortality, Bleeding and Pathology Among Patients Hospitalized with COVID-19: A Single Health System Study

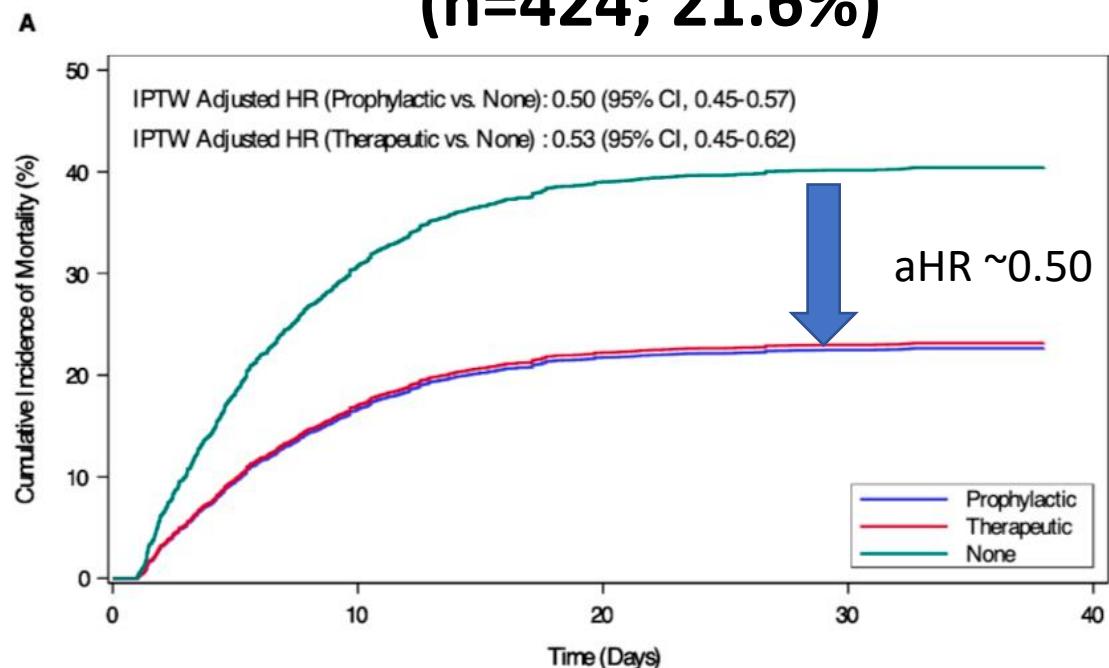
Girish N. Nadkarni, Anuradha Lala, Emilia Bagiella, Helena L. Chang, Pedro Moreno, Elisabet Pujadas, Varun Arvind, Sonali Bose, Alexander W. Charney, Martin D. Chen, Carlos Cordon-Cardo, Andrew S. Dunn, Michael E. Farkouh, Benjamin Glicksberg, Arash Kia, Roopa Kohli-Seth, Matthew A. Levin, Prem Timsina, Shan Zhao, Zahi A. Fayad and Valentin Fuster

Exclusion

- Hospitalized <24 hours
- Received prophylaxis AND therapeutic anticoagulation



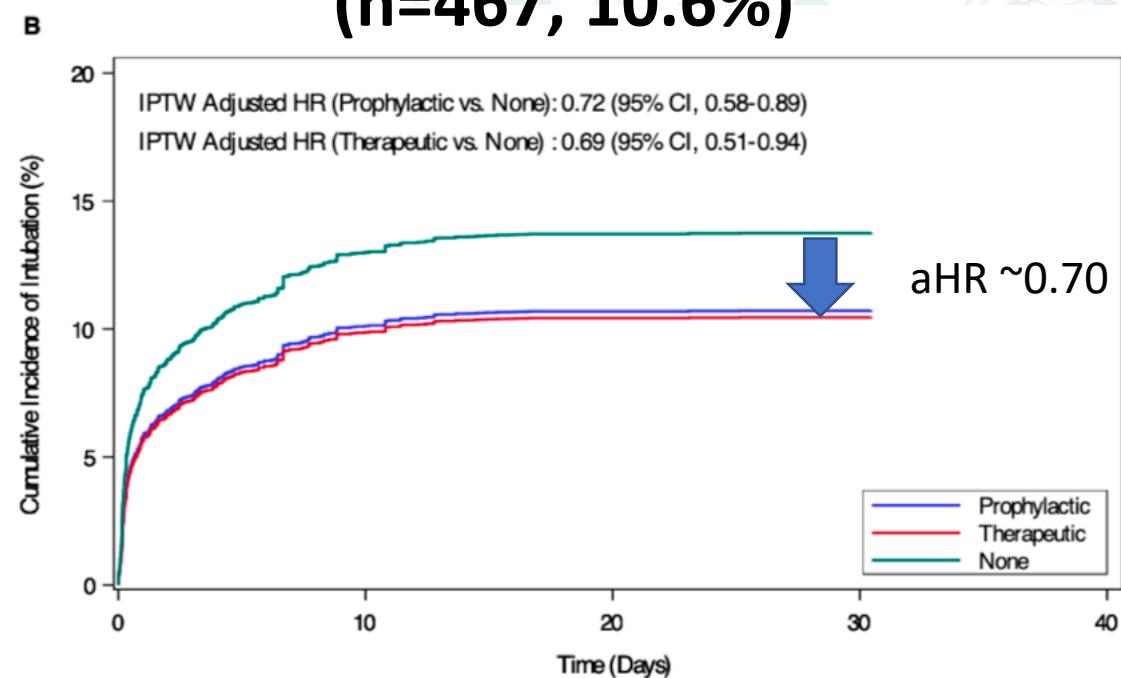
In-hospital Mortality (n=424; 21.6%)



