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WHITE PAPER

# Vaccine trials benefit from equitable participation

September 2024

## In this white paper, we discuss strategies to:

- Improve participation in flu vaccination trials
- Ensure equitable access to flu vaccination trials
- Overcome other common vaccine research challenges

# Introduction

Vaccination is considered one of the most cost-effective methods to avoid disease and the associated morbidity and mortality, preventing 2-3 million deaths a year globally.[1] Despite the availability of vaccines against common infectious diseases such as influenza, only 48.5% of adults and 53.9% of children were vaccinated against influenza in the 2023-2024 season in the US.[2] As a result, seasonal influenza infections continue to be a public health concern, with the Centers for Disease Control and Prevention (CDC) estimating that the flu resulted in the following in the United States from October 1, 2023, through June 15, 2024[3]:

**35-65 million**
**illnesses**

**390,000-830,000**
**hospitalizations**

**16-30 million**
**medical visits**

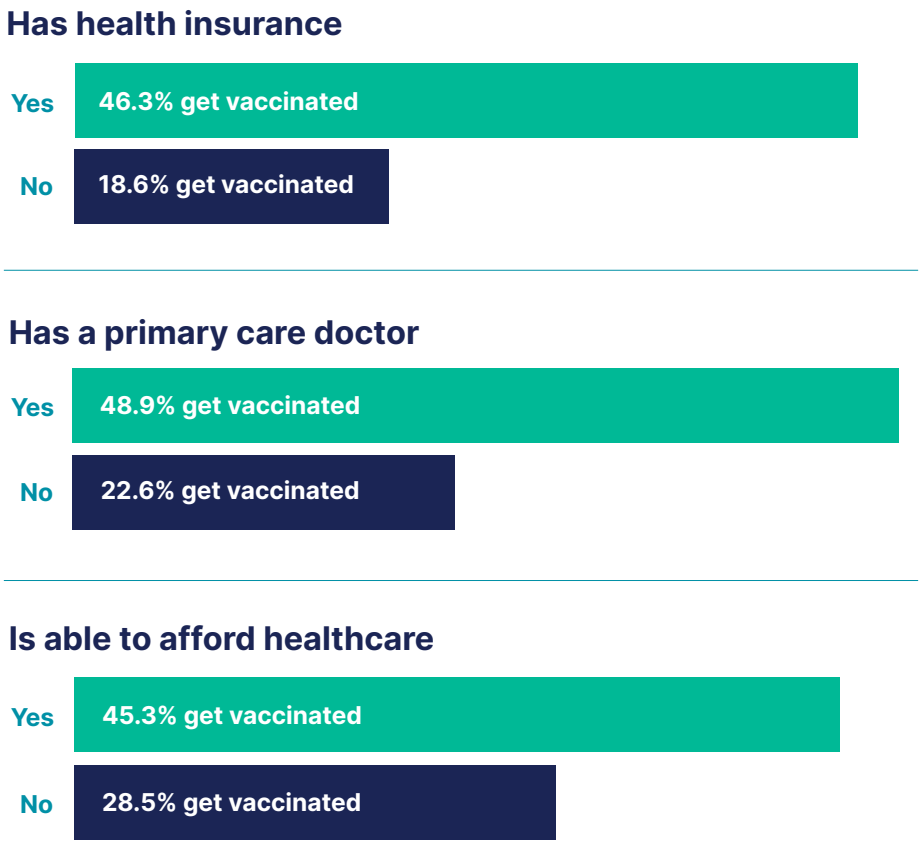
**25,000-72,000**
**deaths**

# Barriers to flu vaccination

A lack of trust and limited knowledge of flu vaccines represent the most common reasons for not being vaccinated, with many people feeling that the flu "does not represent a sufficient health threat to seek out vaccination."[4] When vaccination is already a low priority, the need to be vaccinated annually due to the seasonal evolution of influenza viruses becomes even more inconvenient.

Factors influencing healthcare availability also play a role in vaccine uptake. A recent study reported that access to preventive health care, represented by health insurance, having a primary care doctor, and being able to afford healthcare, were important factors influencing decisions around flu vaccination.[5] These structural issues around healthcare access contribute to inequities around vaccination, and therefore influenza mortality, for adults and children alike.

## How healthcare availability influences vaccination rates



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# Vaccine equity

Social determinants of health (SDOH) such as education level, income level, and housing situation affect knowledge about and access to healthcare, including vaccines.[5] For example, individuals with a college education are two times more likely to be vaccinated than those without a high school education.

These SDOH have a profound impact on minority racial and ethnic groups, contributing to lower vaccine uptake by Black (36.7%), Hispanic (33.9%), American Indian/Alaskan Native (36.6%), and Native Hawaiian/other Pacific Islander (37.9%) individuals when compared with White (46.5%) and Asian (44.1%) individuals.[5]

This pattern is also reflected among older adult Medicare beneficiaries.[6] However, to ensure that vaccines are effective for everyone who could be affected by a disease, it is important that the trial participants resemble the real-life population.



