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

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| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2018-023290 |
| Article Type: | Research |
| Date Submitted by the Author: | 04-Apr-2018 |
| Complete List of Authors: | Duintjer Tebbens, Radboud; Kid Risk, Inc. Pallansch, Mark; Centers for Disease Control and Prevention, Division of Viral Diseases Diop, Ousmane; World Health Organization, Global Polio Eradication Initiative Oberste, M Steven; Centers for Disease Control and Prevention, Division of Viral Diseases; Centers for Disease Control and Prevention, Division of Viral Diseases Thompson, KM; Kid Risk, Inc., |
| Keywords: | poliovirus, surveillance, eradication, cost, global health |
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3 1 **Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis**
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7 3 Authors: Radboud J. Duintjer Tebbens PhD (rdt@kidrisk.org),¹ Ousmane M. Diop PhD
8 4 (diopo@who.int),² Mark A. Pallansch PhD (map1@cdc.gov),³ M. Steven Oberste PhD
9
10 5 (mbo2@cdc.gov),³ and Kimberly M. Thompson ScD (kimt@kidrisk.org)¹
11
12 6
13
14 7 Affiliations:
15
16 8 1. Kid Risk, Inc., 605 N. High St. #253, Columbus, OH 43215
17
18 9 2. Global Polio Eradication Initiative, World Health Organization, Geneva, CH-1211,
19
20 10 Switzerland
21
22 11 3. Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333,
23
24 12 USA
25
26
27 14 Correspondence to: Kimberly M. Thompson, Kid Risk, Inc., 605 N. High St. #253, Columbus,
28
29 15 OH 43215, USA, Email: kimt@kidrisk.org
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3 19 **Abstract**
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6 20 **Objective:** To characterize the costs, including for environmental surveillance (ES), of the
7 21 Global Polio Laboratory Network (GPLN) that provides laboratory support to the Global Polio
8 22 Eradication Initiative (GPEI).

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10 23 **Design and participants:** We conducted a survey of the 146 GPLN laboratories and 3
11 24 laboratories (outside the GPLN) dedicated to concentration of environmental samples to collect
12 25 information about their activities, characteristics, and costs during 2016. We estimate the total
13 26 GPLN costs using regression of reported responses and complementing the findings with GPEI
14 27 data.

15
16 28 **Results:** We received responses from 132 (89%) of the 149 laboratories, with variable response
17 29 rates for individual questions. We estimate that processing samples of patients with acute flaccid
18 30 paralysis leads to total costs of approximately \$28 million per year (2016 US dollars) based on
19 31 extrapolation from reported costs of \$16 million, of which 61% were supported by internal
20 32 (national) funds. Fifty-nine (45%) of the 132 responding laboratories reported supporting ES
21 33 and we estimate an additional \$5.3 million of recurring costs for ES activities performed by the
22 34 GPLN. The reported costs do not include an estimated additional \$10 million of annual global
23 35 and regional costs to coordinate and support the GPLN. On average, the polio-supported staff in
24 36 the responding laboratories spent 30% of their time on non-polio activities. We estimate total
25 37 costs for laboratory support provided by the GPLN of approximately \$43 million (note that this
26 38 estimate does not include any field or other non-laboratory costs of polio surveillance).

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28 39 **Conclusions:** Although countries contribute significantly to the GPLN financing, many
29 40 laboratories currently depend on GPEI funds, and these laboratories also support the laboratory
30 41 component of surveillance activities for other diseases. Sustaining critical global surveillance for
31 42 polioviruses and transitioning support for other disease programs will require continued
32 43 international funding after polio certification.

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35 45 **Strengths and limitations of this study:**

36 46 • Contributes to the very limited literature about the laboratory costs of global surveillance
37 47 activities by providing updates estimates of the laboratory costs of the Global Polio
38 48 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

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3 80 poliovirus risks. First, certification of wild poliovirus eradication and subsequent OPV cessation
4 cannot safely occur without high confidence about the absence of transmission. Second, the risk
5 of outbreaks continues to exist after OPV cessation,^{6 9} as already demonstrated by circulating
6 vaccine-derived poliovirus outbreaks after serotype 2 OPV cessation,¹⁰ virus releases from polio
7 vaccine manufacturing facilities,¹¹ and the existence of long-term excretors of
8 immunodeficiency-associated vaccine-derived polioviruses.^{12 13}
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87 The Global Polio Laboratory Network (GPLN) supports poliovirus surveillance activities in
88 countries by testing stool samples from patients with acute flaccid paralysis (AFP) (and
89 sometimes their contacts) for the presence of polioviruses. In addition to AFP surveillance,
90 which exists in all countries except for 20 high-income countries, some GPLN laboratories
91 support supplemental surveillance through testing of environmental samples (e.g., sewage), or
92 stool collected from non-paralytic individuals (e.g., healthy children surveys or patients with
93 central nervous system diseases such as aseptic meningitis). Some laboratories also test for polio
94 antibodies from sera (e.g., from serological surveys). The GPLN currently consists of 146
95 laboratories with different roles (i.e., subnational, national, regional reference, and global
96 specialized laboratories) and capacities (i.e., sewage concentration, virus isolation, intratypic
97 differentiation (ITD), sequencing, and serology testing) that form a comprehensive global
98 referral system to ensure testing of any specimen for the presence of poliovirus and sequencing
99 of specific polioviruses (e.g., suspected wild or vaccine-derived polioviruses).

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101 The GPEI systematically tracks its resource requirements for the GLPN, which estimated a
102 budget of \$16.4 million for 2017 (compared to \$79 million for 'surveillance and running costs'
103 in the field, and \$1.1 billion for all GPEI activities).¹⁴ However, no mechanism exists to
104 systematically track the contributions by the countries hosting GPLN laboratories. A survey of
105 GPLN laboratories conducted in 2003 found that external GPEI funds accounted for only 34% of
106 the reported GLPN costs, with 47% coming from internal (i.e., national) funds and 13% from
107 bilateral cooperation funds not included in the GPEI budget.¹⁵ The analysis estimated total
108 GPLN costs of \$21 million (2002 USD dollars, equal to \$28 million in 2016 US dollars),
109 including \$9 million for various coordinating and supporting activities by the GPEI and the
110 global specialized laboratories. Since the 2003 survey, the number of countries dealing with

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3 111 polio outbreaks decreased significantly, the poliovirus detection and characterization algorithms
4 changed, and the GPEI significantly increased its ES activities. Analysis of ES samples involves
5 a concentration step not needed for AFP samples, requires a separate work space, and impacts
6 laboratory workloads and workflows.^{16 17} Given these changes and questions about the financial
7 resources required to sustain the GLPN, we conducted a survey following the same general
8 approach as the 2003 survey¹⁵ to update the full GPLN cost estimates and better understand the
9 extent and costs of ES activities supported by the GPLN.
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15 118 **Methods**

