#194

SECOND INTERIM REPORT OF THE TWENTY-SECOND STATEWIDE GRAND JURY

INTRODUCTION

For the last four years, Floridians have all been directed so often to "follow the science" by politicians, public officials, researchers and medical professionals that at this point, there is probably no deader horse in all of healthcare. Don't understand why your government is imposing this restrictive mandate? Follow the science. Don't understand why you should be taking this drug and not the drug that was recommended last month? Follow the science. Don't understand why you are being treated exactly the same as everyone else around you, regardless of age, comorbidities or other mitigating factors? You, sir, must not be following the science. Since its first session, this Grand Jury has been grappling with a question that has been simmering below this tired aphorism: What exactly is "the science?" When qualified, similarly-credentialed experts in the same fields do not agree; when new, inconsistent study results are unveiled on a regular basis; how is the general public supposed to make sense of these contradictions? As jurors, an unbiased pursuit of answers to these questions has occupied a substantial amount of our time and our resources for the last year. Still, in some areas, we do not have satisfying answers. No member of the public could be expected to do anything like this and also have time left over to perform the vital functions required for our society to exist.

So, we outsource. We rely upon scientists, researchers, academics, institutions and government agencies to provide valid, reliable scientific information for the protection and betterment of our families' health without having to dedicate huge portions of our own lives to determine these answers on our own. A block mason does not expect an epidemiologist to understand the mechanisms and measurements behind building the corner foundation of a house; the mason's competency is assumed, if not expected. Just so, we expect our researchers to have similar levels of certitude as they go about researching the spread of a novel virus in a community, the effectiveness of given treatment modalities or the benefits conferred by prior infections. The problem with this analogy is that science is not blocks. The scientific process can be imperfect. By design, it fails more often than it succeeds. To some degree, it is unreasonable of the public to expect as much certainty from our epidemiologists as we might from our block masons, especially amid a global pandemic involving a novel virus. By the same token, it may also be unreasonable for those who disseminate clinical medical guidance amid a global pandemic to display the kind of certitude a block mason would display when laying a foundation, particularly when that certitude is followed by a dismissive instruction to "follow the science." Even where these

pronouncements mollify people in the moment, often "the science" will later render them suspect, as we saw in the First Interim Report and we will see below.

In our First Interim Report, this Grand Jury began to tackle this issue of Covid-19 risk. We identified five of the primary risks associated with the SARS-CoV-2 virus: "Infection Risk," "Disease Risk," "Hospitalization Risk," "Death Risk" and "Long-Term Risk." We also discussed a series of "risk modifiers," various innate factors like age, culture, geography or the existence of one or more comorbidities that could either multiply or divide one or more of those risks on an individual level. We then directed the majority of our efforts toward a specific category of human-driven risk modifiers, nonpharmaceutical interventions (NPIs), examining their effectiveness at modifying these primary risks and the externalities associated with them.

In this Second Interim Report, we examine two additional risk modifiers: Infection-Derived Immunity (often referred to as "Natural Immunity") and the development of effective treatment modalities for Covid-19. Like NPIs, both have effects that can be expressed in the language of a SEIR (Susceptible, Exposed, Infected, Recovered) analysis. "Recovered", in its simplest form, presupposes the concept of Infection-Derived Immunity (IDI) by placing the previously infected in the "Recovered" category, not the "Susceptible" category. For treatments, the goal is to move people expeditiously from the "Infected" category to the "Recovered" category, avoiding prolonged illness, long-term sequelae and death.

These modifiers also have their own externalities, some of which can be expressed in the language of SEIR and some of which lie outside the boundaries of that model. To receive IDI, for example, one must first become infected with the SARS-CoV-2 virus. Depending on the individual, this may be a risky proposition. Treatments have varying externalities like side effects which wax and wane for each individual modality, but there are also issues of development time, expense and uneven access to contend with. As we will discuss in detail below, the development of effective treatments is often a bumpy road at the best of times, and the last four years have obviously not been the best of times. Our primary focus here, however, is not to vilify this modality or vindicate that one, but rather to get an accurate picture of how the rise of IDI and the development of effective treatments have affected the primary risks associated with the SARS-CoV-2 virus. This will enable us to better answer the questions posed by the Governor's Petition and the Florida Supreme Court Order. With that said, there are some notable, avoidable mistakes that have occurred surrounding these risk modifiers that are worth exploring in some detail, lest they occur again in the future.

INFECTION-DERIVED IMMUNITY

The first concept we will explore in this Report is IDI and the degree to which it mitigates future risks for individuals who convalesce from prior SARS-CoV-2 infections. Like mass vaccination, high density of population-level IDI can also achieve "herd immunity," which prominent government public health officials repeatedly expressed as one of the primary goals of the Covid-19 vaccination campaigns in 2021. There is, of course, a significant externality involved in achieving IDI: One must endure a prior infection, and often a bout with Covid-19. Before delving into the science, we wish to make it clear that nothing described below should be read as an endorsement of anyone intentionally becoming infected with the SARS-CoV-2 virus. However, ignoring the substantial benefits conferred by IDI, both to individuals and at a population level, would not adequately address the issue of SARS-CoV-2 risks.

The Human Immune System

The best place to start any discussion of immunity is by describing the objects the human immune system is designed to thwart, referred to as "antigens." Simply put, an antigen is a molecule that can exist on the surface of some pathogen (typically a bacteria or virus, but occasionally a free-floating toxin) which is able to interface with the surface of one or more types of human cells and cause an immune reaction. For thousands of years, human immunity has co-evolved in a cat & mouse game with millions of potential antigens. The result of this evolution is a multi-level reactive system that can physically eliminate or neutralize most antigens; but even where they are able to get through and infect our cells, our immune system can effectively "learn" and "remember" new antigen structures as it eliminates them.

The first level of this system is our skin. The outer layers of the human epidermis create a crude but highly effective barrier for potential antigens. Areas where the skin cannot cover are often mucous membranes like our respiratory tract. Potential pathogens captured in these mucus membranes cannot make contact with cell walls and therefore cannot begin the infection process.

