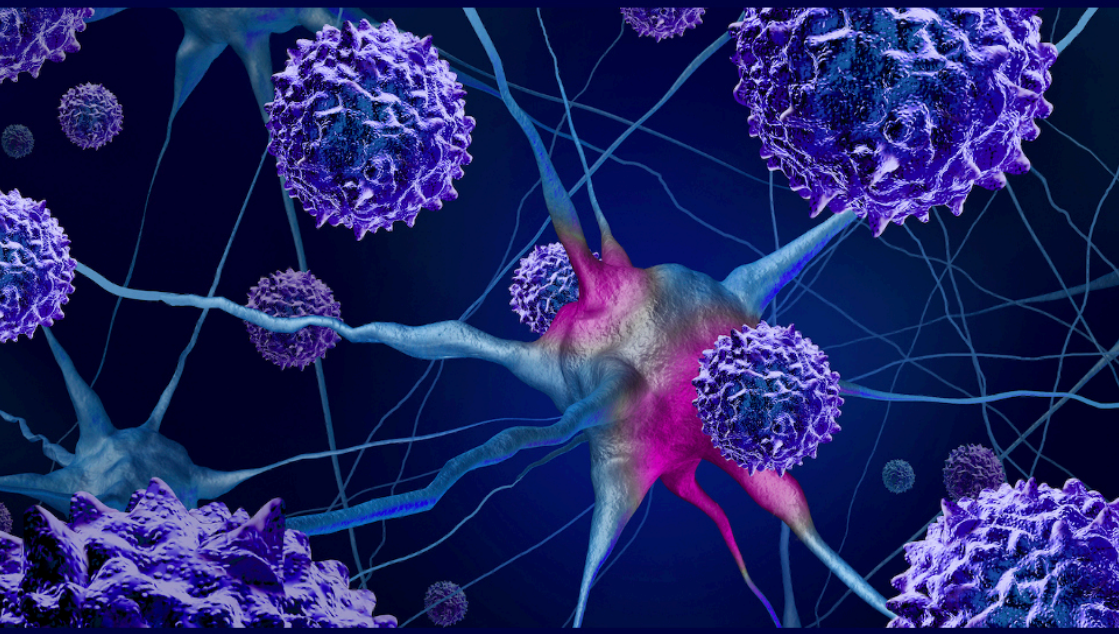
Natalia A. Molodecky, PhD

Understanding POLIO Fundamentals

A technical handbook for a non-technical audience



Understand the key technical principles driving one of the largest global health initiatives in history.

Understanding Polio Fundamentals

A technical handbook for a non-technical audience

Natalia A. Molodecky, PhD

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This book is dedicated to all the heroes of the polio eradication programme around the world, especially my dear friends in Pakistan. Your strength and dedication is a true inspiration, one that I carry with me each day.

Author's Note

When you work in a highly technical field but are in operations and not in research, it is helpful to have a handbook that translates the critical information you need to know into practical knowledge that you can easily apply to your area of expertise. Typically, literature on polio is written to the technical expert or global policy audience, which often excludes implementers at the country level. This is why I wrote **Understanding Polio Fundamentals.** This handbook will give you an in-depth understanding of the science behind the effort to eradicate polio in a way that is simple and easy-to-understand. Understanding the technical principles guiding strategy and policy will enable you to not only be more effective in your work, but also to make more informed decisions when faced with challenging or unexpected circumstances. My hope for this book is to empower you and all the true heroes of this global effort.

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Introduction

The **Global Polio Eradication Initiative** is a very complex global effort. Billions of dollars and intensive research have been invested into the programme over more than three decades. It involves a massive amount of information and research on polio. Thus, it is rich with many layers of data and information. It incorporates movement patterns with infectious disease spread, anthropology, communications, clinical trials, genetics, monitoring and evaluation. Not only is there huge breadth of information but each piece has incredible depth. Due to its diversity, no matter your skill set or the discipline you come from, you can find a home within the polio programme. It is a place where you can grow in different directions and never feel stagnant because there is so much to experience and learn. This is partly why people who begin working on polio often dedicate their lives to the programme and ultimate goal of polio eradication. The people that make up the polio programme are so close to it and know the complexities inside and out; therefore, it can be easy to forget that not everyone affiliated with the programme has that depth of knowledge or the same duration of experience in polio eradication.

Over the past decade and a half I have worked in polio eradication, across various disciplines — informing policy at the global level, in academia and at the regional and country levels. I have worked on seroprevalence surveys, clinical trials, informing policy on WPV1 and cVDPV2 and putting together risk assessments, outbreak response plans and national-level strategies. I completed a PhD in modelling of poliovirus in Pakistan and Afghanistan, and led technical teams at the

country level. I recently evaluated the global withdrawal of OPV2, guiding strategy for future withdrawal efforts. While my focus has largely been on the technical aspects of polio eradication, I have come to realise that the key to eradication is empowering the people at the country level. While in Pakistan, I came to know that the people at the country are highly intelligent, dedicated and driven to rid their country of this devastating disease. Their work ethic is incredible and their resilience inspiring. Due to the emergency nature of the polio programme and the continuous urgent priorities, they are often overwhelmed with the day-to-day challenges that building their capacity on technical issues (although highly desired) is often not feasible.

Literature on polio is typically written to the technical expert or global policy audience. This often excludes those who focus on the operational aspects of programme implementation at the country level. It would be incorrect to assume that just because someone focuses on the implementation or operations side of polio eradication that they won't strongly benefit from understanding technical fundamentals of poliovirus and the polio eradication programme. It would also be incorrect to assume that they do not have a desire. My time at the country level showed me how much desire there is for greater understanding and building of capacity. We must also recognise the extreme pressure and time constraints at the country level. They are working around the clock at maximum capacity, every day, every month of every year. Assuming that if they wanted to learn they would find the time, is unreasonable. It is important to make technical information about polio easily accessible to everyone working in the polio programme, no matter their role. When people are empowered through knowledge and capacity building they are more effective in their work and the whole programme benefits.

There are some fundamental technical principles of polio eradication that are key to understanding the programme. These are concepts I believe everyone working on polio eradication should have access to in order to empower them to feel confident tackling problems in their own area of work. For example, an operations person may know about how to implement a strategy but not what went into deciding where to target the response. It is helpful for them to understand why the intervention is taking place under the conditions that it is. Also, given that the programme integrates people across organizations and disciplines using a one-team approach, people focusing on operations often sit in on meetings where technical content is presented. Additionally, any new staff supporting the polio programme without extensive experience in polio eradication or public health could benefit from an introduction into technical aspects of the programme. Finally, government officials or donors would benefit from understanding key technical principles that are driving polio eradication efforts.

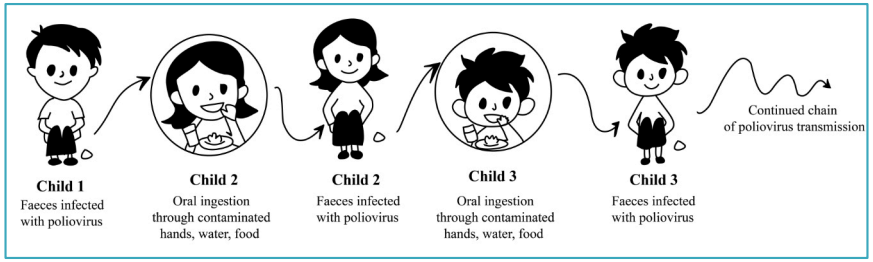
1
What is polio? How does it transmit?

I was first introduced to the polio programme back in 2011 through a friend that had done an internship at the World Health Organization (WHO) in Geneva. I was interested in working at WHO and he suggested that polio would be a great programme to get involved with. I still remember my first day at WHO in Geneva as if it were yesterday. I walked to the office from the residence I was staying at, and was filled with nerves and excitement. I could never have predicted the journey that would begin on that day — one that would take me all over the world and enable me meet the most incredible people. I can genuinely say that working on polio has been an honour and the greatest privilege of my life. At the time, like most people, I knew very little about polio. Spending over a decade working and collaborating with the research team at WHO in Geneva has given me first-hand exposure to and an incredible appreciation for the amount of research that has been invested into better understanding polio. The wealth of information from clinical trials and seroprevalence surveys is the foundation that helps guide every aspect of the polio programme. To understand the polio programme and the strategies being used, one must first understand what the disease is and how it spreads from person to person, or more commonly in the context of polio, from child to child….

What is polio? Polio is a paralytic disease caused by the poliovirus, which is a highly contagious virus that spreads from person-to-person either through the oral-oral route via saliva and mucous infected with poliovirus or the faecal-oral route (oral ingestion of something contaminated with faeces containing poliovirus). The oral-oral route is more common in developed countries and the faecal-oral route is more predominant in developing countries with poor sanitation. Faecal-oral transmission poses the greatest challenge for polio eradication.

What the faecal-oral route of transmission means is that a child infected with poliovirus will shed virus in their stool and it will somehow be ingested orally by another child (through contact with contaminated hands, water or food) (**Figure 1**). Once a child ingests faecal matter that contains poliovirus, the virus starts replicating (i.e., producing copies of itself), in the child's gut. If the child does not have immunity (developed by either being previously exposed to poliovirus or through vaccination), their gut won't be able to contain the virus and they will excrete virus in their stool for 3-6 weeks. This excreted virus is then orally ingested by another child, which if they also lack immunity (i.e., are susceptible to poliovirus), will excrete virus and continue the chain of transmission. This chain of transmission continues if there are sufficient numbers of susceptible children, and environmental conditions (such as poor sanitation) that make it easier for children to come in contact with poliovirus. That is why sanitation is so important for polio eradication — improved sanitation makes it much more difficult for poliovirus to transmit.

Figure 1. Chain of poliovirus transmission.



Poliovirus transmission is highly seasonal, with the peak occurring in summer months due to the increased stability of poliovirus in humid conditions. This is why polio outbreaks tend to occur in the autumn months, with reduced burden in winter. However, it is important to note that vaccination strategies can often dampen the observed seasonal patterns that would naturally be observed without intervention (as vaccination campaign plans have prepared for this inherent seasonal peak by ensuring sufficient vaccination in the winter and spring).

The majority of poliovirus transmission is from children less than five years of age, as is the majority of cases that are reported; however, older children and young adults may play a small role in transmission. This small role becomes more meaningful in high transmission settings (or in circumstances whereby there have been historic gaps in vaccination, resulting in a susceptible cohort of older children and adults). This is why children less than five years of age are targeted for vaccination campaigns and why in certain settings with high transmission, older age vaccination is considered.

Most children infected with poliovirus either develop mild flu-like symptoms or no symptoms at all, and only less than 1% of children develop paralysis (this occurs if poliovirus reaches the central

nervous system and damages motor neurons in the spinal cord), most commonly in the lower limbs. This paralysis is permanent, with the limbs typically atrophying because of the loss of motor neurons. Neurons that impact the respiratory muscles can also be damaged, resulting in difficulty breathing, swallowing and talking. Historically, iron lungs were used in cases of respiratory paralysis to assist in breathing. In 5-10% of polio cases, the result is fatal (typically resulting from paralysed breathing muscles).

There are three serotypes (or simply "types") of poliovirus — 1, 2 and 3 — which differ slightly in their composition. Serotype simply means a group of microorganisms with similar properties that lead to a distinct immune response. All three serotypes of poliovirus can cause paralysis but the probability of being paralysed after infection differs. For serotype 1, paralysis will develop on average once in every 200 children that are infected. For serotype 2, much greater numbers of infected children are required before cases develop, with estimates between 1000-2000 (or even higher) infections per one case. Serotype 3 has paralysis rates in between serotype 1 and 2. This is why we say the "virulence" (or ability to cause damage to the host) is greatest for serotype 1.

When we talk about poliovirus we are usually referring to wild indigenous poliovirus. This is the poliovirus that has been circulating uninterrupted for thousands of years, with the earliest records dating as far back as ancient Egyptian times. This wild poliovirus (WPV) spreads through populations that lack immunity. This has been the predominant focus of eradication efforts. A type of poliovirus that has recently become increasingly important is vaccine-derived poliovirus (VDPV). Given the complexity (and often misconceptions) about VDPV, we will spend a bit of time reviewing what it is and how it spreads.

Definitions

Polio: polio (or poliomyelitis) is a disease caused by poliovirus, a highly-infectious virus. Although poliovirus is highly infectious, less than 1% of infected children develop paralysis. Paralysis occurs if the virus reaches the central nervous system and damages motor neurons responsible for muscle movement. This damage is permanent and lifelong. In rarer cases, the damage also impacts neurons responsible for breathing, which can lead to death (5-10% of paralysed children).

Poliovirus transmission: the spread of poliovirus from person-to-person (most commonly from child-to-child). It is mostly through the faecal-oral route which is when the stool infected with poliovirus from one person, enters the mouth of another (through contact with contaminated hands, water or food). In developed countries with good hygiene and sanitation, the oral-oral route is more likely, occurring through coughing or sneezing.

Wild poliovirus (WPV): poliovirus that is indigenous and has been circulating persistently (and uninterrupted) for thousands of years. The earliest records date as far back as ancient Egyptian times.

Serotype: a group of microorganisms (viruses or bacteria) with similar properties that lead to a distinct immune response based on the characteristics (antigens or other molecules) on the protein shell that encloses its genetic material. There are three distinct poliovirus serotypes — 1, 2 and 3. Each stimulates a distinct immune response (based on the antigens on its protein shell), and differs in its ability to cause damage to its host (in the form of paralysis).

2

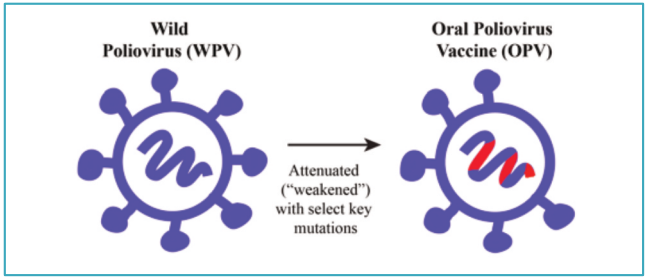
What is vaccine-derived poliovirus (VDPV)?

"So, wait just a minute, does that mean the vaccine you are giving is causing a type of polio in children?" "No… Well, not directly." I've worked in the polio programme for a long time, and the greatest misconceptions and lack of understanding are around vaccine-derived poliovirus (VDPV). I think, perhaps, if we could go back to the naming of the strain we should request a name change. While, yes, the strain does originally stem from the vaccine, it is much more complicated than that. It is not as if you give a child the vaccine and they develop poliovirus. I remember sitting in the Pakistan office with the communications team after the circulating VDPV2 (cVDPV2) emerged in the northern areas in 2019. We were discussing all of the technical details of cVDPV2. The news of something called "vaccine-derived poliovirus" was a nightmare situation in a country like Pakistan, with endemic WPV1 transmission and substantial challenges with vaccine refusals. It is also a place where news spreads like wildfire, especially bad news, as we saw repeatedly in the polio programme. Misconceptions about this strain could have disastrous consequences not only for stopping the cVDPV2 outbreak but also for continued efforts to eradicate WPV1. Having a clear explanation and communication strategy was critical.

In contrast to WPV, VDPV is a more recent phenomenon. While (as the name suggests) VDPV originally stems from the vaccine (specifically the oral poliovirus vaccine [OPV]), another factor must also be present — a large pool of susceptible children (i.e., low population immunity; **Chapter 5** will provide more detail on immunity). Let's explore the process of how OPV goes from being a helpful tool used to stop poliovirus transmission (and the main vaccine used in most countries that have eradicated polio) into creating outbreaks of VDPV.

One of the greatest strengths of OPV is also its greatest challenge and drawback — its similarity to WPV (but with select "attenuating" or weakening mutations that prevent it from causing paralysis) **(Figure 2).** It is this similarity with WPV that ensures OPV can stimulate an effective immune response. As with WPV, when you give OPV to a susceptible child, the child can excrete vaccine virus in their stool and it can be passed onto another child (following a similar process as we saw with poliovirus transmission in **Chapter 1**). This on its own can be positive as this process allows for some immunity to spread within a population, albeit to a limited degree. The problem comes in when a large part of that population is susceptible (more specifically, lacks mucosal immunity, as will be described in **Chapter 5**).

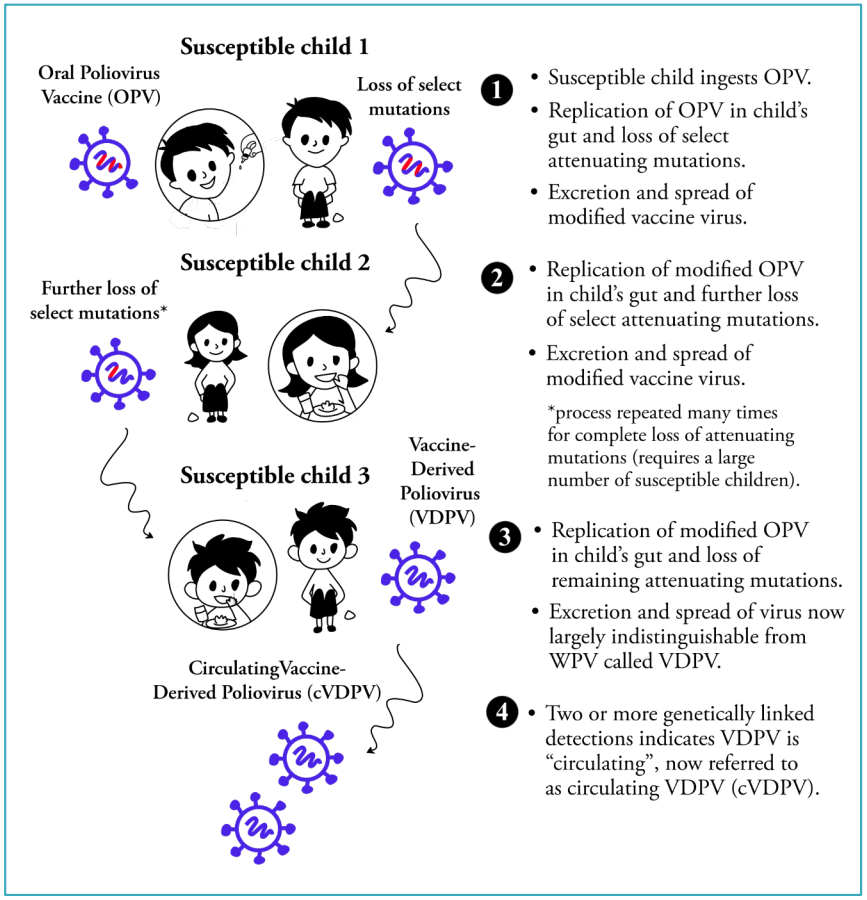
Figure 2. Oral Poliovirus Vaccine (OPV).



OPV (like all viruses) replicate in a host and typically mutate before they move from one host to another. Mutations occur because they don't have very good proofreading skills and sometimes when they replicate they create copies of themselves that aren't perfect matches. If those accidental mutations make it easier for the virus to thrive (e.g., easier to replicate or invade cells, etc.), it will outcompete the other strains and become dominant. Over time, if there are enough susceptible children, the vaccine virus can develop enough key mutations that it ends up reverting back to being just like WPV. It can then spread through populations of susceptible children and cause paralysis indistinguishable to that caused by WPV, but it is now called VDPV. Because viruses can't replicate on their own — they need a human host to do so — this takes time and susceptible children **(Figure 3).** Note that if enough children have mucosal immunity (which prevents poliovirus from replicating in their gut, as will be discussed in detail in **Chapter 5**) they won't be excreting the virus in their stool (or only in a limited amount) so this chain of events will halt. Therefore, the potential for VDPV outbreaks is greatest when OPV is introduced into an environment where there are many susceptible children without mucosal immunity. The virus is considered VDPV once there is at least 1% difference (0.6% for

serotype 2) in the key genetic region (referred to as the viral protein 1 [VP1] region) from the original OPV. Once there are at least two genetically linked VDPV cases or evidence of VDPV circulation in the environment we call this *"circulating"* VDPV (or cVDPV).

Figure 3. Process of OPV evolving into cVDPV.



Like WPV, there are three strains of cVDPV (i.e., cVDPV1, cVDPV2, and cVDPV3), corresponding to the three OPVs. Of the three strains of cVDPV, serotype 2 (i.e., cVDPV2) is the most commonly observed. There are many factors that have made cVDPV2 more common than the other two serotypes, which we will discuss in the subsequent chapters.

Now, let's explore the historic epidemiology of WPV and why polio became the focus of the largest public health intervention in history, with the formation of the Global Polio Eradication Initiative (GPEI).

Definitions

Circulating vaccine-derived poliovirus (cVDPV): vaccine-derived poliovirus (VDPV) is a strain of poliovirus that initially stems from the oral polio vaccine (OPV), but requires a large group of unimmunized (or under-immunized) children. If OPV is able to circulate through populations that lack immunity to poliovirus for long enough, the vaccine can revert back to a form that causes paralysis, largely indistinguishable from WPV. Once the VDPV has not only reverted but started to circulate in a population in its virulent form, it is referred to as circulating VDPV (cVDPV). There are three serotypes of cVDPV, because there are three OPVs, one for each serotype of WPV.

3
Why polio eradication? Historic wild poliovirus (WPV) epidemiology

There I was, in 2020, nearly a decade from the first time I stepped foot into the WHO office in Geneva. I walked into the weekly polio meeting, where every week a full update on the global polio situation is presented. Projected at the front of the large room were maps providing a snapshot of the global situation of poliovirus. What struck me was how much had changed over the years. Some battles had been won, and new battles had emerged. The maps no longer showed any serotype 3 wild poliovirus (WPV) cases. It was striking to see the global map free of serotype 1 WPV, well mostly free. Pakistan and Afghanistan remained, as it did back in 2011, but now under a spotlight. The progress in the world was clear, but there was still much to do. It is always helpful to look back in time before looking forward. Therefore, in order to understand how to get to where we want to go, let's review where we have been and where we currently are…..

The question most people ask me when I say I work on polio eradication is "wasn't polio eradicated already?" It has been a long journey towards eradication — and we are not there yet. In the early-to-mid 1900s, polio was one of the most feared diseases. It would spread through populations rapidly paralysing children, in what appeared to be at random. Parents were terrified that their children would fall ill and become paralysed for life. Because polio is highly asymptomatic, it was difficult to determine which children would develop paralysis and which would be spared. Polio epidemics began to appear in the US and Europe, followed by more explosive and far-reaching pandemics across Europe, North America, Australia and New Zealand. In 1952, the US reported a record of over 57,000 cases of polio. After the vaccines were developed in the 1950s there was a dramatic decline of polio in the Americas and Europe and by 1979 the US reported its final polio case.

