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Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis

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Abstract

Objective: To characterize the costs, including for environmental surveillance (ES), of the Global Polio Laboratory Network (GPLN) that provides laboratory support to the Global Polio Eradication Initiative (GPEI).

Design and participants: We conducted a survey of the 146 GPLN laboratories and 3 laboratories (outside the GPLN) dedicated to concentration of environmental samples to collect information about their activities, characteristics, and costs during 2016. We estimate the total GPLN costs using regression of reported responses and complementing the findings with GPEI data.

Results: We received responses from 132 (89%) of the 149 laboratories, with variable response rates for individual questions. We estimate that processing samples of patients with acute flaccid paralysis leads to total costs of approximately $28 million per year (2016 US dollars) based on extrapolation from reported costs of $16 million, of which 61% were supported by internal (national) funds. Fifty-nine (45%) of the 132 responding laboratories reported supporting ES and we estimate an additional $5.3 million of recurring costs for ES activities performed by the GPLN. The reported costs do not include an estimated additional $10 million of annual global and regional costs to coordinate and support the GPLN. On average, the polio-supported staff in the responding laboratories spent 30% of their time on non-polio activities. We estimate total costs for laboratory support provided by the GPLN of approximately $43 million (note that this estimate does not include any field or other non-laboratory costs of polio surveillance).

Conclusions: Although countries contribute significantly to the GPLN financing, many laboratories currently depend on GPEI funds, and these laboratories also support the laboratory component of surveillance activities for other diseases. Sustaining critical global surveillance for polioviruses and transitioning support for other disease programs will require continued international funding after polio certification.

Strengths and limitations of this study:

- Contributes to the very limited literature about the laboratory costs of global surveillance activities by providing updates estimates of the laboratory costs of the Global Polio Laboratory Network.

- Highlights both the importance of contributions that countries make to the Global Polio Laboratory Network and the need to sustain external funding to support laboratories worldwide in their surveillance efforts for poliovirus and other diseases.
- Results depend on self-reported costs estimates with possible difference in interpretation of the questions and availability of cost information.
- Analysis relied on extrapolation from relatively sparse data to estimate missing values, which may have introduced biases.

Keywords: poliovirus, surveillance, polio eradication, cost study, global health

Background

Launched in response to the 1988 World Health Assembly resolution to globally eradicate all paralytic poliomyelitis caused by polioviruses, the Global Polio Eradication Initiative (GPEI) seeks to stop all polio.[1] By the end of 2017, the GPEI succeeded in limiting indigenous transmission of wild polioviruses to three countries (Afghanistan, Nigeria, and Pakistan) by focusing on four key strategies: strengthening routine polio immunization, supplemental immunization activities, surveillance, and outbreak response.[2] Four of the 6 World Health Organization (WHO) regions have been certified polio-free and of the three wild poliovirus serotypes, serotypes 2 and 3 have not been detected since 1999 and 2012, respectively.[3 4] High-quality surveillance represents a key contributor to these successes because it allows the GPEI to 1) monitor eradication progress, 2) determine where poliovirus transmission still occurs, 3) rapidly respond to any outbreaks in previously polio-free areas, and 4) achieve high confidence about the absence of transmission after the last detected poliovirus in any given area.

As part of the global strategy to manage the risks associated with the oral poliovirus vaccine (OPV),[5 6] and following the certification of serotype 2 wild poliovirus eradication in 2015,[7] cessation of attenuated serotype 2-containing OPV occurred in April-May 2016. The virologic monitoring of the disappearance of serotype 2 vaccine-related viruses from AFP cases and the environment represented an integral activity of the vaccine switch.[8] Even after the eradication of the last circulating wild polioviruses, surveillance will remain critical to manage future poliovirus risks. First, certification of wild poliovirus eradication and subsequent OPV cessation cannot safely occur without high confidence about the absence of transmission. Second, the risk of outbreaks continues to exist after OPV cessation,[6 9] as already demonstrated by circulating vaccine-derived poliovirus outbreaks after serotype 2 OPV cessation,[10] virus releases from polio vaccine manufacturing facilities,[11] and the existence of long-term excretors of immunodeficiency-associated vaccine-derived polioviruses.[12 13]

The Global Polio Laboratory Network (GPLN) supports poliovirus surveillance activities in countries by testing stool samples from patients with acute flaccid paralysis (AFP) (and sometimes their contacts) for the presence of polioviruses. In addition to AFP surveillance, which exists in all countries except for 20 high-income countries, some GPLN laboratories support supplemental surveillance through testing of environmental samples (e.g., sewage), or stool collected from non-paralytic individuals (e.g., healthy children surveys or patients with central nervous system diseases such as aseptic meningitis). Some laboratories also test for polio antibodies from sera (e.g., from serological surveys). The GPLN currently consists of 146 laboratories with different roles (i.e., subnational, national, regional reference, and global specialized laboratories) and capacities (i.e., sewage concentration, virus isolation, intratypic differentiation (ITD), sequencing, and serology testing) that form a comprehensive global referral system to ensure testing of any specimen for the presence of poliovirus and sequencing of specific polioviruses (e.g., suspected wild or vaccine-derived polioviruses).

The GPEI systematically tracks its resource requirements for the GLPN, which estimated a budget of $16.4 million for 2017 (compared to $79 million for ‘surveillance and running costs’ in the field, and $1.1 billion for all GPEI activities).[14] However, no mechanism exists to systematically track the contributions by the countries hosting GPLN laboratories. A survey of GPLN laboratories conducted in 2003 found that external GPEI funds accounted for only 34% of the reported GLPN costs, with 47% coming from internal (i.e., national) funds and 13% from bilateral cooperation funds not included in the GPEI budget.[15] The analysis estimated total GPLN costs of $21 million (2002 USD dollars, equal to $28 million in 2016 US dollars), including $9 million for various coordinating and supporting activities by the GPEI and the global specialized laboratories. Since the 2003 survey, the number of countries dealing with polio outbreaks decreased significantly, the poliovirus detection and characterization algorithms changed, and the GPEI significantly increased its ES activities. Analysis of ES samples involves a concentration step not needed for AFP samples, requires a separate work space, and impacts laboratory workloads and workflows.[16 17] Given these changes and questions about the financial resources required to sustain the GLPN, we conducted a survey following the same general approach as the 2003 survey[15] to update the full GPLN cost estimates and better understand the extent and costs of ES activities supported by the GPLN.

Methods

Survey instrument

We developed an online survey instrument (reviewers can find the instrument available at http://kidrisk.org/mainFrame/KRGPLNSurvey2017.pdf) modeled after the 2003 survey.[15] With respect to costs, the instrument requests annual estimates for 11 major cost categories (see below) each for analysis of samples obtained through AFP surveillance and ES. For the cost categories "equipment" and "durable supplies," we asked for annual amortized costs, defined as purchase, packing, freight, and insurance costs divided by expected useful lifetime, and we provided a spreadsheet to help respondents compute the annual amortized costs. In addition, for laboratories that recently (i.e., between 2010 and 2016) established or significantly expanded their ES capacity, we requested estimates of the ES set-up costs for 10 largely overlapping cost categories relevant to establishing ES capacity. For all of these, we asked respondents to provide the breakdown of costs by funding source (i.e., internal, external (GPEI), bilateral (non-GPEI, non-national)). The instrument further included questions about the role and capacities of the laboratories, geographical areas served, staff time spent on different activities, number of samples processed for different tests (e.g., virus isolation, ITD, sequencing, and, for ES samples, concentration), serological testing activities, non-polio surveillance activities by polio-supported staff, the nature of ES activities, and anticipated future changes in workload or workflow.

Process

We piloted the survey among all WHO regional coordinators of the GPLN and a small subset of laboratories before launching the revised, final instrument online and in PDF form in July, 2017, in English, Chinese, and Russian. We targeted all 145 active GPLN laboratories (we excluded one laboratory considered dormant) and 3 concentration-only laboratories not technically part of the GPLN but recently established to facilitate ES in countries with no easy access to a GPLN laboratory for sewage sample concentration and processing. We followed up with responding laboratories to resolve any ambiguities or apparent inconsistencies in the responses. We followed up four times with non-responding laboratories to increase the response rate through November 2017 and closed the online survey instrument at the end of 2017.

Processing and analysis of results

We collected all original responses directly from the online survey instrument and manually entered any changes indicated by respondents during the follow-up. For rare instances in which a laboratory provided a range of costs for a category, we used the midpoint. Some respondents noted that they reported costs for consumable supplies or shared consumable supplies on a per-sample basis rather than as an annual total, which prompted us to systematically convert consumable supply costs to annual totals when we suspected responses per sample. Specifically, when both the (shared) consumable supply costs per reported virus isolation test equaled less than $20 and the absolute (shared) consumable supply costs equaled less than $400, we multiplied the reported costs by the reported number of virus isolation tests. The second condition served to ensure no undue multiplication by the number of virus isolation tests for some laboratories with very large numbers of reported virus isolation tests but modest reported (shared) consumable supplies. This approach resulted in multiplication by the number of virus isolation tests of the reported consumable and shared consumable supplies for AFP sample processing for 59 and 25 laboratories, respectively. With the exception of two laboratories that clearly reported (shared) consumable supplies per sample for ES sample processing, we did not adjust any of the reported (shared) consumable supply costs for ES sample processing. We converted all monetary estimates to 2016 US dollars ($) using publicly available exchange rates from July 1, 2016.[18] We classified laboratories based on the 2016 World Bank income levels of their host countries.[19] Unless otherwise noted, all results represent the annual totals for 2016.

To account for missing cost responses, we interpreted unanswered or zero responses differently depending on the cost category. We assumed that all laboratories incur costs under the six cost categories of personnel, equipment, durable supplies, consumable supplies, operations, and shipping/transport (i.e., non-zero categories, NZCs). In contrast, we assume that some laboratories may truly not incur any costs for the five categories of training, shared consumable supplies, donated supplies, technical support, and other (i.e., possible zero categories, PZCs). Furthermore, we pre-processed the cost data before further analysis because some respondents indicated challenges in separating costs between analysis of AFP and ES samples and others explicitly indicated that they reported only the combined costs. Compared to samples from AFP patients, the processing of ES samples follows a more involved algorithm (i.e., three times as many cell cultures),[16] more often yields viruses that require ITD testing or sequencing (i.e., because an ES sample represents a composite sample from many individuals), and requires about four times the processing time by trained staff.[20] Based on the average total costs per sample processed for virus isolation reported among all laboratories that provided separate costs for AFP and ES, we assume that, on average, ES samples require seven times the cost per virus isolation test as AFP samples. Specifically, for NZCs, if a laboratory reported non-zero costs for AFP processing and either indicated that they combined AFP and ES costs or reported zero recurring or set-up ES costs for the cost category, then we estimated the portion of reported AFP costs attributable to ES based on the number of ES samples processed for virus isolation times seven, divided by the total samples (i.e., the number of ES samples times seven plus the number of AFP samples processed for virus isolation). We then subtracted the estimated ES-attributable costs from the reported AFP costs. For PZCs, we estimated and subtracted the ES-attributable costs only if the laboratory reported non-zero AFP costs and explicitly indicated that they combined ES and AFP costs (i.e., not if they reported 0 ES costs for the category). Recognizing uncertainty about the true ratio of costs per sample processed for virus isolation for ES compared to AFP samples, we explored the impact of varying this ratio from three to ten.

We further treated the pre-processed data differently depending on the type of cost category. For NZCs, we interpreted any response not corresponding to a positive number as a missing estimate requiring estimation (i.e., even if a laboratory responded with 0, we interpreted this as an indication that the laboratories did not have access to the data required to estimate the costs). For PZCs, we interpreted zeroes, blanks, or any text indicating an inability to estimate the costs (e.g., not applicable, unknown, unable to estimate) as a true zero. For these categories, we only estimated costs for non-responding laboratories or laboratories that did not provide an estimate for any of the cost categories in the corresponding question (see appendix A1 for tables that summarizes how we interpreted different responses in each cost category).

To account for non-responding laboratories, we considered variables that we could obtain outside of the survey for all laboratories from the web-based GPLN management system, including number of employee full-time equivalents (FTEs) employed for poliovirus surveillance, and number of virus isolation tests, ITD tests, and sequences performed on AFP samples. Based on differences between laboratories and descriptive analysis of relationships by WHO region, income level, and laboratory role, we grouped the laboratories by income level and capacity (i.e., virus isolation only, ITD and virus isolation but no sequencing, and sequencing (with or without ITD capacity)) for regression analyses. Within each group, we used univariate linear regression on the number of samples processed for virus isolation to estimate missing costs. In the event of negative intercepts or slopes in a given cost category and group, we forced the intercept to 0, thus effectively reverting to estimation based on the simple average cost per sample processed for virus isolation for the given cost category and group. We also considered linear regression on the number of FTEs, multilinear regression on all variables, and different grouping approaches, but found no substantial improvement or differences in the totals.

Patient and Public Involvement

This survey did not involve patients or public opportunities for engagement.

Results

Overall survey response and grouping

We received responses from 132 of 149 (89%) surveyed laboratories. Figure 1 provides the breakdown of the response rate by laboratory role, region, and income level, which shows a response rate of at least 78% for all breakdowns, except for the 3 concentration-only laboratories, from which we received only 1 response (i.e., response rate 33%). Based on the reported capacities, we grouped the 131 responding GPLN laboratories into 30 (23%) laboratories with virus isolation capacity only, 67 (51%) laboratories with virus isolation and ITD capacity, and 35 (27%) laboratories with sequencing capacity (regardless of virus isolation and ITD capacity), with the concentration-only laboratory equipped with neither of those capacities. For the estimation of costs to process AFP samples, we further grouped the laboratories by income level into low- and lower middle-income vs. upper middle- and high-income to allow more appropriate cost extrapolation while maintaining sufficient numbers of laboratories in each group. For the estimation of costs to process ES samples, we did not stratify by income level because of the smaller numbers of laboratories in this group.

AFP sample processing costs

The response rates related to the various categories of costs to process samples from AFP cases and contacts (Table 1, numbers in parenthesis in the top half) remained markedly lower than the overall survey response rates (Figure 1), with the highest rates for personnel and consumable supplies. The responding laboratories reported approximately $16 million in total AFP-related costs (Table 1). This does not include $510,000 in reported AFP-related costs from 12 laboratories that we re-allocated to processing of ES samples. Personnel accounted for 44% of all reported costs, followed by consumable supplies (21%) and equipment (20%). The bottom half of Table 1 shows the costs estimated for each group and cost category. The resulting total AFP costs equal approximately $28 million. Although the sequencing laboratories account for only 26% of the total number of GPLN laboratories, they account for 34% of the estimated lab-specific costs for processing of AFP samples.

Figure 2 shows the breakdown by cost category and source of funding for the costs reported in the top half of Table 1. Internal (national) funds accounted for a large proportion of personnel (76%), training (66%), equipment (64%), operations (79%), and technical support (85%) costs, while external (GPEI) funds accounted for a large proportion of costs for consumable supplies (72%), donated supplies (75%), and shared consumable supplies (54%). Overall, 61%, 36%, 2.4%, and 1.3% of all reported funds to process AFP samples came from internal, external, bilateral, and unspecified funds, respectively. Twenty-six percent of laboratories reported dependence on non-internal funds for at least 50% of their budget, with regional percentages of

0%, 3.3%, 6.7%, 50%, 58% and 86% for the American, Western Pacific, European, Eastern Mediterranean, Southeast Asian, and African WHO regions, respectively.

ES sample processing costs

Fifty-nine (45%) of all 132 responding laboratories reported supporting ES activities, including one concentration-only laboratory. One additional laboratory that reported not analyzing ES samples estimated the costs of supporting national ES activities with a staff member providing technical support. We excluded the latter laboratory and the concentration-only laboratory due to the absence of numbers of ES samples processed for virus isolation needed for inclusion in the regression. Seven non-responding GPLN laboratories support ES according to unpublished WHO data, leading to a total of 65 (45%) of the 145 GPLN laboratories supporting ES activities in 2016. Table 2 shows the reported and estimated recurring costs for ES based on the variable response rates for each cost category. The responding laboratories reported approximately $3.2 million in total recurring ES-related costs, which includes $510,000 in AFP costs that we attributed to ES. Varying the ratio of per-sample ES processing costs to per-sample AFP processing cost from 3 to 10 changed the AFP processing costs attributed to ES processing from $340,000 to $590,000, respectively. Thus, the impact of this assumption on overall costs remains modest because it only affects 12 laboratories with ambiguity about whether reported AFP processing costs included ES processing costs. The breakdown by cost category remained similar to the costs for processing of AFP samples and similarly, the sequencing laboratories accounted for a large portion of all reported recurring ES costs (i.e., 58%). The bottom half of Table 2 shows the extrapolated costs estimated in each group and for each cost category. The resulting total recurring ES costs equal approximately $5.3 million. Figure 3 shows the breakdown by cost category and funding source for the costs reported in the top half of Table 2, which shows a similar breakdown as for AFP sample processing costs. Overall, 65%, 22%, 0.3%, and 12% of all reported recurring ES costs came from internal, external, bilateral, and unspecified funds, respectively. Table 2 does not factor in the relatively small costs from the one concentration-only laboratory that responded to the survey, which reported only some internally-funded recurring ES costs for personnel with other costs captured in the ES set-up costs or unquantified because they paid for by external resources.

