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Environmental surveillance system characteristics and impacts on confidence about no undetected serotype 1 wild poliovirus circulation

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Abstract

Surveillance for poliovirus during the polio endgame remains uncertain. Building on prior modeling of the potential for undetected poliovirus transmission for conditions like those in Pakistan and Afghanistan, we use a hypothetical model to explore several key characteristics of the poliovirus environmental surveillance (ES) system (e.g., number and quality of sites, catchment sizes, and sampling frequency) and characterize their impacts on the time required to reach high (i.e., 95%) confidence about no circulation (CNC95%) following the last detected case of serotype 1 wild poliovirus. The nature and quality of the existing and future acute flaccid paralysis (AFP) surveillance and ES system significantly impact the estimated CNC95% for places like Pakistan and Afghanistan. The analysis illustrates the tradeoffs between number of sites, sampling frequency, and catchments sizes, and suggests diminishing returns of increasing these three factors beyond a point that depends on site quality and the location of sites. Limitations in data quality and the hypothetical nature of the model reduce the ability to assess the extent to which actual ES systems offers benefits that exceed their costs. Thus, although poliovirus ES may help to reduce the time required to reach high confidence about the absence of undetected circulation, the effect strongly depends on the ability to establish effective ES sites in high-risk areas. The costs and benefits of ES require further analysis.

Keywords

Disease eradication; Infection transmission modeling; Poliomyelitis; Poliovirus; Disease surveillance; Environmental surveillance

1. INTRODUCTION

Since its launch in 1988 (World Health Assembly, 1988), the Global Polio Eradication Initiative (GPEI) achieved many milestones toward the global eradication of wild polioviruses (WPVs). Active surveillance reported no cases of paralytic poliomyelitis (polio) caused by serotype 2 WPV (WPV2) since 1999 (Global Polio Eradication Initiative, 2017), no polio caused by serotype 3 WPV (WPV3) since November 2012 (World Health Organization, 2018), and as of early 2018, only Pakistan, Afghanistan, and Nigeria continue

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to sustain indigenous transmission of serotype 1 WPV (WPV1) (Kew et al., 2014). The Global Certification Commission declared successful WPV2 eradication in September 2015 (Global Polio Eradication Initiative, 2015). This enabled the globally-coordinated switch in late April-early May 2016 from oral poliovirus vaccine (OPV) that contains attenuated strains of all three serotypes (i.e., trivalent OPV or tOPV), to bivalent OPV (bOPV), which only contains the attenuated strains of serotypes 1 and 3 (Hampton et al., 2016). This switch stopped the use of serotype 2-containing OPV (except for serotype 2 monovalent OPV released and used for emergency outbreak response). The current GPEI strategic plan (World Health Organization, 2013) calls for certification of WPV1 and WPV3 eradication following the interruption of transmission of all WPVs, which represents a requirement for the cessation of the last two serotypes of oral poliovirus vaccine (OPV) (Hampton et al., 2016). Consequently, the timing of certification influences the timing of a major global change in vaccination, with significant impacts on global costs and risks (Thompson and Duintjer Tebbens, 2015). However, observing the interruption of WPV transmission remains challenging because extended silent transmission can occur due to the asymptomatic nature of the vast majority of poliovirus infections (i.e., approximately 199 out of 200 susceptible individuals infected with WPV1 do not develop paralysis (Nathanson & Kew, 2010) and asymptomatic reinfection also occurs in individuals with immunity to polio disease) and surveillance gaps (e.g., WPV1 re-emerged in Borno, Nigeria in 2016 after nearly 3 years with no reported cases (Nnadi et al., 2017)).

A recent review of the polio environmental surveillance (ES) literature highlighted the lack of standardization in the development and design of poliovirus ES systems (Duintjer Tebbens, Zimmermann, Pallansch, & Thompson, 2017). Prior mathematical modeling studies explored the probability of undetected circulation of WPVs in the absence of reported cases or poliovirus detections by an ES system. Our 2015 study (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015) used a stochastic adaptation of a poliovirus dynamic transmission model (Duintjer Tebbens et al., 2013) and included an analysis of the 2013 serotype 1 WPV introduction into Israel followed by more than a year of transmission detected by the extensive ES system in Israel (Kalkowska, Duintjer Tebbens, Grotto, et al., 2015). The study considered the impact of acute flaccid paralysis (AFP) surveillance and ES on the confidence about no undetected poliovirus circulation as a function of time after the last detection through either system (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015). The results suggested that it takes up to 3 years without paralytic cases to reach 95% confidence about no circulation in the context of perfect (i.e., detecting every case) AFP surveillance (without ES). Less than perfect AFP surveillance implies longer times, while the addition of high-quality ES reduces the times to reach 95% confidence (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015). The GPEI generally considers 3 years of high-quality AFP surveillance with no reported polio AFP cases as providing sufficient confidence to certify the eradication of a WPV serotype. The development of ES raises questions about whether the criteria used to certify the world as free of WPV1 and/or WPV3 should include the time since the last detected event (i.e., either a polio AFP case or a positive isolate from an ES sample). We previously demonstrated that poliovirus transmission can continue to occur in the absence of cases, and that die out (i.e., clearance of the virus from the last excreting individual) will well occur after the last reported AFP case

(Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015). Evaluating the potential for ES to effectively increase confidence about no undetected circulation depends on understanding the extent to which the AFP and ES surveillance systems will detect transmission.

Using a model developed to characterize poliovirus transmission dynamics in Pakistan and Afghanistan (Duintjer Tebbens et al., 2018), which appear likely to become the last epidemiological region with WPV1 transmission, a subsequent analysis (Kalkowska, Duintjer Tebbens, Pallansch, & Thompson, 2018) focused on modeling the active use of some ES to detect the transmission of any and all live polioviruses (LPVs, include WPV, OPV, OPV-related, and vaccine-derived poliovirus (VDPV)). The circulation of LPVs remains complicated in Pakistan and Afghanistan as both countries continue to pursue WPV1 eradication and monitor the disappearance of serotype 2 LPVs. Using the same framework as a prior study (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015), the subsequent analysis (Kalkowska et al., 2018) used a more detailed approach to model the ES system, and explored the likely future confidence about the end of transmission in the absence of any epidemiological signals (i.e., after the last reported AFP case and/or detection of poliovirus in ES based on analysis of limited data available). We emphasize that our prospective modeling (Kalkowska et al., 2018) differs from and complements epidemiological modeling efforts that seek to characterize retrospective events using the currently available incomplete and/or inconsistent data (Mercer et al., 2017; Molodecky et al., 2017; O'Reilly et al., 2018). Building on our prospective analysis (Kalkowska et al., 2018), we sought to explore key assumptions about the ES systems and their impacts on the time required to reach high confidence about no circulation following the last detected event of WPV1 in conditions like those in Pakistan and Afghanistan. This analysis uses a hypothetical approach that allows us to explore the impacts of varying key ES system design choices. This hypothetical model does not consider the potential for ES systems to aid in the identification of specific individual poliovirus excretors (which has not been demonstrated successfully to date), and it represents an abstraction of the poorly-characterized actual ES systems that exist in Pakistan and Afghanistan (Kalkowska et al., 2018).