4389 patients total

900 therapeutic; 1959 prophy; 1530 "none"

Intubation (n=467, 10.6%)



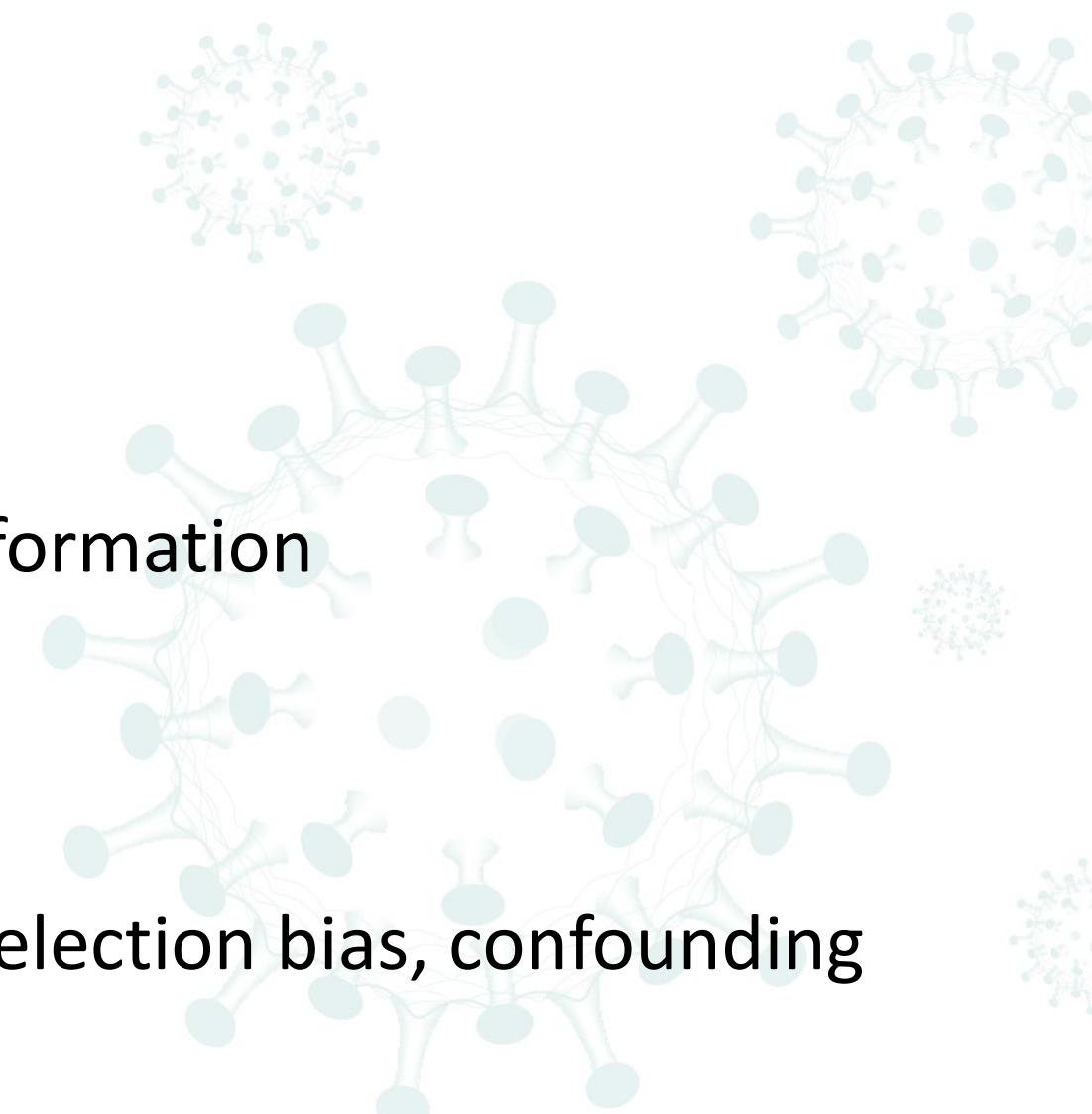
Major bleeding in 89 patients

3.0% therapeutic, 1.7% prophy, 1.9% "none"



Take Away Message

- Anticoagulation prevents thrombosis formation
 - Treatment dose \cong Prophylactic dose?
- Overall major bleeding rates are low
- Observational Study → potential for selection bias, confounding





Study Design

COVID-19 Cohort

- Adult patients discharged with COVID-19
March 3 – May 7, 2020
- Follow up through June 17, 2020
- 2 Hospitals in London, UK

Research Question

- What is risk of post-discharge hospital-associated VTE?

Post-discharge venous thromboembolism following hospital admission with COVID-19

Lara N Roberts , Martin Brunel Whyte, Loizos Georgiou, Gerard Giron, Julia Czuprynska, Catherine Rea, Bipin Vadher, Raj Patel, Emma Gee, Roopen Arya

Check for updates

Blood [blood.2020008086](https://doi.org/10.1182/blood.2020008086).