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17 119 *Survey instrument*

18 120 We developed an online survey instrument (reviewers can find the instrument available at
19 121 <http://kidrisk.org/mainFrame/KRGPLNSurvey2017.pdf>) modeled after the 2003 survey.¹⁵ With
20 122 respect to costs, the instrument requests annual estimates for 11 major cost categories (see
21 123 below) each for analysis of samples obtained through AFP surveillance and ES. For the cost
22 124 categories “equipment” and “durable supplies,” we asked for annual amortized costs, defined as
23 125 purchase, packing, freight, and insurance costs divided by expected useful lifetime, and we
24 126 provided a spreadsheet to help respondents compute the annual amortized costs. In addition, for
25 127 laboratories that recently (i.e., between 2010 and 2016) established or significantly expanded
26 128 their ES capacity, we requested estimates of the ES set-up costs for 10 largely overlapping cost
27 129 categories relevant to establishing ES capacity. For all of these, we asked respondents to provide
28 130 the breakdown of costs by funding source (i.e., internal, external (GPEI), bilateral (non-GPEI,
29 131 non-national)). The instrument further included questions about the role and capacities of the
30 132 laboratories, geographical areas served, staff time spent on different activities, number of
31 133 samples processed for different tests (e.g., virus isolation, ITD, sequencing, and, for ES samples,
32 134 concentration), serological testing activities, non-polio surveillance activities by polio-supported
33 135 staff, the nature of ES activities, and anticipated future changes in workload or workflow.
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48 138 *Process*

49 139 We piloted the survey among all WHO regional coordinators of the GPLN and a small subset of
50 140 laboratories before launching the revised, final instrument online and in PDF form in July, 2017,
51 141 in English, Chinese, and Russian. We targeted all 145 active GPLN laboratories (we excluded
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3 142 one laboratory considered dormant) and 3 concentration-only laboratories not technically part of
4 the GPLN but recently established to facilitate ES in countries with no easy access to a GPLN
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6 143 laboratory for sewage sample concentration and processing. We followed up with responding
7 laboratories to resolve any ambiguities or apparent inconsistencies in the responses. We
8 followed up four times with non-responding laboratories to increase the response rate through
9 November 2017 and closed the online survey instrument at the end of 2017.
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16 149 *Processing and analysis of results*
17 150 We collected all original responses directly from the online survey instrument and manually
18 entered any changes indicated by respondents during the follow-up. For rare instances in which
19 a laboratory provided a range of costs for a category, we used the midpoint. Some respondents
20 noted that they reported costs for consumable supplies or shared consumable supplies on a per-
21 sample basis rather than as an annual total, which prompted us to systematically convert
22 consumable supply costs to annual totals when we suspected responses per sample. Specifically,
23 when both the (shared) consumable supply costs per reported virus isolation test equaled less
24 than \$20 and the absolute (shared) consumable supply costs equaled less than \$400, we
25 multiplied the reported costs by the reported number of virus isolation tests. The second
26 condition served to ensure no undue multiplication by the number of virus isolation tests for
27 some laboratories with very large numbers of reported virus isolation tests but modest reported
28 (shared) consumable supplies. This approach resulted in multiplication by the number of virus
29 isolation tests of the reported consumable and shared consumable supplies for AFP sample
30 processing for 59 and 25 laboratories, respectively. With the exception of two laboratories that
31 clearly reported (shared) consumable supplies per sample for ES sample processing, we did not
32 adjust any of the reported (shared) consumable supply costs for ES sample processing. We
33 converted all monetary estimates to 2016 US dollars (\$) using publicly available exchange rates
34 from July 1, 2016.¹⁸ We classified laboratories based on the 2016 World Bank income levels of
35 their host countries.¹⁹ Unless otherwise noted, all results represent the annual totals for 2016.
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3 173 shipping/transport (i.e., non-zero categories, NZCs). In contrast, we assume that some
4 laboratories may truly not incur any costs for the five categories of training, shared consumable
5 supplies, donated supplies, technical support, and other (i.e., possible zero categories, PZCs).
6 Furthermore, we pre-processed the cost data before further analysis because some respondents
7 indicated challenges in separating costs between analysis of AFP and ES samples and others
8 explicitly indicated that they reported only the combined costs. Compared to samples from AFP
9 patients, the processing of ES samples follows a more involved algorithm (i.e., three times as
10 many cell cultures),¹⁶ more often yields viruses that require ITD testing or sequencing (i.e.,
11 because an ES sample represents a composite sample from many individuals), and requires about
12 four times the processing time by trained staff.²⁰ Based on the average total costs per sample
13 processed for virus isolation reported among all laboratories that provided separate costs for AFP
14 and ES, we assume that, on average, ES samples require seven times the cost per virus isolation
15 test as AFP samples. Specifically, for NZCs, if a laboratory reported non-zero costs for AFP
16 processing and either indicated that they combined AFP and ES costs or reported zero recurring
17 or set-up ES costs for the cost category, then we estimated the portion of reported AFP costs
18 attributable to ES based on the number of ES samples processed for virus isolation times seven,
19 divided by the total samples (i.e., the number of ES samples times seven plus the number of AFP
20 samples processed for virus isolation). We then subtracted the estimated ES-attributable costs
21 from the reported AFP costs. For PZCs, we estimated and subtracted the ES-attributable costs
22 only if the laboratory reported non-zero AFP costs and explicitly indicated that they combined
23 ES and AFP costs (i.e., not if they reported 0 ES costs for the category). Recognizing
24 uncertainty about the true ratio of costs per sample processed for virus isolation for ES compared
25 to AFP samples, we explored the impact of varying this ratio from three to ten.
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3 204 for any of the cost categories in the corresponding question (see appendix A1 for tables that
4 summarizes how we interpreted different responses in each cost category).
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8 207 To account for non-responding laboratories, we considered variables that we could obtain
9 outside of the survey for all laboratories from the web-based GPLN management system,
10 including number of employee full-time equivalents (FTEs) employed for poliovirus
11 surveillance, and number of virus isolation tests, ITD tests, and sequences performed on AFP
12 samples. Based on differences between laboratories and descriptive analysis of relationships by
13 WHO region, income level, and laboratory role, we grouped the laboratories by income level and
14 capacity (i.e., virus isolation only, ITD and virus isolation but no sequencing, and sequencing
15 (with or without ITD capacity)) for regression analyses. Within each group, we used univariate
16 linear regression on the number of samples processed for virus isolation to estimate missing