The second level of the human immune system, referred to as "innate" immunity, occurs in the 0-12 hours after an antigen successfully invades a host cell. Human cells exposed to antigens typically emit chemical emergency signals that cause inflammation, increasing blood flow around the cell, attracting phagocytes to engulf and remove foreign stimuli and facilitating healing of the affected area once that stimuli is removed. The innate immune system has a limited "memory" for past infections via "Natural Killer" lymphocytes, but its key feature is speed. Often, innate immune

responses can stop antigens before they have a chance to replicate in sufficient numbers to produce symptoms we would normally associate with disease.

For antigens that are able to begin replicating at scale, the immune system has a third stage, "adaptive" immunity. Characterized by the production of powerful lymphocytes called "B" and "T" cells, the human immune system effectively "learns" the molecular structure of a subject antigen and tailors its immune response to search for, engulf and destroy cells affected by that antigen. This response is slower, often taking from 12 hours up to 7 days, but it is much more comprehensive. Moreover, antigen structures learned during this third stage are effectively imprinted and "remembered" so that this comprehensive response can occur more quickly should a similar infection reemerge.

This immunological memory is the key to IDI. Second and subsequent responses to identical or similar antigens are quicker, more accurate and less destructive. The adaptive immune system also continues to "learn" new variations in these responses, updating our "immunological memory" to include whatever variations occurred in the last antigen it addressed. All of this manifests clinically as significantly less severe disease, with milder symptoms and shorter duration. This is not to say that immunological memory is perfect. For many coronaviruses including SARS-CoV-2, IDI does not confer permanent protection from subsequent infection, and our immune responses can be complicated by new viral variants. Nevertheless, IDI mitigates the underlying risks associated with SARS-CoV-2 to such a degree that this Grand Jury believes it is irresponsible for policymakers to not consider those with IDI in a separate category from those without it.

SARS-CoV-2 Immunity

In late 2019 and early 2020, no human on earth had an immune system prepared to fend off an infection of the SARS-CoV-2 virus. Today, circumstances are different. Nearly halfway through 2024, easily accessible statistics show over 775 million documented cases of Covid-19 worldwide. Keep in mind, that number refers to "cases," meaning reports of symptomatic Covid-19. Given the difficulty of gathering data from every human on Earth, as well as how many infections are asymptomatic or otherwise unconfirmed, it is safe to say that an enormous proportion of human beings may now count themselves as having some degree of IDI. Many have been infected multiple times.

Even when one disambiguates the protective effect of Covid-19 vaccines—as we have done in some of the studies below[1]—our immunological familiarity with the SARS-CoV-2 virus is a far cry from what it was in early 2020. Most studies show that, on average, IDI lowered chances of reinfection from the Ancestral, Alpha and Delta variants of SARS-CoV-2 in the unvaccinated by roughly 80%. This immunity generally began to decline around 40 weeks after infection but leveled off to what appeared to be a roughly stable 50% that lasted from 60 to 80 weeks after infection. Few studies have looked beyond this point, but there was no obvious indication of a further downward trend in the studies that had.

These promising IDI numbers did not just appear out of the blue in 2024. They were echoed in numerous studies produced at different times over the course of the last four years. An Israeli study from 2021, for example, showed that unvaccinated people with IDI had an overall effective protection rate of approximately 86% against the Delta variant. A study of data from New York and California in late 2021 showed that infections per 1,000 unvaccinated persons were roughly 129 for those with no IDI, and only 5 among the IDI, a 96% relative risk reduction rate. A study of Italian populations from May to September in 2021 showed that the risk of re-infection over the course of nine months after developing IDI was 21.8%, but this was the lowest overall re-infection rate of the three categories studied, which included those with IDI, those with vaccine-induced immunity, and in those with no previous immunity.

A large-scale meta-analysis of 65 individual studies from 19 countries found that protection against reinfection by Ancestral, Alpha, and Delta variants at the 40-week point remained above 78% while protection against Omicron variants was 36.1%. Significantly, however, protection against severe infection and hospitalization was over 90% for Ancestral, Alpha, and Delta and over 88% for Omicron.

None of these statistics should have been a surprise to anyone in healthcare. In fact, the science we described above is so well understood that the broad strokes of it could be found in virtually any high school biology textbook. Understandably, researchers in 2020 could not affirmatively know for certain whether SARS-CoV-2 would follow the path of normal immunity, but it was a coronavirus; it would have been atypical for it to behave otherwise. To be sure, new

---

[1] This Grand Jury does acknowledge the concept of "hybrid" immunity, which consists of some combination of vaccination and IDI. Hybrid immunity was not included in this Report because we have not yet fully examined the risk mitigation potential and externalities involved in the Covid-19 vaccines, the administration of which would be necessary to achieve hybrid immunity.

mechanisms of action, cell receptors, enzymes, catalysts and protein structures are being discovered all the time, but it was unwise to focus on the uncertainties presented by these emerging scientific discoveries at the expense of the well-understood principles of human IDI. Our understanding of immunology and the statistical data have never pointed in any other direction but this one: IDI harnesses the power of the human immune system to produce robust and long-lasting immunity. Even vaccines work by stimulating a truncated version of the very same immune response that produces IDI. The protection provided by IDI is so robust, it would easily surpass FDA's Emergency Use Authorization target efficacy of 50% risk reduction laid out for vaccines in October of 2020.

This understanding changes the risk-benefit profile for all other risk modifiers. By way of example, people with IDI in 2020 and 2021 had little to nothing to gain from NPIs. Their risk profiles were dramatically different than the uninfected, yet they were forced along with everyone else to endure all the externalities. Given that there were testing modalities available that could easily confirm whether a person had IDI, ***this Grand Jury believes it was irresponsible of government agencies not to have advised tailoring their mitigation measures to divide those at decreased risk due to IDI in the same way they would later divide the vaccinated***, especially those of lower age with fewer comorbidities who were already at reduced risk.

The best argument we have seen against this type of bifurcation is that extending privileges to those with IDI might encourage people to become infected at the risk of a serious bout with Covid-19. While we do understand that concern, we still do not believe it is appropriate for public health officials to tailor the information they provide based on a set of preferred behavioral outcomes. An argument that designates the vaccinated for special treatment but not those with IDI is simply at odds with the facts and data; it always has been. Where officials have concerns about certain behaviors, they should absolutely communicate those concerns and discourage those behaviors, but not at the expense of suppressing or ignoring "the science." Even in repressive countries in other parts of the world, the ability of the government to suborn compliance is limited. In the United States, it is almost nonexistent. Public health as a social asset works because people believe in it and comply. When they stop believing, they stop complying.

