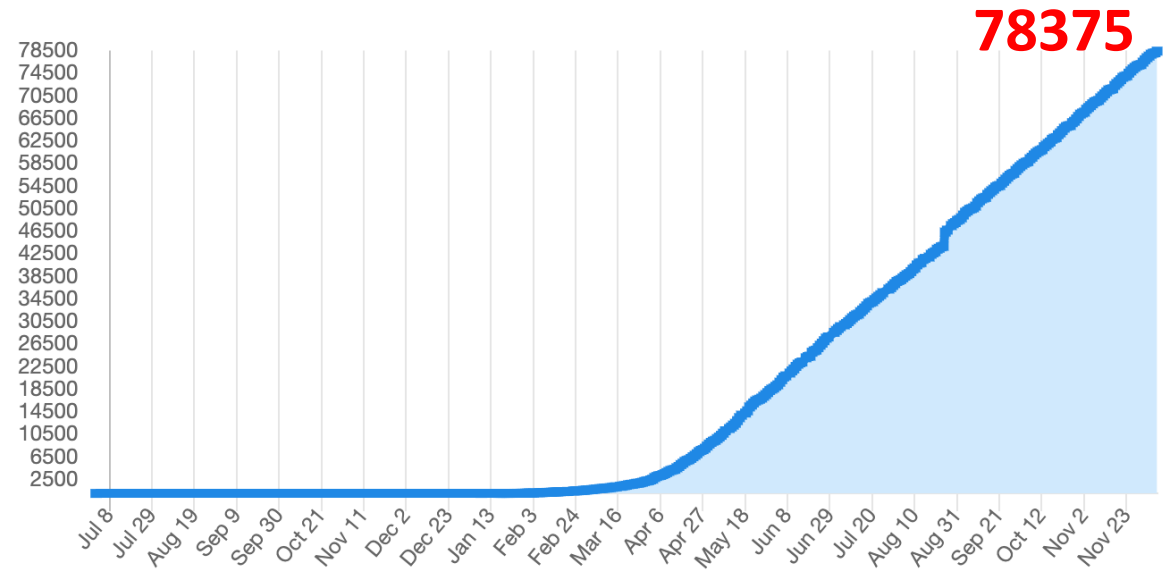


# Updates and Controversies in COVID-19

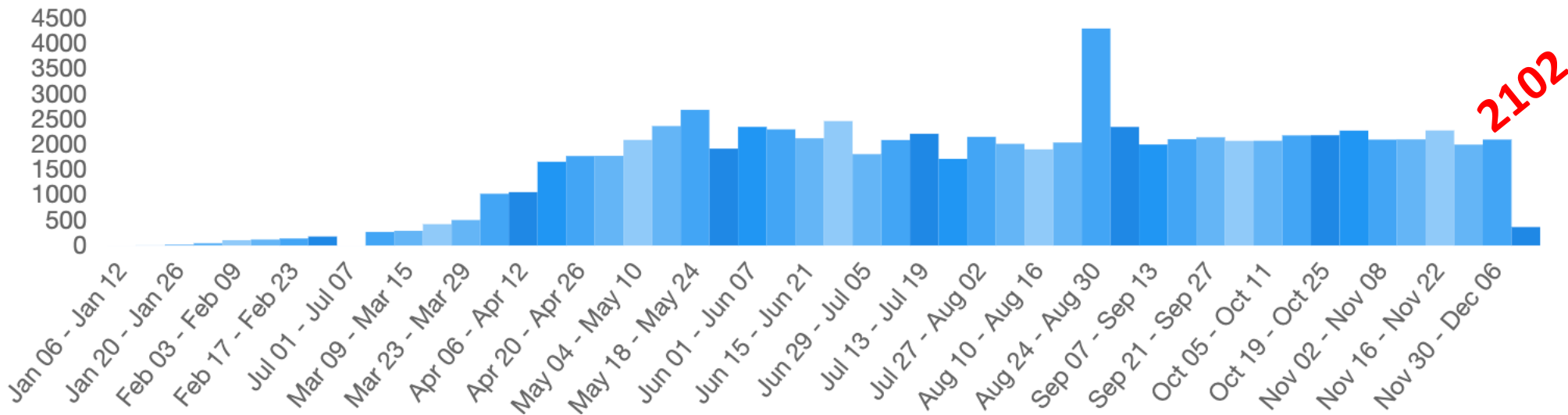
W. Cameron McGuire, MD, MPH

PCCSM Fellow

UC San Diego Health



Cumulative growth of papers in LitCovid



Hydroxychloroquine still does not work...