2. METHODS

We base our analysis on a deterministic, differential equation-based poliovirus transmission and OPV evolution model for Pakistan and Afghanistan (Duintjer Tebbens et al., 2018). We transformed the model into a stochastic model and expanded its characterization of the AFP surveillance and ES systems to estimate the confidence about no circulation after the last detection (Kalkowska et al., 2018). We divide the modeled population into 8 immunity states further subdivided into 5 immunity waning stages (Duintjer Tebbens et al., 2018; Duintjer Tebbens et al., 2013), and eleven age groups, which we combine into 3 preferentially mixing age groups (Duintjer Tebbens et al., 2018). We model all LPV infections using a 6-stage infection process and model OPV evolution using a 20-stage reversion process for both fecal-oral and oropharyngeal transmission (Duintjer Tebbens et al., 2018; Duintjer Tebbens et al., 2013). Following our prior work (Duintjer Tebbens et al., 2018; Kalkowska et al., 2018), we divide both countries into a general population and an under-vaccinated subpopulation. We further adopt the demographic model inputs, assumptions about poliovirus transmissibility and seasonality, and mixing between the four subpopulations

(Duintjer Tebbens et al., 2018; Kalkowska et al., 2018). For all analyses we used the mixing assumptions that reflect the "more" isolated under-vaccinated subpopulation (Duintjer Tebbens et al., 2018). The model characterizes both routine immunization (RI) and supplemental immunization activities (SIAs) (World Health Organization, 2013) based on historical information about the use of OPV and inactivated poliovirus vaccine (IPV), as summarized in Table 1 (see details elsewhere (Duintjer Tebbens et al., 2018)). We focus on the effect of ES strategies on the confidence about no WPV1 circulation within Pakistan and Afghanistan while considering bounds on the detection probabilities for the AFP surveillance system (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015), which we use as a metric to describe AFP quality. Given our focus on confidence about no WPV1 circulation, we assume Pakistan and Afghanistan use proactive strategies (Duintjer Tebbens & Thompson, 2018) to stop WPV1 such that looking for undetected circulation becomes relevant.

Our prior analysis suggested that the immunization plans as of late 2017 would not result in WPV1 eradication in the deterministic model for Pakistan and Afghanistan (Duintjer Tebbens et al., 2018), which leads to concern about achieving the goal of globally eradicating WPV1. As in our previous work (Kalkowska et al., 2018), we consider two alternative immunization scenarios that increase the relative SIA coverage in the under-vaccinated subpopulations compared to the general population in the same country by 0.20 or 0.15 from 2018 onward (i.e., "increased relative SIA coverage 0.20" or "increased relative SIA coverage 0.15," respectively). We use a previously-generated set of 1,000 distinct realizations of the stochastic model from which we recorded the following for each subpopulation: (1) the times when polio cases occur and (2) the infectiousness-weighted numbers of infectious individuals (EI) at each time step (Kalkowska et al., 2018). Polio cases may result in potential detections by AFP surveillance (i.e., if a stool sample taken from the case yields WPV1), and the presence of infections of individuals within a population may result in potential detections by ES (i.e., if the fecal waste of the infectious individual(s) ends up in the catchment area of an ES site with sufficient concentration for WPV1 recovery in an ES sample).

We estimate the probability of no circulation in each month since the last detected event (i.e., detection of WPV1 from an AFP case stool sample or identification of WPV1 from an ES sample) (Eichner & Dietz, 1996; Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015; Kalkowska et al., 2018; Kalkowska, Duintjer Tebbens, & Thompson, 2012). We define the confidence about no circulation as one minus the number of detected-event-free-periods of t months with ongoing WPV1 circulation divided by the total number of detected-event-free-periods of t months (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015; Kalkowska et al., 2018). We present the results in terms of the time when the confidence about no WPV1 circulation in Pakistan and Afghanistan first exceeds 95% (i.e., CNC95%) (Kalkowska, Duintjer Tebbens, Pallansch, et al., 2015; Kalkowska et al., 2018). In the absence of ES, the CNC95% values for AFP alone ranged from 1.42 years to 3.33 years, and with the addition of ES our previous analysis suggested CNC95% values from 0.7 years (i.e., 8 months) to 3.25 years with no detections, depending on the specific characteristics of the surveillance system (Kalkowska et al., 2018). We refer to the prior analysis for discussion about the limitations of the available data, which provided motivation for the use of an abstract and

hypothetical model for this analysis of tradeoffs (Kalkowska et al., 2018). With a CNC95% of one year apparently attainable by a well-performing ES system, we further present results in terms of the minimal combinations of ES characteristics (i.e., number of sites, sampling frequency, and catchment areas) required to achieve a CN95% of less than one year.

We describe AFP surveillance using the probability of detecting a polio AFP case in a series of sequentially detected AFP cases in a subpopulation (i.e., a cluster). We consider different case detection probabilities for the general and under-vaccinated subpopulations, with a lower-and upper-bound in both under-vaccinated subpopulations (Table 1) (Kalkowska et al., 2018). We use two previously-developed approaches to describe the ES system: the site-specific approach (SS) and the system-wide approach (SW) (Kalkowska et al., 2018). Briefly, the SS approach determines the probability of detecting poliovirus for each sampling site using the detection limit $\left(DL_{50}^{i}\right)$, defined as "the effective (i.e., infectiousness-weighted) number of infected individuals (EI) per person required in the catchment area of the site to achieve a 50% probability of detecting the virus" (Kalkowska et al., 2018). We determine the site-specific prevalence for ES sampling site i (EIi) proportionally based on catchment area population size (Kalkowska et al., 2018). The SW approach determines the probability of detecting poliovirus by any sampling site as a function of the total EI in all subpopulations with ES sites and the total catchment area from all ES sites in both countries. The coefficient C dictates how fast the probability increases from 0 (i.e., for 0% ES coverage) to 1 (i.e., for 100% ES coverage) for non-zero EI, with lower values resulting in a faster increase (due to the nature of the assumed exponential function, with the coefficient C in the exponent (Kalkowska et al., 2018)).

