

VIEWPOINT

Sensible Medicine—Balancing Intervention and Inaction During the COVID-19 Pandemic

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Audio

More than 38 million people worldwide have been infected with the severe acute respiratory syndrome (SARS) coronavirus 2, creating intense pressure on clinicians to offer state-of-the-art, life-saving treatment to patients.¹ The conundrum is that few effective treatments are available, and among those treatments tested in clinical trials, even fewer have demonstrated benefit compared with no treatment. Treating patients with coronavirus disease 2019 (COVID-19) is challenging, and clinicians encounter harrowing emergencies in the intensive care unit where, early during the pandemic, 1 in 4 critically ill patients with severe COVID-19 died.²

The natural response at the bedside of a patient with COVID-19 is to act and to act decisively.³ Imbued with determination, clinicians seek to make a difference for patients who are seriously ill. In 2012, Taleb⁴ described an “illusion of control that leads to a default to action rather than inaction.” For many medical emergencies, such as cardiac arrest, pulmonary embolism, or tension pneumothorax, this illusion is a reality for clinicians because immediate intervention can prevent avoidable death. But what if it is unclear what to do? What if no medication or device will lead to a cure? Should clinicians do

nothing? It is certain of the futility of treatment, ineffectiveness of most medications, and corrupting influence of financial incentives. In the middle is a sensible approach, which acknowledges that some interventions are effective but, perhaps, confidence should be tempered. With sensible medicine, the translation of knowledge to the bedside is appropriately calibrated to the rigor and reasoning of the available evidence and the severity of the outcome to be avoided.

A sensible approach has been threatened by the complexity of COVID-19, public demand for progress, and the pace and volume of pandemic science. Clinicians and scientists have been led astray as often as uncovering new COVID-19 biology and treatments.¹ An attainable strategy for sensible medicine is required.

How to Practice Sensible Medicine During a Pandemic

Strategy 1: Medicine Without Magic

Clinicians must first embrace the improbability that a single treatment for severe COVID-19 will be a so-called magic bullet.⁵ Treatments that approach this ideal focus on a unifying pathophysiology and effectively mitigate the constitutive cause of the disease. Insulin may be such a therapy, not by eliminating a target, but by restoring normal physiology. In contrast, the biology of severe COVID-19 is complex.⁶ It is a potentially lethal combination of immunopathogenic and immunoprotective responses on a backdrop of a prothrombotic milieu. No single mechanism or pathway yet discovered accounts for all of the pathophysiology. Similar to acute respiratory distress syndrome caused by sepsis or

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something, when the best option may be measured or supportive care? During the COVID-19 pandemic, clinicians' tension between interventionism and measured action is ever present.

This Viewpoint proposes that sensible medicine for COVID-19 may better serve patients than unreasoned treatment using unproven interventions in the moment.

What Is Sensible Medicine?

Sensible medicine is an approach to treatment that seeks a balance along the spectrum of the strength of evidence and the pace of knowledge translation (Figure). On one hand, a hawkish interventionist has little doubt about the effectiveness of a new treatment and rapidly adopts it into practice. There is a tendency to favor adoption of the new, acceptance of less rigor in research methods and results, and a glance away from subconscious biases. This contrasts with the medical nihilist who is highly skeptical of new evidence and hopes to intervene even less. The medical ni-

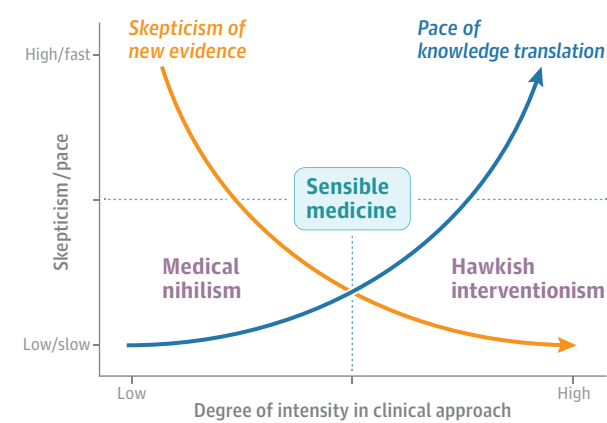
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Strategy 2: Practice Doing (Almost) Nothing

