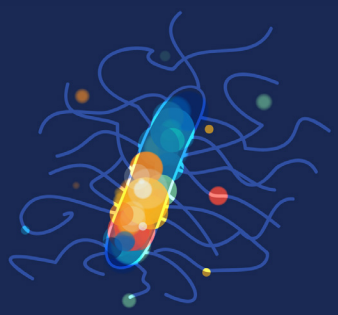

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# OVERCOMING CHALLENGES IN VACCINE CLINICAL DEVELOPMENT: STRATEGIES FOR SUCCESS IN THE EVOLVING LANDSCAPE

Authors: Brian Murphy, *MD, MPH, FIDSA*, Beth Tulip, Christiane Bonde, *PhD*, and Britania O'Brien

## INTRODUCTION TO VACCINE CLINICAL DEVELOPMENT

Over the past 50 years, immunizations have saved an estimated 154 million lives by protecting against more than 30 life-threatening diseases and infections.[1] Many life-threatening diseases have vanished thanks to the success of vaccines.

Vaccines are a powerful tool in public health and their impact is reflected in the global vaccine market, which was valued at $86.06 billion in 2024. Driven by innovation and a continued unmet medical need, the market is expected to grow at a compound annual growth rate of 10.5% from 2025 to 2032.[2] With continued scientific advances, there is a significant opportunity in the vaccine clinical development landscape.

Despite this growth and success, a global decline in vaccination rates is impacting both pediatric and adult populations, largely due to challenges in access and a shift in public perception regarding the need for vaccinations. This trend requires innovative clinical development strategies to address this issue. Vaccinations are critical for controlling infectious diseases, but they can only be effective if enough people get vaccinated. In 2023, more than 14.5 million children under the age of 1 did not receive basic vaccines—nearly 2.7 million more than 2019.[3] Alarmingly, the number of children receiving the first dose of the measles vaccine fell from 86% in 2019 to 83% in 2023.[4]

This decline in immunization rates is concerning. For instance, among children under 5 years of age, infectious diseases accounted for over 40% of deaths in 2021, many of which could have been prevented by vaccines.[5] Furthermore the CDC estimates there have been at least 47 million illnesses, 610,000 hospitalizations, and 26,000 deaths from the 2025 flu season so far, underscoring the persistent threat of infectious diseases in the community.[6]

## CHALLENGES OF VACCINE CLINICAL DEVELOPMENT

The global need for vaccines is evident, driven by emerging infectious diseases and declining immunization rates; however, bringing new vaccines to market is complex. It requires navigating challenges such as vaccine hesitancy and fatigue within the community due to the evolving perception of vaccines, uncertainties about vaccine safety and efficacy, and the amplification of issues through social media and news outlets.

Vaccine hesitancy is defined as a delay in acceptance of vaccines despite the availability and supporting evidence. According to ESCMID Global, "Vaccination hesitancy was identified in the World Health Organization's top ten biggest threats to global health in 2019 that has only continued to grow with each passing year." Medpace works closely with sites and feedback suggests that sites have seen a hesitancy from subjects participating in vaccine trials. Dr. Sarah Smiley, Chief Physician Officer at Velocity Clinical Research says, "There has definitely been a trend in reluctance of subjects to participate in vaccine trials. This does vary by location and even more by indication—especially for COVID-19 and influenza vaccines." Individuals are experiencing a reduced willingness to receive vaccinations due to a variety of factors, impacting the number of subjects participating in clinical trials.

One reason people hesitate to get vaccinated is the spread of misinformation. False information about vaccines can lead to distrust and an increased skepticism around the efficacy and safety. Ineffective communication further worsens this issue, as unclear messages can leave people uncertain about receiving vaccines or participating in vaccine clinical trials.

The growing volume of vaccines available, coupled with increased frequency and diversity of vaccine recommendations, can be overwhelming and has led to confusion around which vaccines are necessary. Information overload and overwhelming vaccine campaigns can contribute to vaccine fatigue, where people are emotionally exhausted by constant reminders and campaigns.

The rapidly changing industry and a lack of trust in government, the pharmaceutical industry, and the media further complicates the vaccine landscape. Changes in regulatory and governmental stances on vaccines can create confusion and uncertainties for the public. There are also potential disruptions in vaccine clinical development due to changes in funding, research delays, and layoffs in public health agencies like BARDA, Health Human Services, and the FDA. At the same time, advisory groups like the Advisory Committee on Immunization Practices (ACIP) are experiencing capacity issues, impacting their ability to make vaccine recommendations. These limitations contribute to delays in guidance and may further impact confusion around necessary vaccines.

