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Understanding vaccine hesitancy in COVID-19

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Vaccines are one of the greatest medical innovations of all time, but there has been skepticism about them throughout history. Although initial concerns about scarcity increased public demand for COVID-19 vaccines, as supply meets demand, vaccine hesitancy may become a defining theme of the next stage of the COVID-19 pandemic.

Vaccines are one of the greatest medical innovations of all time, having produced a remarkable decline in the incidence of diseases that have long plagued humankind. But for as long as there have been vaccines, there has been skepticism, if not outright antagonism, toward vaccination as a medical technology.[1] Although the initial scarcity of COVID-19 vaccines led to an immense public demand for them, as production and availability increase, supply is meeting and will ultimately exceed this demand. When this time comes, COVID-19 vaccine hesitancy may become a defining theme of the next stage of the pandemic.

Coronavirus disease-19 (COVID-19), which is caused by the novel coronavirus SARS-CoV-2, has a range of clinical manifestations and outcomes. While ~30% or more of those infected with SARS-CoV-2 are asymptomatic, asymptomatic people are responsible for most SARS-CoV-2 transmission.[2,3] In a large study from China early in the pandemic, ~80% of symptomatic people had mild disease, ~14% had severe respiratory disease, and ~5% were critically ill with respiratory failure.[4] Disease severity and mortality are strongly influenced by age and comorbidities, such as cardiac and pulmonary disease, obesity, and diabetes mellitus.[2] Mortality is also disproportionately higher for Black and Hispanic individuals relative to white individuals.[2] As of April 3, 2021, more than 550,000 people across the United States have died from COVID-19 according to the CDC COVID Data Tracker (https://covid.cdc.gov/covid-data-tracker/#datatracker-home). Given that proven therapeutic options remain limited, vaccination is the only reliable strategy to prevent COVID-19 and its devastating consequences.

There are now three SARS-CoV-2 (COVID-19) vaccines authorized for emergency use in the United States, and compelling evidence that each can prevent severe COVID-19 and death.[5] There is also emerging evidence that asymptomatic infection and the ability to transmit SARS-CoV-2 is reduced in vaccinated individuals, suggesting that vaccine-acquired herd immunity can be achieved.[6] However, at a minimum, herd immunity will require vaccination of an estimated 60% to 80% of the population.[5] The development and authorization of effective COVID-19 vaccines in less than a year is an unprecedented achievement, a testament to the power of science in the service of humanity, and is nothing short of miraculous. It is therefore all the more tragic that many people are declining these vaccines and, even worse, are advocating against their use.

It is important to differentiate vaccine hesitancy from "vaccine refusal," which is ideological and corrosive. Vaccine refusal often carries deep political, cultural, and emotional underpinnings that can be difficult to overcome.[7] Individuals in this group, often described as "anti-vax," tend to congregate in insular communities, whether physical or online, that are highly resistant to change.[7,8] Misinformation promoted by these groups has its roots in anti-vaccine propaganda that dates back more than a century.[1] The same arguments appear time and again irrespective of the specific vaccine: that vaccine side effects are worse than the diseases they prevent; vaccines introduce toxins or cause disease in otherwise healthy people; mandatory vaccines infringe on civil liberties or religious beliefs; and most insidious, that doctors are biased by conflicts of interest (or engaged in full-fledged conspiracies with drug makers) in promoting vaccines.[1] These views are currently being propagated by groups and individuals opposing COVID-19 vaccines.[7] Alarmingly, online anti-vaccine activity has also been linked to foreign disinformation campaigns intended to strategically undermine public health efforts against the pandemic.[8]

Despite outsized media coverage, total vaccine refusal is far less common than vaccine hesitancy.[9,10] Vaccine hesitancy is a complex phenotype, capturing a range of motivations and concerns. For some, hesitancy around vaccination is grounded in insufficient knowledge, lack of confidence in the benefits of vaccination, or overconfidence in one's ability to avoid the disease in question.[9,10] Others feel anxious or uncertain about vaccines, either due to tangible fears (e.g., of needles or medical settings), concerns

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about side effects, or an unconscious association of vaccines with illness or harm (this latter, in large part, a consequence of the misinformation actively perpetuated by anti-vaccine groups).[9,10] As time passes, reduced cases of COVID-19 may lead to complacency, another variant of vaccine hesitancy, whereby individuals forego vaccination because they do not perceive COVID-19 to be a threat to their health.[11] Finally, and significantly for COVID-19, vaccine hesitancy may also stem from distrust or suspicion of the medical system itself, from concerns that the vaccines were rushed, or from beliefs that corners were cut in vetting the vaccines for public use.[7] Often, these subtypes are intertwined, resulting in a wide range of individual perspectives. Rather than staunchly opposing vaccination, vaccine-hesitant individuals are often uncertain and may change their minds and accept vaccination with focused interventions that address their concerns.[10]