Of the 59 laboratories (i.e., 58 GPLN laboratories and 1 concentration-only laboratory) that reported supporting ES activities, 35 (59%) reported that they recently (i.e., between 2010 and 2016) set-up or significantly expanded their ES capacity. Of these 35 laboratories, 25 (71%) provided set-up cost estimates for at least one cost category, leading to total reported set-up costs of approximately $1.8 million, for an average of approximately $73,000 per laboratory. This includes estimates from 16 ITD laboratories, 6 sequencing laboratories, 2 virus isolation laboratories, and 1 concentration-only laboratory. Only 6 of the 25 (24%) laboratories reported becoming fully operational during 2016 and therefore we assume that only a fraction of the reported set-up costs occurred in 2016. Figure 4 shows the breakdown of the $1.8 million of reported ES set-up costs, with the legend also showing the response rates for each set-up cost category. New equipment for concentration represented the largest contributor to all reported set-up cost (38%), followed by new equipment for expanded poliovirus processing capacity (12%), new personnel (12%), new consumable supplies (11%) and facility costs (10%).

Other findings

Table 3 show the breakdown of polio-supported staff time spent on polio and non-polio diseases, by WHO region. Only 1 of 132 (1%) of laboratories that responded to the survey did not provide estimates for the total number of polio-supported FTEs or the percentages spent on polio and other diseases. Overall, polio-supported staff spent approximately 30% of time supporting activities for other diseases or viruses, including non-polio enteroviruses (11%), measles and/or rubella viruses (7%), and a wide range of other diseases not specifically asked about in the survey (5%) (Table 3, see appendix A2). The American (41%) and European (46%) regions reported the lowest percentages of staff time spent on polio, while the Eastern Mediterranean region (87%), which includes one laboratory serving two polio-endemic countries (i.e., Afghanistan and Pakistan), reported the highest percentage.

Table 4 summarizes the reported number of samples or isolates processed in the context of different activities. Not surprisingly given the primary focus of the GPLN on supporting AFP surveillance, Table 4 shows almost 250,000 samples from AFP cases and their contacts processed for virus isolation, with approximately 4.5% ITD-tested and less than 1% sequenced.

These numbers reflect the reality that, given the current prevalence of wild polioviruses and level of OPV use, roughly 4.5% of stool samples from AFP cases grow in the L20B cells used for virus isolation. Of these, approximately 7% appear as possible wild or vaccine-derived poliovirus, which then undergo sequencing. In contrast, ES accounted for only 12,000 samples processed for virus isolation originating from 8,200 environmental sample concentrates, 67% of which were concentrated using the WHO-recommended two-phase method.[16] The difference between the number of concentrates and the number of isolates probably comes from laboratories that (re)tested samples already concentrated by another laboratory, including third-party laboratories not part of the GPLN. A much larger fraction of isolates from ES samples compared to AFP samples underwent ITD testing (54%) and sequencing (15%), probably because ES samples comprise a composite from potentially thousands of individuals and they often yield complex mixtures of viruses. This results in higher costs on a per-sample basis for ES than AFP, with the ES algorithm additionally requiring three times as many cell cultures as the AFP algorithm. Laboratories also reported analyzing almost 2,000 ES samples in the context of research activities and 82 ES samples using direct detection methods. Forty responding laboratories further reported analyzing over 50,000 serum samples for the presence of antibodies, which they estimated took almost 13,000 employee hours (i.e., 12.7 FTEs assuming 2,000 employee hours per year). Laboratories analyzed almost 40,000 samples in the context of non-polio enterovirus surveillance and approximately 150,000 other samples, reflecting the reality that many GPLN laboratories perform non-polio services (not necessarily funded by polio surveillance), particularly in countries with no recent polio outbreaks. While 49 laboratories reported testing other samples, 3 of these laboratories accounted for 83% of the 150,000 samples and indicated that their reported numbers included routine diagnostic services. Laboratories also reported analyzing approximately 6,900 and 4,300 samples in the context of healthy children or adult stool surveys and clinical trials, respectively. See appendix A3 for additional results.

Estimated overall GPLN costs

Table 5 estimates the full costs of the GLPN for 2016 based on the results of the survey complemented with data from the WHO and the CDC global specialized laboratory in Atlanta, GA. Using the results from Tables 1 and 2, we estimate the total laboratory-specific costs to support AFP surveillance and ES at approximately $33 million. This does not include the reported recent ES set-up costs of $1.8 million, which represents only a fraction of the WHO-supported ES set-up costs for 2016, or the costs for the analysis of serum samples. For the analysis of serum samples, we assume costs of $10 per sample for consumables and equipment and the reported average personnel costs per FTE in upper middle- and high-income countries, which tested most of the reported serum samples, to estimate total costs of serology of approximately $1 million for 2016. We estimate the costs of research and development activities at $3 million based on extrapolation of data from the largest global specialized laboratory. We estimate the global overhead costs for coordination, training, technical support not incurred by individual laboratories at $6 million. The resulting estimated total GPLN cost for 2016 equal to $43.3 million.

For comparison, the 2003 survey estimated substantially lower total GPLN costs of $28 million per year (i.e., 21 million in year 2002 US dollars). This estimate broke down as: (1) $16 million of AFP-related costs for the (sub)-national and regional reference laboratories, (2) $8 million for all polio-related activities by global specialized laboratories, including limited ES conducted at the time, and (3) $4 million in global coordination costs.[15] In this study, the corresponding AFP-related costs for the (sub)-national and regional reference laboratories equals approximately $25 million. The total estimated AFP and recurring ES costs for the global specialized laboratories equals only $3.5 million, but increases to over $7 million if we add the estimated research and development, serology, coordination, training, and technical support costs.

Discussion

This study confirms the important contributions of both GPEI and internal funds to the maintenance of a well-functioning GPLN.[15] While direct comparison of the absolute costs in 2016 to those in the 2003 study[15] remains somewhat challenging due to differences in the specific cost requested, this study finds an apparent increase in the proportion of GPLN costs paid for by internal funds from 53% in 2003 [15] to 62% in 2016. This may reflect increasing self-funding of the laboratory component of polio surveillance activities by polio-free countries no longer at a high risk of outbreaks. In addition, after largely externally-funded capital investment to set up laboratories with the capacity to apply molecular methods in many countries, the more often internally funded personnel costs now represent a relatively larger share of the total costs. The investments in capital costs may also have reduced the recurring costs compared to the 2003 survey, despite the increase from approximately 85,000 AFP samples tested in 2002 to almost 250,000 in 2016. Nevertheless, with 50% or more of GPLN laboratories in the African, Eastern Mediterranean, and Southeast Asian WHO regions depending on external GPEI funds for at least half of their budgets for AFP sample analysis, planning for GPLN financing after the GPEI resources decline post-certification remains of critical importance. In this context, we note that the GPEI budget for 2017 of $16.4 million reflects only 17% of the GPEI budget for all surveillance activities and 1.5% of the overall GPEI budget for 2017.[14] This study further documents the significant contributions made by the GPLN to a large number of other disease surveillance efforts, with 30% of all polio-supported staff time reportedly used for surveillance of other diseases. Thus, we hope that this study highlights both the importance of contributions that countries make to the GPLN and the need to sustain external funding to support laboratories worldwide in their surveillance efforts for poliovirus and other diseases. As global population immunity to poliovirus transmission decreases after OPV cessation,[21] successfully controlling any future outbreaks will require continued vigilance and a rapid immunization response.[22] However, questions remain after the certification of eradication about the long-term financial sustainability of poliovirus surveillance and the functions of the GPLN, because of the expected transition of key GPEI responsibilities and resources to other programs.

Based on our results, the GPLN costs to support ES remain relatively small compared to the AFP costs. This reflects the reality that despite the ongoing global ES expansion, ES remains limited to parts of some countries, while the global AFP surveillance system remains (almost) universal. With the first phase of ES expansion continuing during 2017 and 2018, we expect both increased set-up costs during those years and higher recurring ES costs going forward compared to the ES costs estimated for 2016. With further expansion, the GPLN costs for ES could exceed those for AFP, particularly if AFP surveillance declines, although we urge careful consideration of the costs and effectiveness of doing allowing AFP surveillance to decline.[23]

This survey relied on self-reported estimates of laboratory costs. While we attempted to formulate the questions unambiguously and provided translations of the survey instrument and during follow up where possible, we cannot rule out possible differences in interpretation of the questions. Some respondents reported difficulties separating costs between categories and activities or amortizing costs of equipment purchased long ago. Although we achieved a high overall response rate of 89%, the response rates for individual cost categories remained variable. Therefore, we relied on estimation based on regression of relatively sparse data to characterize missing values, which may have introduced biases. For example, laboratories receiving funding from the GPEI may be more likely to have omitted estimates for individual cost categories, potentially leading to relatively greater errors in the estimation of the external cost. On the contrary, laboratories may not have accounted for all equipment, supplies, and operations cost (e.g., utilities, building maintenance) paid for by their hosting institutions, potentially leading to underestimation of the share of costs funded by internal sources. Despite its limitations, we hope this study provides valuable insights regarding the costs and cost structure of the GPLN. Future research to inform global long-term poliovirus and broader surveillance may include detailed cost studies of the field component of AFP surveillance and economic analyses of the value of AFP surveillance and ES.

Conclusions

Although countries contribute significantly to the GPLN, many laboratories currently depend on GPEI funds, and these laboratories also support the laboratory component of surveillance activities for other diseases. Sustaining critical global surveillance for polioviruses and other diseases will require continued international funding as GPEI resources decline, particularly after global certification. Paying the costs to sustain surveillance represents an essential element for securing a polio-free world, and offers the opportunity to transition GPLN resources to control/eliminate other vaccine-preventable or emerging/re-emerging communicable diseases.[24]

List of abbreviations

AFP, acute flaccid paralysis; ES, poliovirus environmental surveillance; GPEI, Global Polio Eradication Initiative; GPLN, Global Polio Laboratory Network; ITD, intratypic differentiation; NZC, non-zero (cost) category; OPV, oral poliovirus vaccine; PZC, possible zero (cost) category

DECLARATIONS

Authors' contributions

All authors (RDT, DMO, MAP, MSO, KMT) contributed to the study design, survey instrument development, interpretation of data, manuscript writing, and revisions. The first author (RDT) performed the data analysis, the last author (KMT) coded and administered the survey instrument in Survey Monkey™, the second author (DMO) contacted the laboratories, the first and second authors (RDT, DMO) recruited participants and followed up with respondents on any questions.

Ethics approval and consent to participate

Not applicable

Consent to publish

Not applicable

Competing interests

None

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Data sharing statement

Technical appendix available on request from the authors.

References

1. World Health Assembly. Global eradication of poliomyelitis by the year 2000 (resolution 41.28). Geneva: World Health Organization, 1988.
2. Global Polio Eradication Initiative. Strategy 2017 [Available from: http://polioeradication.org/ accessed December 14 2017.
3. Global Polio Eradication Initiative. Global eradication of wild poliovirus type 2 declared 2015 [updated September 20, 2015. Available from: http://www.polioeradication.org/mediaroom/newsstories/Global-eradication-of-wild-poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx accessed November 30 2015.
4. Kew OM, Cochi SL, Jafari HS, et al. Possible eradication of wild poliovirus type 3--worldwide, 2012. *MMWR Morb Mortal Wkly Rep* 2014;63(45):1031-33.
5. World Health Organization. Global Polio Eradication Initiative: Polio Eradication and Endgame Strategic Plan (2013-2018). Geneva, 2013.
6. Duintjer Tebbens RJ, Pallansch MA, Kew OM, et al. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. *Risk Anal* 2006;26(6):1471-505.
7. Hampton LM, Farrell M, Ramirez-Gonzalez A, et al. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine - Worldwide, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65(35):934-38. doi: 10.15585/mmwr.mm6535a3
8. Diop OM, Asghar H, Gavrilin E, et al. Virologic Monitoring of Poliovirus Type 2 after Oral Poliovirus Vaccine Type 2 Withdrawal in April 2016 - Worldwide, 2016-2017. *MMWR Morb Mortal Wkly Rep* 2017;66(20):538-42. doi: 10.15585/mmwr.mm6620a4
9. Duintjer Tebbens RJ, Pallansch MA, Cochi SL, et al. An economic analysis of poliovirus risk management policy options for 2013-2052. *BMC Infect Dis* 2015;15:389. doi: 10.1186/s12879-015-1113-7
10. Jorba J, Diop OM, Iber J, et al. Update on Vaccine-Derived Polioviruses - Worldwide, January 2016-June 2017. *MMWR Morb Mortal Wkly Rep* 2017;66(43):1185-91. doi: 10.15585/mmwr.mm6643a6
11. Duizer E, Ruijs WL, van der Weijden CP, et al. Response to a wild poliovirus type 2 (WPV2)-shedding event following accidental exposure to WPV2, the Netherlands, April 2017. *Euro Surveill* 2017;22(21) doi: 10.2807/1560-7917.ES.2017.22.21.30542
12. Duintjer Tebbens RJ, Pallansch MA, Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the

potential benefits of antiviral drugs. *BMC Infect Dis* 2015;15:379. doi: 10.1186/s12879-015-1115-5

13. Dunn G, Klapsa D, Wilton T, et al. Twenty-Eight Years of Poliovirus Replication in an Immunodeficient Individual: Impact on the Global Polio Eradication Initiative. *PLoS Pathog* 2015;11(8):e1005114. doi: 10.1371/journal.ppat.1005114
14. Global Polio Eradication Initiative. GPEI Budget 2017 2017 [updated June 1, 2017. Available from: http://polioeradication.org/financing/financial-needs/financial-resource-requirements-frr/gpei-budget-2017/ accessed December 14 2017.
15. de Gourville EM, Sangrujee N, Duintjer Tebbens RJ, et al. Global Surveillance and the value of information: The case of the global polio laboratory network. *Risk Anal* 2006;26(6):1557-69.
16. Global Polio Eradication Initiative. Guidelines on environmental surveillance for detection of polioviruses - working draft - March 2015, 2015.
17. World Health Organization. Guidelines for environmental surveillance of poliovirus circulation. Geneva: Department of Vaccines & Biologicals, WHO, 2003.
18. XE.com. Current and historical rate tables 2017 [Available from: http://www.xe.com/currencytables/?from=USD&date=2016-07-01 accessed November 15 2017.
19. World Bank. World Bank analytical classifications - calendar year 2016 GNI per capita in US$ (Atlas methodology) 2017 [Available from: http://databank.worldbank.org/data/download/site-content/OGHIST.xls accessed December 13 2017.
20. Hovi T, Shulman LM, van der Avoort H, et al. Role of environmental poliovirus surveillance in global polio eradication and beyond. *Epidemiology and Infection* 2012;140(1):1-13. doi: 10.1017/S095026881000316X
21. Duintjer Tebbens RJ, Hampton LM, Thompson KM. Implementation of coordinated global serotype 2 oral poliovirus vaccine cessation: Risks of potential non-synchronous cessation. *BMC Infect Dis* 2016;16:237.
22. Duintjer Tebbens RJ, Pallansch MA, Wassilak SGF, et al. Characterization of outbreak response strategies and potential vaccine stockpile needs for the polio endgame. *BMC Infect Dis* 2016;16:137. doi: 10.1186/s12879-016-1465-7
23. Duintjer Tebbens RJ, Zimmermann M, Pallansch MA, et al. Insights from a systematic search for information on designs, costs, and effectiveness of poliovirus environmental surveillance systems. *Food and Environmental Virology* 2017;9(4):361-82. doi: 10.1007/s12560-017-9314-4
24. Rutter PD, Hinman AR, Hegg L, et al. Transition Planning For After Polio Eradication. *J Infect Dis* 2017;216(suppl_1):S287-S92. doi: 10.1093/infdis/jix026

Table 1: Reported and estimated costs to process acute flaccid paralysis samples, based on regression of reported total number stool samples processed for virus isolation. This excludes the costs for the concentration-only laboratories and global and regional costs to coordinate the GPLN.

