# Innovation for Eradication

By Nellie Bristol & Michaela Simoneau | JULY 2020

This seventh installment in our series on U.S. support for global polio eradication explores how ongoing research has allowed the eradication program to learn and adapt in real time, overcoming new obstacles and building a body of knowledge that can be applied to other global health campaigns.

## Introduction

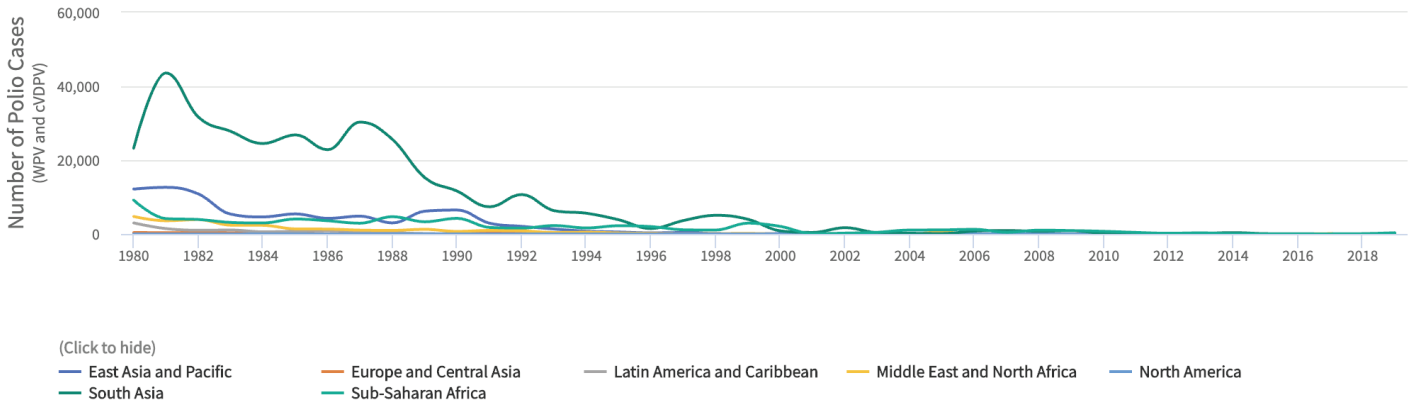
When the World Health Assembly committed all nations to the global eradication of polio in 1988, it did so thinking there was a solid game plan that would surely lead to success, if not by the original 2000 target, then soon after.[1] After all, developed countries already had made substantial progress against the disease. Furthermore, the Americas region, which included countries at all economic levels, was on the verge of scoring a major public health victory by eliminating the disease in under a decade.[2]


Source: Nigeria/WHO

> "Certainly, the program has had different phases where research was not needed. We had tools, we had two good vaccines. One-hundred countries eliminated the circulation of polio quite readily with the application of the basic approaches."
>
> — *Mark Pallansch, Director, Division of Viral Diseases, U.S. Centers for Disease Control and Prevention*

## Global Polio Cases by World Bank Regions, 1980-2019

This chart breaks down the number of cases per World Bank region each year. To see the original World Health Organization region breakdown of case, click here for the data from 1980–2016, 2017–2018, or 2019.




But after substantial early successes, which drove down the number of cases by more than 99 percent, the program met unexpected obstacles as it strove to vaccinate all children everywhere. In addition to encountering problems with the polio vaccine itself, the Global Polio Eradication Initiative (GPEI) struggled to reach communities that were constantly on the move, disenfranchised from their own governments, or plagued by insecurity.

These developments made it clear that some of the original assumptions about polio operations were overly simplified or incorrect and could threaten the eradication goal itself. In response, the GPEI, including the U.S. Centers for Disease Control and Prevention (CDC), and other eradication supporters, such as the U.S. Agency for International Development (USAID), began funding a variety of research projects to better understand how to move the initiative forward.

Source: UNICEF/Serge Wingi

But as progress continued to stall, it became apparent that a more coordinated approach was needed. In response, the GPEI established the Polio Research Committee in 2008, leading to the rapid implementation of program innovations.[3] Research conducted for polio eradication led to changes not only in vaccination approaches but also in operations and communications. Many of these innovations developed for polio eradication also have been applied to other public health programs. Ongoing research will continue to be critical to the initiative as it faces its toughest challenges in the final push for eradication.