COVID-19 vaccine acceptance varies across the world, with ~90% acceptance in China compared to ~55% in Russia.[7,12] In the United States, vaccine hesitancy was high throughout the early months of the pandemic, reflecting both the novelty of the coronavirus vaccines as well as the deeply politicized climate surrounding their development.[13] Since the rollout of the first COVID-19 vaccines to millions of Americans in January of 2021, hesitancy has steadily decreased.[13] Nevertheless, in late March of 2021, 20% of Americans still reported that they would definitely decline a COVID-19 vaccine or only take one if required for school or work.[13] Another 31% reported that they would wait and see how the vaccine was working before accepting one.[13] Different demographic groups in the United States vary in the rate and intensity with which they express COVID-19 vaccine hesitancy. While 34% of Black respondents and 33% of 18- to 29-year-olds reported they would "wait and see" before being vaccinated, 28% of Republicans and 24% of those in rural communities were most likely to state they would "definitely not" accept a vaccine.[13] It is notable that few in the "definitely not" category reported being swayed by pro-vaccine messages and information, suggesting that this group may reflect a nascent COVID-19 vaccine refusal movement rather than vaccine hesitancy.[13]

It is impossible to discuss vaccine hesitancy and medical mistrust without addressing the enormous contribution of race and health disparities to the morbidity and mortality of COVID-19. Black and Hispanic communities have been devastated by the pandemic, with rates of hospitalization and death that far exceed white populations, yet these groups also remain among the least vaccinated in the U.S. to date.[2,13] This disparity is frequently attributed to higher rates of vaccine hesitancy in these communities; for Black populations, such hesitancy is often attributed to medical mistrust, which is described as an after-effect of historical atrocities like the Tuskegee trials.[7,13,14] In reality, Tuskegee rarely comes up as a reason for COVID-19 vaccine hesitancy in surveys of Black individuals.[14] Instead, safety concerns, contemporary racism, and barriers to care (e.g., lack of insurance or internet access, transportation constraints, appointment hours or openings) appear to play a much larger role in COVID-19 undervaccination.[13,14] This raises a potential pitfall of an overemphasis on vaccine hesitancy: not only can this framing place implicit blame on undervaccinated individuals (e.g., the idea that they simply need to change their attitudes), but it can potentially detract from the true source of disparities.[14] Bias and systemic racism in our present-day healthcare system have unquestionably hindered the COVID-19 vaccine rollout. Efforts to counteract vaccine hesitancy can only succeed if they are accompanied by interventions addressing structural barriers to vaccine availability and access.

Overcoming COVID-19 vaccine hesitancy will require a multipronged approach (Table 1). There is no one-size-fits-all solution; to succeed, we must target interventions by focusing on the needs and concerns of individuals, families, and communities. Information and messaging must emphasize that vaccinated individuals will be protected from severe illness and death from COVID-19 and will be less likely to pass the virus to others.[10,13] This protection, in turn, will make it possible for them to work, support their families, and plan for their futures. Stepwise interventions over multiple times can increase acceptance of immunization, highlighting the importance of starting conversations early.[9] Using narrative in addition to data, by highlighting vaccine success stories and positive experiences, can also help to counteract negative biases linking vaccines with illness.[9] While discussing potential side effects may deter some from vaccination, the potential harm of not addressing such side effects is far greater in the long term.[13] It is important to be realistic and transparent about what we know and don't know about COVID-19 vaccines, and clear anticipatory guidance about side effects and adverse reactions should be provided.[10,11,13] Equally important is that available data show that the benefits of COVID-19 vaccines far outweigh their potential risks. Among those for whom COVID-19 has produced feelings of powerlessness and loss of control, framing vaccines as a way to regain control over one's life could be potentially empowering and should be explored in future studies. Interventions aimed at increasing knowledge, awareness, and confidence must be matched by efforts to improve convenience and access to vaccines, particularly in high-risk and rural populations,

Table 1. A framework for communicating about COVID-19 vaccine hesitancy

	Knowledge/confidence subtype	Fear subtype	Mistrust subtype
Sample statements	"I've avoided COVID so far. Anyway, I'm healthy so I don't think I need it." "I don't think the vaccines even work, I heard some people still got COVID after taking them."	"The vaccine isn't safe. It's making people sick." "The vaccines were developed too fast. They're still being tested."	"The drug companies are just trying to make money." "I don't want to be experimented on."
Suggested interventions[9,10,13,15]	make a strong positive recommendation; emphasize that the vaccines are highly effective in preventing illness from COVID-19, and are the best way to get back to normal life; highlight the dangers of COVID-19, including the potential for new variants with increased transmission/virulence; use narrative in addition to data; if possible, speak from personal experience with the illness and/or vaccine	provide context on the history of the vaccines (e.g., the platforms were developed over years) and the number that have been distributed so far (e.g., 100 million people have already been vaccinated); reassure that adverse events are tracked and monitored; serious adverse events are extremely rare; be honest and set expectations; acknowledge that the vaccine may result in mild and temporary side effects while providing long-lasting benefits	remain open and empathetic; ask questions to elicit individual concerns; provide answers to specific questions when possible; spend time discussing vaccines; reinforce vaccine benefits at multiple encounters if needed; engage respected community leaders (e.g., religious leaders, politicians, sports figures) to promote vaccination in their communities

and to engage community leaders in promoting vaccination.

