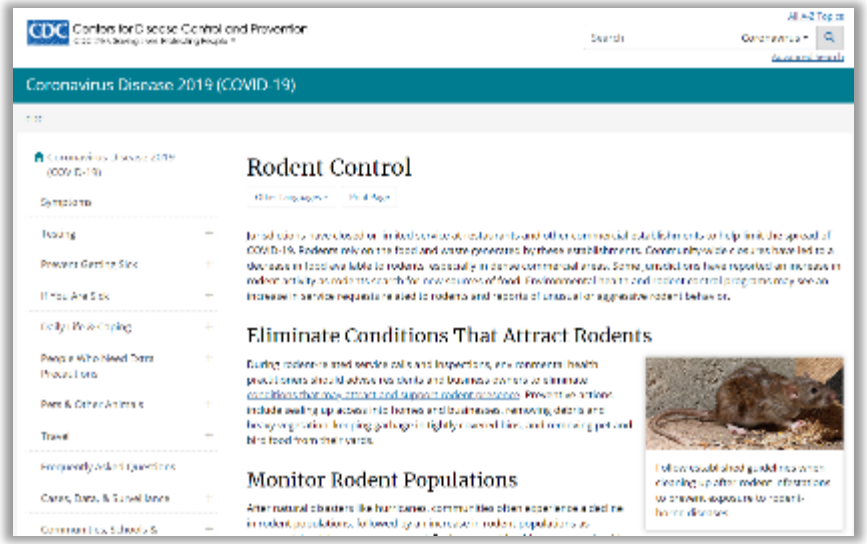
5-28-2020

# Covid-19 Clinical Update 5/28/2020

George Washington University

1. EPIDEMIOLOGY
2. TRANSMISSION
3. PATHOPHYSIOLOGY
4. TREATMENT
5. GW UPDATES



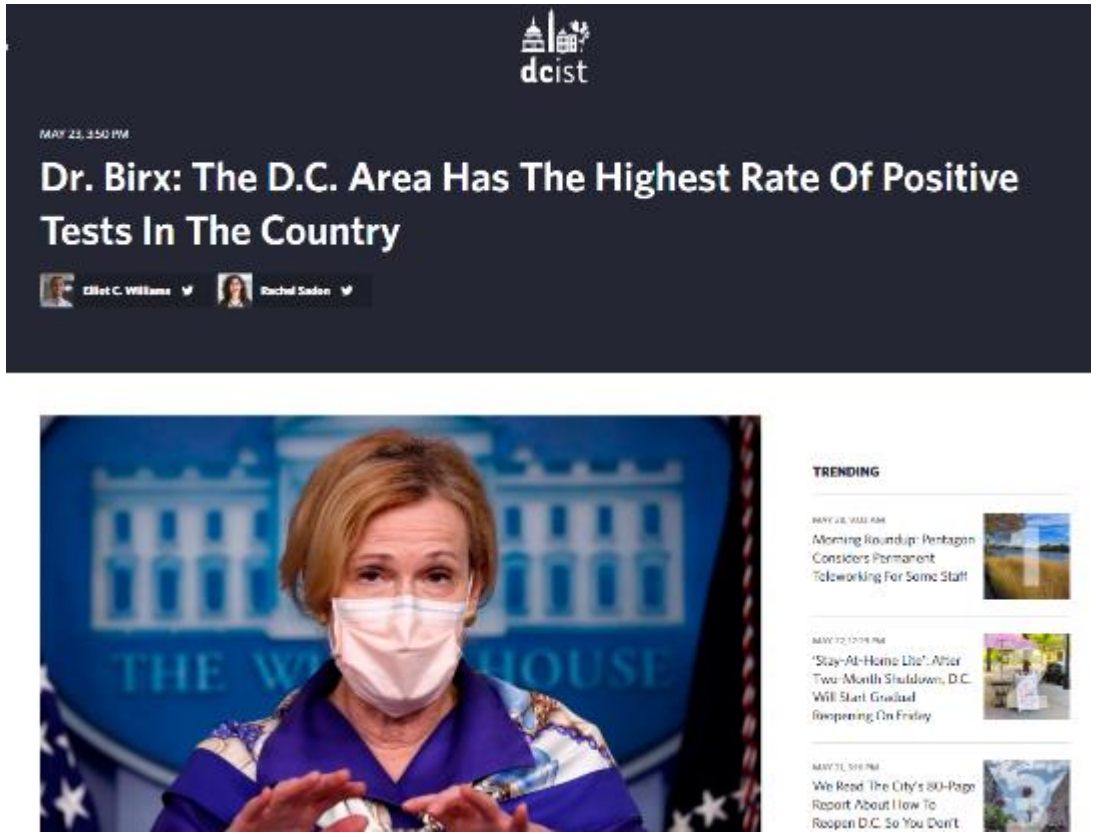

# COVID-19 UPDATE

HANA AKSELROD, MD, MPH
GW DIVISION OF INFECTIOUS DISEASES
5/28/2020

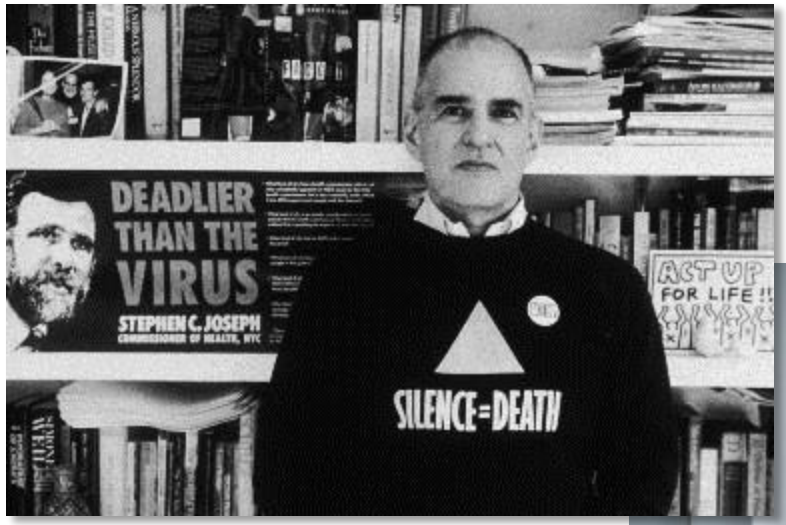
https://www.popville.com/2020/05/expect-the-unexpected-in-coronaville/
https://www.cdc.gov/coronavirus/2019-ncov/community/rodents.html