# A Proven Strategy Hits New Obstacles

Global polio eradication was predicated on a four-pronged approach:

1. Strengthening immunization systems, which include polio vaccination as part of essential childhood immunizations;
2. Conducting mass polio vaccination campaigns using the inexpensive and easily administered oral polio vaccine (OPV);
3. "Mop up" activities to ensure vaccination of any children missed through the first two approaches; and
4. Strong surveillance systems able to detect any new cases and trigger a rapid response.[4]

While groundbreaking scientific research had made the initiative possible, continuing studies were not originally prioritized by the GPEI since it already had a proven approach and program resources were needed to support an ongoing wave of vaccination campaigns.

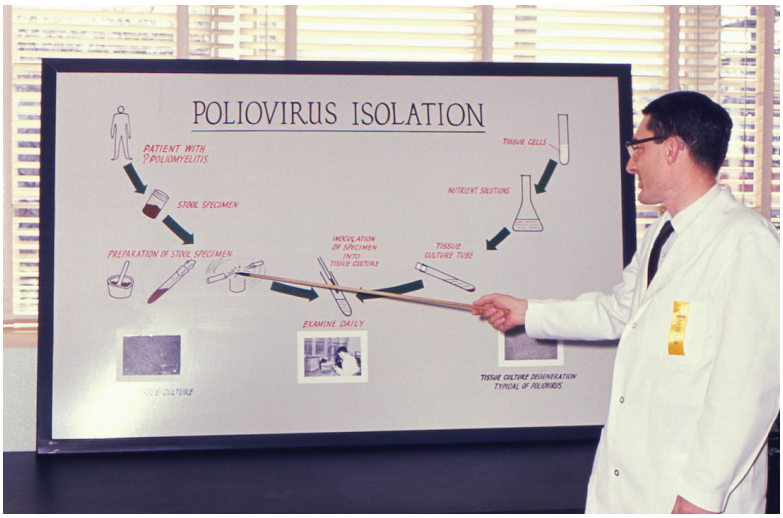
Yet despite the strategy's success throughout much of the world, daunting challenges developed, particularly in areas with weak immunization systems and low polio immunity:

- A growing number of polio cases emerged stemming from the live virus OPV;[5]
- The three vaccine doses deemed sufficient to immunize children in most of the world were ineffective in poor areas of India with inadequate sanitation;[6]
- The program struggled to reach nomads and refugees who typically were underserved by traditional primary health services;[7] and
- As the initiative dragged on, more communities began to refuse the vaccine.

Members of the Afghanistan polio eradication initiative go door to door on their mission to vaccinate every child.
Source: WHO Afghanistan/Tuuli Hongisto

As the downward trend in polio cases flattened out in the first decade of the 2000s, it became evident that fresh ideas were needed. The GPEI began to devote substantial funding, focus, and attention to polio research, which has produced findings related to vaccine dosing schedules, disease tracking and surveillance, and negotiating social norms.[8]

The GPEI's experiences show that devoting resources to social research is as critical to public health efforts as focusing on more technical issues. Overall, the biggest lesson is the need to dedicate funding and attention to research throughout a disease eradication effort to effectively adapt program operations to the range of biomedical and cultural situations found throughout the globe.




Source: CDC/Wallace Richter

# A Well-researched Disease

> "The GPEI invests in research and innovation as vital assets to inform and optimize polio eradication efforts."
> — *Abhijeet Anand, MBBS, Epidemiologist, Polio Eradication Branch, CDC's Center for Global Health*