17 costs. In the event of negative intercepts or slopes in a given cost category and group, we forced
18 the intercept to 0, thus effectively reverting to estimation based on the simple average cost per
19 sample processed for virus isolation for the given cost category and group. We also considered
20 linear regression on the number of FTEs, multilinear regression on all variables, and different
21 grouping approaches, but found no substantial improvement or differences in the totals.
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25 222 *Patient and Public Involvement*
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28 224 This survey did not involve patients or public opportunities for engagement.
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32 226 **Results**
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37 228 *Overall survey response and grouping*
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42 230 We received responses from 132 of 149 (89%) surveyed laboratories. Figure 1 provides the
43 breakdown of the response rate by laboratory role, region, and income level, which shows a
44 response rate of at least 78% for all breakdowns, except for the 3 concentration-only laboratories,
45 from which we received only 1 response (i.e., response rate 33%). Based on the reported
46 capacities, we grouped the 131 responding GPLN laboratories into 30 (23%) laboratories with
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3 235 virus isolation capacity only, 67 (51%) laboratories with virus isolation and ITD capacity, and 35
4 236 (27%) laboratories with sequencing capacity (regardless of virus isolation and ITD capacity),
5 237 with the concentration-only laboratory equipped with neither of those capacities. For the
6 238 estimation of costs to process AFP samples, we further grouped the laboratories by income level
7 239 into low- and lower middle-income vs. upper middle- and high-income to allow more
8 240 appropriate cost extrapolation while maintaining sufficient numbers of laboratories in each
9 241 group. For the estimation of costs to process ES samples, we did not stratify by income level
10 242 because of the smaller numbers of laboratories in this group.
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19 244 *AFP sample processing costs*
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24 246 The response rates related to the various categories of costs to process samples from AFP cases
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26 and contacts (Table 1, numbers in parenthesis in the top half) remained markedly lower than the
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28 overall survey response rates (Figure 1), with the highest rates for personnel and consumable
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30 supplies. The responding laboratories reported approximately \$16 million in total AFP-related
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32 costs (Table 1). This does not include \$510,000 in reported AFP-related costs from 12
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34 laboratories that we re-allocated to processing of ES samples. Personnel accounted for 44% of
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36 all reported costs, followed by consumable supplies (21%) and equipment (20%). The bottom
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38 half of Table 1 shows the costs estimated for each group and cost category. The resulting total
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40 AFP costs equal approximately \$28 million. Although the sequencing laboratories account for
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42 only 26% of the total number of GPLN laboratories, they account for 34% of the estimated lab-
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44 specific costs for processing of AFP samples.
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3 266 0%, 3.3%, 6.7%, 50%, 58% and 86% for the American, Western Pacific, European, Eastern
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5 267 Mediterranean, Southeast Asian, and African WHO regions, respectively.
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9 269 *ES sample processing costs*
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12 271 Fifty-nine (45%) of all 132 responding laboratories reported supporting ES activities, including
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14 272 one concentration-only laboratory. One additional laboratory that reported not analyzing ES
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16 273 samples estimated the costs of supporting national ES activities with a staff member providing
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18 274 technical support. We excluded the latter laboratory and the concentration-only laboratory due
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20 275 to the absence of numbers of ES samples processed for virus isolation needed for inclusion in the
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22 276 regression. Seven non-responding GPLN laboratories support ES according to unpublished
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24 277 WHO data, leading to a total of 65 (45%) of the 145 GPLN laboratories supporting ES activities
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26 278 in 2016. Table 2 shows the reported and estimated recurring costs for ES based on the variable
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28 279 response rates for each cost category. The responding laboratories reported approximately \$3.2
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30 280 million in total recurring ES-related costs, which includes \$510,000 in AFP costs that we
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32 281 attributed to ES. Varying the ratio of per-sample ES processing costs to per-sample AFP
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34 282 processing cost from 3 to 10 changed the AFP processing costs attributed to ES processing from
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36 283 \$340,000 to \$590,000, respectively. Thus, the impact of this assumption on overall costs
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38 284 remains modest because it only affects 12 laboratories with ambiguity about whether reported
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40 285 AFP processing costs included ES processing costs. The breakdown by cost category remained
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42 286 similar to the costs for processing of AFP samples and similarly, the sequencing laboratories
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44 287 accounted for a large portion of all reported recurring ES costs (i.e., 58%). The bottom half of
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46 288 Table 2 shows the extrapolated costs estimated in each group and for each cost category. The
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48 289 resulting total recurring ES costs equal approximately \$5.3 million. Figure 3 shows the
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50 290 breakdown by cost category and funding source for the costs reported in the top half of Table 2,
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52 291 which shows a similar breakdown as for AFP sample processing costs. Overall, 65%, 22%,
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54 292 0.3%, and 12% of all reported recurring ES costs came from internal, external, bilateral, and
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56 293 unspecified funds, respectively. Table 2 does not factor in the relatively small costs from the one
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58 294 concentration-only laboratory that responded to the survey, which reported only some internally-
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60 295 funded recurring ES costs for personnel with other costs captured in the ES set-up costs or
296 unquantified because they paid for by external resources.

