Advancing Care in Public Health Emergencies

Changing the Paradigm from Anecdotal- to Data-driven Patient-centric Care

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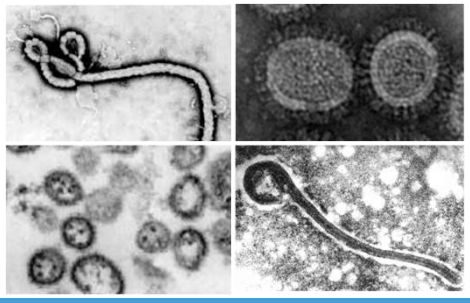

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1

Outcomes depend on *early* (trust) supportive care + safe and effective disease-specific therapies

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2

Challenging research response yields uncertain results

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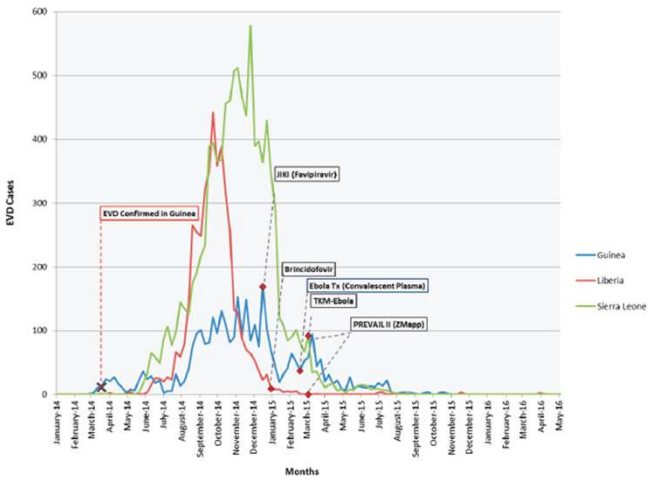

- Late start of studies
- Use of historical controls
- Variable standard of care
- Did not achieve targeted enrollment
- MCM use outside of clinical trials

→ Uncertain results

https://www.nationalacademies.org/projects/IOM-HSP-15-08/publication/24739

3

RCTs change care in public health emergencies

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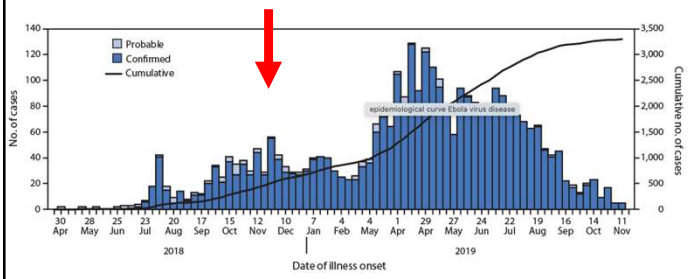
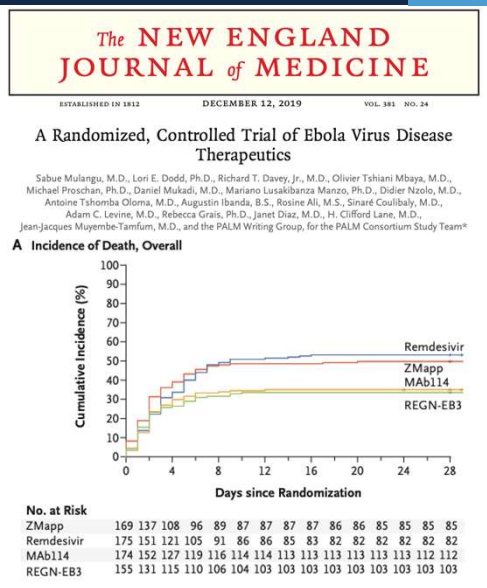
Outbreak to enrollment: 111 days





Aruna, A. et al. MMWR 2019
Mulangu, S. et al. NEJM 2019

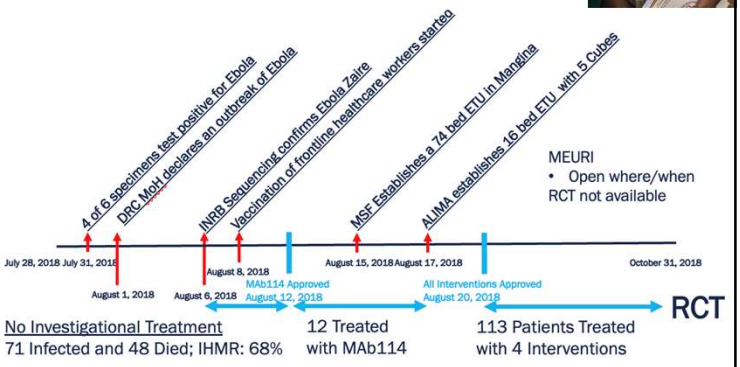
4

MEURI – a model for EA programs

World Health Organization

Notes for the record: Consultation on Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI) for Ebola Virus Disease (EVD)