TREATING COVID-19

Covid-19's status as a novel disease meant that as SARS-CoV-2 infections began to grow exponentially in early 2020, the world's government, private and public health organizations had no firm understanding of how to effectively treat it. Early treatments were based on symptomology

and disease analogues; they involved a lot of experimentation and trial-and-error. It took time for doctors, researchers and public health organizations to understand the disease, develop candidate modalities, gather reliable data and ultimately settle on the most effective regimens.

The SARS-CoV-2 Virus & Covid-19 Disease

Some of the most basic information about SARS-CoV-2 is communicated by the name of the virus itself. "SARS" stands for "Severe Acute Respiratory Syndrome," a moniker that differentiates this particular virus by describing an illness associated with it. "CoV" means that this particular virus belongs to a family called "CoronaViruses", so named for their "crownlike" appearance in electron microscopy. The "spikes" of this microscopic "crown" are the antigens we discussed in the section above that facilitate cell entry and set off immune responses. The "2" means that this is the second known virus of this kind. Importantly, all coronaviruses, including SARS-CoV-2, are RNA viruses, meaning that they reproduce in a way that causes many genomic anomalies in subsequent copies, making them prone to comparatively rapid mutation. Moreover, all coronaviruses can also infect epithelial cells found in human respiratory tracts, making them "airborne," at least to some degree. Indeed, many non-SARS coronavirus variants are associated with what is colloquially called the "common cold."

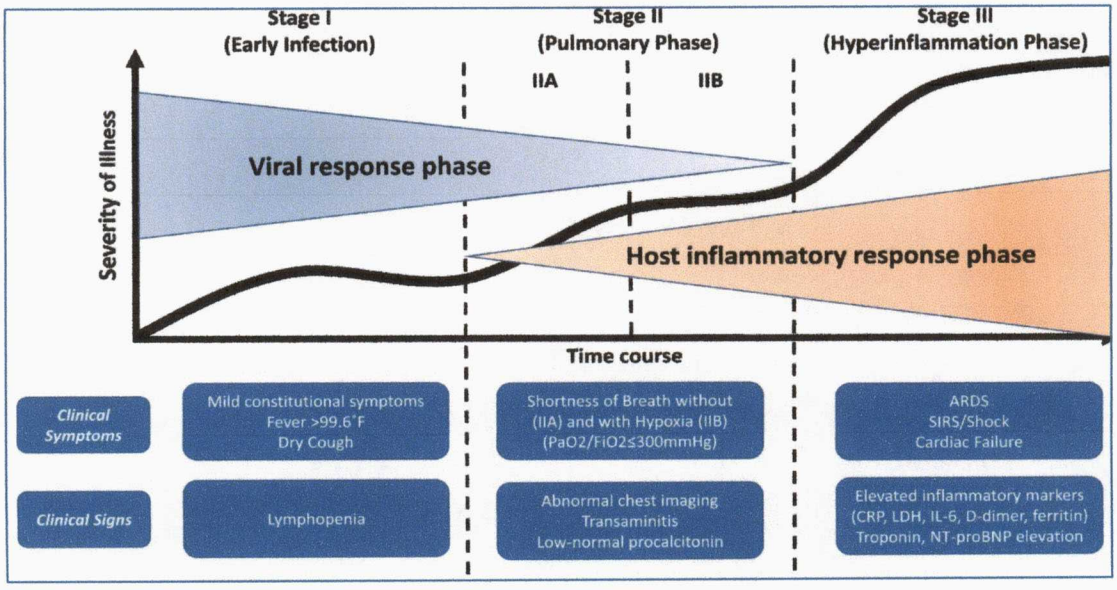
These more pedestrian coronaviruses have coexisted with humans for thousands of years, but there have been two notable "novel" coronavirus outbreaks in the 20 years preceding the Covid-19 Pandemic. SARS-CoV-1 first appeared in China in November of 2002 and had an initial Case Fatality Rate (CFR) of approximately 10%. The SARS-CoV-1 outbreak was not nearly as large as the Covid-19 pandemic, but it did continue at a comparatively low rate for the better part of two years before finally ending in 2004. SARS-CoV-1 has not been seen outside of a lab since. MERS-CoV (MERS is short for "Middle Eastern Respiratory Syndrome"), was first seen in Saudi Arabia in 2012, then had a second outbreak in South Korea in 2015. MERS-CoV's CFR was calculated to be very high at approximately 33%. Cases have been appearing sporadically since 2015 and are usually associated with recent travel to the Middle East or to South Korea.

For purposes of comparison, SARS-CoV-2 is dramatically more infective than both SARS-CoV-1 and MERS-CoV, and has a much lower CFR than those viruses. Researchers believe the increased infectivity of SARS-CoV-2 is due to its ability to replicate in both the upper and lower airways and to be transmitted by asymptomatic hosts. Furthermore, the spike protein of SARS-CoV-2 binds to a site known as the ACE2 receptor, relatively common in a wide variety of human cells including the lungs, heart, liver, kidneys, GI tract and blood vessels. This versatility

can cause variation in clinical symptoms depending on which systems of the host's body experience high viral loads. The incubation period of SARS-CoV-2 after infection is approximately 3-10 days, roughly similar to SARS-CoV-1 and MERS-CoV. Above and beyond the incubation period, it is estimated that approximately 35% to 55% of SARS-CoV-2 infections are asymptomatic, which does not appear to altogether prevent these individuals from spreading the virus to others.

The remaining 45% to 65% of cases all fall within the broad category of "Covid-19 disease." Upwards of 85% of these cases are considered mild, with a typical laundry list of familiar symptoms like fever, chills, cough, shortness of breath, fatigue, muscle & body aches, headache, loss of taste, loss of smell, sore throat, congestion, nausea and diarrhea. Moderate cases are distinguished by the symptoms described above plus some level of lower respiratory involvement or dyspnea (difficulty breathing). Severe Covid-19 illness is characterized by hypoxia with an oxygen saturation level of below 94%, typically accompanied by dyspnea or pneumonia (inflammation and fluid in the lungs). Critical Covid-19 is characterized by acute respiratory failure and often requires intubation or the use of an Extracorporeal Membrane Oxygenation machine to assist breathing. Acute disease can also result in sepsis or multiple organ disfunction, and ultimately death. Complications from Covid-19 include cardiac injury, blood clots, liver injury, stroke and rhabdomyolysis.

