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Considerations for pediatric vaccine trials in developing countries

Contributors

Susanne Schmidt, MD, PhD; Senior Medical Director, Rare Disease, Advanced Therapies and Pediatrics Team (RAPT), Fortrea

Julie Maher, Senior Director, Advanced Therapies and Pediatrics Team (RAPT), Fortrea

Alberto Vicens, PhD; Global Feasibility Lead II, Strategic Feasibility and Analytics, Fortrea

Infectious diseases disproportionately affect developing nations, accounting for 90% of preventable cases globally.[1] These low- and middle-income countries (LMICs) have historically been underrepresented in vaccine research and development, despite bearing the brunt of this burden. However, this landscape is shifting, offering promise for more equitable representation in vaccine research.

Clinical trials landscape in pediatric vaccines

The geographic distribution of vaccine trial locations has shifted significantly in recent years, expanding to include a wider range of regions as well as including upper middle, low middle and low income countries.[2] China, India and Japan have been major drivers of geographic diversification, and South Africa recently joined the top 10 countries for pediatric vaccine trials (figure 1, 2).[3]

Figure 1. Pediatric vaccine trials per region over time

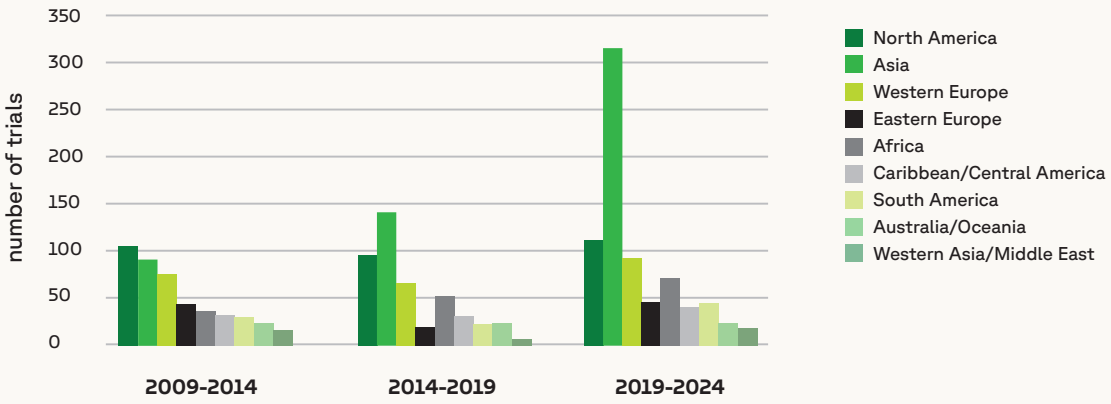
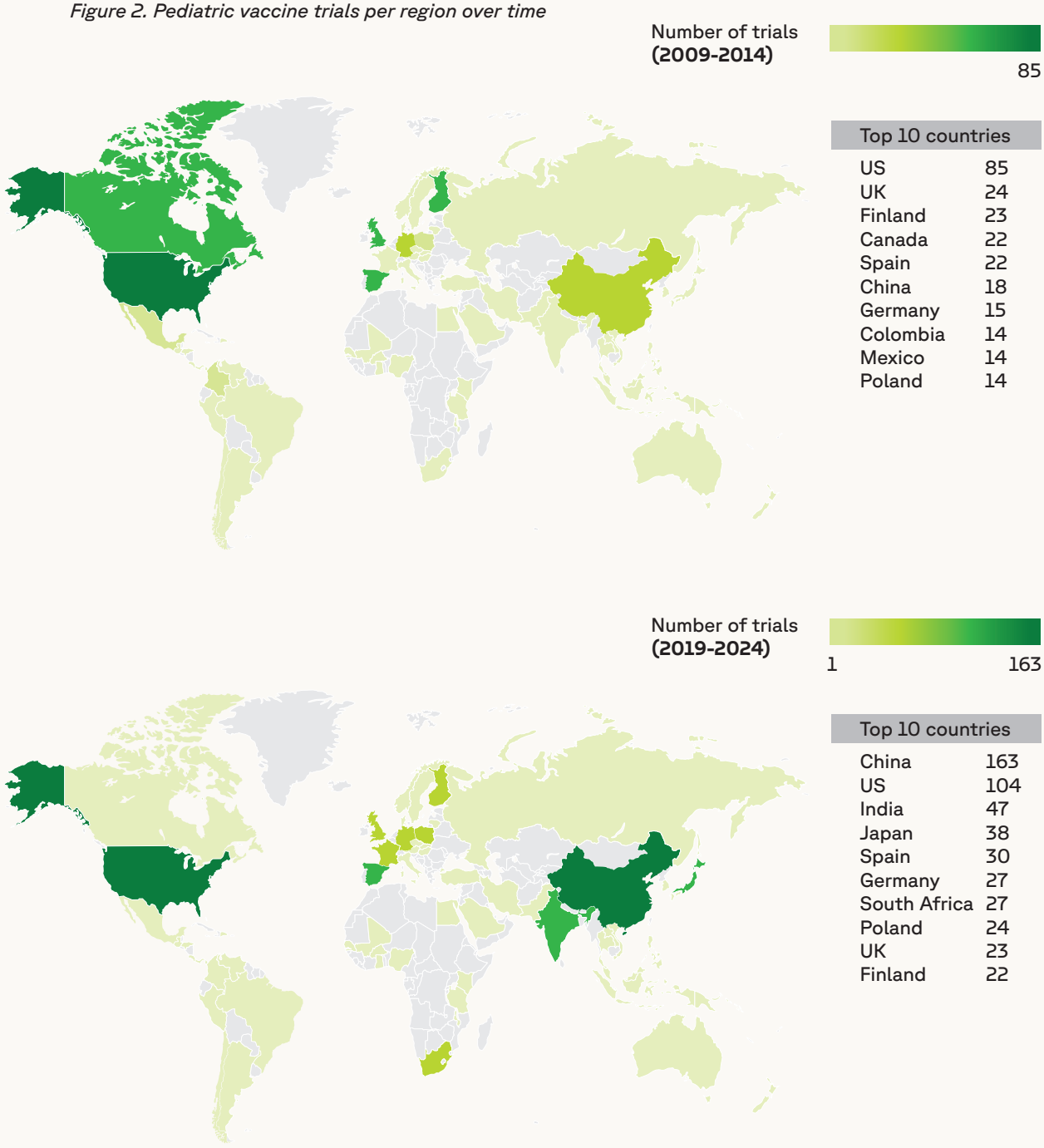