<https://doi.org/10.1182/blood.2020008086>

Article history

Non-COVID-19 Cohort

- Adult patients hospitalized 2019



VTE Prophylaxis Regimen



Table. Weight based dosing of thromboprophylaxis for acutely ill medical patients at high VTE risk (without bleeding risk factors)

Weight	No renal impairment, eGFR \geq 30ml/min	Renal impairment, eGFR 15-30ml/min	End stage renal impairment, eGFR <15ml/min or dialysis dependent
<50kg	Enoxaparin 20mg daily	Contact haematology for advice	Unfractionated heparin 5000 units bd
50-100kg	Enoxaparin 40mg daily	Enoxaparin 20mg daily	Unfractionated heparin 5000 units bd
101-150kg	Enoxaparin 40mg bd or 80mg daily	Enoxaparin 20mg daily	Unfractionated heparin 5000 units tds
>150kg	Enoxaparin 60mg bd or 120mg daily	Contact haematology for advice	Unfractionated heparin 5000 units tds

VTE, venous thromboembolism; bd, twice daily; tds, three times daily; GFR, glomerular filtration rate.

Prophylaxis “intensified” for ICU patients



Results

	COVID-19 London	2019 London
Total Discharges	1877	18,159
All Hosp-associated VTE	84 (2.9%)	
Post-hospital VTE (42 day)	9 (0.5%)	56 (0.3%)
Time to VTE (median, days)	8 (range 3-33)	29 (IQR 16-51)



Take Away Message

- Post-hospital VTE risk only slightly higher in COVID vs. non-COVID patients
 - Low rates of in-hospital VTE as well
- Utility of post-hospital VTE prophylaxis?
- No data on which patients are highest risk



COVID-19 and VTE: How to Manage?

- In-hospital VTE prophylaxis for ALL
- Selective use of “intermediate” dose prophylaxis (e.g, ICU patients)
- Limited use of post-hospital prophylaxis
- Participate in clinical trials of prophylaxis vs. treatment anticoagulation