# Disclosures

- No financial COI
- Pre-print/investigational information discussed
- DC resident




https://dcist.com/story/20/05/23/dr-birx-the-d-c-area-has-the-highest-rate-of-positive-tests-in-the-country/




# “Show me a plague, and I’ll show you the world!”
-- Larry Kramer (1935-2020)

https://www.nytimes.com/2020/03/28/nyregion/coronavirus-larry-kramer-aids.html

# Known coronavirus deaths and cases in D.C., Maryland and Virginia

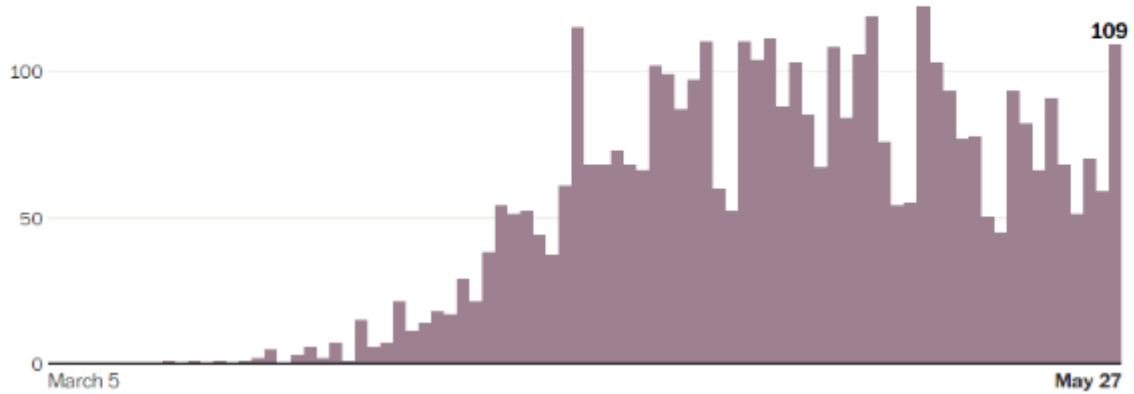
There are a total of **4,118 deaths** and **97,078 cases** confirmed in the region.

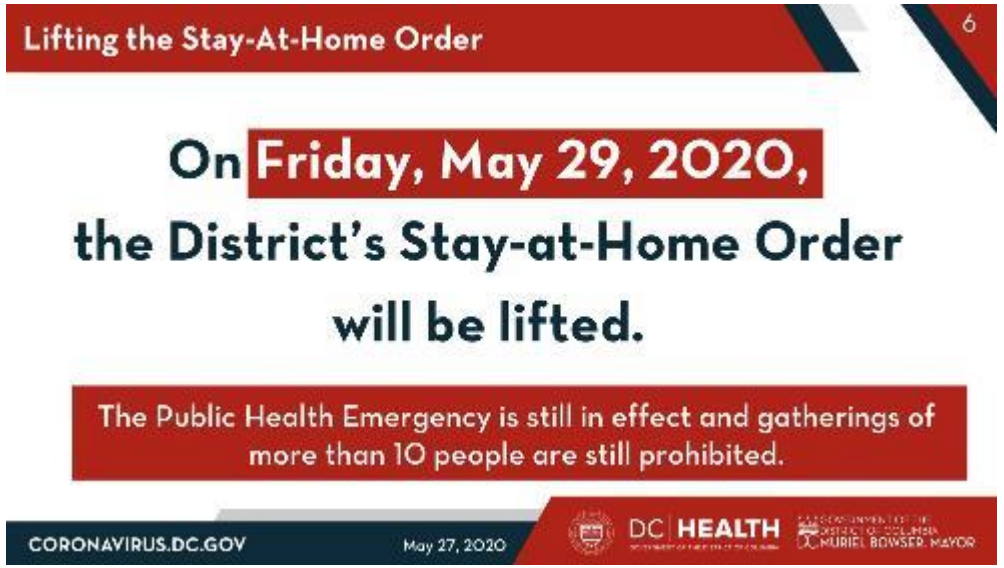
| District of Columbia | Maryland | Virginia |
|---|---|---|
| 445 | 2,392 | 1,281 |
| 8,406 cases | 48,423 cases | 40,249 cases |

By Rebecca Tan, Fenit Nirappil, Kevin Uhrmacher, Gabriel Florit and Danielle Rindler

Updated May 27 at 10:15 a.m.