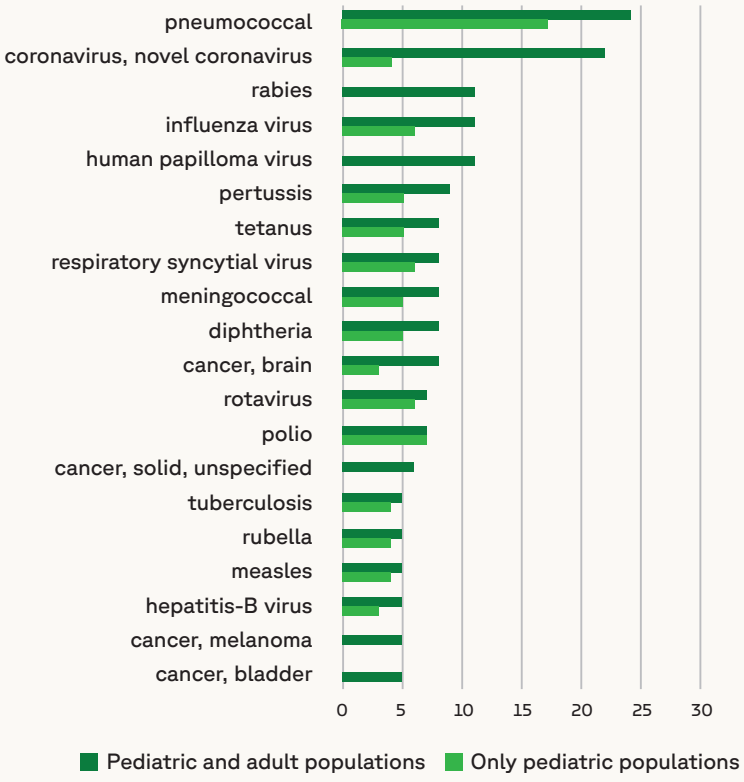
Figure 2. Pediatric vaccine trials per region over time