Effect of Hydroxychloroquine  
in Hospitalized Patients with Covid-19

**NEJM 11/19/2020**

The RECOVERY Collaborative Group\*

Hydroxychloroquine with or without  
Azithromycin in Mild-to-Moderate Covid-19

**NEJM 11/19/2020**

A Cluster-Randomized Trial of  
Hydroxychloroquine for Prevention of Covid-19

**NEJM 11/24/2020**

# Hydroxychloroquine still, still does not work

## HCQ Shows Benefit

STUDY	Location	Study Type	N
Chen	In Hospital	Case-Cohort	568
Gautret 1	In Hospital	Retrospective	42
Gautret 2	In Hospital	Retrospective	80
Henry Ford	In Hospital	Retrospective	2541

**N = 3151**

## HCQ Doesn't Show Benefit

STUDY	Location	Study Type	N
Rosenberg	In Hospital	Retrospective	1438
VA Study	In Hospital	Retrospective	368
Boulware	PrEP	RCT	821
Spanish	PrEP	RCT	2300
Recovery	In Hospital	RCT	4674
Orchid*	In Hospital	RCT	470
Solidarity*	In Hospital	RCT	x
Cavalcanti	In Hospital	RCT	667
Discovery	In Hospital	RCT	Ongoing

**N = 10738**

**N = 8932**

# Convalescent Plasma Hasn't Panned Out

JAMA | **Original Investigation**

**Effect of Convalescent Plasma Therapy on Time to Clinical Improvement  
in Patients With Severe and Life-threatening COVID-19**

A Randomized Clinical Trial

**JAMA June 3, 2020**

Ling Li, MD, PhD; Wei Zhang, MD; Yu Hu, MD, PhD; Xunliang Tong, MD, PhD; Shangen Zheng, MD; Juntao Yang, PhD; Yujie Kong, MD;  
Lili Ren, PhD; Qing Wei, MD; Heng Mei, MD, PhD; Caiying Hu, MD; Cuihua Tao, MD; Ru Yang, MD; Jue Wang, MD; Yongpei Yu, PhD;  
Yong Guo, PhD; Xiaoxiong Wu, MD; Zhihua Xu, MD; Li Zeng, MD; Nian Xiong, MD; Lifeng Chen, MD; Juan Wang, MD; Ning Man, MD;  
Yu Liu, PhD; Haixia Xu, MD; E. Deng, MS; Xuejun Zhang, MS; Chenyue Li, MD; Conghui Wang, PhD; Shisheng Su, PhD; Linqi Zhang, PhD;  
Jianwei Wang, PhD; Yanyun Wu, MD, PhD; Zhong Liu, MD, PhD

**Convalescent plasma treatment of severe  
COVID-19: a propensity score-matched control  
study**

**Nature Med Sept 20, 2020**

**A Randomized Trial of Convalescent Plasma  
in Covid-19 Severe Pneumonia**

**NEJM Nov 24, 2020**

# There is Equipoise with Remdesivir...

## WHO recommends against the use of remdesivir in COVID-19 patients

20 November 2020

### 7. RECOMMENDATIONS FOR THERAPEUTICS

#### 7.1 Remdesivir

Hospitalized patients with COVID-19, regardless of disease severity

Conditional recommendation

We suggest against administering remdesivir in addition to standard care.

## FDA Approval of Remdesivir — A Step in the Right Direction

**NEJM Dec 2, 2020**

Daniel Rubin, Ph.D., Kirk Chan-Tack, M.D., John Farley, M.D., M.P.H., and Adam Sherwat, M.D.

## The place for remdesivir in COVID-19 treatment

**Lancet Nov 26, 2020**

# There is Equipoise with Remdesivir...

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

**JAMA Sept 15, 2020**

**Remdesivir for 5 or 10 Days in Patients  
with Severe Covid-19**

**NEJM Nov 5, 2020**

Jason D. Goldman, M.D., M.P.H., David C. Lye, M.B., B.S., David S. Hui, M.D.

Kristen M. Marks, M.D., Raffaele Iacono, M.D.,  
Christoph D. Spinner, M.D., Mass

Ronald G. Nahass, M.D., Yao-She

Robert H. Hyland, D.Phil., Anu C

Christiana Blair, M.S., Xuelian W

Diana M. Brainard, M.D., William

Kathleen M. Mullane, D.O., Ph

Karen T. Tashima, M.D., George Dia

**Remdesivir for the Treatment of Covid-19 — Final Report**

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu,  
A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapon, L. Hsieh, T.F. Patterson,  
R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios,  
T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett,  
J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane,  
for the ACTT-1 Study Group Members\*