1. No proven effective treatment
2. RCT not possible
3. Supportive efficacy/safety data
4. Use suggested by scientific committee
5. Approved by relevant country/ethics committees
6. Risks can be minimized
7. Informed consent is obtained
8. Emergency use is monitored and results are shared



→How to operationalize therapeutics
→High risk populations
→Key clinical endpoints

5

Streamlined, inclusive RCT can be highly impactful

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RECOVERY

Randomized Evaluation of COVID-19 Therapies

March 19, 2020 (<70 days)
Inclusive Enrollment
Data entry minimal
Follow up at a single timepoint

The NEW ENGLAND JOURNAL of MEDICINE

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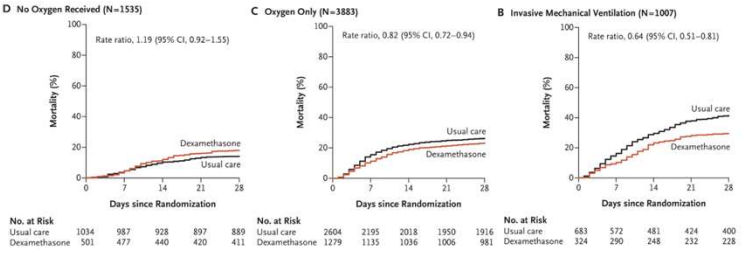
Dexamethasone in Hospitalized Patients with Covid-19

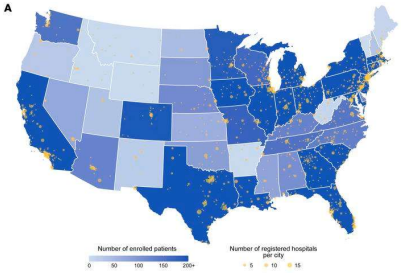
The RECOVERY Collaborative Group*



→1,000,000 lives saved in first 9 months

6

EA-IND provides early insight into safety + logistics



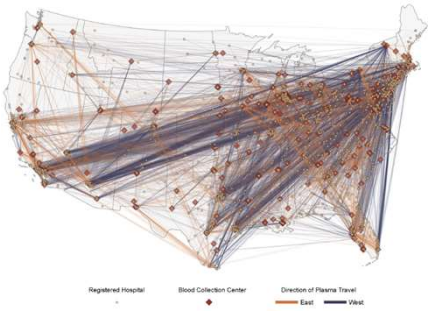


Table 2. Serious adverse event characteristics (n = 5,000)

Four-hour reports	Reported (n = 36)	Related[A] (n = 25)	Estimate (95% CI)
Mortality	15	4	0.08% (0.03%, 0.21%)
Transfusion-associated circulatory overload	7	7	0.14% (0.07%, 0.29%)
Transfusion-related acute lung injury	11	11	0.22% (0.12%, 0.39%)
Severe allergic transfusion reaction	3	3	0.06% (0.02%, 0.18%)
Seven-day reports			
Mortality	602		14.9% (13.8%, 16.0%)[B]

N=105,717 → 500,000

Joyner, M. et al JCI 2020
Senefeld, J. et al. Plos Medicine 2021

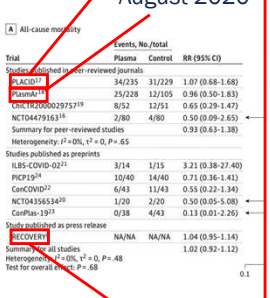
7

No benefit associated with convalescent plasma in severe or critical COVID-19

October 2020

August 2020

January 2021



JAMA | Original Investigation

Association of Convalescent Plasma Treatment With Clinical Outcomes in Patients With COVID-19
A Systematic Review and Meta-analysis

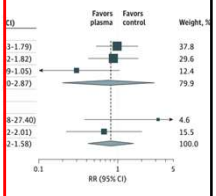
ONLINE SPECIAL ARTICLE

Surviving Sepsis Campaign Guidelines on the Management of Adults With Coronavirus Disease 2019 (COVID-19) in the ICU: First Update