Social media has historically been weaponized by anti-vaccine groups to sow public doubts of vaccine safety.[8] Throughout the COVID-19 pandemic, coordinated anti-vaccine campaigns by both foreign and domestic actors have proliferated, compelling social media companies to actively reign in vaccine disinformation.[8] While social media consistently ranks among the least trusted sources of COVID-19 health information, social media platforms also provide a mechanism for positive vaccine discourse.[8,13,15] Trusted public figures can help promote confidence by documenting and publicizing their own COVID-19 vaccines and encouraging others to follow suit—as countless celebrities, sports figures, and politicians from both sides of the aisle (including President Joe Biden) have already done. These public endorsements, together with countless photographs and stories depicting grandparents, healthcare workers, and others benefitting from COVID-19 vaccines, are powerful and may gradually help to shift public sentiment.

When it comes to promoting COVID-19 vaccines, trust cannot be manufactured at will. But previously established trust between physicians and patients can and should be marshalled and reinforced. Prior to the pandemic, healthcare providers were consistently ranked as the most reliable and trusted source of information on vaccines and were frequently able to assuage the concerns of those initially hesitant about vaccines with person-to-person dialog.[9,10] Surveys during the COVID-19 pandemic show that the majority of people consider their personal physicians to be their most trusted source of vaccine information.[13,15] Primary care providers must therefore be at the forefront of efforts to combat COVID-19 vaccine hesitancy. They are uniquely able to meet patients where they are and should be prioritized in future vaccine distribution schema.

Vaccine hesitancy is at its highest following the introduction of any new vaccine. In one survey, of those currently reporting COVID-19 vaccine hesitancy in the U.S., 48% stated they would get the vaccine later if it proved to be safe.[15] As more and more people are vaccinated and the pandemic abates, providing proof that the vaccines work and are safe, fear and doubt of COVID-19 vaccination should decrease. As we look forward to a time when the pandemic will eventually end, a critical focus within healthcare must be on rebuilding longitudinal relationships centered on trust and mutual respect, particularly within marginalized and disadvantaged communities. The rise of "on-demand care" centered on convenience and speed has had the unwanted effect of slowly siphoning away from the relationship-based model of healthcare. As this pandemic lays bare, there is an irreplaceable role to be played by physicians, and primary care providers especially, in safeguarding the health of individuals and communities. It is crucial that we advocate for increased investment in the medical home and in primary care, as well as the development of a health care workforce that reflects the patient population it serves with respect to race, ethnicity, and socioeconomic background. For this crisis, and all that will follow, trust in the medical community is a resource we cannot do without.

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DECLARATION OF INTERESTS

The authors have no competing interests.

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Defining long COVID: Going back to the start

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"Long COVID" is the condition whereby affected individuals do not recover for several weeks or months following the onset of symptoms suggestive of COVID-19, whether tested or not.[1] The name "long COVID" was created by the people experiencing it in Spring 2020 to describe their journeys of not recovering.[2] Here, we suggest a way to standardize its definition through outlining what constitutes initial infection with COVID-19.

In previously hospitalized COVID-19 patients, persistent ill health seems to be very common, with ongoing symptoms including breathlessness, cough, fatigue, and mental health problems.[3] However, long COVID is not restricted to those with initial severe disease. In many so-called "mild" COVID-19 cases, recurring symptoms include persistent fatigue and breathlessness, headache, chest heaviness, muscle aches, and palpitations. They involve many systems and are wide-ranging, with a mostly fluctuating or relapsing nature. A large proportion of those who do not fully recover also develop cognitive problems, including poor memory and concentration, as well as what "long haulers" describe as "brain fog."[4] There is emerging evidence of long-term health impairment and organ damage across the spectrum of the clinical presentation of COVID-19 infection.[5] However, much is still unknown about long COVID. Most importantly, it is still not well defined for the purposes of clinical diagnosis, disease surveillance, and research.

How common is long COVID?

Measuring COVID-19 morbidity is an immediate priority in this pandemic. There are two main issues to be taken in account when measuring the prevalence of long COVID, particularly in non-hospitalized individuals with non-laboratory confirmed infections. First, everyone infected with COVID-19, or at least all those initially symptomatic, should be counted in the denominator. Second, standardization of case definitions, especially for the comparison across different settings and population groups, needs to be applied.

Evidence from relatively small studies suggests approximately one-third of

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