## New daily deaths reported in D.C., Maryland and Virginia

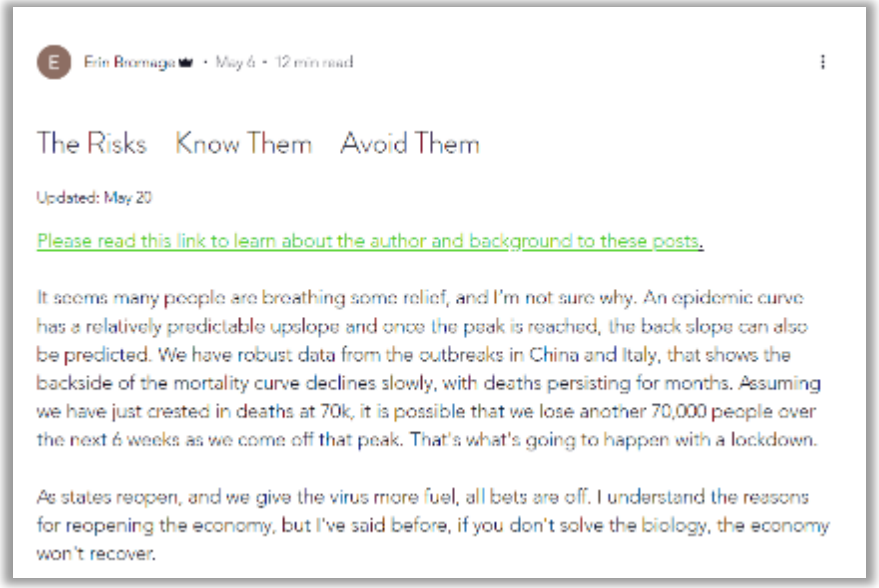




https://www.washingtonpost.com/graphics/local/dc-maryland-virginia-coronavirus-cases/
https://coronavirus.dc.gov/reopendc

# Transmission Updates



Erin Bromage • May 6 • 12 min read

The Risks Know Them Avoid Them

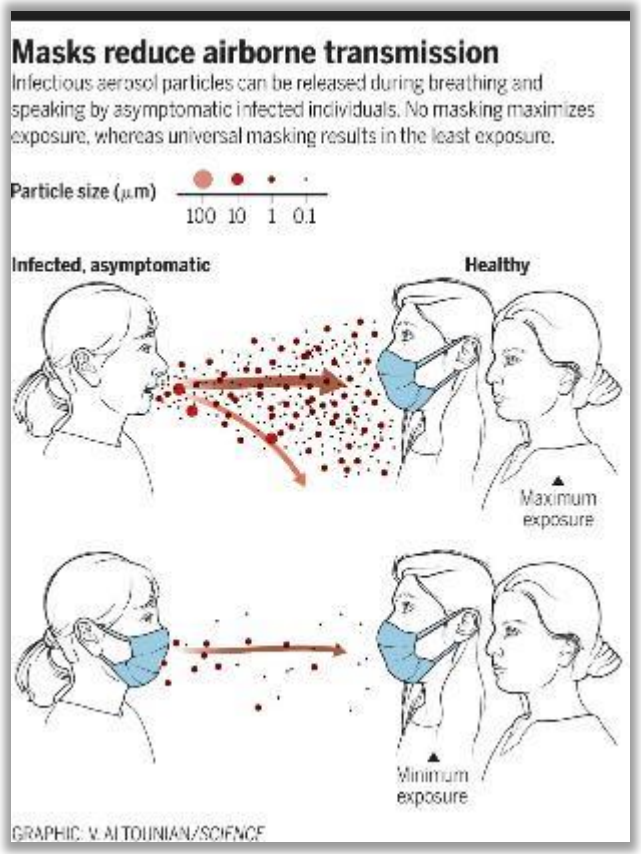
Updated: May 20

Please read this link to learn about the author and background to these posts.

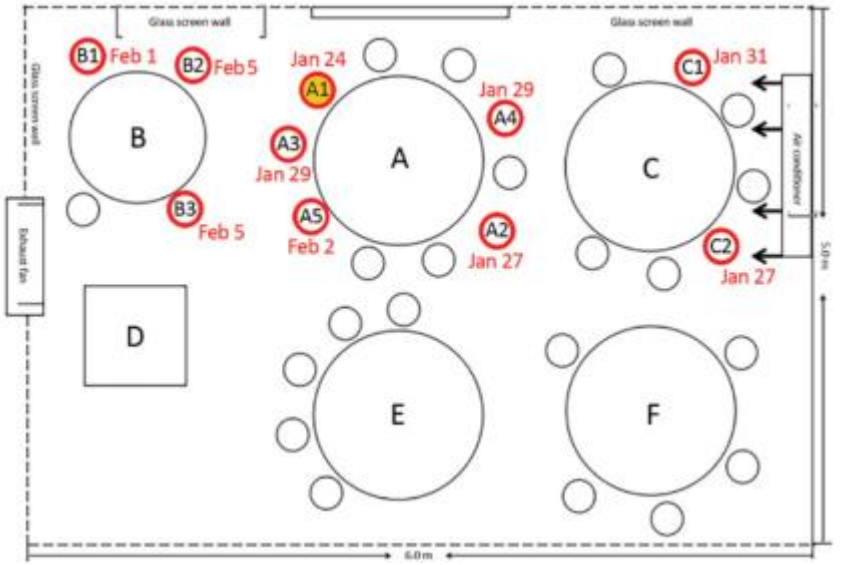
It seems many people are breathing some relief, and I'm not sure why. An epidemic curve has a relatively predictable upslope and once the peak is reached, the back slope can also be predicted. We have robust data from the outbreaks in China and Italy, that shows the backside of the mortality curve declines slowly, with deaths persisting for months. Assuming we have just crested in deaths at 70k, it is possible that we lose another 70,000 people over the next 6 weeks as we come off that peak. That's what's going to happen with a lockdown.

As states reopen, and we give the virus more fuel, all bets are off. I understand the reasons for reopening the economy, but I've said before, if you don't solve the biology, the economy won't recover.

https://www.erinbromage.com/post/the-risks-know-them-avoid-them




Prather KA, et al. Reducing transmission of SARS-CoV-2. *Science*. 2020. https://science.sciencemag.org/content/early/2020/05/27/science.abc6197




Lu J, et al. COVID-19 outbreak associated with air conditioning in restaurant, Guangzhou, China, 2020. *Emerg Infect Dis*. 2020.