Following the rapid success of wiping out polio from the Americas and Europe, the world was confident this could be done across the entire globe. That would mean that only for the second time in history, the world would be free of an infectious disease and no longer need to vaccinate children globally. The only time an infectious disease had been eradicated was smallpox in 1980. By 1988, the world was confident from the success of smallpox eradication and all the success of the polio vaccine so far, that the world committed to eradicating polio globally, and the Global Polio Eradication Initiative (GPEI) was formed. A resolution was passed at the World Health Assembly (WHA) in 1988 with all member states committing to eradicating polio globally by the year 2000. There were four main partners in GPEI: World Health Organization (WHO), United Nations Children's Fund (UNICEF), Rotary International and US Centers for Disease Control and Prevention (CDC). Recently two

additional partners were added to the GPEI: Bill & Melinda Gates Foundation (BMGF) and Global Alliance for Vaccines and Immunization (GAVI). At that time, polio was endemic (i.e., transmission had never been interrupted) in 125 countries, with an estimated >350,000 cases occurring annually **(Figure 4)**.

The GPEI made rapid progress and by 2001, only 10 countries remained endemic and less than 1,000 cases were reported, a decrease of more than 99%. Moreover, serotype 2 wild poliovirus (WPV2) was last isolated in 1999 from northern India, leaving only two serotypes in circulation (serotypes 1, WPV1 and 3, WPV3). Progress steadily continued and by 2002, three WHO Regions (the Americas, Western Pacific and European Regions) had been certified polio-free. By 2010, only 4 countries remained endemic to WPV1 — Pakistan, Afghanistan, India and Nigeria; however, outbreaks in other countries continued to be reported (typically ~15-20 additional countries annually), mainly across Africa. India was able to eliminate WPV1 from most of the country with the remaining hotspots of Uttar Pradesh (UP) and Bihar proving to be the greatest challenges. In early 2011, the last case of WPV1 was reported in India, proving that eradication could be achieved in the most difficult environments. India (along with the entire South-East Asia Region) was certified polio free in 2014. Nigeria, after a long battle with WPV1 with more than 1,000 cases reported annually at its peak in 2006, reported its last case of WPV1 in 2016 from Borno State. Three years after the last case in Nigeria, the country was taken off the WPV1 endemic list, leaving only Pakistan and Afghanistan. The last case of WPV3 globally was reported in Northern Nigeria in 2012. Global WPV2 eradication was officially declared in 2015 and in 2019, global WPV3 eradication was declared.

The last bit is proving to be increasingly challenging with WPV1 cases continuing to be reported in Pakistan and Afghanistan. Since late-2023, there has been an upswing of WPV1 transmission, resulting in 99 cases reported in 2024. This is a substantial increase from the 12 cases (6 in each Pakistan and Afghanistan) reported in 2023, 21 cases (20 in Pakistan and 1 in Afghanistan) in 2022 and 4 cases (1 in Pakistan and 3 in Afghanistan) in 2021. While there had been substantial progress over the past few years (176 and 140 cases reported in 2019 and 2020, respectively), poliovirus continues to persist (especially in core hotspots, often referred to as reservoirs of poliovirus; and once it travels out, it exploit pockets of under-immunized children). Challenges in Pakistan and Afghanistan include vaccine hesitancy, community fatigue, issues with access in certain key areas, political instability and substantial population movement. With the introduction of Emergency Operation Centres (EOCs) at the national and provincial levels in 2014 in the endemic countries of Pakistan and Afghanistan (and Nigeria, which has since eradicated WPV), better coordination among all partner agencies and between provinces and national level was possible.

In addition to continued transmission in Pakistan and Afghanistan, increasingly alarming is the exportation of WPV1 to other countries (Malawi [1 case] and Mozambique [8 cases] in 2021 and 2022, respectively). Given that we live in a highly connected world, there continues to be a risk of poliovirus being exported to other countries, reminding us that until all poliovirus is interrupted everywhere, the world continues to be at risk.

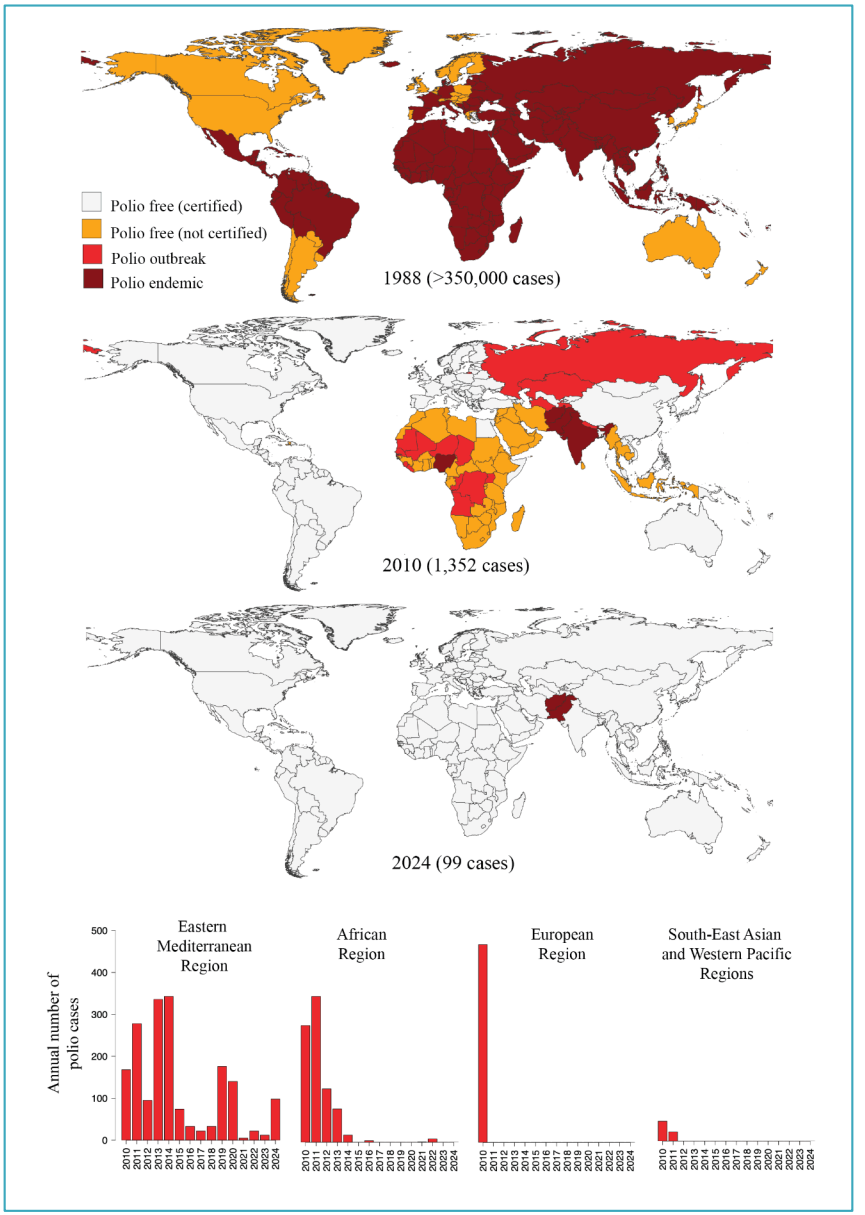
For polio eradication the key is eradicating everywhere — success is dependent on eradicating from every corner of the earth. Until that day comes, the entire world will need to make sure they are remaining vigilant with their vaccination and ensuring the high

immunity of their populations. This high level of immunity will need to be maintained across every country of the world until Pakistan and Afghanistan become WPV1 free. Billions of dollars each year are spent ensuring the world's children are protected from polio. Once WPV1 is gone, these funds can be diverted to other priorities.

Polio eradication is an all-or-nothing initiative. Unlike other programs that focus on eliminating diseases from their own countries, what happens in Pakistan and Afghanistan is directly linked to the wellbeing of children in other countries. Polio eradication is both a global priority and a national level priority. This is an important message because it can be difficult for communities in endemic countries to understand why polio is so important, especially given that the morbidity and mortality attributed to other diseases is currently far greater than polio. It is important to note that the burden of WPV1 would substantially increase if less focus was placed on polio in these countries and would lead to high case burden. In the current context of relatively low case numbers, communicating the potential risk of decreasing polio efforts as well as the importance to the global context is critical messaging to the communities.

Where are we now? There are two countries endemic (constantly present) with WPV1 — Pakistan and Afghanistan. Serotypes 2 and 3 WPV have been eradicated. In 2024, 99 cases were reported and more than 741 samples from the environment have detected presence of WPV1 (as of 14 March 2025). In order to consider a country to be polio free, a period of three years without any poliovirus isolations is required. Therefore, while there is much to celebrate how far the world has come, there is also still work to be done.

Figure 4. Polio endemic and outbreak countries over time and annual number of cases by region.



Definitions

Global Polio Eradication Initiative (GPEI): the GPEI is a public-private partnership made up of six global health agencies, including WHO, UNICEF, US CDC, Rotary International, BMGF and GAVI, with the goal to eradicate polio globally. It was formed in 1988 after representatives from WHO member states passed a resolution at the World Health Assembly to eradicate polio. The initial goal was set for the year 2000, with timelines continuously needing to be extended.

Endemic: a disease that is constantly present or indigenous in a population within a geographic area. For poliovirus, a three year period free of WPV1 cases or detections in the environment is required to consider a geography as polio free (or no longer endemic). Certification of polio-free status occurs at the WHO regional level, and requires all countries within the region to fulfill this criteria before certification can be granted.

4
What about vaccine-derived poliovirus (VDPV) epidemiology?

"Is now the time?" This was the question on everyone's mind. It was 2015 and the number of circulating VDPV (cVDPV) outbreaks had far surpassed WPV, with the serotype 2 strain (cVDPV2, which originally stems from OPV2 use) posing particular concern. How do we justify continuing to use OPV2 if there is no WPV2, and large outbreaks are being seeded from its use (along with the rare but increasingly unacceptable burden of vaccine-associated paralytic poliomyelitis, VAPP)? Yes, it needs to be withdrawn in order for us to reach our goal of polio eradication, but the process of removing it is extremely difficult. It is currently our only tool of stopping cVDPV2. So the only tool for stopping cVDPV2, is what is creating new outbreaks. I was sitting with the team at Imperial College London working on estimating serotype 2 immunity globally. These would be used to guide decision-making on the number of campaigns to be implemented before the global OPV2 withdrawal to ensure sufficient levels of immunity. It would be disastrous if a cVDPV2 outbreak occurred when immunity already started to decline. The first few years following OPV2 withdrawal would be the most important, with new children being born never exposed to OPV2, and waning of

immunity to serotype 2 in those that had previous exposure. It was like a forest during a drought. All it would take is one match to set off a catastrophic event. But it had to be done now, and done quickly. The world was free of any persistent cVDPV2. Nobody knew when an opportunity like this would present itself again. And that is how it happened, in a two week window in all 155 OPV2 using countries. There could not be any OPV2 left in any facility, in any clinic, anywhere in the world. You can imagine how incredible that was to achieve. Let's go through how we got there, and what has happened since this monumental moment in history…..

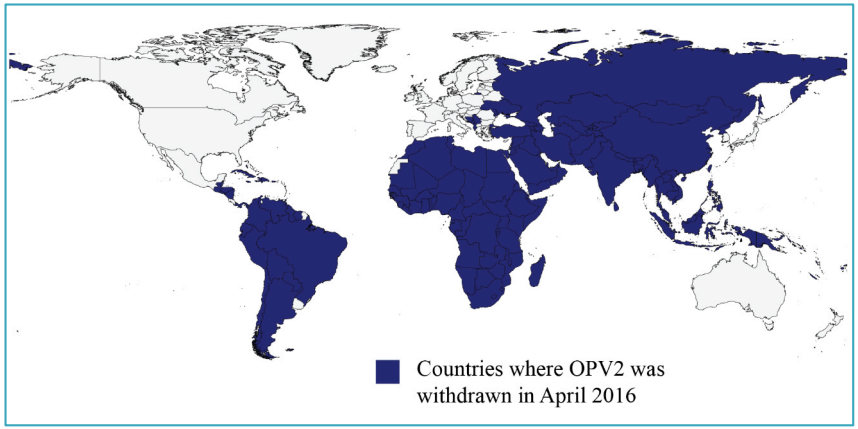
Adding to the already complex challenges to eradicating polio globally are the increasing outbreaks of circulating vaccine-derived poliovirus (cVDPV), especially those of serotype 2 (i.e., cVDPV2, stemming from OPV2). Similar risks are observed for serotypes 1 and 3 (i.e., cVDPV1 and cVDPV3, stemming from OPV1 and OPV3, respectively), however, with a lower probability, especially serotype 3.

The first reported cVDPV outbreak occurred in 2000 (on Hispaniola). Between January 2010 to May 2016, there were 319 cases reported from 15 countries, with the greatest outbreaks seen in Pakistan and Nigeria. Outbreaks started to occur due to decline in serotype 2 immunity when Supplementary Immunization Activities (SIAs — vaccination campaigns undertaken in places where routine vaccination practices do not adequately reach all children) transitioned from using predominantly the trivalent OPV (tOPV) vaccine to the new formulations of monovalent OPV1 and OPV3 (mOPV1, and mOPV3) and bivalent OPV (bOPV, containing serotype 1 and 3). This was done to accelerate eradication of WPV1 and WPV3, following WPV2 elimination. The outbreaks typically occurred in areas with suboptimal routine immunisation (RI).

cVDPV typically emerges and spreads when OPV is used in a population of low immunity and sub-optimal coverage. Due to the potential for cVDPV outbreaks, in order to achieve global eradication of polio, eventual withdrawal of OPV is required. While there were still many WPV cases being reported annually, justification of using OPV remained strong (and benefits outweighed its risks); however, with the success of the polio programme leading to declining WPV cases and relatively larger number of cVDPV cases (along with the increasingly unacceptable burden of VAPP [a rare direct adverse event of OPV], at approximately 200 to 400 cases globally per year), the withdrawal of OPV use became an important consideration.

Since the last detection of WPV2 was in 1999 and there were cVDPV2 outbreaks being reported each year (due to continued use of OPV2), OPV2 became the first vaccine serotype to be withdrawn globally. This globally synchronised withdrawal of OPV2 took place in 2016 (over a two week period across all 155 OPV-using countries) in both RI and campaigns **(Figure 5)**. It was the best window to withdraw the vaccine as the world was currently clear of any persistent cVDPV2. The global withdrawal needed to be synchronised to ensure there was no OPV2 left anywhere (i.e. vials not properly disposed of, any remaining OPV2 that was not detected by surveillance before OPV2 withdrawal, etc.) as it posed a major threat to creating cVDPV2 outbreaks at a time when OPV2 was no longer being used. The first few years following OPV2 withdrawal were critical, as susceptible birth cohorts (children born shortly before or sometime after the 2016 global withdrawal who did not receive doses of OPV2) accumulated and mucosal immunity to serotype 2 had waned (more details on waning of mucosal immunity in **Chapter 5**).

Figure 5. Countries where OPV2 was withdrawn from routine immunization (RI) in April 2016.



The withdrawal of OPV2 took place in April 2016 and was a globally synchronised initiative that took place in a two-week window globally. All OPV2 needed to be destroyed because any that was left in the environment could pose big problems with creating VDPV2. The requirement for this withdrawal was that for 6-months leading up to the decisions for withdrawal, there could be no cVDPV2 globally and serotype 2 immunity would need to be high everywhere. This is why there were so many trivalent OPV (tOPV, including OPV2) SIAs implemented in late 2015 and early 2016 despite bivalent OPV (bOPV, excluding OPV2) being the primary vaccine used in SIAs at that point. cVDPV2s emerge from OPV2 and spread in environments with low serotype 2 immunity and the only way to stop a cVDPV2 outbreak is by using OPV2.

In the first year following OPV2 withdrawal, there were 13 cVDPV2 cases from 4 countries (Nigeria, Pakistan, Democratic Republic of Congo (DRC) and Syria), most of which were seeded from OPV2 use prior to withdrawal. OPV2 was required to respond to these outbreaks. With the accumulation of susceptible birth cohorts who had never received OPV2, the outbreaks emerged more quickly and spread faster. In 2020, 2021 and 2022 there were 1082, 682 and 571 cases of cVDPV2 from 24, 22 and 19 countries, respectively. While the annual number of cVDPV2 cases has since declined, with 396 cases reported in 2023, and 288 cases reported in 2024, cVDPV2 continues to circulate in 33 countries (18 of which are reporting cases) (based on detections over the past 12-months). Since OPV2 withdrawal in 2016, there have been more than 3600 cVDPV2 cases from 45 countries (as of 14 March 2025). The majority of the outbreaks have been seeded from monovalent OPV2 (mOPV2) use as part of outbreak response. More recent outbreaks have been seeded by the more genetically stable novel OPV2 (nOPV2), which will be discussed in **Chapter 6**.

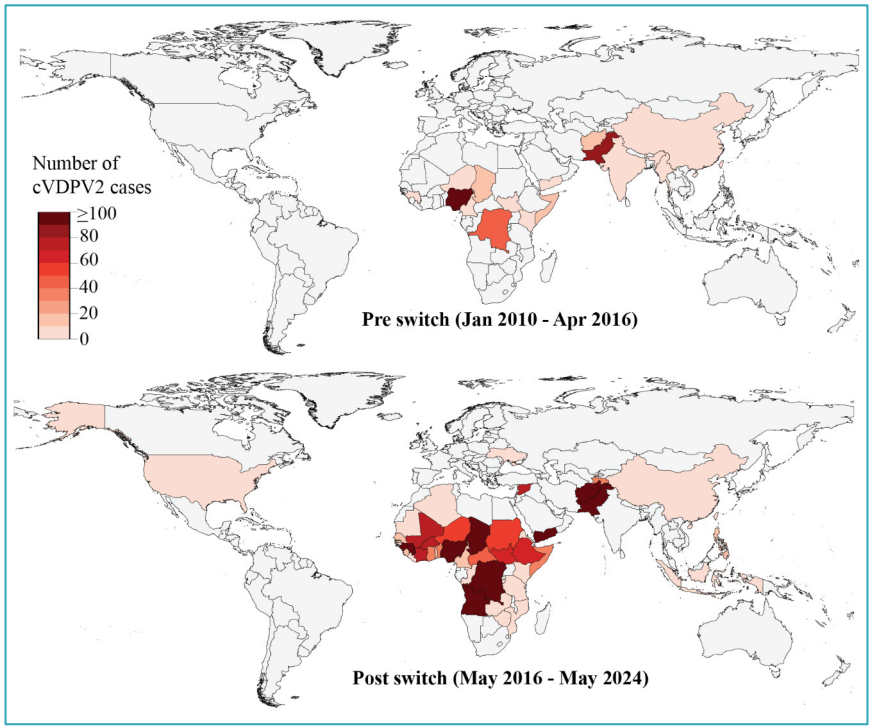
In addition to cVDPV2, the risk of cVDPV1 is increasingly becoming important with 17 cVDPV1 cases in 2021, 192 cVDPV1 cases in 2022 and 134 cVDPV1 cases in 2023. The increase in cVDPV1 cases come mostly from DRC, which reported 149 and 106 cases in 2022 and 2023, respectively. Other countries typically reporting cVDPV1 cases include Madagascar and Mozambique (as well as Yemen, Malawi and Congo). Low numbers of cVDPV3 cases are typically reported (1 cases in 2022 and 0 cases in 2020-2021). With the decline in OPV campaigns in many countries (with low RI coverage), resulting in low serotype 1 immunity, cVDPV1 poses a risk if OPV1 (e.g., tOPV in response to a cVDPV2 outbreak) is used in non-WPV1 endemic settings with an infrequent SIA schedule. The increased number of cVDPV1 cases is an important consideration to monitor, and further demonstrates why strategic technical guidance is required for planning outbreak response. This is especially important as decision-making continues about the timelines and strategy for withdrawing OPV serotypes 1 and 3.

Where are we now? In 2024, 288 cVDPV2 cases were reported from 18 countries. In addition, 11 cVDPV1 cases were reported from two countries (DRC and Mozambique). Only 4 cVDPV3 cases were reported globally in 2024, all from Guinea.

It is clear that the global withdrawal of OPV2, which was intended to reduce cVDPV2 case burden and move the programme's efforts closer to eradication, did not go as planned, with approximately a 10-fold increase in case burden compared to pre-switch era **(Figure 6)**. There are key events that led to widespread cVDPV2 outbreaks. A formal evaluation of OPV2 withdrawal took place to generate critical lessons learned to inform the programme's strategy moving forward. It highlighted a key issue to be insufficient outbreak response, due to poor quality (i.e., low vaccination coverage in the targeted

population), inadequate scope (i.e., targeted geographic area not large enough) and lengthy delays (i.e., from notification of outbreak to first vaccination round or between vaccination rounds) of vaccination with OPV2. Outbreak response capacity must be improved before any future OPV withdrawal efforts take place.

Figure 6. Global cVDPV2 cases pre- and post-switch from tOPV to bOPV.



Definitions

Vaccine-associated paralytic poliomyelitis (VAPP): a rare adverse event of OPV, with approximately 200 to 400 cases globally per year. Children with immune deficiencies are at much greater risk of developing VAPP after receiving OPV, due to the vaccine virus being able to replicate in the child for extended periods of time.

Global OPV2 withdrawal: the globally-coordinated withdrawal of OPV2 and replacement of tOPV with bOPV (often referred to as "the switch") in RI and campaigns, that took place in April 2016 across a two-week period across all 155 OPV-using countries. Prior to OPV2 withdrawal, the world was expected to be free of any persistent cVDPV2 for at least 6-months leading up to the decision and all OPV using countries were to introduce at least 1 IPV dose into RI. The goal of OPV2 withdrawal was to eliminate cVDPV2 case burden (in addition to preventing VAPP); however, since the switch, there have been more than 3600 cVDPV2 cases across 45 countries, representing an approximate 10-fold increase in case burden compared to the pre-switch era.

Insufficient outbreak response: includes poor quality (i.e., low vaccination coverage in the targeted population), insufficient scope (i.e., targeted geographic area not large enough) and lengthy delays (i.e., from notification of outbreak to first vaccination round or between vaccination rounds).

5

How to protect against polio? Immunity basics

It was August 2019, and I was standing in front of a room full of government officials in Pakistan explaining the difference between humoral and mucosal immunity. In this room were leading administrators of key remaining strongholds of poliovirus. "You can think of mucosal immunity as preventing spread of poliovirus from one child to another and humoral immunity as protecting an individual child from being paralysed, if infected with poliovirus." You would think this level of detail in information would be unnecessary for this audience; however, it is critically linked to all polio strategy. The interplay between the different types of immunity induced by the different vaccines (if administered alone, together, and in which order, and which age group) all play a central role in devising strategy. Understanding these key distinctions ensure that the most effective strategy is supported and implemented.

Why is understanding basics of immunology so important when working in polio eradication? Everything really comes down to immunity of the individual and immunity of individuals within a population. That's the ultimate goal — to make sure all children or enough children are immune for long enough that the virus can no longer sustain itself and then is gone, forever. "Enough" here just means a threshold level often referred to as herd immunity, which is what happens when a large enough proportion of the population is immune and therefore the chances of a susceptible person coming into contact with an infected person is low (the herd immunity threshold is different for different infectious diseases and geographies).

