03/29/22 • COVID › NEWS

Researchers Seek Real-World Data From 2.5 Million People for Global COVID Vaccine Safety Study

In an interview with The Defender, Aditi Bhargava, Ph.D., the principal investigator of the

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The researchers behind an ambitious and far-reaching new university study on COVID-19 vaccine safety and efficacy hope to collect responses from 2.5 million people worldwide.

The principal investigator of the PROVES (People's Response to COVID-19 Vaccine Efficacy and Safety) study is Aditi Bhargava, Ph.D., a professor in the department of Ob/Gyn and the Center for Reproductive Sciences at the University of California San Francisco (UCSF).

Bhargava, who has a background in molecular and developmental biology, was involved in the development in 1990 of one of the first PCR diagnostic kits for the detection of mycobacterium tuberculosis.

Her co-investigator, Sabra Inslicht, Ph.D., is also affiliated with UCSF as an associate professor practicing clinical psychology and stress research in the university's department of psychiatry.

Organized as a survey, the PROVES study seeks to gather real-world data from respondents on "vaccine efficacy, safety, severity of COVID illness, health outcomes, course of recovery, and mortality in vaccinated and unvaccinated controls."

The study is open to individuals from across the world, regardless of vaccination or COVID status.

In an interview with The Defender about her work and the study, Bhargava explained how her particular scientific background helped inform the study:

> "My work focuses a lot on stress biology. In a way, viral infections are a huge stressor. Also, [I am] studying sex differences. Males and females. Their functions and physiology differ for various reasons. And when they have a particular disease, some of them can also have different outcomes. So that's where I am coming from."

San Francisco, where Bhargava lives, on March 13, 2020, enacted one of the first COVID-related lockdowns in the U.S. She said her research into the effects of such restrictive measures on mental health began that same day:

> "Stress is a big contributor to mental health problems. And we [Bhargava and her collaborator, Dr. Inslicht] at that time had a hypothesis that these lockdowns and mandates … will actually have a huge mental health impact, not just on people who already suffer from mental health issues, such as PTSD, but on the general population."

At the time though, according to Bhargava, this line of research was not widely accepted within the scientific community:

> "We actually submitted five grant applications that were not funded, and most of the critiques [said] that mental health problems due to shutdowns and mandates are not of 'great significance' … and, in fact, as you know, mental health issues associated with the lockdowns and the COVID-19 pandemic have emerged as one of the most significant factors that have impacted us all, especially children."

Further inspiring Bhargava's research was the "warp-speed" rollout of the COVID vaccines. As she explained:

> "The other issue that came about was, of course, implementation of the vaccines at such rapid speed. For the first time, at least since science [became] modern science … has there been such disregard of natural immunity."

The differences across countries in terms of the COVID vaccines that have been made available to the general population helped inform Bhargava's decision to collect responses from a global sample of survey participants.

She stated:

> "In the U.S., it's primarily the mRNA, as well as the recombinant adeno-associated viral DNA vector-based vaccines that have been deployed.
>
> "But in the rest of the world, there are other traditional vaccines that use the inactivated virus or the dead virus. And so, we do not really know what's the efficacy of the vaccines that are in the U.S. compared to the other vaccines, as well as safety issues associated with those vaccines.
>
> "Hence, this particular survey combines both of those interests of mine."

Bhargava told The Defender she was not at liberty to reveal the exact hypotheses her study is working with, in order to not influence the outcome of the research or the responses received.

"I really don't want to influence [the results], since it's a survey-based study, by giving out my hypothesis, because it … would then dictate the outcome," she said.

However, Bhargava did highlight, in broad terms, key issues she aims to address through the study:

> "There's a long list, the main ones [include] trying to compare the actual efficacy of the vaccines that are deployed in the U.S., which are mostly the mRNA-based vaccine, Pfizer and Moderna, compared to the other vaccines that are used in other parts of the world, and to natural immunity."

According to Bhargava, this broad goal is closely connected to concerns about how the COVID vaccines were rolled out to the public:

> "And not just efficacy, but the adverse events associated with these vaccines is an important issue that has not been studied enough. For example, myocarditis and pericarditis (inflammation of the heart muscle and membrane covering, respectively) were not recognized or listed as adverse events when the trials first started.
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> "As you know, the clinical trials were very short. They were only for two months. And within two months, the placebo arm was folded into the vaccine arm, and this was declared as a big success, as no prior vaccine had achieved 95% efficacy.
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> "This is not something that has ever happened in my experience, where you have an approved clinical trial that states they are going to follow people for two years … it didn't happen. Given that these vaccines are mandated, and given to a large population without any long-term follow-up, a systematic data collection and analysis is much needed."