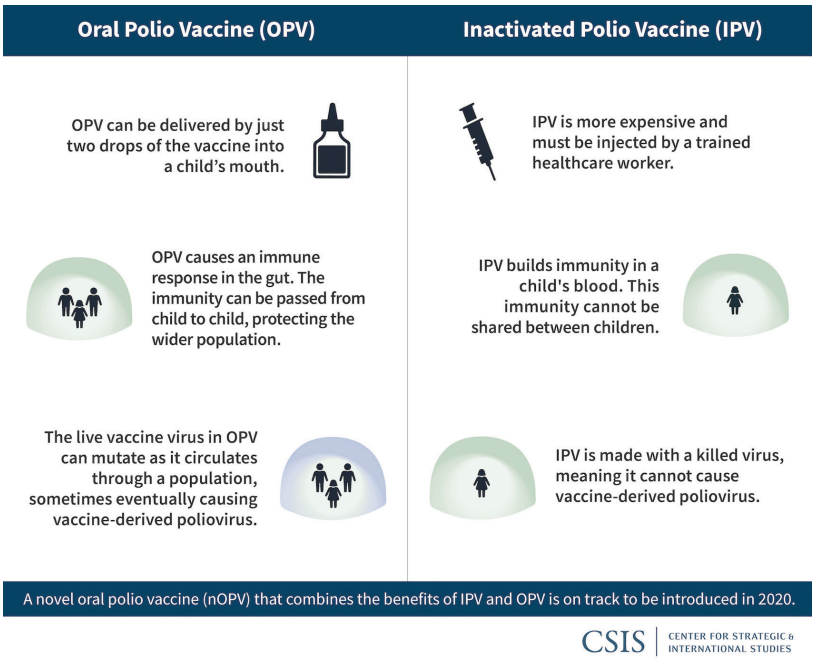
The polio virus is one of the most thoroughly researched pathogens of the modern age, principally because of its structure. It is a simple virus that is easy to work with in the laboratory, and because the disease is vaccine preventable, scientists can work with it safely. It proved to be an ideal model for researchers at the CDC, the World Health Organization (WHO), and elsewhere to understand how viruses worked and how they affect the host.

Starting in the mid-1970's, even before the global eradication effort began, researchers were able to distinguish between wild and vaccine-derived poliovirus and understand how the virus mutates over time. With the development of genome sequencing technology in the early 1980's, researchers at the CDC were able to determine the geographical origin of a particular virus by studying how it mutated and through those discoveries follow its path to other regions. This allowed the GPEI to pinpoint the origin of outbreaks in areas that previously had been polio-free and helped set vaccination strategies.

Genome sequencing is now a routine part of viral research and disease surveillance, tracking global circulation of not only polio but other viruses such as measles and yellow fever.[9]

# Optimizing Polio Vaccines

But even with advanced knowledge and proven approaches, further innovations were needed. Research conducted for the initiative in the early 2000's helped devise strategies to ensure children in high-risk areas of India were able to achieve immunization levels required to stop viral transmission. Researchers discovered that children in these areas were subject to other intestinal diseases that hindered the polio vaccine's effectiveness.[10] As a result, they required 8, 10, and sometimes more vaccinations to be fully protected.[11] By better understanding these interactions, the GPEI tinkered with the vaccine's formulation to make it more effective in that environment.[12]




Research led to other innovations as well. As part of an eventual phased global withdrawal of OPV to stop the circulation of the vaccine-derived disease, the program recommended that all countries provide at least one dose of inactivated poliovirus vaccine (IPV).[13] IPV protects individuals from polio but is a more expensive, injectable vaccine requiring a more complex administration regime and does not provide the type of immunity found to be most effective in developing countries.[14]

Unfortunately, IPV manufacturers were not able to provide the supply needed in a timely manner.[15] Research funded through the GPEI discovered the minimal amounts of IPV required per dose to achieve immunity and pioneered dose sparing administration methods, allowing the initiative to ensure the scarce vaccine reached the maximum number of children possible.[16] Some of these new techniques are now being used for hepatitis B and yellow fever vaccines.[17]

# Stemming Vaccine-derived Polio

> "The long-term use of traditional OPV is not compatible with polio eradication."
> *— Ondrej Mach, Polio Research Team, World Health Organization*

Source: UNFoundation/Christine McNab

The initiative now is conducting research to address the Achilles heel of the entire eradication effort: vaccine-derived poliovirus. OPV, the primary vaccine used by the initiative, is a weakened live virus vaccine. In populations with low vaccine coverage, the vaccine virus can be passed among unimmunized populations, mutating as it circulates until it reaches a state where it can cause outbreaks with the same paralyzing effects as those of wild poliovirus.