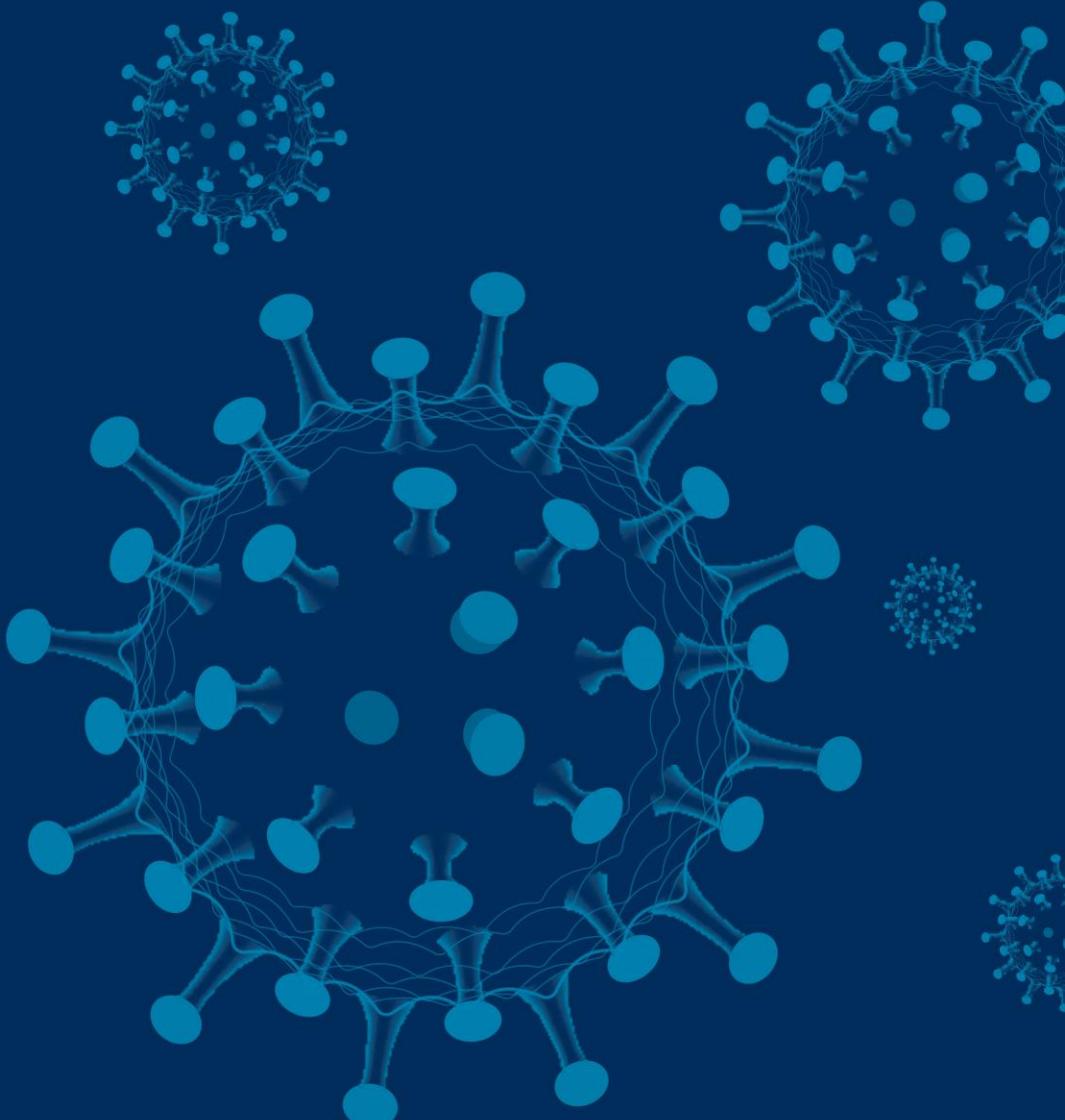


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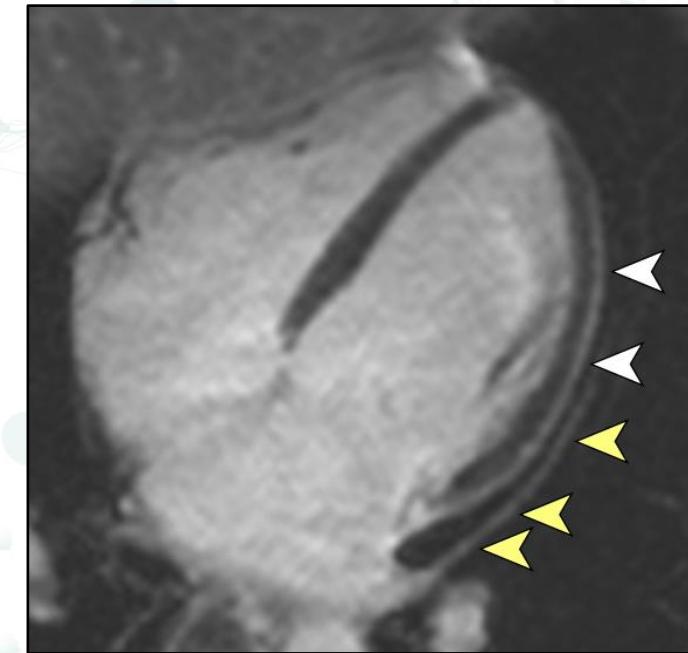
Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered from COVID-19

Puntmann et al. JAMA Cardiol. 2020; Jul 27



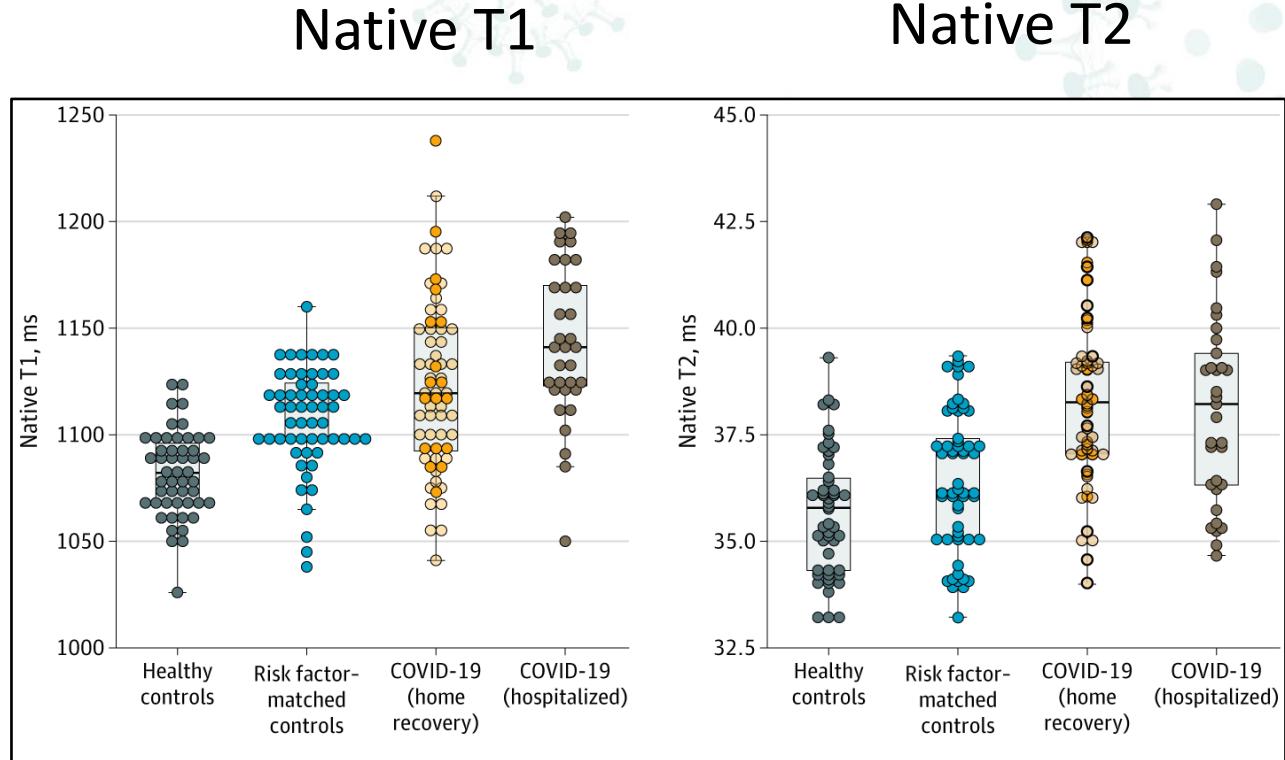


- N=100 pts in University of Frankfurt COVID-19 registry, ≥ 2 wks from initial dx, with respiratory recovery
- Patients referred for clinical CMR excluded
- Healthy and risk-factor matched controls
- CMR protocol: native T1 and T2 mapping, late gadolinium enhancement (LGE) imaging
- Mean age 49 yrs, 53% male
- COVID severity: 33% hospitalized, 2% ventilated, 15% with hsTnT ≥ 13.9 pg/ml in hospital
- At time of CMR, hsTnT detectable (> 3 pg/ml) in 71%