Covid-19 is also characterized by a series of distinct phases, illustrated in the following diagram:



During the first phase, the primary driver of disease progression is relatively unchecked viral replication. Gradually, however, the balance begins to shift, and the disease becomes driven not by the virus itself, but by the inflammatory response of the host's own immune system. The severest complications appear to result from a poorly timed, overwrought immune response known as a cytokine storm. Currently, there are no biological markers that can reliably predict in whom this "storm" will appear, but younger people with less comorbidities are less likely to develop cytokine storms and tend to be better able to "weather" them when they do occur.

Public Health & The Covid-19 Pandemic

Before we delve fully into the issue of Covid-19 treatments, we wish to reiterate a maxim that has been expressed to us in one way or another by every witness who has testified in this area: The development of effective treatments for any disease is challenging work, even under the best of circumstances. In early 2020, an ad-hoc, worldwide patchwork of government agencies, nongovernment organizations, multinational corporations, academic centers, and medical facilities ranging from large hospital networks to small walk-in clinics essentially conducted a large-scale, population-level experiment to determine the best courses of treatment. The question of which treatments were most beneficial was further complicated by the various stages, severities and populations affected by Covid-19. Sometimes it could be something as simple as gathering basic health data. Pulse oximeters, for example, were ubiquitous during the early months of the pandemic, but were also widely known to be less accurate for dark-skinned patients. This could introduce an additional degree of complication in determining Covid-19 severity and progression for those patients, and it was yet another variable treating physicians needed to understand and account for as they went about their work. The fact that this patchwork—often referred to generically as "public health"—was able to collectively develop effective treatments and disseminate accurate and specific information about them worldwide in a comparatively short period is truly a remarkable achievement and a triumph of science. It is worthy of our praise and respect.

With that said, however, developing effective treatment regimens was far from perfect. Mistakes were certainly made, but these mistakes were largely unavoidable. Early in the pandemic, treatment regimens and modalities that were championed by prominent voices in the public health community based on their limited knowledge of Covid-19 were later proved by more reliable data to be ineffective. Similarly, some treatments that were initially rejected were later shown by reliable data to be effective by modulating medication dose or timing. Through this trial-and-error

process, the complex public health apparatus was able to pare down effective treatment modalities from thousands, to hundreds, to dozens over a course of months. This paring can only occur because a lot of things that a lot of people tried didn't work. This gradual movement from uncertainty to certainty—ever in doubt, and often with frustrating setbacks—is what "following the science" actually looks like. While much was accomplished, there were still mistakes, and those mistakes cost lives and resources.

Finally, we also want to be clear that our examination of individual treatment modalities is necessarily limited by both our available time and our mandate. We are aware that the question of whether some treatments are or are not effective has been controversial, and we do intend to discuss some of science behind these controversial treatments below. The goal of this analysis, however, is not to analyze every shred of evidence to vindicate this theory or vilify that one, but instead to highlight avoidable mistakes, many of which have to do with messaging and communication, not science. That goal is adjacent to our overarching goal of determining how the establishment of effective treatment modalities modified the primary risks associated with the SARS-CoV-2 virus, but we believe that discussing these avoidable errors, both how they occurred and the harms they brought forth, may be of value in any future public health crisis.

Development of Treatments for Covid-19

The development cycle of all treatment modalities for pathogens, even novel viruses like SARS-CoV-2, must necessarily follow a broadly similar course. First, one must gain some baseline knowledge about the underlying pathogen and the symptoms it causes. From there, one can then begin to hypothesize a treatment regimen, usually based on some theory about how a pathogen or disease progresses and how some drug or therapy might inhibit that progression. The treatment could be something completely new, or it could be some repurposed drug (already established as safe & effective in the context of other diseases) that shows promise in the management of the disease under investigation. After that, the only way to determine whether the treatment works is to administer it to some patients and see whether it is effective.

In the midst of a pandemic, the first step in determining this effectiveness will often be anecdotal. Researchers may often be front-line doctors who administer a candidate treatment modality, sometimes alone or sometimes in combination with other treatments, to one or more patients. If patient outcomes suggest a given treatment might be effective, the next step would be to form a cohort study, administering the candidate treatment to some patients but not others in the hopes of determining whether there is some difference in disease progression or other adverse

events. Cohort studies can also be done retrospectively, by gathering patient records and comparing outcomes between patients who did and did not receive a candidate treatment.

The underlying problem with cohort data is always the same—confounding variables. These can come from a multitude of sources: How similar are the patient populations who received and did not receive a candidate treatment? If a doctor is administering a candidate treatment as part of a regimen, how can one be sure the candidate treatment is producing the result and not some other part of the regimen? How well will the results found in one patient population translate to other patient populations? Is the perceived benefit due to the way the doctor is selecting patients for treatment? Or even from the placebo effect? There are an infinite variety of possible confounders that can obscure the effectiveness of meritorious candidate treatments or even can make treatments appear to be effective where they are not. This is not to say the results of cohort studies are never valuable or that they are always misleading; it is merely to say that to reach conclusions based on this kind of data, one must look beyond the abstracts, carefully examining the means by which the data was collected and the methods used to evaluate it.

One of the better ways to potentially reduce or eliminate these shortfalls is to run a randomized controlled trial (RCT), isolating the effectiveness of a candidate treatment from potential confounders. RCTs, however, are not infallible. They are expensive, time-consuming and like cohort studies, designed by researchers and research teams consisting of human beings, making them subject to human error. Furthermore, there are also many ways that even "randomized" data can be intentionally manipulated to reflect outcomes that are not ultimately accurate. In a global pandemic caused by a novel disease in which people are dying every day, policymakers often relied on whatever faulty studies were currently available to make treatment recommendations, only to have some of those recommendations invalidated by updated, more reliable data, whether from an RCT or a better-constructed cohort study. It can also be ethically challenging to conduct RCTs because by design they require physicians to withhold potentially life-saving courses of treatment to control groups of hundreds or even thousands of people.