Cost category	Laboratories with virus isolation capacity only (N=38)		Laboratories with ITD (and no sequencing) capacity (N=70)		Laboratories with sequencing capacity (N=38)		All GPLN laboratories (N=146)
	Low- and lower middle-income (N=8)	Upper middle- and high-income (N=30)	Low- and lower middle-income (N=32)	Upper middle- and high-income (N=38)	Low- and lower middle-income (N=6)	Upper middle- and high-income (N=32)	
Total reported costs (% of all labs in group reporting non-zero costs)							
Personnel	1,700 (25)	750,000 (60)	2,100,000 (78)	1,100,000 (63)	490,000 (67)	2,400,000 (78)	6,900,000 (67)
Training	2,500 (13)	8,900 (37)	37,000 (25)	36,000 (55)	250 (17)	51,000 (41)	130,000 (38)
Equipment	36,000 (25)	190,000 (60)	690,000 (72)	1,000,000 (63)	3,000 (17)	1,200,000 (69)	3,100,000 (62)
Durable supplies	2,400 (25)	170,000 (57)	120,000 (59)	110,000 (63)	9,400 (33)	110,000 (59)	530,000 (57)
Consumable supplies	34,000 (50)	190,000 (60)	1,300,000 (59)	620,000 (71)	900,000 (50)	280,000 (75)	3,300,000 (65)
Shared consumable supplies	2,700 (38)	44,000 (40)	84,000 (41)	180,000 (53)	290,000 (33)	88,000 (53)	690,000 (46)
Donated supplies	4,000 (13)	10,000 (3)	5,600 (6)	770 (3)	0 (0)	480 (9)	21,000 (5)
Operations	4,500 (25)	53,000 (17)	170,000 (53)	140,000 (50)	53,000 (33)	300,000 (28)	730,000 (37)
Shipping/transport	1,200 (25)	24,000 (30)	53,000 (66)	32,000 (61)	100 (17)	91,000 (53)	200,000 (50)
Technical support	200 (13)	14,000 (23)	39,000 (16)	43,000 (26)	200 (17)	19,000 (13)	120,000 (19)
Other	0 (0)	7,500 (3)	7,400 (6)	1,400 (3)	0 (0)	1,600 (3)	18,000 (3)
All cost categories	90,000	1,500,000	4,600,000	3,300,000	1,800,000	4,500,000	16,000,000
Estimated total costs							
Personnel	9,100	1,200,000	2,600,000	1,700,000	770,000	2,700,000	9,000,000
Training	2,900	9,000	44,000	39,000	250	63,000	160,000
Equipment	4,200,000	290,000	930,000	1,200,000	18,000	1,700,000	8,400,000
Durable supplies	270,000	260,000	200,000	180,000	33,000	260,000	1,200,000
Consumable supplies	150,000	280,000	1,400,000	810,000	1,500,000	450,000	4,600,000
Shared consumable supplies	8,400	63,000	87,000	230,000	290,000	110,000	790,000
Donated supplies	4,600	15,000	6,200	830	0	600	27,000
Operations	540,000	550,000	330,000	250,000	1,000,000	440,000	3,100,000
Shipping/transport	150,000	40,000	57,000	55,000	600	170,000	470,000
Technical support	230	21,000	40,000	46,000	200	20,000	130,000
Other	0	11,000	8,200	1,500	0	2,200	23,000
All cost categories	5,300,000	2,800,000	5,700,000	4,500,000	3,600,000	6,000,000	28,000,000

565 **Table 2: Reported and estimated recurring costs to process environmental samples, based on regression by reported total**
566 **number of environmental samples processed for virus isolation (results exclude costs from one responding concentration-only**
567 **laboratory).**

Cost category	Laboratories with virus isolation capacity only (N=20)	Laboratories with ITD (and no sequencing) capacity (N=22)	Laboratories with sequencing capacity (N=23)	All GPLN laboratories doing ES (N=65)
Total reported costs (% of all labs in group reporting non-zero costs)				
Personnel	110,000 (40)	290,000 (77)	1,100,000 (70)	1,500,000 (63)
Training	7,400 (15)	17,000 (41)	42,000 (35)	66,000 (31)
Equipment	24,000 (35)	340,000 (73)	160,000 (52)	520,000 (54)
Durable supplies	22,000 (40)	42,000 (82)	20,000 (52)	84,000 (58)
Consumable supplies	51,000 (35)	210,000 (68)	120,000 (57)	380,000 (54)
Shared consumable supplies	5,600 (20)	18,000 (50)	80,000 (35)	100,000 (35)
Donated supplies	8,100 (5)	29,000 (9)	1,200 (4)	38,000 (6)
Operations	1,900 (5)	110,000 (73)	190,000 (35)	300,000 (38)
Shipping/transport	8,500 (25)	33,000 (77)	46,000 (43)	88,000 (49)
Technical support	1,600 (15)	6,300 (18)	51,000 (17)	59,000 (17)
Other	0 (0)	0 (0)	25,000 (9)	25,000 (3)
All cost categories	240,000	1,100,000	1,800,000	3,200,000
Estimated total costs				
Personnel	180,000	320,000	1,700,000	2,200,000
Training	15,000	17,000	61,000	94,000
Equipment	66,000	470,000	360,000	890,000
Durable supplies	47,000	52,000	42,000	140,000
Consumable supplies	120,000	310,000	340,000	760,000
Shared consumable supplies	12,000	18,000	130,000	160,000
Donated supplies	18,000	29,000	2,000	49,000
Operations	37,000	130,000	540,000	710,000
Shipping/transport	44,000	36,000	98,000	180,000
Technical support	2,100	6,300	73,000	81,000
Other	0	0	40,000	40,000
All cost categories	540,000	1,400,000	3,400,000	5,300,000

568

569 **Table 3: Polio-supported staff time spent on polio and non-polio diseases, by World Health Organization Region**

Disease/virus	Number (%) of employee full-time equivalents, by World Health Organization region (N=number of responses)						
	European (N=39)	Western Pacific (N=42)	Southeast Asian (N=14)	African (N=15)	Eastern Mediterranean (N=12)	American (N=8)	All (N=130)
Polio	59 (46)	83 (60)	171 (82)	137 (83)	83 (87)	25 (41)	558 (70)
Non-polio enteroviruses	30 (23)	24 (18)	11 (5)	5 (3)	3 (3)	15 (24)	88 (11)
Measles and/or rubella viruses	7 (5)	13 (9)	22 (10)	14 (9)	3 (3)	1 (1)	59 (7)
Rotavirus	5 (3)	4 (3)	3 (1)	2 (1)	2 (2)	1 (2)	16 (2)
Influenza	12 (9)	3 (2)	1 (0)	2 (1)	1 (1)	1 (1)	20 (3)
Japanse encephalitis	0 (0)	4 (3)	0 (0)	0 (0)	0 (0)	0 (0)	4 (1)
Yellow fever	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	2 (0)
Other arboviruses or hemorrhagic fever viruses	2 (2)	1 (0)	0 (0)	1 (0)	0 (0)	1 (1)	4 (1)
Other	15 (11)	5 (4)	2 (1)	1 (1)	4 (4)	14 (22)	41 (5)
All diseases	129	137	209	164	95	57	792

570

571 **Table 4: Reported number of samples/isolates processed for different activities**

Activity	Nature of testing/activity	Number of samples/isolates
Acute flaccid paralysis surveillance	Virus isolation	243,897
	Intratypic differentiation	10,380
	Sequencing	751
	Other[a]	925
Environmental surveillance	Concentration (two-phase method)	5,509
	Concentration (other methods)	2,703
	Virus isolation	12,170
	Intratypic differentiation	6,638
	Sequencing	1,847
	Research	1,971
	Direct detection	82
Serology	Serum antibody testing	52,020
Other	Non-polio enterovirus surveillance	38,589
	Healthy children/adults surveys	6,907
	Clinical trial support	4,337
	Other[b]	149,345

572 [a] Includes serotyping and polymerase chain reaction analysis of non-polio enteroviruses identified in acute flaccid paralysis cases,
573 Sanger sequencing, and next generation sequencing of complete genomes
574 [b] See appendix A2
575

Table 5: Estimated overall GPLN costs for 2016

Cost component	Amount ($ millions)
Processing of samples from acute flaccid paralysis surveillance	
- Reported	16
- Estimated	28
Processing of samples from environmental surveillance	
- Reported	3.2
- Estimated	5.3
Serology	1.0
Research and development	3.0
Global and regional overhead (e.g., coordination, training, technical support)	6.0
Total estimated annual GPLN costs	43

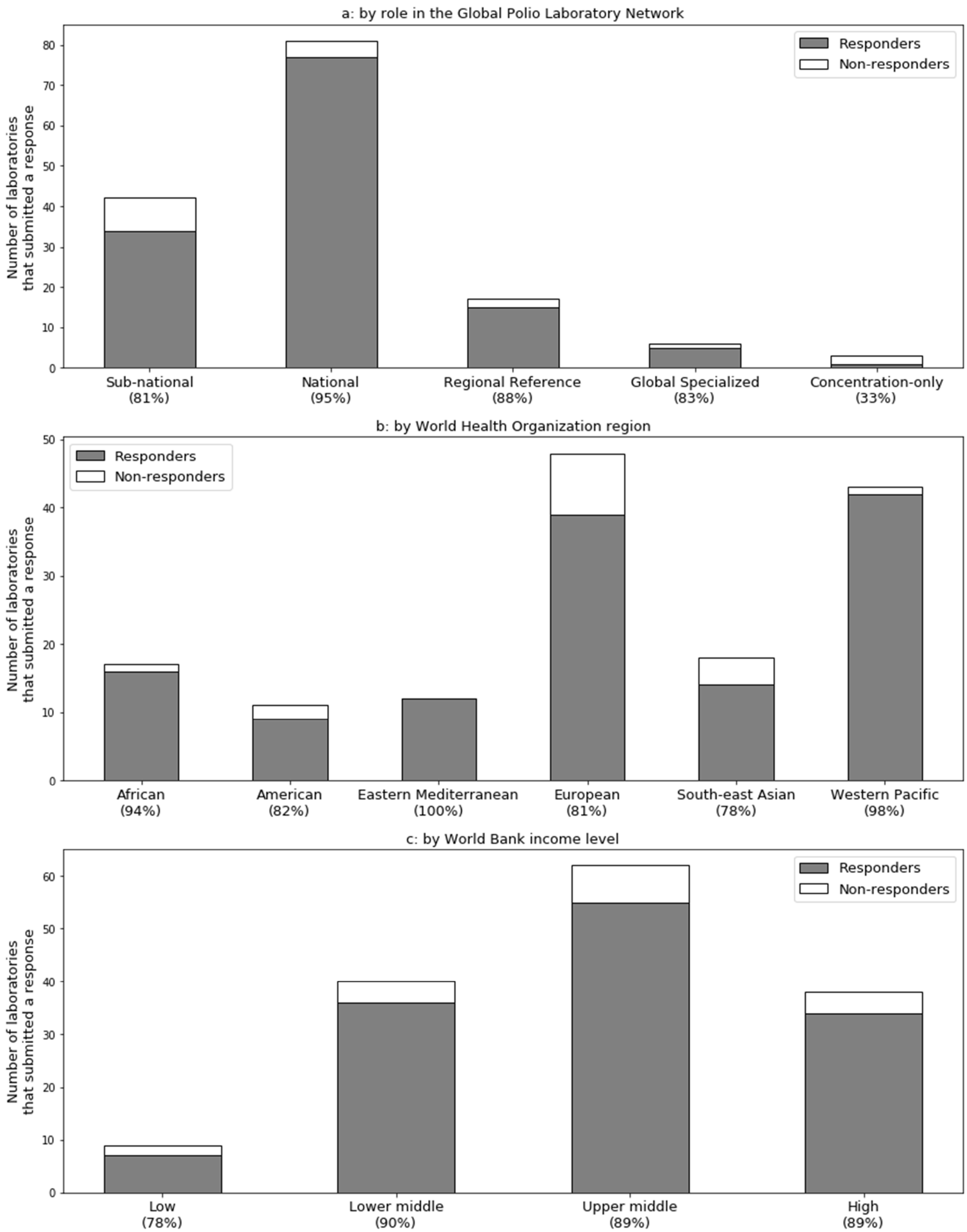
Figure Captions

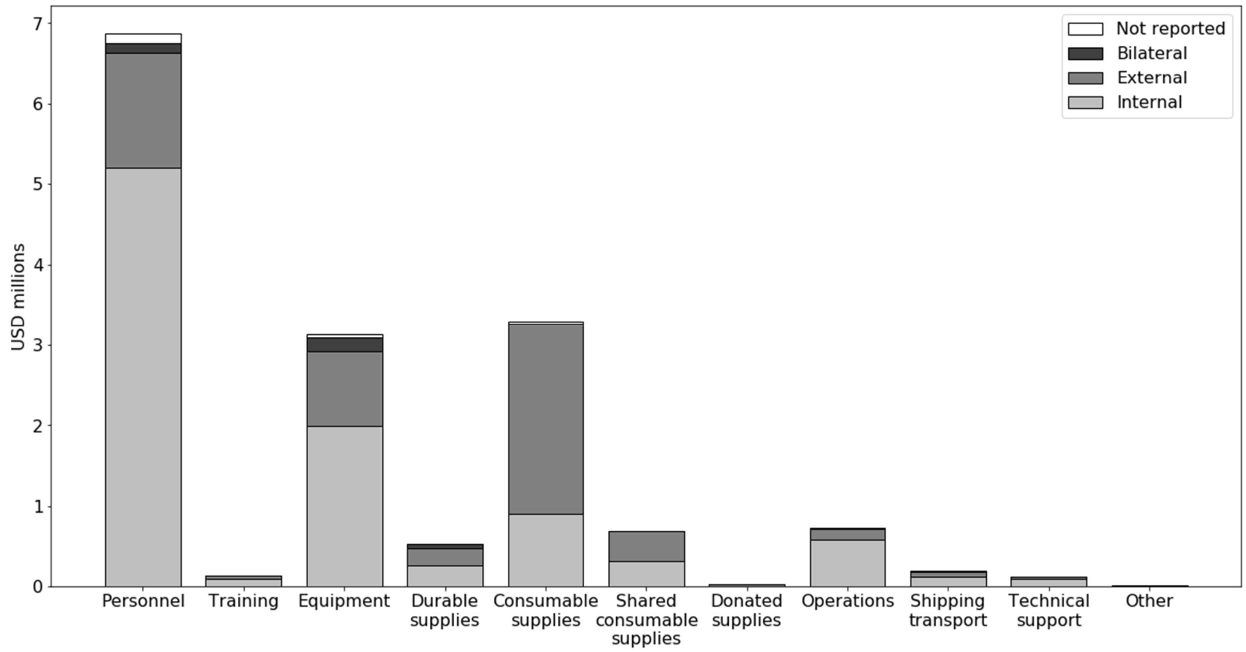
Figure 1: Survey response rates by role, region, and income level

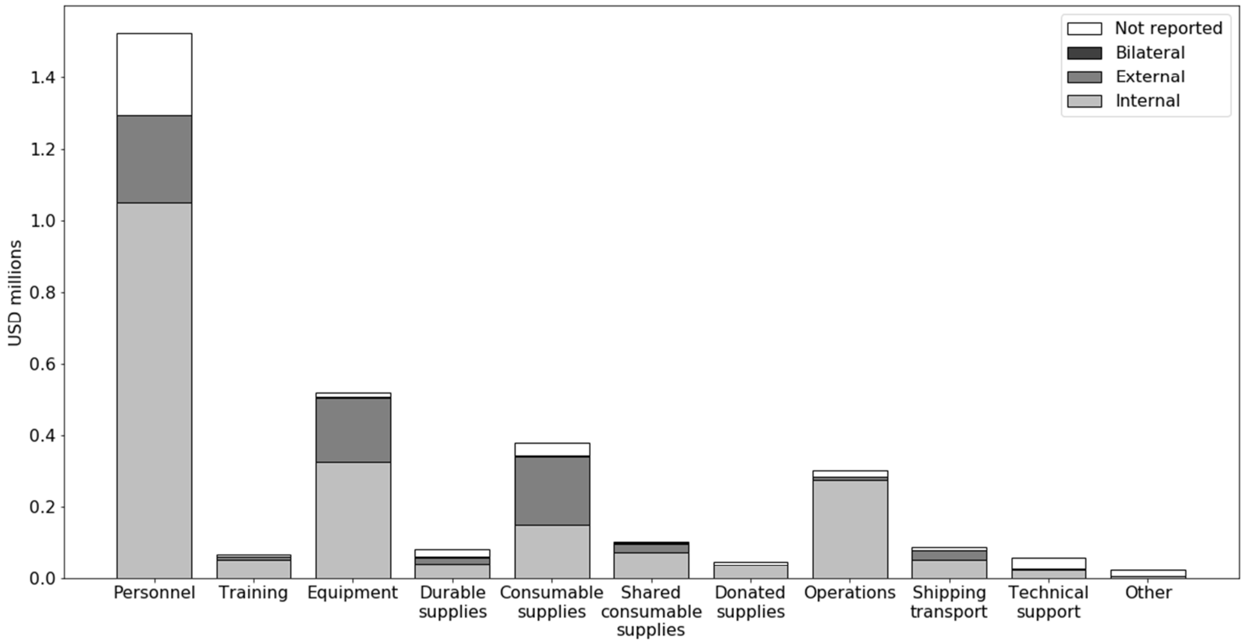
Figure 2: Reported costs to process acute flaccid paralysis samples by cost category and source of funding

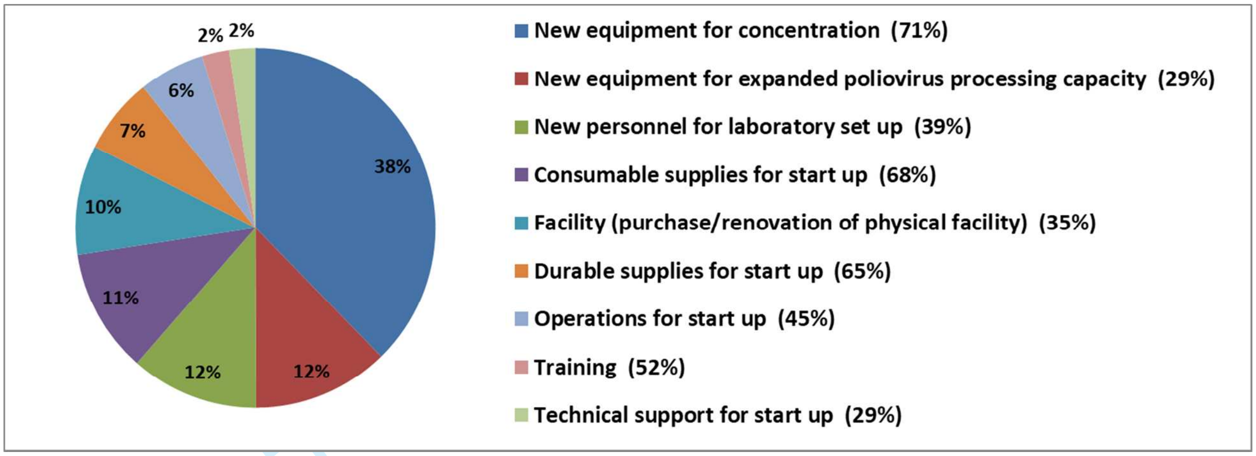
Figure 3: Reported recurring costs to process environmental samples by cost category and source of funding

Figure 4: Breakdown by cost categories of reported environmental surveillance set-up costs. Numbers in parenthesis indicate the response rates among 30 laboratories that reported having set-up or significantly expanded poliovirus environmental surveillance capacity between 2010 and 2016. The total reported set-up costs equal $1.8 million.