Since the model characterizes under-vaccinated subpopulations that preferentially mix abstractly based on various characteristics (i.e., not specifically linked to geographies) (Duintjer Tebbens et al., 2018), we cannot explicitly match the actual ES sampling sites to the modeled subpopulations. With this hypothetical model, we sought to develop simplified situations that would provide some context about the bounds of the information provided by ES, which most likely will represent a mixture of the three situations we used (Kalkowska et al., 2018). Consequently, we consider the following possible distributions of ES sites relative to the four subpopulations: (i) national sites (NS) (i.e., all ES sampling sites distributed evenly over the country), (ii) under-vaccinated subpopulation sites (US) (i.e., all ES sampling sites distributed evenly only in the under-vaccinated subpopulation of the country), and (iii) general population sites (GS) (i.e., all ES sampling sites distributed evenly only in the general subpopulation of the country) (Kalkowska et al., 2018).

The CNC95% estimates from our previous analysis (Kalkowska et al., 2018) depended on limited information about ES and the methods available to characterize the ES system. Given that the available data on catchment areas remains incomplete and/or inconsistent with expectations for the ES system (Kalkowska et al., 2018), we used a more hypothetical approach to explore the impact of different ES strategies for Pakistan and Afghanistan.

For this analysis, we characterized the ES system according to the number of sampling sites and their quality, catchment area, and sampling frequency. Specifically, to explore ES strategies, we consider a hypothetical ES system that uses from 1 to 20 sampling sites per

country. The estimated catchment areas in Pakistan and Afghanistan based on elevation maps (Novel-T Innovative Solutions) vary widely from very small (i.e., <1,000 people) to almost 1 million people. The upper limit remains consistent with published catchment areas for some urban, developing country settings (Deshpande, Shetty, & Siddiqui, 2003; Duintjer Tebbens et al., 2017). Therefore, we consider a catchment area of 1,000, and catchment areas between 10,000 and 100,000 people using increments of 10,000, and between 100,000 and 1,000,000 people using increments of 100,000. Thus, an ES system with 6 sites per country and a catchment area of 100,000 each covers 600,000 people per country and a total of 1,200,000 people for both countries.

Based on values fitted by comparing our transmission and surveillance model to observed isolation rates (Kalkowska et al., 2018), we consider four quality levels (i.e., good, medium, bad, or very bad) by varying the values of DL_{50}^{i} and C (see Table 1) for all sites simultaneously (i.e. all good sites versus all bad sites). Finally, we consider different sampling frequencies (f) ranging from 0 to 24 times per year (Table 1), with the sampling times evenly distributed over a year (e.g., for $f = 2$ per year, sampling occurs at six-month intervals for all active sites at the same time in June and December). We also explored the effect of varied sampling times within the year among sites (e.g., for $f = 2$ per year, sampling occurs six months apart in each active site but at different times in different sites, such as January and July, February and August, March and September, etc.) using the "increased relative SIA coverage 0.20" scenario with the lower bound AFP detection level in the under-vaccinated subpopulations and good ES quality.

3. RESULTS

The nature and quality of AFP surveillance and ES significantly impact the estimated CNC95% for Pakistan and Afghanistan, which we found varied from 0.2 years (i.e., 2 months) to 3.4 years over all considered combinations of AFP surveillance quality and ES strategies. Figures 1 and 2 show the CNC95% for WPV1 in Pakistan and Afghanistan for "increased relative SIA coverage 0.20" and "increased relative SIA coverage 0.15," respectively, as a function of catchment area size per site and number of sites per country using the lower-bounds (Figures 1a–c, 2a–c) and upper-bounds (Figures 1d–f, 2d–f) of the AFP case detection probabilities in the under-vaccinated subpopulations. While we evaluated all combinations of the ES model inputs in Table 1, we show only the worst ES performance with the SS approach to characterize the ES system (i.e., very bad quality and sampling frequency of 0 times/year in Figures 1a, 1d, 2a and 2d), the best ES performance with the SS approach (i.e., good quality and sampling frequency of 24 times/year in Figures 1b, 1e, 2b and 2e), and the best performance with the SW approach (Figures 1c, 1f, 2c and 2f).

As expected, the ES system performs the worst when the sampling frequency equals 0 times/year (i.e., in the absence of any ES) and the resulting CNC95% values in Figures 1a and 2a reflect the performance of AFP surveillance alone, regardless of the site quality level or the distribution of ES sites over the subpopulations. The CNC95% does not change with the GS distribution (i.e., putting all of the ES sites in the general population) regardless of quality or frequency since transmission happens almost exclusively in the under-vaccinated

subpopulations (results not shown). For the NS and US distributions of ES sampling sites, we see that both better site quality and more frequent sampling reduce the CNC95%. As mentioned, the under-vaccinated subpopulations sustain most of the transmission, thus placing all ES sites in those subpopulations (i.e., US distribution) naturally yields better results than distributing them nationally (i.e., NS distribution) with a reduction of up to 2.33 years in CNC95%, depending on all other modeling choices. The ES system performs the best using the US distribution with good quality and a sampling frequency of 24 times/year.

With the SS approach, the CNC95% improves equally with increases in both frequency and quality. For the SW approach the improvement appears slower (compared to the SS approach, due to the nonlinear nature of the SW approach (Kalkowska et al., 2018)), for both frequency and quality. Using small numbers of sampling sites per country and small catchment areas per site, the SS approach produces up to 1.75 years shorter CNC95% values compared to the SW approach (Figures 1b, 1e, 2b, 2e compared to Figures 1c, 1f, 2c, 2f, respectively). This difference decreases to 1 month with the increase in number of sampling sites per country and catchment area per site.

A separate analysis that varied the temporal distribution of sampling among the sites showed that spreading the sample times among different months in a year (e.g., to optimize the transportation and sampling processing logistics), may increase the CNC95% by up to approximately 0.5 years for very infrequent sampling (less than 2 samples/year), which creates sporadic, low coverage ES when combined with a small number of sites (less than 8) or low catchment area (less than 30,000 per site). On the contrary, the temporal distribution of sampling in conjunction with the higher number of sites (more than 8) and higher catchment area (more than 30,000) compensates for the low frequency and effectively decreases the CNC95% by up to 0.67 years. However, as the frequency increases, the effect reduces to 0.1 years (i.e., approximately 1 month), because shifting the sampling times among the sites in a dense ES system will lead to an overlap with the original schedule.

Table 2 shows that it may not be possible to reach a CNC95% of 1 year for WPV1 in the hypothetical model for Pakistan and Afghanistan regardless of the ES approach for very low sampling frequencies of less than 2 times/year. Depending on the levels of vaccination and the quality of AFP surveillance, the ES system requires a minimum of 2–6 samples per year and good site quality with all sites located in the under-vaccinated subpopulations (i.e., US) to achieve CNC95% values of less than a year. Once the site distribution becomes less precise (NS), the minimum frequency needs to broaden (e.g., 2–24 samples per year in Table 2). As ES quality decreases from good to very bad, the sampling frequency needs to further increase up to a level of more than 24 times/year, thus becoming not feasible (as indicated by an “x” in Table 2).