For most physicians, it is difficult to do (almost) nothing for patients. The list of the experimental therapies proposed for COVID-19 is long, including hyperbaric oxygen therapy (NCT04358926), mesenchymal stem cells (NCT04444271), and even the administration of thalidomide (NCT04273529). The lack of control groups in some recent trials of COVID-19 treatments further highlights the do-something mentality.⁷ But there is an alternative. Sensible medicine accepts that unreasoned intervention with experimental treatment may lead to

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Figure. Conceptual Model for Sensible Medicine



more harm than good. A drug like hydroxychloroquine may be safe when used in the correct dose for a proven indication in a patient who is relatively healthy, whereas it may have unknown adverse effects when used in a critically ill patient who is receiving many other therapies. Clinicians should advocate for randomized trials with appropriate controls, and counsel patients that standard care may be as effective as tomorrow's best idea. Clinicians must learn while doing,³ and accept that (almost) nothing is in fact something.

Strategy 3: Elevate Usual Care

Sensible medicine is still labor intensive. For patients with COVID-19 who have acute illness, guidelines include supportive or usual measures like lung protective ventilation or prone positioning, both of which reduce mortality.¹ Usual care also includes optimizing care for chronic health conditions. During the 2004 SARS outbreak, for example, patients were far less likely to obtain outpatient care due to concern about nosocomial infection.⁸ Missed opportunities to manage chronic conditions, such as diabetes and hypertension, could affect the likelihood of surviving COVID-19.

Strategy 4: Focus on High-Quality Evidence

Some clinical research is biased. Even the best research methods, such as randomized trials, can be unreliable. This has been amplified by the rapid pace of research undertaken during the COVID-19

pandemic. Moreover, the public demand for an effective intervention can generate unwarranted visibility for sensational results from small, unblinded, or nonrandomized trials, as illustrated with hydroxychloroquine. But to be confident that an intervention is effective for COVID-19, as Califf et al⁹ have suggested, requires the reliance on evidence from only the highest-quality randomized trials.

Strategy 5: Think Bayesian

In 2009, Friedman¹⁰ wrote that "new treatments are a bit like the proverbial new kid on the block: they have an allure that is hard to resist." The pandemic has accelerated attraction to new treatments and promoted rapid translation to the bedside. But should clinicians be so aggressive? A simple application of the Bayes theorem may help. For example, assume H is a hypothesis that a new COVID-19 treatment is effective and E is the evidence for that treatment being effective. By the Bayes theorem, the odds that the new treatment is effective given the evidence is:

$$P(E|H)/P(E|\text{not } H) \times \text{Prior Odds}$$

During the pandemic, the following assumptions would be expected:

The prior odds are low given the lack of a unifying biological mechanism and multiple neutral clinical trials.

$$P(E|H)/P(E|\text{not } H)$$

This is the ratio of observing the (weak) evidence assuming the treatment is or is not effective, and this ratio is close to 1.

Thus, the posterior odds that a new COVID-19 treatment is effective should be low and hardly changed from a small prior value. It follows that treatment guidelines, national mandates, and bedside care adapt to new data only when the evidence is rigorous, reproducible, and sufficiently strong.

To be clear, sensible medicine does not mean clinicians should not intervene. Rather, it proposes a gentler, moderate, and humble view of available treatment options and their effectiveness in patients with COVID-19. The approach encourages clinicians to elevate usual care, reduce unnecessary interventionism, and focus and rely on scientific rigor. Rather than choose between action and inaction, sensible medicine encourages supportive restraint and heightened therapeutic humility.

ARTICLE INFORMATION

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