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5 298 Of the 59 laboratories (i.e., 58 GPLN laboratories and 1 concentration-only laboratory) that
6 reported supporting ES activities, 35 (59%) reported that they recently (i.e., between 2010 and
7 2016) set-up or significantly expanded their ES capacity. Of these 35 laboratories, 25 (71%)
8 provided set-up cost estimates for at least one cost category, leading to total reported set-up costs
9 of approximately \$1.8 million, for an average of approximately \$73,000 per laboratory. This
10 includes estimates from 16 ITD laboratories, 6 sequencing laboratories, 2 virus isolation
11 laboratories, and 1 concentration-only laboratory. Only 6 of the 25 (24%) laboratories reported
12 becoming fully operational during 2016 and therefore we assume that only a fraction of the
13 reported set-up costs occurred in 2016. Figure 4 shows the breakdown of the \$1.8 million of
14 reported ES set-up costs, with the legend also showing the response rates for each set-up cost
15 category. New equipment for concentration represented the largest contributor to all reported
16 set-up cost (38%), followed by new equipment for expanded poliovirus processing capacity
17 (12%), new personnel (12%), new consumable supplies (11%) and facility costs (10%).
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29 312 *Other findings*
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31 313 Table 3 show the breakdown of polio-supported staff time spent on polio and non-polio diseases,
32 by WHO region. Only 1 of 132 (1%) of laboratories that responded to the survey did not provide
33 estimates for the total number of polio-supported FTEs or the percentages spent on polio and
34 other diseases. Overall, polio-supported staff spent approximately 30% of time supporting
35 activities for other diseases or viruses, including non-polio enteroviruses (11%), measles and/or
36 rubella viruses (7%), and a wide range of other diseases not specifically asked about in the
37 survey (5%) (Table 3, see appendix A2). The American (41%) and European (46%) regions
38 reported the lowest percentages of staff time spent on polio, while the Eastern Mediterranean
39 region (87%), which includes one laboratory serving two polio-endemic countries (i.e.,
40 Afghanistan and Pakistan), reported the highest percentage.
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50 324 Table 4 summarizes the reported number of samples or isolates processed in the context of
51 different activities. Not surprisingly given the primary focus of the GPLN on supporting AFP
52 surveillance, Table 4 shows almost 250,000 samples from AFP cases and their contacts
53 processed for virus isolation, with approximately 4.5% ITD-tested and less than 1% sequenced.
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3 328 These numbers reflect the reality that, given the current prevalence of wild polioviruses and level
4 329 of OPV use, roughly 4.5% of stool samples from AFP cases grow in the L20B cells used for
5 330 virus isolation. Of these, approximately 7% appear as possible wild or vaccine-derived
6 331 poliovirus, which then undergo sequencing. In contrast, ES accounted for only 12,000 samples
7 332 processed for virus isolation originating from 8,200 environmental sample concentrates, 67% of
8 333 which were concentrated using the WHO-recommended two-phase method.¹⁶ The difference
9 334 between the number of concentrates and the number of isolates probably comes from
10 335 laboratories that (re)tested samples already concentrated by another laboratory, including third-
11 336 party laboratories not part of the GPLN. A much larger fraction of isolates from ES samples
12 337 compared to AFP samples underwent ITD testing (54%) and sequencing (15%), probably
13 338 because ES samples comprise a composite from potentially thousands of individuals and they
14 339 often yield complex mixtures of viruses. This results in higher costs on a per-sample basis for
15 340 ES than AFP, with the ES algorithm additionally requiring three times as many cell cultures as
16 341 the AFP algorithm. Laboratories also reported analyzing almost 2,000 ES samples in the context
17 342 of research activities and 82 ES samples using direct detection methods. Forty responding
18 343 laboratories further reported analyzing over 50,000 serum samples for the presence of antibodies,
19 344 which they estimated took almost 13,000 employee hours (i.e., 12.7 FTEs assuming 2,000
20 345 employee hours per year). Laboratories analyzed almost 40,000 samples in the context of non-
21 346 polio enterovirus surveillance and approximately 150,000 other samples, reflecting the reality
22 347 that many GPLN laboratories perform non-polio services (not necessarily funded by polio
23 348 surveillance), particularly in countries with no recent polio outbreaks. While 49 laboratories
24 349 reported testing other samples, 3 of these laboratories accounted for 83% of the 150,000 samples
25 350 and indicated that their reported numbers included routine diagnostic services. Laboratories also
26 351 reported analyzing approximately 6,900 and 4,300 samples in the context of healthy children or
27 352 adult stool surveys and clinical trials, respectively. See appendix A3 for additional results.
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3 359 support AFP surveillance and ES at approximately \$33 million. This does not include the
4 reported recent ES set-up costs of \$1.8 million, which represents only a fraction of the WHO-
5 supported ES set-up costs for 2016, or the costs for the analysis of serum samples. For the
6 analysis of serum samples, we assume costs of \$10 per sample for consumables and equipment
7 and the reported average personnel costs per FTE in upper middle- and high-income countries,
8 which tested most of the reported serum samples, to estimate total costs of serology of
9 approximately \$1 million for 2016. We estimate the costs of research and development activities
10 at \$3 million based on extrapolation of data from the largest global specialized laboratory. We
11 estimate the global overhead costs for coordination, training, technical support not incurred by
12 individual laboratories at \$6 million. The resulting estimated total GPLN cost for 2016 equal to
13 approximately \$43.3 million.
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17 371 For comparison, the 2003 survey estimated substantially lower total GPLN costs of \$28 million
18 per year (i.e., 21 million in year 2002 US dollars). This estimate broke down as: (1) \$16 million
19 of AFP-related costs for the (sub)-national and regional reference laboratories, (2) \$8 million for
20 all polio-related activities by global specialized laboratories, including limited ES conducted at
21 the time, and (3) \$4 million in global coordination costs.¹⁵ In this study, the corresponding AFP-
22 related costs for the (sub)-national and regional reference laboratories equals approximately \$25
23 million. The total estimated AFP and recurring ES costs for the global specialized laboratories
24 equals only \$3.5 million, but increases to over \$7 million if we add the estimated research and
25 development, serology, coordination, training, and technical support costs.
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29 381 **Discussion**
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34 383 This study confirms the important contributions of both GPEI and internal funds to the
35 maintenance of a well-functioning GPLN.¹⁵ While direct comparison of the absolute costs in
36 2016 to those in the 2003 study¹⁵ remains somewhat challenging due to differences in the
37 specific cost requested, this study finds an apparent increase in the proportion of GPLN costs
38 paid for by internal funds from 53% in 2003¹⁵ to 62% in 2016. This may reflect increasing self-
39 funding of the laboratory component of polio surveillance activities by polio-free countries no
40 longer at a high risk of outbreaks. In addition, after largely externally-funded capital investment
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3 390 to set up laboratories with the capacity to apply molecular methods in many countries, the more
4 391 often internally funded personnel costs now represent a relatively larger share of the total costs.
5 392 The investments in capital costs may also have reduced the recurring costs compared to the 2003
6 393 survey, despite the increase from approximately 85,000 AFP samples tested in 2002 to almost
7 394 250,000 in 2016. Nevertheless, with 50% or more of GPLN laboratories in the African, Eastern
8 395 Mediterranean, and Southeast Asian WHO regions depending on external GPEI funds for at least
9 396 half of their budgets for AFP sample analysis, planning for GPLN financing after the GPEI
10 397 resources decline post-certification remains of critical importance. In this context, we note that
11 398 the GPEI budget for 2017 of \$16.4 million reflects only 17% of the GPEI budget for all
12 399 surveillance activities and 1.5% of the overall GPEI budget for 2017.¹⁴ This study further
13 400 documents the significant contributions made by the GPLN to a large number of other disease
14 401 surveillance efforts, with 30% of all polio-supported staff time reportedly used for surveillance
15 402 of other diseases. Thus, we hope that this study highlights both the importance of contributions
16 403 that countries make to the GPLN and the need to sustain external funding to support laboratories
17 404 worldwide in their surveillance efforts for poliovirus and other diseases. As global population
18 405 immunity to poliovirus transmission decreases after OPV cessation,²¹ successfully controlling
19 406 any future outbreaks will require continued vigilance and a rapid immunization response.²²
20 407 However, questions remain after the certification of eradication about the long-term financial
21 408 sustainability of poliovirus surveillance and the functions of the GPLN, because of the expected
22 409 transition of key GPEI responsibilities and resources to other programs.
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26 411 Based on our results, the GPLN costs to support ES remain relatively small compared to the AFP
27 412 costs. This reflects the reality that despite the ongoing global ES expansion, ES remains limited
28 413 to parts of some countries, while the global AFP surveillance system remains (almost) universal.
29 414 With the first phase of ES expansion continuing during 2017 and 2018, we expect both increased
30 415 set-up costs during those years and higher recurring ES costs going forward compared to the ES
31 416 costs estimated for 2016. With further expansion, the GPLN costs for ES could exceed those for
32 417 AFP, particularly if AFP surveillance declines, although we urge careful consideration of the
33 418 costs and effectiveness of doing allowing AFP surveillance to decline.²³
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3 420 This survey relied on self-reported estimates of laboratory costs. While we attempted to
4 421 formulate the questions unambiguously and provided translations of the survey instrument and
5 422 during follow up where possible, we cannot rule out possible differences in interpretation of the
6 423 questions. Some respondents reported difficulties separating costs between categories and
7 424 activities or amortizing costs of equipment purchased long ago. Although we achieved a high
8 425 overall response rate of 89%, the response rates for individual cost categories remained variable.
9 426 Therefore, we relied on estimation based on regression of relatively sparse data to characterize
10 427 missing values, which may have introduced biases. For example, laboratories receiving funding
11 428 from the GPEI may be more likely to have omitted estimates for individual cost categories,
12 429 potentially leading to relatively greater errors in the estimation of the external cost. On the
13 430 contrary, laboratories may not have accounted for all equipment, supplies, and operations cost
14 431 (e.g., utilities, building maintenance) paid for by their hosting institutions, potentially leading to
15 432 underestimation of the share of costs funded by internal sources. Despite its limitations, we hope
16 433 this study provides valuable insights regarding the costs and cost structure of the GPLN. Future
17 434 research to inform global long-term poliovirus and broader surveillance may include detailed
18 435 cost studies of the field component of AFP surveillance and economic analyses of the value of
19 436 AFP surveillance and ES.

