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A Deadly Race Against Time: Lessons from COVID-19 On Pandemic Policy During Emergent Outbreaks

I. ABSTRACT:

The COVID-19 pandemic has ravaged the international community, creating worldwide devastation and pain for millions. Now with developed vaccines and a proven antiviral drug, the immediate clinical urgency is somewhat abating. It thus has become imperative to scrutinize the national and international pandemic response, not only to derive lessons about effective pandemic management, but also to identify practical recommendations for citizens and governmental agencies in future emergent outbreaks. Specifically, in the context of the United States, the federal government failed in the delicate balancing of clinical efficiency to maximize patient outcomes with medical due diligence, poignantly illustrated in the management of early SARS-CoV-2 testing and the hydroxychloroquine debacle as examples, leading to numerous deaths. The most significant causes behind the mismanagement were a lack of bureaucratic organization and a fundamental deficiency in reciprocal trust between lawmakers and citizens. The theoretical solution—creating a communicative, inter-departmental agency that is transparent and garners trust through comprehensive, evidence-based practices—is a target to strive for, but reality is messy, and outbreak management is invariably infiltrated by politics and self-interest. Nonetheless, by examining other historical outbreak investigations in addition to COVID-19, there are two simple yet critical and practical steps everyday citizens can take in future emergency situations to perhaps create an environment where collaborative, nuanced discourse on the best course of action is easier: engaging

in local advocacy and being mindful of our own rhetoric. Thus, perhaps when the next pandemic strikes, we won't witness the same desolation in our families and communities as we did in 2020.

II. THE EARLY FAILURES OF COVID-19

"Pneumonia of Unknown Cause":

I vividly remember waking up one morning in December 2019 and gazing out our four-story window into the gusty, chilly courtyard surrounding my grandparents' apartment complex in China. It was a lazy, entirely unremarkable start to the day—one befitting of a winter break vacation—except for a core interaction that forever marred this seemingly nondescript memory. It was a simple interaction. My mom, diligent as always, had gotten up early to read the morning news. In there, buried behind the latest sensational stories and color-laden advertisements, was a simple report that she read out to me: "multiple cases of atypical pneumonia detected in Wuhan." Fatefully at that time, I had just finished reading *Spillover* by David Quammen, which included a section on China's Severe Acute Respiratory Syndrome (SARS) outbreak of 2003. Feeling an uneasy *deja vu,* I responded with an off-handed, "yeah, that might not turn out well."

In hindsight, that might have been an understatement.

The facts are clear from then on. By January 23rd, not more than a month since that day, Wuhan was entirely in quarantine. A week later, the WHO issued a Global Health Emergency. By May 28th, 100,000 alone in the United States were dead, and the sobering reality of the COVID-19 pandemic gripped the world (AJMC Staff 2021). Everything, from geopolitical stability to the economy to actual human life centered around how governments around the world responded.

SARS-CoV-2 Testing - A Tale of Two Countries:

When it became clear that SARS-CoV-2, or COVID-19, would be an epidemic-level pathogen of significant importance early in February 2020, the United States national response could only be described as fractured, particularly in the sector of distributing SARS-CoV-2 tests. While countries like South Korea "acted like an army" by summoning "representatives from more than 20 medical companies" to develop and streamline such tests through the regulatory pipeline, the United States became mired in "congested [bureaucracy]," "cautious leadership," and "a reliance on protocol." The United States relied on CDC-developed kits as was customary during previous outbreaks, "some of which proved faulty" (Terhune 2020). Furthermore, "South Korea took a risk, releasing briskly vetted tests, then circling back later to spot check their effectiveness. By contrast, the United States FDA said it wanted to ensure, upfront, that the tests were accurate before they went out to millions of Americans." (Terhune 2020). The result was ultimately catastrophic—broader, earlier testing would have dampened the exponential portion of the logistic growth characteristic of pandemics, saving innumerable lives.

While it is normal to expect mistakes when dealing with such uncertain and emergent situations, the reality is that the United States' botched handling of the pandemic's earliest stages induced ripple effects that propagate to this very day. In the case of SARS-CoV-2 testing, the scientific consensus is generally clear: screening tests are an instrumental "mitigation strategy" in public health emergencies (Yukari 2020). Naturally, this fact was well-known to US policymakers and advising epidemiologists in February 2020. The difference in outcomes for South Korea and the United States (at least early on in the pandemic) arose because of differences in execution, stemming from fundamental paradigm differences between the two countries about conducting medical-related investigations during emergent pandemics.