a: by role in the Global Polio Laboratory Network
Responders
Non-responders
Number of laboratories that submitted a response
Sub-national (81%)
National (95%)
Regional Reference (88%)
Global Specialized (83%)
Concentration-only (33%)
b: by World Health Organization region
African (94%)
American (82%)
Eastern Mediterranean (100%)
European (81%)
South-east Asian (78%)
Western Pacific (98%)
c: by World Bank income level
Low (78%)
Lower middle (90%)
Upper middle (89%)
High (89%)


Not reported
Bilateral
External
Internal
USD millions
0
1
2
3
4
5
6
7
Personnel
Training
Equipment
Durable supplies
Consumable supplies
Shared consumable supplies
Donated supplies
Operations
Shipping transport
Technical support
Other


Not reported
Bilateral
External
Internal
USD millions
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
Personnel
Training
Equipment
Durable supplies
Consumable supplies
Shared consumable supplies
Donated supplies
Operations
Shipping transport
Technical support
Other


38%
12%
12%
11%
10%
7%
6%
2%
2%
New equipment for concentration (71%)
New equipment for expanded poliovirus processing capacity (29%)
New personnel for laboratory set up (39%)
Consumable supplies for start up (68%)
Facility (purchase/renovation of physical facility) (35%)
Durable supplies for start up (65%)
Operations for start up (45%)
Training (52%)
Technical support for start up (29%)

APPENDIX

A1. Interpretation of cost responses

Table A1: Logic for interpretation of AFP cost responses (after any subtractions as a result of logic in Table A2)

Value	Type of cost category	Interpretation	Treatment
Non-response or no cost provided for entire question	Any	No information available	Estimate based on extrapolation
Positive number	Any	Laboratory-estimated value available	Keep response (influence extrapolation)
Zero	PZC	True zero	Keep as 0 (influence extrapolation)
	NZC	Costs not actually zero	Estimate based on extrapolation
Other text (e.g., unknown)	PZC	Costs actually zero	Set to 0 (influence extrapolation)
	NZC	Non-zero costs, but unknown	Estimate based on extrapolation

NZC, non-zero (cost) category; PZC, possible zero (cost) category

Table A2: Logic for interpretation of ES recurring cost responses

Value	Type of cost category	Corresponding set-up cost category	Corresponding AFP cost category	Interpretation	Treatment
Non-response or no cost provided for entire question	Any	Any	Any	No information available	Estimate based on extrapolation
Positive number	Any	Any	Any	Laboratory-estimated value available	Keep response (influence extrapolation)
Zero	PZC	Any	Any	True zero	Keep as 0 (influence extrapolation)
	NZC	Positive number	Any	Assume cost included in set-up costs	Keep as 0 to avoid double-counting (influence extrapolation)
	NZC	Not a positive number	Positive number	Assume costs included in AFP costs	Estimate based on ES-attributable costs, then subtract from corresponding AFP cost category
	NZC	Not a positive number	Not a positive number	Non-zero costs, but unknown	Estimate based on extrapolation
Respondent indicated cost included in AFP costs	PZC	Any	Positive number	Assume included in AFP costs	Estimate based on ES-attributable costs, then subtract from corresponding AFP cost category
	PZC	Any	Not a positive number	Costs actually zero	Set to 0 (influence extrapolation)
	NZC	Any	Positive number	Assume included in AFP costs	Estimate based on ES-attributable costs, then subtract from corresponding AFP cost category
	NZC	Any	Not a positive number	Non-zero costs, but unknown	Estimate based on extrapolation (but do not subtract from corresponding AFP cost category)
Other text	PZC	Any	Any	Costs actually	Set to 0 (influence extrapolation)

(e.g., unknown)				zero	
	NZC	Any	Any	Non-zero costs, but unknown	Estimate based on extrapolation

NZC, non-zero (cost) category; PZC, possible zero (cost) category

A2. Other diseases

Respondent laboratories collectively reported spending 41 FTEs on diseases/conditions not specifically listed in Table 3. The laboratories reported that these other diseases/conditions included TORCH, exanthemal infections, urogenital, immunology, intestinal and parasitic infection groups, human immunodeficiency virus, hepatitis, acute respiratory viral infections, teratogenic infections, mycoplasma, chlamydophyll, transgenic organisms control, astrovirus, norovirus, sapovirus, adenovirus, rabies, non-influenza respiratory diseases, non-rotavirus acute gastroenteritis, herpes group viruses, mumps, rhinovirus, parainfluenza virus, respiratory syncytial virus, metapneumovirus, parechovirus, polyomavirus, varicella virus, diphtheria, tetanus, pertussis, cytomegalovirus, crystalli, parotitis, severe fever with thrombocytopenia syndrome, meningitis, and encephalitis.

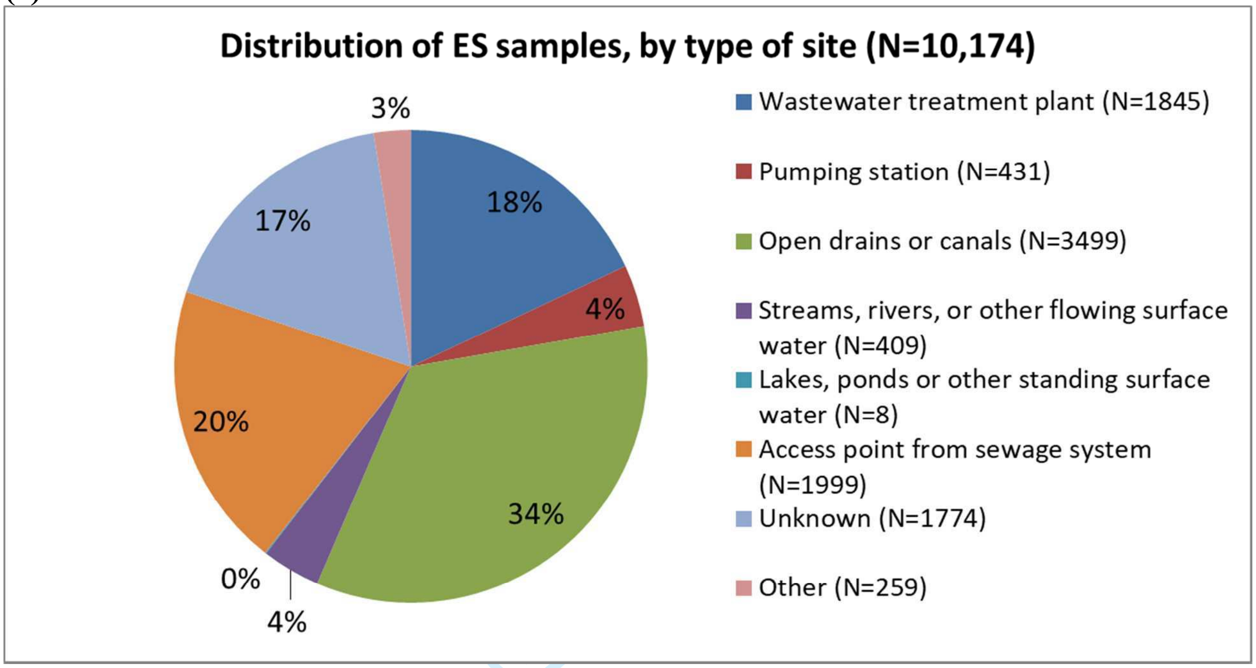
The other types of laboratory tests in Table 4 include ELISA, PCR, RT-PCR, HBsAg, microtitration, genotyping, and serology for numerous viruses and on various sample types (i.e., sera, nasopharyngeal washings, blood, feces, urine, urogenital scrapings, sectional material, mites, spinal fluid, rectal swab and vomitus from diarrhea and food poisoning cases, ice and drinking water, soil) as well as virus isolation on fecal samples from AFP cases over age 15, AFP samples from provinces outside of the areas normally served by the laboratory, fecal samples from non-AFP patients not part of a survey, and research activities.

A3. Additional results related to ES systems

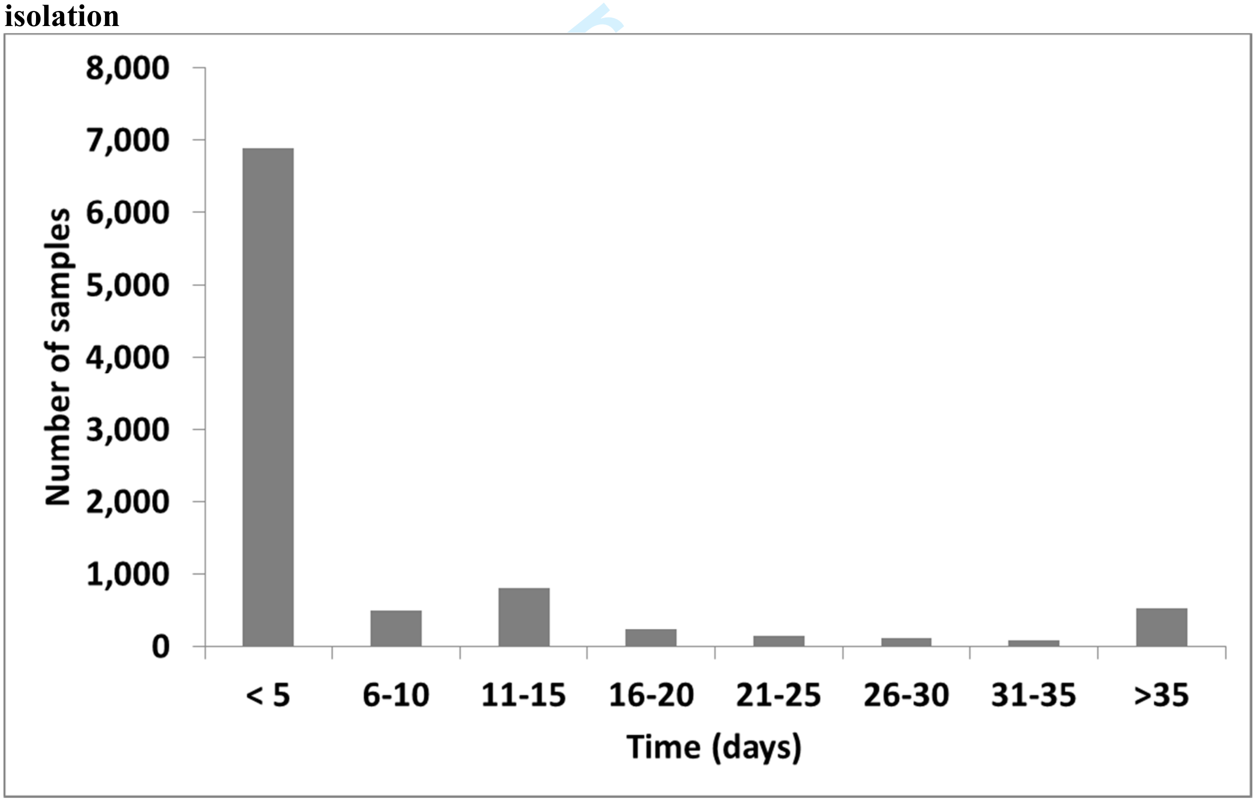
Figure A1 summarizes characteristics of the ES systems based on reported results for approximately 10,000 ES samples (the total numbers of samples differ from Table 4 due to incomplete responses for some (sub)questions and possible double-counting of samples analyzed by multiple laboratories through the referral system). The majority of ES samples came from open drains or canals (34%), followed by other access points from sewage systems (19%), wastewater treatment plants (18%), and unknown sources (18%). Eighty percent of samples started processing for virus isolation within 5 days of sample collection, which likely reflects the routine handling of ES samples collected in the context of ongoing ES (see Figure A1b). However, the reported 6% of samples taking more than 35 days until virus isolation began suggests a long tail of the distribution of transportation and processing delays (Figure A1b). The delays may relate to a supply shortage situation during the rapid global expansion of ES, which efforts to streamline quality assurance and quality control may limit as the system become more established. Moreover, ES conducted in the context of research activities may follow different timelines.

Figure A1: Reported results related to the ES systems.

(a) Nature of ES sites



(b) Distribution of duration from sample collection to beginning of processing for virus isolation



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Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis

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Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis

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Abstract

Objective: To characterize the costs, including for environmental surveillance (ES), of the Global Polio Laboratory Network (GPLN) that provides laboratory support to the Global Polio Eradication Initiative (GPEI).

Design and participants: We conducted a survey of the network across 92 countries of the 146 GPLN laboratories plus 3 non-GPLN laboratories that concentrate environmental samples to collect information about their activities, characteristics, and costs during 2016. We estimate the total costs using regression of reported responses and complementing the findings with GPEI data.

Results: We received responses from 132 (89%) of the 149 laboratories, with variable response rates for individual questions. We estimate that processing samples of patients with acute flaccid paralysis leads to total costs of approximately $28 million per year (2016 US dollars) based on extrapolation from reported costs of $16 million, of which 61% were supported by internal (national) funds. Fifty-nine (45%) of the 132 responding laboratories reported supporting ES and we estimate an additional $5.3 million of recurring costs for ES activities performed by the laboratories. The reported costs do not include an estimated additional $10 million of annual global and regional costs to coordinate and support the GPLN. On average, the staff supported by funding for polio in the responding laboratories spent 30% of their time on non-polio activities. We estimate total costs for laboratory support of approximately $43 million (note that this estimate does not include any field or other non-laboratory costs of polio surveillance).

Conclusions: Although countries contribute significantly to the GPLN financing, many laboratories currently depend on GPEI funds, and these laboratories also support the laboratory component of surveillance activities for other diseases. Sustaining critical global surveillance for polioviruses and transitioning support for other disease programs will require continued significant funding after polio certification.

Strengths and limitations of this study:

- High overall response rate from laboratories allows for estimation of costs across geographies, income levels, and laboratory types.
- Results depend on self-reported costs estimates with possible difference in interpretation of the questions and availability of cost information.

- Analysis relied on extrapolation from relatively sparse data to estimate missing values, which may have introduced biases.

Keywords: poliovirus, surveillance, polio eradication, cost study, global health

Background

Launched in response to the 1988 World Health Assembly resolution to globally eradicate all paralytic poliomyelitis caused by polioviruses, the Global Polio Eradication Initiative (GPEI) seeks to stop all polio.[1] Bymid-2018, the GPEI succeeded in limiting indigenous transmission of wild polioviruses to three countries (Afghanistan, Nigeria, and Pakistan) by focusing on four key strategies: strengthening routine polio immunization, supplemental immunization activities, surveillance, and outbreak response.[2] Four of the 6 World Health Organization (WHO) regions have been certified polio-free and of the three wild poliovirus serotypes, and wild poliovirus serotypes 2 and 3 have not been detected since 1999 and 2012, respectively.[3 4] High-quality surveillance represents a key contributor to these successes because it allows the GPEI to 1) monitor eradication progress, 2) determine where poliovirus transmission still occurs, 3) rapidly respond to any outbreaks in previously polio-free areas, and 4) achieve high confidence about the absence of transmission after the last detected poliovirus in any given area.

As part of the global strategy to manage the risks associated with the oral poliovirus vaccine (OPV),[5 6] and following the certification of serotype 2 wild poliovirus eradication in 2015,[7] cessation of attenuated serotype 2-containing OPV occurred in April-May 2016. The virologic monitoring of the disappearance of serotype 2 vaccine-related viruses from acute flaccid paralysis (AFP) cases and the environment represented an integral activity of the vaccine switch.[8] Even after the eradication of the last circulating wild polioviruses, surveillance will remain critical to manage future poliovirus risks. First, certification of wild poliovirus eradication and subsequent OPV cessation cannot safely occur without high confidence about the absence of transmission. Second, the risk of outbreaks continues to exist after OPV cessation,[6 9] as already demonstrated by circulating vaccine-derived poliovirus outbreaks after serotype 2

OPV cessation,[10] virus releases from polio vaccine manufacturing facilities,[11] and the existence of long-term excretors of immunodeficiency-associated vaccine-derived polioviruses.[12 13]

Established in 1990, the Global Polio Laboratory Network (GPLN) supports poliovirus surveillance activities in countries by testing stool samples from patients with AFP (and sometimes their contacts) for the presence of polioviruses.[14] AFP may indicate a poliovirus infection, but also occurs at a relatively predictable rate due to other causes (e.g., Guillain-Barre Syndrome), making the rate of non-polio AFP cases detected a good indicator of the ability of the surveillance system to detect AFP caused by poliovirus infection in a population.[15] Currently the GPLN analyzes over 200,000 stool samples per year from AFP cases and their contacts. In addition to AFP surveillance, which exists in all countries except for 20 high-income countries, some GPLN laboratories support supplemental surveillance through testing of environmental surveillance (ES) samples (e.g., sewage), or stool collected from non-paralytic individuals (e.g., healthy children surveys or patients with central nervous system diseases such as aseptic meningitis). Some laboratories also test for polio antibodies from sera (e.g., from serological surveys). The GPLN currently consists of 146 laboratories across 92 countries with different roles (i.e., subnational, national, regional reference, and global specialized laboratories) and capacities (i.e., sewage concentration, virus isolation, intratypic differentiation (ITD), sequencing, and serology testing) that form a comprehensive international referral system to ensure testing of any specimen for the presence of poliovirus and sequencing of specific polioviruses (e.g., suspected wild or vaccine-derived polioviruses).