In the polio context, there are two main types of immunity that are important to consider, mucosal and humoral immunity— mucosal immunity is key for stopping poliovirus transmission and humoral immunity protects individual children from being paralysed. Understanding the two types of immunity is critically important for devising appropriate strategies as the they play different roles in the eradication strategy.

Mucosal immunity

We will first focus on mucosal immunity, which in the polio context is immunity in the child's gut (or mucous membranes of the gastrointestinal system) and prevents the child from excreting poliovirus in its stool. Mucosal immunity is key to polio eradication because it stops children from excreting virus and therefore stops transmission of poliovirus. If a child has mucosal immunity, this will limit the replication of poliovirus in the child's intestines and they will

not excrete poliovirus in their stool, which stops the chain of transmission from child-to-child.

With mucosal immunity, there are degrees of protection. Over time, even when a child has full mucosal immunity, this immunity can wane and the child can again be susceptible to poliovirus and excrete virus. It is assumed that waning of mucosal immunity occurs within one year to a level where they are only 50% as protected as they were at the time of complete mucosal immunity. Ensuring that mucosal immunity remains high is the reason that vaccination campaigns with OPV (i.e., the source of mucosal immunity, described in more detail in **Chapter 6**) remain frequent, and continued repeat vaccination is required. Because mucosal immunity keeps waning, ensuring it is consistently high as long as poliovirus is circulating is necessary.

Humoral immunity

We've discussed mucosal immunity and its role in halting the transmission of poliovirus, and now we turn to the role of humoral immunity — which is protection from paralysis.

If a child has humoral immunity, they have poliovirus neutralising antibodies so that they won't be paralysed if infected with poliovirus. The antibodies in the blood prevent poliovirus from reaching the central nervous system. This does not mean they won't be infected with poliovirus. If they don't have mucosal immunity only humoral immunity, they are *just* as likely as someone who doesn't have humoral immunity to be infected with poliovirus and shed virus in their stool. Protection against paralysis (humoral immunity) for all three poliovirus serotypes persists across most OPV vaccinated

children for many years (at least five years), and is largely considered lifelong.

Preventing paralysis is important and is a main concern for the polio programme; however, it has no impact on poliovirus eradication — which is stopping poliovirus transmission everywhere. Humoral immunity does not wane like mucosal immunity and typically once a child is protected from paralysis, they are protected for life. While there are degrees of protection for humoral immunity, there is a cut-off value which defines either protected or not protected from paralysis (details on this will be provided in **Chapter 8** on Serology) — essentially providing an all or nothing response.

Comparisons between humoral and mucosal immunity, and duration of protection are presented in **Figures 7 and 8**.

It is important to note that immunity needs to be not only reached but maintained above the immunity threshold required to interrupt transmission until all transmission is interrupted everywhere. This is especially important in highly-connected geographies with substantial population movement (e.g., Pakistan). Thresholds differ in different geographies and are based on contact rates, influenced by population density, movement patterns and sanitation (i.e., anything that make it more likely for a child to come into contact with poliovirus, will result in higher required immunity thresholds). Highly populated areas (e.g., Karachi, Pakistan) have extremely high immunity thresholds, while lower levels of immunity are required in areas where contact rates are much lower (e.g., Balochistan and interior Sindh, Pakistan).

Figure 7. Comparison between humoral and mucosal immunity.

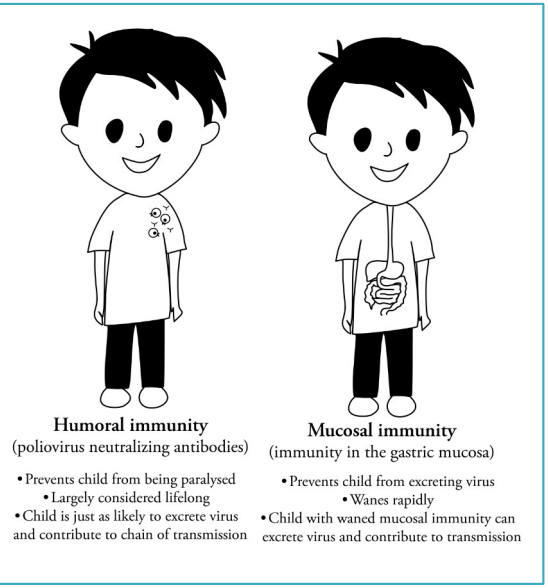
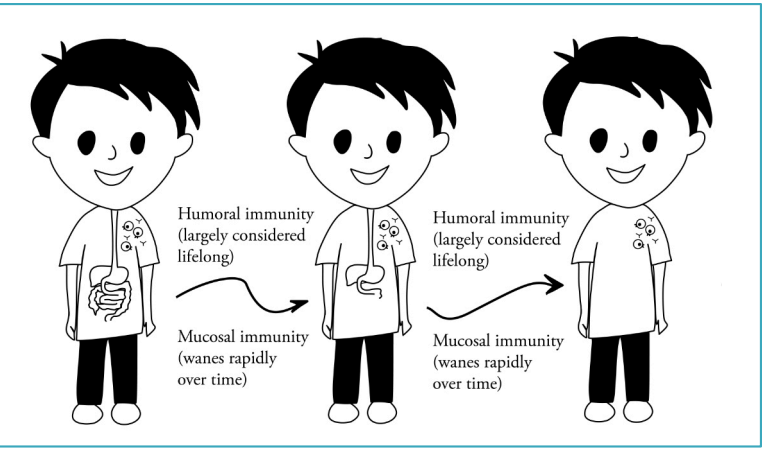


Figure 8. Duration of humoral and mucosal immunity.



Definitions

Immunity threshold: immunity levels that are required to be achieved and maintained to interrupt transmission. Thresholds differ in different geographies and are based on rates of contact, influenced by population density, movement patterns and sanitation.

Mucosal immunity (in the polio context): immunity of the gut (or more specifically the mucous membranes of the gastrointestinal system). This immunity limits the replication of poliovirus in the intestines and limits the amount of virus that is shed in stool, thereby stopping the chain of transmission from child-to-child.

Humoral immunity (in the polio context): immunity that protects a child from being paralysed, if infected with poliovirus. A child with humoral immunity has poliovirus neutralising antibodies in their blood that prevents poliovirus from reaching the central nervous system. This does not mean they won't be infected with poliovirus or shed poliovirus in their stool.

6

How to induce polio immunity? Oral poliovirus vaccine (OPV)

"How many OPV doses are enough?" That is the most common question I've been asked in all of my years in the polio programme. In settings like Pakistan, children receive more than seven OPV doses and still develop polio or contribute to the chain of transmission. How is that possible? This was a question that has often been asked, especially by government officials overseeing key polio hotspots. The answer is just as complex as the question. There are many reasons why consistent and continuous vaccination with OPV is required. The efficacy of OPV has been demonstrated to be highly variable, and while a three dose OPV schedule is typically sufficient in developed countries, efficacy is substantially reduced in tropical developing countries. In these settings the high prevalence of enteric infections and diarrheal illness interfere with the immune response, resulting in serotype 1 per-dose OPV efficacy estimates as low as 12% for trivalent OPV (tOPV) and 25% for bivalent OPV (bOPV). Under these estimates, it would take up to eight bOPV doses to achieve a 90% probability that a child is protected against poliovirus. This relatively low serotype 1 efficacy of OPV (in developing countries), coupled with the rapid waning of mucosal immunity (as we saw in **Chapter 5**) and high birth cohorts in areas with sub-optimal RI coverage, sets up challenging conditions to not

only achieve but maintain serotype 1 immunity beyond thresholds required to interrupt transmission (which are very high in many of the highest risk geographies). These levels of immunity must be consistently maintained until poliovirus transmission is interrupted everywhere. Otherwise, if poliovirus is not interrupted everywhere, it can find its way into pockets of lower immunity and re-establish itself, especially in highly-connected geographies (as we have recently seen in Pakistan).

How do we ensure that children have immunity (i.e., are protected) against poliovirus? — Vaccines. Exposure to vaccines ensures that the body is able to remember the virus so that when encountered again, it will be prepared to mount an effective response against it. Not only does polio have an effective vaccine, it has multiple effective vaccines — all of which have distinct properties and benefits. Understanding which one to use when (and in which order, and sometimes which age group) is a commonly asked question and critically important for devising strategy.

We will go through the different vaccines, how they impact the immune system, how to use them together and in which order, and why children need to be vaccinated so many times. Let us start with the oral poliovirus vaccine (OPV) as it plays the greatest role in the eradication efforts.

Oral poliovirus vaccine (OPV)

OPV is given orally (via drops) and is a live-attenuated vaccine, mimicking the immune response following WPV, thereby protecting both from paralysis and stopping transmission. What live-attenuated means is that it contains live poliovirus strains that have been weakened ('attenuated'). This attenuation prevents the vaccine from causing paralysis, while its similarity to poliovirus enables it to induce an immune response that mimics poliovirus infection — stimulating both humoral and mucosal immunity (as described in **Chapter 5**). Protection against paralysis (humoral immunity) for all three poliovirus serotypes persists across most OPV vaccinated children for many years (at least five years), and is largely considered lifelong. While the mucosal immune response stimulated by OPV is strong, it is not

lifelong and wanes over time, with evidence suggesting significant waning within one year of vaccination. Children with waned mucosal immunity can excrete poliovirus and contribute to transmission. Following OPV vaccination, susceptible children (or those with waned mucosal immunity) can also excrete vaccine virus, indirectly immunizing other children. The amount of secondary exposure to OPV is highly variable by setting and serotype.

Because there are three serotypes of poliovirus (1, 2 and 3) there are three types of OPV (OPV1, OPV2 and OPV3). The three OPV types are combined in various vaccine formulations, including: trivalent OPV (tOPV, with OPV1, OPV2 and OPV3), bivalent OPV (bOPV, with OPV1 and OPV3), and monovalent OPV for each serotype (mOPV1, mOPV2 and mOPV3). Each formulation has its strengths and most appropriate circumstances under which to be used, based on how the different components behave when combined. Currently, the vaccine of choice for stopping WPV1 is bOPV (and mOPV1 to a much lesser degree), and stopping cVDPV2 outbreaks is mOPV2 (and more recently novel OPV2, nOPV2, described later in this Chapter).

Historically, the most commonly used vaccine has been tOPV, which includes all three OPV serotypes and therefore provides blanket protection against all poliovirus strains. This was critically important when all three WPV serotypes were in circulation, and the reason that tOPV was the vaccine of choice for more than two decades. However, after WPV2 was eradicated (followed more recently by WPV3), vaccination against all three serotypes became less important, and bOPV began to replace tOPV in SIAs (note that tOPV remained in RI until global OPV2 withdrawal in 2016). One could argue that wouldn't it just be better to err on the side of caution and ensure protection is high against all three serotypes and use tOPV, especially

given that logistically you would still be only administering one vaccine? It comes down to the efficacy of the different formulations. Given how challenging it can be to repeatedly reach children through campaigns, it is important to maximise the impact of each vaccination activity to ensure the highest possible immunity can be achieved.

The efficacy of OPV (i.e., the performance of the vaccine under ideal circumstances) differs between the different serotypes (i.e., 1, 2 or 3) and the combination of serotypes used in the vaccine. For tOPV, the serotype 1 efficacy of tOPV in developed (industrialised) countries is high, where the per-dose efficacy is up to 50% (with three doses resulting in seroconversion of nearly 100%). What that means is that for every tOPV dose you give a child from a developed country, they have a 50% probability of seroconverting to serotype 1 (i.e. developing a strong enough immune response to protect them from poliovirus, see **Chapter 8** for details on seroconversion). The probability of a child developing an immune response following OPV is not dependent on how many doses they received in the past, and is an all-or-nothing response. If with the first tOPV dose, 50% of children develop an immune response, this leaves 50% still susceptible. The second dose will result in 50% of those susceptible children developing immunity. At this point 75% of the children are protected, leaving only 25% still susceptible. With the third tOPV dose, 50% of the remaining 25% will become protected, resulting in nearly 90% of children protected after three tOPV doses. This is why the routine immunization (RI) schedule historically included at least three tOPV doses.

This is for developed countries with good hygiene and sanitation practices, and low prevalence of other infections. The efficacy becomes much lower in countries with poor hygiene and sanitation and high prevalence of other infections, which are common

factors in polio endemic countries. This is because it is much more difficult for children to mount an immune response when battling many different infections, diarrheal illness or are malnourished. In these settings efficacy is much lower and therefore many more doses of OPV are required. The serotype 1 efficacy of tOPV in endemic (or previously endemic) countries is as low as 12.5-19%, with considerable intra-country variability. As a result, a three tOPV RI schedule is not sufficient to ensure high levels of immunity in these populations (based on this efficacy, only ~40% of the population would be immune to serotype 1 after three tOPV doses). This low serotype 1 efficacy of tOPV in polio endemic countries created a substantial challenge to eradication efforts and resulted in the need for a very high number of tOPV doses to be administered in order to achieve and sustain sufficient levels of immunity.

The low serotype 1 efficacy of tOPV in developing countries was helped by the introduction of bOPV in SIAs. The serotype 1 efficacy of bOPV is higher than that of tOPV, and estimated between 20-30% in polio endemic or previously endemic countries. Why is this the case? In tOPV, the OPV2 component outcompetes OPV1 and OPV3 (because of the strength of response it elicits) and therefore children preferentially develop immunity to serotype 2, ultimately reducing the efficacy of response to the other two serotypes (i.e. serotypes 1 and 3). This is because you are essentially giving the child three vaccines but together, so the child must mount separate immune responses to each of the three components. The same impact does not occur when removing OPV3 from bOPV in terms of serotype 1 efficacy (i.e., efficacy of serotype 1 in mOPV1 and bOPV are fairly comparable). Therefore, despite WPV3 being eradicated, a similar transition to the use of mOPV1 from bOPV was not observed.

Putting it into practice

Let's say we want to determine how many times it would take for a population to become immune using a particular vaccine. If we are interested in serotype 1 and using bOPV, we can assume the per-dose efficacy of ~25% or 0.25 (**Table 1**). Following 1 bOPV dose, to determine the susceptible population, you would take the total population (here as 100% or 1) and subtract the proportion that is immune based on the efficacy (here as 25% or 0.25); therefore, after 1 bOPV dose, 25% of the population is now immune and 75% remains susceptible. The total immune and susceptible should always equal 100% or 1. For the second bOPV dose, you would take the proportion that are still susceptible (now 75% or 0.75 and multiply that by the efficacy, i.e., 0.25). This gives you 56% (0.56) of the population remaining susceptible after 2 bOPV doses. Subtracting this from 100% or 1, you get 44% that are immune. In this example you can replace 0.25 with the type specific efficacy you are interested in. For example, if you were considering tOPV (with efficacy of 0.125) you would replace any mention of 0.25 in the table with 0.125. Since the efficacy is lower, it will take many more tOPV doses to reach the same level of immunity in the population.

To determine the number of children immune or susceptible, you would multiply the total population by the proportion either immune or susceptible. For example, if you had vaccinated all children in a population five times with bOPV, you would assume that 76% of the population was immune (and 24% susceptible). If 500,000 children lived in the

population, you would assume 500,000 x 0.76 = 380,000 children were immune. However, you wouldn't expect every child in the population to be vaccinated five times, since SIA coverage is rarely 100%. You would then incorporate coverage into the equation. Let's say coverage was 85% (or 0.85), you would modify the equation to be 500,000 x 0.76 x 0.85 = 323,000. Therefore, the equation can be summarised as: Population size x proportion immune x coverage. Remember, when you are doing any of these calculations, you must use the 0 to 1 scale for immunity, susceptibility and coverage – so divide the percent (%) values by 100.

Table 1. Calculating immunity based on the number of OPV doses and vaccine efficacy (assuming per-dose efficacy of 25% or 0.25).

Number of OPV doses	Proportion of population susceptible	Proportion of population immune
1	1-0.25 = 0.75	1-0.75 = 0.25
2	0.75-(0.75x0.25) = 0.56	1-0.56 = 0.44
3	0.56-(0.56x0.25) = 0.42	1-0.42 = 0.58
4	0.42-(0.42x0.25) = 0.315	1-0.315 = 0.685
5	0.315-(0.315x0.25) = 0.24	1-0.24 = 0.76
6	0.24-(0.24x0.25) = 0.18	1-0.18 = 0.82
7	0.18-(0.18x0.25) = 0.135	1-0.135 = 0.865
8	0.135-(0.135x0.25) = 0.10	1-0.10 = 0.90
9	0.10-(0.10x0.25) = 0.075	1-0.075 = 0.925
10	0.075-(0.075x0.25) = 0.06	1-0.06 = 0.94

cVDPV2 vaccines: mOPV2 and nOPV2

The main tool for stopping cVDPV2 outbreaks is monovalent OPV2 (mOPV2, monovalent just means that it is only OPV2).

OPV2 is a highly effective vaccine, and induces the strongest immune response of all the OPV serotypes (which reiterates why its removal improved the efficacy of the other OPV serotypes). The per-dose efficacy of mOPV2 is typically estimated to be greater than 50%. The benefit of this is that it is highly effective at stopping cVDPV2 outbreaks, which are becoming increasingly evident. While this is an effective tool for stopping cVDPV2 outbreaks, it is also the source of cVDPV2 to emerge in susceptible populations (which is why outbreak response strategy for cVDPV2 is critically important as we will see in **Chapter 13**). Therefore, its use requires caution to prevent any further seeding of cVDPV2. It is the ultimate catch-22 — its use is effective at stopping the initial outbreak but can easily create a new one. Due to this critical issue, intense focus was placed to create an OPV2 vaccine that was more genetically stable and had a reduced probability of creating more cVDPV2. That's how novel OPV2 (nOPV2) was born.

nOPV2 was created with additional modifications, making the process of it mutating back to being virulent more difficult. It basically added in extra steps for the vaccine virus to be able to find its way back to having the potential to cause paralysis. The correct balance point needed to be found to ensure the OPV remained similar enough to still induce immunity, but a slightly increased (meaningful) difference to make it harder for the OPV to regain virulent potential. This was no small feat and took a large effort by the GPEI (since 2011). nOPV2 was expected to be more stable in populations and therefore less likely to revert back to virulence and result in cVDPV2 outbreaks. This was

the solution the polio programme was looking for. It would reduce the risks of using OPV2 to stop outbreaks of cVDPV2.

In late 2020, nOPV2 was released for use under a WHO Emergency Use Listing (EUL), meaning that countries could use the vaccine in emergency settings, but additional preparation measures would be required (including authorization of its importation/use, and monitoring before and after campaign) that could potentially delay activities. Early users of nOPV2 included Nigeria, Liberia, Benin, Congo, Tajikistan, Sierra Leone and Niger. Supply constraints posed an issue, with many countries continuing to use mOPV2 for cVDPV2 outbreak response (now largely resolved).

nOPV2 has since replaced mOPV2 (it was fully licensed in December 2023) and is demonstrating to have a lower probability of reverting back to virulence and causing cVDPV2 outbreaks than mOPV2. This is promising for polio eradication efforts; however, it has not fully eliminated the risk of cVDPV2.

The per-dose efficacy estimates of OPV in developing countries by poliovirus serotype and vaccine formulation are presented in **Table 2**.

Table 2. Per-dose efficacy of OPV in developing countries by serotype and vaccine formulation.

Vaccine	Serotype 1	Serotype 2	Serotype 3
tOPV	12.5-19.4%	48%	13-18.0%
bOPV	23.4-31%	--	23.8%
mOPV1	32.1-34.5%	--	--
mOPV2	--	54-68%	--
nOPV2	--	52%	--
mOPV3	--	--	43.2%

Definitions

Oral Poliovirus Vaccine (OPV): OPV is a live-attenuated vaccine, mimicking the immune response following WPV, thereby protecting both from paralysis and stopping transmission (i.e., inducing both humoral and mucosal immunity). The efficacy of OPV has been demonstrated to be highly variable, and while a three dose OPV schedule is typically sufficient in developed countries, efficacy is substantially reduced in tropical developing countries (due to high prevalence of other infections, diarrheal illness and malnutrition). The relatively low serotype 1 efficacy of OPV in tropical developing countries, coupled with waning of mucosal immunity and high birth cohorts in areas with sub-optimal RI coverage, sets up challenging conditions to not only achieve but maintain serotype 1 immunity beyond thresholds required to interrupt transmission (which are very high in many of the highest risk areas).

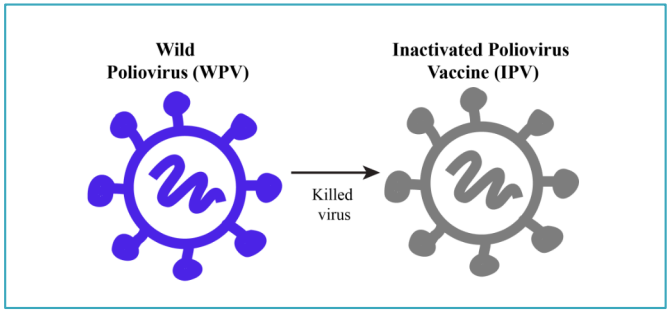
7
What about inactivated poliovirus vaccine (IPV)? Vaccine choice

It was nearing the end of the high transmission season in 2018. We were at the National Emergency Operations Centre (NEOC) in Pakistan discussing the challenges in Karachi, arguably the most complex poliovirus reservoir. It has all of the factors that support poliovirus to thrive (high population density, movement patterns, birth rates, malnutrition, prevalence of other infections, and poor sanitation), thereby requiring very high levels of immunity to stop transmission. Despite repeated campaigns in the reservoir area, population immunity has largely remained inadequate to stop and prevent transmission. What to do? OPV was largely the tool used in campaigns, but there was another effective tool that was mostly reserved for routine immunization and that is inactivated poliovirus vaccine (IPV). This was the environment that was perfectly aligned with the strengths of IPV. IPV can help quickly close (humoral) immunity gaps in high risk populations due to its greater efficacy as compared to OPV and can be particularly useful when the immunity required to stop transmission is very high. We were also at a time more than two years following OPV2 withdrawal, and there were very real risks of cVDPV2 outbreaks as were being observed in other parts of the world. While giving IPV to children less than two years of age

provided them with protection from paralysis (across all three serotypes), in children over the age of two who had previously received OPV2, a dose of IPV would boost their waned mucosal immunity (and act as an effective preventative measure against any cVDPV2). Implementing a large IPV campaign in Karachi for the more than 2 million children between 4-59 months of age would be a huge undertaking. It would also be the first time using fractional IPV (fIPV, 1/5 dose of IPV) in a large setting with needle-free jet injectors. Understanding the rationale for using IPV, in which settings and age groups is critical to not only devising operational strategy, but also for communication.

