

# COVID-19: KEEPING UP WITH A MOVING TARGET JUNE 10, 2020 UPDATE

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# COVID-19: Keeping Up with a Moving Target

Twice Weekly @ [COVID19.DKBmed.com](https://COVID19.DKBmed.com)



# CME Information

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Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials. These include hydroxychloroquine/chloroquine, hydroxychloroquine/chloroquine in combination with azithromycin, lopinavir plus ritonavir, tocilizumab, corticosteroids, and COVID-19 convalescent plasma. All activity, content, and materials have been developed solely by the activity directors, planning committee members, and faculty presenters, and are free of influence from a commercial entity.



# CME Information

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**COVID19.DKBmed.com**



# Learning Objectives

- **Discuss common misperceptions about COVID-19 preventive measures**
- **Describe the relationship between trust in news and adherence to public health recommendations**
- **Discuss data pertaining to use of convalescent plasma in people with severe COVID-19**



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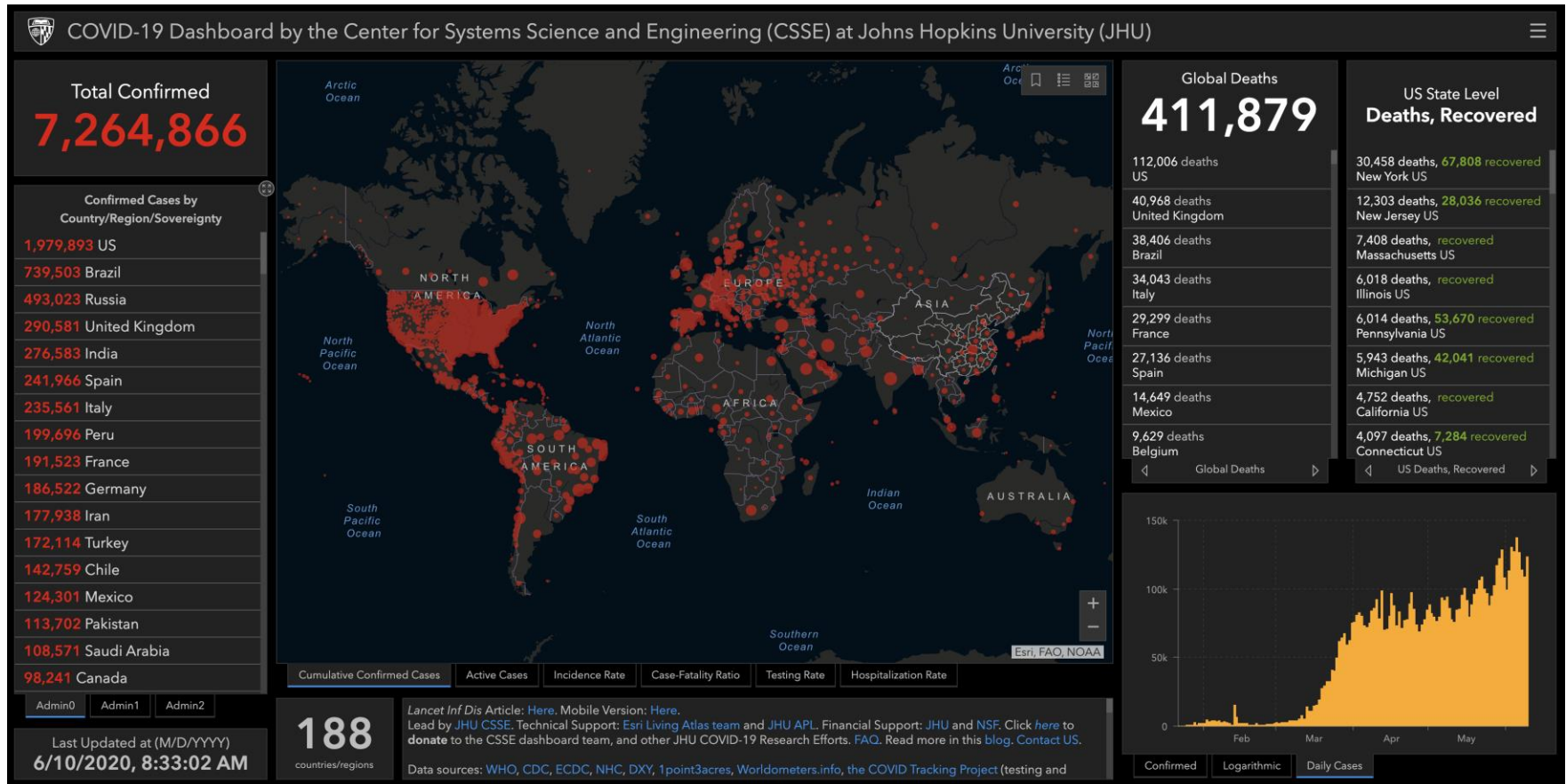
# Thank You