The GPEI systematically tracks its resource requirements for the GLPN, which estimated a budget of $16.4 million for 2017 (compared to $79 million for "surveillance and running costs" in the field, and $1.1 billion for all GPEI activities).[14] However, no mechanism exists to systematically track the contributions by the countries hosting GPLN laboratories. A survey of GPLN laboratories conducted in 2003 found that external GPEI funds accounted for only 34% of the reported GLPN costs, with 47% coming from internal (i.e., national) funds and 13% from bilateral cooperation funds not included in the GPEI budget.[15] The analysis estimated total GPLN costs of $21 million (2002 USD dollars, equal to $28 million in 2016 US dollars), including $9 million for various coordinating and supporting activities by the GPEI and the global specialized laboratories. Since the 2003 survey, the number of countries dealing with polio outbreaks decreased significantly, the poliovirus detection and characterization algorithms changed, and the GPEI significantly increased its ES activities. Analysis of ES samples involves a concentration step not needed for AFP samples, requires a separate work space, and impacts laboratory workloads and workflows.[16 17] Given these changes and questions about the financial resources required to sustain poliovirus surveillance during the polio endgame, we conducted a survey following the same general approach as the 2003 survey[15] to update the full laboratory cost estimates and better understand the extent and costs of poliovirus ES activities.

Methods

Survey instrument

We developed an online survey instrument (see appendix A1 modeled after the 2003 survey.[15] With respect to costs, the instrument requests annual estimates for 11 major cost categories (see below) each for analysis of samples obtained through AFP surveillance and from ES. For the cost categories “equipment” and “durable supplies,” we asked for annual amortized costs, defined as purchase, packing, freight, and insurance costs divided by the expected useful lifetime, and we provided a spreadsheet to help respondents compute the annual amortized costs. In addition, for laboratories that recently (i.e., between 2010 and 2016) established or significantly expanded their ES capacity, we requested estimates of the ES set-up costs for 10 largely overlapping cost categories relevant to establishing ES capacity. For all of these, we asked respondents to provide the breakdown of costs by funding source (i.e., internal, external (GPEI), bilateral (non-GPEI, non-national)). The instrument further included questions about the role and capacities of the laboratories, geographical areas served, staff time spent on different activities, number of samples processed for different tests (e.g., virus isolation, ITD, sequencing, and, for ES samples, concentration), serological testing activities, non-polio surveillance activities by supported by funding for polio (i.e., polio-supported staff), the nature of ES activities, and anticipated future changes in workload or workflow.

Process

We piloted the survey among all WHO regional coordinators of the GPLN and a small subset of laboratories before launching the revised, final instrument online and in PDF form in July 2017, in English, Chinese, and Russian. We targeted all 145 active GPLN laboratories (we excluded one laboratory considered dormant) and 3 non-GPLN laboratories recently established to facilitate ES in countries with no easy access to a GPLN laboratory for sewage sample concentration and processing (i.e., concentration-only laboratories). We followed up with responding laboratories to resolve any ambiguities or apparent inconsistencies in the responses (see appendix A2 for a list of the responding laboratories). We reached out four times to non-responding laboratories to increase the response rate through November 2017 and closed the online survey instrument at the end of 2017.

Processing and analysis of results

We collected all original responses directly from the online survey instrument and manually entered any changes indicated by respondents during the follow-up. For rare instances in which a laboratory provided a range of costs for a category, we used the midpoint. Some respondents noted that they reported costs for consumable supplies or shared consumable supplies on a per-sample basis rather than as an annual total, which prompted us to systematically convert consumable supply costs to annual totals when we suspected responses per sample (see appendix A3). We converted all monetary estimates to 2016 US dollars ($) using publicly available exchange rates from July 1, 2016.[18] We classified the income levels of laboratories based on the 2016 World Bank income levels of their host countries.[19] Unless otherwise noted, all results represent the annual totals for 2016.

To account for missing cost responses from responding laboratories, we interpreted unanswered or zero responses differently depending on the cost category. We assumed that all laboratories incur costs under the six cost categories of personnel, equipment, durable supplies, consumable supplies, operations, and shipping/transport (i.e., non-zero categories, NZCs). In contrast, we assume that some laboratories may truly not incur any costs for the five categories of training, shared consumable supplies, donated supplies, technical support, and other (i.e., possible zero categories, PZCs). Furthermore, we pre-processed some of the cost data before further analysis because some respondents indicated challenges in separating costs between analysis of AFP and ES samples and others explicitly indicated that they reported only the combined costs. Compared to samples from AFP patients, the processing of ES samples follows a more involved algorithm (i.e., three times as many cell cultures),[16] more often yields viruses that require ITD testing or sequencing (i.e., because an ES sample represents a composite sample from many individuals), and requires about four times the processing time by trained staff.[20] The type and nature of adjustment depended on the nature of the missing data (see appendix A3)

To account for non-responding laboratories, we considered variables that we could obtain outside of the survey for all laboratories from the web-based GPLN management system, including number of employee full-time equivalents (FTEs) employed for poliovirus surveillance, and number of virus isolation tests, ITD tests, and sequences performed on AFP samples. Based on differences between laboratories and descriptive analysis of relationships by WHO region, income level, and laboratory role, we grouped the laboratories by income level and capacity (i.e., virus isolation only, ITD and virus isolation but no sequencing, and sequencing (with or without ITD capacity)) for regression analyses. Within each group, we used univariate linear regression on the number of samples processed for virus isolation to estimate missing costs. In the event of negative intercepts or slopes in a given cost category and group, we forced the intercept to 0, thus effectively reverting to estimation based on the simple average cost per sample processed for virus isolation for the given cost category and group. We also considered linear regression on the number of FTEs, multilinear regression on all variables, and different grouping approaches, but found no substantial improvement or differences in the totals.

Other cost assumptions

To estimate the costs of analysis of serum samples, we assume costs of $10 per sample for consumables and equipment. For the personnel costs, we multiply the reported average personnel costs per FTE in upper middle- and high-income countries (since these countries test most of the reported serum samples) by the reported number of FTEs for processing of serum samples. We estimate the costs of research and development activities based on extrapolation of data from the largest global specialized laboratory (i.e., the U.S. Centers for Disease Control and Prevention laboratory in Atlanta, GA) (MAP,MSO). We estimate the global overhead costs for coordination, training, and technical support not incurred by individual laboratories based on WHO surveillance budgets (OMD).

Patient and Public Involvement

This survey did not involve patients or public opportunities for engagement.

Results

Overall survey response and grouping

We received responses from 132 of 149 (89%) surveyed laboratories, which included one concentration-only laboratory. Figure 1 provides the breakdown of the response rate by laboratory role, region, and income level, which shows a response rate of at least 78% for all breakdowns, except for the 3 concentration-only laboratories, from which we received only 1 response (i.e., response rate 33%). Based on the reported capacities, we grouped the 131 responding GPLN laboratories into 30 (23%) laboratories with virus isolation capacity only, 67 (50%) laboratories with virus isolation and ITD capacity, and 35 (27%) laboratories with sequencing capacity (regardless of virus isolation and ITD capacity), with the concentration-only laboratory equipped with neither of those capacities. For the estimation of costs to process AFP samples, we further grouped the laboratories by income level into low- and lower middle-income vs. upper middle- and high-income to allow more appropriate cost extrapolation while maintaining sufficient numbers of laboratories in each group. For the estimation of costs to process ES samples, we did not stratify by income level because of the smaller numbers of laboratories in this group.

AFP sample processing costs

Table 1 (top) summarizes the breakdown in the laboratory types and the numbers of laboratories in each category. The reported costs to process samples from AFP cases and contacts for each individual cost category reflect different response rates for the various categories (Table 1, numbers in parenthesis next to the reported costs show the percent of laboratories reporting). The reported costs for each category remained markedly lower than the overall survey response rates (compare Figure 1 with Table 1), and show the highest reporting percentages for personnel and consumable supplies. The responding laboratories reported approximately $16 million in total AFP-related costs (Table 1), which does not include $510,000 in reported AFP-related costs from 12 laboratories that we re-allocated to processing of ES samples. Personnel accounted for 44% of all reported costs, followed by consumable supplies (21%) and equipment (20%).

Figure 2a shows the source of funding by cost category for the costs reported. Internal (national) funds accounted for a large proportion of personnel (76%), training (66%), equipment (64%), operations (79%), and technical support (85%) costs, while external (GPEI) funds accounted for a large proportion of costs for consumable supplies (72%), donated supplies (75%), and shared consumable supplies (54%). Overall, 61%, 36%, 2.4%, and 1.3% of all reported funds to process AFP samples came from internal, external, bilateral, and unspecified funds, respectively. Twenty-six percent of laboratories reported dependence on non-internal funds for at least 50% of their budget, with regional percentages of 0%, 3.3%, 6.7%, 50%, 58% and 86% for the American, Western Pacific, European, Eastern Mediterranean, Southeast Asian, and African WHO regions, respectively.

Finally, Table 1 (bottom section) also reports the total costs estimated for each laboratory group and cost category, based on extrapolation to the entire network of laboratories. The resulting total AFP costs equal approximately $28 million. Although the sequencing laboratories account for only 26% of the total number of GPLN laboratories, they account for 34% of the estimated lab-specific costs for processing of AFP samples.

ES sample processing costs

Fifty-nine (45%) of all 132 responding laboratories reported supporting ES activities, including one concentration-only laboratory. One additional laboratory that reported not analyzing ES samples estimated the costs of supporting national ES activities with a staff member providing technical support. We excluded the latter laboratory and the concentration-only laboratory due to the absence of numbers of ES samples processed for virus isolation needed for inclusion in the regression. Seven non-responding GPLN laboratories support ES according to unpublished WHO data, leading to a total of 65 (45%) GPLN laboratories supporting ES activities in 2016.

Table 2 shows the reported and estimated recurring costs for ES based on the variable response rates for each cost category. The responding laboratories reported approximately $3.2 million in total recurring ES-related costs, which includes $510,000 in AFP costs that we attributed to ES. Varying the ratio of ES processing cost per sample to the AFP processing cost per sample from 3 to 10 changed the AFP processing costs attributed to ES processing from $340,000 to $590,000, respectively. Thus, the impact of this assumption on overall costs remains modest, because it only affects 12 laboratories with ambiguity about whether reported AFP processing costs included ES processing costs. The breakdown by cost category remained similar to the costs for processing of AFP samples, and similarly the sequencing laboratories accounted for a large portion (58%) of all reported recurring ES costs.

Figure 2b shows the breakdown by cost category and funding source for the reported costs in Table 2, which shows a similar breakdown as for AFP sample processing costs. Overall, 65%, 22%, 0.3%, and 12% of all reported recurring ES costs came from internal, external, bilateral, and unspecified funds, respectively.

The bottom half of Table 2 shows the extrapolated costs estimated in each group and for each cost category. The resulting total recurring ES costs equal approximately $5.3 million. Table 2 does not factor in the relatively small costs from the one concentration-only laboratory that responded to the survey, which reported only some internally-funded recurring ES costs for personnel with other costs captured in the ES set-up costs or unquantified because they paid for by external resources.

Of the 59 laboratories (i.e., 58 GPLN laboratories and 1 concentration-only laboratory) that reported supporting ES activities, 35 (59%) reported that they recently (i.e., between 2010 and 2016) set-up or significantly expanded their ES capacity. Of these 35 laboratories, 25 (71%) provided set-up cost estimates for at least one cost category, leading to total reported set-up costs of approximately \$1.8 million. This includes estimates from 16 ITD laboratories, 6 sequencing laboratories, 2 virus isolation laboratories, and 1 concentration-only laboratory. Only 6 of the 25 (24%) laboratories reported becoming fully operational during 2016, which suggests that most of the reported set-up costs did occurred sometime between 2010 and 2015. Figure 3 shows the breakdown of the \$1.8 million of reported ES set-up costs, with the legend also showing the response rates for each set-up cost category. New equipment for concentration represented the largest contributor to all reported set-up cost (38%), followed by new equipment for expanded poliovirus processing capacity (12%), new personnel (12%), new consumable supplies (11%) and facility costs (10%). These results suggest that establishing new ES capacity in a laboratory costs approximately \$75,000.

Other findings

We explored the breakdown of reported staff time spent on polio and non-polio diseases by WHO region for staff supported by funding for polio (see appendix A4). We also characterized the reported number of samples or isolates processed in the context of different activities (see appendix A4), with the approximately 250,000 samples from AFP cases and their contacts processed for virus isolation dominating the results and reflecting the primary focus of the GPLN on supporting AFP surveillance. Given the current prevalence of wild polioviruses and level of OPV use, roughly 4.5% of stool samples from AFP cases grow in the L20B cells used for virus isolation. Of these, approximately 7% appear as possible wild or vaccine-derived poliovirus, which then undergo sequencing. In contrast, ES accounted for only 12,000 samples processed for virus isolation originating from 8,200 environmental sample concentrates, 67% of which were concentrated using the WHO-recommended two-phase method.[16] The difference between the number of concentrates and the number of isolates probably comes from laboratories that (re)tested samples already concentrated by another laboratory, including third-party laboratories not part of the GPLN.

Estimated overall GPLN costs

Table 3 estimates the full polio laboratory costs for 2016 based on the results of the survey complemented with data from the WHO and the CDC global specialized laboratory in Atlanta, GA. Using the results from Tables 1 and 2, we estimate the total laboratory-specific costs to support AFP surveillance and ES at approximately $33 million. This does not include the reported recent ES set-up costs of $1.8 million, which represents only a fraction of the WHO-supported ES set-up costs for 2016, or the costs for the analysis of serum samples. For 2016, we estimate total costs of serology of approximately $1 million, total costs of research and development activities of approximately $3 million, and global overhead costs for coordination, training, technical of approximately $6 million. The resulting estimated total poliovirus laboratory costs for 2016 equal to $43.3 million.

Discussion

This study confirms the important contributions of both GPEI and internal funds to the maintenance of a well-functioning poliovirus surveillance laboratories.[15] For comparison, the 2003 survey estimated substantially lower total costs of $28 million per year (i.e., 21 million in year 2002 US dollars). This estimate broke down as: (1) $16 million of AFP-related costs for the (sub)-national and regional reference laboratories, (2) $8 million for all polio-related activities by global specialized laboratories, including limited ES conducted at the time, and (3) $4 million in global coordination costs.[15] In this study, the corresponding AFP-related costs for the (sub)-national and regional reference laboratories equals approximately $25 million. The total estimated AFP and recurring ES costs for the global specialized laboratories equals only $3.5 million, but increases to over $7 million if we add the estimated research and development, serology, coordination, training, and technical support costs.

While direct comparison of the absolute costs in 2016 to those in the 2003 study[15] remains somewhat challenging due to differences in the specific cost requested, this study finds an apparent increase in the proportion of costs paid for by internal funds from 53% in 2003 [15] to 62% in 2016. This may reflect increasing self-funding of the laboratory component of polio surveillance activities by polio-free countries no longer at a high risk of outbreaks. In addition, after largely externally-funded capital investments helped to set up laboratories with the capacity to apply molecular methods in many countries, the more often internally-funded personnel costs now represent a relatively larger share of the total costs.

The investments in capital costs may also have reduced the recurring costs compared to the 2003 survey, despite the increase from approximately 85,000 AFP samples tested in 2002 to almost 250,000 in 2016. Nevertheless, with 50% or more of GPLN laboratories in the African, Eastern Mediterranean, and Southeast Asian WHO regions depending on external GPEI funds for at least half of their budgets for AFP sample analysis, planning for financing after the GPEI resources decline post-certification remains of critical importance. In this context, we note that the GPEI budget for 2017 for the GPLN of $16.4 million reflects only 17% of the GPEI budget for all surveillance activities (i.e., costs associated with the field components of AFP surveillance dominate the costs in the GPLN budget for surveillance) and 1.5% of the overall GPEI budget for 2017.[14]

This study further documents the significant contributions made by poliovirus laboratoriesto a large number of other disease surveillance efforts, with 30% of all polio-supported staff time reportedly used for surveillance of other diseases. Thus, we hope that this study highlights both the importance of contributions that countries make to poliovirus surveillance and the need to sustain funding to support laboratories worldwide in their surveillance efforts for poliovirus and other diseases. As global population immunity to poliovirus transmission decreases after OPV cessation,[21] successfully controlling any future outbreaks will require continued vigilance and a rapid immunization response.[22] However, questions remain after the certification of eradication about the long-term financial sustainability of poliovirus surveillance and the functions of the GPLN, because of the expected transition of key GPEI responsibilities and resources to other programs.

Based on our results, the poliovirus laboratory costs to support ES remain relatively small compared to the AFP costs. This reflects the reality that despite the ongoing global ES expansion, ES remains limited to parts of some countries, while the global AFP surveillance system remains (nearly) universal. With the first phase of ES expansion continuing during 2017 and 2018, we expect both increased set-up costs during those years and higher recurring ES costs going forward compared to the ES costs estimated for 2016. With significant further expansion, the poliovirus laboratory costs for ES could exceed those for AFP, particularly if AFP surveillance declines, although we urge careful consideration of the costs and effectiveness of allowing AFP surveillance to decline.[23]

This survey relied on self-reported estimates of laboratory costs. While we attempted to formulate the questions unambiguously and provided translations of the survey instrument and during follow up where possible, we cannot rule out possible differences in interpretation of the questions. As described above, some respondents reported difficulties separating costs between categories and activities or amortizing costs of equipment purchased long ago. Although we achieved a high overall response rate of 89%, the response rates for individual cost categories remained variable. Therefore, we relied on estimation based on regression of relatively sparse data to characterize missing values, which may have introduced biases. For example, laboratories receiving funding from the GPEI may be more likely to have omitted estimates for individual cost categories, potentially leading to relatively greater errors in the estimation of the external cost. In addition, laboratories may not have accounted for all equipment, supplies, and operations cost (e.g., utilities, building maintenance) paid for by their hosting institutions, potentially leading to underestimation of the share of costs funded by internal sources. We also did not consider alternative data collection methods, which might have yielded different results (e.g., instead of asking the entire population of laboratories to report annual estimates based on available data and recall we could have attempted to visit a sample of laboratories and observed activities and costs over some period of time and then extrapolated to the full year and full population).