If OPV is so important why do we also need IPV? OPV and IPV are very different vaccines and have different benefits and downsides. Unlike OPV, IPV does not contain live virus — it is a killed vaccine **(Figure 9)** — and is administered by injection (in contrast to the OPV drops). IPV, like tOPV, is a trivalent vaccine and includes protection against all three poliovirus serotypes (1, 2 and 3). IPV is better than any OPV at protecting against paralysis. In contrast to OPV, the efficacy of IPV is dependent on previous exposure. In developing countries, one dose of IPV has a serotype 1 efficacy of at least 50% and the second IPV dose brings up the efficacy to 90%, when administered at or after 14 weeks of age. Therefore, IPV can be used to quickly close any (humoral) immunity gaps since it will prevent paralysis effectively in a population. This is particularly important in high-risk settings where immunity thresholds are very high (as will be discussed in **Chapter 13)**, or in areas that have not been recently reached through immunization.

Figure 9. Inactivated Poliovirus Vaccine (IPV).

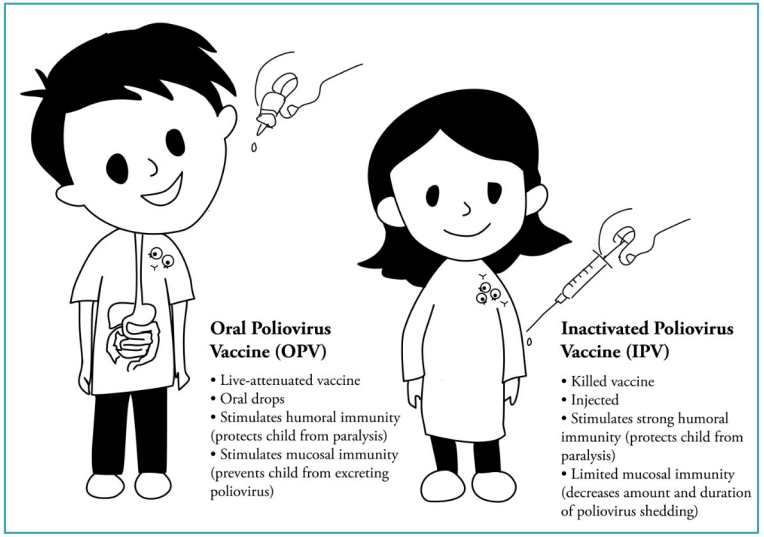


The age of administration of IPV is important, as when administered in young children, their maternal antibodies (i.e., temporary immune protection received directly from the mother) can interfere with the immune response to IPV. Therefore, IPV is significantly more immunogenic when given at or after 14 weeks of age. The humoral immune response to IPV is considered dose dependent, with a priming (or enhancing) effect often observed with the first dose on the subsequent dose.

In advance of OPV2 withdrawal in 2016, at least one dose of IPV was introduced into RI in all OPV using countries, as an additional measure to protect children from paralysis, particularly against cVDPV2.

Despite being more effective than OPV at protecting from paralysis, IPV on its own has little impact on mucosal immunity (mostly reducing the amount and duration of viral shedding), and therefore is less effective at preventing poliovirus transmission. In addition, it is much more difficult to administer and requires trained personnel, which can create problems (especially logistically) in the field. It is also more expensive than OPV and historically there have been supply constraints (which have since been addressed). Comparisons between OPV and IPV are provided in **Figure 10**.

Figure 10. Comparison between OPV and IPV.



Due to supply constraints around IPV (largely now resolved), fractional IPV (fIPV, i.e., 1/5 a regular IPV dose) was introduced as a dose-sparing mechanism. Studies have shown that the efficacy of 1 fIPV is only modestly lower than 1 full dose IPV and 2 fIPV are better than 1 IPV. fIPV can be more challenging to administer since it is most often administered intradermally instead of intramuscularly (like full dose IPV). Recently, needle-free jet injectors have been used that make administering fIPV easier and do not require highly trained personnel. Evidence from Pakistan (and Nigeria and Somalia) has demonstrated increased acceptance among communities and vaccinators of fIPV using jet injectors compared to IPV or OPV.

There are some key factors to consider when deciding on IPV use, as outlined in **Table 3.**

Table 3. Considerations for IPV use.

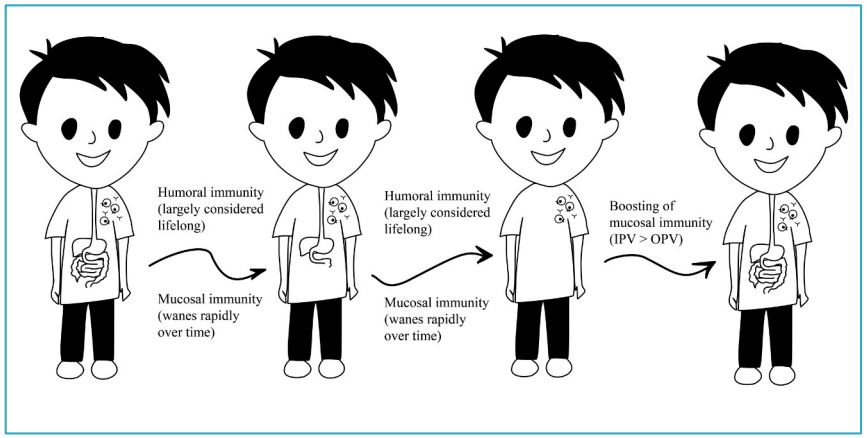
IPV Consideration	Details
Poliovirus risk	IPV can help close the (humoral) immunity gap in high risk populations due to its greater efficacy as compared to OPV.
Serotype 1 population immunity and immunity threshold	IPV can be particularly useful when the immunity required to stop transmission is very high (population size/density, movement patterns, birth rate) (e.g., Karachi, Pakistan).
Improvements in accessibility	IPV is useful in quickly closing the immunity gap in areas that have not been recently reached through immunization.
Potential to achieve high SIA coverage	If not possible to achieve good coverage, use of IPV may not have much impact. However, acceptance of IPV (compared to OPV) has been shown to be higher in select settings.
Exposure to previous IPV doses	IPV efficacy is dependent on previous IPV exposure (in contrast to independence of OPV doses).
Timing (force of infection; seasonality of transmission)	IPV can be particularly useful just before the high season (April-May) to boost immunity in preparation for increased force of transmission; also particularly useful in low season since greater probability of stopping transmission.
Age group	When administered in children <14 weeks of age, maternal antibodies may interfere with immune response.

Combining OPV and IPV. Order matters

So we have OPV which mimics infection with poliovirus. It induces mucosal immunity which is key for stopping person-to-person transmission. It also induces humoral immunity. IPV does not directly induce mucosal immunity but it is great at inducing humoral immunity (better than OPV).

This addresses how to use OPV and IPV on their own, but how about combining them? There is an interesting phenomenon that happens when you give the two vaccines together. We talked about waning of mucosal immunity, that even if a child develops mucosal immunity from OPV, that immunity can wane rapidly over time and the child can then again be susceptible to poliovirus and shed virus in their stool. If you give IPV to a child who has waned mucosal immunity, the IPV boosts their mucosal immunity back to a protective level (even better than another dose of OPV) **(Figure 11)**. And it doesn't matter if you use IPV or fIPV, both have a similar effect. By giving even a little bit of IPV to a child, their mucosal immunity is boosted. So IPV on its own has little impact on mucosal immunity, but when given to children who have previously been exposed to OPV (or poliovirus), it is very effective at boosting their waned mucosal immunity and preventing the transmission of poliovirus.

Figure 11. Waning and boosting of mucosal immunity.



Giving IPV before OPV also has a beneficial effect. In addition to cVDPV2, OPV also comes with another unlikely risk — vaccine associated paralytic paralysis (VAPP) — which occurs in 1 in 2.7 million doses of OPV. VAPP can occur in recently vaccinated children or their close contacts, and unlike cVDPV (which requires time and many susceptible children), VAPP is a more direct consequence of OPV. If you give a child IPV before OPV, it dramatically reduces their risk of VAPP.

Table 4 outlines the impact of OPV and IPV on mucosal and humoral immunity.

Table 4: Impact of OPV and IPV (alone or in combination) on mucosal and humoral immunity.

Vaccine	Impact on mucosal immunity (preventing excretion of virus and person-to-person transmission) (Yes/No)	Impact on humoral immunity (protection against paralysis) (Yes/No)
OPV alone	Yes (OPV is the best tool for inducing mucosal immunity and preventing transmission).	Yes (OPV also induces humoral immunity and protects child against paralysis)
IPV alone	No (IPV alone induces little mucosal immunity; has been shown to reduce the amount and duration of virus shedding).	Yes (IPV is greater at protecting against paralysis than OPV).
IPV after OPV	Yes. IPV boosts mucosal immunity that has waned from previous OPV exposure (even better than another OPV dose).	Yes (great for closing immunity gap since IPV has higher efficacy than OPV).
IPV before OPV	No (IPV before OPV induces little mucosal immunity; has been shown to reduce the amount and duration of virus shedding).	Yes (also protects against VAPP, a rare direct consequence of OPV).

Vaccine choice

OPV has largely been the vaccine of choice in the developing world, due to its lower cost, ease of administration and ability to induce both humoral and mucosal immunity (and ability to indirectly immunize secondary contacts). For over 30 years, tOPV was the primary vaccine of choice in developing countries, until in 2005 and 2009, mOPV (mOPV1 and mOPV3) and bOPV (serotypes 1 and 3)

were licensed. mOPV2 has been used since April 2016 to respond to outbreaks of cVDPV2, with nOPV2 being used in select countries since 2020 and more recently fully replacing mOPV2 for cVDPV2 outbreak response. IPV is used in developed countries where there is a low risk of poliovirus transmission (especially through the faecal-oral route due to their good hygiene and sanitation practices). IPV was also introduced globally into RI to provide additional protection against paralysis (this was done in preparation of OPV2 withdrawal). IPV is also used under special circumstances in SIAs, where closing any gaps in immunity is important. **Table 5** highlights strengths and limitations of OPV and IPV.

Table 5: Strengths and limitations of OPV and IPV.

Vaccine	Strengths	Limitations
OPV	• OPV is the best tool for inducing mucosal immunity and preventing transmission. • Easy to use (drops) and less expensive than IPV. • OPV induces humoral immunity and protects child against paralysis (but less effective than IPV).	• Efficacy of OPV (especially OPV1) in tropical developing countries is low, necessitating a large number of doses. Exacerbated by rapid waning of mucosal immunity (~50% per year). • Risk of reversion to cVDPV. • Resistance to OPV and poorly accepted in certain high-risk communities.
IPV	• IPV is superior to OPV at protecting against paralysis, which is great for quickly closing humoral immunity gaps. • IPV boosts waned mucosal immunity (even better than another OPV dose) in children previously exposed to OPV or WPV/cVDPV. • IPV alone has been shown to decrease amount and duration of shedding. • IPV (especially fIPV) is more accepted than OPV in certain settings. • No risk of reversion to cVDPV. • Protects against VAPP.	• IPV alone does not induce substantial mucosal immunity to stop transmission (shown to decrease amount and duration of shedding). • Requires priming (dose-dependent). • Maternal antibodies in young infants interfere with immune response. • Injectable (requiring needles, syringes, etc.) • Cost (more expensive than OPV). • Challenges with widespread implementation (especially in SIAs). • Until recently we didn't have a way to easily administer house-to-house (now have needle-free jet injectors).

Definitions

Inactivated Poliovirus Vaccine (IPV): IPV is an injectable vaccine that is highly effective at preventing paralysis from poliovirus infection (more so than OPV). However, unlike OPV, IPV does not contain live virus and therefore it does not directly induce mucosal immunity, which is required to interrupt transmission. While IPV's direct impact on stopping transmission is limited (mostly reducing the amount and duration of viral shedding), it is highly effective at boosting waned mucosal immunity (with fIPV just as effective as IPV in boosting mucosal immunity, and better accepted by communities than either IPV or OPV).

8

How to determine humoral immunity? Serology

It was Monday morning at Pakistan's NEOC. The surveillance team was presenting the weekly update, highlighting reported WPV1 cases, including their dose histories and serology results. While dose histories are not always reliable (as they are often based on parent recall), serology results provide a wealth of information, and can make the child's vaccination history clear. It is like piecing together a puzzle, which becomes easier the more you understand how the different vaccines behave and how they (along with poliovirus) impact the antibody (humoral immune) response in a child. When going through the WPV1 case data, the clear pattern was that the majority of WPV1 cases had high antibodies to serotype 1 (indicative of WPV1 infection) and undetectable antibodies to serotypes 2 and 3, which is indicative of not being vaccinated. However, there were cases that showed different patterns. Someone asked, "How does that WPV1 case have high antibodies against serotype 3? Wouldn't this mean they were vaccinated with bOPV? So how could they have become a case? What about those WPV1 cases with high antibody titers to all three serotypes?" From their recalled dose histories, they appeared to be fully vaccinated. How do we make sense of this? Serology results can help clarify vaccination histories, but only once you become comfortable interpreting them. This is what we will go through….

How do we know if a child is protected from paralysis caused by infection with poliovirus (i.e., has humoral immunity)? — through serology.

Serology is a measure of humoral immunity and tells us whether a child is protected from paralysis (either by being immunized with vaccine or previously exposed to poliovirus) and to what degree. What serology measures is the amount of antibodies in the child's blood that are able to bind to poliovirus and make it ineffective (i.e., poliovirus neutralizing antibodies).

The way to test for the amount of antibodies is through serial dilutions — a process of repeatedly diluting the sample of serum (blood plasma) and determining whether that diluted sample has enough antibodies to make poliovirus ineffective. You first mix each of the diluted samples with poliovirus and then add cells to see if that sample had enough antibodies to make the poliovirus ineffective. If not, you will see cells that have been destroyed (a common marker of cell destruction is viral plaques). Cell destruction and plaque formation is a marker of low neutralising antibody concentration. You can imagine that if you have a very diluted sample of serum and are still able to neutralise virus, the concentration of antibodies in the person's blood is high. The final dilution that is able to neutralise virus is taken as the result and a value is assigned to this sample, called the titer value. The titer value is a measure of the amount (concentration) of antibodies found in the person's blood. The higher the titer value, the greater the concentration of antibodies.

For poliovirus, the serial dilution of the sample is done repeatedly in half, and therefore they correspond to: 1/2, 1/4, 1/8, 1/16, 1/32, 1/64, etc. **(Figure 12)**. Often the titers are expressed using the ratio of the initial concentration (i.e., 1) to the diluted

concentration (i.e., 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, etc) or just expressed by the denominator only (e.g., 2, 4, 8, 16, 32, 64). In order to make these easier to represent, this is converted to the $\log_2$ scale (i.e. $\log_2(2)=1$, $\log_2(4)=2$, $\log_2(8)=3$, $\log_2(16)=4$, etc), which also corresponds to the sequence number of dilution. It is assumed that if the person is able to neutralize poliovirus at the 1:8 serial dilution they have enough antibodies in their blood to protect them from paralysis. This is often represented as titer $\geq$1:8, 8 or 3 (on the $\log_2$ scale) (these three values are interchangeable and represent seroprotection). Therefore, you will typically see a value of $\geq$3 (or 8 or 1:8) when referred to as seropositive (or seroprotected). For simplicity, we will use the value of $\geq$3 for seropositive throughout the rest of the chapter but keep in mind it can also be presented as $\geq$8 or $\geq$1:8. The last serial dilution for poliovirus antibody testing is typically 1/1024 (corresponding to the 10^{th} dilution). Different ways of representing titer values are presented in **Table 6.**

Figure 12. Polio serial dilutions.

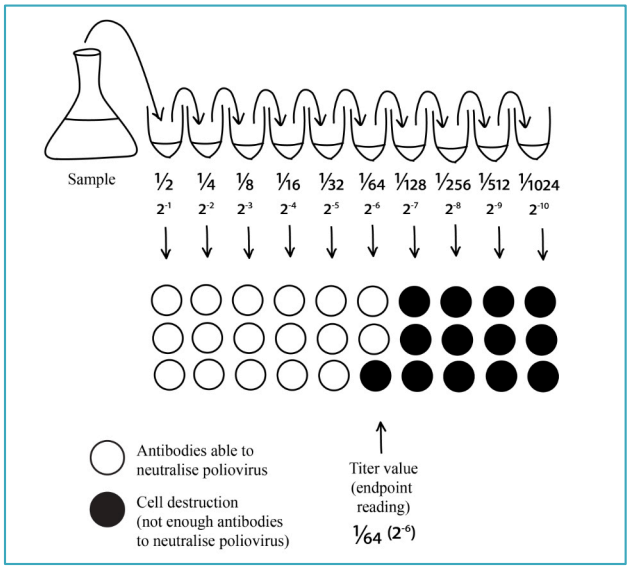


Table 6. Different ways of representing antibody titer values.

Serial dilutions	Initial to diluted concentr.	Exponential scale	Denominator value	Log_2 scale	Interpretation
1/2	1:2	2^{-1}	2	$Log_2(2) = 1$	Seronegative
1/4	1:4	2^{-2}	4	$Log_2(4) = 2$	Seronegative
1/8	1:8	2^{-3}	8	$Log_2(8) = 3$	Seropositive
1/16	1:16	2^{-4}	16	$Log_2(16) = 4$	Seropositive
1/32	1:32	2^{-5}	32	$Log_2(32) = 5$	Seropositive
1/64	1:64	2^{-6}	64	$Log_2(64) = 6$	Seropositive
1/128	1:128	2^{-7}	128	$Log_2(128) = 7$	Seropositive
1/256	1:256	2^{-8}	256	$Log_2(256) = 8$	Seropositive
1/512	1:512	2^{-9}	512	$Log_2(512) = 9$	Seropositive
1/1024	1:1024	2^{-10}	1024	$Log_2(1024) = 10$	Seropositive

Putting it into practice

Now that we know what titer values means, how do we interpret child level data to determine their protection against paralysis? There are a few important things to keep in mind. The results don't distinguish whether the child was exposed to poliovirus or vaccine virus of the same type. They have the same impact on the serology results. Also, there are three poliovirus serotypes and different vaccines including combinations of protection against the serotypes. Even though vaccines can include components that protect against poliovirus for more than one serotype, each one is distinct. Therefore, just because a child was given a vaccine meant to protect against multiple serotypes (e.g., bOPV) does not mean they will mount the same immune response to all serotypes, and may only respond to one serotype. The child will need to respond to each serotype separately, so there is a possibility that child was able to mount an immune response against one serotype and not another.

Let's start out by interpreting the serology results for WPV1 cases **(Table 7)**. Because you can't distinguish whether a child was exposed to poliovirus or vaccine virus, the WPV1 cases will have high titers (i.e., ≥3) to serotype 1 (unless there are problems with their immune system). So how do you determine the vaccination history of a WPV1 case? That's why for WPV1 cases we look at the titers of other serotypes, most commonly serotype 3 (since bOPV, which contains OPV1 and OPV3, is currently the most common vaccine used in campaigns) to determine whether they were vaccinated. If a WPV1 case has serotype 3 titer values <3, this means that either the child did not

receive any bOPV (or IPV) or was not able to mount an immune response. If a child does have high serotype 3 titer values, they could have preferentially responded to OPV3 and not OPV1, which left them susceptible to WPV1. This is because each vaccine has a certain probability of a child responding and these two events are independent. What about serotype 2? Since April 2016, there has not been any OPV2 so there are only two reasons for a child to have a serotype 2 titer ≥3 and that would be either as a result of IPV or if they were covered in an OPV2 response (historically mOPV2 and more recently nOPV2). As a WPV1 case, it is unlikely that they received IPV because the serotype 1 efficacy of IPV is high and therefore chances of them being paralysed is low (but still possible). Now that OPV2 is being used in outbreak response, this is a more likely scenario for a WPV1 case to have high serotype 2 titers.

Now what about serology results from healthy children? This is easier to interpret than WPV1 cases since the serotype 1 titer information can provide you information with vaccination history (unlike WPV1 cases where it is masked by infection with WPV1). We would expect that if a healthy child was repeatedly vaccinated with bOPV (containing OPV1 and OPV3) they would have a protective titer (i.e., ≥3) for serotype 1 and serotype 3 but <3 for serotype 2 (since bOPV does not contain serotype 2 OPV). If a child was vaccinated with IPV, we would expect titers ≥3 for serotypes 1, 2 and 3 (since IPV is a trivalent vaccine).

Table 7: Interpreting antibody titer values of WPV1 cases and healthy children.

Sample type	Ab titer serotype 1	Ab titer serotype 2	Ab titer serotype 3	Interpretation
WPV1 case	5	2.5	4	Likely vaccinated with bOPV and preferentially seroconverted to serotype 3 and not serotype 1 (remained susceptible to serotype 1 and was infected with WPV1); higher serotype 1 titer (i.e. >3) is due to WPV1 infection
WPV1 case	7	2.5	2.5	Likely unvaccinated child since undetected antibodies for serotype 2 and serotype 3; higher serotype 1 titer (i.e. >3) is due to WPV1 infection
WPV1 case	4	5	6	Likely vaccinated with tOPV or bOPV + OPV2; cases are unlikely with IPV but possible; higher serotype 1 titer (i.e. >3) is due to WPV1 infection
Healthy child	5	7	6	Likely vaccinated with IPV since high titers across all three serotypes and healthy child.
Healthy child	6	2.5	8	Likely vaccinated with bOPV since high serotypes 1 and 3 titers but undetected serotype 2 titer
Healthy child	2.5	6	2.5	Likely vaccinated with OPV2 without receiving any other vaccination (this scenario is unlikely; and only in an areas with previous cVDPV2 outbreak, without regular bOPV SIAs and poor RI).

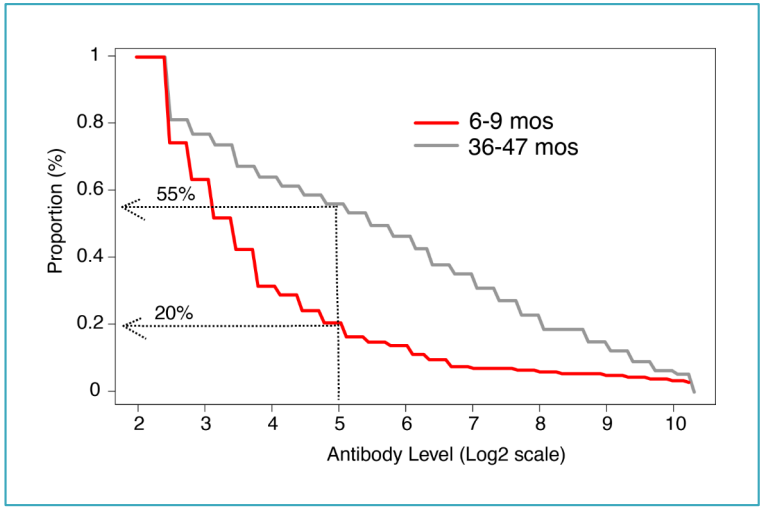
Note that values ≥3 could be any value between 3 to 10.5 and the interpretation would remain largely consistent (apart from IPV typically inducing a stronger antibody response as compared to OPV). The main distinguisher is between 2.5 (undetectable antibodies) and values ≥3.