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34 438 **Conclusions**
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36 439 Although countries contribute significantly to the GPLN, many laboratories currently depend on
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38 440 GPEI funds, and these laboratories also support the laboratory component of surveillance
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40 441 activities for other diseases. Sustaining critical global surveillance for polioviruses and other
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42 442 diseases will require continued international funding as GPEI resources decline, particularly after
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44 443 global certification. Paying the costs to sustain surveillance represents an essential element for
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46 444 securing a polio-free world, and offers the opportunity to transition GPLN resources to
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48 445 control/eliminate other vaccine-preventable or emerging/re-emerging communicable diseases.²⁴
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3 449 AFP, acute flaccid paralysis; ES, poliovirus environmental surveillance; GPEI, Global Polio
4 450 Eradication Initiative; GPLN, Global Polio Laboratory Network; ITD, intratypic differentiation;
5 451 NZC, non-zero (cost) category; OPV, oral poliovirus vaccine; PZC, possible zero (cost) category
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10 456 **DECLARATIONS**
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3 480 Nicksy Gumeche-Moeletsi, Sirima Pattamadilok, Gloria Rey, Yan Zhang for helpful feedback on
4 the survey instrument, and Patrick Briand, Steve Cochi, Lee Hampton, Maria Iakovenko, Fem
5 481 Paladin, Everardo Vega, Steve Wassilak, Marita Zimmermann for input at various stages of the
6 482 process.
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11 485 **Data sharing statement**
12 486 Technical appendix available on request from the authors.
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17 488 **References**
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27 497 [poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx](http://www.polioeradication.org/mediaroom/newsstories/Global-eradication-of-wild-poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx) accessed November 30
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3 562 **Table 1: Reported and estimated costs to process acute flaccid paralysis samples, based on regression of reported total number**
4 563 **stool samples processed for virus isolation. This excludes the costs for the concentration-only laboratories and global and**
5 **regional costs to coordinate the GPLN.**
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| 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) |
| <i>All cost categories</i> | 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 |
| <i>All cost categories</i> | 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) |
| <i>All cost categories</i> | 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 |
| <i>All cost categories</i> | 540,000 | 1,400,000 | 3,400,000 | 5,300,000 |