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THE SOLUTION

# Strategies to improve participation in flu vaccination trials

Clinical trials represent one method of overcoming some of the access-related barriers to vaccines, such as cost and availability. This can be particularly important given that flu vaccination campaigns are not federally funded, leaving states to decide whether to offer coverage programs for lower income individuals and resulting in a fractured vaccine landscape.

## Recommendation from a healthcare provider

Receiving a recommendation from a trusted healthcare provider is one of the strongest promoters of vaccine uptake and could also increase participation in clinical trials.[4,7,8] This is especially true given the increase in vaccine hesitancy that has been observed since the COVID-19 pandemic. Defined as the "reluctance or refusal to vaccinate despite the availability of vaccines," the World Health Organization listed vaccine hesitancy as one of the top 10 threats to global health even before the pandemic.[1] A lack of vaccination has been contributing to increasing cases of measles and other infectious diseases, even in countries where the diseases were nearly eliminated.

The reasons for vaccine hesitancy and anti-vaccine sentiment are multifactorial, including lack of confidence in the vaccines, mistrust of public officials and policies, safety concerns, political polarization, complacency, and inconvenient access.[9] Multiple experts and organizations have documented the negative role that misinformation and amplified awareness of vaccine risks on social media and websites is playing in vaccine uptake, both in clinical trials and once they are approved. In addition, poor and conflicting communication by the scientific community has been suggested as contributing to the public's concerns about vaccines.[10] It is not surprising that the public (and even some healthcare professionals) is unsure about whether it is in their best interest to be vaccinated, especially with an unproven vaccine during a clinical trial.

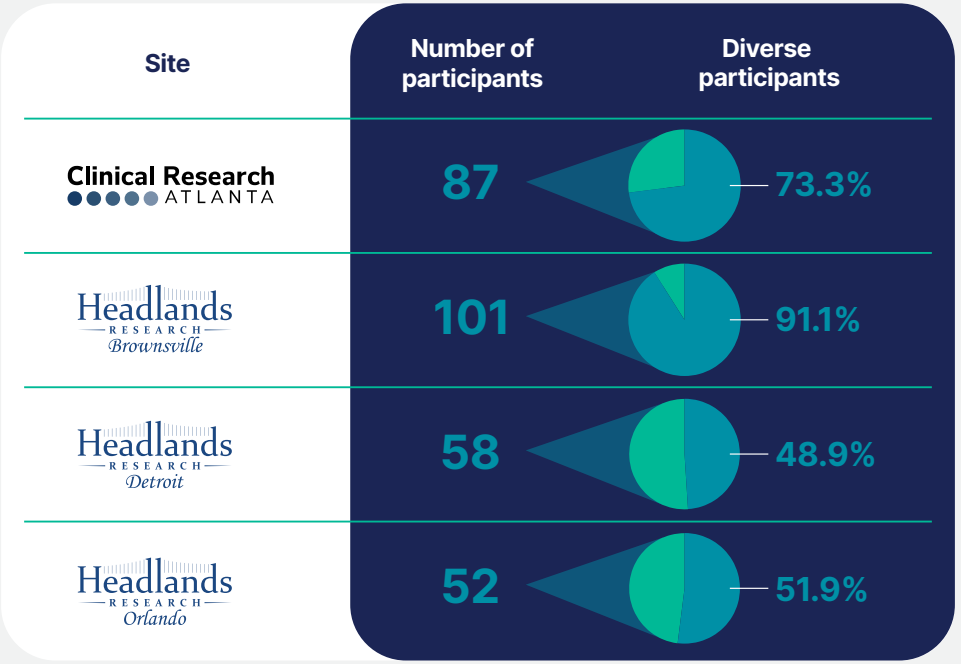
To help increase physicians' knowledge of vaccine clinical trials and improve recruitment rates, our sites have successfully fostered relationships with local physician offices by conducting lunch-and-learn educational sessions, visiting their offices, and treating their patients respectfully when they're referred to a clinical trial.

## Improving accessibility

Convenient vaccine availability is another facilitator of vaccination.[4] Going directly to the community through targeted outreach activities such as educational sessions at community centers and having a presence at community health fairs also increases vaccine knowledge and awareness. Since younger adults, men, and individuals living in rural areas are less likely to be vaccinated against the flu than their counterparts,[5] finding ways to reach those populations within the community could have a significant impact on public health. At the same time, encouraging vaccine trial participation by older adults, minority racial and ethnic populations, and men would help address their long-standing underrepresentation in vaccine trials.[11] Improving accessibility to study locations by providing transportation for potential participants has also contributed to more successful enrollment across our sites.