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Please see **COVID19.DKBmed.com** for additional resources and educational activities



# Total Cases: N. America (6/10/20)







# Viral Transmission

- What does the evidence point to for the top 3 interventions for protection?
- What does the public know and who do they trust?
- How are they getting their information?



# Transmission Prevention

## Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis



Derek K Chu, Elie A Akl, Stephanie Duda, Karla Solo, Sally Yaacoub, Holger J Schünemann, on behalf of the COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors\*



172 observational studies, no RCTs, 44 comparative studies, overall 25,697 patients  
SARS, MERS and COVID-19 studies

	Studies and participants	Relative effect (95% CI)	Anticipated absolute effect (95% CI), eg, chance of viral infection or transmission		Difference (95% CI)	Certainty*	What happens (standardised GRADE terminology) <sup>29</sup>
			Comparison group	Intervention group			
Physical distance ≥1 m vs <1 m	Nine adjusted studies (n=7782); 29 unadjusted studies (n=10736)	aOR 0.18 (0.09 to 0.38); unadjusted RR 0.30 (95% CI 0.20 to 0.44)	Shorter distance, 12.8%	Further distance, 2.6% (1.3 to 5.3)	-10.2% (-11.5 to -7.5)	Moderate†	A physical distance of more than 1 m probably results in a large reduction in virus infection; for every 1 m further away in distancing, the relative effect might increase 2.02 times
Face mask vs no face mask	Ten adjusted studies (n=2647); 29 unadjusted studies (n=10170)	aOR 0.15 (0.07 to 0.34); unadjusted RR 0.34 (95% CI 0.26 to 0.45)	No face mask, 17.4%	Face mask, 3.1% (1.5 to 6.7)	-14.3% (-15.9 to -10.7)	Low‡	Medical or surgical face masks might result in a large reduction in virus infection; N95 respirators might be associated with a larger reduction in risk compared with surgical or similar masks§
Eye protection (faceshield, goggles) vs no eye protection	13 unadjusted studies (n=3713)	Unadjusted RR 0.34 (0.22 to 0.52)¶	No eye protection, 16.0%	Eye protection, 5.5% (3.6 to 8.5)	-10.6% (-12.5 to -7.7)	Low	Eye protection might result in a large reduction in virus infection



# Transmission Prevention

Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis



*Derek K Chu, Elie A Akl, Stephanie Duda, Karla Solo, Sally Yaacoub, Holger J Schünemann, on behalf of the COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors\**



- Best 3 interventions
  - > 1 meter physical distance--likely > 2m even better
    - Pooled aOR 0.18 [95% CI 0.09-0.38]
    - Relative risk 2.02 per meter = increased protection
  - Face mask use
    - aOR 0.15 [95% CI 0.07-0.34]
    - Stronger associations with N95 or similar mask wear than surgical masks
  - Eye protection
    - aOR 0.22 [95% CI 0.12-0.39]



# Asymptomatic transmission – mixed messages

## The W.H.O. walks back an earlier assertion that asymptomatic transmission is ‘very rare.’

A top expert at the World Health Organization on Tuesday walked back her earlier assertion that transmission of the coronavirus by people who did not have symptoms was “very rare.”

Dr. Maria Van Kerkhove, who made the original comment at a W.H.O. briefing on Monday, said that it was based on just two or three studies and that it was a “misunderstanding” to say asymptomatic transmission was rare globally.

“I was just responding to a question; I wasn’t stating a policy of W.H.O. or anything like that,” she said.

Dr. Van Kerkhove said that estimates of transmission from people without symptoms come primarily from models, which may not provide an accurate representation. “That’s a big open question, and that remains an open question,” she said.