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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) |
| 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 |

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 |

^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 appendix A2

576 **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 |

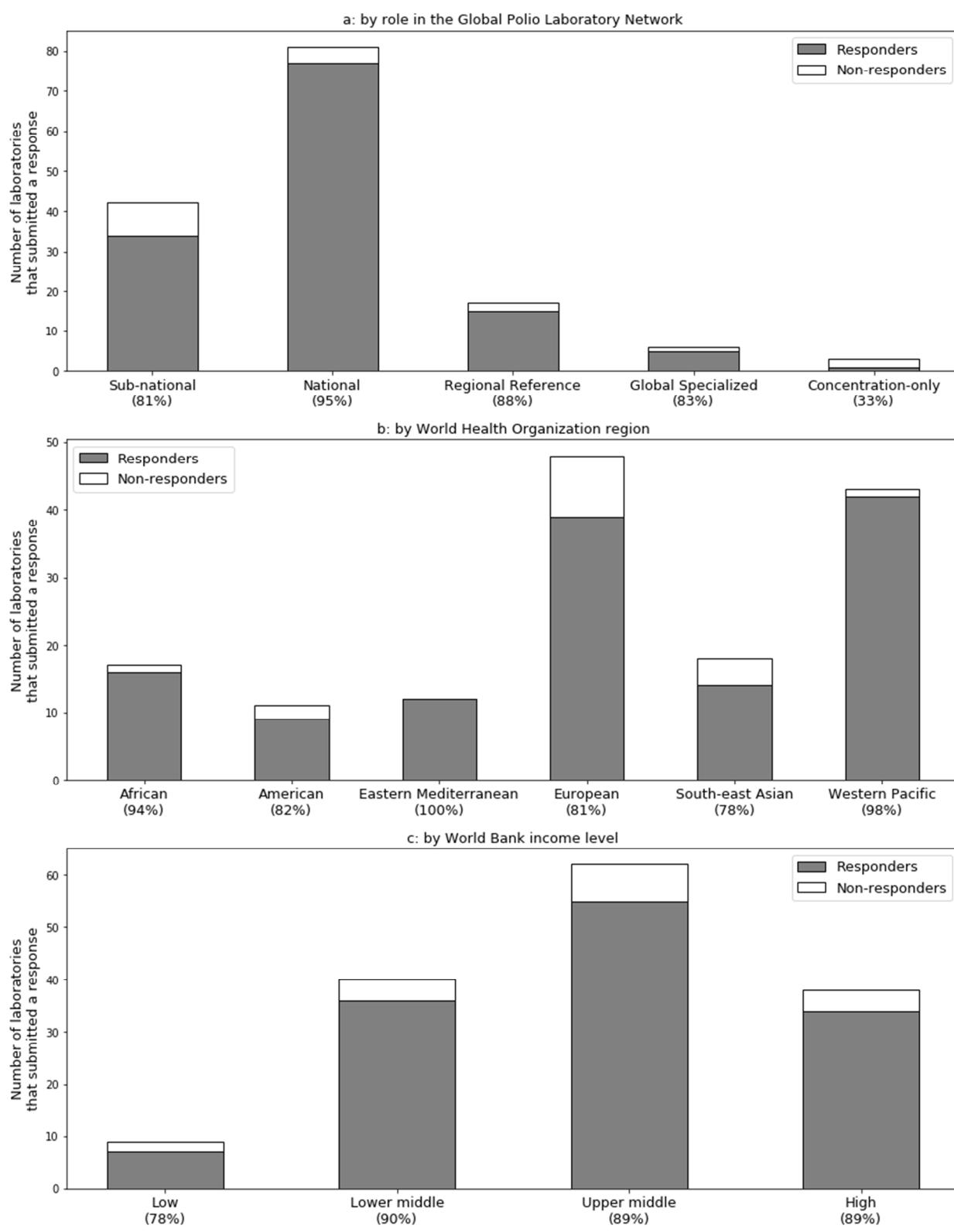
Figure Captions

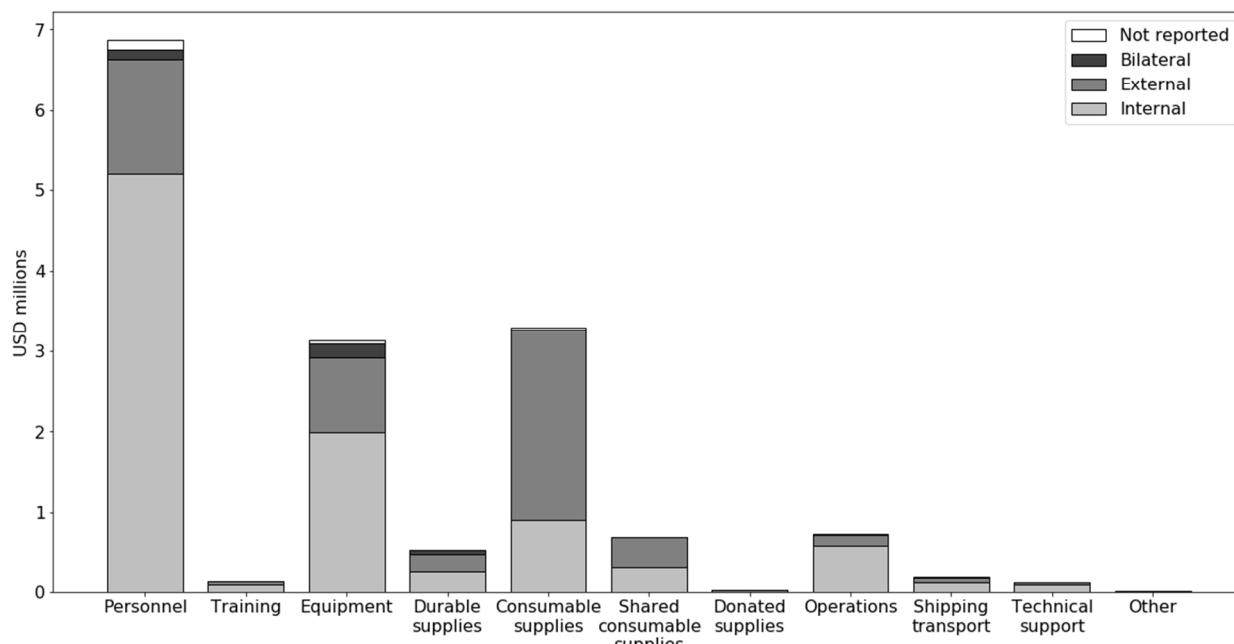
Figure 1: Survey response rates by role, region, and income level

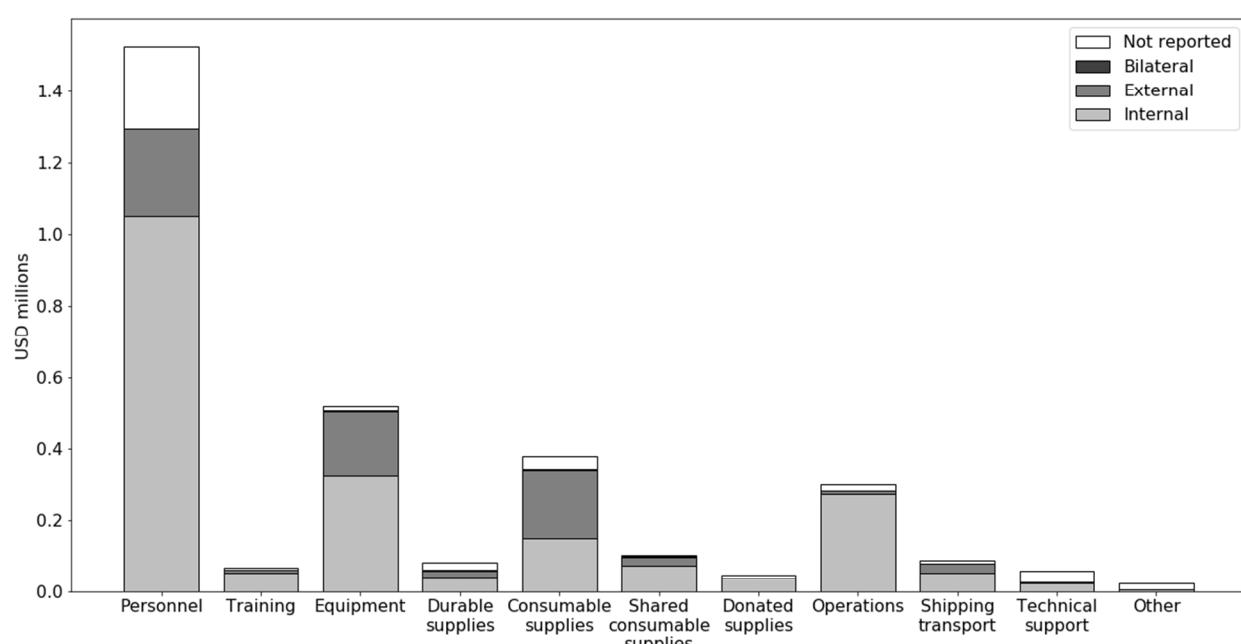
Figure 2: Reported costs to process acute flaccid paralysis samples by cost category and source of funding

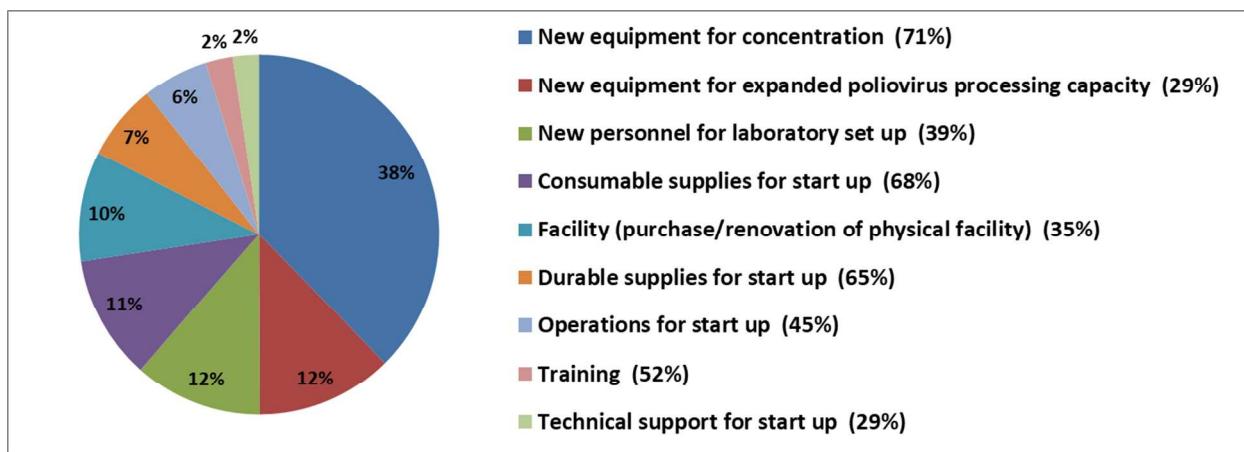
Figure 3: Reported recurring costs to process environmental samples by cost category and source of funding

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.