Figures 3 and 4 present the minimum catchment area per site required to reach CNC95% within one year for the “increased relative SIA coverage 0.20” and “increased relative SIA coverage 0.15” scenarios, respectively, and for combinations of the number of sites per country and sampling frequency that support reaching CNC95% within one year. Both figures use the lower-bound AFP case detection probability in the under-vaccinated subpopulations and compare the ES site distribution options for three ES quality levels

(good, medium, bad): SS-NS (Figures 3a–c and 4a–c) and SS-US (Figures 3d–f and 4d–f), using varied sampling frequencies. Figures 3 and 4 show that a trade-off exists between key ES choices about the number of ES sites, their catchment areas, and the sampling frequency. For example, Figure 3a shows that with 10 sites per country, increasing the sampling from 3 to 24 samples/year reduces the catchment area size required for each site for a CNC95% of less than one year by a factor of eight. Both figures further show that once the sampling frequency becomes large enough to attain a CNC95% of less than one year, further increasing the sampling frequency lowers the number of sites per country needed to maintain a CNC95% of less than one year for any given catchment area size. With increasing numbers of sampling sites, the minimum catchment area per site decreases to a point beyond which no advantages come from adding more sampling sites (i.e., diminishing returns).

Figures 3 and 4 illustrate that the point of diminishing returns depends on the location of sites and site quality. For example, with sampling 12 times/year and catchment areas of 10,000 people per nationally distributed site (i.e., NS), increasing the number of good quality sites per country beyond 12 results in diminishing returns for both considered scenarios and AFP surveillance levels. Using the same settings except with a more precise site distribution relative to where transmission occurs (i.e. US), the model shows diminishing returns for catchment areas of only 1,000 people per site (Figures 3a and 4a compared to Figures 3b and 4b, respectively).

4. DISCUSSION

The benefit of ES with respect to the confidence that it provides about the lack of poliovirus transmission appears highly dependent on critical components of the ES system and will vary with the level of AFP quality (i.e., the background ability to detect poliovirus transmission). Our systematic approach provides insights about the tradeoffs between ES system attributes (i.e., sampling frequencies, number of sites, quality, and catchment areas). These tradeoffs further depend on the population immunity to transmission and levels of vaccination, which suggests the need for frequent testing in under-served subpopulations and less value of sampling in general populations. Our model suggests that a CNC95% of less than one year may not be possible in Pakistan and Afghanistan in the context of low quality and/or low sampling frequency. However, while adding more sampling sites and/or increasing the catchment areas increases performance, our analysis also finds diminishing returns beyond a point with respect to the value of the information (independent of consideration of costs). The costs of poliovirus surveillance remain a significant concern, particularly as national governments will need to increasingly support (or secure external funding to support) the real costs (Duintjer Tebbens, Diop, Pallansch, Oberste, & Thompson, 2018) of any activities that occur throughout the remainder of the polio endgame.

Our analysis remains limited by the availability and quality of data (Kalkowska et al., 2018), and our framing and assumptions. The existing ES data remain incomplete (i.e., missing estimates) and inconsistent (i.e., surprisingly-low estimates) regarding the watershed population (i.e., catchment size) of specific sites (Kalkowska et al., 2018). Moreover, unlike for AFP surveillance, to the best of our knowledge, objective and universally accepted

criteria to evaluate the quality of the existing ES sampling sites do not yet exist. While the hypothetical characterization of ES sampling sites circumvents some of the data limitations, our results also remain limited to the space of possibilities that we explored (e.g., maximum number of sites of only 20 per country) and their abstract utility for actual field conditions and insights. Specifically, in real ES systems, the available options for ES sites will come with various sizes of catchment areas that depend on the conditions in the field (e.g., the existence of converging sewage networks), and countries cannot simply divide up the geography according to a target population size and find watershed areas and sampling sites that will match. In reality, large cities may represent ideal ES sampling sites because of the water and sewage management, but if these areas collect samples from the general population alone, they may not provide confidence about the absence of transmission nationally (i.e., for countries with significant heterogeneity in immunization coverage and surveillance quality).

Our model provides a simplified characterization of mixing between subpopulations that truncates very low level transmission and involves significant uncertainty (Duintjer Tebbens et al., 2018). In reality, limited transmission may occur stochastically, even in better-vaccinated communities, and may result in environmental detections in those communities (Alam et al., 2016). With respect to our assumptions, the use of a transmission threshold to approximate die-out instead of absolute 0 total infected individuals simplifies the transmission die-out dynamics (Duintjer Tebbens et al., 2018; Duintjer Tebbens et al., 2013). While use of a stochastic transmission model results in some variability in time when the prevalence hits the die-out threshold, in reality, transmission may stop stochastically before or after reaching this threshold, influencing the CNC95% estimates from this analysis. The SW approach also does not explicitly account for the dilution effect of polioviruses excreted into large catchment areas, and the SS approach does not explicitly model characteristics of the sewage system (e.g., flow rate, time delays), which should remain of topics of further empirical and modeling research (Hovi, Stenvik, Partanen, & Kangas, 2001; Ranta, Hovi, & Arjas, 2001). We suggest that the tradeoffs of ES quality, quantity, and catchment area size and sampling frequency combinations should provide useful insights about the potential impact of these factors on ES performance and should motivate improvements in data quality. Further analyses may better characterize the tradeoffs as data quality improves. In addition, mapping the quality descriptors (from very bad to good), which we characterized using assumptions fitted to the very limited and relatively low-quality available ES data (Kalkowska et al., 2018), does not map back to actual ES sites. Finally, review of the literature demonstrated a wide range of different types of sampling sites, the conditions of which most likely impact the likelihood of detection (Duintjer Tebbens et al., 2017). This analysis implicitly assumed all sites of equal quality, when in reality the quality of sites varies and would require additional modeling to better characterize (e.g., in the context of less-hypothetical analyses that explore actual system behavior). The available data do not currently support this type of analysis, and the ES system continues to evolve, which makes it a moving target.

We hope that this analysis will motivate serious discussions within the GPEI and countries about the actual quality of the information that comes from ES systems, and lead to significantly improved data collection related to the characteristics and performance of ES

sites. Since choices about ES systems significantly influence the role of ES in increasing national and global confidence about the absence of circulation in the absence of observed cases, improved understanding and characterization of the costs and benefits of ES appears warranted. Although ES may reduce the time required to reach high confidence about the absence of undetected circulation, the effect strongly depends on the ability to detect transmission in high-risk areas. Since ES remains sensitive to the location of its sampling sites, it does not serve as a replacement for AFP surveillance, which remains universal in its ability to detect polioviruses wherever case reporting occurs. The potential role and value of ES may shift if AFP quality declines. National and global polio stakeholders must continue to recognize the critical role that poliovirus surveillance plays in the polio endgame.