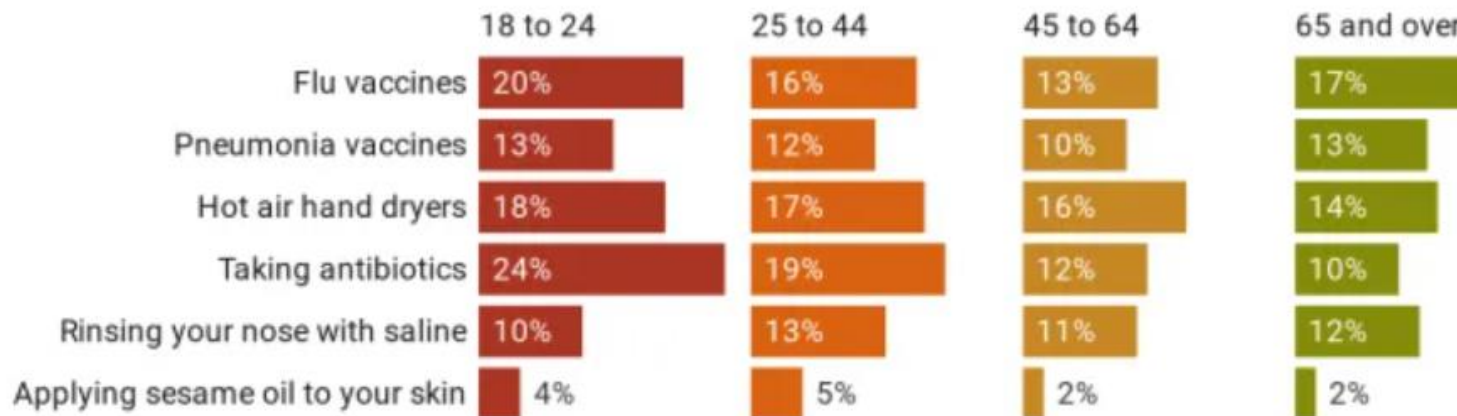


# What is the Message? From Where?

Shorenstein Center Media Politics and Public Policy (Harvard)

## COVID-19 prevention misperceptions by age group

To the best of your knowledge, are the following ways of preventing a coronavirus (COVID-19) infection effective or not? [ Percent respondents who say "effective" ]



National sample, N = 18,132, Time period: 5/16/2020-5/31/2020

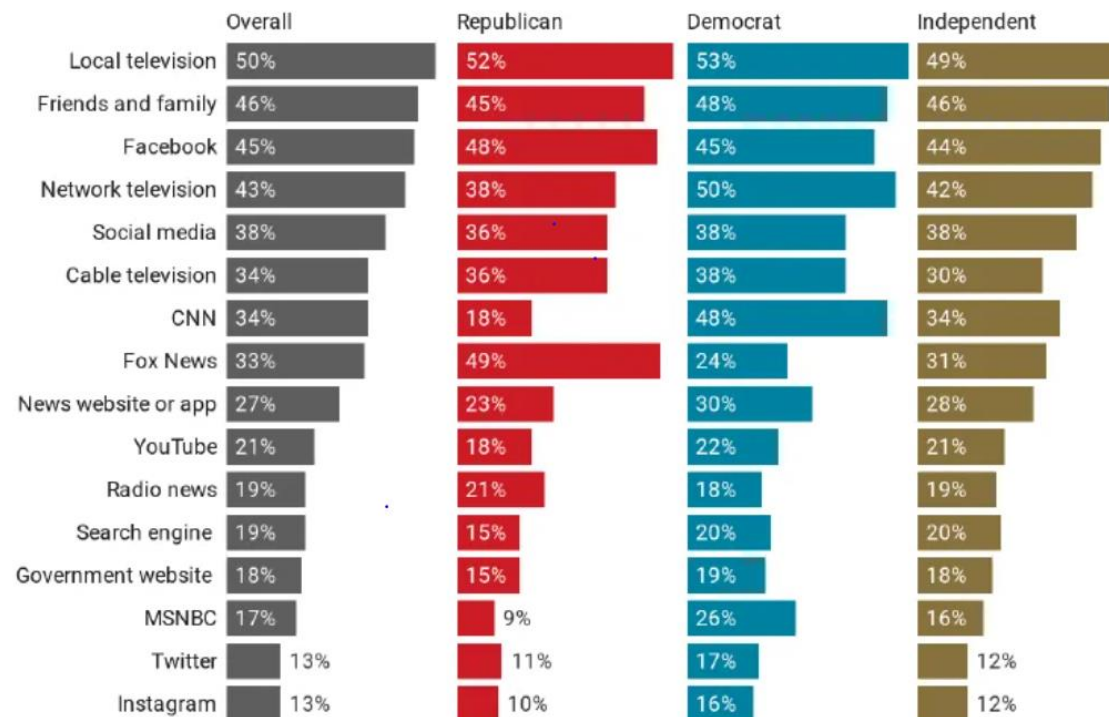
Source: The COVID-19 Consortium for Understanding the Public's Policy Preferences Across States (A joint project of: Northeastern University, Harvard University, Rutgers University, and Northwestern University) [www.covidstates.org](http://www.covidstates.org)