# Symptomatic vs. Asymptomatic Infection

- 78 patients from 26 transmission cluster series
- Wuhan, China, 12/24/2019-2/24/2020
- Asymptomatic patients were:
  - Younger, 37 [26-45] vs. 56 [34-63] y/o
  - More women, 66.7% vs 31.%
  - Lower rate of abnormal LFTs, 3% vs. 20%
  - Higher CD4 count during recovery, 719 [538-963] vs. 474 [354-811]
  - Faster CT improvement, 9 vs. 15 days
  - **Shorter duration of viral shedding by NP swab RT-PCR, 8 [3-12] vs. 19 [16-24] days**

Research Letter | Infectious Diseases

May 27, 2020

**Comparison of Clinical Characteristics of Patients with Asymptomatic vs Symptomatic Coronavirus Disease 2019 in Wuhan, China**

Rongrong Yang, PhD[1]; Xien Gui, MBBS[1]; Yong Xiong, PhD[1]

» Author Affiliations | Article Information

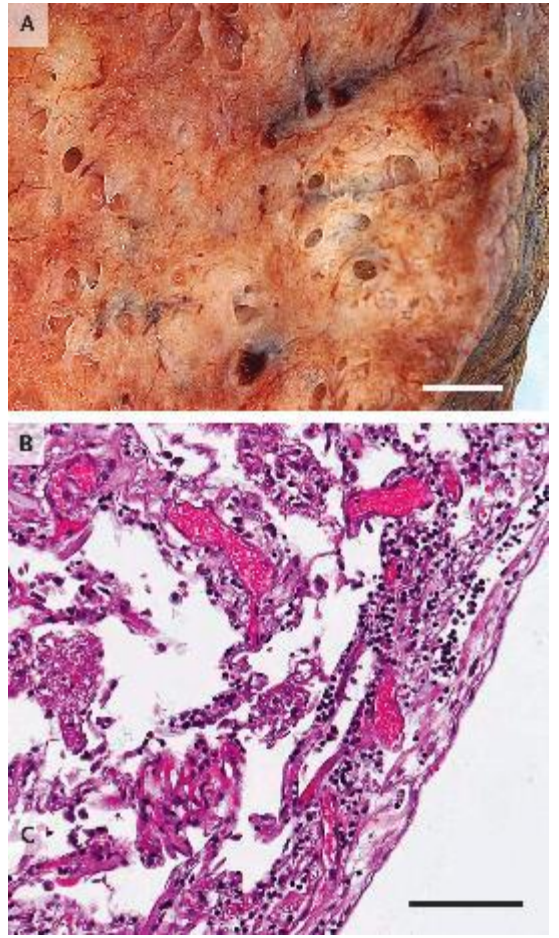
*JAMA Netw Open*. 2020;3(5):e2010182. doi:10.1001/jamanetworkopen.2020.10182

ORIGINAL ARTICLE

# Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19

Maximilian Ackermann, M.D., Stijn E. Verleden, Ph.D., Mark Kuehnel, Ph.D., Axel Haverich, M.D., Tobias Welte, M.D., Florian Laenger, M.D., Arno Vanstapel, Ph.D., Christopher Werlein, M.D., Helge Stark, Ph.D., Alexandar Tzankov, M.D., William W. Li, M.D., Vincent W. Li, M.D., et al.

- Distinctive vascular features, severe endothelial injury associated with the presence of intracellular virus and disrupted cell membranes
- Alveolar capillary microthrombi were 9 times as prevalent in patients with Covid-19 as in patients with influenza (P<0.001)
- The amount of **new vessel growth** — predominantly intussusceptive angiogenesis — was 2.7 times as high as that in the lungs from patients with influenza (P<0.001)