As detailed by Terhune, the United States stubbornly clung to codified regulations and internalized precedents when designing tests. In contrast, South Korea abandoned those rules by

identifying the emergent nature of SARS-CoV-2 early on and decisively choosing to take early action, resulting in a minimization of cases. From an initial outcomes perspective, both in garnering the public's trust toward government competency and delivering actual clinical benefit, it seems like South Korea's approach is superior.

While the United States ultimately ramped up its testing program later on toward the middle of 2020, the delayed reaction already had effects. During those critical first few months, every policy decision was amplified—South Korea seemed poised for more successful virus containment, while an environment of fear and uncertainty was cultivated in the United States.

The Central Question:

The parallel case study of the US and South Korea's implementation of nationwide testing thus raises an extremely prescient question: Is it true, then, that circumventing established regulations for the sake of rapid efficiency in the context of developing medical therapeutics is the most desirable policy when responding to emergent situations, at least early on? More broadly, is there a preferred strategy that governments and scientists should employ to maximize clinical benefit and public trust during emergencies? As one might expect, the answer is not so simple, particularly when addressing the multifaceted issue of pandemic response, which weaves together disparate aspects of public policy, epidemiology, human psychology, biological investigation, and more into a proverbial Gordian Knot.

The stakes associated with testing were minimal. Rapid SARS-CoV-2 tests could hardly cause any real physiological harm to the body, the test was relatively noninvasive and thus well-received, and general consensus agreed testing was positive. Yet in virtually all other cases, be it vaccines, antiviral drugs, or enacting nationwide lockdowns, few if any of these three aforementioned conditions are true. As demonstrated by the controversy surrounding hydroxychloroquine, which

occurred shortly after and partly as a consequence of the initial testing failure, adopting the strategy of speed over clinical due diligence can produce devastating consequences as well.

Hydroxychloroquine - A Case Study:

On March 20th, 2020, a new preprint article was posted onto medRxiv. Titled "Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial," authors Gautret et al. detailed the use of hydroxychloroquine, a then relatively obscure antiparasitic, as a potential therapeutic for patients suffering from SARS-CoV-2. The study was grounded in biological plausibility—chloroquine had been proposed as an effective *in vitro* (in the lab) antiviral for COVID-19, so the next logical step was expanding the compound to *in vivo* (in human) testing. The stakes were high, and the scientific community was eagerly awaiting an urgently needed drug to combat the virus as it inched toward catastrophic pandemic status. Thus, when Gautret reported that their "survey [showed] that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients," researchers were cautiously optimistic (Guatret et al. 2020). Despite the promising results, Gautret himself acknowledged that the study had a "small sample size," while other scientists warned of potential biases involved in the study—after all, whoever discovered the miracle antiviral that could eradicate the SARS-CoV-2 plague would benefit tremendously in status and money for discovering this panacea. Specifically, all of the control patients were patients who refused hydroxychloroquine treatment, and the viral load quantification through PCR techniques delivered potential inconsistencies (Machiels 2020). It was clear overall that, in order for hydroxychloroquine (HCQ) to clear minimal standards as a potential therapeutic during so-called "normal times," much more work would need to be done.

However, almost simultaneously in March 2020, President Trump announced during a White House briefing that HCQ was a "game changer" in terms of treating COVID-19. Google searches for HCQ spiked, and as the FDA released an Emergency Use Authorization (EUA), HCQ came flying off the shelves. Soon, the FDA declared a national shortage (Englund 2020). Despite the FDA attempting to qualify their EUA by stating that HCQ research was based on "limited in-vitro and anecdotal clinical data," the governmental authorization and messaging lent substantial credibility. This triggered a "norm cascade" "into consumer interest and behavior" that would be extremely difficult to stop—any reversal in policy decision-making would have to contend with humanity's natural instinct to try every treatment possible during times of desperation (Englund 2020).

Unfortunately, on June 15th, 2020, the FDA revoked its EUA for HCQ as further research revealed that it was "unlikely to be effective in treating COVID-19." Furthermore, the literature described a risk for "serious cardiac adverse events and other potential serious side effects," triggering the worst-case scenario (FDA 2020). Not only were people purchasing HCQ and depleting the global supply for patients who actually needed it as a malaria antiparasitic, but many were also duped into a false sense of security, leading to a poorer prognosis for SARS-CoV-2 infection—not to mention the potential side effects.