**Repurposed Antiviral Drugs for Covid-19 —  
Interim WHO Solidarity Trial Results**

**NEJM Dec 2, 2020**

WHO Solidarity Trial Consortium\*

# So Where Does That Leave Us Therapeutically...?

	Mortality	Mechanical ventilation	Adverse events	Admission to hospital	Viral clearance at 7 days	Duration of hospitalization	ICU length of stay	Duration of mechanical ventilation	Time to symptom resolution	Time to viral clearance	Ventilator free days
Standard care*	130 per 1,000	116 per 1,000	15 per 1,000	43 per 1,000	484 per 1,000	13 days	13 days	15 days	11 days	10 days	11 days
Azithromycin	6 (-40 to 62)	1 (-60 to 90)				0.4 (-2.9 to 3.9)					-1.7 (-5.1 to 1.8)
Colchicine	-106 (-129 to 42)					-1.6 (-2.8 to -0.3)**					
Corticosteroids	-17 (-34 to 1)***	-29 (-54 to 1)****			5 (-426 to 458)	-0.9 (-3.4 to 1.7)	-3.8 (-5.9 to -1.8)	-1.4 (-3.4 to 0.62)			2.6 (0.2 to 5.0)
Favipiravir	63 (-113 to 773)				81 (-301 to 399)						
Hydroxychloroquine	11 (-11 to 38)**	20 (-18 to 76)****	16 (-11 to 192)**	-26 (-38 to 12)**	18 (-293 to 334)	0.1 (-1.9 to 2.0)			-2.0 (-4.0 to 0.1)	-0.7 (-4.3 to 4.8)**	
Hydroxychloroquine + azithromycin	-48 (-103 to 66)	58 (-32 to 216)				0.6 (-1.2 to 2.4)**					
Interferon beta	2 (-35 to 35)	-13 (-60 to 45)									
Interferon gamma					436 (-215 to 516)						
Interferon kappa+ trefoil factor 2					290 (-334 to 503)						
Lopinavir-ritonavir	-12 (-31 to 10)	10 (-31 to 60)****			-235 (-449 to 164)	-0.4 (-1.7 to 0.6)**			-1.0 (-4.1 to 3.2)		
rhG-CSF	-102 (-124 to -41)***	-96 (-108 to -68)				-0.7 (-2.3 to 1.0)**			-0.8 (-4.5 to 4.6)		
Remdesivir	-12 (-35 to 14)**	-33 (-65 to 1)****	0 (-9 to 40)		14 (-429 to 460)	-0.2 (-1.9 to 1.2)**		-1.3 (-4.1 to 1.5)	-2.0 (-4.2 to 0.9)		
Tocilizumab	5 (-46 to 81)	-35 (-80 to 54)	-8 (-15 to 300)**			-2.5 (-6.9 to 1.8)	-4.5 (-13.8 to 4.9)		-1.8 (-5.0 to 3.4)		4.7 (-4.2 to 13.9)
Umifenovir	-130 (-130 to 870)										
	Most beneficial	Intermediate benefit	Not different from SC	Harmful							
High/ moderate certainty											
Low/ very low certainty											
*Numbers presented are absolute risk differences (95% CI) per 1000 patients or mean difference (95% CI) when compared to standard care											
** The best estimate of effect was obtained from direct evidence											
*** Fixed effects NMA estimates (vs standard care): Corticosteroids, -18 (-30 to -7); Hydroxychloroquine, 10 (-5 to 29); Lopinavir-Ritonavir, -14 (-26 to 0); Remdesivir, -10 (-26 to 9)											
**** Fixed effects NMA estimates (vs standard care): Corticosteroids, -57 (-85 to -27); Hydroxychloroquine, 30 (-5 to 66); Lopinavir-Ritonavir, 29 (-3 to 63); Remdesivir, -24 (-51 to 5)											
Empty cells: there was no evidence for the specific intervention											
rSG-CSF: Recombinant human granulocyte colony-stimulating factor											
<b>Fig 2. Summary of effects compared with standard care</b>											