# The Sources...yet

## Sources of news and information about COVID-19 by party

In the last 24 hours, did you get any news or information related to the current coronavirus (COVID-19) outbreak from the following sources? [ Percent respondents who selected each source ]



National sample, N = 18,132, Time period: 5/16/2020-5/31/2020

Source: The COVID-19 Consortium for Understanding the Public's Policy Preferences Across States (A joint project of: Northeastern University, Harvard University, Rutgers University, and Northwestern University) [www.covidstates.org](http://www.covidstates.org)

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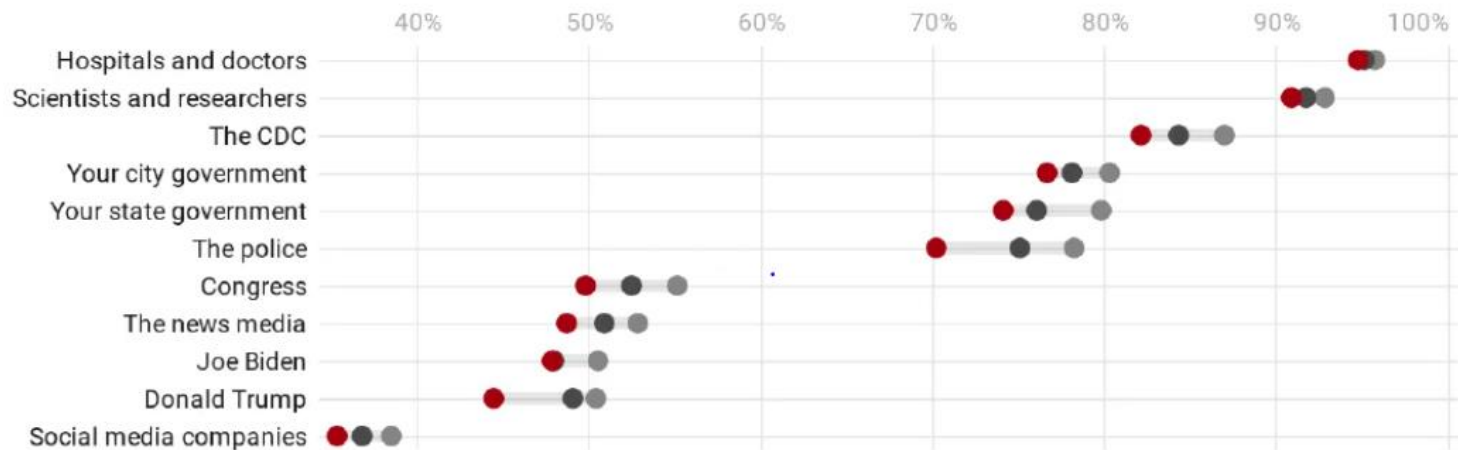


# Who is Trusted?

## Trust in individuals and institutions to handle the COVID-19 pandemic

How much do you trust the following people and organizations to do the right thing to best handle the current coronavirus (COVID-19) outbreak? [ Percent respondents who say "some" or "a lot" ]

● Late April ● Early May ● Late May



National sample, N1 = 19,505 (4/16/2020-4/30/2020), N2 = 20,333 (5/2/2020-5/15/2020), N3 = 18,132 (5/16/2020-5/31/2020)

