

Politics of Science
in a pandemic:
Impact on
Evidence-based medicine

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Sevagram

Outline

1	Politics of Science
2	Evidence based Medicine
3	Possible to do randomized controlled trials during a pandemic?
4	Why do we need randomized controlled trials?
5	Perils of untested therapies
6	Penchant for untested therapies
7	Is there a hope?

WHEN WRITTEN IN CHINESE, THE WORD

CRISIS

IS COMPOSED OF TWO CHARACTERS

ONE REPRESENTS

DANGER

危

AND THE OTHER REPRESENTS

OPPORTUNITY

机

John F. Kennedy



“**Medicine** is a social science and **politics** is nothing else but **medicine** on a large scale.”

Rudolph Virchow



EVERY
DISASTER MOVIE
STARTS WITH THE
GOVERNMENT
IGNORING
A SCIENTIST



**People are
tired of hearing
Fauci and
all these idiots!**



Covid-19 has created a crisis throughout the world. This crisis has produced a test of leadership. With no good options to combat a novel pathogen, countries were forced to make hard choices about how to respond. Here in the United States, our leaders have failed that test. They have taken a crisis and turned it into a tragedy.

Dying in a leadership Vacuum

COVID-19 in Brazil: “So what?”

These are hopeful actions. Yet, leadership at the highest level of government is crucial in quickly averting the worst outcome of this pandemic, as is evident from other countries. In our 2009 Brazil Series, the authors concluded: “The challenge is ultimately political, requiring continuous engagement by Brazilian society as a whole to secure the right to health for all Brazilian people.” Brazil as a country must come together to give a clear answer to the “So what?” by its President. He needs to drastically change course or must be the next to go. ■ *The Lancet*

flouting and discouraging the sensible measures of physical distancing and lockdown brought in by state governors and city mayors but has also lost two important and influential ministers in the past

because of severe cuts in the science budget and a more general demolition of social security and public services. In the context of COVID-19, many organisations have launched manifestos aimed at



Bruna Prado/Getty Images

For a Portuguese translation see
Online for appendix



THE COVID-19 CATASTROPHE

**WHAT'S GONE WRONG AND HOW
TO STOP IT HAPPENING AGAIN**

**RICHARD
HORTON**

**How did two of the richest,
most powerful and most
scientifically advanced
countries in the world
get it so wrong,
and cause such ongoing pain
for their citizens?**

Again using the United Kingdom as an example, he suggests that researchers were insufficiently informed or understanding of the crisis unfolding in China, and were too insular to speak to Chinese scientists directly. The model for action at times seemed to be influenza, a drastic underestimation of the true threat of the new coronavirus. Worse, as the UK government's response went off the rails in March, ostensibly independent scientists would "speak with one voice in support of government policy", keeping up the facade that the country was doing well. In Horton's view, this is a **corruption of science policymaking at every level**. Individuals failed in their responsibility to procure the best scientific advice, he contends; and the advisory regime was too close to – and in sync with – the political actors who were making decisions. **"Advisors became the public relations wing of a government that had failed its people,"** he concludes.

COVID-19 in India: the dangers of false optimism

Despite a strong response at the outset of the pandemic, as of Sept 22, India has the world's fastest growing outbreak of COVID-19 in absolute numbers according to WHO, reporting more than 5.6 million infections. Restrictions began to be lifted in June, and this relaxation has continued in the face of a continuing dramatic increase in case numbers nationally. Beneath these alarming national figures, the pattern of spread in India is nuanced and complex, with marked differences between states, and between rural and urban areas. For example, cities like Kolkata and rural areas in the north of India were relatively spared the outbreak initially, whereas Delhi, with strong international connections, was at the forefront of the first wave. Even so, India is clearly facing a dangerous period.

The country has responded well in many regards, especially for such a large and diverse nation. India instigated a national lockdown in March, which was praised by WHO. During the lockdown period, tertiary care provision was increased, including access to specialist equipment such as ventilators. Testing numbers also increased quickly, with India being among the first to roll out innovations like pooled testing. India has also been at the forefront of efforts to develop and manufacture a vaccine, both through domestic vaccine candidates and manufacturers such as the Serum Institute of India preparing production capacity for internationally developed vaccine candidates.

distancing. The epidemic in India is far from over, with a potentially huge burden of mortality and morbidity to come unless public health measures are used and adhered to. Without clear and honest communication of the risks of COVID-19 to the population, stemming the epidemic will be impossible.