Given these limitations, often the best a treating physician or researcher can hope for in the midst of a global pandemic is quality cohort data. Indeed, most treating physicians simply do not have the time to review the developing, expanding, messy mountain of studies and articles related to scores of prospective treatments. After all, they do have patients to treat. To accomplish that, they often must make potentially life or death decisions quickly. For this reason, many large organizations have propounded standards describing the currently-known effective treatments for

a given disease, explaining when, how and to whom they should be administered, and providing at least a snapshot of the supporting research behind these various treatment modalities. These standards exist to support physicians dealing with all manner of diseases, from various cancers, to heart disease, to communicable diseases like malaria or even psychological problems like depression. Indeed, the various "Institutes" and "Centers" that collectively make up the National Institutes of Health (NIH) have been specifically tasked with collating the available research in specific subspecialties and propounding standards for practicing physicians in those areas.

To be clear, these large-scale, government-sponsored standards are not accompanied by formal force of law. Individual doctors have always enjoyed wide latitude in determining what regimens would provide the most benefit to their patients and have the authority to prescribe drugs "off-label" or for a use not approved or promoted by one of these agencies. But the standards do possess a kind of soft power over the larger medical community for two primary reasons. First, they effectively impose "standards of care" for the treatment of different diseases. Yes, by letter of law, doctors have broad latitude, but substantial deviation from these standards, especially in the absence of informed consent, may subject doctors or hospitals to liability for patient injuries. This can have a chilling effect—if not on the doctors themselves—on the hospitals and medical conglomerates that employ them, or on the insurance companies that underwrite them and ultimately reimburse their patients.

Secondly, medical professionals' training, education and experience conditions them to favor the conclusions of these entities. This can make their confidence very difficult to dislodge, even when it is misplaced. On multiple occasions, this Grand Jury has watched a peculiar cognitive dissonance suddenly take hold of an otherwise reasonable medical professional when that professional is forced to confront valid research findings that may challenge the supposed infallibility of some instruction propounded by one of these entities. Similarly, on more than one occasion, it was obvious to us that these medical professionals did not even prepare for their own testimony by beyond reading the standards and regurgitating the abstracts of whatever scientific studies those standards claimed supported the preferred modalities. Once we did progress beyond these top-line conclusions, however, it was clear to us, and even clear to some of those experts, that there sometimes were significant problems with the underlying research.

For our purposes, one of the most prominent standards guiding the treatment of this disease is the Covid-19 Treatment Guidelines published by the National Institute of Allergy and Infectious Diseases, one of the many "Institutes" of the National Institutes of Health. First propounded on

April 21, 2020, and receiving their final update on February 29, 2024, the Guidelines have been continuously updated throughout the last four years to reflect the Institute's latest guidance regarding the dose and timing of various Covid-19 treatments. A virtual version of the Guidelines is available online and in a downloadable PDF file. The website also indicates that it will be removed on August 16, 2024.

The current version of the Guidelines is divided into multiple sections providing instructions for all manner of Covid-19-related issues from testing, to prevention, to clinical management and critical care. There are separate sections devoted to the treatment of adults and children. There are numerous medication-specific recommendations involving dozens of treatment modalities divided into various categories, with a shorthand method describing the strength of evidence related to each modality and a separate section devoted to treatment modalities characterized as having "insufficient evidence." There are specific treatment guidelines for various "Special Populations": The immunocompromised, pregnant women, cancer patients, the HIV positive, transplant recipients and influenza patients. The PDF version of the Guidelines also provides long, comprehensive lists of studies and research findings to support its recommendations in each of the areas discussed above. The overall impression given by the current version of the Guidelines is one of certitude—the hard-won intellectual fruits of a victory of science and medicine over a novel and deadly pathogen. One other thing this website provides which has been immensely helpful to this Grand Jury is a downloadable archive of prior versions of the Guidelines. Analyzing this archive has allowed us to look beyond the definitive version available today and do a time-based analysis of which treatments were recommended when and how those recommendations developed and changed over time. Ultimately, the lens of this time-based analysis tells a different story, one of uncertainty and a rapidly changing research environment.

The following are some overall time-related statistics: The Guidelines were reissued with updated information a total of 67 times between 2020 and 2024; that is an average of every 18.5 days. The bulk of these changes were concentrated in 2020 and 2021, when they were often updated multiple times per month and occasionally multiple times per week. Excluding vaccines, we analyzed a total of 23 different treatment modalities associated with Covid-19, including relatively uncontroversial drugs like dexamethasone and monoclonal antibodies, newly patented

and approved medications like remdesivir, molnupiravir and nirmetrivir/ritonavir[2], and more controversial repurposed drugs like hydroxychloroquine and Ivermectin. Just as the Guidelines did, we separated those modalities into four broad categories:

(1) "Insufficient Evidence" where there is not sufficient evidence to support the administration of a given modality;

(2) "Emergency Recommended" (or "Emergency Use Authorized") where there is sufficient evidence to support administration, but not yet conclusive evidence of effectiveness;

(3) "Recommended" (or "Authorized") where there is conclusive evidence of effectiveness; or

(4) "Not Recommended" (or "Not Authorized") where there is conclusive evidence of ineffectiveness or harmfulness.

These categories broadly outline the scientific process, moving from low-evidence uncertainty to high-evidence certainty.

For many of these modalities, that is exactly what happened. Dexamethasone, for example, moved from "Insufficient Evidence" to "Emergency Recommended" status in June of 2020, and thereafter in July of 2020 from "Emergency Recommended" to "Recommended" status. It has stayed there ever since, although its dosage and timing has been adjusted on a total of 14 occasions in subsequent versions of the Guidelines. Given the importance of timing the administration of this powerful immunosuppressant to the latter phase of Covid-19, these frequent adjustments are not at all surprising. Similarly, remdesivir first appeared as "Emergency Recommended" in May of 2020, later moving from "Emergency Recommended" to "Recommended" in November of that year. It, too, has stayed in the "Recommended" category ever since, with five dosage adjustments in subsequent versions of the Guidelines. Even well-publicized mistakes like early recommendations around the use of ventilators were quickly addressed. In June of 2020, two months after the initial Guidelines were published, an updated version propounded a set of protocols aimed at reducing ventilator-related infections and ventilator-induced lung injuries once it became clear that ventilators were introducing new complications in the seriously and critically

[2] We did conduct an analysis of nirmetrivir/ritonavir in a manner similar to the other drugs mentioned in this Report, but we are still in the process of gathering data regarding this medication and intend to address it in the future once we have completed our investigation.

ill patients who required them. The Guidelines were again updated in December of 2020 in an effort to reduce the incidence of Ventilator-Assisted Pneumonia.