Despite its limitations, we hope this study provides valuable insights regarding poliovirus laboratory costs and the cost structure of the GPLN. Future research to inform global long-term poliovirus and broader surveillance may include detailed cost studies of the field component of AFP surveillance and economic analyses of the value of AFP surveillance and ES.

Conclusions

Although countries contribute significantly to poliovirus laboratory finances, many laboratories currently depend on GPEI funds, and these laboratories also support the laboratory component of surveillance activities for other diseases. Sustaining critical global surveillance for polioviruses and other diseases will require continued funding as GPEI resources decline, particularly after global certification. Paying the costs to sustain surveillance represents an essential element for securing a polio-free world, and offers the opportunity to transition at least some of the current poliovirus laboratory resources to control/eliminate other vaccine-preventable or emerging/re-emerging communicable diseases.[24]

List of abbreviations

AFP, acute flaccid paralysis; ES, poliovirus environmental surveillance; GPEI, Global Polio Eradication Initiative; GPLN, Global Polio Laboratory Network; ITD, intratypic differentiation; NZC, non-zero (cost) category; OPV, oral poliovirus vaccine; PZC, possible zero (cost) category

DECLARATIONS

Authors' contributions

All authors (RDT, DMO, MAP, MSO, KMT) contributed to the study design, survey instrument development, interpretation of data, manuscript writing, and revisions. The first author (RDT) performed the data analysis, the last author (KMT) coded and administered the survey instrument in Survey Monkey™, the second author (DMO) contacted the laboratories, the first and second authors (RDT, DMO) recruited participants and followed up with respondents on any questions.

Ethics approval and consent to participate

Not applicable

Consent to publish

Not applicable

Competing interests

None

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Data sharing statement

Technical appendix available on request from the authors.

References

1. World Health Assembly. Global eradication of poliomyelitis by the year 2000 (resolution 41.28). Geneva: World Health Organization, 1988.
2. Global Polio Eradication Initiative. Strategy 2017 [Available from: http://polioeradication.org/ accessed December 14 2017.
3. Global Polio Eradication Initiative. Global eradication of wild poliovirus type 2 declared 2015 [updated September 20, 2015. Available from: http://www.polioeradication.org/mediaroom/newsstories/Global-eradication-of-wild-poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx accessed November 30 2015.
4. Kew OM, Cochi SL, Jafari HS, et al. Possible eradication of wild poliovirus type 3--worldwide, 2012. *MMWR Morb Mortal Wkly Rep* 2014;63(45):1031-33.

5. World Health Organization. Global Polio Eradication Initiative: Polio Eradication and Endgame Strategic Plan (2013-2018). Geneva, 2013.
6. Duintjer Tebbens RJ, Pallansch MA, Kew OM, et al. Risks of paralytic disease due to wild or vaccine-derived poliovirus after eradication. *Risk Anal* 2006;26(6):1471-505.
7. Hampton LM, Farrell M, Ramirez-Gonzalez A, et al. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine - Worldwide, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65(35):934-38. doi: 10.15585/mmwr.mm6535a3
8. Diop OM, Asghar H, Gavrilin E, et al. Virologic Monitoring of Poliovirus Type 2 after Oral Poliovirus Vaccine Type 2 Withdrawal in April 2016 - Worldwide, 2016-2017. *MMWR Morb Mortal Wkly Rep* 2017;66(20):538-42. doi: 10.15585/mmwr.mm6620a4
9. Duintjer Tebbens RJ, Pallansch MA, Cochi SL, et al. An economic analysis of poliovirus risk management policy options for 2013-2052. *BMC Infect Dis* 2015;15:389. doi: 10.1186/s12879-015-1113-7
10. Jorba J, Diop OM, Iber J, et al. Update on Vaccine-Derived Polioviruses - Worldwide, January 2016-June 2017. *MMWR Morb Mortal Wkly Rep* 2017;66(43):1185-91. doi: 10.15585/mmwr.mm6643a6
11. Duizer E, Ruijs WL, van der Weijden CP, et al. Response to a wild poliovirus type 2 (WPV2)-shedding event following accidental exposure to WPV2, the Netherlands, April 2017. *Euro Surveill* 2017;22(21) doi: 10.2807/1560-7917.ES.2017.22.21.30542
12. Duintjer Tebbens RJ, Pallansch MA, Thompson KM. Modeling the prevalence of immunodeficiency-associated long-term vaccine-derived poliovirus excretors and the potential benefits of antiviral drugs. *BMC Infect Dis* 2015;15:379. doi: 10.1186/s12879-015-1115-5
13. Dunn G, Klapsa D, Wilton T, et al. Twenty-Eight Years of Poliovirus Replication in an Immunodeficient Individual: Impact on the Global Polio Eradication Initiative. *PLoS Pathog* 2015;11(8):e1005114. doi: 10.1371/journal.ppat.1005114
14. Global Polio Eradication Initiative. GPEI Budget 2017 2017 [updated June 1, 2017. Available from: http://polioeradication.org/financing/financial-needs/financial-resource-requirements-frr/gpei-budget-2017/ accessed December 14 2017.
15. de Gourville EM, Sangrujee N, Duintjer Tebbens RJ, et al. Global Surveillance and the value of information: The case of the global polio laboratory network. *Risk Anal* 2006;26(6):1557-69.
16. Global Polio Eradication Initiative. Guidelines on environmental surveillance for detection of polioviruses - working draft - March 2015, 2015.
17. World Health Organization. Guidelines for environmental surveillance of poliovirus circulation. Geneva: Department of Vaccines & Biologicals, WHO, 2003.
18. XE.com. Current and historical rate tables 2017 [Available from: http://www.xe.com/currencytables/?from=USD&date=2016-07-01 accessed November 15 2017.
19. World Bank. World Bank analytical classifications - calendar year 2016 GNI per capita in US$ (Atlas methodology) 2017 [Available from: http://databank.worldbank.org/data/download/site-content/OGHIST.xls accessed December 13 2017.
20. Hovi T, Shulman LM, van der Avoort H, et al. Role of environmental poliovirus surveillance in global polio eradication and beyond. *Epidemiology and Infection* 2012;140(1):1-13. doi: 10.1017/S095026881000316X

21. Duintjer Tebbens RJ, Hampton LM, Thompson KM. Implementation of coordinated global serotype 2 oral poliovirus vaccine cessation: Risks of potential non-synchronous cessation. *BMC Infect Dis* 2016;16:237.
22. Duintjer Tebbens RJ, Pallansch MA, Wassilak SGF, et al. Characterization of outbreak response strategies and potential vaccine stockpile needs for the polio endgame. *BMC Infect Dis* 2016;16:137. doi: 10.1186/s12879-016-1465-7
23. Duintjer Tebbens RJ, Zimmermann M, Pallansch MA, et al. Insights from a systematic search for information on designs, costs, and effectiveness of poliovirus environmental surveillance systems. *Food and Environmental Virology* 2017;9(4):361-82. doi: 10.1007/s12560-017-9314-4
24. Rutter PD, Hinman AR, Hegg L, et al. Transition Planning For After Polio Eradication. *J Infect Dis* 2017;216(suppl_1):S287-S92. doi: 10.1093/infdis/jix026

547 **Table 1: Reported and estimated costs to process acute flaccid paralysis samples, based on regression of reported total number**
548 **stool samples processed for virus isolation for the number of laboratories (N) in the category (excluding the costs for the**
549 **concentration-only laboratories and global and regional costs for research and coordination).**

Cost category	Laboratories with virus isolation capacity only (N=38)		Laboratories with ITD (and no sequencing) capacity (N=70)		Laboratories with sequencing capacity (N=38)		All GPLN laboratories (N=146)
	Low- and lower middle-income (N=8)	Upper middle-and high-income (N=30)	Low- and lower middle-income (N=32)	Upper middle-and high-income (N=38)	Low- and lower middle-income (N=6)	Upper middle-and high-income (N=32)	
Total reported costs (% of all labs in group reporting non-zero costs)							
Personnel	1,700 (25)	750,000 (60)	2,100,000 (78)	1,100,000 (63)	490,000 (67)	2,400,000 (78)	6,900,000 (67)
Training	2,500 (13)	8,900 (37)	37,000 (25)	36,000 (55)	250 (17)	51,000 (41)	130,000 (38)
Equipment	36,000 (25)	190,000 (60)	690,000 (72)	1,000,000 (63)	3,000 (17)	1,200,000 (69)	3,100,000 (62)
Durable supplies	2,400 (25)	170,000 (57)	120,000 (59)	110,000 (63)	9,400 (33)	110,000 (59)	530,000 (57)
Consumable supplies	34,000 (50)	190,000 (60)	1,300,000 (59)	620,000 (71)	900,000 (50)	280,000 (75)	3,300,000 (65)
Shared consumable supplies	2,700 (38)	44,000 (40)	84,000 (41)	180,000 (53)	290,000 (33)	88,000 (53)	690,000 (46)
Donated supplies	4,000 (13)	10,000 (3)	5,600 (6)	770 (3)	0 (0)	480 (9)	21,000 (5)
Operations	4,500 (25)	53,000 (17)	170,000 (53)	140,000 (50)	53,000 (33)	300,000 (28)	730,000 (37)
Shipping/transport	1,200 (25)	24,000 (30)	53,000 (66)	32,000 (61)	100 (17)	91,000 (53)	200,000 (50)
Technical support	200 (13)	14,000 (23)	39,000 (16)	43,000 (26)	200 (17)	19,000 (13)	120,000 (19)
Other	0 (0)	7,500 (3)	7,400 (6)	1,400 (3)	0 (0)	1,600 (3)	18,000 (3)
All cost categories	90,000	1,500,000	4,600,000	3,300,000	1,800,000	4,500,000	16,000,000
Estimated total costs							
Personnel	9,100	1,200,000	2,600,000	1,700,000	770,000	2,700,000	9,000,000
Training	2,900	9,000	44,000	39,000	250	63,000	160,000
Equipment	4,200,000	290,000	930,000	1,200,000	18,000	1,700,000	8,400,000
Durable supplies	270,000	260,000	200,000	180,000	33,000	260,000	1,200,000

Consumable supplies	150,000	280,000	1,400,000	810,000	1,500,000	450,000	4,600,000
Shared consumable supplies	8,400	63,000	87,000	230,000	290,000	110,000	790,000
Donated supplies	4,600	15,000	6,200	830	0	600	27,000
Operations	540,000	550,000	330,000	250,000	1,000,000	440,000	3,100,000
Shipping/transport	150,000	40,000	57,000	55,000	600	170,000	470,000
Technical support	230	21,000	40,000	46,000	200	20,000	130,000
Other	0	11,000	8,200	1,500	0	2,200	23,000
All cost categories	5,300,000	2,800,000	5,700,000	4,500,000	3,600,000	6,000,000	28,000,000

Table 2: Reported and estimated recurring costs to process environmental samples, based on regression by reported total number of environmental samples processed for virus isolation (results exclude costs from concentration-only laboratories).

Cost category	Laboratories with virus isolation capacity only (N=20)	Laboratories with ITD (and no sequencing) capacity (N=22)	Laboratories with sequencing capacity (N=23)	All GPLN laboratories doing ES (N=65)
Total reported costs (% of all labs in group reporting non-zero costs)				
Personnel	110,000 (40)	290,000 (77)	1,100,000 (70)	1,500,000 (63)
Training	7,400 (15)	17,000 (41)	42,000 (35)	66,000 (31)
Equipment	24,000 (35)	340,000 (73)	160,000 (52)	520,000 (54)
Durable supplies	22,000 (40)	42,000 (82)	20,000 (52)	84,000 (58)
Consumable supplies	51,000 (35)	210,000 (68)	120,000 (57)	380,000 (54)
Shared consumable supplies	5,600 (20)	18,000 (50)	80,000 (35)	100,000 (35)
Donated supplies	8,100 (5)	29,000 (9)	1,200 (4)	38,000 (6)
Operations	1,900 (5)	110,000 (73)	190,000 (35)	300,000 (38)
Shipping/transport	8,500 (25)	33,000 (77)	46,000 (43)	88,000 (49)
Technical support	1,600 (15)	6,300 (18)	51,000 (17)	59,000 (17)
Other	0 (0)	0 (0)	25,000 (9)	25,000 (3)
All cost categories	240,000	1,100,000	1,800,000	3,200,000
Estimated total costs				
Personnel	180,000	320,000	1,700,000	2,200,000
Training	15,000	17,000	61,000	94,000
Equipment	66,000	470,000	360,000	890,000
Durable supplies	47,000	52,000	42,000	140,000
Consumable supplies	120,000	310,000	340,000	760,000
Shared consumable supplies	12,000	18,000	130,000	160,000
Donated supplies	18,000	29,000	2,000	49,000
Operations	37,000	130,000	540,000	710,000
Shipping/transport	44,000	36,000	98,000	180,000
Technical support	2,100	6,300	73,000	81,000
Other	0	0	40,000	40,000

All cost categories	540,000	1,400,000	3,400,000	5,300,000

Table 3: Estimated overall poliovirus surveillance laboratory costs for 2016

Cost component	Amount ($ millions)
Processing of samples from acute flaccid paralysis surveillance	
- Reported	16
- Estimated	28
Processing of samples from environmental surveillance	
- Reported	3.2
- Estimated	5.3
Serology	1.0
Research and development	3.0
Global and regional overhead (e.g., coordination, training, technical support)	6.0
Total estimated annual laboratory costs	43

Figure Captions

Figure 1: Survey response rates by role, region, and income level

Figure 2: Reported costs by cost category and source of funding
(a) Costs to process acute flaccid paralysis samples
(b) Costs to process environmental samples

Figure 3: Breakdown by cost categories of reported environmental surveillance set-up costs. Response rates for each cost category represent percentages among 30 laboratories that reported having set-up or significantly expanded poliovirus environmental surveillance capacity between 2010 and 2016. The total reported set-up costs equal $1.8 million.

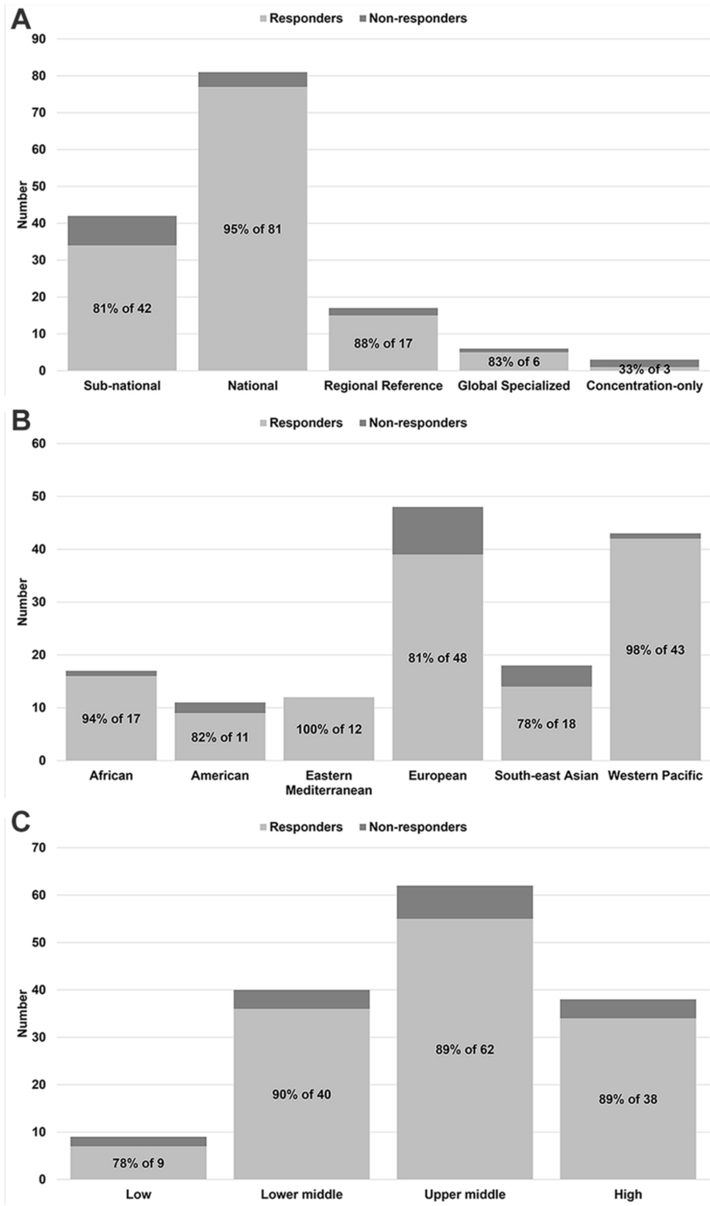
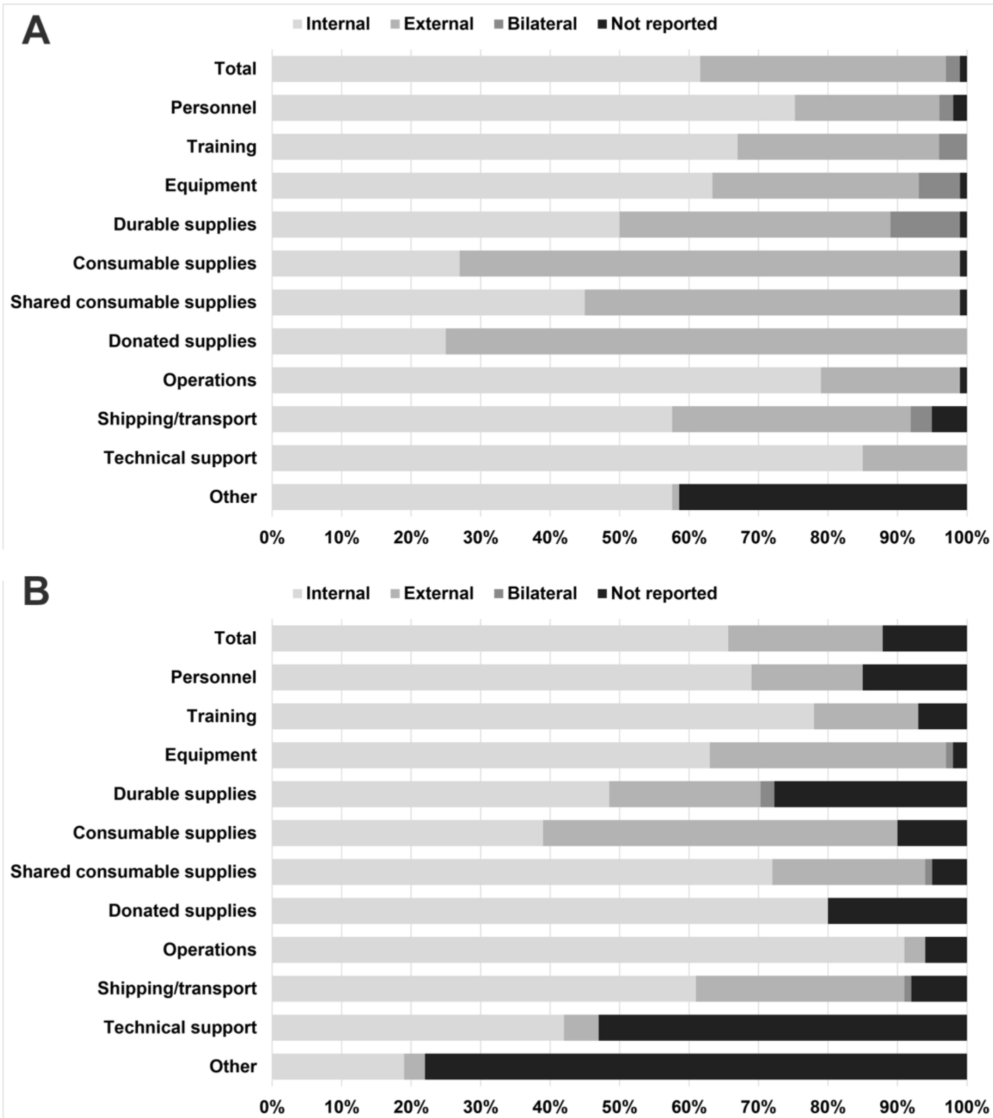


Figure 1: Survey response rates by role, region, and income level



hope you are well.