Currently, 83 of 171 vaccines in development specifically target pediatric populations only.[4] Pediatric vaccine trials from the last five years cover a broad range of ages, ranging from 0-5 years (26% of trials) to trials that include both pediatric and adult populations.[4] Additionally, most trials from this time period (64%) have been industry-sponsored.[4]

Of the vaccines currently in development, major pediatric indications include pneumococcal disease, polio, rotavirus, and RSV (figure 3).[4] A shift toward more inclusive research is crucial for addressing the unique health needs of children in LMICs, where preventable diseases such as these are a significant concern.

Figure 3. Top 20 vaccine indications



While progress has been made in expanding pediatric vaccine trials to LMICs, these regions continue to present unique considerations for pediatric vaccine trials. From ethical and regulatory concerns to logistical challenges, navigating these complexities is essential for ensuring these trials effectively address community needs and contribute to improved global health outcomes.

Challenges and considerations for pediatric vaccine trials in LMICs

While pediatric vaccine trials in LMICs offer significant potential benefits, they also present unique challenges that researchers must carefully navigate. These concerns include both general issues in pediatric research and specific hurdles encountered in resource-limited settings.

Community engagement and participation

Limited understanding of research processes among potential participants and their families can hinder recruitment and informed consent.[7] Low literacy rates in some LMICs further complicate this issue, necessitating innovative approaches to explain trial procedures, risks and benefits. Socioeconomic factors, such as poverty, underdevelopment and high disease burden, also significantly influence families' decisions regarding trial enrollment. These factors can also affect trial outcomes by impacting a child's overall health and immune response.

Cultural and linguistic barriers present additional challenges. Researchers must navigate local customs, beliefs and hierarchies that may influence trial participation. For example, obtaining consent may require consultation with community elders or other authority figures before approaching individual caregivers.[7]

Infrastructure and resource limitations

Limited trial site infrastructure and experience in some LMICs can affect the quality and efficiency of vaccine trials. While recent years have seen improvements, many areas still lack the necessary facilities, equipment and trained personnel to conduct complex clinical studies. This underscores the need for ongoing investment in strengthening research capacity within these regions.

Ethical and regulatory considerations

Ethical considerations are paramount in LMIC settings, particularly given the history of unethical research practices in some regions.[8] This historical context can create apprehension surrounding clinical trials, requiring researchers to build trust and demonstrate clear benefits to local communities.

Ensuring equipoise and selecting appropriate comparators—whether placebo or an existing vaccine—is also crucial. This choice must be scientifically and ethically justified, considering local standards of care, which may differ from those in high-income countries (HICs). This often requires careful consultation with local health authorities and ethics committees to ensure alignment with local health priorities and ethical standards while maintaining scientific rigor.

Navigating regulatory variability across LMICs presents another hurdle. Each country has its own set of regulations, which can differ significantly from international standards, affecting various aspects of trial conduct, from protocol approvals to data reporting. In some LMICs, regulatory bodies may have limited experience with complex clinical trials, potentially leading to longer approval processes or inconsistent interpretations of international guidelines. Despite ongoing harmonization efforts, researchers and sponsors must carefully navigate these differences.