The point is this: Even if the system is functioning as it should, the process of developing and optimizing treatment modalities is a bumpy ride. Behind each of the 14 adjustments to dexamethasone are one or more negative patient outcomes. Medicine only learned about ventilator-assisted pneumonia because people got sick with it. The story is likely similar with the five changes made to remdesivir, just as it is with each of the 185 adjustments to dosage, timing and method across each of the 23 modalities we examined. Effectively, the NIH was faced with a Hobson's choice: They could continuously update their recommendations at the risk of appearing inconsistent, or they could update less frequently, appearing more consistent at the expense of being accurate.

This is what makes the areas where the treatment modalities move unpredictably, from "Recommended" to "Not Recommended," or from some degree of certainty back to "Insufficient Evidence," so interesting. In a few cases, this type of movement should be expected. Monoclonal antibodies, for example, are highly variant-dependent in their effectiveness, so an antibody that works well against one variant might not work at all on another. When it comes to bamlanivimab & etesevimab, casirivimab & imdevimab, sotrovimab, tixagevimab & cilgavimab and bebtelovimab, this is pretty much exactly what we see, a pattern of positive recommendation that abruptly changes to negative recommendation. More perplexing are the changes to two of the more controversial modalities, hydroxychloroquine and Ivermectin.

As of 2020, hydroxychloroquine was approved by the FDA as safe and effective for the first line treatment of Malaria, Lupus and Rheumatoid Arthritis; it was widely prescribed off-label for Porphyria Cutanea Tarda and Chronic Q Fever. Across these uses, it is prescribed in a variety of doses ranging from 100 to 800 milligrams. The side effects of hydroxychloroquine include retinal damage, cardiac effects, aggravation of existing psoriasis, proximal myopathy and neuropathy. Fortunately, all of these side effects are comparatively rare and tend to disappear once the medication is discontinued. In 2020, there were scientific articles explaining plausible mechanisms of action through which hydroxychloroquine could impede replication of the SARS-CoV-2 virus, and some early cohort studies did indeed support the argument that hydroxychloroquine had utility as an outpatient treatment for high-risk patients. This research is reflected in the Guidelines, where it stood as "Emergency Recommended" from the time the initial version was published until June of 2020. The FDA also moved quickly, granting an "Emergency

Use Authorization" (EUA) for the treatment of Covid-19. On June 15, 2020, the FDA revoked its EUA, citing more recent preliminary RCT data that did not support the drug's effectiveness and highlighting a series of serious adverse cardiac events associated with the administration of hydroxychloroquine and chloroquine for Covid-19 in the FDA's Adverse Event Reporting System (FAERS). Importantly, however, 92 of the 109 reported events involved patients who were on at least one other medication that could produce similar adverse events, and the FAERS system could not provide any denominator of treated patients from which one could produce a rate at which these adverse events could be expected to occur. Nevertheless, the Guidelines moved hydroxychloroquine to "Not Recommended," where it has remained ever since.

Scientifically, this seems to be an open and shut case. Cohort data suggested utility against Covid-19, but later on, once the confounders had been removed, more reliable RCT data disproved that theory and the FAERS system showed possible harms. Interestingly, however, these changes in the stance of the NIH and FDA did not seem to curtail hydroxychloroquine's widespread administration as a treatment modality. When the President of the United States became sick with Covid-19 in October of 2020—months after the EUA was revoked—he was administered hydroxychloroquine as part of his treatment regimen. Why?

We believe the answer is twofold: First, a small but significant group of well-credentialed scientists and clinicians were dissatisfied with the way the RCTs disproving the effectiveness of hydroxychloroquine had been conducted. According to these proponents, the RCTs quoted by the FDA focused on using the drug in hospitalized patients as opposed to outpatients, contained large numbers of low-risk individuals, utilized small numbers of outcomes which made randomization useless, utilized less than desirable statistical analysis to base their findings or had poor scientific rigor. Given these issues, they continued to find preexisting cohort data showing effectiveness more persuasive. In essence, they "followed the science" into disagreement with the FDA.

Second, a large number of clinicians—including, apparently, the doctor who treated the President of the United States—took a look at the long history of hydroxychloroquine, the plausible mechanisms of action and the limited side effect profile and concluded, "why not?" In an environment where "the science" is changing all the time and the amount of harm a drug can cause is relatively limited, we also do not believe it was unreasonable to include hydroxychloroquine in an early outpatient treatment regimen for Covid-19. Prominent government public health officials, of course, did not agree, widely stigmatizing the drug, vilifying the doctors who prescribed it, the researchers who advocated it and the people who took it. In April of 2020,

a mere two days after the Guidelines were initially published with an "Emergency Recommendation" for hydroxychloroquine, a prominent newspaper characterized interviews with hydroxychloroquine proponents as "a big dose of dumb[,]" and noting that "[c]laims about hydroxychloroquine to treat Covid-19 have gained traction despite a lack of scientific evidence." From there, the information war was on. Even after the Guidelines changed hydroxychloroquine's status to "Not Recommended," news agencies continued to criticize those who researched the drug, calling hydroxychloroquine "the most disappointing, disavowed drug that researchers keep studying for Covid-19."

A journal article from 2020 attempted to apply some scientific methodology to the conversations around hydroxychloroquine occurring on Twitter (now X), analyzing more than 14,000 tweets from April of 2020 in an attempt to discern some pattern to these conversations. Their findings? The five most common words employed by those who wrote tweets in favor of the use of hydroxychloroquine were "patient," "doctor," "treat," "treatment" and "drug." Those who wrote tweets disfavoring hydroxychloroquine, on the other hand, most commonly used three of those same words: "drug," "patient," and "treatment," to which they added the word "study." But that only makes 4. Number 5, and by far the most common word, used more than twice as much by opponents of hydroxychloroquine, was "trump."