As the authors have stated that the research will be deposited into the Dryad repository, you should have submitted/uploaded the research data into Dryad. Once completed, you will receive an email with the DOI number. We require this DOI number so this is included in the data sharing statement of the article.

Thank you and I am looking forward to your prompt response.

Please be advised that once you have addressed above point/s, I will then forward your paper to Production Team. The email with the payment link will then follow in the next 24 hours after that.

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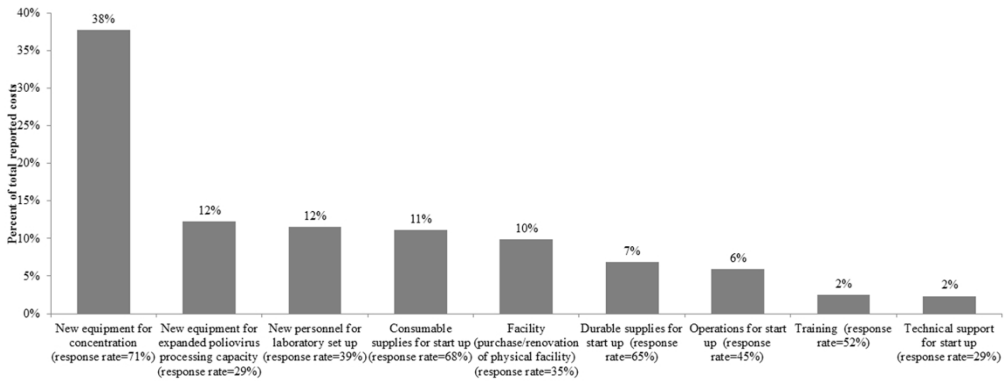

Figure 3: Breakdown by cost categories of reported environmental surveillance set-up costs. Response rates for each cost category represent percentages among 30 laboratories that reported having set-up or significantly expanded poliovirus environmental surveillance capacity between 2010 and 2016. The total reported set-up costs equal $1.8 million.

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APPENDIX for Duintjer Tebbens et al., "Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis"

A1. Survey instrument

Introduction: Poliovirus Laboratory Survey

The World Health Organization (WHO)-led Global Polio Laboratory Network (GPLN) continues to play an essential role in global polio eradication, and periodic efforts to quantify its overall value provide important information that helps to motivate financial support for GPLN laboratories. Assessing the value of the GPLN is of utmost importance at this stage of the GPEI, as the partners discuss the strategies to maintain polio laboratory functions pre- and post-certification of wild poliovirus eradication and global containment of live polioviruses. This GPLN survey aims to collect data on activities and costs of all of the GPLN laboratories to support an overall synthesis. The objectives of this survey include to: (1) update estimates of the total costs of the GPLN reported based on a similar 2003 survey, (2) better understand the different cost components, including environmental surveillance, and (3) characterize the extent to which the GPLN contributes to surveillance of other diseases. The survey form should take approximately 60 minutes to complete, and we expect that collecting data and calculating some of the costs may take an additional 1-4 hours, depending on the size and complexity of the laboratory. Please start the survey as soon as possible, so if you have any questions or if you need to compile data, you will have time to do so. The survey includes questions about acute flaccid paralysis (AFP) surveillance (i.e., stool samples from AFP cases and contacts) and environmental surveillance (i.e., sewage samples).

Please note:
· we pre-filled some answers based on data collected in GPLNMS annual reports for 2016 as of June 2017, and we ask that you please check the pre-filled answers carefully and correct the information as appropriate.
· please do not leave any answers blank, because we cannot interpret these correctly, so please enter "0" for zero, "unknown" for unknown, "not applicable" for not applicable, or "data not available" or other appropriate text. If you find any question too difficult to answer, please do not quit the entire question or survey, but instead reply with "unable to answer" and please add any information that can help us understand the reason.

We provided a glossary to promote consistent interpretation of survey language. If you have any questions, please contact Dr. Radboud Duintjer Tebbens (Kid Risk) and Dr. Ousmane Diop (WHO). Thank you very much for your time and effort to respond to the survey. We look forward to hearing from you - please complete your response by September 1, 2017. We will share the results with all polio laboratory directors for dissemination once they become available.

1. Please provide information about how to contact you and about your laboratory
Laboratory Name:
Your Name:
Phone number:
Email address:

City:
Country:
WHO Region:
* Total employee full-time equivalents (FTEs) for poliovirus surveillance employed by the laboratory:
Please enter the percent (between 0-100, without the % sign) of FTEs reported for the line with the * above supported by National/internal funds:
Please enter the percent (between 0-100, without the % sign) of FTEs reported for the line with the * above supported by GPEI external funds:
Please enter the percent (between 0-100, without the % sign) of FTEs reported for the line with the * above supported by Other external funds (non GPEI-external funds, including bi-lateral support) - This line should total 100 minus the percents on the prior 2 lines.

2. What role did your laboratory play in the global polio laboratory network in 2016?
Subnational
National
Regional reference
Specialized
Other (please specify)

3. Please list the geographic areas (country, state, region) that your laboratory served in 2016 for each laboratory capacity (enter "None" for any you do not do and please note any special activities by including the word "Special" after the name of the geographic area indicated, for example to help with overflow from another lab, if applicable for 2016):
Virus isolation:
Intratypic differentiation (ITD):
Sequencing:
Serology:
Environmental surveillance:

4. Please estimate what percentages (without including the "%" sign) of polio-supported staff time and equipment your laboratory spends on poliovirus surveillance and research activities (including methods development, serology, clinical trials, next generation or complete genome sequencing, etc.) versus surveillance and research activities for other diseases.
Poliovirus activities (indicate 100 here and 0 on all other answers if your lab supports poliovirus surveillance activities exclusively):
Non-polio enteroviruses:
Measles and/or rubella viruses:
Rotavirus:
Influenza:
Japanese encephalitis:
Yellow fever:
Other arboviruses (e.g., Zika, dengue) or hemorrhagic fever viruses:
Other (please provide percentage here and details about what this includes in Question 9):

5. Did your laboratory perform the following for poliovirus environmental surveillance in 2016 (if none indicate no for all)?
Site selection: Y/N
Sample collection: Y/N
Sample transportation: Y/N
Concentration: Y/N
Virus isolation: Y/N
Intratypic differentiation: Y/N
Sequencing: Y/N
Other (please specify): Y/N

6. Please tell us about any poliovirus serology testing you did in 2016 (if none, then enter "None" for this question).
How many serum samples did you test for poliovirus antibodies in 2016?
Approximately how many employee hours did your laboratory spend in 2016 for poliovirus serum sample processing?
What laboratory method do you use for poliovirus serology testing?
Please indicate the purpose(s) for the poliovirus serology sampling (e.g., seroprevalence assessment, support for vaccine trials, etc.)

7. Please tell us the number of samples your laboratory processed in 2016 related to other activities (i.e., non-AFP, non-poliovirus environmental surveillance, and non-poliovirus serology activities) for the following (please specify details about the methods used and your role in sample collection in Question 9)
Non-polio enterovirus surveillance:
Healthy children / adult surveys (e.g., stool surveys) that are not part of AFP surveillance:
Clinical trial support:
Other (please specify the nature of these samples in Question 9):

8. What currency do you use to track laboratory costs and will you use to report costs in this survey?

9. Please specify details here if you answered "other" for Question 4 and/or 7, please also describe any research activities conducted by your laboratory in 2016 related to polioviruses, and please use this space to enter any other comments you would like to make related to the questions on this page.

10. How many samples/isolates from AFP cases and their contacts did you process in 2016?
Acute flaccid paralysis (AFP) surveillance:
Virus isolation:
Intratypic differentiation:
Sequencing:
Other (please enter the number here and specify the type of processing in Question 14):

11. How many people (full-time equivalents) worked on the different steps of processing AFP samples in 2016?

Cell culture:
Virus isolation:
Intratypic differentiation:
Sequencing:
Management (including supervisors, data management, analytics, recording, and reporting):
Other (please enter number here and specify the type of processing in Question 14):

12. How much did your laboratory spend (in the currency you specified in Question 8) for analysis of AFP samples in 2016 for each cost category?
Personnel (costs should correspond to number of people in Question 11 plus any staff not on payroll):
Training (please exclude any costs counted in the personnel row above):
Equipment, please estimate the amortized annual cost, see Excel worksheet:
Durable supplies, please estimate the amortized annual cost, see Excel worksheet:
Consumable supplies attributable to each sample:
Shared consumable supplies purchased by laboratory not easily attributable to each sample:
Donated supplies provided by your lab to other labs (please specify the other labs you provide these to in Question 14):
Operations:
Shipping/transport:
Technical support (not otherwise captured):
Other (please specify in Question 14):

13. Please indicate the approximate percents of the amounts spent in Question 12 for each c ost category by contribution type: 1. National/internal; 2. GPEI external; and 3. Bilateral and non-GPEI external. For example, if all support came from national sources then indicate "100; 0; 0" OR if all contributions came from the GPEI indicate "0; 100; 0" OR if approximately equal support came from each indicate "33.4; 33.3; 33.3" and please verify that the totals of all three components of the answer for each row add to 100)
Personnel
Training
Equipment
Durable supplies
Consumable supplies
Shared consumable supplies
Donated supplies
Operations
Shipping/transport
Technical support
Other

14. Please specify details here about Questions 10-13 for which you answered "other" or enter any comments you would like to make related to the questions on this page.

15. Did your laboratory support any poliovirus environmental surveillance or research activities in 2016 (please verify)?

No
Yes

16. Did your laboratory first establish its capacity to process poliovirus environmental samples between 2010 and 2016 (i.e., relatively recently)? (If yes, the survey will ask you to estimate set up costs. If your laboratory established its capacity to process environmental samples before 2010, but made significant investments in 2016 to expand its capacity, then answer yes and estimate the costs for expanding the capacity in 2016 in Question 18).
No
Yes

17. Please enter the dates your laboratory first began to develop the capacity to support poliovirus environmental surveillance efforts and became fully operational (if exact date unknown, please estimate month and enter "14" for day)?
Date laboratory began to develop the poliovirus ES capacity: MM/DD/YYYY
Date your lab became fully operational to support poliovirus environmental surveillance: MM/DD/YYYY

Environmental surveillance SET UP questions (for capacity established AFTER 2009 OR expanded during 2016 ONLY):

18. Please estimate the costs your laboratory spent to SET UP poliovirus ES capacity between the dates you reported in Question 17 (in the currency you specified in Question 8) for each cost category.
Facility (purchase/renovation of physical facility)
New personnel for laboratory set up
Training
New equipment for concentration (e.g., centrifuge, refrigerators, funnels, filtration devices, etc.)
New equipment for expanded poliovirus processing capacity
Durable supplies for start up
Consumable supplies for start up
Operations for start up
Technical support for start up
Other (please specify in Question 20)

19. If you included estimates of SET UP costs in Question 18, please indicate the approximate percents of the amounts for each cost category by contribution type: 1. National/internal; 2. GPEI external; and 3. Bilateral and non-GPEI external. For example, if all support came from national sources then indicate "100; 0; 0" OR if all contributions came from the GPEI indicate "0; 100; 0" OR if approximately equal support came from each indicate "33.4; 33.3; 33.3" and please verify that the totals of all three components of the answer for each row add to 100)
Facility
New personnel for laboratory set up
Training for start up
New equipment for concentration
New equipment for expanded poliovirus processing capacity

Durable supplies for start up
Consumable supplies for start up
Operations for start up
Technical support for start up
Other (please specify in Question 20)

20. Please specify details here about Questions 18-19 for which you answered "other" or enter any comments you would like to make related to the questions on this page.

21. Which organization(s) collect the poliovirus environmental samples that your laboratory receives?

22. Please enter the total number of environmental samples your laboratory received in 2016 from each of the following types of water source(s) sampled (if known). If only unknown water source(s) sampled, then please indicate the total number of environmental samples for 2016 in the second-to-last row.
Wastewater treatment plant
Pumping station
Open drains or canals
Streams, rivers, or other flowing surface water
Lakes, ponds or other standing surface water
Access point from sewage system
Unknown
Other (please indicate type in Question 27)

23. Please enter the number of environmental samples for which your laboratory took the indicated number of days between the time of sample collection and starting the process of virus isolation. Your internal data for all poliovirus ES samples should provide the sample collection date and the date your lab started sample processing.
Less than 2 days
3 to 5 days
6 to 10 days
11 to 15 days
16 to 20 days
21 to 25 days
26 to 30 days
31 to 35 days
More than 35 days

24. How many environmental samples did your laboratory process in 2016 for each of the following?
Concentration using
WHO-recommended two-phase separation
Concentration using other methods (please specify method(s) used in Question 27)
Virus isolation
Intratypic differentiation

Sequencing
Research
Direct detection
Other (please specify type of processing in the comment field at the bottom of this page in Question 27)

25. How much did your laboratory spend (in the currency you specified in Question 8) for analysis of environmental samples in 2016 (excluding any costs for SET UP that occurred in 2016, which you should have reported in Question 18) and excluding any costs already reported in Question 12 related to AFP processing that applied to processing environmental samples.
Personnel (FTEs for environmental surveillance activities)
Training
Equipment, please estimate the amortized annual cost, see Excel worksheet
Durable supplies, please estimate the amortized annual cost, see Excel worksheet
Consumable supplies
Shared consumable supplies
Donated supplies (please specify the other labs you provide these to in Question 27)
Operations
Shipping/transport
Technical support
Other (please specify in Question 27)

26. Please indicate the approximate percent of the amounts spent in Question 25 for each c ost category by contribution type: 1. National/internal; 2. GPEI external; and 3. Other external. For example, if all support came from national sources then indicate "100; 0; 0" OR if all contributions came from the GPEI indicate "0; 100; 0" OR if approximately equal support came from each indicate "33.4; 33.3; 33.3" and please verify that the totals of all three components of the answer for each row add to 100)
Personnel
Training
Equipment
Durable supplies
Consumable supplies
Shared consumable supplies
Donated supplies
Operations
Shipping/transport
Technical support
Other (please specify in Question 27)

27. Please specify details here about Questions 21-26 for which you answered "other" or enter any comments you would like to make related to the questions on this page.

28. Please list and indicate the nature and source of all in-kind contributions your laboratory receives that support AFP and/or ES sample processing (please provide a brief description that

includes the amount, source, and purpose of the in-kind support). If your laboratory provides in-kind support to other laboratories, please provide details about this.

No

Yes (please specify)

29. Did your laboratory experience any significant changes in its workload/workflow in 2016 compared to 2015, if so please describe reasons (e.g., increased/decreased AFP, contact samples, special surveys, serology or clinical trials, introduction of environmental surveillance, implementation of polio laboratory containment and GAP III requirements or other activities, and impacts of changes in financials support, etc.)?

No

Yes (please specify)

30. Does your laboratory expect to make any significant changes in its workload/workflow in the future compared to 2016, if so please describe reasons (e.g., increased/decreased AFP, contact samples, special surveys, serology or clinical trials, or other activities, introduction of environmental surveillance)?

No

Yes (please specify)

31. What other costs or issues related to poliovirus laboratories do you think we should consider? What questions should we ask that we did not ask? Please use this space to make any final comments on the survey. Thank you very much for your responses.