According to news reports, hours before announcing the national lockdown, Prime Minister Narendra Modi told owners and editors from India's largest media organisations that it was important to tackle the spread of pessimism, negativity, and rumour. This pressure to avoid negative news, and to offer reassurance, appears to have been felt by several professional scientific organisations in India. The Indian Council of Medical Research (ICMR) has been singled out by experts for straying from scientific evidence, appearing at worst politically motivated and at best overly optimistic. A letter from the Director General of the ICMR, Balram Bhargava, said that the ICMR envisaged launching a coronavirus vaccine on Aug 15 (Indian Independence Day; a deadline considered unrealistic by most medical experts); ICMR has supported treatment with hydroxychloroquine despite insufficient evidence; and news reports claim that data on coronavirus infection were removed from a scientific paper.

Transparency of the data on COVID-19 cases and deaths, especially those underpinning the case fatality rate, has also been questioned, as detailed in a recent



Barcroft Media/Getty Images

For more on **pooled testing in India** see <https://www.livemint.com/news/india/pooling-can-help-india-optimize-its-testing-strategy-11587578644506.html>

For **Modi's comments to journalists** see <https://www.theguardian.com/global-development/2020/jul/31/india-arrests-50-journalists-in->

'Govt relying on bureaucrats, not epidemiologists': Top health experts slam Covid handling

Statement issued by Indian Public Health Association, Indian Association of Preventive and Social Medicine & Indian Association of Epidemiologists have called the lockdown 'draconian'.

FATIMA KHAN 31 May, 2020 2:38 pm IST

Senior AIIMS doctor slams Modi govt's response to COVID-19 in medical journal

Dr Anoop Saraya, Head of Gastroenterology and Human Nutrition Unit at AIIMS, said success of any advisory group of scientists depended on a culture of openness, independence and diversity of opinion

HEALTH

ICMR Must Decide if it Is India's Council for Medical Research or its Master's Voice

Today, no one expects ICMR to contradict the Centre's COVID-19 response strategy on any count, irrespective of the enormity of a transgression.

What is Evidence Based Medicine

David Sackett
Gordon Guyatt

Editorials

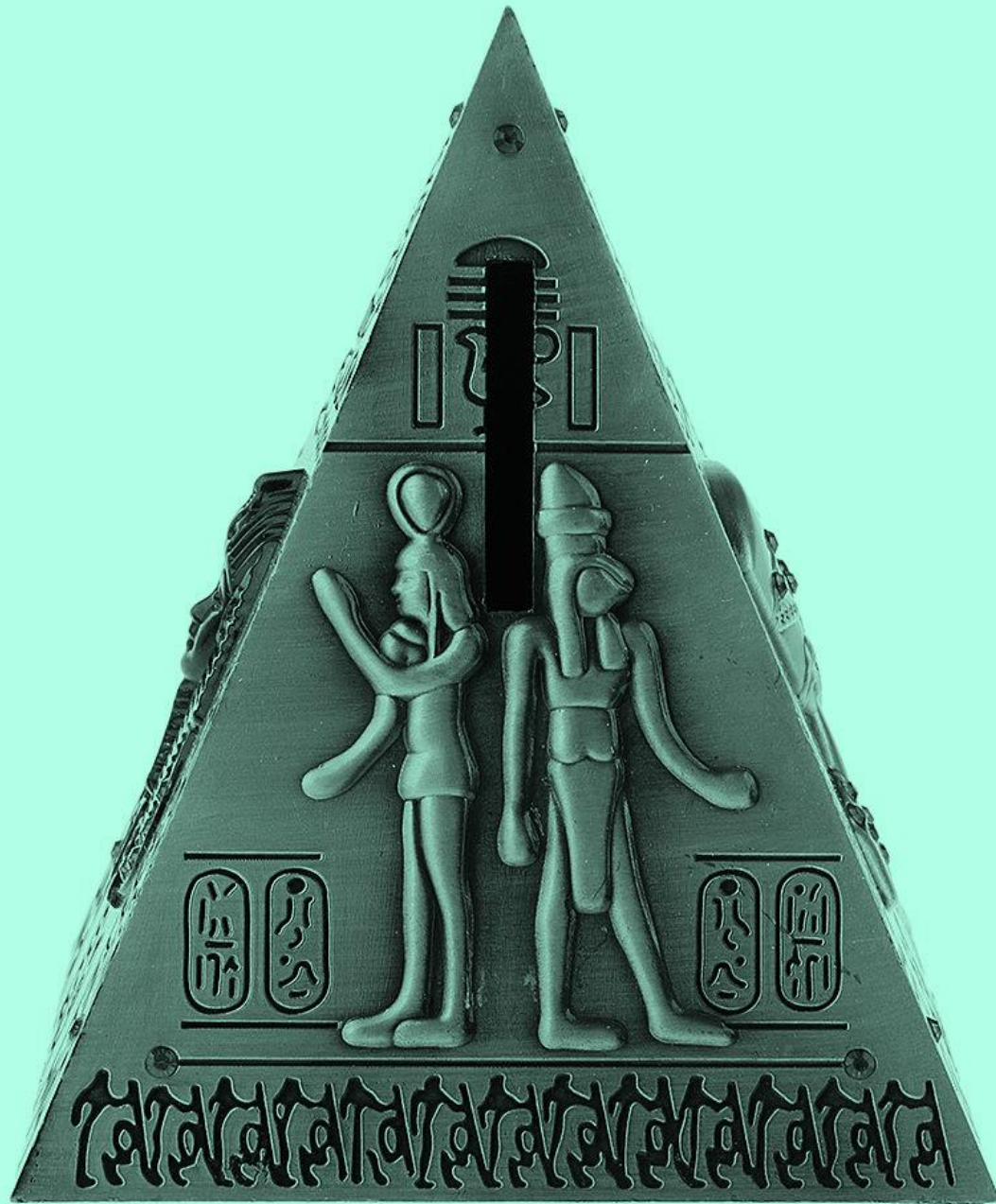
Evidence based medicine: what it is and what it isn't