The story of Ivermectin, from the perspective of the Guidelines, is even more bizarre. It was rated as "Insufficient Evidence" until July of 2020, when its rating was then changed to "Not Recommended." It remained in that status until January of 2021, when it was again changed to "Insufficient Evidence," where it remained until April of 2022, when it was finally changed to "Not Recommended," where it has remained ever since. How did science progress from being uncertain about Ivermectin, to being certain that it was ineffective or harmful, to being uncertain about it, to once again being certain it was ineffective or harmful?

We begin again with a general description. Ivermectin is an antiparasitic medication first approved for human use in 1987 and widely prescribed all over the world to treat roundworm infections and parasites. Common off-label human uses for Ivermectin include head lice, scabies and other similar mites, worms and insects. Ivermectin is well tolerated by most patients, with a long list of generally mild and infrequent side effects. Just like hydroxychloroquine, there were hopeful scientific research articles in early 2020 touting a mechanism for potential antiviral effects of Ivermectin, and that hope was quickly backed up by cohort data of debatable value supporting its effectiveness at preventing the progression of Covid-19 severity. Once again, there were other

studies, including cohort data and RCTs, that later claimed not to be able to find any effectiveness against Covid-19. Once again, we had a pointless, ugly war of words over a proven-safe drug with questionable effectiveness. The most responsible messaging for public health officials to deploy in this environment would probably have been to say something along the lines of *We are not satisfied with the data that show Ivermectin is effective against Covid-19, so please do not use it at the expense of other treatment modalities, but it is a safe medication when used under proper medical supervision.*

We did not get that. We got this:

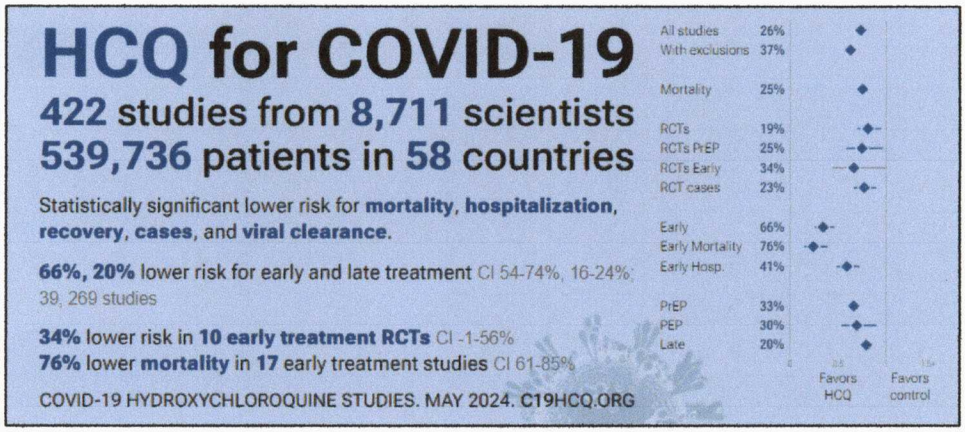
The tweet above (which the FDA later had to retract after settling a lawsuit) was just a small part of an unnecessary war to stigmatize the use of Ivermectin as a treatment for Covid-19. Wall-to-wall media coverage characterized this human medication as "horse paste," and the people who were interested in learning more about it as unsophisticated bumpkins who did not "follow the science." In some states, licensing bodies—who, unlike the NIH, do have legal power over doctors in their states—began to threaten the livelihoods of doctors who prescribed Ivermectin to their patients for Covid-19. Proponents of Ivermectin who publicly called for further studies to adequately evaluate its overall effectiveness were portrayed as purveyors of misinformation, stripped of their professional associations and ostracized. These proponents were only doing what they had been taught to do for their entire careers: Think like scientists. Using new, contrary research to challenge conventional wisdom and debate the merits of new paradigms, formerly regarded as one of the cornerstones of the scientific process, now carried with it the additional risk of being labeled a pariah. Through all of this, none of these opponents were able to effectively

articulate a good reason for their contempt towards Ivermectin. To this day, the best we can come up with is that it didn't work. That's a fine (and likely a correct) conclusion, but there was, especially early on, at least some evidence it might be effective. In such a fast-moving research environment, what was the harm in letting people try it as part of a Covid-19 treatment regimen?

Because the opponents of Ivermectin were not able to provide any good reasons for people to reject this drug as a potential treatment, bad ones began to take hold. "Ivermectin is being deliberately suppressed as part of a conspiracy between the government and pharmaceutical companies to push the vaccine," said some. "The media is pushing against Ivermectin too, so they must be in on it," said others. Where accurate information would probably have quieted the storm, the credibility vacuum created by Ivermectin's unnecessary vilification fanned the flames of these conspiracy theories. Some people became so desperate to get this supposed miracle drug, so sure they were being lied to, that they began to resort to doses and formulations of the drug meant for animals, resulting in a number of well-publicized Ivermectin overdoses. Once again, opponents looked down their noses at the foolishness of these desperate, misguided fools. Late night comedians made jokes at their expense and everybody who knew how to "follow the science" laughed. This Grand Jury is not laughing. This was a profound failure of public health messaging. ***We lay every overdose that occurred at the feet of those who authored this campaign of vilification.*** Regardless of whether Ivermectin was effective in treating Covid-19, it was a mistake to make policy designed to prevent people from getting this medication given its relative safety. Had these people been able to acquire Ivermectin from their own doctors, it may not have cured their Covid-19, but we doubt those overdoses would have taken place at all.

The sad consequence of all of this messaging nonsense has been to undermine much of the trust many members of the public are willing to place in these institutions. And when members of the public began to mistrust the information provided by FDA, NIH, CDC and the like, they sought that information elsewhere. One prominent source of "alternative" data that has been repeatedly brought to our attention is a website, C19early.org (C19), that purports to collect and collate all data associated with a wide variety of both conventional and unconventional treatments. These data include "meta-analyses" for scores of treatments, many of which purport to show remarkable efficacy, even from over-the-counter medications, vitamins and other easily obtainable modalities like sunlight. This is a far cry from the limited cross-section of treatments discussed in the Guidelines. Over the course of the last year, C19 has been regularly sourced to this Grand Jury as a foundation for many divergent viewpoints on Covid-19 treatments.