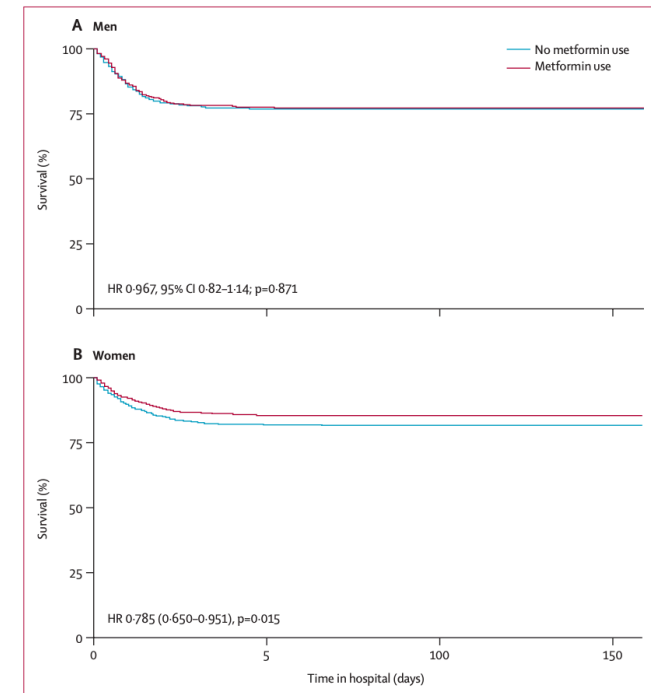
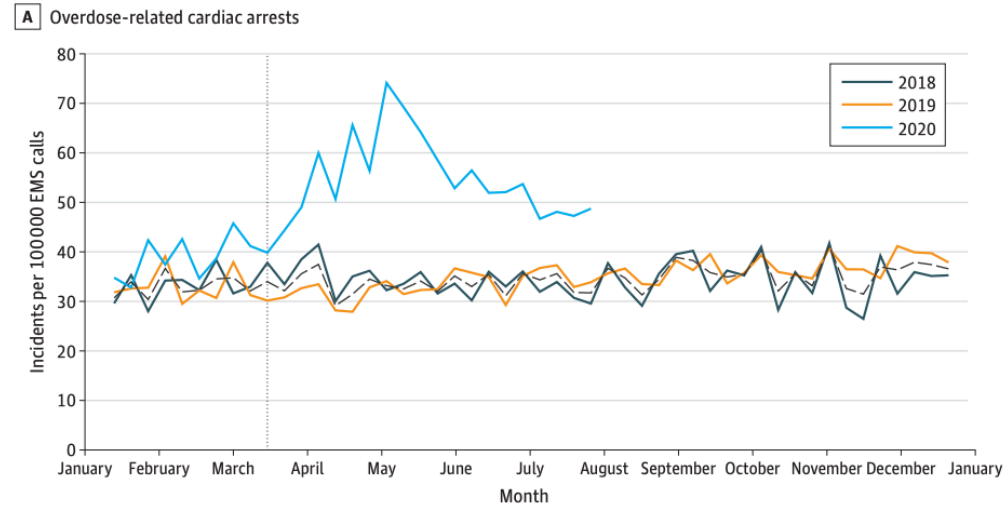
# Some Quick Hitters...

## Overdose-Related Cardiac Arrests Observed by Emergency Medical Services During the US COVID-19 Epidemic

Joseph Friedman, MPH<sup>1</sup>; Leo Beletsky, JD, MPH<sup>2</sup>; David L. Schriger, MD, MPH<sup>3</sup>

[» Author Affiliations](#) | [Article Information](#)

*JAMA Psychiatry*. Published online December 3, 2020. doi:10.1001/jamapsychiatry.2020.4218



## Metformin and risk of mortality in patients hospitalised with COVID-19: a retrospective cohort analysis

Carolyn T Bramante, MD • Nicholas E Ingraham, MD • Thomas A Murray, PhD • Schelomo Marmor, PhD •

Shane Hovertsen, PhD • Jessica Gronski, PhD • et al. [Show all authors](#) • [Show footnotes](#)

**Open Access** • Published: December 03, 2020 • DOI: [https://doi.org/10.1016/S2666-7568\(20\)30033-7](https://doi.org/10.1016/S2666-7568(20)30033-7) •



# Some (More) Quick Hitters...

## Aspergillus Rates Aren't Increased in COVID-19 ARDS

JCM Accepted Manuscript Posted Online 4 December 2020

J Clin Microbiol doi:10.1128/JCM.02278-20

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Frequency of Positive Aspergillus Tests in COVID-19 Patients in Comparison to Other Patients with  
Pulmonary Infections Admitted to the ICU


Erlangga Yusuf<sup>1</sup>, Alieke Vonk<sup>1</sup>, Johannes P.C. van den Akker<sup>2</sup>, Lonneke Bode, Gregorius J. Sips<sup>1</sup>, Bart

JA Rijnders<sup>1</sup>, Jurriaan de Steenwinkel<sup>1</sup>, Nelianne J. Verkaik<sup>1</sup>, Marius Vogel<sup>1</sup>, Menno van der Eerden<sup>3</sup>,

Mireille van Westreenen<sup>1</sup>

## VAP Rates in COVID-19 ECMO Patients are Increased

Ventilator-associated pneumonia in patients with SARS-CoV-2-associated acute respiratory distress syndrome requiring ECMO: a retrospective cohort study

[Charles-Edouard Luyt](#) , [Tarek Sahnoun](#), [Melchior Gautier](#), [Pauline Vidal](#), [Sonia Burrel](#), [Marc Pineton de Chambrun](#), [Juliette Chommeloux](#), [Cyrielle Desnos](#), [Jeremy Arzoine](#), [Ania Nieszkowska](#), [Nicolas Bréchet](#), [Matthieu Schmidt](#), [Guillaume Hekimian](#), [David Boutolleau](#), [Jérôme Robert](#), [Alain Combes](#) & [Jean Chastre](#)

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