While the case of hydroxychloroquine is but one of the many examples of mishandled decisions in the early pandemic by the Trump administration, it remains an instructive and representative example for understanding the underlying reasoning for why seemingly poor decisions can happen.

III. WHY WE FAILED

Internal Political Pressure:

In the Englund study into hydroxychloroquine using Google Trends search volume data, a fascinating trend emerged: relative search volumes for HCQ were greatest in "the United States, Brazil, and India, which also had support from political leadership for treatment of COVID-19… Of note, these three countries have had the highest confirmed cases and deaths from COVID-19 through October 2020" (Englund 2020). This provides insight into why President Trump and other world leaders in Brazil and India were so eager to promote HCQ despite the fact it was poorly studied: there was significant political pressure ramping up internally within their countries. Indeed, it is no coincidence that the countries that fared worst in terms of clinical outcomes early on tended to lean heavily toward favoring quick, perhaps performative action over the necessary medical due diligence. As Philip Bump describes in a Washington Post article, hydroxychloroquine became "a sign of… confidence in [President Trump's] instincts and as a way of promoting what they see as an optimistic view of the pandemic" when the situation had already become dire (Bump 2020).

Unfortunately, as alluded to earlier, this internal pressure to produce some sort of medicinal solution can be linked to the Trump administration's initial inaction in the earliest stages of the pandemic, where more directed and centralized testing could have minimized case counts. South Korea, for instance, felt no such pressure to jump on hydroxychloroquine as a vehicle to assuage the fears of the general public since case counts were lower. Perhaps even more importantly, the South Korean public retained more trust in the government, which meant the officials felt minimal pressure to immediately take action as a demonstrative political gesture of competency—empirical evidence proved that they were already making sound decisions.

While I've used South Korea as a foil to the American COVID-19 response, the same applies to any other country. Although there are certainly geopolitical differences that make each case unique, in broad strokes, the same snowballing effect of competency leading to trust and

incompetence leading to misguided, potentially harmful attempts to regain trust is broadly generalizable.

Norm Entrepreneurs:

Even if most of the political leadership in the country holds firm against internal pressure, the unfortunate reality is that just a single, powerful individual can completely disconcert a coordinated national pandemic response. President Trump in the United States was a "norm entrepreneur," a single individual who triggered the devastating "norm cascade" that bounced around through influential media channels and word-of-mouth spread until the issue of hydroxychloroquine use lay firmly outside of the FDA's hands (Englund 2020). Indeed, the effects that Trump had on hydroxychloroquine were quantified by Niburski et al. in 2020, with Figure 1 below taken from their article "Impact of Trump's Promotion of Unproven COVID-19 Treatments and Subsequent Internet Trends: Observational Study." Section B of Figure 1 describes search trends for "hydroxychloroquine," with the orange line corresponding to purchases and the blue to Google search volume. Section A corresponds to "chloroquine."