Personal experiences or perceived experiences of others also play a significant role in someone's willingness to receive a vaccine. Common concerns that can amplify hesitancy include needle fear and expectations of adverse reactions, such as pain, injection site soreness, fatigue, or headaches. Therefore, it is critical for physicians to compassionately address concerns about vaccines and provide support to ensure that the vaccination experience is positive.

Practical challenges can also deter people from getting vaccinated. Accessibility—for example, waiting time at the clinic or pharmacy, distance to the next vaccination center, and lack of local access—impacts the amount of people receiving vaccinations. In the case of seasonal vaccine, the delay in vaccine availability further complicates matters. If the timing is not right, subjects wanting to be vaccinated might have already opted for an alternative option or may have decided to forego it for the year.

The perceived importance of vaccines has changed over time due to medical advancements and better disease management. With improved treatments and availability of over-the-counter pain relievers, many individuals reassess the risk-benefit of a vaccine. The growing number of treatment options (e.g., effective antivirals for COVID-19 and flu, multiple over-the-counter therapies for symptomatic relief, and improved medical supportive care for serious infections) also minimizes the perceived severity of the disease or post-infection complications. Additionally, younger generations who haven't experienced extreme diseases like measles, mumps, and polio may underestimate the importance of vaccines, resulting in a diminished sense of need around immunizations. Many people also lack an understanding of how certain viral diseases mutate and how the severity of the disease may change over time. This gap in knowledge may impact understanding the importance of a vaccine.

There have always been challenges in vaccine clinical development:

- **Scientific and Technical Challenges**
  - Understanding Disease Mechanisms: In early vaccine development, limited knowledge of pathogens made it difficult to design effective vaccines.
  - Manufacturing Limitations: Before modern biotechnology, producing vaccines in large quantities while maintaining safety and efficacy was difficult.
  - Cold Chain Requirements: Many vaccines require refrigeration, posing distribution challenges, especially in low-resource settings.
  - Mutation of Pathogens: Diseases like influenza mutate rapidly, requiring frequent vaccine updates.

- **Safety Concerns and Adverse Events**
  - Contamination and Production Errors: Cutter Polio Vaccine Incident (1955): A batch of polio vaccine contained live poliovirus, leading to cases of paralysis and deaths in children.
  - Side Effects: Even rare adverse reactions (e.g., Guillain-Barré syndrome with some influenza vaccines) raised public alarm.
  - Public Mistrust of New Technologies: mRNA vaccines (e.g., COVID-19) faced skepticism, in part due to the accelerated timelines, despite strong evidence for safety and efficacy.
- **Misinformation and Vaccine Hesitancy**
  - The Wakefield Study (1998): A fraudulent paper falsely linking the MMR vaccine to autism sparked a global anti-vaccine movement.
  - Social Media and Misinformation: False claims spread rapidly online, undermining public confidence in vaccines.
  - Religious or Philosophical Objections: Some groups oppose vaccines on moral or religious grounds.
- **Ethical and Equity Challenges**
  - Informed Consent: In early studies (e.g., Tuskegee Syphilis Study), participants were often not fully informed.
  - Access and Equity: Developing countries often receive vaccines much later than wealthier nations. COVID-19 vaccine distribution highlighted global inequality.
- **Political and Legal Obstacles**
  - Mandates vs. Personal Freedom: Vaccine mandates (e.g., for school entry) have sparked legal battles and political protests.
  - Nationalism in Distribution: 'Vaccine nationalism' during COVID-19 disrupted global collaboration and equity.
  - Distrust in Government or Institutions: Historical abuses (e.g., in marginalized communities) have led to deep-rooted skepticism.
- **Logistical and Distribution Barriers**
  - Rural and Remote Areas: Reaching isolated populations requires significant infrastructure and planning.
  - Conflict Zones: War and political instability have disrupted vaccination campaigns (e.g., polio eradication efforts in Afghanistan and Nigeria).
  - Supply Chain Bottlenecks: Shortages in raw materials or manufacturing delays have hindered timely vaccine availability.

Although vaccine development has always been complex, the challenges are now heightened due to social media, news, online information, political landscape shifts and greater public access to resources. Online platforms can easily amplify misinformation, leading to increased levels of uncertainty and apprehension.

As vaccine development and deployment have accelerated—particularly during the COVID-19 pandemic—it has become more important than ever to address the challenges that impact vaccine uptake and effectiveness. Tackling these issues is essential for protecting public health against outbreaks of vaccine-preventable diseases and ensuring that scientific advancements translate to real impact.

## STRATEGIES TO MOVE FORWARD DURING VACCINE HEADWINDS

Successfully addressing these challenges requires collaboration among Sponsors, CROs, sites, regulators, and patients. This approach ensures vaccines are not only developed efficiently but guarantees they are effectively delivered and embraced by communities worldwide. Read on to explore key strategies to address the challenges of vaccine clinical development.