The website itself collates literally hundreds of scientific studies, presenting summaries of the data involving various treatment modalities for Covid-19 in the form of its own "meta-analyses." Here, for example, is C19's "meta-analysis" of the studies supporting hydroxychloroquine:



These results sound amazing; certainly a far cry from the conclusions in the Guidelines. Ever-skeptical, this Grand Jury hired our own unbiased biomedical research scientist with many years of experience as a grant reviewer, journal referee and over 50 peer-reviewed publications to his own credit to review these studies and attempt to reconstruct C19's meta-analyses for some of the more prominent treatment modalities (including hydroxychloroquine and Ivermectin). After several attempts using different mathematical models and different variations of popular meta-analysis software, he was simply unable to reconcile the results published on the website with the data from the studies. Moreover, after reviewing a sizeable sample of the studies included on C19, our own researcher came to the following additional conclusions:

- C19 routinely fails to consider what the primary endpoint of the study is, and often includes studies in its meta-analyses using their secondary endpoints. These unconsidered primary outcomes tend to be omitted from the graphical representations of the studies.
- C19 routinely pools studies with different endpoints, different statistical analyses and different interventions in its meta-analyses.
- C19 regularly misrepresents data in its graphical descriptions of studies.

- C19 criticizes the methodology of studies that do not show results that support the effectiveness of certain preferred modalities but does not apply the same rigor to those that reach the opposite conclusion.
- C19 is critical in a general sense of studies that show negative results for certain preferred modalities, and often uses unscientific criticisms in its analyses such as conflicts of interest.
- C19 arbitrarily employs exclusion criteria to remove or include studies based on whether their findings were in line with certain preferred modalities.

Given the above, we probably do not need to reiterate that we do not find C19 to be a credible source of data, but we are sympathetic to how the haughty, dismissive approach of government agencies like FDA, NIH and CDC to public health communication gave rise to a funhouse-mirror version of what these large agencies were doing. With the resources at our disposal, it was comparatively easy for this Grand Jury to uncover C19's faults, but what hope does an average person have? Do they go hire a research scientist at great personal expense to spend many hours determining whether a website they found is accurate? The growth of websites like C19 are a direct manifestation of the cost of bad messaging.

In the end, the story of the developing treatments for Covid-19 is ultimately one of remarkable success under the most challenging of circumstances. When we turn our attention to a limited subset of controversial treatment modalities, however, we see a series of avoidable blunders that undermined much of what so many worked so hard to accomplish. It will likely take years for these institutions to regain the public trust that they squandered on what appear to be inconsequential disagreements.

CONCLUSION

As of 2024, the combined effect of IDI and the development of numerous successful treatment modalities have dramatically changed the overall risk profile of Covid-19 from where it was in 2020 and 2021. IDI has been repeatedly shown to substantially lower the risk of reinfection, hospitalization and even transmission for a long period, completely changing the risk/benefit profile of those who have previously been infected, even patients previously at high risk. Similarly, treatments for Covid-19 have improved precipitously in the past four years, dramatically lowering hospital and death risks for those who are able to access them. The combined effect of these risk

modifiers has been to lower risk to such a degree that in 2024, it is hard to measure risks related to Covid-19 because there simply are too few bad clinical outcomes at this point to run effective studies.

With that said, there were policy mistakes in the way the subject of IDI was treated, and in the messaging around some of the more controversial treatment modalities. The result of these unforced errors led directly to a trust deficit with many of the people it was tasked with protecting at precisely the time when that trust was most needed, and people suffered as they searched for reliable answers in the vacuum of those failures. Unfortunately, these failures of effective communication are becoming something of a theme. They came up in our First Interim Report, they also came up here, and we will continue to examine and critique them when they come up in the future.

CERTIFICATION

THIS REPORT IS RESPECTFULLY SUBMITTED in Open Court to the HONORABLE CHRISTOPHER C. SABELLA, Presiding Judge of the Twenty-Second Statewide Grand Jury, this 21st day of May, 2024.

Juror # 5
Foreperson
Twenty-Second Statewide Grand Jury of Florida

I, NICHOLAS B. COX, Statewide Prosecutor and Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

NICHOLAS B. COX
Statewide Prosecutor
Legal Adviser

I, JEREMY B. SCOTT, Chief Assistant Statewide Prosecutor and Assistant Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

JEREMY B. SCOTT
Chief Assistant Statewide Prosecutor
Assistant Legal Adviser

I, BRIAN L. FERNANDES, Chief Assistant Statewide Prosecutor and Assistant Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

BRIAN L. FERNANDES
Chief Assistant Statewide Prosecutor
Assistant Legal Adviser

I, PAUL DONTENVILLE, Chief Assistant Statewide Prosecutor and Assistant Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

PAUL DONTENVILLE
Chief Assistant Statewide Prosecutor
Assistant Legal Adviser

I, JAMES R. HARRIS, Assistant Statewide Prosecutor and Assistant Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

JAMES R. HARRIS
Assistant Statewide Prosecutor
Assistant Legal Adviser

I, JAE HEE KIM, Assistant Statewide Prosecutor and Assistant Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

JAE HEE KIM
Assistant Statewide Prosecutor
Assistant Legal Adviser

I, NATHANIEL S. BAHILL, Assistant Statewide Prosecutor and Assistant Legal Adviser, Twenty-Second Statewide Grand Jury of Florida, hereby certify that I, as authorized and required by law, have advised the Grand Jury which returned this report on this 21st day of May, 2024.

NATHANIEL S. BAHILL
Assistant Statewide Prosecutor
Assistant Legal Adviser

THE FOREGOING Second Interim Report of the Twenty-Second Statewide Grand Jury was returned before me in Open Court this 21st day of May, 2024, and is hereby sealed until further order of this Court, upon proper motion of the Statewide Prosecutor.

HONORABLE CHRISTOPHER C. SABELLA
Chief Judge of the Thirteenth Judicial Circuit
Presiding Judge, Twenty-Second Statewide Grand Jury