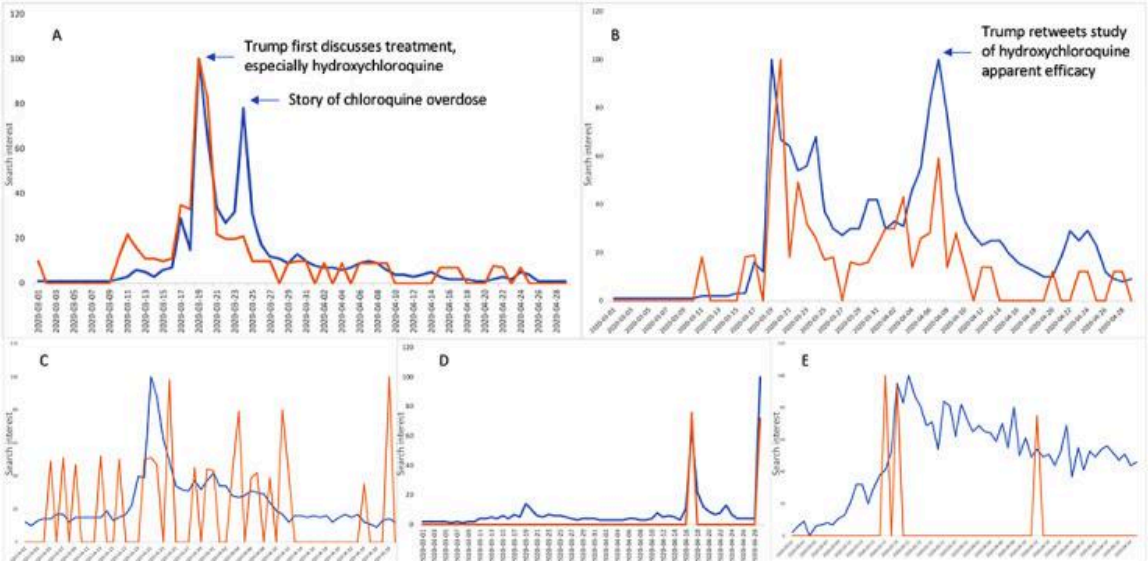

Figure 1: Search Volume and Purchases for "Chloroquine," "Hydroxychloroquine," and other terms.

It is clear from the trends that both purchases and search volume spiked after Trump's promotion, either through official White House channels or through his social media presence. In contrast, a widely publicized story about chloroquine overdose generated less search volume, and it's certain that a subset of those who heard the story nonetheless continued seeking out HCQ.

Norm entrepreneurship makes logical sense: "individuals often seek out influential figures for guidance and knowledge," and Trump's message of wholehearted approval was indeed much more appealing than Fauci's scientific and thus inherently uncertain warning to "look at [hydroxychloroquine] in a scientific way" and not to immediately believe in the "buzz" (Fox News 2020).

The existence of norm entrepreneurs highlights the importance of a centralized, national response team that can communicate and coordinate without the impediments of bureaucracy. If the adoption of hydroxychloroquine had not been spearheaded by President Trump in a viral manner online before other federal agencies and leaders could come to a consensus, it is likely that the subsequent fallout could have been minimized.

IV. RECOMMENDATIONS: WHAT WE SHOULD DO

Our Role:

While the debacle surrounding SARS-CoV-2 testing and hydroxychloroquine can both be easily attributed to the "classic conflict between the clinical bedside medicine and academic medicine," where "clinical bedside medicine… allows for prescription of the therapies which may not be based on the most rigorous clinical evidence" in hopes of creating better clinical outcomes, that conclusion would be simplistic and reductive (Neeraj 2020). Accepting that premise would be inherently accepting that in emergent situations like pandemics, there would be almost an intrinsic, uncontrollable risk that ultimately harmful medications like HCQ can be prescribed and promoted

on an international level, or needed interventions like efficient testing may be delayed out of overcautiousness.

While that risk does always exist, I contend that each and every person, be it a world leader or an everyday citizen, has at least some agency in working toward preventing what can only be described as the disastrous mishandling of the COVID-19 pandemic in early 2020 from occurring in the future.

The Ideal:

As previously discussed, navigating a pandemic response with millions of lives on the line is a messy, complicated, and ultimately intractable affair. No country, federal department, or leader will make all the right choices, and similarly, there is no prescribable formula that can be followed for success. Nonetheless, examining the COVID-19 pandemic, particularly in its earliest phases, has provided invaluable insight into a number of different guiding principles that should be adopted for future emergent situations.

First, on the conflict between speed and clinical validation (also framed as the conflict between clinical bedside medicine and academic medicine), the speed should be proportional to the amount of harm, be it to trust, health, or social systems, that may occur. Testing, which is minimally invasive with significant upside, should be implemented as quickly as possible. In contrast, the adoption of novel pharmaceutical agents like hydroxychloroquine would require more due diligence. Compared to so-called "normal times," urgency becomes more important in emergency situations, but that does not trump clinical validation in cases where the stakes are large and norm cascades may occur.

This case-by-case evaluation of different proposed policies is the challenging, "easier-said-than-done" assertion, as there are many instances where "invasiveness" and "upside" is

extremely difficult to quantify among numerous other different factors. This is why a centralized, inter-agency task force must be established, with frequent communication and buy-in from every member involved. As evidenced by the existence of "norm entrepreneurs," it only takes one "bad-faith" actor in the governmental response to derail an entire coordinated plan. It is only in this way that companies, agencies, departments, and national governments can collaborate in a manner that generates clear and decisive decision-making. Politics should not enter the equation—in essence, the members of the task force must trust the citizens enough to transparently present comprehensive, factual breakdowns of what we know or don't know. If distrust, be it a fear of reputational damage (i.e. Trump overcompensating for testing failures by adopting HCQ) or a belief that the public should not know critical information for fear of misguided action (i.e. the "noble lie" told by Fauci about how masking doesn't work to ensure nurses have their own supply (Powell, Kerrington, and Prasad 2021)), becomes entangled in the pandemic response, that distrust snowballs and creates mass misinformation that results in preventable deaths.