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LIST OF ABBREVIATIONS

AFP	acute flaccid paralysis
bOPV	bivalent OPV
CNC	confidence about no circulation
EI	effective number of infected individuals
ES	environmental surveillance
GPEI	Global Polio Eradication Initiative
GS	general population sites
IPV	inactivated poliovirus vaccine
LPV	live poliovirus
NS	national sites
OPV	oral poliovirus vaccine
R_0	basic reproduction number
RI	routine immunization
SIA	supplemental immunization activity
SS	site-specific
SW	system-wide
tOPV	trivalent OPV

US	under-vaccinated subpopulation sites
WPV(1,2,3)	wild poliovirus (of serotype 1, 2, 3, respectively)

REFERENCES

Alam MM, Sharif S, Shaukat S, Angez M, Khurshid A, Rehman L, & Zaidi SS (2016). Genomic surveillance elucidates persistent wild poliovirus transmission during 2013–2015 in major reservoir areas of Pakistan. Clin Infect Dis, 62(2), 190–198. doi:10.1093/cid/civ831 [PubMed: 26417032]

Deshpande JM, Shetty SJ, & Siddiqui ZA (2003). Environmental Surveillance System To Track Wild Poliovirus Transmission. Applied and Environmental Microbiology, 69(5), 2919–2927. [PubMed: 12732567]

Duintjer Tebbens RJ, Diop OM, Pallansch MA, Oberste MS, & Thompson KM. (2018). Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis. In preparation.

Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Ehrhardt DT, Farag NH, Hadler SC,… Thompson KM (2018). Modeling poliovirus transmission in Pakistan and Afghanistan to inform vaccination strategies in undervaccinated subpopulations. Risk Analysis, 38(8), 1701–1717. doi:10.1111/risa.12962 [PubMed: 29314143]

Duintjer Tebbens RJ, Pallansch MA, Kalkowska DA, Wassilak SG, Cochi SL, & Thompson KM (2013). Characterizing poliovirus transmission and evolution: Insights from modeling experiences with wild and vaccine-related polioviruses. Risk Analysis, 23(4), 703–749.

Duintjer Tebbens RJ, & Thompson KM (2018). Evaluation of proactive and reactive proactive strategies for polio eradication activities in Pakistan and Afghanistan Risk Analysis. 10.1111/risa.13194.

Duintjer Tebbens RJ, Zimmermann M, Pallansch MA, & Thompson KM (2017). Insights from a systematic search for information on designs, costs, and effectiveness of poliovirus environmental surveillance systems. Food and Environmental Virology, 9(4), 361–382. doi:10.1007/s12560-017-9314-4 [PubMed: 28687986]

Eichner M, & Dietz K (1996). Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated? American Journal of Epidemiology, 143(8), 816–822. [PubMed: 8610692]

Global Polio Eradication Initiative. (2015, September 20, 2015). Global eradication of wild poliovirus type 2 declared. Retrieved from http://www.polioeradication.org/mediaroom/newsstories/Global-eradication-of-wild-poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx

Global Polio Eradication Initiative. (2017). Eradication within reach. Annual report 2016. Retrieved from Geneva: http://polioeradication.org/wp-content/uploads/2017/08/AR2016_EN.pdf

Hampton LM, Farrell M, Ramirez-Gonzalez A, Menning L, Shendale S, Lewis I,…Immunization Systems Management Group of the Global Polio Eradication Initiative. (2016). Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine - Worldwide, 2016. Morbidity and Mortality Weekly Report, 65(35), 934–938. doi:10.15585/mmwr.mm6535a3 [PubMed: 27606675]

Hovi T, Stenvik M, Partanen H, & Kangas A (2001). Poliovirus surveillance by examining sewage specimens. Quantitative recovery of virus after introduction into sewerage at remote upstream location. Epidemiology and Infection, 127, 101–106. [PubMed: 11561962]

Kalkowska DA, Duintjer Tebbens RJ, Grotto I, Shulman LM, Anis E, Wassilak SGF,…Thompson KM (2015). Modeling options to manage type 1 wild poliovirus imported into Israel in 2013. Journal of Infectious Diseases, 211(11), 1800–1812.

Kalkowska DA, Duintjer Tebbens RJ, Pallansch MA, Cochi SL, Wassilak SGF, & Thompson KM (2015). Modeling undetected live poliovirus circulation after apparent interruption of transmission: Implications for surveillance and vaccination. BMC Infect Dis, 15(66), 1. doi:10.1186/s12879-015-0791-5 [PubMed: 25567701]

Kalkowska DA, Duintjer Tebbens RJ, Pallansch MA, & Thompson KM (2018). Modeling undetected live poliovirus circulation after apparent interruption of transmission in Pakistan and Afghanistan. Risk Analysis, Submited.

Kalkowska DA, Duintjer Tebbens RJ, & Thompson KM (2012). The probability of undetected wild poliovirus circulation after apparent global interruption of transmission. American Journal of Epidemiology, 175(9), 936–949. [PubMed: 22459121]

Kew OM, Cochi SL, Jafari HS, Wassilak SG, Mast EE, Diop OM,…Centers for Disease Control and Prevention (CDC). (2014). Possible eradication of wild poliovirus type 3--worldwide, 2012. Morbidity and Mortality Weekly Report, 63(45), 1031–1033. [PubMed: 25393222]

Mercer LD, Safdar RM, Ahmed J, Mahamud A, Khan MM, Gerber S,…Chabot-Couture G (2017). Spatial model for risk prediction and sub-national prioritization to aid poliovirus eradication in Pakistan. BMC Med, 15(1), 180. doi:10.1186/s12916-017-0941-2 [PubMed: 29017491]

Molodecky NA, Blake IM, O'Reilly KM, Wadood MZ, Safdar RM, Wesolowski A,… Grassly NC (2017). Risk factors and short-term projections for serotype-1 poliomyelitis incidence in Pakistan: A spatiotemporal analysis. PLoS Med, 14(6), e1002323. doi:10.1371/journal.pmed.1002323 [PubMed: 28604777]

Nathanson N, & Kew OM (2010). From emergence to eradication: the epidemiology of poliomyelitis deconstructed. American Journal of Epidemiology, 172(11), 1213–1229. [PubMed: 20978089]