### *Patient Recruitment and Retention Strategies*

Effective recruitment and retention are critical to the success of vaccine clinical trials. As trials become more complex and vaccine acceptance becomes more nuanced, it is important to deploy a multifaceted strategy to ensure adequate and representative enrollment.

A foundational step in successful recruitment is understanding the subject population, including their motivation, concerns, and needs to participate in a vaccine trial. People participate in clinical trials for various reasons: a personal connection to the disease, a desire to protect a loved one, financial compensation, or pure altruism. Recognizing and understanding these diverse motivations helps tailor outreach efforts to appeal to each perspective. Effective geotargeting messaging is key and should be tailored to resonate with specific subgroups. Emotional appeals, such as framing participation around the 'why' (e.g., "wouldn't you like to avoid missing work due to the flu?"), can be more persuasive and effective than purely information messages.

Moreover, messaging should not only encourage participation but should also validate that a subject made the right decision when receiving the vaccine. This reinforces confidence in the subject and validates the impact of vaccines. Focusing on countering misinformation in a neutral way is also important. This can be done through using quotes or messaging from celebrities or personalities that the subject can relate to, which can be particularly powerful when combined with scientifically accurate information.

Implementing creative recruitment approaches can be effective in expanding the reach of a trial. Some effective approaches include fostering patient referrals through clinics and healthcare networks, implementing robust digital advertising campaigns, educational recruitment campaigns via flyers, emails, phone calls, and apps, as well as partnering with advocacy groups. Collaborating with popular personality podcasts that may align with the targeted audience also can be a powerful method. Expanding the number of sites and extending the enrollment period can help increase trial participation while expanding outreach.

High-quality educational materials play a vital role in patient recruitment and retention. By equipping clinics with patient education materials with accurate and relatable information backed by scientific data, we can ensure the participant is comfortable and confident in their choice to participate in the trial. The development of patient education materials should highlight the positive impact of vaccines and should include Q&A to address common concerns or misconceptions.

### *Reducing Patient Burden*

Minimizing the burden on patients is a proven way to increase participation and adherence. This can be achieved through collaboration with the Sponsor to streamline the protocol, reducing travel burdens, and providing incentives such as stipends or reimbursements to alleviate financial barriers to participate.

Flexible scheduling is another aspect to help reduce patient burden. Initiatives like mobile vaccine centers and extended hours for vaccine centers in the evening and weekends make it easier for participants to get the vaccine with minimal interruption to their personal or professional obligations. By placing patients at the center of a trial, it helps reach enrollment goals while helping yield successful outcomes in terms of study design, participation, adherence, satisfaction, and data collection.

### *Strong Collaboration Between Key Stakeholders*

Strong communication, collaboration, and transparency among patients, sites, Sponsors, CROs, and regulators is key to ensuring a seamless clinical trial. CROs can provide sites and Sponsors with invaluable insights gained from managing comparable vaccine trials, helping them navigate common challenges and roadblocks that arise.

Sites networks have a strong influence and play a pivotal role in vaccine clinical trials. Real-time updates on timelines and enrollment progress allows sites to adapt quicky and make changes as needed. Early and ongoing engagement with regulators is important for expediting the approval process. By identifying potential challenges early on, strategies can be implemented to streamline the study, ensuring a seamless path to approval.

## CONCLUSION

Vaccine development is essential in the prevention of high-risk diseases, but there are nuances Sponsors and CROs must understand to successfully advance vaccine development and minimize the impact of infectious diseases on the community. The Medpace infectious diseases and vaccines team has global experience and expertise, offering comprehensive support for vaccine clinical trials across a wide range of vaccine types and populations.

Through our interdepartmental, multidisciplinary approach, we leverage the experience of colleagues across functional and therapeutic focus areas to pool our collective knowledge to support your program. Additionally, our medical experts are embedded directly within the project team and remain fully involved throughout the study. This integration of specialized physicians with our functional teams ultimately drives the highest quality performance throughout the trial.

Our strong relationships with investigators, key sites, regulators, institutions, specialized laboratories, and KOLs enable us to streamline site selection, start-up, and recruitment efforts. These long-standing relationships, combined with our deep expertise, translate into successful and timely recruitment, study conduct, and delivery. Furthermore, our comprehensive CRO services are supported by wholly-owned Central Laboratories, as well as ClinTrak®, a seamless Clinical Trial Management System, providing real-time access to all patient and study data, perfect for rapidly enrolling vaccine trials.

With our experienced, cross-functional infectious diseases and vaccines team, integrated services, and extensive site and investigator relationships, we are equipped to assist you in navigating vaccine hesitancy and the complexities of vaccine clinical development.

Do you have an upcoming vaccine clinical trial that needs seamless execution? Contact us today to discuss how Medpace can help accelerate your clinical development.

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