David L Sackett, William M C Rosenberg, J A Muir Gray, R Brian Haynes, W Scott Richardson

It's about integrating individual clinical expertise and the best external evidence

Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.





Politicians

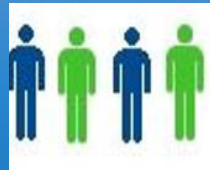




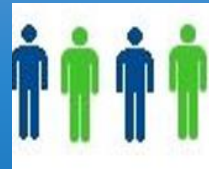
Assess
for
eligibility



Excluded



Intervention



Control



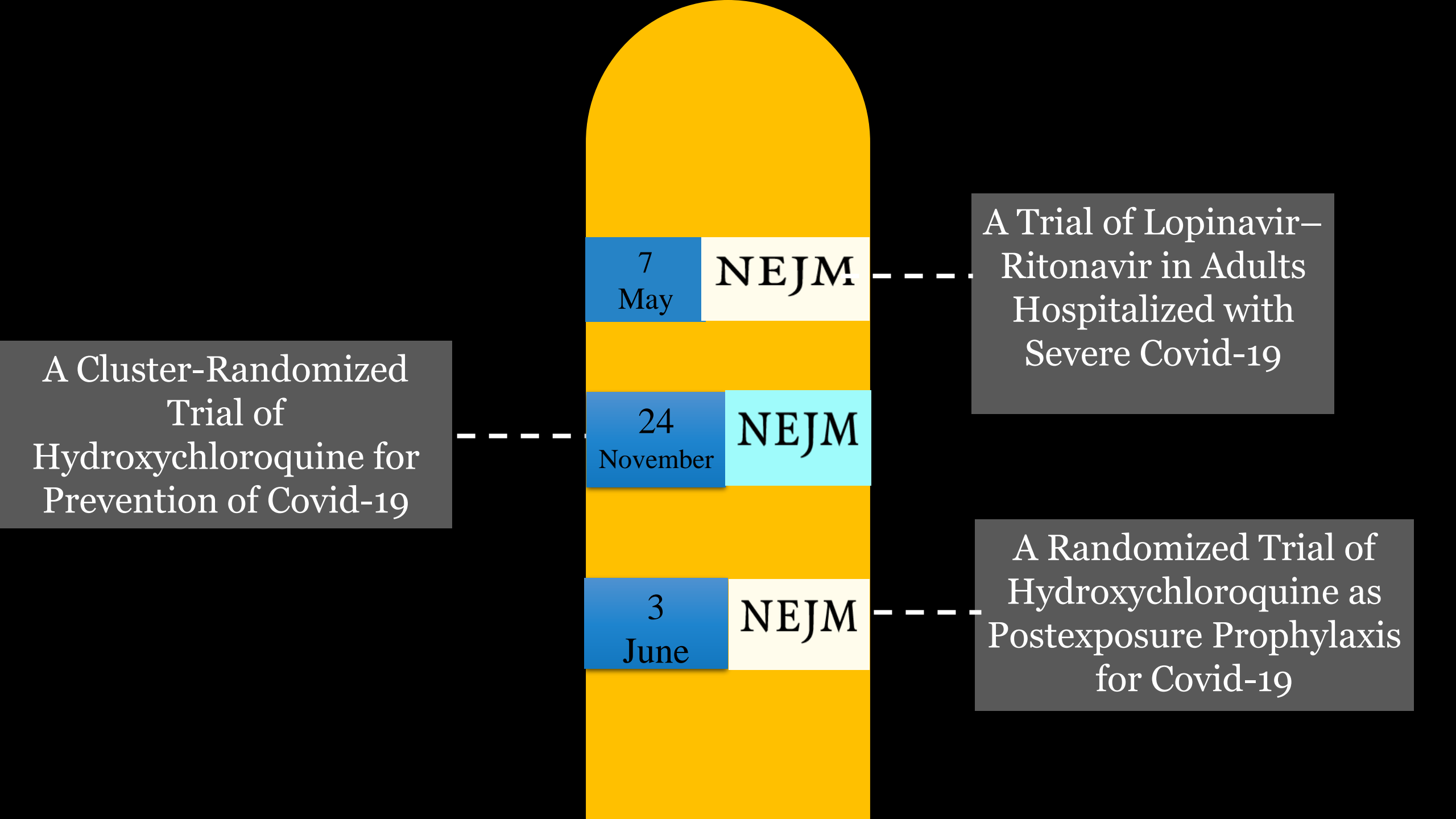
Assess Outcome

Is it possible to do RCT
during a pandemic?

Yes

Start to Finish 60 days





7
May

NEJM

A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

24
November

NEJM

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

3
June

NEJM

A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19

Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19

16 July Annals of Int Med

Hydroxychloroquine in Nonhospitalized Adults with Early COVID-19

8 October NEJM

JAMA The Journal of the American Medical Association

9 Nov

Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19

Remdesivir in adults with severe COVID-19: a randomised, double blind, placebo-controlled, multicentre trial.

23
July

NEJM

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

29 Apr

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LANCET

5
Nov

NEJM

Remdesivir for the Treatment of Covid-19 —

24
November

NEJM

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

Convalescent plasma in
the management of
moderate covid-19
in India:
(PLACID Trial)

12 Oct

thebmj

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

6
August

NEJM

Efficacy of Tocilizumab
in Patients Hospitalized
with Covid-19

JAMA The Journal of the
American Medical Association

20 Oct

NEJM

10 Dec

JAMA The Journal of the
American Medical Association

20 Oct

Effect of tocilizumab vs
usual care in adults
hospitalized with COVID-
19 and moderate or severe
pneumonia: a randomized
clinical trial.

Effect of tocilizumab vs
standard care on clinical
worsening in patients
hospitalized with COVID-
19 pneumonia: a
randomized clinical trial.