## Outreach activities by Headlands Research sites ensure inclusive recruitment

**COVID-19/flu combination vaccine study**



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## Convenience of combination vaccines

Another strategy used by sponsors to improve convenience is the development of combination vaccines for common infectious respiratory illnesses with a public health impact, such as influenza, respiratory syncytial virus (RSV), and COVID-19. To date, separate vaccinations have been required. Although generally considered safe by the CDC and other organizations, questions persist within the public regarding the safety and efficacy of being vaccinated against multiple illnesses through multiple vaccinations simultaneously. In addition, getting more than one vaccination in a single visit can result in more and more severe side effects such as arm pain, swelling, headache, and fatigue, which is often a concern.[12] In clinical trials, combination vaccines have demonstrated advantages of a higher immune response without more side effects than with a single vaccination, in addition to the convenience of a single administration.[13]



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# How greater equity in vaccine trials could help overcome common research challenges

Successful development of vaccines against infectious diseases relies on a few population characteristics that could be met using broader recruitment strategies:

- Exposure of trial participants to the target infectious disease in late-stage trials (to test efficacy)
- Unvaccinated status (at least to the vaccine under investigation)

Each requirement benefits from tailored strategies, some of which are presented here based on our network's experience with vaccine clinical trials, using influenza as the example disease.

## Exposure to influenza

How well the vaccine protects against influenza is the most common endpoint for prophylactic vaccine clinical trials. To measure this, in later-phase trials, participants need to be at risk of being exposed to the pathogen (i.e., influenza must be occurring in the participants' areas).

Although evaluating the ability of a vaccine to provide protection typically requires a large number of participants, the level of pathogen exposure can also affect the required enrollment timeframe for the trial and therefore the trial length and cost. For example, if the incidence of disease is low in a trial area, it may require a longer period of time to conduct the trial to appropriately enroll the number of participants needed to estimate vaccine efficacy; in contrast, if the disease incidence is higher, it may take a shorter amount of time to enroll the number of participants needed for the trial.

Understanding the disease epidemiology, including age-specific incidence, age-specific death rates, prevalence of the disease, risk of transmission, clinical manifestations, and seasonality of exposure, is essential to determining where and when trials should be conducted.[14] In addition, as we observed during the COVID-19 pandemic, the epidemiology can quickly change, moving from one geographic area to another and affecting age groups in different ways depending on the most prevalent variant. Therefore, adapting to changes in disease epidemiology is also important for a successful trial.

We've found that engaging sites within a geographically dispersed site network can help to not only more quickly determine the local disease epidemiology but also follow changes in the epidemiology by adapting recruitment efforts to sites in disease hot spots for later-phase studies that require the disease to be occurring.



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## Unvaccinated status

Participants who have previously been vaccinated against the disease of interest or a similar disease create challenges in determining the efficacy of the vaccine under investigation. These individuals are more likely to have a faster, better immune response to subsequent vaccines.[10] This immune memory functions differently depending on the pathogen, its variants, seasonality, and type of vaccine. However, it remains important to determine which vaccines and timing can interfere with the investigational vaccine and to clearly document this in the inclusion/exclusion criteria in the protocol.

Being able to reach populations who typically don't get vaccinated requires targeted recruitment strategies and close community involvement. For sites and investigators, knowing when particular vaccine trials will begin (especially seasonal trials for diseases like the flu) provides an opportunity to be proactive and let the community know about the trials through social media or research database outreach. Potential participants can then make an informed decision whether to participate and receive a vaccine at one of our clinical trial sites or receive it from their physician or local pharmacy.

## Working with an experienced partner

In addition to our proven outreach strategies, our network of 18 sites across the United States and Canada has deep expertise in vaccine trials, including enrolling thousands of participants in influenza vaccine trials with an overall 95% retention rate. Our approach to participant engagement, Principal Investigators who are representative of their communities, and multilingual staff at each site contribute to our ability to provide trusted services that people want to be involved in and remain compliant with. Together, we can ensure equitable access to flu vaccines across our communities, for better public health outcomes.

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### 100% eDiary compliance in an RSV/flu combination vaccine trial

- **77% participants enrolled in 12 days**
- **Site's first vaccine trial**
- **Only site within the network to have 100% eDiary compliance on this trial (all other sites: 95-97%)**
- **Trained on Headlands Research vaccine standards**
- **Not only met but exceeded eDiary compliance**

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Headlands Research is a multinational integrated clinical trial site organization with a mission to improve lives by advancing innovative medical therapies. Its network of sites focuses on large-volume recruitment and retention of diverse, inclusive populations through its extensive site databases and physician partnerships. With key opinion leaders, experienced principal investigators and site staff, and a broad range of therapeutic area expertise, the sites deliver meaningful participant experiences, operational excellence, and the highest quality data. To date, Headlands Research has successfully supported more than 5,000 clinical trials. Additional information about the company is available at www.headlandsresearch.com.

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