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

Dr. SP Kalantri
Professor of Medicine
Mahatma Gandhi Institute of Medical Sciences
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 and the other represents opportunity.

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
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.

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
'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
Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.
Is it possible to do RCT during a pandemic?

Yes
Start to Finish 60 days
A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19

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

A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19
Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19

Hydroxychloroquine in Nonhospitalized Adults with Early COVID-19

Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19
Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19

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

Remdesivir for the Treatment of Covid-19 —
A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia

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

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

A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia
Effect of tocilizumab vs usual care in adults hospitalized with COVID-19 and moderate or severe pneumonia: a randomized clinical trial.

Efficacy of Tocilizumab in Patients Hospitalized with Covid-19

Effect of tocilizumab vs standard care on clinical worsening in patients hospitalized with COVID-19 pneumonia: a randomized clinical trial.
An mRNA Vaccine against SARS-CoV-2

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

WHO Solidarity Trial
Dexamethasone in Hospitalized Patients with Covid-19

Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19
Favipiravir to treat mild to moderate Covid-19

Itolizumab to treat Patients with Covid-19

Immunity booster Coronil in mild Covid-19

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!
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.
“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
“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.”

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

Lee Iacocca

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?

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) 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. 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.

Sahaj Rathi, Pranav Ish, Ashwini Kalantri, *Shriprakash Kalantri
sp.kalantri@gmail.com
"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.”

©Randy Glasbergen
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?
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.
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.