- Abnormal CMR findings: 78%
 - Increased native T1: 73%
 - Increased native T2: 60%
 - Myocardial LGE: 32%
 - Pericardial LGE: 22%
- Biopsy in 3 pts → lymphocytic inflammation, no viral genome
- AUC in pts vs. healthy controls
 - Native T1: 0.86
 - Native T2: 0.84
 - LVEF: 0.70
 - RVEF: 0.74
 - hsTnT: 0.79
 - NT-proBNP: 0.56 (P=NS)



CMR in COVID: unanswered questions

- Are non-cardiac muscles also affected?
- What are the clinical implications of mild CMR abnormalities?
- How should these patients be followed?
- What about exercise?

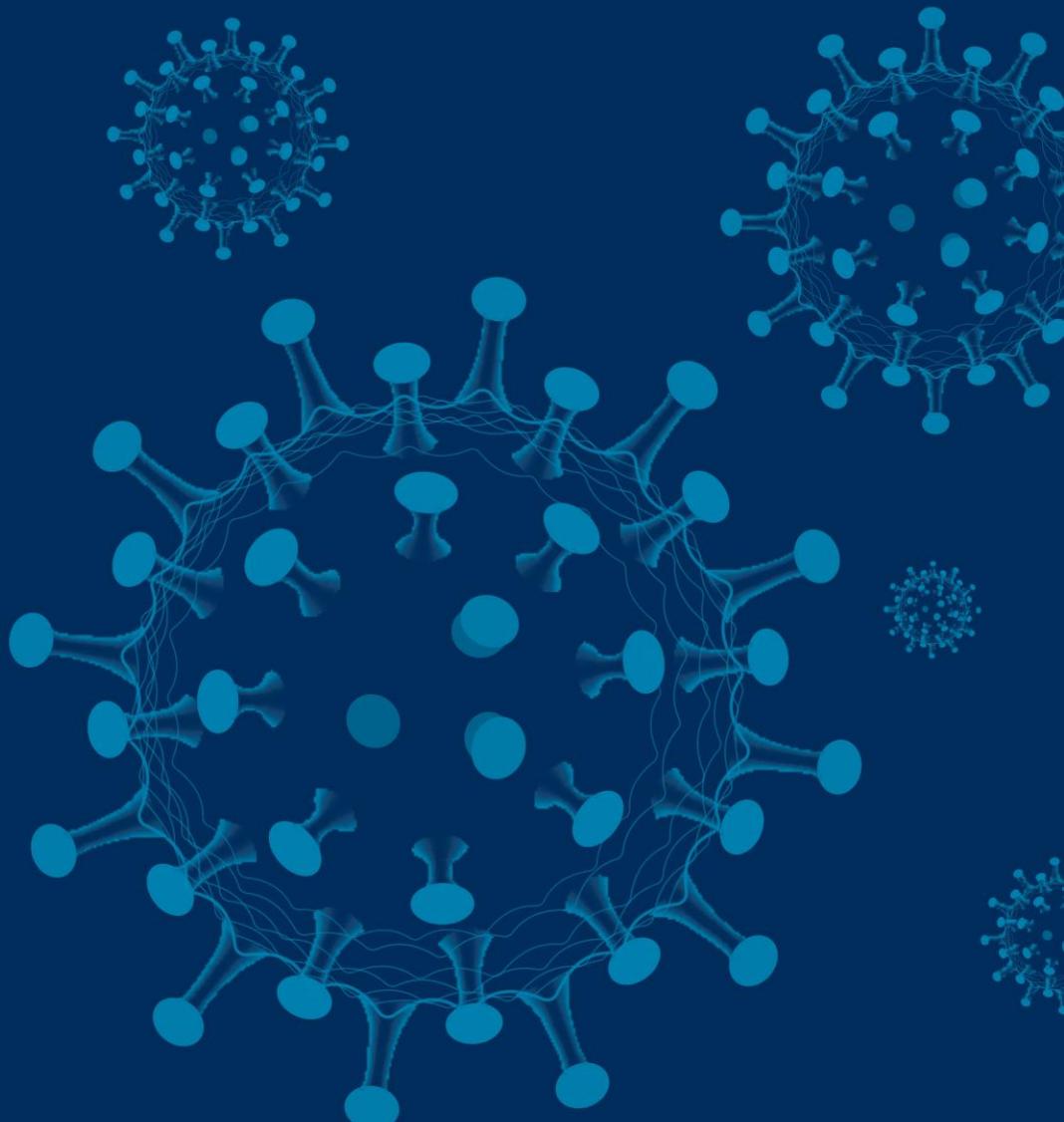


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Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19