Designing effective pediatric vaccine trials in LMICs

Addressing the unique challenges and ethical considerations of pediatric vaccine trials in LMICs requires carefully designed trials appropriate for these settings. Several key strategies can help achieve this goal.

Parallel trials in HICs and LMICs

Conducting parallel trials in both HICs and LMICs can provide valuable comparative data and ensure that vaccines are effective across diverse populations. This approach allows for the identification of any region-specific factors that might influence vaccine efficacy or safety. It also helps address concerns about equity in research, ensuring that LMIC populations benefit from advances in vaccine technology simultaneously with HIC populations.

Prioritizing local relevance and disease burden

Effective trial design in LMICs must prioritize diseases that represent a significant local health burden. This focus ensures that research resources are directed toward addressing the most pressing health needs of the population. For example, trials for vaccines against diseases like malaria or dengue fever may take precedence in regions where these illnesses are endemic.

Improving consent processes

Given the challenges related to informed consent in LMIC settings, innovative approaches are necessary. This might include using visual aids, storytelling techniques or community-based education programs to explain trial procedures and potential risks and benefits. Engaging local community leaders in the consent process also is critical to help build trust and understanding.

Addressing socioeconomic inequalities

Trial designs must account for the socioeconomic realities of LMIC settings. This could involve providing transportation to trial sites, ensuring that participation does not result in lost wages for families or offering ancillary care for participants. Such measures help ensure that economic factors do not unduly influence participation or skew trial results.

Posttrial considerations

While the focus of pediatric vaccine trials in LMICs is often one of the immediate challenges of design and implementation, it is also crucial to consider the long-term implications and responsibilities that extend beyond the trial's conclusion.

Ensuring posttrial access to effective vaccines is a key ethical obligation. Once a vaccine proves effective, there's a responsibility to make it available to the communities that participated in its development. This may involve agreements with pharmaceutical companies or governments to provide the vaccine at reduced cost or through donation programs. For example, the WHO provides vaccines through its Expanded/Essential Programme on Immunization (EPI). The program has grown from six vaccines at its inception to 13 and continues to work with other public health programs with a goal of universal vaccine access.[9]

Technology transfer to local manufacturers is another important consideration. By sharing knowledge and production capabilities with manufacturers in LMICs, we can enhance local capacity to produce vaccines, potentially reducing costs and improving supply chain reliability. This approach not only benefits the immediate region but can also contribute to global vaccine supply resilience.

Building sustainable research capacity

Beyond individual studies, pediatric trials can begin to build long-term research capacity that can support ongoing health improvements. This can be achieved by investing in local scientific talent, including training programs for researchers, laboratory technicians and clinical staff. Collaborations between LMIC institutions and experienced research centers in HICs can facilitate knowledge transfer and skill development.

Strengthening local ethical review boards and regulatory bodies is another essential step for ensuring high-quality, ethically sound research. This might involve providing training in Good Clinical Practice (GCP) standards, supporting the development of local ethical guidelines and facilitating participation in international regulatory harmonization efforts.

Partnerships are another tool for building research capacity. Academic partnerships can foster knowledge exchange and collaborative research. Product development partnerships bring together diverse stakeholders to address specific health challenges. Clinical trial networks can help standardize practices and share resources across multiple sites.

Support for your pediatric vaccine trial

Pediatric vaccine trials in LMICs offer opportunities to address global health disparities. By carefully navigating ethical considerations, focusing on local relevance and planning for long-term impact, researchers can conduct trials that not only advance vaccine development but also contribute to broader improvements in pediatric health outcomes.

Fortrea provides support for organizations conducting pediatric vaccine trials in LMICs. With experience in managing complex trials across diverse settings, Fortrea offers guidance on regulatory compliance, ethical considerations and community engagement strategies. Contact us for more information on how Fortrea can assist with your research.

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