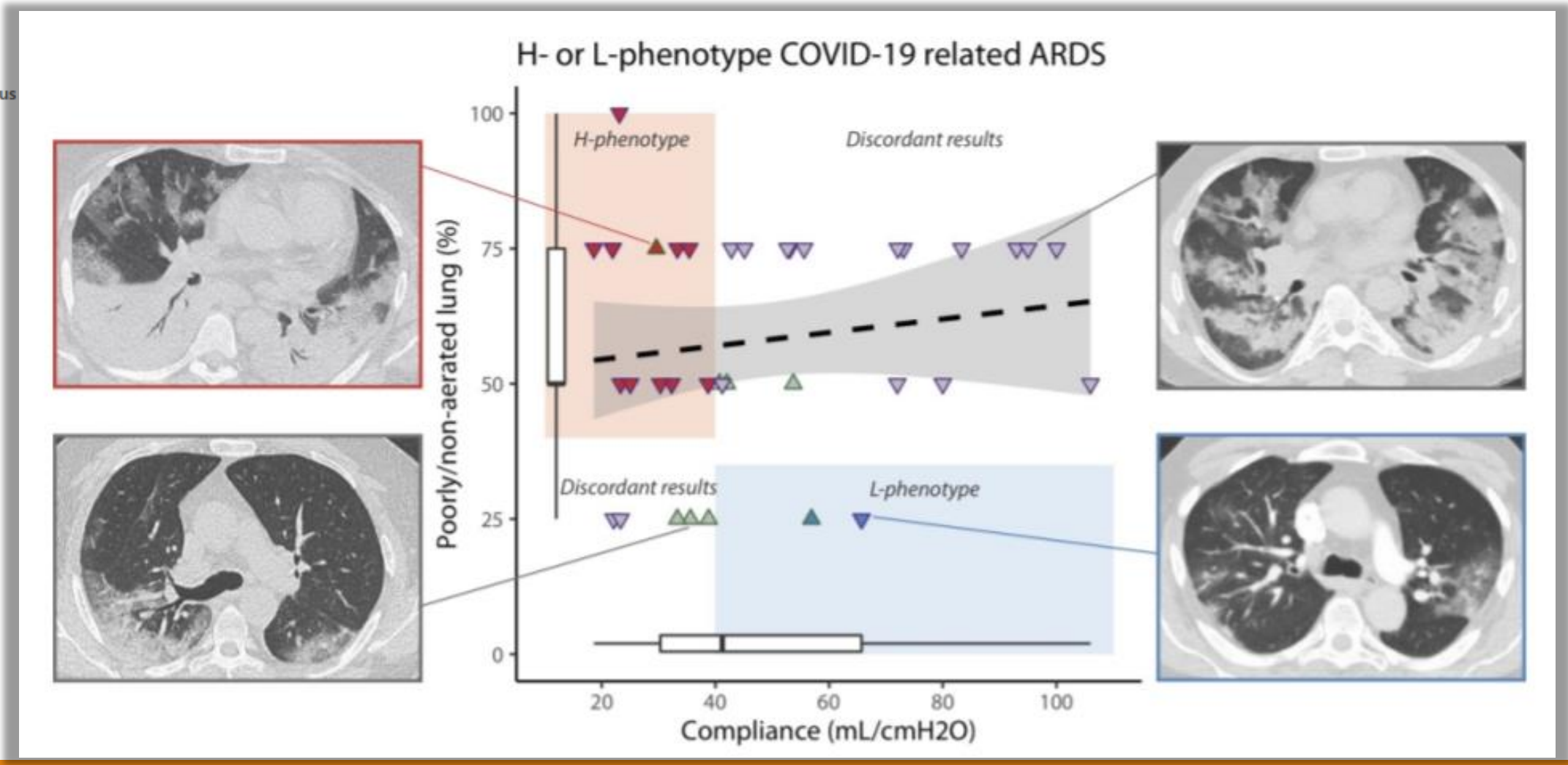
Annals of the American Thoracic Society



# Subphenotyping ARDS in COVID-19 Patients: Consequences for Ventilator Management

Data is empty

Lieuwe DJ Bos , Frederique Paulus



# Early Corticosteroids?

- Quasi-experiment design
- Multi-center health system in Michigan, March 2020
- Adult patients with confirmed moderate-severe COVID
- 81 (38%) got no steroids; 132 (62%) got steroids
  - Methylprednisolone 0.5-1 mg/kg/day x 3 days
- Composite endpoint of escalation of care from ward to ICU, new requirement for ventilation, and mortality
- Composite endpoint observed in 34.9% of steroids group vs. 54.3% of no-steroids group (p=0.005)
  - Treatment effect observed within each component
- LOS lower in steroids group, 8 vs. 5 days (p < 0.001)
- Multivariate regression demonstrated independent reduction in composite endpoint at 14-days (aOR: 0.45; 95% CI [0.25-0.81]).

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**Early Short Course Corticosteroids in Hospitalized Patients with COVID-19**

Raef Fadel, Austin Morrison, Amit Vahia, Zachary R Smith, Zohra Chaudhry, Pallavi Bhargava, Joseph Miller, Rachel Kenney, George Alangaden, Mayur S Ramesh, Henry Ford COVID-19 Management Task Force

doi: https://doi.org/10.1101/2020.05.04.20074609



| Treatment | Total (n=213) | Pre-Protocol (n=81) | Post-Protocol (n=132) | p-value |
|---|---|---|---|---|
| **Antimicrobials** | | | | |
| Empiric antibiotic prescribed for pneumonia – no. (%) | 163 (76.5) | 65 (80.2) | 98 (74) | 0.316 |
| Median time to empiric antibiotics (IQR) – days | 1 (0-1) | 1 (0-1) | 0 (0-1) | 0.631 |
| Median duration of antimicrobials (IQR) - days | 4 (2-5) | 5 (3-5) | 3 (2-5) | 0.009 |
| Hydroxychloroquine use - no. (%) | 161 (75.6) | 57 (70.4) | 104 (78.8) | 0.167 |
| Median time to hydroxychloroquine initiation (IQR) - days | 2 (1-3) | 3 (1-4) | 1 (0-2) | 0.126 |
| Lopinavir/ritonavir and ribavirin use - no. (%) | 10 (4.7) | 9 (11.1) | 1 (0.76) | 0.001 |
| Remdesivir use – no. (%) | 5 (2.3) | 5 (6.2) | 0 (0) | 0.004 |
| Tocilizumab use – no. (%) | 14 (6.6) | 8 (10.1) | 6 (4.5) | 0.126 |
| **Corticosteroid treatment** | | | | |
| Corticosteroids received at any time - no. (%) | 136 (63.8) | 46 (56.8) | 90 (68.2) | 0.094 |
| Corticosteroids received in first 48 hours - no. (%) | 65 (30.5) | 10 (12.4) | 55 (41.7) | <0.001 |
| Median time to steroid initiation from admission (IQR) – days | 2 (1-4) | 5 (3-7) | 2 (1-3) | <0.001 |
| Median methylprednisolone dose (IQR) – mg | 40 (40-50) | 40 (40-50) | 40 (35-50) | 0.851 |
| Median duration of corticosteroids (IQR) – days | 3 (3-3) | 3 (3-3) | 3 (3-3) | 0.812 |