Source: The COVID-19 Consortium for Understanding the Public's Policy Preferences Across States (A joint project of: Northeastern University, Harvard University, Rutgers University, and Northwestern University) [www.covidstates.org](http://www.covidstates.org)

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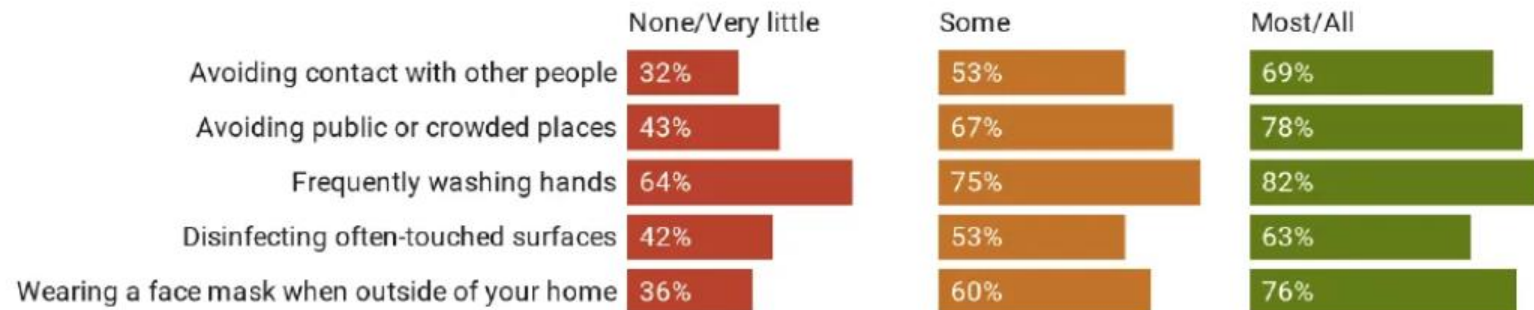




# Belief = actions

## Americans who think COVID-19 news is mostly accurate are much more likely to follow health guidelines

*In the last week, how closely did you personally follow the health recommendations listed below?  
[ Percent respondents who say "very closely" ] BY In general, how much of the information you see about the coronavirus (COVID-19) outbreak do you think is accurate or trustworthy?*



*National sample, N = 18,132, Time period: 5/16/2020-5/31/2020*

Source: The COVID-19 Consortium for Understanding the Public's Policy Preferences Across States (A joint project of: Northeastern University, Harvard University, Rutgers University, and Northwestern University) [www.covidstates.org](http://www.covidstates.org)

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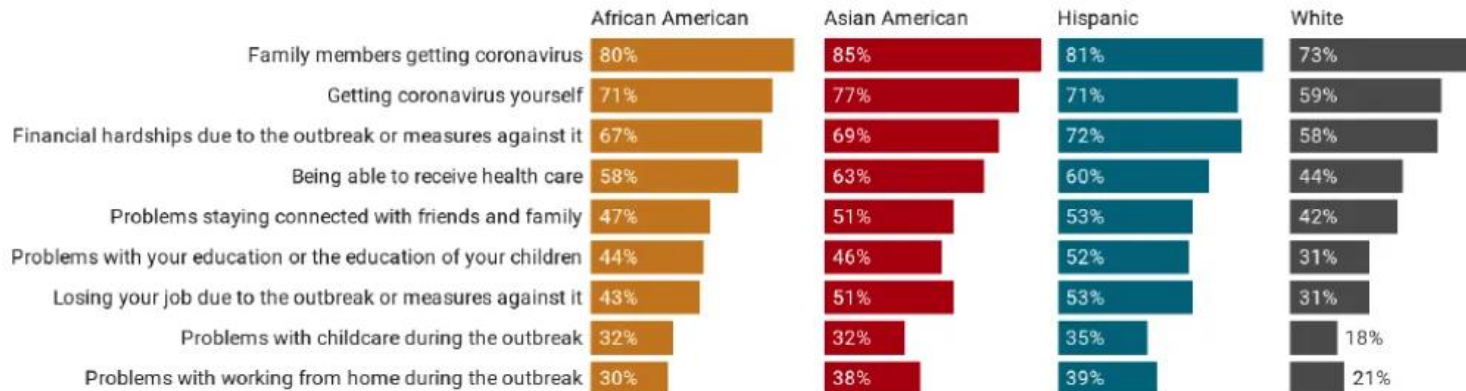
# Non-whites Rightly Concerned

## Are the Messages Heard?

### All concerns about COVID-19 are higher among non-White Americans

How concerned, if at all, do you currently feel about the following?