NEJM

10 Dec

Safety and Efficacy of
the BNT162b2 mRNA
Covid-19 Vaccine

An mRNA Vaccine
against SARS-CoV-2

NEJM

12 Nov

NEJM

2 Dec

WHO Solidarity Trial

SARS-CoV-2
Neutralizing Antibody
LY-CoV555 in
Outpatients with Covid-
19

17
July

NEJM

Dexamethasone in
Hospitalized Patients
with Covid-19

28
Oct

NEJM

11
Dec

NEJM

Baricitinib plus
Remdesivir for
Hospitalized Adults
with Covid-19

PATANJALI

23 June

Immunity booster Coronil
in mild Covid-19

Itolizumab to treat
Patients with Covid-19

 **Biocon**

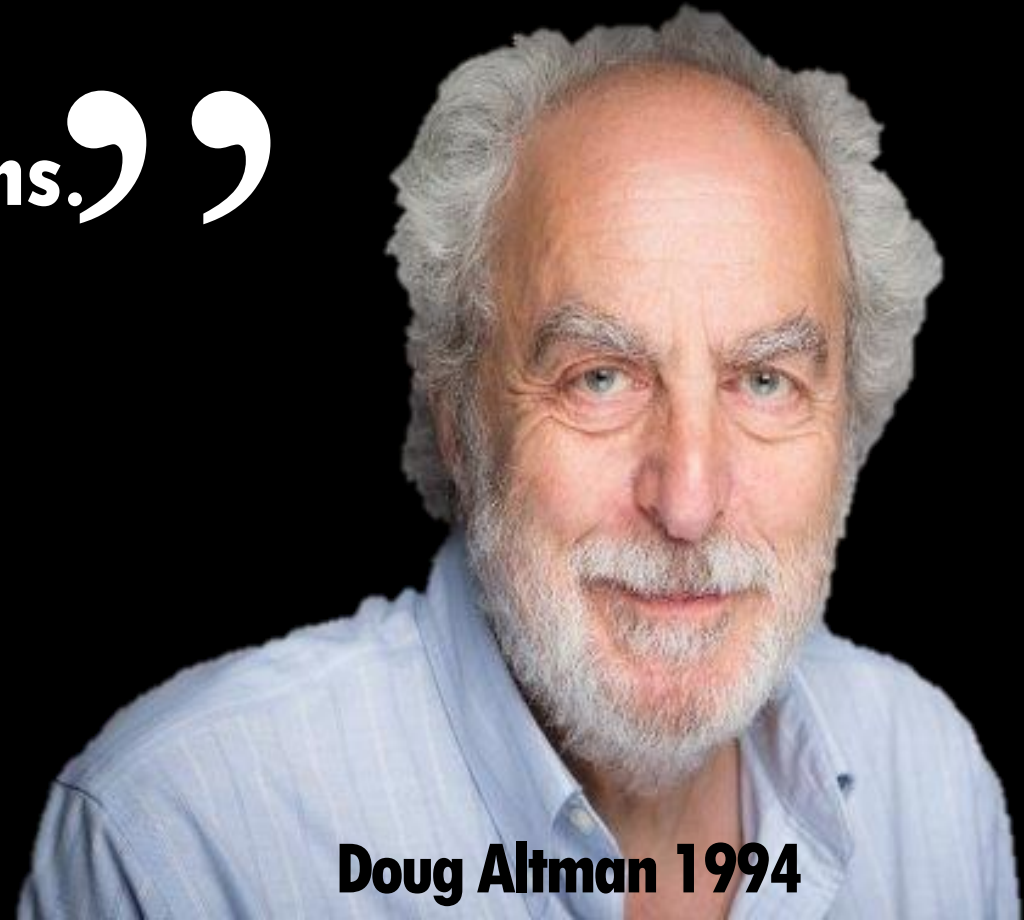
13 July

Glenmark

22 July

Favipiravir to treat mild to
moderate Covid-19

“ “We need **less** research,
better research, and
research done
for the right reasons.” ”



Doug Altman 1994

Why we need randomized
controlled trials?

Cure

A single positive response to a new treatment

Equality

Making unproven treatments to everyone

New Definitions!

A close-up photograph of a hand holding a pencil, poised to write on a lined notebook. The background is a textured, light-colored surface. The text is overlaid in a bold, black, sans-serif font.

**Drugs
that look very appealing and promising
on paper
fall flat
when they are tested in RCTs...**

**Oseltamavir
(Tamiflu)**

Randomized controlled trials are the most reliable way to identify the relative benefits and risks of investigational products, and every effort should be made to implement them during epidemics.

Committee on Clinical Trials During the 2014-2015 Ebola Outbreak.
Busta ER, Mancher M, Cuff PA, et al., editors.

“Scientifically robust and ethically sound clinical research remains the quickest and most efficient pathway to effective treatment and prevention strategies for patients with Covid.”

H. Clifford Lane, and Anthony S. Fauci
NEJM. 17 July 2020

“It is not biological, however; the superinfection I'm talking about is spreading in the hearts and minds of physicians and academics. The superinfection has led us to forget longstanding principles of evidence-based medicine, abandon logic and clear-headedness, and lower the bar for adopting unproven standards of care.”