*IQR denotes Interquartile range

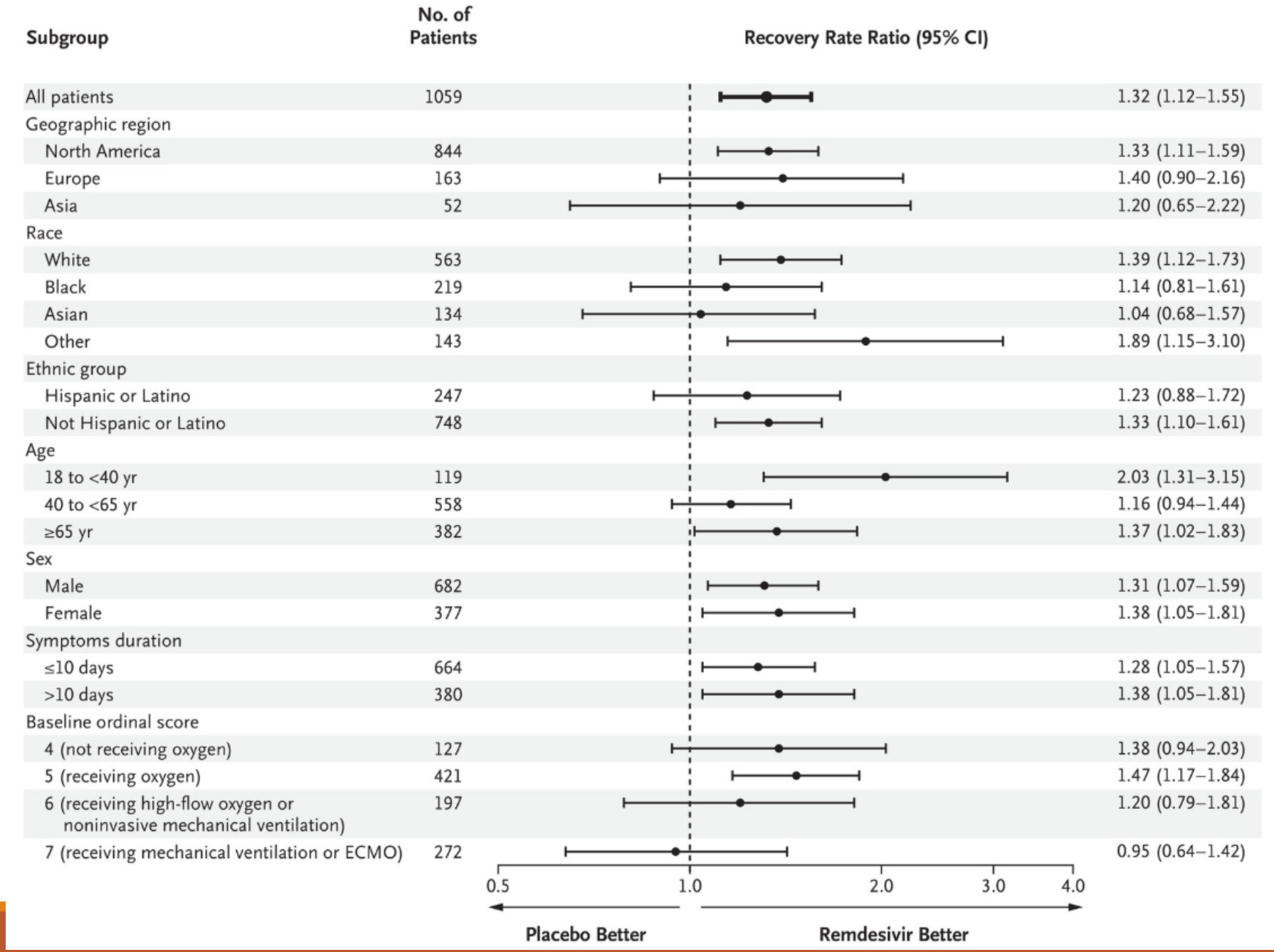
# Remdesivir

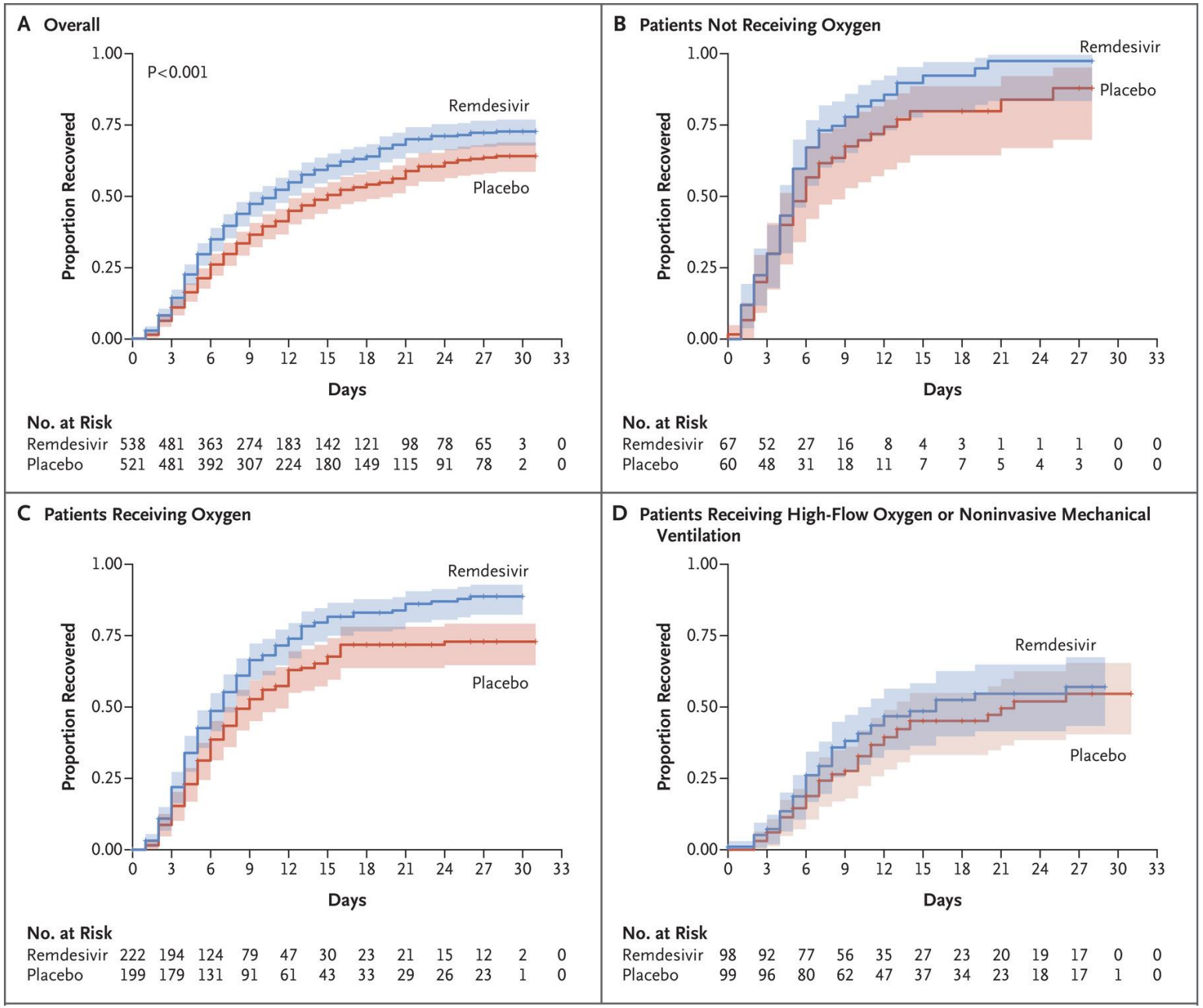
ORIGINAL ARTICLE

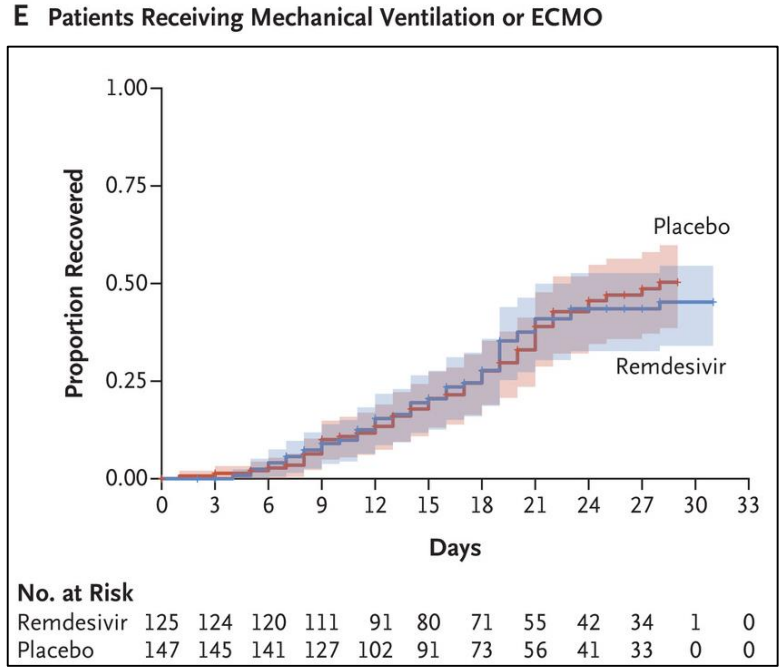
## Remdesivir for the Treatment of Covid-19 — Preliminary Report

John H. Beigel, M.D., Kay M. Tomashek, M.D., M.P.H., Lori E. Dodd, Ph.D., Aneesh K. Mehta, M.D., Barry S. Zingman, M.D., Andre C. Kalil, M.D., M.P.H., Elizabeth Hohmann, M.D., Helen Y. Chu, M.D., M.P.H., Annie Luetkemeyer, M.D., Susan Kline, M.D., M.P.H., Diego Lopez de Castilla, M.D., M.P.H., Robert W. Finberg, M.D., et al., for the ACTT-1 Study Group Members*

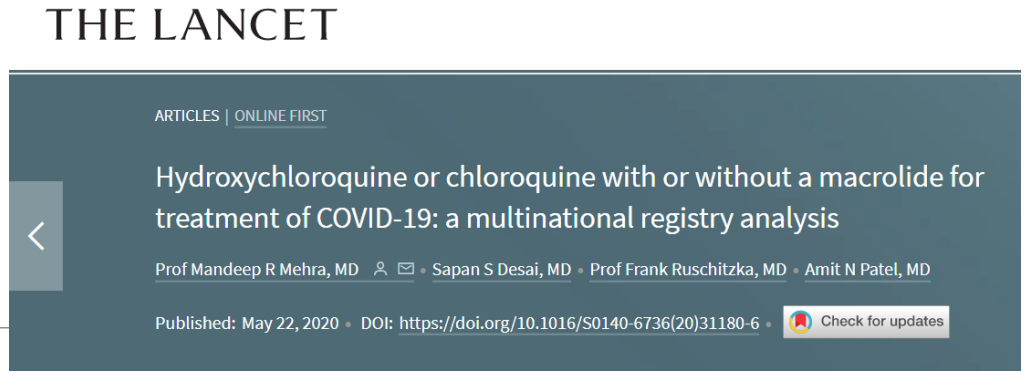
- Double-blind RCT, enrolled 2/2020-4/2020 across trial sites in US (45), EU (17), UK (5), Asia (4), Mexico (2)
- 10-day course of IV remdesivir (200 mg LD + 100 mg daily)
- Preliminary results from 1059 patients (538 assigned to remdesivir and 521 to placebo)
- In remdesivir group:
  - Recovery time 11 days (95% CI, 9 to 12) vs. 15 days (13 to 19); rate ratio for recovery, 1.32; 95% CI, 1.12 to 1.55)
  - Mortality at 14 days was 7.1% with remdesivir and 11.9% with placebo (HR, 0.70; 95% CI, 0.47 to 1.04)
  - SAEs reported for 21.1% in remdesivir group vs. 27.0% in placebo group
- Outcomes differed by subgroup and by severity of disease (next slides)
- Acute respiratory failure, hypotension, viral pneumonia, and AKI (~7%) slightly more common in placebo group
- No deaths were considered to be related to treatment assignment
- Limitations:
  - Patients with impaired renal function were excluded from enrollment