[ Percent respondents who say they are "somewhat concerned" or "very concerned" ]



National sample, N = 18,132, Time period: 5/16/2020-5/31/2020

Source: The COVID-19 Consortium for Understanding the Public's Policy Preferences Across States (A joint project of: Northeastern University, Harvard University, Rutgers University, and Northwestern University) [www.covidstates.org](http://www.covidstates.org)

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# COVID-19 Therapeutics



# Convalescent Plasma

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

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

Primary endpoint: clinical improvement with 28d

103 patients (halted early prior to planned 200 pts, no new cases to enroll)

Lab-confirmed COVID-19. median age = 70

Severe disease (hypoxemic) or critical illness

Convalescent plasma vs. usual care

- There was no significant difference in 28-day mortality (15.7% vs 24.0%; OR, 0.65 [95%CI, 0.29-1.46];  $P = .30$ )
- OR in time from randomization to discharge (51.0% vs 36.0% discharged by day 28; HR, 1.61 [95%CI, 0.88-2.93];  $P = .12$ )
- Convalescent plasma treatment was associated with a negative conversion rate of viral PCR at 72 hours  
87.2% of the convalescent plasma group vs 37.5% of the control group (OR, 11.39 [95%CI, 3.91-33.18];  $P < .001$ )
- Two had reactions to plasma, improved with supportive care



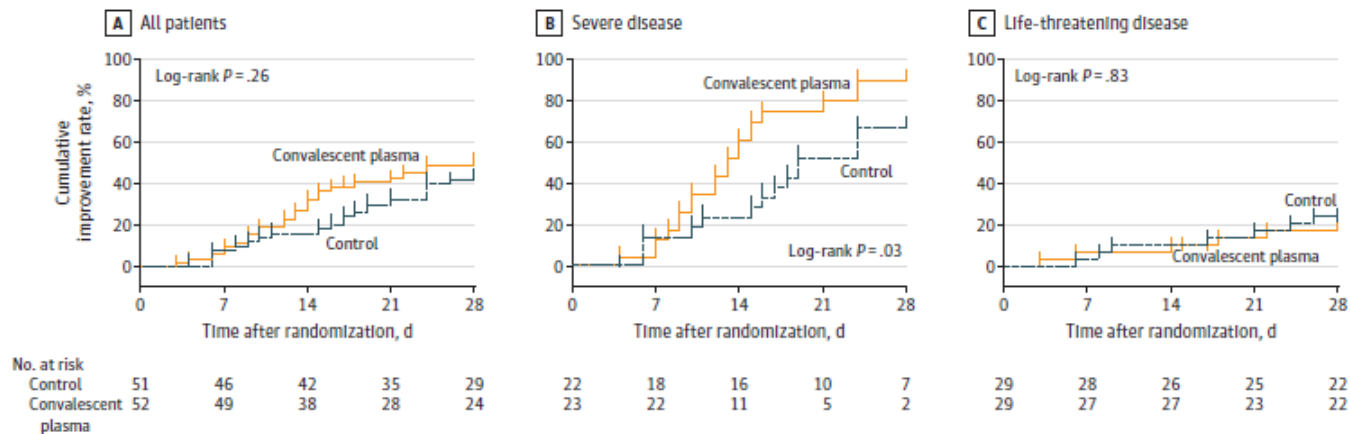
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Figure 2. Time to Clinical Improvement in Patients With COVID-19



The cumulative improvement rate is the percentage of patients who experienced a 2-point improvement or were discharged alive from the hospital. Ticks on the curves indicate censored events. All patients who did not reach clinical improvement were observed for the full 28-day period or until death. COVID-19 indicates coronavirus disease 2019.

The median (IQR) follow-up times for the convalescent plasma group and control group, respectively, were 15 (10-28) days and 24 (13-28) days overall; 13 (10-16) and 18.5 (11-26) days among those with severe COVID-19; and 28 (12-28) and 26 (15-28) days among those with life-threatening COVID-19.