Similarly, it is also our prerogative as citizens to place trust in our government when faced with times of uncertainty (if they haven't done anything egregious to prove otherwise). The relationship must be reciprocal for the government to feel comfortable being transparent and for the citizens to believe in the recommended interventions.

The Reality:

Unfortunately, it would be naive to think that real life could perfectly align with the recommended steps described above. The ever-present political polarization in our country means no more than 50% of citizens at a time trust the government, and while the concept of a collaborative task force exists theoretically, it relies on the participation of completely logical, cooperative political figures. In all cases, politicians are motivated by their own personal agenda in

some form, and although President Trump could be seen as an anomaly for his divisiveness, to an extent all leaders suffer from the same issue. In addition, fear and uncertainty prey on the instinctual aspects of human psychology, driving communities and people to engage in understandable yet ultimately harmful behavior toward pandemic management. To be clear, this is perfectly normal and expected, as we are all human.

V. PRACTICAL STEPS FROM HISTORICAL EPIDEMIOLOGY

Thus, if expecting government leaders and everybody else to just "do the right thing" all the time is a little too hopeful, it thus becomes imperative to—in addition to aiming for the lofty but perhaps at times hollow-ringing goals of communication, collaboration, and mutual trust—codify practical steps that everyday citizens can take during emergent situations to better the discourse and perhaps save lives. In particular, examining the social and scientific tensions during empirical instances of epidemiological investigations is illuminating toward identifying lessons learned and actionable steps to take.

1. The Rajneeshee 1984 Bioterrorist Attack: Advocacy

On September 17th, 1984, researchers and scientists in Wasco County, Oregon began receiving reports of gastroenteritis centered around the small town of The Dalles, Oregon. In the 1980s, the population hovered around 10,500, yet shockingly within the span of a few weeks, 751 people were infected with Salmonella bacteria. Naturally, the Center for Disease Control (CDC) stepped in to investigate, but as cases continued to rise, "there was a tremendous amount of pressure on the CDC to claim a cause for the outbreak and put everyone at ease." Thus, perhaps hastily, the CDC concluded that the outbreak occurred because of poor food worker hygiene at local restaurants

(Sen 2018), much like how political and social pressure altered decision-making during the COVID-19 pandemic.

However, unsatisfied with the response, Congressman James Weaver and his constituents conducted their own investigation, which ultimately brought to light the involvement of the Rajneeshee cult in intentionally spreading the Salmonella pathogen to salad bars in restaurants in The Dalles (Weaver 2001). This incident remains the largest bioterrorism event in the history of the United States. Without the dogged pursuit of Weaver and his colleagues, history may still regard the 1984 outbreak to be from accidental causes, and the future damage caused by the Rajneeshee cult would be immeasurable.

This incident parallels the COVID-19 pandemic because, on a much smaller scale, residents of an entire community were thrust into an all-consuming and fearful emergent situation surrounding pathogens. In addition, the same interplay between politics and governmental intervention remained.

Specifically, the case of the Rajneeshee bioterror attack highlights the critical importance of advocacy, both from everyday people and their corresponding legislative constituents. Many in The Dalles shared concerns about the Rajneeshee cult, who had moved in only a few years ago and had subsequently attempted to seize political power (DBpedia). This resulted in their healthy skepticism toward the findings of the CDC, and thus facilitated the discovery of the truth. Their engagement and investment in the political process encouraged action. Critically, however, they were not mistrustful of the governmental agencies, allowing them to collaborate and share information. In reciprocation, the government acquiesced to the citizens' concerns and continued its epidemiological investigation by involving the FBI, which searched the cult and discovered the contaminating bacteria (DBpedia).

Thus, practically during a pandemic, the first thing we can do is to get involved with our local representatives. People of all different backgrounds and experiences need to come together to coalesce diverse viewpoints through which comprehensive solutions can be created. In times of crisis, it can be easy to retreat or succumb to faux advocacy through bitter internet vitriol where trust is never reciprocated and no effective action can be taken. We as citizens must choose to avoid that natural albeit debilitating consequence and strive to engage in productive dialogue with our governmental policymakers.

