Medical Xpress

Ensuring an ethical path to a 'warp speed' vaccine

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A vaccine for COVID-19 is seen by many—rightly or wrongly—as the finish line for the pandemic, the shot that will mark the resumption of our normal lives.

Yet recent polls suggest that a significant fraction of Americans may opt

not to get a vaccine when one becomes available, or are at least wary of getting it. Especially concerning are poll results indicating that populations that have been hardest hit by COVID-19, specifically Blacks and Latinos, have high rates of vaccine hesitancy.

As dozens of COVID-19 vaccines enter various stages of clinical trials, what is being done to ensure this accelerated process is being conducted ethically? How will an eventual vaccine or vaccines be distributed in a fair manner among the various groups that have jobs, physical conditions, or living circumstances that put them at greater risk? And how can public health officials convince people that a vaccine is safe and worth receiving, especially among populations who not only have been victims of unethical and harmful scientific and clinical processes, but also bear the brunt of the disease a vaccine is aiming to prevent?

Bioethicists, clinicians, and others at Penn have been grappling with these questions about COVID-19 since the earliest days of the pandemic. "Our human tendency is that when we speed up, we cut corners, but here we can't afford to," says Emma Meagher, vice dean at the Perelman School of Medicine. "Public trust is such a critical part of the research enterprise. If it's lost, the price to pay is enormous."

Concerns about ethics and trust, researchers say, may wind up mattering as much as the careful scientific discovery process in the impact of a vaccine on the pandemic.

Testing considerations

In mid-March, much of the clinical research operations around Penn shut down. "We were at about 15 to 17% of our usual capacity," says Meagher. "Our focus switched to COVID research."

At the same time, Penn became a center for a number of clinical trials,

first testing therapies for the disease, such as remdesivir and hydroxychloroquine, and later two vaccines.

Trials are complex; they require oversight and approval, including a rigorous ethics evaluation. And yet with large numbers of patients becoming hospitalized and dying from a disease with no proven effective treatment, the pressure to turn out results and prove that an intervention works is monumental.

"As you might imagine, during this process you have to be exceptionally careful not to lower your standards," Meagher says, noting that Penn's Institutional Review Board, which ensures the protection and welfare of human research participants, met almost daily to review research protocols as quickly as possible.

Vaccine trials present a special ethical consideration, because testing occurs in healthy people who have a lot to lose if the product under study turns out to be unsafe. It's important that trials—especially phase 3 trials, which involve tens of thousands of people and evaluate a vaccine's safety and efficacy—include volunteers who are representative of the population who will eventually receive and benefit from a vaccine.

"With clinical trials we want to make sure there is no undue burden, but also equal opportunity to participate," Meagher says. "We know that the vast majority of the sickest COVID patients were African American and Hispanic. We also know that we are not effective at identifying adequate numbers of African American and Hispanic patients and volunteers who are willing to participate in the trials. This is a real and persistent challenge—of our own making."

Penn Medicine research teams responsible for vaccine clinical trial recruitment are taking a creative approach to build diversity into their pool of volunteers. "They are engaging with community leaders and are

bringing the research opportunity into communities by using a mobile research unit and setting up sites in community centers and churches," Meagher says. To avoid any risk of coercion or improper influence, would-be volunteers go through a thorough informed consent process, with multiple opportunities to opt out of participating.

Meagher is heartened by the care and thought she sees in her Penn colleagues as they carefully consider the ethical implications of this research. "In the current environment where we are so conscious of existing health inequity and social injustice, it is so incredibly important that we get this right."

Outside forces

The approaches taken by an institution like Penn, or any individual vaccine trial site, are only half of the effort necessary to engender necessary public trust. The operation of regulatory bodies like the U.S. Food and Drug Administration (FDA), which oversees the drug and vaccine development process and is responsible for determining whether vaccine products may be marketed and distributed, are likewise crucial.

Holly Fernandez Lynch, a bioethicist at Penn Medicine whose scholarship examines the ethics and regulation of clinical trials and drug development, notes that the FDA has layers of protections in place to help make sure that product approvals are based on solid scientific evidence. "I've been a supporter of the FDA," she says. "They have a difficult job in balancing safety and speed and, although there's room for some criticism, they have largely done it well over the years." She notes also that the FDA has traditionally enjoyed substantial public trust.

But she is concerned about politicization eroding the FDA's commitment to rigorous scientific standards. The FDA has issued emergency use authorizations (EUAs) for drugs heavily touted by President Trump on

the basis of little evidence, she notes. One of these, hydroxychloroquine, had to be withdrawn when it became clear that the drug was ineffective against COVID-19 and carried significant risks. The late-August EUA for convalescent plasma came on the heels of the president's accusation that FDA staff were slow-walking approvals to hurt his election prospects.

Fernandez Lynch also notes that the FDA has planned a meeting of its vaccine advisory committee for Oct. 22, sparking speculation about an "October surprise": a vaccine approval intended to sway people's views leading into the November election.

"All signs are pointing to the agency being used as a puppet to just give the go-ahead for one of these vaccines," Fernandez Lynch says.

Messaging counts

For Joseph Cappella of the Annenberg School for Communication, who studies health and political communication, his thinking about the COVID-19 vaccine centers on the art and science of persuasion.