Seroprevalence: Serology in a population at a snapshot in time.

The last section looked at the serum (blood plasma) of an individual child to determine if they are protected from paralysis. What if we want to know the protection of an entire population? Seroprevalence studies look at a population to see what percentage of the population is seropositive or seroprotected (seropositive and seroprotected can be used interchangeably). Blood samples are taken from children in a population (often to be representative based on a sampling strategy) and tested for poliovirus neutralising antibodies to determine if they are seropositive.

For seroprevalence surveys, the results are presented as the percentage of children that are seropositive for a particular serotype. For example, if the result is 83%, that means 83% of children surveyed had a seropositive (i.e. ≥3 titer) result. Often for seroprevalence studies, it isn't only the ≥3 cut-off that is analysed but the antibody titer values themselves. That tells you what serial dilution the sample was still able to neutralise poliovirus, in other words how strong the antibody response was. These results are often presented in what is referred to as a reverse cumulative distribution plot (RCDP), which displays all the titers across the entire population **(Figure 13)**. The results show the percentage of all children (y-axis) with a titer greater than or equal to a particular titer value (x-axis). The results start at the top left corner and should be 100% (since 100% of the study population have titers greater than or equal to the lowest value). In the Figure below, let's first consider the 6-9 month olds: 100% of subjects had an antibody titer of any value, 60% of subjects had a titer value of at least 8 ($\log_2(8)$ = 3) (i.e. seropositive) and 20% of subjects had a titer of at least 32 ($\log_2(32)$ = 5). In contrast, for the 36-47 month olds, 78% and 55% of subjects had a titer of at least 8 and 32.

Figure 13. Reverse cumulative distribution plots (RCDPs) for antibody titer values.



Seroconversion: Change in serology in a population over time (i.e., comparing two points in time).

So we know how to determine if a child is protected from paralysis, and we know how to determine if a population has protection from paralysis, but these are all snapshots in time. These give you information at one point in time and not how their protection is changing. If you want to consider how seroprotection is changing over time (typically due to vaccination) you are interested in determining the seroconversion of a child and seroconversion of the children in a population. Seroconversion is defined as either: (1) going from seronegative (antibody titer <3, <8, <1:8) to seropositive (antibody titer ≥3, ≥8, ≥1:8) or (2) if the child started out seropositive, a 4-fold rise in antibody titer value. Note, when considering 4-fold rise

in antibody titer value for young infants, you would also need to factor in the expected decline in their maternal antibodies but this is outside the scope of this handbook (and only relevant if you are considering children less than 6 months of age). Because each dilution is already 2-fold, and each dilution increases by a value of 1 (when on the $\log_2$ scale) a 4-fold rise just means you are interested in a change in +2 (i.e. from 3 to 5, 4 to 6, etc.). Therefore, seroconversion is just taking seroprotection at two points in time and comparing them. Seroconversion is often represented as a percentage of the population tested that seroconverted (i.e., fulfilled either criteria (1) or (2)).

Definitions

Serology: a measure of humoral immunity and tells us whether a child is protected from paralysis (either by being immunized with vaccine or previously exposed to poliovirus) and to what degree. Serology measures the amount of antibodies in the child's blood that are able to bind to poliovirus and make it ineffective (i.e., poliovirus neutralizing antibodies).

Seroprevalence: serology in a population at a snapshot in time, reported as the percentage of children in a select population that are seropositive for a particular serotype.

Seroconversion: change in serology in a population over time (i.e., comparing two points in time), typically considered before and after vaccination.

Calculations

Seroprevalence (%) = ((Number of children seroprotected, i.e., titer values >3)/Total number of children assessed)*100

Seroconversion (%) = ((Number of children that went from seronegative to seropositive + Number of children with 4-fold rise in antibody titer value[&])/Total number of children assessed)*100

[&]*over expected decline in maternal antibodies, if considering infants.*

9
How to determine mucosal immunity? Excretion

I still remember the day like it was yesterday. I had been analysing data for a clinical trial looking at the impact of different vaccines on mucosal immunity that had recently been conducted in India. My supervisor in Geneva at the time came into my office and asked me if I could go through the data again. I reviewed the data again….and again. It was correct. The results were incredible. They were showing that IPV was very effective at boosting waned mucosal immunity (even more so than another dose of OPV) in children who had previously been exposed to OPV. This had very important implications for IPV use. IPV had largely been discounted as a tool to get us to eradication. While it was used in a large number of countries and very helpful in protecting children from paralysis, in the countries where we still had poliovirus, stopping transmission was the critical factor that would get us to our goal. One of the reasons so many doses of OPV are required is due to the rapid waning of mucosal immunity. Now we had another tool to help us stop poliovirus transmission in the most challenging places. It wasn't the easiest tool to use in the most complex environments, but an effective tool nonetheless. Excretion studies like these were critical to informing strategy and guiding the action taken at the country level.

If a child is protected from being paralysed does it mean that they can't infect other children? As we have discussed in previous chapters — yes, a child can be protected from paralysis but still shed poliovirus in their stool and add to the chain of transmission. For determining whether a child is protected from paralysis we can take their blood and check for poliovirus neutralising antibodies. This doesn't tell us anything about whether the child is excreting virus. While a child that has high antibodies was likely vaccinated multiple times, it is not possible to determine whether the child received IPV or OPV; therefore, whether or not they have mucosal immunity. You can do some detective work and if a child had high serotype 2 titers and weren't in an area with an OPV2 response or cVDPV2 outbreak, you could assume they received IPV. But it is not possible to know whether they also received OPV.

The gold standard for determining whether a child has mucosal immunity is through looking at the shedding of virus in the stool of a child in what is referred to as a "challenge" with vaccine virus (i.e., OPV). Since OPV behaves like WPV in the gut it mimics what would happen if a child was exposed to live virus. Will the gut immune system neutralise it or will the virus replicate and be excreted in the child's stool? If the child's stool has OPV virus after giving the child the challenge dose of OPV, that means the child's gut or mucosal immune system wasn't able to clear the virus and it was able to replicate, indicating a lack of mucosal immunity. Children who don't excrete any virus have complete mucosal immunity.

There are many challenge studies that give children in certain groups OPV and then take stool samples at increasing intervals after the OPV 'challenge' dose. Often the stool is collected between 7-14 days since by 30 days most children would stop excreting (even those without mucosal immunity). These studies often measure the

proportion of children excreting or shedding any virus and then also consider the amount of virus shed. These are the studies that have determined the boosting effect of IPV on mucosal immunity (as was described in **Chapter** 7). They gave either IPV, bOPV or no vaccine (control) to children with previous OPV exposure and then four weeks later gave all a challenge dose of bOPV. Then measured the amount of vaccine virus in their stool — and found a reduced amount and duration present in the IPV group relative to the bOPV and control groups, representing increased mucosal immunity.

The way to determine the amount of virus in a child's stool is by looking at the viral titers (in a similar process already described for Serology in **Chapter 8**). These are typically determined through a series of 10-fold dilutions and represent the amount of virus per gram of stool. Excretion titers are often represented on the $\log_{10}$ scale and as the concentration at which 50% of the cells are infected in cell culture (TCID50) per gram of stool.

Definitions

Excretion: in the polio context, excretion is the amount and duration of viral shedding. The gold standard for determining whether a child has mucosal immunity is through looking at the shedding (excretion) of virus in the stool of a child in what is referred to as a challenge with vaccine virus (i.e., OPV).

10
Surveillance & Genetic trees

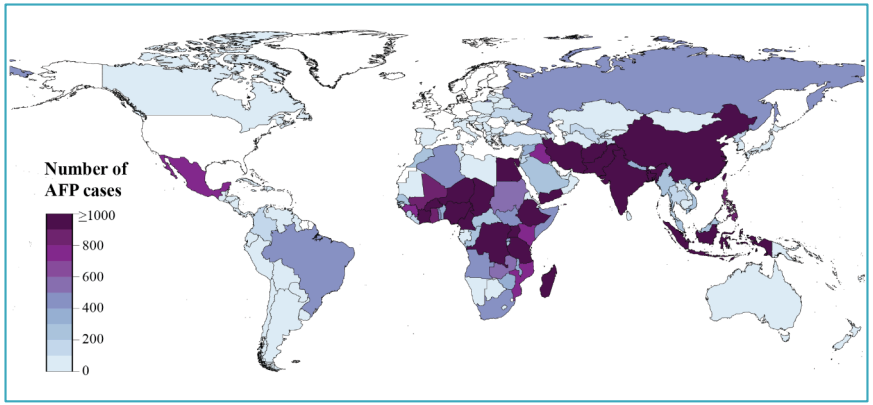
It was July 2019 and we were battling a large WPV1 outbreak in Pakistan (with 47 cases already reported that year). In the midst of the large case burden, the lab notified five new cases, and it was these cases that changed the trajectory of polio eradication with serious consequences in the final two remaining polio endemic countries. The five cases were reported in the northern areas of Pakistan, which are typically free of poliovirus. What distinguished these five cases was that they were not WPV1, but cVDPV2. This was at a time when the population hadn't been exposed to any OPV2 in over three years (meaning nearly the entire at risk population was susceptible), and in a context where we are seeing even less of the total transmission (since for cVDPV2, a case is reported on average for every 2000 children infected, in contrast to 200 for WPV1). While a cVDPV2 outbreak was a challenge on its own at this level of susceptibility, battling both WPV1 and cVDPV2 at this stage of eradication efforts was an enormously challenging feat, pulling resources and focus in two varying directions. We needed to understand clearly (and quickly!) where the virus was and how it was moving in order to plan strategically to prevent further spread. It quickly became clear how important the vast surveillance network in Pakistan had become. The cVDPV2 cases (and environmental surveillance detections) were providing us a clear signal that transmission was focused, but we knew that it would spread rapidly. The surveillance data was also telling us that these cVDPV2 detections had very recently emerged from OPV2 (based on the number of mutations in the genetic material) and therefore, the outbreak was just starting.

Surveillance is a pillar of polio eradication. If you don't know where the virus is how can you stop it and how do you know once you've achieved your goal?

When the GPEI was formed, a global routine surveillance system was established to identify polio cases and infection (in the absence of clinical confirmation) and help achieve eradication. This system identifies all causes of acute flaccid paralysis (AFP), including but not limited to polio. Since AFP is not limited to polio but characteristic of many diseases, it provides a sample of the population to test for the presence of poliovirus. The AFP surveillance system functions through a network of healthcare providers and active AFP surveillance staff to ensure there is a good awareness of AFP diagnosis and reporting by clinicians and traditional health practitioners.

All AFP cases are investigated, detailed information is obtained (e.g., location of residence, date of onset, vaccine dose history), and stool samples are collected and tested in a laboratory for the presence of poliovirus (the tests identify the serotype, i.e., 1, 2, 3, and distinguish between WPV and VDPV). Because there is a minimum AFP rate expected amongst the global population, ensuring AFP rates are maintained above a certain level gives confidence in the surveillance system and that polio cases aren't being missed. Non-polio AFP rate (i.e., AFP rate after excluding those confirmed to be polio) is expected to be at least two cases per 100,000 population less than 15 years of age globally and higher in endemic countries (to ensure all cases are being detected, i.e., need to remain more vigilant in these countries). AFP surveillance is critical to polio eradication **(Figure 14).**

Figure 14. Spatial distribution of AFP cases in 2024.



AFP surveillance is a strong global network and has been critical to the success of polio eradication. However, despite the strength and comprehensive nature of this system, most poliovirus infections are asymptomatic and therefore go undetected (as was described in **Chapter 1**). This is one of the biggest challenges in polio eradication. What that means is that only a small proportion of those infected with poliovirus will develop paralysis and most children will either present with mild flu-like symptoms or no symptoms as all. That makes things very difficult because you know that once a case is reported you already have an outbreak situation. This is why environmental surveillance (ES) is very important for polio eradication (it is also becoming increasingly important with the expanded use of IPV in RI, which can mask outbreaks by preventing paralysis, especially in areas with high RI coverage).

ES is the systematic testing of sewage samples for poliovirus to identify transmission, and has been increasingly used as a method to

test for the presence of poliovirus in the absence of cases. Since infected children excrete virus in their stool, which goes into wastewater or waterways (the latter being common in low-income countries with poor sanitation infrastructure), you can determine if there are children shedding virus in an area. Like for AFP surveillance, it is important to ensure that ES sites are sensitive (i.e., if there was virus present, would the ES site be able to pick it up?). The sensitivity of the ES site is confirmed through the presence of OPV and other enteroviruses, that are typically found in the sewage. Children can shed OPV for up to 30 days following vaccination and therefore there should be some OPV in the sewage for approximately one month after an SIA. In places where poliovirus persists, non-polio enteroviruses (NPEV, which are in the same family of viruses as poliovirus) are very common and therefore these should also be present. While careful consideration goes into selecting ES sites and there are strict sampling protocols, there are many uncontrollable factors when dealing with the environment, and therefore ensuring consistent sensitivity of sites is important.

Unlike AFP surveillance where you can gather information about the extent of transmission simply by asking the family where they primarily reside and their movement patterns/history (along with many other factors, such as immunization history), making inferences about transmission from ES detections is much more difficult. If an ES site is positive for WPV1, it is not possible to determine whether this represents one child shedding, a few or many children shedding virus (however, this is an area of work that is currently being explored). It won't tell you exactly where the virus came from, how much virus is in the population or how widespread it is (i.e., extent of transmission). It simply gives you a flag that poliovirus has been detected. A negative ES result can be even more challenging to interpret, as it does not provide conclusive evidence that the area is free of poliovirus, only that the

particular site did not pick up any virus when sampled that one particular time. While interpretation of a single ES sample has a variety of limitations, there is substantial power that can be gained when looking at the results through the appropriate lens — namely through understanding the catchment area, repeat/consistent sampling of the same site, results of neighbouring/nearby sites (e.g., in the same district), genetic linkages, and finally triangulation with AFP.

We will look at these one-by-one in the *putting it into practice* box, but for now let's delve a bit deeper into the genetic linkages to better understand how one can use genetic trees to piece together the movement patterns of the virus. It can also tell us if we are missing something (i.e., if the surveillance system is failing to capture important pieces of the puzzle). While this is critical for surveillance as a whole, it provides added benefit to piece together information from the extensive ES surveillance system.

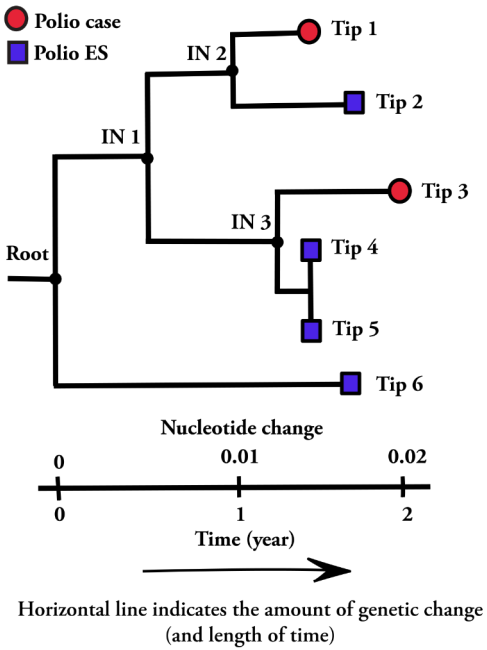
(Phylo)Genetic trees

All poliovirus in AFP and ES results are genetically sequenced to show the relationship between samples. Given that poliovirus (like all viruses) mutate over time we can see how long the virus has been circulating in the population by how much it has mutated and how closely it resembles virus taken from other samples. The longer it has been circulating in the environment, the more mutations it has developed and the less similar it is to previous samples. This is how we can determine whether we are capturing all the poliovirus transmission taking place in a population. If the samples tend to be closely related, we are regularly capturing any changes taking place. However, if there are a lot of differences in samples, they have likely been going

undetected for some time (because the virus has had ample time to mutate without being captured in our samples). These detections are often referred to as "orphan" viruses, because they are not closely related to any other detections. The speed at which the virus mutates over time is referred to as the molecular clock. For poliovirus, which is known to evolve very rapidly over time (i.e.. rapid genomic evolution), the rate of change averages 10^{-2} (or 0.01 or 1%) substitutions per site per year.

Genetic trees show a picture of the relationships between the sequences of all the poliovirus samples that have been collected. They are characterised as having nodes and branches. Internal nodes represent inferred (not observed) branching points indicating where samples diverge. External nodes (or "tips") represent actual viruses sampled and sequenced (for poliovirus, these can be from cases or ES detections). Branches represent the amount of genetic change from the root, which is the last theoretical common ancestor of all samples. Sequences that share the same mutations are grouped together. When a sequence sits on a line on its own, it has unique mutations not found in the other sequences. When sequences are linked by a flat vertical line, their sequences are identical. The number of mutations (corresponding to time) is on the x-axis so the longer the line, the more mutations and typically the more recent the detection. Orphan viruses are those that are genetically distinct from other previously collected samples (greater than 1.5% divergent or different), indicating circulation for long periods without detection. **Figure 15** presents an example schematic of a poliovirus genetic tree.

Figure 15: Schematic of poliovirus genetic tree.



Horizontal line indicates the amount of genetic change (and length of time)

Internal Nodes (INs): most common inferred ancestor

IN 1: common ancestor of Samples 1, 2, 3, 4 and 5.

IN 2: common ancestor of Samples 1 and 2.

IN 3: common ancestor of Samples 3, 4 and 5.

External Nodes (or "Tips"): actual viruses sampled and sequenced

Tip 1: polio case most closely linked with Tip 2 (sharing IN 2).

Tip 2: polio ES most closely linked with Tip 1.

Tip 3: polio case most closely linked with Tips 4 and 5.

Tips 4 and 5: polio ES detections that are identical.

Tip 6: polio ES that is an orphan virus (not closely linked to any other Tip).

Putting it into practice

While interpretation of a single ES sample has a variety of limitations, there is substantial power that can be gained when looking at the results through the appropriate lens—namely through understanding the catchment area, repeat/consistent sampling of the same site, results of neighbouring/nearby sites (i.e., in the same district), genetic linkages and finally triangulation with AFP. Let's take these one-by-one….

Let's start with a positive ES result. What inferences can you make about an ES positive result and what does that actually mean?

First, it is critical to know the catchment area of an ES site (i.e., what population drains into the wastewater or waterway system?). This gives you a reference point and clarifies the population the site represents. Keep in mind that a positive ES sample does not tell you how many children are shedding virus or the amount of virus being shed. This is simply a starting point of investigation.

Second, is this the first ES positive or have there been continued positive detections in the site? While one positive ES sample is very difficult to interpret, consecutive positive ES sites for 3- or 6-months, provides a clearer indication of sustained transmission in the area (again, consider the catchment area to better understand the scale of transmission).

Third, look to neighbouring or nearby sites in the area (e.g., district). Some areas will have many ES samples

representing different catchment areas. If only one ES site is consistently positive that provides support for more localised transmission as compared to multiple (or all) ES sites being consistently positive. We have seen in many circumstances historic reservoirs (which typically have many ES sites) detecting virus across all sites, consistently month after month. This is a clear signal for more widespread transmission in the area.

Fourth, there are instances where due to high levels of movement, virus is continuously being imported into an area in the absence of ongoing local transmission. Through genetic sequencing (all poliovirus in AFP and ES results are sequenced to show the relationship between samples, and because of the mutating nature of viruses, it is possible to draw the history of the virus and show which samples are most closely related, based on the highest probability), we can determine if the ES positive detection is most closely linked locally or from another location. If closely linked to previous detections in the same area, it further supports local transmission.

Finally, it is important to consider both AFP and ES data when formulating conclusions about risk as both sources provide different information, that taken together can clarify the picture of poliovirus transmission **(Table 8)**.

In contrast to an ES positive result which gives you a flag indicating that there may be transmission present, with a negative result it is not possible to make the same type of inference (i.e., that transmission is not present). There is limited information that can be drawn from a negative ES result. Ensuring the sensitivity of negative ES sites is critical.

Table 8: Interpretation of ES and AFP data.

Number of ES+ (current location, 1-month apart)	Another ES in nearby area (yes/no) if yes: (+/-)	Polio cases in current location	Polio cases in nearby location	Interpretation
1	No	None	None	Difficult to make any inferences
1	Yes (-)	None	None	Difficult to make any inferences
1	Yes (+)	None	None	Difficult to make any inferences but may indicate some low level of transmission in the larger area
1	No	≥1 case	None	Outbreak in current location (location where cases reside). Difficult to know whether low level of transmission has spread to nearby area since no ES.
1	Yes (-)	≥1 case	None	Outbreak in current location (appears focused).
1	Yes (+)	≥1 case	None	Outbreak in current location with potentially low level transmission in nearby areas.
1	No	None	≥1 case	Outbreak in nearby location. Possible low level of transmission in current location but difficult to determine.
1	Yes (-)	None	≥1 case	Outbreak in nearby location (check catchment area and sensitivity of ES site). Possible low level of transmission in current location but difficult to determine.
1	Yes (+)	None	≥1 case	Outbreak in nearby location. Possible low level of transmission in current location but difficult to determine.
1	No	≥1 case	≥1 case	Widespread outbreak in both current and nearby location.
1	Yes (-)	≥1 case	≥1 case	Widespread outbreak in both current and nearby location (check catchment area and sensitivity of ES site).
1	Yes (+)	≥1 case	≥1 case	Widespread outbreak in both current and nearby location.
≥2	No	None	None	Possible transmission in current location. Increased probability with increased frequency of positive ES. Check AFP surveillance sensitivity. Check ES catchment area and determine links to high transmission areas/ reservoirs.
≥2	Yes (-)	None	None	Possible focused transmission in current location. Increased probability with increased frequency of positive ES. Check AFP surveillance sensitivity. Check ES catchment area and determine links to high transmission areas/ reservoirs. Check ES sensitivity and catchment area in neighbouring location.
≥2	Yes (+)	None	None	Possible widespread transmission in current and neighbouring locations. Increased probability with increased frequency of positive ES. Check AFP surveillance sensitivity. Check ES catchment area and determine links to high transmission areas/reservoirs.
≥2	No	≥1 case	None	Outbreak in current location. Confirm extent based on location/travel histories of cases.
≥2	Yes (-)	≥1 case	None	Outbreak in current location. Confirm extent based on location/travel histories of cases.
≥2	Yes (+)	≥1 case	None	Outbreak in current location. Potential transmission extended into nearby area. Check catchment area of nearby location (proximity, connectivity with current location).
≥2	No	None	≥1 case	Outbreak in neighbouring location, and possible transmission in current location. Increased probability with increased frequency of positive ES. Check AFP surveillance sensitivity in current location.
≥2	Yes (-)	None	≥1 case	Outbreak in neighbouring location, and possible transmission in current location. Increased probability with increased frequency of positive ES. Check AFP surveillance sensitivity in current location. Check ES sensitivity and catchment area in neighbouring location.