Bavry, ACC.org Trial Summary, 2020
Aug 24





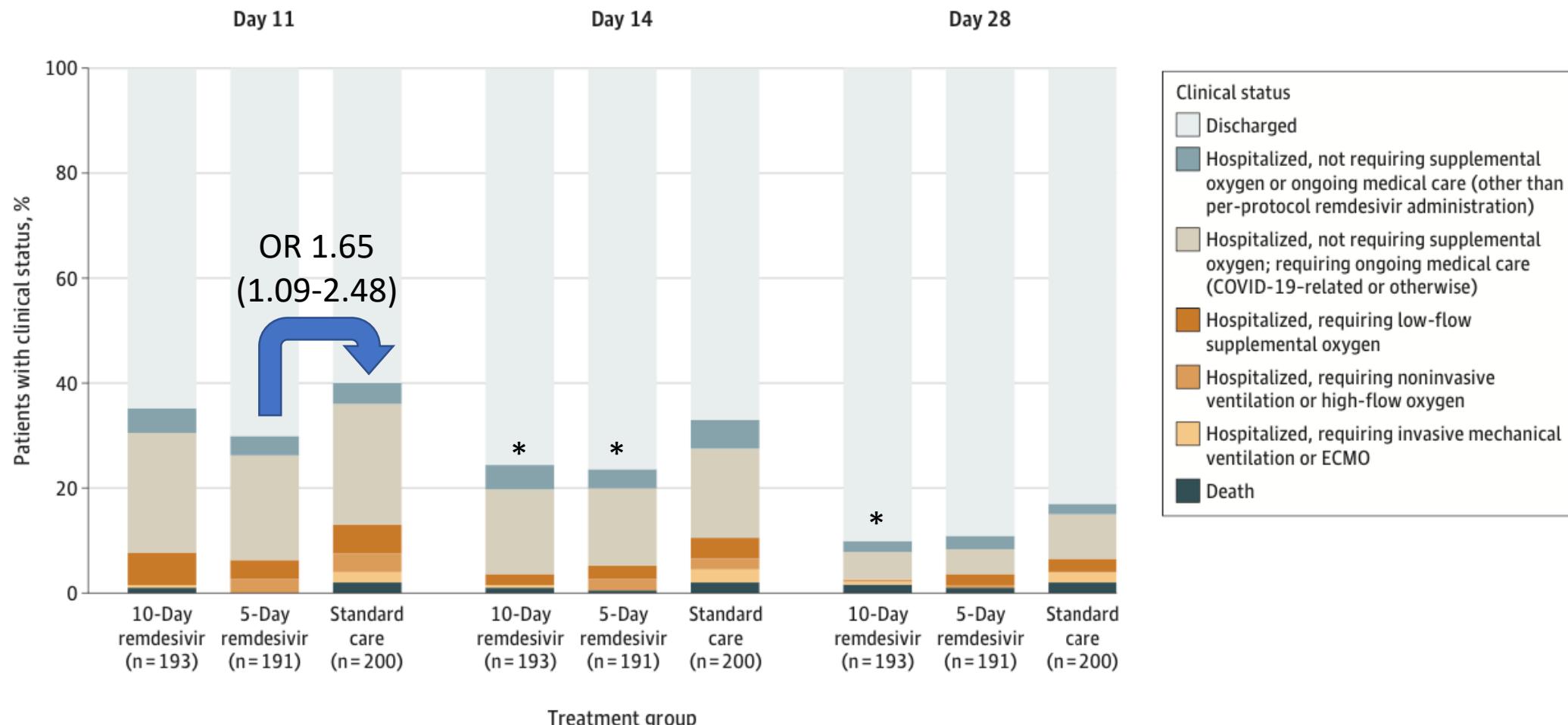
Study Design

- Randomized, parallel, open-label design in US, Europe, Asia (105 hosp)
- Inclusion: COVID-19 infection, moderate pneumonia ($\text{SpO}_2 > 94\%$ on room air)
- Exclusion: $\text{AST}/\text{ALT} > 5 \times \text{ULN}$, $\text{CrCl} < 50 \text{ ml/min}$
- Intervention: remdesivir x10d (n=197), x5d (n=199), or none (n=200)
- Primary outcome: Disease progression

Christoph D. Spinner, MD¹; Robert L. Gottlieb, MD, PhD²; Gerard J. Criner, MD³; [et al](#)