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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) | NZC | Any | Any | zero Non-zero costs, but unknown | Estimate based on extrapolation |
|--------------------|-----|-----|-----|--|---------------------------------|

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

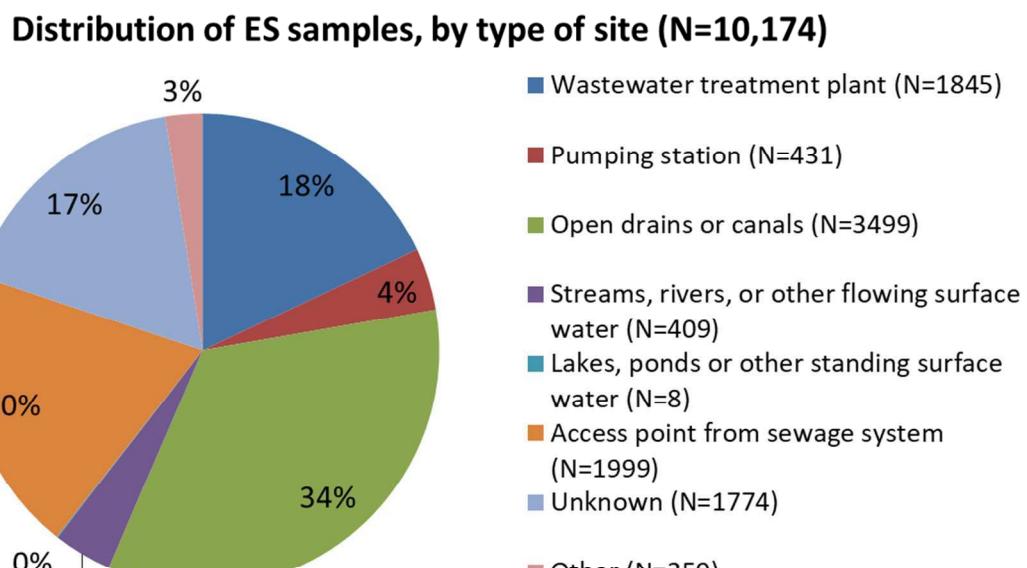
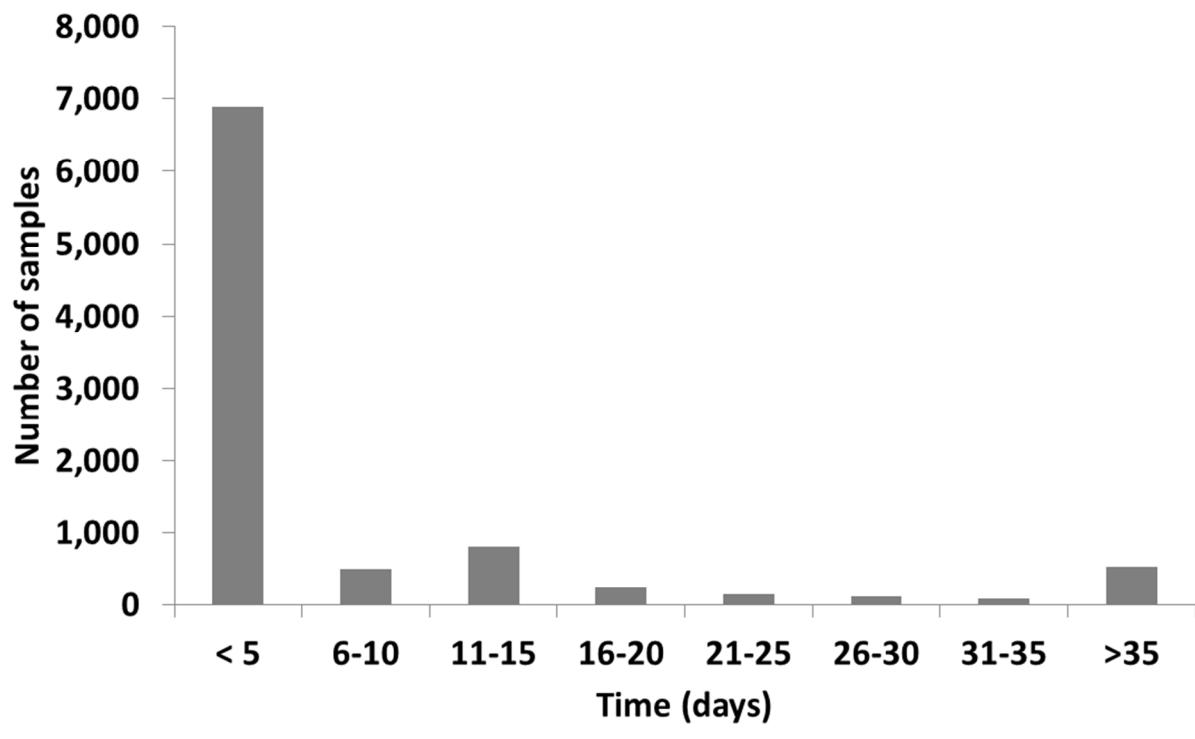
11 12 A2. Other diseases

13 14 Respondent laboratories collectively reported spending 41 FTEs on diseases/conditions not
15 16 specifically listed in Table 3. The laboratories reported that these other diseases/conditions
17 18 included TORCH, exanthemal infections, urogenital, immunology, intestinal and parasitic
19 20 infection groups, human immunodeficiency virus, hepatitis, acute respiratory viral infections,
21 22 teratogenic infections, mycoplasma, chlamydophyll, transgenic organisms control, astrovirus,
23 24 norovirus, sapovirus, adenovirus, rabies, non-influenza respiratory diseases, non-rotavirus acute
25 26 gastroenteritis, herpes group viruses, mumps, rhinovirus, parainfluenza virus, respiratory
27 28 syncytial virus, metapneumovirus, parechovirus, polyomavirus, varicella virus, diphtheria,
29 30 tetanus, pertussis, cytomegalovirus, crystalli, parotitis, severe fever with thrombocytopenia
31 32 syndrome, meningitis, and encephalitis.