Nnadi C, Damisa E, Esapa L, Braka F, Waziri N, Siddique A,…Adamu U (2017). Continued endemic wild poliovirus transmission in security-compromised areas - Nigeria, 2016. MMWR Morb Mortal Wkly Rep, 66(7), 190–193. doi:10.15585/mmwr.mm6607a2 [PubMed: 28233765]

Novel-T Innovative Solutions. Environmental Surveillance Maps. Retrieved November 9, 2017 http://maps.novel-t.ch/#/catalog/all

O'Reilly KM, Verity R, Durry E, Asghar H, Sharif S, Zaidi SZ,… Grassly NC (2018). Population sensitivity of acute flaccid paralysis and environmental surveillance for serotype 1 poliovirus in Pakistan: an observational study. BMC Infect Dis, 18(1), 176. doi:10.1186/s12879-018-3070-4 [PubMed: 29653509]

Ranta J, Hovi T, & Arjas E (2001). Poliovirus surveillance by examining sewage water specimens: studies on detection probability using simulation models. Risk Anal, 21(6), 1087–1096. [PubMed: 11824684]

Thompson KM, & Duintjer Tebbens RJ (2015) Health and economic consequences of different options for timing the coordinated global cessation of the three oral poliovirus vaccine serotypes. BMC Infect Dis 15:374, doi:10.1186/s12879-015-1113-7. [PubMed: 26381878]

World Health Assembly. (1988). Global eradication of poliomyelitis by the year 2000 (resolution 41.28). Geneva: World Health Organization.

World Health Organization. (2013). Global Polio Eradication Initiative: Polio Eradication and Endgame Strategic Plan (2013–2018) (WHO/POLIO/13.02). Retrieved from Geneva: http://www.polioeradication.org/Portals/0/Document/Resources/StrategyWork/PEESP_EN_US.pdf

World Health Organization. (2018). Polio this week as of 3 January 2018. Retrieved from http://polioeradication.org/polio-today/polio-now/this-week/. Access date January 10, 2017.

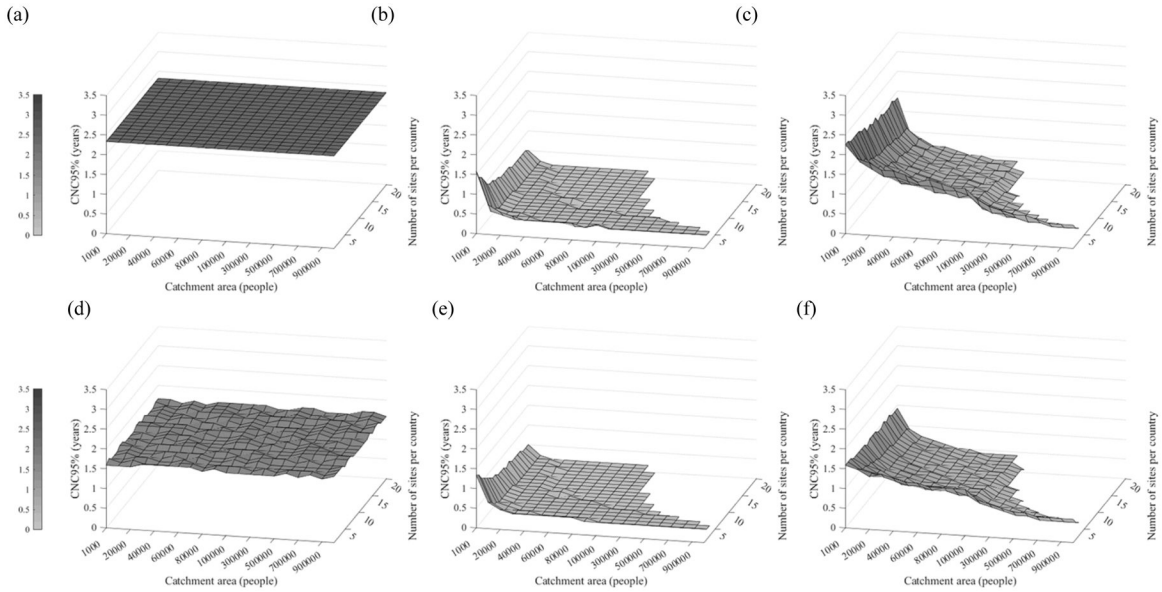

Figure 1.

CNC95% for WPV1 in Pakistan and Afghanistan (z-axis) for the increased relative SIA coverage 0.20 scenario as a function of catchment area per site (x-axis) and number of sites per country (y-axis) using: lower bound AFP detection level in under-vaccinated subpopulations with (a) worst ES performance (any ES approach with very bad quality and sampling frequency 0 times/year), (b) best SS-US performance (with good quality and sampling frequency 24 times/year), and (c) best SW-US performance (with good quality and sampling frequency 24 times/year); upper bound AFP detection level in the under-vaccinated subpopulations with (d) worst ES performance (any ES approach with very bad quality and sampling frequency 0 times/year), (e) best SS-US performance (with good quality and sampling frequency 24 times/year), and (f) best SW-US performance (with good quality and sampling frequency 24 times/year).

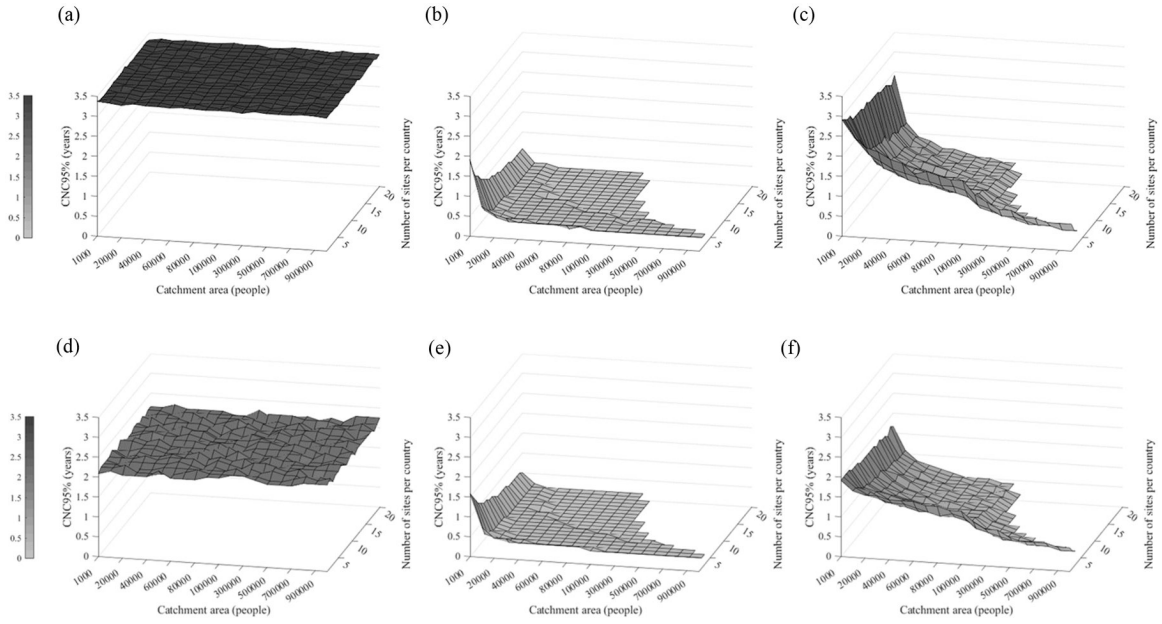

Figure 2.