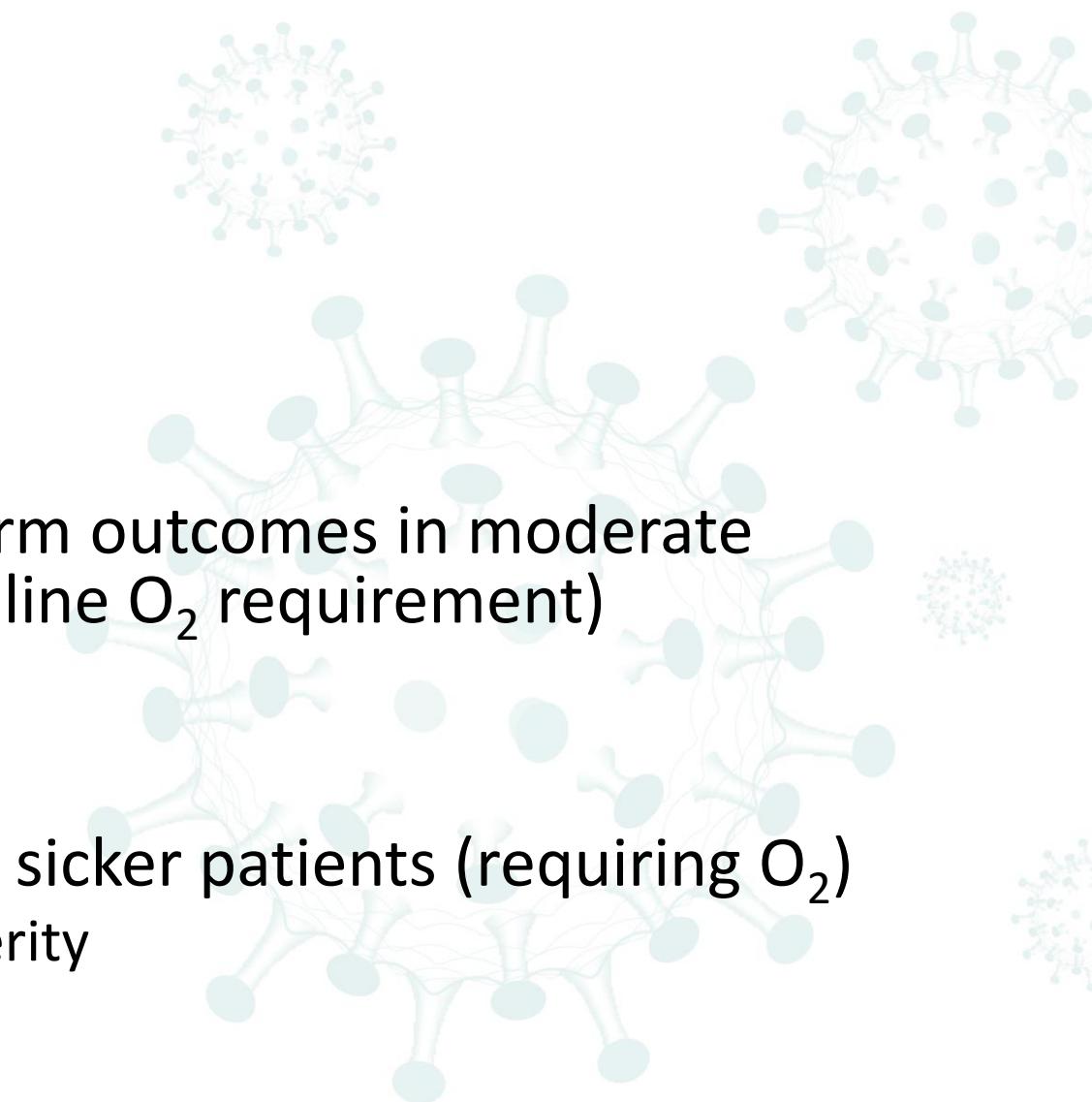
Figure 2. Clinical Status on a 7-Point Ordinal Scale on Study Days 11, 14, and 28 by Treatment Group





Take Away Message

- Remdesivir may slightly improve short-term outcomes in moderate COVID-19 infection (hospitalized, no baseline O₂ requirement)
 - Uncertain clinical importance
- Remdesivir use may be most effective for sicker patients (requiring O₂)
 - Some mixed efficacy results by baseline severity