≥2	Yes (+)	None	≥1 case	Outbreak in nearby area. Confirm extent based on location/travel histories of cases. Check catchment area of ES sites. Check AFP surveillance sensitivity in current location. Check catchment area of current location sites.
≥2	No	≥1 case	≥1 case	Widespread outbreak in both current and nearby location. Confirm extent based on location/travel histories of cases.
≥2	Yes (-)	≥1 case	≥1 case	Widespread outbreak in both current and nearby location. Confirm extent based on location/travel histories of cases. Check catchment area and sensitivity of ES site in nearby area.
≥2	Yes (+)	≥1 case	≥1 case	Widespread outbreak in both current and nearby location. Confirm extent based on location/travel histories of cases.

Definitions

Acute Flaccid Paralysis (AFP) Surveillance: the global routine surveillance system to identify polio cases and infection, established upon formation of the GPEI in order to help achieve eradication. This surveillance system identifies all causes of acute flaccid paralysis (AFP), including but not limited to polio. Since AFP is not limited to polio but characteristic of many diseases, it provides a sample of the population to test for the presence of poliovirus. The AFP surveillance system functions through a network of healthcare providers and active AFP surveillance staff to ensure there is a good awareness of AFP diagnosis and reporting by clinicians and traditional health practitioners.

Environmental Surveillance (ES): ES is the systematic testing of sewage samples for poliovirus to identify transmission, and has been increasingly used as a method to test for the presence of poliovirus in the absence of cases. Since infected children excrete virus in their stool, which goes into wastewater or waterways (the latter being common in low-income countries with poor sanitation infrastructure), you can determine if there are children shedding poliovirus in an area. Like for AFP surveillance, it is important to ensure that ES sites are sensitive (i.e., if there was virus present, would the ES site be able to pick it up?). The sensitivity of the ES site is confirmed through the presence of OPV and other enteroviruses, typically found in the waterways.

Non-polio AFP rate: because there is a minimum AFP rate expected among the global population, ensuring AFP rates are maintained above a certain level gives confidence in the surveillance system and

that polio cases aren't being missed. Non-polio AFP rate is expected to be at least two cases per 100,000 population less than 15 years of age globally and higher in endemic countries (to ensure all cases are being detected, i.e., need to remain more vigilant in these countries).

ES sensitivity: The sensitivity of the ES site is confirmed through the presence of OPV and other enteroviruses, that are typically found in the sewage. Children can shed OPV for up to 30 days following vaccination and therefore there should be some OPV in the sewage for approximately one month after an SIA. In places where poliovirus persists, non-polio enteroviruses (NPEV, which are in the same family of viruses as poliovirus) are very common and therefore these should also be present.

Calculations

Non-polio AFP rate = (number of non-polio AFP cases/population <15 years of age)*100,000

ES sensitivity = (number of ES samples detecting Sabin and/or NPEV / total number of ES samples)*100

11
Vaccination strategies

"Can we extend the time interval between SIAs? Communities are fatigued and don't want to keep seeing polio workers at their doorsteps." This is a common sentiment in Pakistan as there are campaigns planned in most months of the year. While the SIA schedule attempts to maintain a 6-week window, the pre-campaign and post-campaign weeks (where activities in the communities are ongoing), shrink this interval in the eyes of polio workers and communities. Often case responses need to be fit between SIA rounds, further compressing these intervals. While this consistency is critical, there needs to be a balance to combat the exhaustion of the workforce and communities. We have attempted to increase this interval, but without strengthening the underlying RI system (which would reduce the need for frequent SIAs), frequent SIAs are a necessity to ensure sufficient levels of immunity are both achieved and maintained. Pakistan, like many of the highest risk countries, is in an untenable position: it must ensure consistently high immunity in the context of very high population size and density, substantial and widespread population movement, and very high birth rates in areas with low RI coverage. This challenge is exacerbated by a vaccine made ineffective from high prevalence of co-infection with other viruses, diarrheal illness and malnutrition, and rapid waning of mucosal immunity. With SIAs, we are continuously running as fast as we can, simply to stay in the

same place (as susceptible children are born and mucosal immunity wanes), all the while poliovirus is moving from one area to the next exploiting pockets of susceptible children. If only the same emphasis had been placed on improving the RI system as remaining vigilant with SIAs, we may be in a very different place. For strengthening RI is the greatest insurance that polio eradication will be achieved and sustained for generations to come.

There are two main strategies through which a child can be vaccinated against poliovirus: 1) routine immunisation (RI); and 2) supplementary immunization activities (SIAs).

The primary mode through which immunization against polio is received is RI. RI services are provided through the health system of a country, in collaboration with the Expanded Program on Immunization (EPI). They are generally delivered through fixed-sites (i.e., within health facilities), but in developing countries where access to fixed services is often limited, they are supported with outreach services. The RI system ensures delivery of vaccines to all children in the first year of life.

While most developed countries have IPV-only schedules (in the Americas and European Regions), developing countries continue to use OPV in RI (i.e., bOPV, which replaced tOPV in April 2016). In OPV-using countries, children are expected to receive at least 3 OPV doses from the age of 6 weeks, with a minimum interval of 4 weeks between doses (commonly at 6, 10, and 14 weeks of age in the African, Eastern Mediterranean and South-East Asian Regions); and, since 2015, at least one dose of IPV co-administered with an OPV dose at or after 14 weeks of age. Many countries also administer a birth dose of OPV and a second IPV dose (the latter has recently been recommended for all countries by the Strategic Advisory Group of Experts on Immunization, SAGE). Some countries that previously used OPV have recently transitioned to IPV-only (or mostly IPV) schedules, especially in the Americas and Western Pacific. Select countries in South-East Asia use fractional instead of full-dose IPV. RI schedules and number of doses vary by country and region.

Vaccination through RI remains one of the most critical intervention strategies to interrupt poliovirus transmission, with poor

RI performance being the most indicative of endemicity or re-infection. Countries with low RI coverage are those where interruption of poliovirus transmission has been most challenging. RI coverage is often spatially heterogeneous across and within countries and in polio endemic countries is largely sub-optimal to protect children from the disease.

To supplement RI in areas with limited health infrastructure and poor RI coverage, wide-scale and frequent SIAs with OPV (or less commonly IPV) targeting children less than five years of age have been implemented. These are called national or sub-national immunization days (NIDs or SNIDs) depending on the geographic scale of the vaccination campaign. In endemic countries, as many as 10 SIAs are implemented each year per country, with repeat SIAs often targeting high-risk areas. Historically, tOPV was used in SIAs; however, following the eradication of WPV2, there was a renewed focused on eradicating WPV1 and 3. With the licensing of mOPV (mOPV1, mOPV3) and bOPV in 2005 and 2009, respectively, these became the vaccine of choice for SIAs in endemic or high risk countries.

SIA plans are created in advance of each year and are based on an assessment of risk. Areas are classified into risk tiers, with strategies tailored to each tier (discussed in more detail in **Chapter 13** on Risk Assessment). Moreover, the SIA calendar in polio endemic countries reflects transmission dynamics of poliovirus. Specifically, vaccination strategies are tailored to be more frequent in the low transmission season as to try to eradicate when transmission is lowest. In recent years, there has been a strengthened focus on achieving SIA coverage consistently greater than 90%, which has repeatedly demonstrated to play a critical role in interrupting poliovirus transmission.

In addition, there are vaccination responses conducted for each reported case, following detailed case investigation. Furthermore, there are additional strategies that help reach high-risk children, especially those on the move, often through improved tracking and targeted strategies for vaccination (including vaccination at transit points and better incorporating these groups into the detailed operational plans, i.e., microplans).

Definitions

Routine immunization (RI): immunization services provided by the health system of the country in collaboration with the Expanded Program on Immunization (EPI). The RI system ensures delivery of vaccines to all children in the first year of life.

Supplementary immunization activities (SIAs): SIAs are conducted to supplement RI in areas with limited health infrastructure and poor RI coverage. SIAs typically target children less than five years of age and are either national or sub-national immunization days (NIDs, or SNIDs), depending on the geographic scale of the vaccination campaign.

12
Monitoring & Evaluation

It was March 2019 and we had just released the Lot Quality Assurance Sampling (LQAS) results for the most recent SNID. A critical district reported shocking results, with more than 60% of their LQAS lots failing, indicating substantial gaps in their campaign quality. Immediate action ensued, with senior district leadership coming to the NEOC for discussion. The fear about these poor results was palpable. Given the prominence that LQAS had reached as the yardstick with which success was measured and the spotlight on the Pakistan programme, no district wanted to be flagged as the worst performing. The intense focus placed on LQAS was getting out of hand. It was becoming the key measure of SIA performance and was often interpreted to represent more than it was ever designed for. LQAS is not a coverage but simply a flag to indicate where further improvements are required at a fine geographic level. Historically, the standard methods of post campaign evaluation were carried out at a district level and gave a coverage representative of the entire geographic area. As risk became more focused, a measure was required to better zero in on gaps. The transition to LQAS (conducted at the union council [UC] level in Pakistan, the lowest administrative unit), provided more focused attention on gaps, which were often masked when considering larger geographic areas. While this was giving us more

focused feedback, it was coming with its own set of challenges. Because there were so many UCs in Pakistan, we could only conduct LQAS in a select sample following each SIA (many other challenges exist with LQAS, including ensuring follow up and corrective action). How could we decide which UCs to evaluate? Should we prioritise the highest risk areas and sample them repeatedly, or should we sample areas that have not been evaluated in a long time? But if we sample these areas, would we not want to sample them again after the next SIA to check on progress? We needed to come up with a systematic way to select UCs. Based on the four risk tiers, we developed an algorithm to systematically select UCs for LQAS. Distinct criteria was developed for each risk tier based on a variety of factors, including past performance and length since previously assessed. Higher risk tiers were systematically oversampled. In order to capture variability in the lower risk tiers, other indicators of campaign performance (including administrative data and independent monitoring) were incorporated. Selecting UCs for LQAS is an evolving process, one that continues to need careful attention.

Monitoring and evaluation is an important component of the polio programme. While monitoring involves regularly tracking and collecting data on the programme's activities (primarily SIAs), evaluation involves assessing their quality and impact in achieving the programme's goals. After each SIA, the quality (or coverage) is evaluated to determine whether additional strategies are required to reach the target population and to address any identified gaps before the next SIA.

There are many different ways of assessing the quality of SIAs, each with their own strengths and weaknesses. The primary approaches used are through: 1) administrative records; 2) independent monitoring (IM); 3) lot quality assurance sampling (LQAS); and 4) vaccination histories of AFP cases. Here we will go through each method, providing an overview, along with their strengths and limitations.

Administrative data

All countries report vaccination coverage based on administrative data. These data on vaccination status of children are routinely collected through health facilities and service providers within a country, and are captured in their administrative records. Health facility records are then compiled and sent to higher administrative levels of government for further aggregation.

The greatest benefit of administrative data is that it is consistently and routinely collected through the existing health system (a separate mechanism is not required). This provides near real-time information, allows for monitoring of all administrative levels, and ensures a comparable measure of coverage across all sub-units of

geography and over time. This is particularly helpful to better understand how coverage is changing over time at finer geographic scales (e.g., district) or to compare coverage between different locations. While this ensures helpful information can often be gained from the use of administrative data, there are some key limitations to consider.

The main challenge with administrative data is determining the denominator for calculating coverage. Coverage is calculated based on the number of children vaccinated divided by the target population. The denominator here is the target population. It is very difficult to get a reliable target population in countries with infrequent or poor-quality census, or high rates of migration (unfortunately, this applies to most if not all of the endemic and outbreak-prone countries). The targets become even less reliable at lower spatial levels (i.e., national level are likely more reliable than province, which in turn are more reliable than district). The challenge with the target population is why coverage estimates are often greater than 100%.

The challenge posed by the denominator can be circumvented, in part, by considering only the magnitude (or proportion) of missed children. These are children that were recorded to be not vaccinated and provide valuable insight into the quality of the vaccination campaign. Moreover, considering how coverage or missed children estimates are changing over time can help elucidate the progress or decline in campaign quality.

When interpreting administrative data, especially trends over time or comparison between locations, one must be aware of factors that may have impacted the reliability of the data reporting system. It is imperative to keep in mind any events that may have resulted in delays in reporting, or problems with vaccination (e.g., lack of vaccine)

that may have impacted the coverage data, especially if there are sudden changes to the numbers.

Because of the challenges with administrative data, the polio programme has implemented other ways of specifically monitoring the SIAs, including independent monitoring (IM) and more recently lot quality assurance sampling (LQAS).

Independent monitoring

Independent monitoring (IM) is one method of post-SIA evaluation. IM occurs through door-to-door visits or checking children in community markets or known gatherings. IM is often a method of convenience sampling or sampling in specific targeted areas and is likely not fully representative of the coverage in the entire population. The results of IM produce a coverage level estimate typically at a second administrative level (e.g., district). Because the goal of IM is to get a coverage across a fairly large geographic unit, you can get IM coverage estimates across a wide geography and do so consistently across campaigns. This enables having a coverage estimate that can be compared across geographies in a particular campaign and also comparing the coverage trends of the same geography over time.

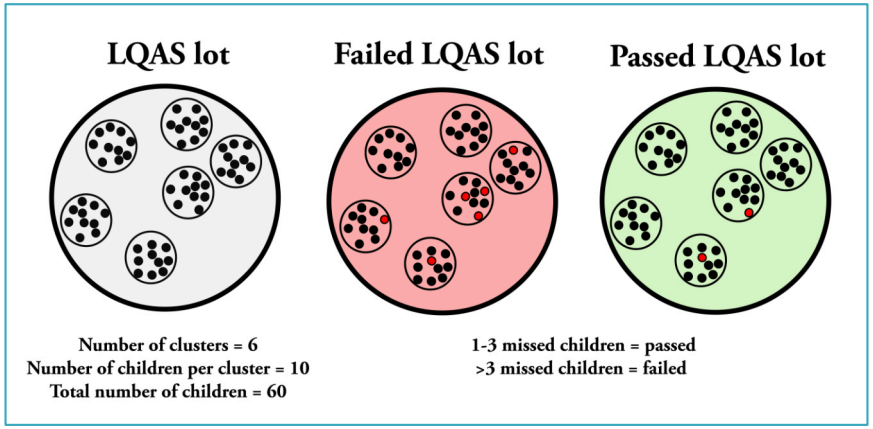
While IM coverage resolved the denominator issue of administrative coverage, it resulted in a blanket coverage across a fairly large geography, limiting inferences at a finer spatial resolution. As polio eradication progressed, the problems became more focused into smaller geographic areas that could be masked by coverage estimates at the district level. Moreover, the IM coverage estimates became consistently high even in areas with continued WPV1 transmission. Therefore, the programme decided to incorporate a new method of

post-campaign evaluation in 2009 — called lot quality assurance sampling (LQAS).

Lot quality assurance sampling (LQAS)

LQAS assesses the performance following a specific SIA in pre-defined areas known as "lots". Lots are selected based on a pre-defined methodology and are typically based on the lowest administrative unit (in Pakistan, this is the union council [UC], in Afghanistan this is the district and in Nigeria this is the local government area [LGA]). Once the lot is selected, 6 different clusters (e.g., villages, settlements) are randomly selected from within the lot, and in each cluster, 10 children are randomly selected. Therefore, in each lot, a total of 60 children are sampled (**Figure 16**). Based on the vaccination status of these 60 children, the lots are classified as either passed or failed, with more than three children missed typically the cut-off.

Figure 16. Lot quality assurance sampling (LQAS) selection strategy.



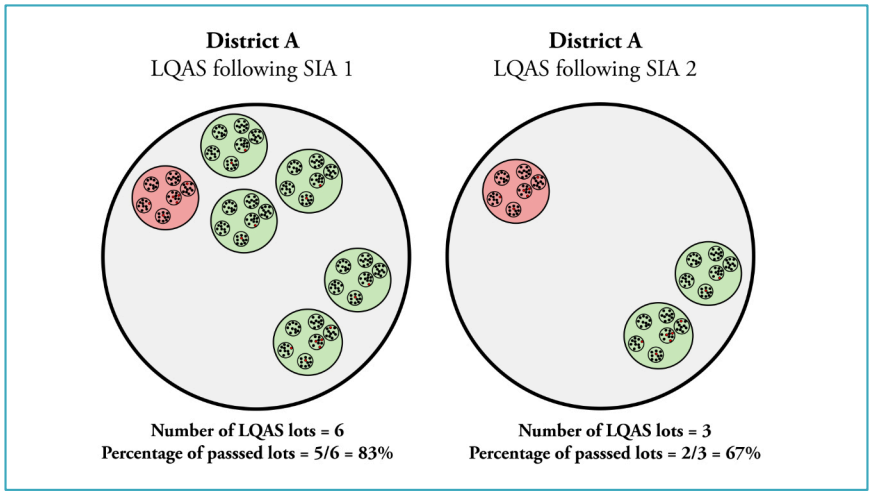
The benefit of this new method was that it enabled making a rapid assessment of SIA quality by selecting a relatively small sample (only 60 children, in contrast to other post SIA evaluation methods, whereby a large number of children were checked for their vaccination status). It also focused at the lowest administrative level, enabling identifying gaps within focused geographic areas (in contrast to IM, where it was not possible to determine where to focus if the overall coverage was poor in the larger administrative level). This ensured (in theory) that gaps could be quickly identified and addressed before subsequent SIAs (in reality, addressing and following up on issues identified through LQAS has been largely ineffective, limiting the role of LQAS in driving SIA improvement).

The challenge of tracking progress and making improvements based on LQAS is due, in part, to its limited reach and inability to consistently evaluate the same lots after each SIA. While LQAS provides greater insight at an in-depth level than the other methods of post-campaign evaluation, it can only be conducted in select areas. In Pakistan, where the sampling basis for LQAS lots is the UC, less than 10% of the nearly 8,000 UCs can be selected following each SIA, and those selected vary from campaign to campaign. The selection of UCs for LQAS is based on risk classification (with oversampling of highest risk areas), previous campaign performance and time since last evaluation. Due to the large number of UCs, many are not routinely selected, making inferences about trends over time difficult (this has partly been addressed in the highest risk areas, as they have been prioritised to be repeatedly sampled; however, it still poses a substantial issue in consistently tracking the majority of areas).

While the lack of consistent sampling of lots poses a challenge, the greatest limitation with LQAS is that, in contrast to the other methods of post SIA evaluation, it is not a coverage. LQAS is simply a

flag indicating how well a particular area performed (in a pass/fail categorization with either 4-5 categories, indicating varying degrees of pass and fail). Therefore, the results must be interpreted with caution, and any aggregation or analyses conducted with LQAS must be ventured into carefully. Often, LQAS results are aggregated at higher administrative levels and presented as the percentage of LQAS lots that passed. Trends over time are routinely presented to give an indication of progress or declines in performance in an area. However, one must take into account that the lots sampled are not the same for each round, and therefore any aggregation over time can be misleading. For example, in Pakistan, a district may go from an 83% LQAS pass rate to 67%, but it could simply be the different lots (UCs) that were selected for evaluation (**Figure 17**). The number of UCs selected in the district could also be different between rounds (making results not comparable and potentially providing misleading results).

Figure 17. Comparison of LQAS lot selection between SIAs for a select geographic area and impact on aggregated results.



Vaccination histories of AFP cases

In contrast to IM and LQAS (which are direct methods of determining SIA quality), AFP surveillance data is another routinely collected data source that can be used to estimate coverage (in addition to administrative data). AFP surveillance data are a rich and consistent source of information, and provide detailed demographic, geographic location and dose history information for each child (and are expected to be fairly representative of the population), enabling estimation of SIA coverage at a focused spatial level.

The SIA vaccination coverage for each non-polio AFP case is calculated by dividing the recorded OPV dose history of that child by the number of SIA campaigns the child is expected to have received (based on their date of birth and date of paralysis onset). For example, let's say a non-polio AFP case is 10 months of age (at the date of paralysis onset), and should have been exposed to 6 SIAs based on the SIA calendar and the location of residence. If the child only received 3 OPV SIAs, the coverage for this child would be 50%. This would be applied to all non-polio AFP cases and aggregated at a geographic level and over time. You would want to exclude the polio cases as they are likely under-immunised and would skew the results (as you want a representative sample of the population of interest). SIA coverage based on non-polio AFP data is also sometimes simply reflected as the proportion of AFP cases that have at least 7 OPV SIA doses.

The primary limitation of using AFP data to estimate SIA coverage is that OPV dose histories are based on parent recall which may be biased, especially when the number of SIAs is large. Also, only some regions (including the Eastern Mediterranean Region) separate OPV dose histories into those received through SIA versus RI. When not separated, the dose histories from SIAs can be difficult to infer.

Moreover, this method doesn't provide you with an estimate of coverage for a specific SIA, but for all the SIAs over a narrow period of time (e.g., 4 or 6 months) (the more AFP cases the narrower the window can be).

The strengths and limitations of each of the above post SIA evaluation tools is provided in **Table 9**. Keeping these in mind (especially when the results from the different sources don't align) and using these tools together can provide a more complete and comprehensive picture of campaign quality.

Table 9: Comparison of the different types of monitoring data, including challenges, benefits and when to use.

	Challenges	Benefits	When to use
Admin. data	Accuracy of denominator, often resulting in coverage >100% (more problematic at lower geographic units). Need to be cautious about fluctuations over time due to problems in the system influencing coverage (i.e., data collection, vaccine availability in an area, etc).	Coverage estimates that can be aggregated across any geographic unit. Can look at trends over time for any geographic area.	Excluding the denominator and considering missed children and refusal children can provide great value, as can trends (but must take into account any changes to the admin system).
Independent monitoring (IM)	Only gives you a coverage estimate at a fairly large geographic unity (e.g., district) and therefore can mask problems at a lower level. Or if coverage is low, you can't identify where the problems are in that geographic unit.	Provides coverage estimate for a geographic unit across a wide geography – therefore can compare different areas in one point in time or the same area over time. Coverage estimates are easier to understand/ interpret.	If you want to understand the progress of an area over time or get a general understanding of the coverage of a campaign across all geographies.
LQAS	Only gives you a pass/fail flag indicating where problems occur. Small sample of LQAS lots so difficult to compare areas and trends over time. Often different areas are selected for LQAS across multiple campaigns and therefore only get a snapshot.	Get in-depth information about campaign quality in a focused area.	If you want to understand the challenges in a focused location at a particular point in time.
Non-polio AFP	Due to limited AFP data, coverage estimate at a fairly large geographic unit (e.g., district) and over periods of time (not for a specific campaign). Influenced by parent recall of child's dose history.	Coverage estimates that can be aggregated across any geographic unit. Can look at trends over time for any geographic area.	If you want to understand the progress of an area over time or get a general understanding of the coverage of campaigns across all geographies.