Subgroup
No. of Patients
Recovery Rate Ratio (95% CI)
All patients 1059 1.32 (1.12–1.55)
Geographic region
North America 844 1.33 (1.11–1.59)
Europe 163 1.40 (0.90–2.16)
Asia 52 1.20 (0.65–2.22)
Race
White 563 1.39 (1.12–1.73)
Black 219 1.14 (0.81–1.61)
Asian 134 1.04 (0.68–1.57)
Other 143 1.89 (1.15–3.10)
Ethnic group
Hispanic or Latino 247 1.23 (0.88–1.72)
Not Hispanic or Latino 748 1.33 (1.10–1.61)
Age
18 to <40 yr 119 2.03 (1.31–3.15)
40 to <65 yr 558 1.16 (0.94–1.44)
≥65 yr 382 1.37 (1.02–1.83)
Sex
Male 682 1.31 (1.07–1.59)
Female 377 1.38 (1.05–1.81)
Symptoms duration
≤10 days 664 1.28 (1.05–1.57)
>10 days 380 1.38 (1.05–1.81)
Baseline ordinal score
4 (not receiving oxygen) 127 1.38 (0.94–2.03)
5 (receiving oxygen) 421 1.47 (1.17–1.84)
6 (receiving high-flow oxygen or noninvasive mechanical ventilation) 197 1.20 (0.79–1.81)
7 (receiving mechanical ventilation or ECMO) 272 0.95 (0.64–1.42)
0.5
1.0
2.0
3.0
4.0
Placebo Better
Remdesivir Better


A Overall
P<0.001
Remdesivir
Placebo
Proportion Recovered
1.00
0.75
0.50
0.25
0.00
0 3 6 9 12 15 18 21 24 27 30 33
Days
No. at Risk
Remdesivir 538 481 363 274 183 142 121 98 78 65 3 0
Placebo 521 481 392 307 224 180 149 115 91 78 2 0
B Patients Not Receiving Oxygen
Remdesivir
Placebo
Proportion Recovered
1.00
0.75
0.50
0.25
0.00
0 3 6 9 12 15 18 21 24 27 30 33
Days
No. at Risk
Remdesivir 67 52 27 16 8 4 3 1 1 1 0 0
Placebo 60 48 31 18 11 7 7 5 4 3 0 0
C Patients Receiving Oxygen
Remdesivir
Placebo
Proportion Recovered
1.00
0.75
0.50
0.25
0.00
0 3 6 9 12 15 18 21 24 27 30 33
Days
No. at Risk
Remdesivir 222 194 124 79 47 30 23 21 15 12 2 0
Placebo 199 179 131 91 61 43 33 29 26 23 1 0
D Patients Receiving High-Flow Oxygen or Noninvasive Mechanical Ventilation
Remdesivir
Placebo
Proportion Recovered
1.00
0.75
0.50
0.25
0.00
0 3 6 9 12 15 18 21 24 27 30 33
Days
No. at Risk
Remdesivir 98 92 77 56 35 27 23 20 19 17 0 0
Placebo 99 96 80 62 47 37 34 23 18 17 1 0


E Patients Receiving Mechanical Ventilation or ECMO
Placebo
Remdesivir
Proportion Recovered
1.00
0.75
0.50
0.25
0.00
0 3 6 9 12 15 18 21 24 27 30 33
Days
No. at Risk
Remdesivir 125 124 120 111 91 80 71 55 42 34 1 0
Placebo 147 145 141 127 102 91 73 56 41 33 0 0

# Hydroxychloroquine




- Multinational registry analysis, 671 hospitals, 6 continents
- Patients hospitalized with laboratory-confirmed SARS-CoV-2, 12/2019-4/2020
- Four treatment groups (CQ, CQ + macrolide, HCQ, HCQ + macrolide) and control group (standard care)
  - Excluded patients who started treatment >48 hours after diagnosis or while on mechanical ventilation
  - Excluded patients who also received remdesivir
- Analysis controlled for age, sex, race/ethnicity, BMI, co-morbidities, baseline severity of disease
- **In-hospital mortality:**
  - **Control (9·3%), HCQ (18·0%; HR 1·335), HCQ/M (23·8%; 1·447), CQ (16·4%; 1·365), CQ/M (22·2%; 1·368)**
- **Clinically significant ventricular arrhythmias:**
  - **Control (0·3%), HCQ (6·1%; 2·369), HCQ/M (8·1%; 5·106), CQ (4·3%; 3·561), CQ/M (6·5%; 4·011)**
- "We were unable to confirm a benefit of hydroxychloroquine or chloroquine, when used alone or with a macrolide, on in-hospital outcomes for COVID-19. Each of these drug regimens was associated with decreased in-hospital survival and an increased frequency of ventricular arrhythmias when used for treatment of COVID-19."

# GW Updates

- Data analysis on hospitalized patients: Shant Ayanian, Juan Reyes
- COVID-19 Specimen Bank study enrolling patients: Adrienne Poon, Aileen Chang
- COVID-19 Intelligence Unit Brief on Serologic Testing
- COVID-19 Virtual Elective for MS3/MS4 students by GW SMHS Clinical Public Health Group
- Got a COVID-19 publication?