Some officials at the U.S. Food and Drug Administration (FDA) as early as 2020 expressed similar concerns over the COVID vaccine rollout, according to Bhargava:

> "You might be aware that in October 2020, during the Vaccine Safety Discussion panel [convened by the Vaccines and Related Biological Products Advisory Committee (VRBPAC)], which was hosted by the FDA, then-deputy director Dr. [Doran] Fink of the Division of Vaccines and Related Products said that widespread deployment of a weakly effective COVID-19 vaccine could result in more harm than good.

> "So, definitely there were concerns about deploying ineffective or weakly effective vaccines. And [Fink] went on to say that these vaccines could provide a false sense of security and interfere with more effective and concrete measures that would bring the pandemic under control.
>
> "In some ways, we've seen that play out."

Numerous scientific studies have been conducted in relation to COVID, as well as the lockdowns, COVID vaccines and other related issues. Bhargava explained what makes her research different from these studies:

> "Most of the studies I've seen have been narrow in their focus and do not include proper controls.
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> "My study differs from most studies in that we're not looking at a specific mechanism here. We don't know what mechanism to really focus on because we really don't understand how this disease affects a lot of people.
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> "So far, attention has been focused on the very sick. And if you look at the number of very sick [people], that's far less than the people who have not been affected in any severe manner.
>
> "Yet, we are imposing treatments and policies based on what may or may not benefit a very small fraction of society."

Bhargava cited specific studies as examples of what she felt was COVID-related research that was lacking or incomplete, including the recent study by Imperial College London, known as the Human Challenge study, where 36 healthy, unvaccinated people were exposed intranasally to the SARS-CoV-2 virus.

The study found only 18 people got mild disease. The others never developed the disease despite being given a big bolus of virus in their nose. Two people were excluded as they got infected before the start of the study.

"So that [tells us] about … how your immune system and your mucosal immunity play the most important part," Bhargava said. "If [despite] being exposed to the virus so closely, they didn't get it, then [what does this say] about social distancing or wearing masks and things like that?

Bhargava added:

> "I can give you examples of two stories that were highlighted in the media and which I refer to in my blog, which talked about how the vaccinated clear the virus sooner than the unvaccinated.
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> "In a study referenced in a letter published by the New England Journal of Medicine [NEJM] … the number of vaccinated people they studied was very small, 37, compared to the unvaccinated group, which was 136.
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> "When you have such unequal group distribution, performing statistical analysis is not easy. You have to look at the data in a different manner. The authors used Bayesian analysis that allows adding an extra layer of computations, which can give them any result they want."

Also, Bhargava pointed out, there have been many, many variants, and vaccinated and unvaccinated individuals were infected by different variants in that NEJM study. "Unless you are comparing vaccinated and unvaccinated individuals infected with the same variant, it is not a valid comparison," she said.

"You can't take a [vaccinated] individual infected with the Delta variant and compare that to an unvaccinated individual infected with Omicron or the Alpha variant. That is because variants differ in growth times (replication cycle time)."

"This is really disconcerting, that these studies are highlighted without understanding what's going on," Bhargava said. "And in the same study, they did mention that the unvaccinated and the vaccinated, at their peak infection, both had very similar loads of the virus."

Bhargava said that when you look at other studies that have taken samples, even from highly infectious people, only 40% of the time can the virus be taken and grown or cultivated.

"That means 60% of the time the virus may not be infectious," she said. "That would suggest that your immune system has, in a way, neutralized the virus.

She added:

> "That would [require] properly understanding the data and the results.
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> "There's also … another example, a Journal of the American Medical Association [JAMA] study that [found] no adverse events from vaccines. But, they were only comparing two groups, which is people vaccinated within 1 to 21 days and after their first dose of [the] vaccine, and the second group was 22 to 42 days … post-vaccination.
>
> "That's not a valid comparison. If you want to look at vaccine adverse effects, you have to include people who were not vaccinated."How can you compare vaccine adverse events in vaccinated people alone?"