32. Are you ready to submit your completed survey?

No (if not, please make sure to select "Prev" below to go back to the prior questions)

Yes (if so, and only if so, select "Done" below, because you will not be able to make any changes after selecting "Done")

A2. Responding laboratories

We received responses from the following 131 Global Polio Laboratory Network (GPLN) laboratories, organized by World Health Organization (WHO) region, laboratory type, and country of laboratory location:

African Region (15 of 16)

Regional reference laboratories in Central African Republic, Ghana, and South Africa

National laboratories in Algeria, Cameroon, Cote d'Ivoire (note: this lab also serves as the National lab for Mali, Burkina Faso, Liberia, and Sierra Léone), Democratic Republic of the Congo, Ethiopia, Kenya, Madagascar, Nigeria (2: Ibadan, Maiduguri), Uganda (note: this lab also serves as the National lab for Burundi, Rwanda, and the Republic of Tanzania, South Sudan), Zambia, and Zimbabwe (note: this lab also serves as the National lab for Malawi)

Region of the Americas (9 of 11)

Global specialized laboratory in the United States of America

Regional reference laboratory in Brazil

National laboratories in Canada, Columbia, Cuba, Mexico, Trinidad and Tobago, and Venezuela
Subnational laboratory in Brazil

Eastern Mediterranean Region (12 of 12)
Regional reference laboratories in Egypt, Kuwait, Pakistan, and Tunisia
National laboratories in Iran, Iraq, Jordan, Morocco, Oman, Saudi Arabia, Sudan, and the Syrian Arab Republic

European Region (39 of 48)
Global specialized laboratories in France and the Netherlands
Regional reference laboratories in Finland, Italy, and the Russian Federation
National laboratories in Albania, Austria, Belarus, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, France, Georgia, Greece, Hungary, Ireland, Israel, Kazakhstan, Latvia, Lithuania, Moldova, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Switzerland, Turkey, Ukraine, United Kingdom, and Uzbekistan
Subnational laboratories in Russian Federation (Khabarovsk), Turkey, and Ukraine (Odessa)

Note: At the time of the survey, we did not contact the National lab in the Democratic People's Republic of Korea because it was considered dormant (i.e., no active or known contact)

South East Asia Region (14 of 16)
Global specialized laboratory in India
Regional reference laboratories in Sri Lanka and Thailand
National laboratories in Bangladesh, India (6 – Bangalore, New Delhi, Ahmedabad, Kasauli, Kolkata, and Lucknow), Indonesia (3 - Bandung, Jakarta, Surabaya), and Myanmar

Western Pacific Region (42 of 43)
Global specialized laboratory in Japan
Regional reference laboratories in Australia and China
National laboratories in China (Hong Kong), Malaysia, Mongolia, New Zealand, Philippines, Republic of Korea, Singapore, and Viet Nam (2 – Hanoi, Ho Chi Minh)
Subnational laboratories in China (30 – Anhui, Beijing, Chongqing, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Jilin, Liaoning, Neimengu, Ningxia, Qinghai, Shaanxi, Shandong, Shanghai, Shanxi, Sichuan, Tianjin, Xinjiang, Yunnan, and Zhejiang)

In addition to these GPLN laboratories, we received a response from the Concentration-only laboratory in Niger.

A3. Technical details for analysis

Adjustment for under-reporting of (shared) consumable costs

When both the (shared) consumable supply costs per reported virus isolation test equaled less than $20 and the absolute (shared) consumable supply costs equaled less than $400, we multiplied the reported costs by the reported number of virus isolation tests. The second condition served to ensure no undue multiplication by the number of virus isolation tests for some laboratories with very large numbers of reported virus isolation tests but modest reported (shared) consumable supplies. This approach resulted in multiplication by the number of virus isolation tests of the reported consumable and shared consumable supplies for AFP sample processing for 59 and 25 laboratories, respectively. The results remained robust to choices of the thresholds of $20 and $400. With the exception of two laboratories that clearly reported (shared) consumable supplies per sample for ES sample processing, we did not adjust any of the reported (shared) consumable supply costs for ES sample processing.

Adjustments to account for missing data

As described in the main text, we separated the cost categories into non-zero categories (NZCs) and possible zero categories (PZCs). Some respondents indicated challenges in separating AFP and ES sample costs, and others explicitly indicated that they reported only the combined costs. This led us to pre-process the data from these laboratories. Based on the average total costs per sample processed for virus isolation reported among all laboratories that provided separate costs for AFP and ES, we assume that, on average, ES samples require seven times the cost per virus isolation test as AFP samples. Specifically, for costs in the NZCs, if a laboratory reported non-zero costs for AFP processing and either indicated that they combined AFP and ES costs or reported zero recurring or set-up ES costs for the cost category, then we estimated the portion of reported AFP costs attributable to ES based on the number of ES samples processed for virus isolation times seven, divided by the total samples (i.e., the number of ES samples times seven plus the number of AFP samples processed for virus isolation). We then subtracted the estimated ES-attributable costs from the reported AFP costs. For PZCs, we estimated and subtracted the ES-attributable costs only if the laboratory reported non-zero AFP costs and explicitly indicated that they combined ES and AFP costs (i.e., not if they reported 0 ES costs for the category). Recognizing uncertainty about the true ratio of costs per sample processed for virus isolation for ES compared to AFP samples, we explored the impact of varying this ratio from three to ten.

In addition to making assumptions to separate combined cost estimates, we further treated the data differently depending on the type of cost category. For NZCs, we interpreted any response not corresponding to a positive number as a missing estimate requiring estimation (i.e., even if a laboratory responded with 0, we interpreted this as an indication that the laboratories did not have access to the data required to estimate the costs). For PZCs, we interpreted zeroes, blanks, or any text indicating an inability to estimate the costs (e.g., not applicable, unknown, unable to estimate) as a true zero. For these categories, we only estimated costs for non-responding laboratories or laboratories that did not provide an estimate for any of the cost categories in the corresponding question according to the logic shown in Table A1 for AFP and Table A2 for ES.

Table A1: Logic for interpretation of AFP cost responses (after any subtractions as a result of logic in Table A2)

Value	Type of cost category	Interpretation	Treatment
Non-response or no cost provided for entire question	Any	No information available	Estimate based on regression
Positive number	Any	Laboratory-estimated value available	Keep response (influence regression)
Zero	PZC	True zero	Keep as 0 (influence regression)
	NZC	Costs not actually zero	Estimate based on regression
Other text (e.g., unknown)	PZC	Costs actually zero	Set to 0 (influence regression)
	NZC	Non-zero costs, but unknown	Estimate based on regression

NZC, non-zero (cost) category; PZC, possible zero (cost) category

Table A2: Logic for interpretation of ES recurring cost responses

Value	Type of cost category	Corresponding set-up cost category	Corresponding AFP cost category	Interpretation	Treatment
Non-response or no cost provided for entire question	Any	Any	Any	No information available	Estimate based on regression
Positive number	Any	Any	Any	Laboratory-estimated value available	Keep response (influence regression)
Zero	PZC	Any	Any	True zero	Keep as 0 (influence regression)
	NZC	Positive number	Any	Assume cost included in set-up costs	Keep as 0 to avoid double-counting (influence regression)
	NZC	Not a positive number	Positive number	Assume costs included in AFP costs	Estimate based on ES-attributable costs, then subtract from corresponding AFP cost category
	NZC	Not a positive number	Not a positive number	Non-zero costs, but unknown	Estimate based on regression
Respondent indicated cost included in AFP costs	PZC	Any	Positive number	Assume included in AFP costs	Estimate based on ES-attributable costs, then subtract from corresponding AFP cost category
	PZC	Any	Not a positive number	Costs actually zero	Set to 0 (influence regression)
	NZC	Any	Positive number	Assume included in AFP costs	Estimate based on ES-attributable costs, then subtract from corresponding AFP cost category
	NZC	Any	Not a positive number	Non-zero costs, but unknown	Estimate based on regression (but do not subtract from corresponding AFP cost category)
Other text (e.g., unknown)	PZC	Any	Any	Costs actually zero	Set to 0 (influence regression)
	NZC	Any	Any	Non-zero costs, but unknown	Estimate based on regression

NZC, non-zero (cost) category; PZC, possible zero (cost) category

A4. Other findings

Other diseases

Table A3 show the breakdown of polio-supported staff time spent on polio and non-polio diseases by WHO region. Only 1 of 132 (1%) of laboratories that responded to the survey did not provide estimates for the total number of polio-supported FTEs or the percentages spent on polio and other diseases. Overall, polio-supported staff spent approximately 30% of time supporting activities for other diseases or viruses, including non-polio enteroviruses (11%), measles and/or rubella viruses (7%), and a wide range of other diseases not specifically asked about in the survey (5%). The American (41%) and European (46%) regions reported the lowest percentages of staff time spent on polio. The Eastern Mediterranean region (87%), which includes one laboratory serving two polio-endemic countries (i.e., Afghanistan and Pakistan), reported the highest percentage.

Respondent laboratories collectively reported spending 41 FTEs on diseases/conditions not specifically listed in Table A3. The laboratories reported that these other diseases/conditions included TORCH, exanthemal infections, urogenital, immunology, intestinal and parasitic infection groups, human immunodeficiency virus, hepatitis, acute respiratory viral infections, teratogenic infections, mycoplasma, chlamydophyll, transgenic organisms control, astrovirus, norovirus, sapovirus, adenovirus, rabies, non-influenza respiratory diseases, non-rotavirus acute gastroenteritis, herpes group viruses, mumps, rhinovirus, parainfluenza virus, respiratory syncytial virus, metapneumovirus, parechovirus, polyomavirus, varicella virus, diphtheria, tetanus, pertussis, cytomegalovirus, crystalli, parotitis, severe fever with thrombocytopenia syndrome, meningitis, and encephalitis.

Table A1: Staff time spent on polio and non-polio diseases by World Health Organization Region for staff supported by funding for polio (i.e., polio-supported staff)

Disease/virus	Number (%) of employee full-time equivalents, by World Health Organization region (N=number of responses)						
	European (N=39)	Western Pacific (N=42)	Southeast Asian (N=14)	African (N=15)	Eastern Mediterranean (N=12)	American (N=8)	All (N=130)
Polio	59 (46)	83 (60)	171 (82)	137 (83)	83 (87)	25 (41)	558 (70)
Non-polio enteroviruses	30 (23)	24 (18)	11 (5)	5 (3)	3 (3)	15 (24)	88 (11)
Measles and/or rubella viruses	7 (5)	13 (9)	22 (10)	14 (9)	3 (3)	1 (1)	59 (7)
Rotavirus	5 (3)	4 (3)	3 (1)	2 (1)	2 (2)	1 (2)	16 (2)
Influenza	12 (9)	3 (2)	1 (0)	2 (1)	1 (1)	1 (1)	20 (3)
Japanese encephalitis	0 (0)	4 (3)	0 (0)	0 (0)	0 (0)	0 (0)	4 (1)
Yellow fever	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	2 (0)
Other arboviruses or hemorrhagic fever viruses	2 (2)	1 (0)	0 (0)	1 (0)	0 (0)	1 (1)	4 (1)
Other	15 (11)	5 (4)	2 (1)	1 (1)	4 (4)	14 (22)	41 (5)
All diseases	129	137	209	164	95	57	792

Other types of polio laboratory tests

Laboratories reported performing several other types of laboratory tests, including ELISA, PCR, RT-PCR, HBsAg, microtitration, genotyping, and serology for numerous viruses and on various sample types (i.e., sera, nasopharyngeal washings, blood, feces, urine, urogenital scrapings, sectional material, mites, spinal fluid, rectal swab and vomitus from diarrhea and food poisoning cases, ice and drinking water, soil) as well as virus isolation on fecal samples from AFP cases over age 15, AFP samples from provinces outside of the areas normally served by the laboratory, fecal samples from non-AFP patients not part of a survey, and research activities.

Table A4 summarizes the reported number of samples or isolates processed in the context of different activities. The difference between the number of concentrates and the number of isolates for ES probably comes from laboratories that (re)tested samples already concentrated by another laboratory, including third-party laboratories not part of the GPLN. A much larger fraction of isolates from ES samples compared to AFP samples underwent Intratypic differentiation (ITD) testing (54%) and sequencing (15%), probably because ES samples comprise a composite from potentially thousands of individuals and they often yield complex mixtures of viruses. This results in higher costs on a per-sample basis for ES than AFP, with ES sample processing additionally requiring three times as many cell cultures as the AFP sample processing. As shown in Table A4, laboratories also reported analyzing almost 2,000 ES samples in the context of research activities and 82 ES samples using direct detection methods.

Forty responding laboratories further reported analyzing over 50,000 serum samples for the presence of antibodies, which they estimated took almost 13,000 employee hours (i.e., 12.7 FTEs assuming 2,000 employee hours per year). Laboratories analyzed almost 40,000 samples in the context of non-polio enterovirus surveillance and approximately 150,000 other samples, reflecting the reality that many GPLN laboratories perform non-polio services (not necessarily funded by polio surveillance), particularly in countries with no recent polio outbreaks. While 49 laboratories reported testing other samples, 3 of these laboratories accounted for 83% of the 150,000 samples and indicated that their reported numbers included routine diagnostic services. Laboratories also reported analyzing approximately 6,900 and 4,300 samples in the context of healthy children or adult stool surveys and clinical trials, respectively.

Table A2: Reported number of samples/isolates processed for different activities

Activity	Nature of testing/activity	Number of samples/isolates
Acute flaccid paralysis surveillance	Virus isolation	243,897
	Intratypic differentiation	10,380
	Sequencing	751
	Other[a]	925
Environmental surveillance	Concentration (two-phase method)	5,509
	Concentration (other methods)	2,703
	Virus isolation	12,170
	Intratypic differentiation	6,638
	Sequencing	1,847
	Research	1,971
	Direct detection	82
Serology	Serum antibody testing	52,020
Other	Non-polio enterovirus surveillance	38,589
	Healthy children/adults surveys	6,907
	Clinical trial support	4,337
	Other[b]	149,345

[a] Includes serotyping and polymerase chain reaction analysis of non-polio enteroviruses identified in acute flaccid paralysis cases, Sanger sequencing, and next generation sequencing of complete genomes

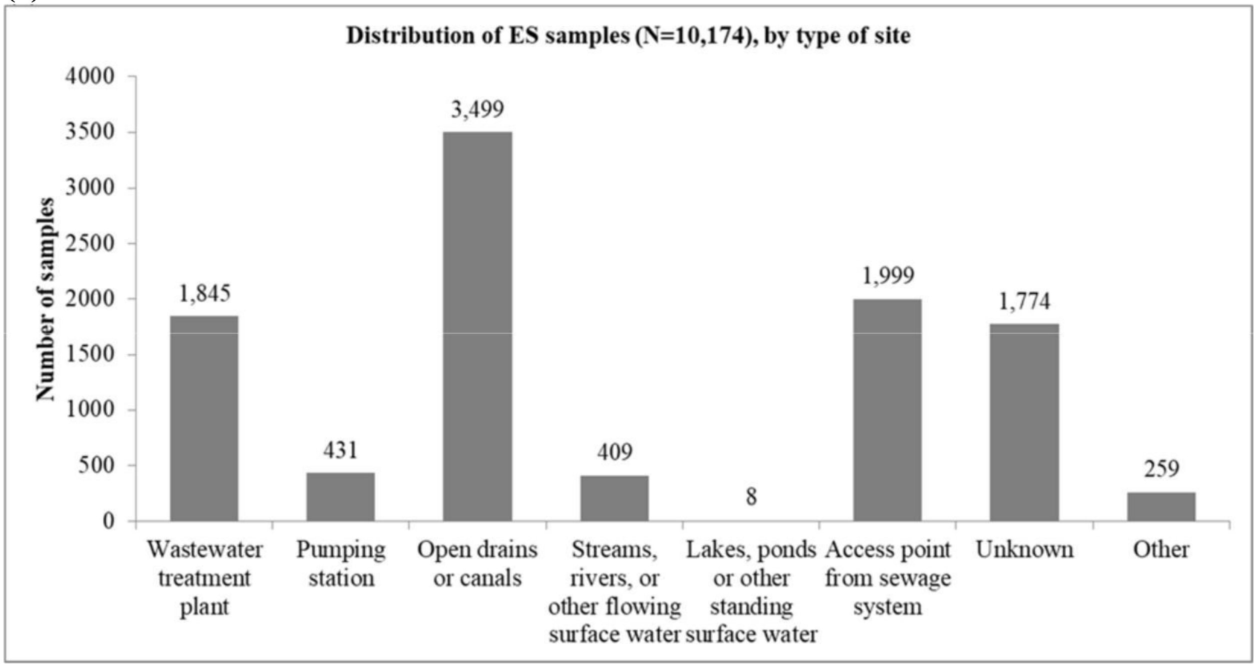
[b] See text

Additional results related to ES sampling

Figure A1 summarizes characteristics of the ES systems based on reported results for approximately 10,000 ES samples (the total numbers of samples differ from Table A4 due to incomplete responses for some (sub)questions and possible double-counting of samples analyzed by multiple laboratories through the referral system). The majority of ES samples came from open drains or canals (34%), followed by other access points from sewage systems (19%), wastewater treatment plants (18%), and unknown sources (18%). Eighty percent of samples started processing for virus isolation within 5 days of sample collection, which likely reflects the routine handling of ES samples collected in the context of ongoing ES (see Figure A1b). However, the reported 6% of samples taking more than 35 days until virus isolation began suggests a long tail of the distribution of transportation and processing delays (Figure A1b). The delays may relate to a supply shortage situation during the rapid global expansion of ES, which efforts to streamline quality assurance and quality control may limit as the system become more established. Moreover, ES conducted in the context of research activities may follow different timelines.

Figure A1: Reported results related to the ES systems

(a) Nature of ES sites



(b) Distribution of duration from sample collection to beginning of processing for virus isolation