In addition to evaluation of SIA performance, monitoring the status and progress of RI coverage is equally important to identify immunization gaps in an area. Given the inequities in health service availability and utilisation within countries, capturing variability of RI coverage helps to better understand the gaps in the foundation of immunity. However, while SIA performance is highly dynamic (necessitating continued and repeat evaluation), RI coverage tends to be marked by gradual (or no) changes. As a result, RI coverage is often evaluated over fairly long periods of time (6-months to 1-year) or at snapshots in time, separated by large intervals of time.

WHO and UNICEF annually produce national RI coverage estimates (referred to as WUENIC estimates), which are derived from administrative and survey data but with adjustments to increase the accuracy and reliability of the estimates. As we saw with SIA coverage estimation, administrative data (based on health service provider registries), faces issues with target populations, thereby limiting the accuracy of coverage. Moreover, survey data is typically sparse and only includes information on a small proportion of areas, often biased to areas with good RI services. The routine surveys that are typically conducted include: EPI cluster survey, the UNICEF Multiple Indicators Cluster Survey (MICS) and the Demographic and Health Survey (DHS).

As with estimating SIA coverage, non-polio AFP cases can provide representative and reliable estimates of RI coverage at fairly fine geographic levels. The estimated RI coverage for each non-polio AFP child is based on the recorded OPV dose history of that child and the expected 3 RI OPV doses the child should have received through RI services. However, as noted for SIAs, OPV doses are often not separated into those received through RI versus SIAs (in select regions), making inferences difficult.

Definitions

Administrative data: all countries report their coverage based on administrative data, which is based on administrative records from health facilities and is collected across all geographies (a separate mechanism is not required). This ensures a consistent measure of coverage across sub-units of geography (e.g., districts) in a country to enable comparison between areas, and over time.

Independent monitoring (IM): is one method of post-SIA evaluation. IM occurs through door-to-door visits or checking children in community markets or known gatherings. IM is often a method of convenience sampling or sampling in specific targeted areas and is likely not fully representative of the coverage in the entire population. The results of IM produce a coverage level estimate typically at a second administrative level (e.g., district).

Lot quality assurance sampling (LQAS): a method that assesses the performance following a specific SIA in pre-defined areas known as "lots". In each lot, 60 children are sampled in six different clusters, each of 10 children), with selection based on a pre-defined methodology. This method focuses at a finer spatial resolution but you do not estimate coverage, what you get is a flag indicating how well the area performed (in a pass/fail categorization with either 4-5 categories).

Calculations

Administrative coverage = number of children vaccinated / target population

Missed children proportion = number of children missed / target population

Still missed children proportion = number of children still missed (after catch-up activities) / target population

Independent Monitoring (IM) coverage = number of children vaccinated / number of children checked

LQAS passed lots proportion (this is not a measure of coverage) = number of passed lots in a specific geographic area / total number of lots in a specific geographic area

SIA coverage based on non-polio AFP cases = number of OPV SIA doses received / number of OPV doses expected based on SIA calendar

These can all be turned into a percent (%) by multiplying the proportion by 100%.

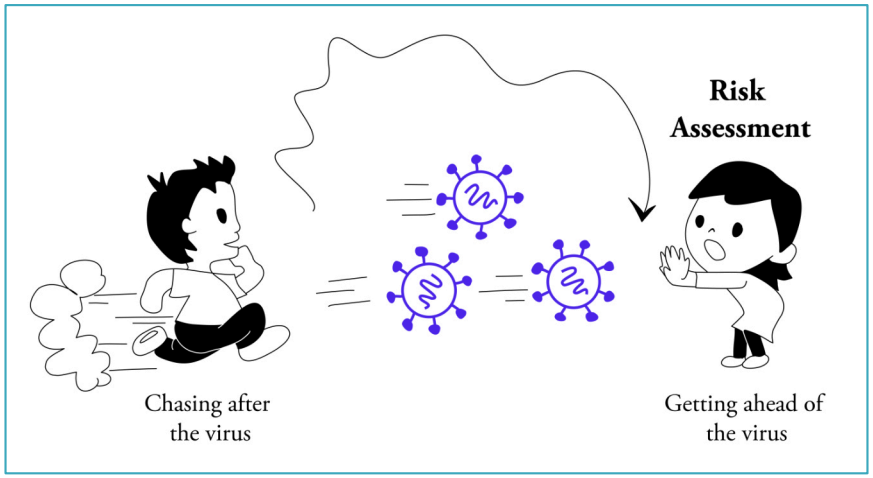
13
Risk assessment & Vaccination response

It was October 2015 and I had just landed in Pakistan for the first time. I was excited and couldn't wait to practically apply the work I had been doing. At the time, I was doing my PhD at Imperial College London (ICL) in the infectious disease epidemiology department, with a focus on modelling poliovirus transmission in Pakistan and Afghanistan. As the WHO collaborating institute for polio analysis and modelling, the ICL team worked on projects that directly informed global and national-level policies. Up to this point, while at WHO in Geneva, I had worked on many countries, including Nigeria and India. However, by 2014, it was clear that Pakistan and Afghanistan would pose the greatest challenge to eradication, and therefore it was decided that my PhD would focus on Pakistan and Afghanistan. I fell in love with Pakistan the minute I arrived. The NEOC was welcoming and engaging, and I had never felt so at home (it is a feeling I still get to this day whenever I land in Pakistan). My first trip in 2015 focused on assessing risk and designing optimal vaccination strategies for WPV1 and cVDPV2 (as ultimately did my PhD). For WPV1, assessing risk was critical for devising the SIA plans for the upcoming year. For cVDPV2 it was a pivotal time because it was leading up to OPV2 withdrawal and there was a requirement to strengthen serotype 2 immunity. Pakistan already had a very tight

SIA schedule, so figuring out how many tOPV rounds needed to be incorporated into the strategy, without compromising on serotype 1 immunity, was essential. It was a balancing act between ensuring sufficient serotype 2 immunity to mitigate risk against cVDPV2 outbreaks post OPV2 withdrawal, without compromising on the efforts to eradicate WPV1 (as tOPV has a lower serotype 1 efficacy compared to bOPV, but bOPV does not include any serotype 2 vaccine). The experience taught me how important it was to work collaboratively with country teams throughout the process, not only to capture context specific information and insights but ensure an iterative process of feedback and refinement. This first trip was followed by subsequent trips and then eventually a move to Pakistan. I have since spent many years working on risk assessments and devising optimal response strategies for WPV1 and cVDPV2 (including during the 2019 cVDPV2 outbreak in Pakistan and Afghanistan, as well as for other countries in the Eastern Mediterranean Region), now applying practical application and context realities. In the Chapter that follows, I will go through the basic principles of assessing risk and considerations for devising optimal vaccination response strategies.

Why is risk assessment important? Poliovirus spreads rapidly through populations and in order to interrupt the chain of transmission, it is critical to get ahead of the virus (**Figure 18**). We must remember that poliovirus is highly asymptomatic (i.e., we are only seeing the tip of the iceberg in the form of cases and ES is not located everywhere). Therefore, finding ways to determine where the virus currently is and predicting where it will go is essential for effective planning and allocation of resources.

Figure 18. Getting ahead of poliovirus transmission through risk assessment.



In endemic countries, risk assessments are used to determine the geographic scope of sub-national SIAs (i.e., sub-national immunization days, SNIDs). While the entire country is immunized multiple times throughout the year during national immunization days (NIDs), additional SIAs are implemented in higher-risk areas. These areas can be at risk for a variety of reasons, which we will go through in detail below. Typically, in endemic countries, SIAs take

place every 6-weeks throughout the year. Procuring sufficient vaccine and ensuring resources are in place for repeated large-scale SIAs takes months of planning and coordination. Therefore, accurately predicting risk in order to plan appropriately scoped SIAs limits modifications required when the time comes for implementation (which can be difficult).

In outbreak countries, it is perhaps even more important to get ahead of the virus and ensure an appropriate scale is targeted. These countries often have lower levels of population immunity due to the reduced frequency of SIAs and capacity to conduct quality outbreak response. This is particularly important in the cVDPV2 context, due to lower baseline levels of serotype 2 immunity (resulting in faster spread of virus), and risk of seeding more cVDPV2 from an inadequate OPV2 response (as will be discussed later in the Chapter).

Before we can review how to approach a poliovirus risk assessment, let's start by considering the key factors that contribute to poliovirus transmission…

Poliovirus risk factors

There are certain factors that make poliovirus more likely to thrive, and spread both within and between populations. These are critically important to consider when devising any strategy to mitigate risk and plan a vaccination schedule or response.

Below are 10 important risk factors for poliovirus transmission (summarized in **Table 10**):

1. **Low population immunity.** The lower the population immunity, the higher the number of susceptible children that can be infected

with poliovirus and the more likely it is to spread within a population. This is particularly problematic when you have pockets of susceptibles clustering in close proximity (e.g., resistant or under-served community), increasing the probability of having a large focused outbreak that can then spread to other areas.

2. **Low RI coverage.** RI coverage provides a foundation of immunity that mitigates against risk of poliovirus transmission. It consistently comes out as one of the strongest predictors of poliovirus transmission. While RI coverage is incorporated when estimating overall population immunity, we often consider RI separately as it can be a proxy for other components of the health system or utilisation patterns that are more difficult to quantify.

3. **Low SIA coverage.** Given that RI coverage is poor in many of the highest risk geographies, high SIA coverage plays a critical role in mitigating against risk of poliovirus transmission. However, SIA coverage is not always strongly correlated with poliovirus risk (unlike RI coverage), as it can be difficult to quantify. Moreover, there are various measures of SIA quality (as discussed in **Chapter 12**) and they are often not aligned or particularly reliable (with coverage greater than 100% in areas with continued poliovirus transmission). While the magnitude of SIA coverage estimates are not always helpful in predicting risk, considering trends over time can help provide insights into the change in risk of an area.

4. **Poor sanitation and hygiene.** Since poliovirus is a faecal-oral transmitted disease, it is spread in areas where the chances of a child coming into contact with poliovirus-infected faeces is high. Therefore, areas with poor sanitation and hygiene are at greatest risk of poliovirus transmission. This can be difficult to quantify but there are various multidimensional indices (e.g., water, sanitation

and hygiene [WASH] index) that use a range of indicators to create summary estimates in an area.

5. **High population size and density.** The higher the population size and density, the more likely it is for contact to occur between susceptible children and infectious material, thereby more readily propagating the chain of poliovirus transmission. This increases the immunity threshold required to interrupt transmission (once it occurs) and is often why the areas at greatest risk are those with very high population sizes and densities (e.g., Karachi, Pakistan).

6. **High rates of malnutrition, diarrheal illness and prevalence of other enteric infections.** These factors increase risk of poliovirus transmission by reducing the efficacy of OPV in the population (by reducing a child's ability to mount an effective immune response). Therefore, when these factors are prevalent, they decrease the impact of OPV SIAs on the immunity of the population, necessitating more OPV SIAs to achieve a certain level of immunity.

7. **High birth rate.** High birth rates rapidly increase the number of susceptible children that could become infected with poliovirus, thereby increasing risk of poliovirus transmission. This is particularly problematic in the context of low RI coverage, as children being born are not receiving the OPV and IPV doses they are expected to receive in the first year of life.

8. **Historic polio cases and detections.** Areas with historic polio cases or persistent detections are often flags for poliovirus risk, as there are certain characteristics of the areas that make them more susceptible to poliovirus transmission.

9. **High population movement and/or connectivity with other populations.** In populations that are highly connected, with substantial population movement, the chances of an infected child spreading poliovirus is more likely. It also makes assessing risk and getting ahead of the virus more challenging. In addition to spreading virus, children on the move can be more easily missed from vaccination campaigns. That is why additional strategies have been implemented to track and reach these populations on the move.

10. **Inaccessibility (or sub-optimal SIA delivery).** Areas that are hard to reach, have sub-optimal SIA delivery (e.g., site-to-site versus house-to-house) and/or that have limited information are at great risk of clustering of susceptibles and undetected transmission. They are also less likely be able to implement successful SIAs. While this may be reflected in SIA coverage, coverage estimates may not fully reflect the risk, especially in the context of limited access/information.

Other factors that are important to consider but must be carefully incorporated to ensure the correct inferences are made:

Surveillance sensitivity. In actuality, low surveillance sensitivity increases risk of missing early detection and having poliovirus spread undetected, ultimately resulting in a larger outbreak. However, a word of caution when incorporating surveillance sensitivity into any risk prediction, as with improvements in surveillance, there is an increased probability of detecting transmission and therefore a positive association is typically observed (i.e., increased

non-polio AFP rate increases the probability of detecting cases, and therefore perceived risk).

Number of SIAs. While one might think that with an increasing number of SIAs, the risk would decrease, this is often not what is observed in practice. SIAs are typically biased to high-risk areas so we often observe the inverse association — increased number of SIAs correlated with increased risk, which can be misleading. Therefore, a word of caution when considering number of SIAs when predicting risk of poliovirus.

Additional risk factors for cVDPV

While the risk factors for cVDPV are largely consistent with those for WPV, there are additional factors that must be carefully considered. Given the risk of seeding more cVDPV through the use of OPV, the additional factors are those that increase risk of cVDPV emergence, namely poor quality (i.e., low vaccination coverage in the targeted population), insufficient scope (i.e., targeted geographic area not large enough) and lengthy delays between responses. When the quality of OPV response is insufficient there may be clustering of susceptibles that can fuel the chain of transmission leading to a cVDPV emergence. Similarly, if the scope of response is insufficient, there is a risk of emergences in areas not targeted with the OPV response. Furthermore, if a second OPV round is substantially delayed, the immunity of the first round may not be sufficient to mitigate the risk of emergence in the targeted area.

Table 10: Risk factors for poliovirus transmission.

Poliovirus risk factors	Details
Low population immunity	The lower the population immunity, the higher the number of susceptible children that can be infected with poliovirus, and the more likely it is to spread within a population.
Low RI coverage	RI coverage provides a foundation of immunity that mitigates risk against poliovirus transmission. It consistently comes out as a strong predictor of poliovirus transmission. It can be a proxy for other components of the health system and utilisation that are more difficult to quantify.
Low SIA coverage	Given that RI coverage is poor in many of the highest risk geographies, high SIA coverage plays a critical role in mitigating risk against poliovirus. SIA coverage can be difficult to measure and has not always had a strong correlation with poliovirus risk.
Poor sanitation and hygiene	Since poliovirus is a faecal-oral transmitted disease, it is spread in areas where the chances of a child coming into contact with faeces containing poliovirus is high.
High population size and density	The higher the population density, the more likely it is for contact to occur between susceptible children and infectious material, thereby more readily propagating the chain of poliovirus transmission.
High rates of malnutrition, diarrheal illness and prevalence of other enteric infections	This makes it more difficult for a child to mount an effective immune response, even after a large number of OPV doses.
High birth rate	This rapidly increases the number of susceptible children in the population that could become infected with poliovirus. This is particularly problematic in the context of low RI coverage.

Historic polio cases and detections	Areas with historic cases or persistent detections are often flags for risk, as there are certain characteristics of the areas that make them more susceptible to poliovirus transmission.
High population movement and/or connectivity with other populations	In populations that are highly connected, with substantial population movement, the chances of an infected child spreading poliovirus across long distances is more likely, and it also makes assessing risk and getting ahead of the virus more challenging. In addition to spreading virus, children on the move can be more easily missed from vaccination campaigns.
Inaccessibility (or sub-optimal SIA delivery)	Areas that are hard to reach, have sub-optimal SIA delivery (e.g., site-to-site versus house-to-house) and/or that have limited information are at great risk of clustering of susceptibles and undetected transmission. They are also less likely to be able to implement successful SIAs.
Other factors (requiring careful consideration)	
Surveillance sensitivity	In actuality, low surveillance sensitivity increases risk of missing early detection and having poliovirus spread undetected, ultimately resulting in a larger outbreak. However, with improvements in surveillance, there is an increased probability of detecting transmission and therefore a positive association is typically observed (i.e., increased non-polio AFP rate increases the probability of detecting cases, and therefore perceived risk).
Number of SIAs	SIAs are typically biased to high-risk areas so we often observe the inverse association — increased number of SIAs correlate with increased risk, which can be misleading. Therefore, a word of caution when considering number of SIAs when predicting risk of poliovirus.
Additional risk factors for cVDPV	
Poor quality, scope and timeliness of OPV response	When the quality of OPV response is insufficient there are sufficient clustering of susceptibles that can fuel the chain of transmission leading to a cVDPV emergence. Similarly, if the scope of response is insufficient, there is a risk of spread and emergences in areas not targeted with the OPV response. Furthermore, if a second OPV round is substantially delayed, the immunity of the first round may not be sufficient to mitigate the risk of emergence in the targeted area.

Now that we know what risk factors are important to consider, let's go through the basic principles of determining poliovirus risk. We will also review two commonly used methods to determine poliovirus risk, each with different strengths and applications.

Determining poliovirus risk

How does one assess risk of poliovirus? We will first consider risk of WPV1 since risks for cVDPV2 have some different considerations.

To determine risk of an outbreak of WPV1, there are six key questions to ask yourself (summarized in **Table 11**). These can be sub-divided into immediate risks and longer-term risks. Note: when designing the response to these risks, one can plan for a multi-staged approach targeting the immediate risks first and then incorporating longer-term risks once additional planning can take place (since it will likely need to increase geographic scope); keeping in mind how quickly the longer term risks will likely become a priority.

Immediate risks

1. **Where is the virus right now?** Start out by identifying where the epicenter (central point) of transmission is located, along with the extent of transmission. To do this you would look at the surveillance information (i.e., AFP and ES data), as outlined in **Chapter 10**. While poliovirus is highly asymptomatic, there is typically a signal — either a cases (or clustering of cases) or repeat positive ES detections (perhaps across multiple sites in a district).

2. **How likely will transmission be sustained in the current location?**

This is where the risk factors we explored come into play. Go through each of the risk factors outlined above to determine what the risk of sustained transmission is in the current location. For example, ask yourself: "what is the population immunity in the current location? Is the RI system strong? Is the location densely or sparsely populated? Are there challenges with access to vaccination? Is sanitation particularly problematic in the area? Are there pockets of resistant communities impacting SIA coverage?" Considering the different risk factors for poliovirus will give you a strong indication of how likely transmission will be sustained in the identified location.

3. **How likely will it be to control transmission in the current location?** Now that we have an idea of the likelihood that transmission will be sustained based on the various risk factors, we must consider how likely it will be to control transmission in the current location. Ask yourself: "What is the level of SIA coverage that is likely to be achieved?" This can be based on historic estimates of SIA coverage. If coverage is expected to be low, consider how many rounds would be required. Are there pockets of vulnerable children with low coverage expected? Special strategies targeting these groups could be devised.

<u>Longer-term risks</u>

4. **Where is the virus likely to go and how quickly?** Are people travelling from the epicenter of transmission? Consider movement patterns, areas with strong connectivity (e.g., due to culturo-linguistic links, economic reasons) and when those movements typically take place. Is there an upcoming festival or event that will result in movement to other locations? What about seasonal

migration? Are the specific locations where people have historically moved? Are there certain factors that have halted movement between certain locations? The "how quickly" part of this will dictate whether this is an immediate or longer-term risk. Some countries have transit points where they vaccinate children. This may also be considered when thinking whether virus will move from one location to another.

5. **How likely will the virus result in sustained transmission in these locations?** Just having strong movement links with the epicenter of transmission doesn't necessarily mean an area is at risk. It is important to consider the specific risks in each connected location, as we did for 2 above. For example, if there is movement into an area from the epicenter of transmission and that area has very high levels of immunity, it would not be considered high risk. We see this often in Pakistan, whereby the most densely populated and highly-connected province (i.e., Punjab) receives the most number of importations of poliovirus, and yet due to its consistently strong RI coverage (and subsequent high immunity), has a low risk of sustained transmission. Moreover, if there are very few people living in an area and they are all sparsely populated, even if there is movement of poliovirus into the area, the chances of the virus reaching enough susceptible children to sustain transmission is likely low.

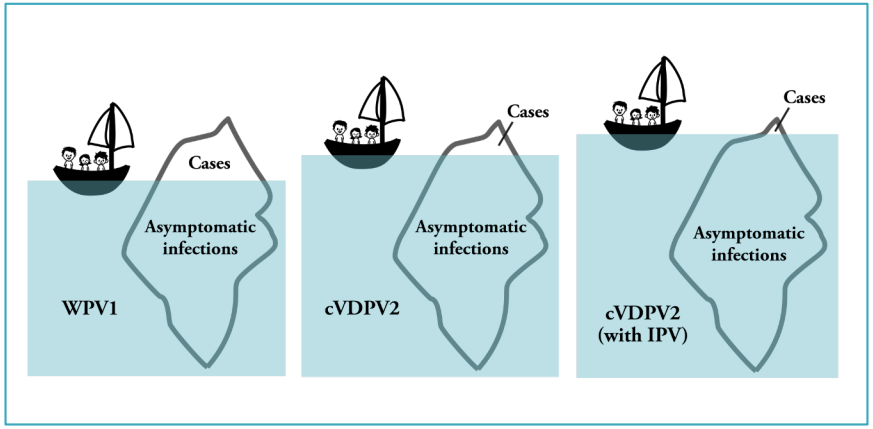
6. **What is the likelihood we will be able to stop it in these locations?** Here again we are referring to the expected SIA coverage in these locations and the speed at which the SIAs can take place.

Special considerations for cVDPV2 risk

For cVDPV2, the assessment of risk is slightly different since serotype 2 mucosal immunity is extremely low. Therefore, the longer term risks now become a priority since the virus will spread rapidly in areas of low immunity. You would repeat the same steps as for WPV1 but the speed and scope (in addition to quality) of response are more important for cVDPV2. You could still consider a two-staged approach, with a fast focused response followed by a larger response, but the time frame will need to be as short as logistically feasible, given that cVDPV2 will spread faster in most settings due to the extremely low serotype 2 mucosal immunity (apart from areas that were recently vaccinated with OPV2).

Moreover, unlike for serotype 1, the difference between mucosal and humoral immunity is very large for serotype 2 since we are using IPV in RI (which will give serotype 2 humoral immunity) but no longer using OPV2 (which gives serotype 2 mucosal immunity). What that means is that you will tend to see fewer cases than expected given a certain amount of infection for cVDPV2 (because children will be immune to paralysis given their humoral immunity, but still be transmitting the virus due to low/no mucosal immunity). Given that you already get more infection per case for cVDPV2 than with WPV1 (2000 versus 200, respectively), the tip of the iceberg gets much smaller **(Figure 19).** This will potentially allow transmission to go undetected in areas without strong ES, making it much more difficult to determine the extent of transmission (and where the risks truly are). When determining risk, you would want to consider what the IPV coverage (either RI or SIA) is in the area. If you have some indication of cVDPV2 transmission in an area that has high IPV coverage, the transmission is likely higher than what is being detected (you may be seeing very few cases spread out geographically).

Figure 19. Polio cases for the same number of infections.