"There are a lot of people out there saying that they are not currently interested in getting a vaccine," he says. "And a much larger fraction of African Americans say they are distrustful, likely based on events in history like the Tuskegee [syphilis study] and other events such as the inequitable distribution of the polio vaccine."

To build back trust, he says, requires effective communication. "You've got to make the case over and over again that the emphasis in developing a vaccine is on safety, that the emphasis is on ensuring a breadth of testing during clinical trials that encompass a significant percentage of African Americans and Latinos," he says. "That information needs to be credible, and the sources sharing this information need to be credible."

There are two parts to credibility, Cappella notes. "One is trustworthiness. What we mean is not expertise, not knowledge. Trustworthy sources are not only self-interested but have the interests of others at heart as well.

"The other aspect is expertise. The best spokespeople are people who have expertise and are trustworthy."

Messaging can make or break a vaccine distribution effort, he says, and nomenclature is part of that. "It's Operation Warp Speed, not Operation Safety or Operation Cure," he notes, referring to the U.S. government's goal to deliver 300 million vaccine doses by January 2021.

To Cappella, just because there's an urgency in getting a vaccine to market doesn't mean that meticulous message testing shouldn't occur. "We're spending billions of dollars on the vaccine, as well we should," he says, "but why not spend half of one of those vaccine contracts lining up expertise in the world of advertising, in the world of communications research, in the world of psychology, in the world of marketing, to put our expertise to work so that people seriously consider this vaccine?"

Ethical allocation

Assuming clinical trials give way to the approval of a vaccine—or a few—the question of who should be first in line to get a shot has no easy answer. Faculty at Penn, however, are among those who have been part of crafting carefully considered proposals.

One aspect of Penn Medicine bioethicist Harald Schmidt's research encompasses how to set priorities in health care; he was even teaching a course on rationing and resource allocation in the spring as the pandemic descended. He says that traditional notions of how to allocate scarce health resources, whether they be ventilators or vaccines, fail to take into

account the reality of our society today.

"Many take it for granted that you start from a utilitarian framework," he says, "that it's about saving the most lives or the most life-years. But in a society such as ours, you can't take that kind of ahistorical perspective. We have highly unequal access to health care, vast differences in how easy it is for people to live healthily, and, for example, in Philadelphia, a difference of 30 years in life expectancy between economically better and worse off zip codes. These are horrific facts that have to do with social determinants of health, with structural racism. That's why to me it's absolutely imperative that any allocation system doesn't proceed in colorblind fashion."

Schmidt's beliefs, which he laid out in a paper for The Hasting Center Report, emphasize prioritizing COVID-19 vaccine distribution for residents of neighborhoods that rank low on measures of housing quality, employment, income, and more. "If you use a measure such as the Area Deprivation Index that captures this," he says, "you don't explicitly deal with race, but the index tracks it quite well, unfortunately, because of a history of redlining and segregated neighborhoods."

This element of prioritizing vulnerable populations is also present in the draft report released for public comment this week by the National Academy of Medicine's ad hoc committee on Equitable Allocation of Vaccine for the Novel Coronavirus, on which the School of Nursing's Alison Buttenheim is serving.

"The public comment period, which runs through midnight Friday [Sept. 4], is central to the framework development process," Buttenheim says, encouraging all to review and comment. "The ad hoc committee is a diverse and thoughtful group representing multiple disciplines and perspectives, all of which have informed the draft framework. Given the rapid timelines for the committee's work, the public comment window is

brief, but comments will be reviewed and will shape the final product."

The committee's framework proposes a phased vaccine distribution, prioritizing health care workers, those with conditions that predispose them to severe disease, and older individuals in the first of four tiers, while also acknowledging a crosscutting need to consider equity, specifically through the lens of the Centers for Disease Control's Social Vulnerability Index.

Schmidt says the draft report is "quite interesting and should really be welcomed for countering in subtle, yet important ways the trend in dominant allocation frameworks to largely turn a blind eye to social justice."

In a separate effort, Vice Provost for Global Initiatives Ezekiel Emanuel has co-authored a plan for vaccine allocation, sharing a proposal deemed the "Fair Priority Model" in this week's issue of the journal *Science*. He and colleagues suggest that earlier ideas of either prioritizing health care workers and high-risk populations or allotting vaccines to different countries based on their population size are "seriously flawed."

"The idea of distributing vaccines by population appears to be an equitable strategy," Emanuel says. "But the fact is that normally, we distribute things based on how severe there is suffering in a given place, and, in this case, we argue that the primary measure of suffering ought to be the number of premature deaths that a vaccine would prevent."

Their model expressly values benefiting people and limiting harm, prioritizing the disadvantaged, and giving equal moral concern for all individuals, with an emphasis on preventing death, especially premature death.

No matter how allocation proceeds, Fernandez Lynch underscores the

need for faith in the product and process. "My biggest concern is the trustworthiness of a vaccine," she says. "A healthy person might just say, "I can continue to cloister myself, I don't have to get this vaccine. I'll wear my mask, I'll use my hand sanitizer." If not enough people trust enough to get a vaccine, then what's the point of having one?"

More information: Harald Schmidt. Vaccine Rationing and the Urgency of Social Justice in the Covid-19 Response, *Hastings Center Report* (2020). DOI: 10.1002/hast.1113

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