Vinay Prasad



Perils of Using Untested therapies

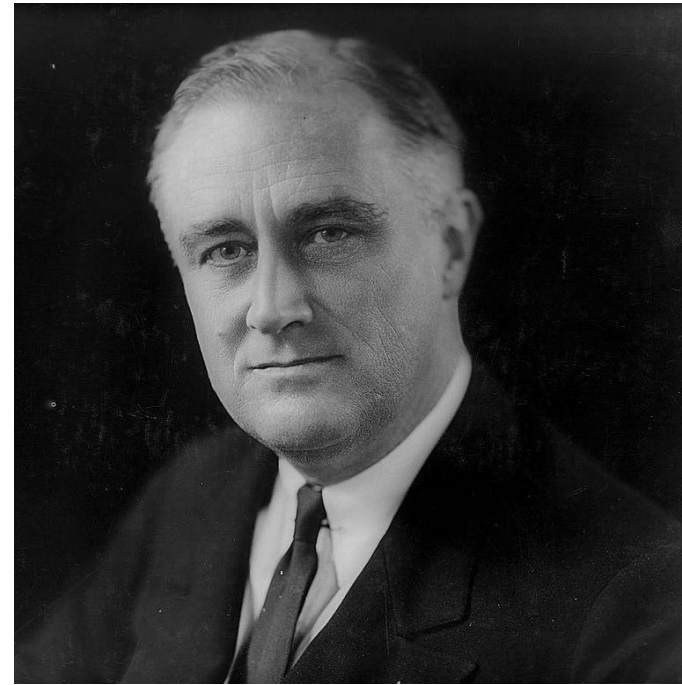
Human response to Crisis

“So what do we do? Anything. Something... . If we screw it up, start over. Try something else. If we wait until we’ve satisfied all the uncertainties, it may be too late.”



Lee Iacocca

“Take a method and try it. If it fails, admit it frankly and try another. But by all means, try something.”



Franklin D. Roosevelt

Perils of Using untested therapies

Though a trial-and-error approach may be appropriate in business and politics, should it be applied to medical decision making during a pandemic?

Zagury-Orly I, Schwartzstein RM. Covid-19 - A Reminder to Reason.
N Engl J Med. 2020 Jul 16;383(3):e12.

Perils of prescribing untested therapies

Primum Non Nocere

Difficult to enroll people in the
randomized controlled trials

Adverse events underestimated

Unproven therapies become the
standard of care

We are deeply concerned that in this environment of global panic, an endorsement by the highest scientific body of India (and also by the President of the USA)⁴ will create an overly optimistic perception of the effectiveness of hydroxychloroquine among the public. Markets in the USA are already reporting a short supply of both hydroxychloroquine and chloroquine.⁴ The situation in India is no different, probably indicating widespread self-medication.

The shortage of chloroquine, an inexpensive antimalarial in low-income malaria-endemic countries

for its efficacy and its potential risks. Additionally, all outcome events should be recorded. If this is not done, the risk–benefit assessment would be skewed, **adverse events accepted as collateral damage**, and a drug accepted provisionally in a time **of crisis could become commonplace as standard of care for a long time to come.**

We declare no competing interests.

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Ashwini Kalantri,
*Shriprakash Kalantri
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“ I have never witnessed a doctor giving five, six, or 10 drugs to treat a virus without any proof that it will help. ”



“Right now I take a blue pill, a purple pill, an orange pill, a white pill, and a yellow pill. I need you to prescribe a green pill to complete my collection.”