CNC95% for WPV1 in Pakistan and Afghanistan (z-axis) for the "increased relative SIA coverage 0.15" scenario as a function of catchment area per site (x-axis) and number of sites per country (y-axis) using: lower bound AFP detection level in the under-vaccinated subpopulations with (a) worst ES performance (any ES approach with very bad quality and sampling frequency 0 times/year), (b) best SS-US performance (with good quality and sampling frequency 24 times/year), and (c) best SW-US performance (with good quality and sampling frequency 24 times/year); upper bound AFP detection level in the under-vaccinated subpopulations with (d) worst ES performance (any ES approach with very bad quality and sampling frequency 0 times/year), (e) best SS-US performance (with good quality and sampling frequency 24 times/year), and (f) best SW-US performance (with good quality and sampling frequency 24 times/year).

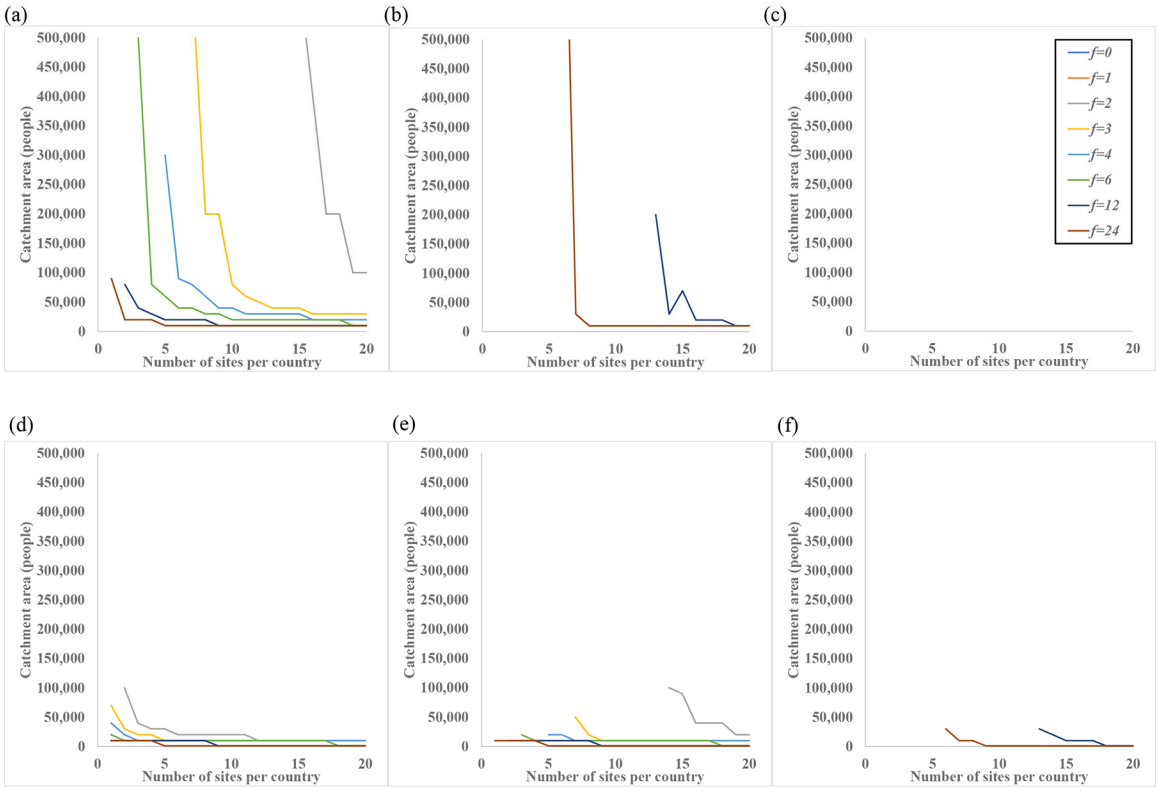

Figure 3.

Minimal catchment area per site required for a CNC95% of 1 year for WPV1 in Pakistan and Afghanistan with the “increased relative SIA coverage 0.20” scenario as a function of the number of sites per country (x-axis) and sampling frequency (*f*, times/year, legend upper right corner) using lower bound AFP detection level in under-vaccinated subpopulations and: SS-NS approach with (a) good, (b) medium, and (c) bad ES quality; or SS-US approach with (d) good, (e) medium, and (f) bad ES quality.