2. HIV, Homophobia, and Hate: Rhetoric

In 1981, the CDC reported five cases of a rare form of pneumonia usually seen in immuno-suppressed individuals in healthy, homosexual men. The disease, then known as the pejorative gay-related immunodeficiency disease (GRID), has since evolved into what we now know as HIV/AIDS (Halkitis 2012). However, this association between HIV/AIDS and homosexual men has never truly been decoupled despite policymakers' best efforts, and it persists to the modern day. A significant driving force behind this association was the rhetoric used initially by news organizations, the government, and other scientists at the time. Be it being dubbed the "gay disease" or having the associated pneumonia described as "gay men's pneumonia," the language used was often patronizing and blaming (HIV/AIDS Timeline). The result was devastating. Famously, "members of the Reagan administration… refused to even mention the word AIDS until 1985" when the epidemic was too big to ignore (Christensen 2016). This culminated in a sense of fear and shunning that enveloped the nation, meaning victims of this horrendous disease were rendered entirely without support as "parents refused to see their sick children, and faith communities called patients with HIV an 'abomination'" (Christensen 2016). The result was undoubted agony for patients and lost time in finding a cure.

On the other hand, following the early ignorance and stigmatization of HIV/AIDS, the rhetoric used by government officials shifted drastically in 1987 when they launched the "everyone is at risk" message campaign in an effort to unravel the association between HIV/AIDS and gay communities. However, the rhetoric was "met with mixed feelings by AIDS workers." The reality was that not everyone was at risk to the same extent, and by spreading out the attention and resources thin to all groups, "some saw the campaign as diverting money and attention away from the communities that needed it the most--leaving gay and minority communities to compete with one another for the little money that remained" (Geiling 13).

The HIV/AIDS pandemic was another instance, much like the COVID-19 pandemic, where social issues and divisions infiltrated epidemiological response due to its wide-spreading effects and propensity to cause fear. As illustrated, the power of rhetoric in shaping public health discourse is clear. We must realize that the way we describe and converse about topics, be it HIV/AIDS or a new and emerging pandemic pathogen like COVID-19, communicates information, even subconsciously. It's important to remove ourselves from the fearmongering that can run rampant during times of uncertainty, and try to ensure our concerns are heard without overreacting. In addition, we must not be quick to assign blame, as the labels can stick within the public consciousness and thus unknowingly influence policy and decision-making. After all, language sways individuals' decisions, and as shown by the HIV/AIDS pandemic, both the initial stigmatization and subsequent efforts to combat the stigma resulted in misdirected use of resources that could have saved lives. The practical manifestation of being careful about our rhetoric can be a simple mindfulness of the information we disseminate to friends, and whether they're merely unsubstantiated rumors or actual, verifiable facts—even just thinking about this in the future pandemic situations as a nation could allow us to take a more measured and nuanced approach to pandemic response.

VI. REFLECTIONS

As is true for many, the COVID-19 pandemic is personal to me. Like many, that first moment when I heard about this small, seemingly insignificant virus during winter break more than three years ago has been seared into my consciousness. And like many, I've been heartbroken from witnessing the suffering of those I love.

When I first set out to investigate the COVID-19 pandemic response, I sincerely hoped that there would be a concrete solution to maximize our pandemic preparedness and ensure the miscommunications and polarization of the past few years don't happen again—something that I could point to, so that the future generations won't suffer the same pain.

However, as research progressed and more nuance emerged, it was clear to me that my initial goal wasn't possible. But nonetheless, I hoped to detail everything we could strive for, both idealistic and practical, to perhaps improve our response when "the next big pathogen" inevitably arrives in the future.

The recommendations are still imprecise. While I've identified a heuristic for the long-standing debate between clinical efficiency and medical due diligence, the implementation of those policies still rests on the combined effort of government policymakers and the everyday citizen. There are actionable steps we can take to foster an environment conducive to positive discourse: citizens can advocate for their beliefs in local government and become more mindful of their immediate reactionary rhetoric to uncertain situations, while government officials should adopt a mindset of trust toward the public and collaborate. But reality is often far more complicated and nuanced.

All I hope is that when the next emergent pandemic occurs, we will be better prepared than we were in December of 2019, on that gusty, chilly morning in China when I first learned about SARS-CoV-2.

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