In an effort to reduce the number of vaccine-derived cases, the GPEI in 2016 re-

moved from OPV the component that causes the majority of outbreaks, which immunized against the type 2 strain of polio. The program began using a bivalent OPV instead that only inoculated against polio types 1 and 3.[18] While the initiative expected to see some additional cases of type 2 vaccine-derived polio after the vaccine switch, it instead is facing an unexpectedly large number outbreaks, mostly in Africa.[19]

Researchers are now fast-tracking development of what is called novel OPV (nOPV), a more stable form of the oral vaccine aimed at type 2 polio that is less likely to mutate into a disease-causing state.[20] "GPEI officials are counting on the vaccine, hoped to be available in 2020, to halt the advent of the vaccine-derived disease and move the initiative into its final stages.[21]

> "The research going into [nOPV] goes back more than 15 years… this is an example of multiple laboratories, including the CDC polio labs, doing basic research into the nature of polio replication that came together with a practical end point of a potential new vaccine."
> — *Mark Pallansch, Director, Division of Viral Diseases, U.S. Centers for Disease Control and Prevention*

Introduction of nOPV will be paired with expanded and simplified environmental surveillance techniques which can detect and categorize poliovirus in sewage samples. Improved environmental surveillance will tell the GPEI where poliovirus is present and whether the sample is wild or vaccine-derived. It also will be able to show whether the correct vaccine is being used in a particular area and if programmatic changes are required to boost immunity.[22]


Source: CDC/Holly Patrick, MS, MPH

## Prioritizing Innovation: The Polio Research Committee

> "In the early years there was no research committee . . . we were trying to get a handle on some of the gaps early on. We funded [projects] that we thought would improve the quality of the program."
> — *Ellyn Ogden, Worldwide Polio Eradication Coordinator, U.S. Agency for International Development*

Individual members of the GPEI partnership—including the CDC, Rotary International, UNICEF, the World Health Organization, the Bill & Melinda Gates Foundation, and recently Gavi, the Vaccine Alliance, as well as donors such as USAID—had been supporting and conducting sporadic research projects even before the initiative began. But the challenges facing the initiative led the GPEI to establish a more formal process to streamline and prioritize as a way to drive program progress.

**A lab technician in Kenya works with samples to test for poliovirus.** Source: WHO Kenya/L. Dore

The Polio Research Committee (PRC), established in 2008 and led by the WHO, CDC, and Bill & Melinda Gates Foundation, is considered by many in the GPEI to be a game-changer for the initiative.[23] It ensures money is set aside to encourage ongoing innovation and streamlines the path from discovery to application in the field. Findings are discussed at PRC meetings and can be incorporated into operations even before they go through the lengthy process of peer-reviewed publication. Furthermore, since funding is specifically earmarked for research, the resources are guaranteed and cannot be diverted to program operations or other needs.

> "The polio program has benefited from dependable donor funds that have allowed it to consistently improve program strategy based on research that has been responsive to the changing realities on the ground."
> *— Abhijeet Anand, MBBS, Epidemiologist, Polio Eradication Branch, CDC's Center for Global Health*

Comprised of experts in virology, epidemiology, sociology, and public health, the committee meets twice a year to publicize priorities, review proposals, and recommend projects for funding. Most funding for research is provided by the International PolioPlus Committee of Rotary International and by the Bill & Melinda Gates Foundation, with some specific funding from the CDC.[24] The bulk of approved projects focus on clinical measures, vaccine optimization, and operations improvements.[25] The PRC gives preference to relatively short-term research (12-24 months) that will have substantial immediate impact on eradication progress.

In addition to the PRC structure, several organizations—both core partners such as CDC and UNICEF and other collaborators and donors such as USAID—continue to conduct their own research on a more project-by-project basis.

## The U.S. Government & Polio Research

Different arms of the U.S. government have contributed substantial new knowledge in support of global polio eradication. The CDC, a core member of the GPEI, has conducted its own research focused on epidemiology, vaccine efficacy, and improving operations during vaccine campaigns.[26] With their premier cadre of scientific expertise and strong bilateral partnerships with labs around the world, CDC staff have led landmark studies to track the spread of the virus, optimize vaccine schedules to improve population immunity, and implement the vaccine "switch" to bivalent OPV.[27] Most recently, CDC scientists have helped lead efforts to develop and test candidates for type 2 nOPV, and they continue to work on novel type 1 and 3 vaccine candidates as well.[28]

USAID, by contrast, has focused more on operational research, "recognizing and raising the importance of mobile populations, cross-border coordination, communications, and the need for women vaccinators."[29] Its efforts extend beyond polio to address other immunizations, water and sanitation, breastfeeding, and handwashing and fit into broader goals around disease surveillance and outbreak response.[30] The agency has worked with the CORE Group Polio Project and a variety of other NGOs to emphasize this communication-based approach to polio eradication.[31]