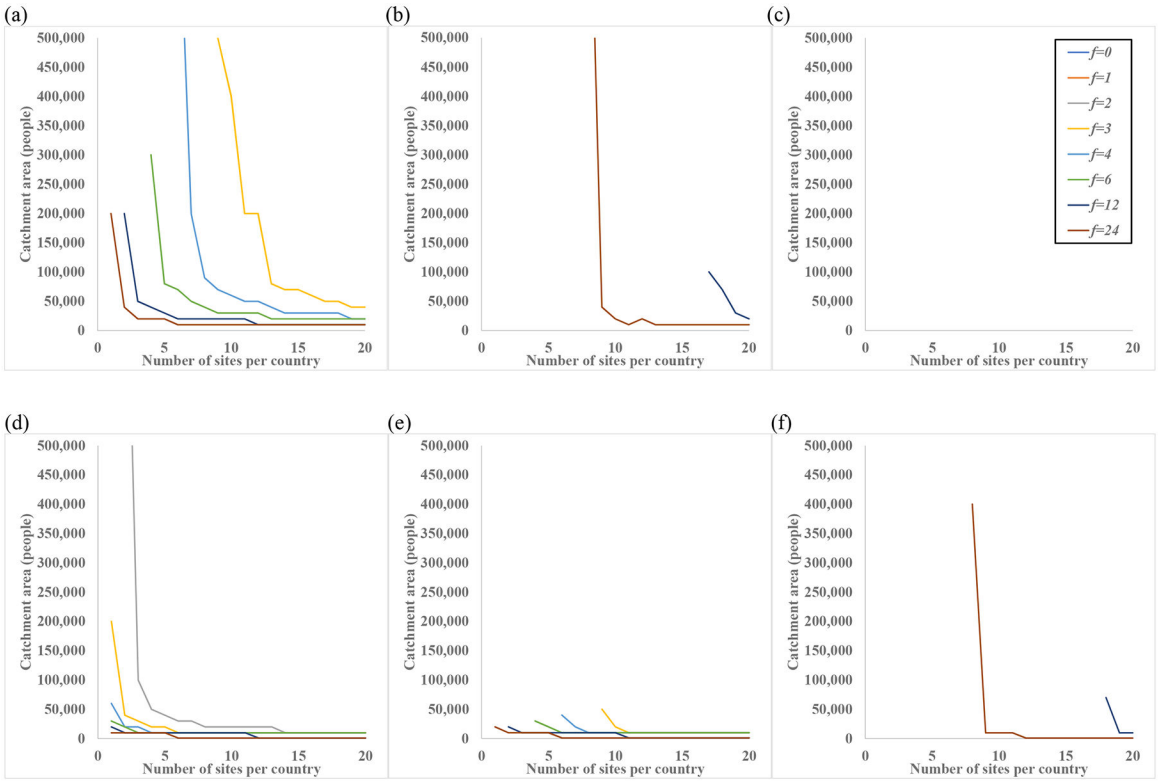

Figure 4.

Minimal coverage per site required to reach CNC95% within 1 year for serotype 1 in Pakistan and Afghanistan under "increased relative SIA coverage 0.15" scenario as a function of the number of sites per country (x-axis) and the sampling frequency (*f*, times/year, legend upper right corner) using lower bound AFP detection level in under-vaccinated subpopulations and: SS-NS approach with (a) good, (b) medium, and (c) bad ES quality; or SS-US approach with (d) good, (e) medium, and (f) bad ES quality.

Table 1

List of model inputs for the transmission model and the surveillance component, based on prior work (Duintjer Tebbens et al., 2018; Kalkowska et al., 2018) and hypothetical ES strategies and characteristics (bottom of table).

Model input (unit if applicable), Symbol	**Value(s)**
Deterministic and stochastic transmission model inputs:	
Stochastic model start year	2018
Paralysis-to-infection ratio for WPV and VDPV	1/200
Average R_0 for WPV1	11
Annual bOPV SIA frequency after 2017 for Pakistan, Afghanistan (Cumulative fraction targeted by all SIAs in a year)	8.2, 6.6
True SIA coverage in the general population after 2017 for Pakistan, Afghanistan	0.80, 0.70
Relative SIA coverage in the under-vaccinated subpopulation after 2017 for Pakistan, Afghanistan	0.25, 0.20
National RI coverage after 2017 for Pakistan, Afghanistan	0.72, 0.57
Relative RI coverage in the under-vaccinated subpopulation after 2017 for Pakistan, Afghanistan	0.40, 0.60
AFP surveillance model inputs:	
Cluster length (days), *cl*	90
Probability of detecting a case by AFP surveillance in general population, $p = (p_1, p_2, \ldots, p_i)$	(0.75, 0.80, 0.85, 0.90, …, 0.90)
Probability of detecting a case by AFP surveillance in under-vaccinated subpopulation, lower bound, $p = (p_1, p_2, \ldots, p_i)$	(0.10, 0.10, …, 0.10)
Probability of detecting a case by AFP surveillance in under-vaccinated subpopulation, upper bound, $p = (p_1, p_2, \ldots, p_i)$	(0.50, 0.53, 0.57, 0.60, …, 0.60)
ES model inputs:	
Effective (i.e., infectiousness-weighted) number of infectious individuals (infections)	From transmission model
Number of people in the population (people)	From transmission model
Detection limit of i^{th} ES sampling site of quality level (infections/people), DL_{50}^{i}:	
Good (g)	1/100000
Medium (m)	1/10000
Bad (b)	1/1000
Very bad (vb)	1/100
Coefficient of system-wide ES for quality level, *C*:	
Good (g)	0.05
Medium (m)	0.1

Model input (unit if applicable), Symbol	Value(s)
Bad (b)	0.3
Very bad (vb)	0.5
Sampling frequency (times/year), f	0, 1, 2, 3, 4, 6, 12, 24
Number of sampling sites	1, 2, …, 20
Catchment area population of the i^{th} sampling site (people), N_i	1,000, 10,000 to 100,000 by 10,000 increments and 100,000 to 1,000,000 by 100,000 increments

Abbreviations: AFP, acute flaccid paralysis; bOPV, bivalent oral poliovirus vaccine; ES, environmental surveillance; PV, poliovirus; R_0, basic reproductive number; RI, routine immunization; SIA, supplementary immunization activity; VDPV, vaccine-derived poliovirus; WPV, wild poliovirus; WPV1, serotype 1 wild poliovirus.

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Table 2

Minimal sampling frequency (*f*, times/year) required to obtain a CNC95% of less than one year for WPV1 in Pakistan and Afghanistan with very bad (vb), bad (b), medium (m) and good (g) sampling site quality. An x indicates the impossibility of reaching CNC95% within one year.

ES approach	**SW**												**SS**											
Site distribution	**GS**				**NS**				**US**				**GS**				**NS**				**US**			
Site quality*	**vb**	**b**	**m**	**g**	**vb**	**B**	**m**	**g**	**vb**	**b**	**m**	**g**	**vb**	**b**	**m**	**g**	**vb**	**b**	**m**	**g**	**vb**	**b**	**m**	**g**
"increased relative SIA coverage 0.20"																								
lower bound AFP detection	x	x	x	x	x	x	x	24	x	x	12	4	x	x	x	x	x	x	12	2	x	12	2	2
upper bound AFP detection	x	x	x	x	x	x	x	12	x	24	6	3	x	x	x	x	x	x	12	2	x	12	2	2
"increased relative SIA coverage 0.15"																								
lower bound AFP detection	x	x	x	x	x	x	x	24	x	x	12	6	x	x	x	x	x	x	12	3	x	12	3	2
upper bound AFP detection	x	x	x	x	x	x	x	12	x	x	12	4	x	x	x	x	x	x	12	2	x	12	2	2

*For ES approach of SW, site quality corresponds to coefficient of system-wide ES for quality level, *C*, (see Table 1), and for ES approach of SS, site quality corresponds to the detection limit of i^{th} ES sampling site of quality level, DL_{50}^{i} (see Table 1).

Abbreviations: AFP, acute flaccid paralysis; b, bad; CNC95%, 95% confidence about no circulation; ES, environmental surveillance; g, good; GS, general sites; m, medium; NS, national sites; SIA, supplementary immunization activity; SS, site-specific; SW, system-wide; US, under-vaccinated sites; vb, very bad

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