Additionally, use of OPV2 poses a risk of creating more cVDPV2 outbreaks in areas with low serotype 2 mucosal immunity. This is why scope and timing (and quality) of OPV2 responses is particularly important. Also, while conducting an SIA with OPV2 must be done quickly, it faces additional challenges as there is a formal process of approval to release OPV2 vaccine (due to its risks).

Table 11: Considerations for risk of WPV1 and cVDPV2.

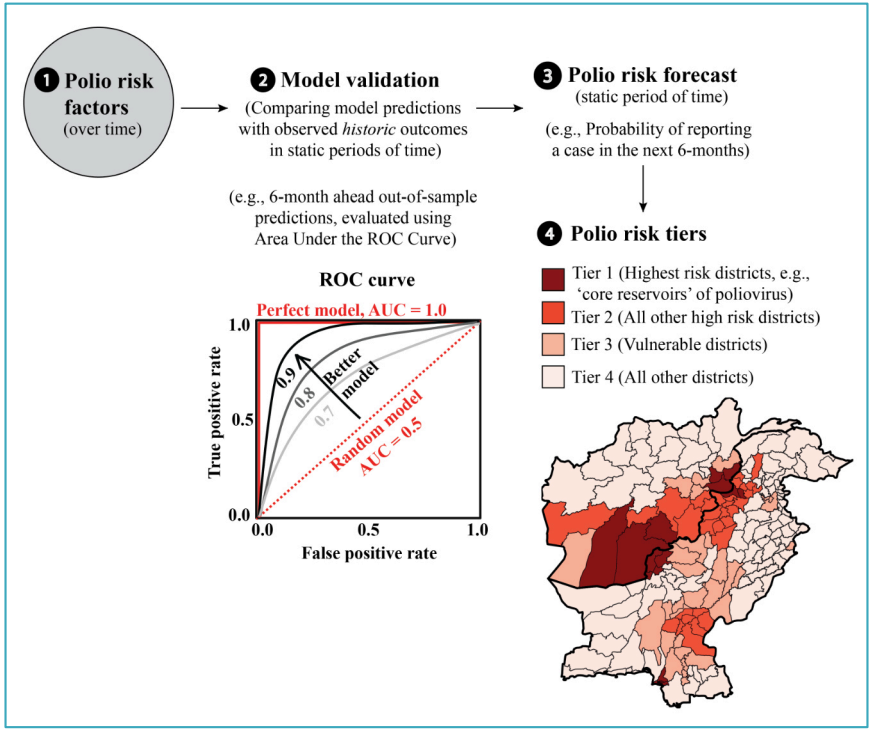
Question	Considerations for WPV1	Additional considerations for cVDPV2
Immediate risks		
Where is the virus right now?	Surveillance information – clustering of polio cases and/or multiple ES positive samples in single or multiple sites	More difficult to detect outbreak because of greater gap between mucosal and humoral immunity; and more infections per case for cVDPV2 than WPV1. Consider IPV coverage to determine whether it is masking the extent of transmission (because preventing paralysis). Determining the entire area of cVDPV2 transmission can be difficult but very important (more than for WPV1).
How likely will the outbreak result in sustained transmission in current location?	Risk factors, including immunity of the population	Because serotype 2 mucosal immunity is extremely low everywhere (apart from areas that already had OPV2 responses), you can assume that any detection of cVDPV2 will result in sustained transmission.
How likely will it be to control transmission in the current location?	Expected SIA coverage; feasibility of conducting an SIA quickly	OPV2 is an effective vaccine and can stop the outbreak of cVDPV2 if targeting the entire area of transmission. Conducting an SIA with OPV2 must be done quickly but faces additional challenges due to the formal process of approval to release OPV2 vaccine (due to its risks).
Longer-term risks		
Where is the virus likely to go and how quickly?	Movement patterns; transit vaccination on the way to these locations	This now becomes an immediate priority since immunity is extremely low (especially mucosal immunity) and therefore cVDPV2 spreads quickly.
How likely will the virus result in sustained transmission in these locations?	Risk factors, including immunity in these other locations	Given the low serotype 2 immunity everywhere (apart from areas with recent OPV2 responses), cVDPV2 will spread rapidly and result in sustained transmission.
What is the likelihood we will be able to stop it in these locations?	Expected SIA coverage in these places and speed at which SIAs can take place	OPV2 is an effective vaccine and can stop the outbreak of cVDPV2 if targeting the entire area of transmission. Conducting an SIA with OPV2 must be done quickly but faces additional challenges due to the formal process of approval to release OPV2 vaccine (due to its risks). Use of OPV2 poses a risk of creating more cVDPV2 outbreaks in areas with low serotype 2 mucosal immunity. That is why the scope of OPV2 is particularly important — it needs to be big enough to stop the current cVDPV2 outbreak but no bigger because of the risks of creating more cVDPV2.

Methods for determining poliovirus risk

There are two different methods commonly used in polio to formally predict poliovirus risk, each with its strengths and limitations.

The **first** is using statistical models to predict polio risk and is often used for planning of SIAs **(Figure 20)**. It typically provides a static picture of risk in a certain period of time (e.g., the next 6-months) within a certain geographic unit (e.g., district or province), based on various estimated risk factors. It takes data from the past and explores the relationship between various risk factors and the outcome (i.e., typically WPV1 cases), and uses a model to predict risk over a certain period of time. It checks that the predictions are reasonable, using historic predictions and outcomes, to provide more reliability to the predictions in the future we have yet to observe. The outcome is often a probability that a certain geographic unit with report at least 1 WPV1 case in the next 6-months. The greater the probability, the greater the risk. Each geographic unit would have a distinct probability based on its historic data, and therefore each area would have a certain risk. Geographies can be grouped based on risk, which is often what the SIA plans are based off of, as SIA plans are typically grouped into 4 tiers with different strategies for different tiers of risk.

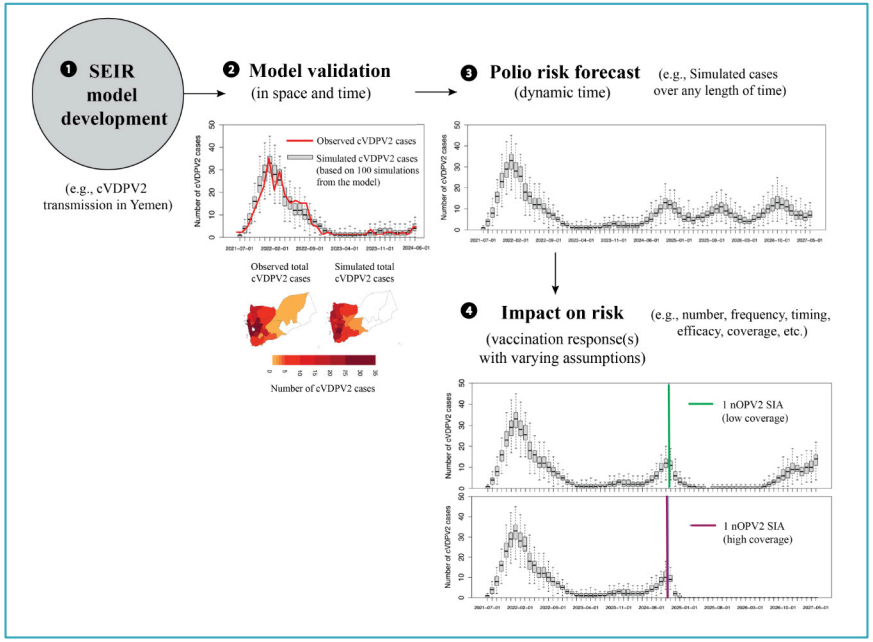
Figure 20. Static polio risk forecast (e.g., Pakistan and Afghanistan).



The **second** is to model poliovirus transmission itself, which is more dynamic and allows for forward simulations over longer periods of time **(Figure 21).** It also allows for a lot more flexibility in exploring optimal vaccination response scenarios. The transmission model attempts to capture as closely as possible the reality of the dynamics of children moving through different states of susceptible, exposed, infected and recovered (commonly referred to as an SEIR model, with each state called a compartment). Based on what we know about poliovirus natural history, vaccine efficacy, RI and SIA coverage, vaccination schedule, waning rates, birth rates, population size and

movement patterns, we can create a model and validate it based on historic data to ensure the model is able to replicate what we've seen in the past. Often the model is validated based on historic daily or weekly case data to ensure it reliably captures reality. The validation process typically goes through an iterative process of checking various estimates in the model (mostly rates between each of the SEIR compartments) and determines the estimates that maximise the likelihood of the case data given the model (with those combination of rates). Once you have a model you feel confident replicates reality, you can use it to simulate transmission dynamics moving forward. Then adjustments can be made to the response conditions (i.e., number of SIAs, SIA coverage, scope of responses, type of vaccine used, etc.) to see what strategies are needed to stop transmission (or explore what would happen if you stopped vaccinating in certain areas). This second method is particularly useful in the cVDPV2 context, because of the lower case to infection ratio (i.e., more infections per case), meaning that for every case you have thousands of infected children. Devising an appropriate response strategy is also more critical, given the risk of seeding more cVDPV2 (in contrast to the approach in WPV1 eradication, where there are limited risks with large-scale responses).

Figure 21. Dynamic polio risk forecast (using SEIR model) (e.g., Yemen).



Vaccination Response

Now that we know where the risks are — both the immediate and longer-term risks — we need to come up with a vaccination response plan. When you have an understanding of where the risks are, the geographic scope of response is fairly straightforward, at least for WPV1. The question comes in whether you want to keep each round the same size or conduct the first round just where the immediate risks are and the subsequent rounds where the immediate and longer term risks are. It is often about trading off speed versus quality versus size — it is easier to plan for a small focused response and therefore this can

be done quickly. If coverage is expected to be poor, multiple additional rounds may be required (however, really it would be important to come up with a way to increase coverage, but realistically this may not be feasible; whether the extra rounds reach only the same children may be often the case).

Additionally, for serotype 1, if you want to stop an outbreak you would want to choose the vaccine with the greatest efficacy. There is only a marginal difference in seroconversion between mOPV1 and bOPV; however, mOPV1 has been shown to produce a stronger antibody response. IPV is the most effective vaccine at protecting from paralysis and while it does not directly induce mucosal immunity (needed to stop transmission; as was discussed in **Chapter** 7), it is highly effective at boosting waned mucosal immunity (more so than another OPV dose) in children previously exposed to OPV. In endemic countries, given the extensive use of OPV, IPV is a great tool to not only protect children effectively from paralysis but also to boost mucosal immunity that has waned (as has been demonstrated in Pakistan). The challenge of implementation of IPV does pose some drawbacks; however, acceptance has been shown to be high.

Special considerations for cVDPV2 response

For cVDPV2, the outbreak response strategy is much more complicated than for WPV1 and requires careful consideration, given that the primary tool for stopping the outbreak (i.e., OPV2) is what caused the outbreak in the first place. As we discussed in **Chapter 2**, cVDPV2 is caused by OPV2 spreading from child-to-child in settings of low serotype 2 mucosal immunity. In the current global context of very low serotype 2 immunity levels, the use of OPV2 poses a risk of

further seeding of cVDPV2. Therefore, the response must be big enough to stop the cVDPV2 outbreak but no bigger given the risk of seeding even more cVDPV2. Seeding of cVDPV2 typically occurs when outbreak response with OPV2 is of insufficient quality, scope and timing, enabling vaccine virus to spread through susceptible populations, replicate unimpeded and lose its attenuating mutations. While the risk of seeding more cVDPV2 is a very important one to consider, the immediate risk of the cVDPV2 outbreak tends to outweigh any longer-term risk of additional seeding. This is because of how explosive the cVDPV2 outbreaks can be as most children under the age of five have never received any OPV2, resulting in a fully susceptible populations (apart from areas that have conducted OPV2 responses).

In addition to OPV2, IPV has a role to play in cVDPV2 outbreak response. IPV is very effective at preventing paralysis and could substantially reduce the case burden from the outbreak (and provide time to mount an effective OPV2 response, without the immediate consequences of cases). There are many areas that have used OPV2 over the past few years and therefore, use of IPV in these areas would boost mucosal immunity. However, it would have little impact on transmission in places that have not responded to cVDPV2 outbreaks since 2016.

The outbreak response strategy for cVDPV2 often comes down to the trade-offs between immediate versus longer term risks. The immediate risk is the current cVDPV2 outbreak, whereas the longer term risks are the potential for seeding new cVDPV2 outbreaks from OPV2 use. The immediate risk is the greatest priority given how low serotype 2 immunity levels are and therefore the potential for explosive outbreaks that spread rapidly, resulting in very high case burden. This often outweighs any potential for future seeding of

cVDPV2, but both are important to keep in mind when devising appropriate outbreak response strategy.

Finally, given the risks of OPV2 use, there are strict requirements and processes in place for release of vaccine. The OPV2 advisory group typically reviewed risk assessments and outbreak response plans globally to ensure appropriate responses were being conducted, while mitigating risk. However, this led to substantial delays in release of vaccines and implementing responses. Moreover, vaccine supply constrains (both with mOPV2 and nOPV2) posed challenges with ensuring appropriate response strategies to stop cVDPV2 outbreaks. While many of these challenges have since been resolved, factors continue to hamper rapid implementation of effective cVDPV2 outbreak response.

Definitions

Risk assessment: a process of gathering information from multiple sources to understand and predict the risk of poliovirus transmission, with the intention of "getting ahead" of the virus in order to effectively plan and allocate resources. Poliovirus spreads rapidly and is highly asymptomatic — therefore, assessment of risk plays a critical role in interrupting the chains of transmission.

Risk factors: characteristics or factors of the population that are associated with a higher likelihood of poliovirus transmission. For poliovirus, these include: low population immunity; low RI and SIA coverage; poor sanitation and hygiene; high population size and density; high rates of malnutrition, diarrheal illness and prevalence of other enteric infections; high birth rate; historic polio cases and detections; high population movement and/or connectivity with other populations; and inaccessibility (or sub-optimal SIA delivery).

SEIR model: a model used to analyse the dynamics of poliovirus transmission, whereby the population is subdivided into susceptible (S), exposed (E), infected (I), and recovered (R) compartments. It is often used to predict the changes to risk under various assumptions, especially following vaccination campaigns (including modifications to the number and coverage of rounds, and/or choice of vaccine) in order to guide strategy and decision-making.

Conclusion. Final thoughts.

Since formation of the GPEI in 1988 there has been substantial progress, including >99.9% reduction in global WPV case burden, reduction in number of endemic countries from 125 to 2, eradication of 2 out of the 3 WPV serotypes (WPV2 last detected in 1999; WPV3 in 2012; WPV1 still circulating in Pakistan and Afghanistan) and withdrawal of the first OPV serotype (i.e., OPV2). Despite the remarkable progress, the GPEI has faced substantial setbacks and is struggling to cross the finish line.

The GPEI has failed to achieve its goal of eradicating WPV1 in Pakistan and Afghanistan. While substantial progress was demonstrated in 2021-22, since September 2023 there has been an expansion of transmission across both Pakistan and Afghanistan, and re-established transmission in historic reservoirs (i.e., Karachi, Peshawar, Quetta Block, Kandahar). Re-established transmission in these areas is a major setback and poses an increased challenge in achieving WPV1 eradication. In 2024, 99 WPV1 cases were reported in Pakistan and Afghanistan, with widespread transmission indicating that 2025 will be a challenging year. Drastic strategy changes are required to put the programme on track to be able to interrupt transmission in the 2025/26 low season. The rest of eradication efforts, including withdrawal of remaining OPV serotypes, depend on eradication of WPV1 on the shortest possible timeline. Any delay, results in continued need to fund the global programme at over $1 billion per year, which is continuing to lead to donor fatigue. Given that absence of WPV1 transmission is required for a three year period

before certification of eradication, the earliest eradication can be achieved is 2028/29. At the current level of transmission in Pakistan and Afghanistan, this timeline is optimistic and requires bold and swift decision-making to course correct.

The withdrawal of OPV2 in 2016 was a failure, resulting in continued and uncontrolled cVDPV2 outbreaks. Globally more than 3,600 cVDPV2 cases have been reported since the switch across 45 countries; with a total of 60 countries detecting cVDPV2. Since 2019-20, cVDPV2 has become endemic-like in many high-risk countries, especially in the African Region. While there has been progress demonstrated over the past couple of years, much work remains to be done. Currently, discussions around bOPV cessation are taking place, however, this hinges on eradication of WPV1 and elimination of all cVDPVs (including the ongoing cVDPV2 outbreaks and any persistent cVDPV1/3 in the year leading to bOPV withdrawal). Given the three year period required to certify eradication of WPV1 and elimination of cVDPV2, the earliest possible timeline for bOPV withdrawal is 2030 (based on an optimistic forecast of interrupting all WPV1 transmission at the end of 2025 and cVDPV2 at the end of 2026). The next two years will decide the fate of the GPEI, with the next 6-months critical to ensuring we are on the right course to achieve these optimistic targets.

In addition to eradication of WPV1 and control of cVDPV2, there is an increasing concern of cVDPV1 outbreaks, which have been detected in DRC, Madagascar, Mozambique, Yemen, Malawi and Congo. The potential for cVDPV1 (and less likely cVDPV3) will increase with the use of tOPV in the context of declining frequency of bOPV (or any type 1 OPV) SIAs. Careful planning is required in using tOPV in settings with infrequent SIAs and low RI coverage. This will

continue to be important as discussions are ongoing regarding the withdrawal of bOPV.

The current and remaining challenges to eradicating WPV1 include poor RI coverage, inaccessible areas, vaccine hesitancy and operational issues (especially sub-optimal campaign quality and modalities, i.e., site-to-site/mosque-to-mosque versus house-to-house). Very high immunity thresholds required to be achieved and maintained in many of the highest-risk geographies (e.g., Karachi, Peshawar, etc.), coupled with substantial population movement exacerbate these challenges. For cVDPV2, inability to close out outbreaks through effective outbreak response remains the biggest issue in interrupting transmission. Inadequate outbreak response has led to not only ongoing transmission but high cVDPV2 case burden. That was fuelled by a variety of factors, including the lack of urgency and narrative that cVDPVs are of lower importance than WPV. Moreover, despite the replacement of mOPV2 with the more-genetically stable nOPV2, seeding of new cVDPV2 poses continued concern in managing the ongoing transmission and re-seeding. In addition, poor RI infrastructure and resulting low coverage of IPV has contributed to high cVDPV2 case burden. Countries with strong RI coverage have reduced or fully prevented cVDPV2 cases, despite extensive ongoing transmission and sub-optimal outbreak response with OPV2 (e.g., Egypt). In most of the highest-risk countries, there has been limited progress in RI, with challenges in reaching adequate levels of coverage.

While there are many challenges to achieving global polio eradication (which includes interruption of both WPV and withdrawal of all OPVs), it is possible. However, we must recognise that the same strategies and ways of thinking that led us to this point will not lead us to eradication. Until some of the root issues are

resolved we will continue focusing on details without meaningful impact.

I believe that there are **six key foundational aspects that need to be addressed in order for us to achieve eradication**:

1. **Streamline accountability by making government fully accountable at all levels.** While GPEI has a role to play, it should play a more supportive and advisory role, as was always intended. Ensuring one line of responsibility and accountability from field to national level will ensure that there is always someone responsible for gaps or issues in an area. Currently, the responsibilities and accountabilities at each level are distributed amongst a number of staff from both government and partner agencies, creating confusion over roles and diffusion of responsibly.

2. **Integrate polio with EPI and health.** This is linked with the first point above, as when government takes full ownership of the programme, it will be the responsibility of health officials at the sub-national level, who also oversee EPI and health related services. While SIAs will still take place, they will be better coordinated and integrated with other health-related activities taking place, representing a more cohesive approach. This will also strengthen community acceptance as resistance is often fuelled by polio being the sole (and separate) focus in these communities.

3. **Strengthen the reach and coverage of IPV through every possible modality (i.e., fixed site, extended outreach, door-to-door strategies).** Considering out-of-the-box strategies and innovative approaches (such as house-to-house fIPV) could be game-changers to increase reach of vaccination in high-risk populations. These strategies must be carefully thought out to ensure impact where it

is most needed. While initiatives such as the Big Catch Up were intended to increase the reach of IPV, the impact will likely be limited in many of the highest risk areas due to the target group selected (i.e., zero dose across any antigen) and poor coverage.

4. **Focus on a back-to-basic approach, one that prioritises consistently achieving the essential principles for effective SIAs.** While innovation has a role to play, it is the basic principles that need to be consistently achieved across all areas. These include things like ensuring funds are available at the field level on the first day of the SIA to ensure vaccinators and monitors/supervisors are able to go where they need to, that data is used for action to ensure presence of vaccinators and monitors in the interior and remote areas, and training quality is sufficient to ensure implementers are empowered with the knowledge and skills to effectively do their job. As a programme, we tend to focus on adding innovations, instead of ensuring the basics are consistently achieved.

5. **Prioritise support for frontline workers.** While this is often discussed (and there is a strong awareness that this is a key issue that needs to be addressed), it is often considered amongst a sea of other topics that require solutions. This needs to be treated as the *top* priority, and immediate strategies implemented to ensure frontline workers are supported with the resources, finances and capacity building that is needed for them to effectively do their job. Without this we will not achieve eradication.

6. **Finally, better incorporate (and truly listen to) community perspectives when designing strategies.** This is critically important, especially in the final strongholds of the endemic countries. Currently, communities are pressured to receive the vaccine instead of listened to and supported. Communities

rightfully do not understand the sole and continued focus on polio, when their basic needs are not being met. While it is not directly under the polio programme's mandate to provide health related services to communities, we must remember that poliovirus is able to thrive in settings where these basic needs (i.e., clean water and sanitation) are not being met. Moreover, small improvements in the basic health needs of communities go a long way to building trust and acceptance. These don't need to be expensive, but smartly designed and executed. It is time to think outside-of-the-box and approach this as a collaborative effort with the many organizations working to improve the health of communities in the field. Truly understanding the needs of communities may also help with access issues or at least help with negotiations.

We are at a critical point in the polio eradication efforts and the decisions taken now will affect the course of one of the largest global health programmes in history. As the saying goes, history continues to repeat itself and therefore it is imperative for the GPEI to take a sobering look at the current situation and devise a new track forward to reach eradication.

The final thought I will leave you with is a call to action:

Let us collectively bring compassion and care back into the programme, especially for communities and frontline workers.

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Understanding Polio Fundamentals

When you work in a highly technical field but are in operations and not in research, it is helpful to have a handbook that translates the critical information you need to know into practical knowledge that you can easily apply to your area of expertise. Typically, literature on polio is written to the technical expert or global policy audience, which often excludes implementers at the country level. This is why I wrote Understanding Polio Fundamentals. This handbook will give you an in-depth understanding of the science behind the effort to eradicate polio in a way that is simple and easy-to-understand. Understanding the technical principles guiding strategy and policy will enable you to not only be more effective in your work, but also to make more informed decisions when faced with challenging or unexpected circumstances. My hope for this book is to empower you and all the true heroes of this global effort.

Photo by: Dan Abramovici

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