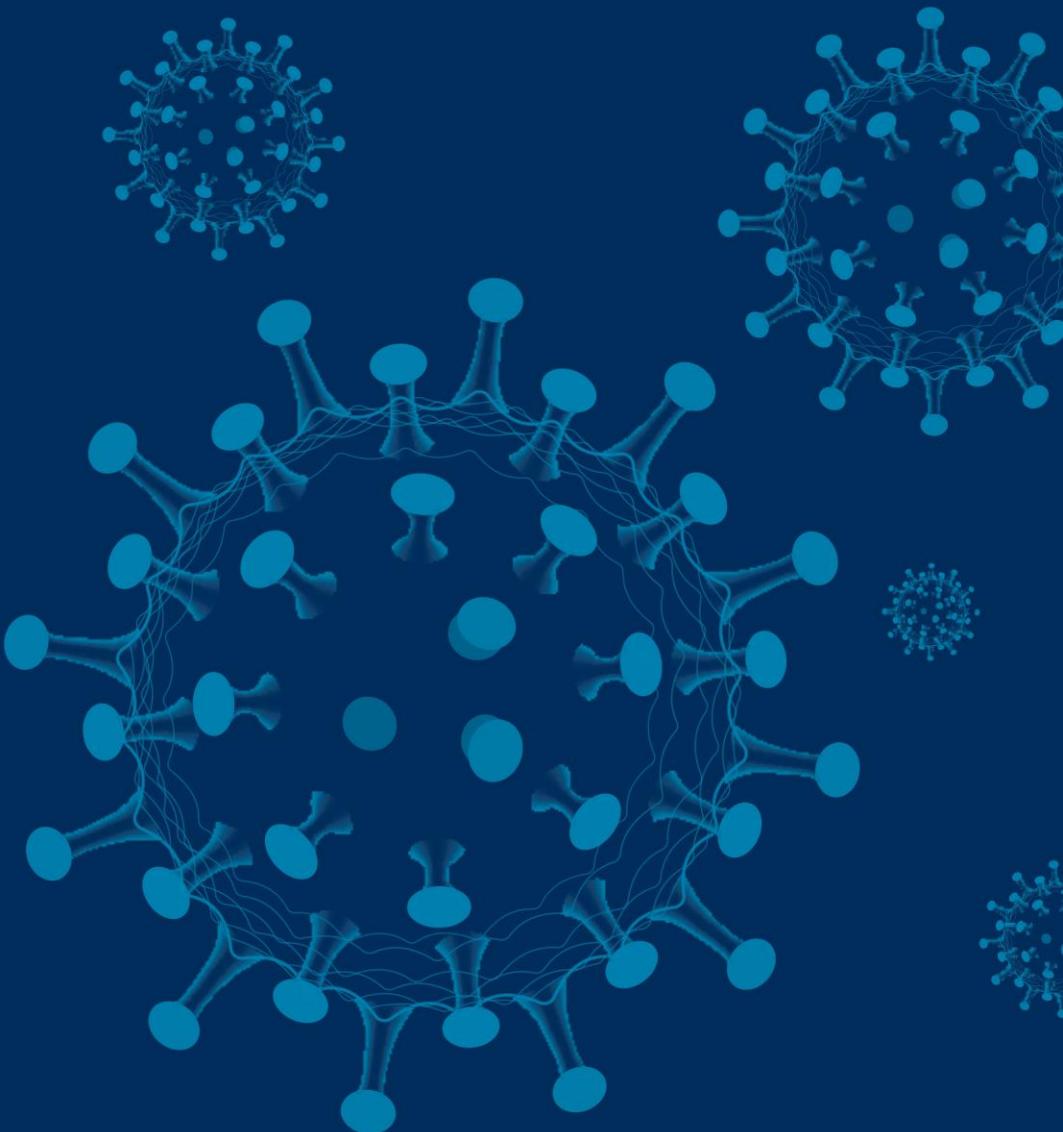


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COVID-19

Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report

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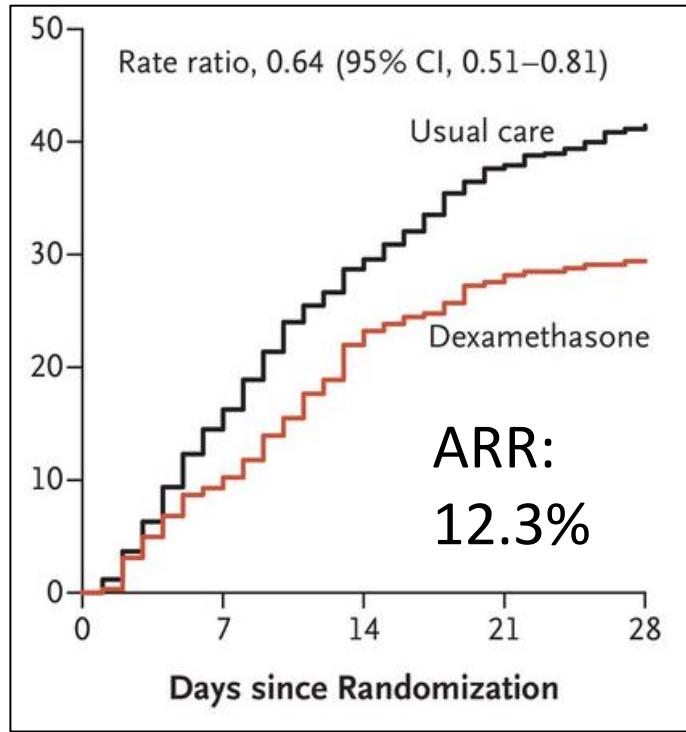


Dexamethasone in COVID-19

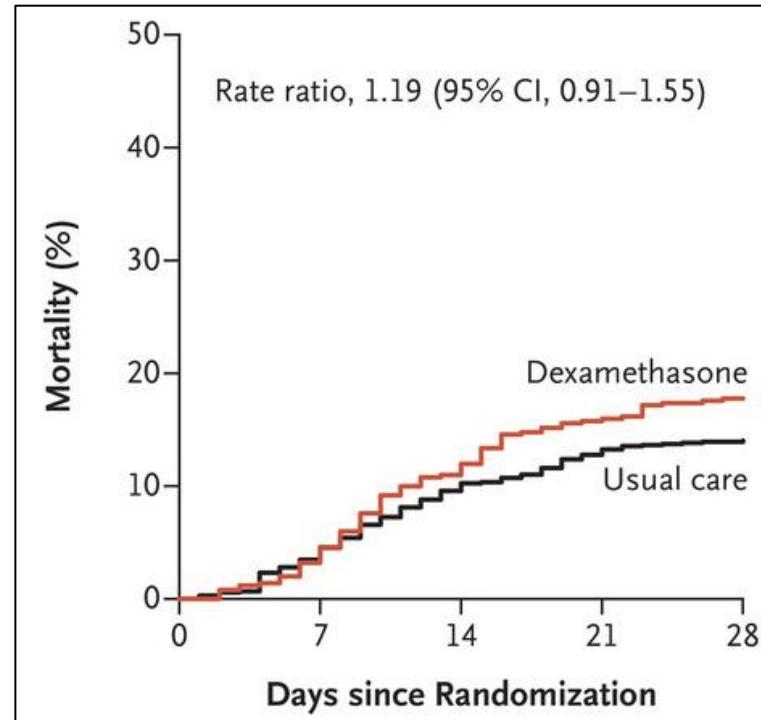
- Open-label trial at 176 UK sites
- Dexamethasone 6 mg daily: 2104 pts; usual care: 4321 pts
- Other treatments studied: tocilizumab, convalescent plasma, azithromycin (hydroxychloroquine, lopinavir-ritonavir stopped)
- Data collection: web-based forms
- Primary endpoint, all-cause mortality at 28 days: 22.9% dex, 25.7% usual care (rate ratio 0.83, 95% CI 0.75-0.93, $P<0.001$)



Ventilation (N=1007)



No oxygen (N=1535)



Perspective

- Dexamethasone on WHO essential med list; widely available at low cost
- Need data on cardiovascular effects of steroids
- Hyperglycemia must be managed



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