Bhargava also explained how her study differs from data collected and made available by the U.S. Centers for Disease Control and Prevention (CDC):

> "CDC controls the release of data on whatever studies they're conducting. I'm not sure how to get hold of the raw data, per se.
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> "The Vaccine Adverse Event Reporting System data … has been analyzed, as you know, in great detail by many people … but there are no control groups in that. It is a very skewed data set. Only people who are sick report into that system. So you really don't have [the] full breadth of data."

She further explained that, as of May 2021, the CDC stopped collecting data on breakthrough COVID infections, except in cases where "people were hospitalized or died … so again, you've skewed the data."

Bhargava added, "They were supposed to release that data [regarding breakthrough cases] way back in October [2021], but I haven't seen any of that released."

She also referred to the recent release of documents related to the FDA's Emergency Use Authorization of the Pfizer-BioNTech COVID vaccine, highlighting how it has contradicted findings from previous published trial studies:

> "The data that was released showed that between December 2020 and February 2021, there were far more deaths, over 1,200 deaths due to vaccine-related events, than they reported in the NEJM paper, which said that only two people died in their trials. So, which data set to believe? I have published an analysis of this online."

According to Bhargava, there has been a direct connection between the results of skewed, improperly conducted or otherwise incomplete scientific studies, and media reporting related to COVID — with real-world impacts that are, in part, the focus of the PROVES study:

> "There has been just so much hype, or media working as an echo chamber in spreading misinformation and fear, which is what has driven these policies."

For Bhargava, all of the above factors created a need for the PROVES study.

"I've been in this field for a long time," she said. "The data that I generate or I collect — I know what my methods were. I can rely on it … so, hopefully, we should be able to get data that people can trust."

According to Bhargava, while she is obliged to keep the specific sources of her funding confidential, the PROVES study has not received funding from any federal source and is, to a significant extent, crowdfunded.

She said:

> "I'm afraid [we're] not allowed to give that information [referring to specific funding sources]. Donors don't have any influence on the design or data analysis aspects of the study. They didn't see the questionnaire. That's not how the studies are conducted, so they don't have any influence.
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> "[The study] is not funded by the NIH [National Institutes of Health] or any other federal source. It was partly funded by some donor funds … there have been a few big donors that have given some money, and there have been over 100 or 150, maybe more, individual donors who have donated small amounts of money.
>
> "Cumulatively, we've been able to fundraise over $180,000, which will hopefully be able [sic] to fund a statistician's salary to help with data analysis."

Similarly, according to Bhargava, the PROVES study is not receiving any official institutional support in terms of recruiting new participants. Instead, snowball sampling — referrals from person to person — is being heavily relied upon:

> "We are not advertising … so far, our way of spreading this [study] is basically personal contact by both non-professional and professional contacts and putting it on university servers for students, faculty and others, sharing it with other colleagues who are then requested to share it with their colleagues, putting it on my LinkedIn profile.
>
> "The idea is that when [the invitations to participate in the study] come from people that you trust, then you would be more willing to take the survey and also hopefully provide truthful information, which is key to getting good, robust data that we can rely on."

The online survey, according to Bhargava, has been active for approximately two weeks. During that period, nearly 15,000 responses have been received, "mostly from the U.S., but [also] Canada, Australia, New Zealand and some European countries," according to Bhargava, who added:

> "We've started to see some increase in traffic from South American countries, which is really important for us, because those are the countries that did not receive the Pfizer or the Moderna vaccine, but the dead virus vaccine, so it's a different kind of vaccine and that's really important data for us.
>
> "We are also hoping that countries such as Brazil, the Philippines, India, that have multiple kinds of vaccines that are not from Pfizer or Moderna, that we'll see an uptake [from] those places."

Bhargava said the hoped-for sample size is large in order to deliver results that have a higher degree of validity:

> "Once we have enough [responses] and a number for different kinds of vaccines, then we can start to put out some results.

> "We don't want to analyze small numbers … because, as we know, small numbers can be very skewed. We waited two years [since the pandemic was declared], so a few more months will hopefully not make such a big difference, but it will make a big difference in the quality of the data."

The PROVES study is open to both vaccinated and non-vaccinated participants, with or without COVID, with no geographical restrictions. It is also open to participants under the age of 18 if parents or guardians answer on their behalf.

The online survey questionnaire is available here.

SUGGEST A CORRECTION

Michael Nevradakis, Ph.D.

Michael Nevradakis, Ph.D., is an independent journalist and researcher based in Athens, Greece.