Convalescent Plasma

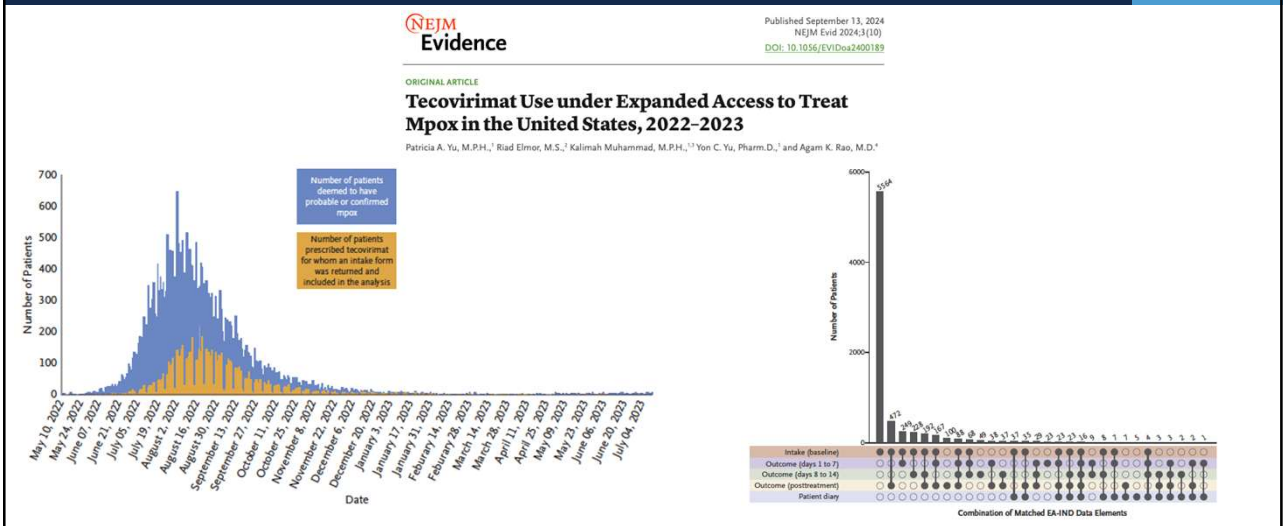
Recommendation:

5. For adults with severe or critical COVID-19, we suggest against the use of convalescent plasma outside clinical trials (weak recommendation, low-quality evidence).



8

A large number of people contributed little data



NEJM Evidence

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ORIGINAL ARTICLE

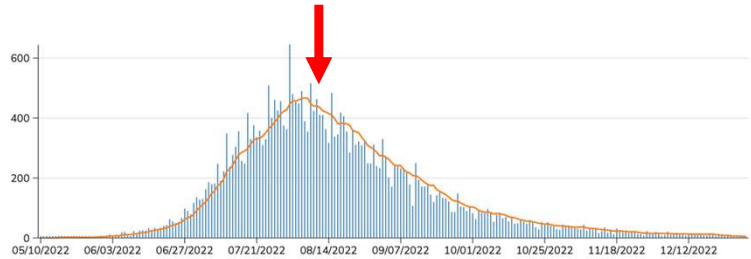
Tecovirimat Use under Expanded Access to Treat Mpox in the United States, 2022–2023

Patricia A. Yu, M.P.H.,[1] Riad Elmor, M.S.,[2] Kalimah Muhammad, M.P.H.,[1,3] Yon C. Yu, Pharm.D.,[1] and Agam K. Rao, M.D.[4]

9

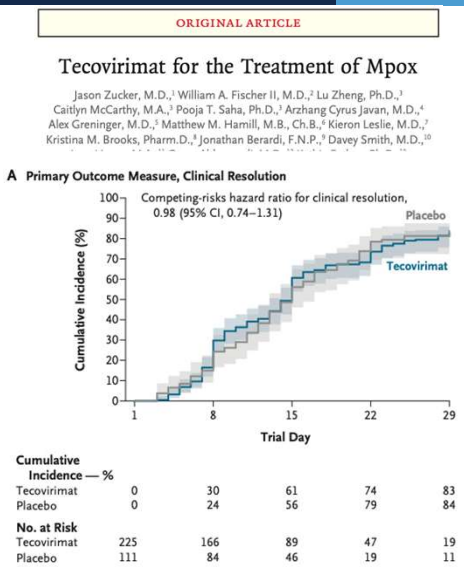
Negative results can change care and improve efficiency

Outbreak to enrollment: 130 days
Funding to enrollment: 60 days



Collaboration facilitated study design and enrollment

https://www.cdc.gov/monkeypox/data-research/cases/index.html



ORIGINAL ARTICLE

Tecovirimat for the Treatment of Mpox

Jason Zucker, M.D.,[1] William A. Fischer II, M.D.,[2] Lu Zheng, Ph.D.,[3] Caitlyn McCarthy, M.A.,[3] Pooja T. Saha, Ph.D.,[3] Arzhang Cyrus Javan, M.D.,[4] Alex Greninger, M.D.,[5] Matthew M. Hamill, M.B., Ch.B.,[6] Kieron Leslie, M.D.,[7] Kristina M. Brooks, Pharm.D.,[8] Jonathan Berardi, F.N.P.,[9] Davey Smith, M.D.,[10]

A Primary Outcome Measure, Clinical Resolution

Cumulative Incidence — %					
Tecovirimat	0	30	61	74	83
Placebo	0	24	56	79	84
No. at Risk					
Tecovirimat	225	166	89	47	19
Placebo	111	84	46	19	11

10

We can move faster and be more effective

- RCTs change care and build trust
  - Minimize bias and confounding through randomization
  - Fewest number of people are exposed to the least effective intervention
  - Improves efficiency of response
- Trial designs can be optimized to balance speed and rigor
  - Streamline regulatory processes
  - Pre-approve protocols/frameworks
  - Coordinated international collaboration
- Use complimentary evidence sources
  - EA-IND/observational studies can improve RCTs

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11

Thank You

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12