# TOCIVID-19 Trial

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## Tocilizumab for patients with COVID-19 pneumonia. The TOCIVID-19 phase 2 trial

 Francesco Perrone, Maria Carmela Piccirillo, Paolo Antonio Ascierto, Carlo Salvarani, Roberto Parrella, Anna Maria Marata, Patrizia Popoli, Laurenzia Ferraris, Massimiliano M Marrocco Trischitta, Diego Ripamonti, Francesca Binda, Paolo Bonfanti, Nicola Squillace, Francesco Castelli, Maria Lorenza Muiesan, Miriam Lichtner, Carlo Calzetti, Nicola Duccio Salerno, Luigi Atripaldi, Marco Cascella, massimo costantini, Giovanni Dolci, Nicola Cosimo Facciolongo, Fiorentino Fraganza, Marco Massari, Vincenzo Montesarchio, Cristina Mussini, Emanuele Alberto Negri, Gerardo Botti, Claudia Cardone, Piera Gargiulo, Adriano Gravina, Clorinda Schettino, Laura Arenare,  Paolo Chiodini,  Ciro Gallo

doi: <https://doi.org/10.1101/2020.06.01.20119149>

- Phase II, multicenter, 1221 patients
- 1 or 2 infusions, 8 mg/kg tocilizumab
- 60% had delay in receiving drug
- Most had concurrent therapies



# Tocilizumab and concurrent Rx

	ITT Phase 2	ITT Validation
	N=301	N=920
<b>Concurrent treatment, no. (%)</b>		
Antiretroviral	179 (63.5%)	549 (66.9%)
Hydroxy-chloroquine	205 (72.7%)	627 (76.4%)
Antibiotics	117 (41.5%)	421 (51.3%)
Steroids	61 (21.6%)	277 (33.7%)
LMW heparin	64 (22.7%)	158 (19.2%)
Unknown	19	99
<b>C-reactive protein – Median (IQR)</b>	37.6 (14.7, 120.0)	36.3 (13.7, 137.0)
Missing or not tested	181	255



# Efficacy

	Phase 2	Validation
<b>14 days intention-to-treat</b>		
No. of events/no. of patients at risk	55/299	101/884
<b>Lethality rate, % (97.5% CI)</b>	<b>18.4% (13.6-24.0)</b>	<b>11.4% (9.1-14.0)</b>
P value (P0=20%)	<b>0.52</b>	<b>&lt;0.001</b>
<b>14 days modified intention-to-treat</b>		
No. of events/no. of patients at risk	28/180	56/515
Lethality rate, % (95% CI)	15.6% (10.6-21.7)	10.9% (8.3-13.9)
<b>30 days intention-to-treat</b>		
No. of events/no. of patients at risk	67/299	158/858
<b>Lethality rate, % (97.5% CI)</b>	<b>22.4% (17.2-28.3)</b>	<b>18.4% (15.5-21.6)</b>
P value (P0=35%)	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Median time of death, days (IQR)	8 (4-14)	11 (4-18)
<b>30 days modified intention-to-treat</b>		
No. of events/no. of patients at risk	36/180	99/495
Lethality rate, % (95% CI)	20.0% (14.4-26.6)	20.0% (16.6-23.8)



# Conclusions

- Impact on 30d mortality, not 14d
  - Single arm prevents firm conclusion
  - Comparison (null hypothesis) for validation
    - 43,000 patients Italy, another view
      - ❖ 14d = 22%, 30d = 27.6%
    - This study
      - ❖ 14d = 18.4%, 30d = 22%
- Multiple logistic regressions
  - Most benefit for those not yet on mechanical ventilation
- Only 1 death of 35 attributable to tocilizumab
  - 3% had severe elevation of LFTs





To submit your own question, please email  
[QA@dkbmed.com](mailto:QA@dkbmed.com)



**Can you comment on whether COVID-19 appears to be weakening as it mutates?**



**How will infection rates affect the ability of schools to reopen? What criteria should be most important when considering opening schools in the fall?**



**Some reports suggest that blood type may be associated with risk of COVID-19 infection and disease severity, with type O blood being protective. Can you comment on this?**



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## **To ask your own question to Dr. Auwaerter:**

- Email [QA@dkbmed.com](mailto:QA@dkbmed.com)