Source: WHO Afghanistan/Tuuli Hongisto

# Expanding the Research Portfolio

> "It went beyond just knowing about the disease. It went to looking at attitude and intentions. Then to follow through and look at actual coverage. Actual acceptance of the vaccine."
> — *Rustam Haydarov, Senior Communication Manager, Polio, Health Section, Program Division, UNICEF*

While the PRC has been pivotal in encouraging needed research, it and the GPEI overall have been criticized for focusing too much on biomedical approaches at the expense of social research. The bulk of research by the GPEI and other eradication supporters focused on understanding the poliovirus, improving surveillance, and optimizing the vaccine,[32] but the program needed better guidance to improve communications and operations. The need for a broader re-

search portfolio became apparent as the initiative faced increasing vaccine fatigue and refusals and struggling to reach mobile populations and disenfranchised and remote communities.[33]

Vaccinators traverse rural Pakistan by camel to reach villages with otherwise inaccessible children. Source: UNICEF/PAK2016/Waseem Niaz

The GPEI partners realized that negotiating social norms and weaving vaccination into the existing fabric of these communities would be critical to lasting success. They also discovered that being able to identify and quantify social obstacles in a scientific manner lent credence to the findings, making them more palatable to the largely medically-oriented GPEI operations officials.

UNICEF and USAID have supported and partnered with institutions such as Harvard University in using surveys to reveal and quantify community norms that were hindering acceptance of the polio vaccine.[34] The studies identified illiteracy as a major barrier to knowing about specific vaccine campaigns and gaps in understanding the lack of a cure for polio, spurring development of alternative forms of communication. UNICEF worked with BBC Media Action to produce vaccine information in a variety of new formats, including radio and television, to assess their effects on vaccine uptake.[35] These studies also revealed the importance of working with local leaders to gain community trust of the vaccine and the organizations behind the GPEI.[36]

Religious leaders are trained on the basics of social mobilization, communication, health, and hygiene. They also learn about the religious justifications for polio vaccination. Source: WHO Pakistan/Dawood Batozai

Anthropological research became critically important as the GPEI struggled to vaccinate nomadic and mobile populations. Such research was able to illuminate social norms among different populations that allowed the program to provide better access to vaccination. For example, a study of Somali pastoralists led the program to offer vaccination at cattle water points and markets, doing so in concert with veterinarian services.[37] The research has now been applied by programs focused on tuberculosis in the Horn of Africa.[38]

In Pakistan, one of the three countries where wild poliovirus remains endemic, research helped formulate hyper-local programming to address vaccine acceptance on a neighborhood-by-neighborhood basis, another set of findings now being adapted for broader immunization programs.[39] These tailored programs will be essential as GPEI becomes increasingly focused on the remaining wild polio hotspots during the eradication endgame.[40]


Source: Adek Berry/AFP/Getty Images

## Eradication Needs Innovation

> "If there is one lesson from polio that is broadly applicable, it's to never assume you know enough . . . there is no reason, even going into an eradication effort, to stop research."
> — *Mark Pallansch, Director, Division of Viral Diseases, U.S. Centers for Disease Control and Prevention*

Ongoing research has been and continues to be critical to global polio eradication. Although the poliovirus and its vaccines were well known and the Americas presented an effective proof of concept for global eradication, the need to vaccinate every child in the world living in every possible geography and culture presented challenges that in many cases could not be foreseen. Continued exploration of effective vaccination doses and strategies along with operational adjustments were imperative.

In addition to fast-tracking novel approaches to address polio and other diseases, social and cultural research pioneered by program supporters will continue to provide insights into ensuring health services reach and are accepted by all communities. Research will continue to be a high priority for the GPEI as it moves into the difficult eradication endgame and likely will add to the collection of new approaches useful to the broader health community.

# About the Authors

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SPECIAL THANKS TO:

Abhijeet Anand, MBBS, MPH, Epidemiologist, Polio Eradication Branch, Center for Global Health, U.S. Centers for Disease Control and Prevention

Jason Cecil, Public Health Analyst, U.S. Centers for Disease Control and Prevention

Rustam Haydarov, Senior Communication Manager, Polio, Health Section, Program Division, UNICEF

Ondrej Mach, Polio Research Team, World Health Organization

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*This project is made possible through the generous support of the Bill & Melinda Gates Foundation.*

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