Perils of Using untested therapies

Paisa

Power

Politicians

Policymakers

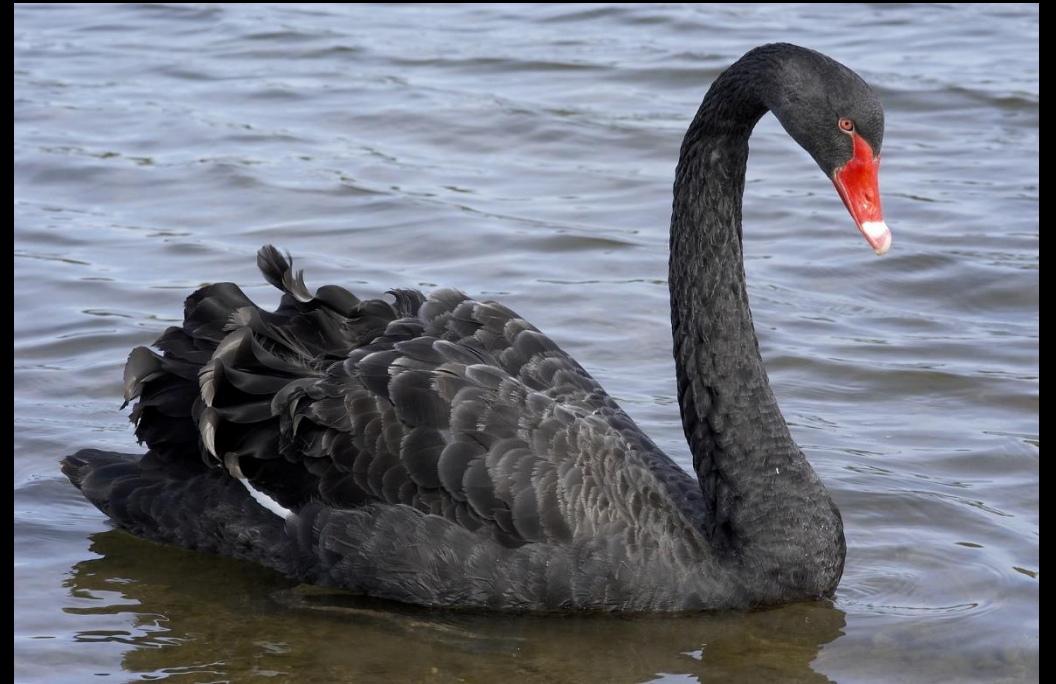
Poor research

can mislead the people and physicians—
into believing that many worthless or
unproven treatments are effective.

What makes people want,
and physicians try,
untested drugs?

COVID-19

It is unpredictable;
it carries a massive impact;
and, after we concoct an explanation that
makes it appear less random, and more
predictable, than it was.



What if HCQ turns out to be effective?

Then, what do we do?

What do I have to lose?

“The evidence doesn’t matter, because in my experience they work”

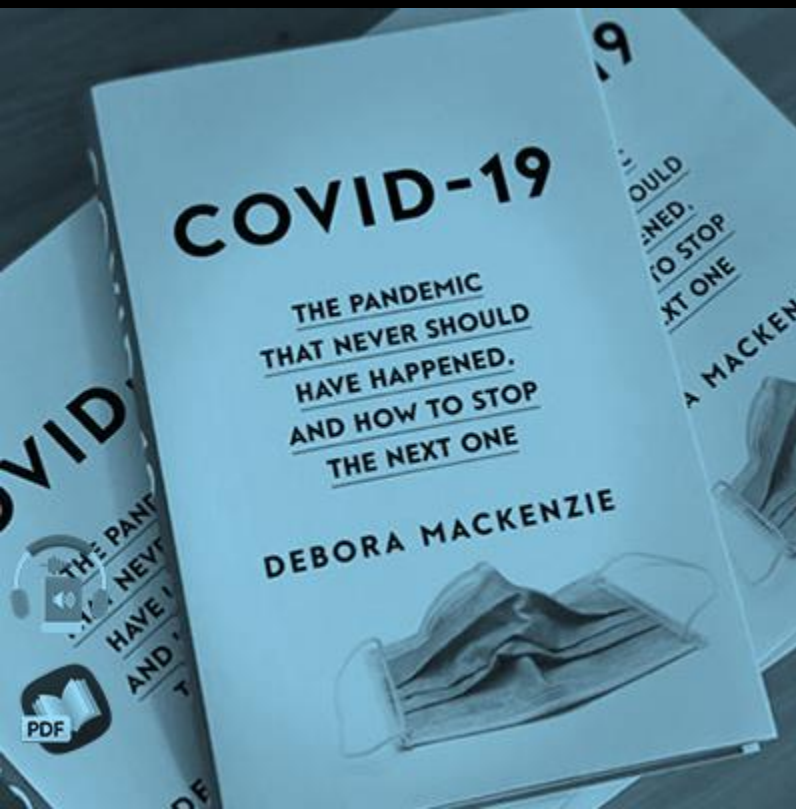
We feel compelled to do something

The government questions why I did not use this drug



So, Is there a hope?

But we can at least hope listening to scientists will become more of a norm. Now that Covid-19 has shown us how desperately a modern society needs to rely on facts, evidence, and honesty, rather than secrecy, ideology, or wishful thinking.



THE LANCET



India has the expertise in medicine, public health, research, and manufacturing to lead the nation through the COVID-19 pandemic.

To capitalise on these attributes, the country's leaders must respect scientific evidence, expert commentary, and academic freedom, and not provide false optimism.