33 34 The other types of laboratory tests in Table 4 include ELISA, PCR, RT-PCR, HBsAg,
35 36 microtitration, genotyping, and serology for numerous viruses and on various sample types (i.e.,
37 38 sera, nasopharyngeal washings, blood, feces, urine, urogenital scrapings, sectional material,
39 40 mites, spinal fluid, rectal swab and vomitus from diarrhea and food poisoning cases, ice and
41 42 drinking water, soil) as well as virus isolation on fecal samples from AFP cases over age 15,
43 44 AFP samples from provinces outside of the areas normally served by the laboratory, fecal
45 46 samples from non-AFP patients not part of a survey, and research activities.

47 48 A3. Additional results related to ES systems

49 50 Figure A1 summarizes characteristics of the ES systems based on reported results for
51 52 approximately 10,000 ES samples (the total numbers of samples differ from Table 4 due to
53 54 incomplete responses for some (sub)questions and possible double-counting of samples analyzed
55 56 by multiple laboratories through the referral system). The majority of ES samples came from
57 58 open drains or canals (34%), followed by other access points from sewage systems (19%),
59 60 wastewater treatment plants (18%), and unknown sources (18%). Eighty percent of samples
61 62 started processing for virus isolation within 5 days of sample collection, which likely reflects the
63 64 routine handling of ES samples collected in the context of ongoing ES (see Figure A1b).
65 66 However, the reported 6% of samples taking more than 35 days until virus isolation began
67 68 suggests a long tail of the distribution of transportation and processing delays (Figure A1b). The
69 70 delays may relate to a supply shortage situation during the rapid global expansion of ES, which
71 72 efforts to streamline quality assurance and quality control may limit as the system become more
73 74 established. Moreover, ES conducted in the context of research activities may follow different
75 76 timelines.

51 **Figure A1: Reported results related to the ES systems.**52 **(a) Nature of ES sites**53 **(b) Distribution of duration from sample collection to beginning of processing for virus**
54 **isolation**

BMJ Open

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

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|--|---|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2018-023290.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 10-Sep-2018 |
| Complete List of Authors: | Duintjer Tebbens, Radboud; Kid Risk, Inc. Diop, Ousmane; World Health Organization, Global Polio Eradication Initiative Pallansch, Mark; Centers for Disease Control and Prevention, Division of Viral Diseases Oberste, M Steven; Centers for Disease Control and Prevention, Division of Viral Diseases; Centers for Disease Control and Prevention, Division of Viral Diseases Thompson, KM; Kid Risk, Inc., |
| < b > Primary Subject Heading < /b >: | Infectious diseases |
| Secondary Subject Heading: | Public health, Global health |
| Keywords: | poliovirus, surveillance, eradication, cost, global health |
| | |

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3 1 **Characterizing the costs of the Global Polio Laboratory Network: A survey-based analysis**
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6
7 3 Authors: Radboud J. Duintjer Tebbens PhD (rdt@kidrisk.org),¹ Ousmane M. Diop PhD
8 4 (diopo@who.int),² Mark A. Pallansch PhD (map1@cdc.gov),³ M. Steven Oberste PhD
9 5 (mbo2@cdc.gov),³ and Kimberly M. Thompson ScD (kimt@kidrisk.org)¹
10
11 6
12
13 7 Affiliations:
14
15 8 1. Kid Risk, Inc., 605 N. High St. #253, Columbus, OH 43215
16
17 9 2. Global Polio Eradication Initiative, World Health Organization, Geneva, CH-1211,
18
19 10 Switzerland
20
21 11 3. Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333,
22
23 12 USA
24
25
26 14 Correspondence to: Kimberly M. Thompson, Kid Risk, Inc., 605 N. High St. #253, Columbus,
27
28 15 OH 43215, USA, Email: kimt@kidrisk.org
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2
3 19 **Abstract**
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6 20 **Objective:** To characterize the costs, including for environmental surveillance (ES), of the
7 21 Global Polio Laboratory Network (GPLN) that provides laboratory support to the Global Polio
8 22 Eradication Initiative (GPEI).

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10 23 **Design and participants:** We conducted a survey of the network across 92 countries of the 146
11 24 GPLN laboratories plus 3 non-GPLN laboratories that concentrate environmental samples to
12 25 collect information about their activities, characteristics, and costs during 2016. We estimate the
13 26 total costs using regression of reported responses and complementing the findings with GPEI
14 27 data.

15
16 28 **Results:** We received responses from 132 (89%) of the 149 laboratories, with variable response
17 29 rates for individual questions. We estimate that processing samples of patients with acute flaccid
18 30 paralysis leads to total costs of approximately \$28 million per year (2016 US dollars) based on
19 31 extrapolation from reported costs of \$16 million, of which 61% were supported by internal
20 32 (national) funds. Fifty-nine (45%) of the 132 responding laboratories reported supporting ES
21 33 and we estimate an additional \$5.3 million of recurring costs for ES activities performed by the
22 34 laboratories. The reported costs do not include an estimated additional \$10 million of annual
23 35 global and regional costs to coordinate and support the GPLN. On average, the staff supported
24 36 by funding for polio in the responding laboratories spent 30% of their time on non-polio
25 37 activities. We estimate total costs for laboratory support of approximately \$43 million (note that
26 38 this estimate does not include any field or other non-laboratory costs of polio surveillance).

27
28 39 **Conclusions:** Although countries contribute significantly to the GPLN financing, many
29 40 laboratories currently depend on GPEI funds, and these laboratories also support the laboratory
30 41 component of surveillance activities for other diseases. Sustaining critical global surveillance for
31 42 polioviruses and transitioning support for other disease programs will require continued
32 43 significant funding after polio certification.

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35 45 **Strengths and limitations of this study:**

36 46 • High overall response rate from laboratories allows for estimation of costs across
37 47 geographies, income levels, and laboratory types.
38 48 • Results depend on self-reported costs estimates with possible difference in interpretation
39 49 of the questions and availability of cost information.

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3 50 • Analysis relied on extrapolation from relatively sparse data to estimate missing values,
4 51 which may have introduced biases.
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8 53 **Keywords:** poliovirus, surveillance, polio eradication, cost study, global health
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11 55 **Background**
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14 57 Launched in response to the 1988 World Health Assembly resolution to globally eradicate all
15 58 paralytic poliomyelitis caused by polioviruses, the Global Polio Eradication Initiative (GPEI)
16 59 seeks to stop all polio.¹ By mid-2018, the GPEI succeeded in limiting indigenous transmission of
17 60 wild polioviruses to three countries (Afghanistan, Nigeria, and Pakistan) by focusing on four key
18 61 strategies: strengthening routine polio immunization, supplemental immunization activities,
19 62 surveillance, and outbreak response.² Four of the 6 World Health Organization (WHO) regions
20 63 have been certified polio-free and of the three wild poliovirus serotypes, and wild poliovirus
21 64 serotypes 2 and 3 have not been detected since 1999 and 2012, respectively.^{3,4} High-quality
22 65 surveillance represents a key contributor to these successes because it allows the GPEI to 1)
23 66 monitor eradication progress, 2) determine where poliovirus transmission still occurs, 3) rapidly
24 67 respond to any outbreaks in previously polio-free areas, and 4) achieve high confidence about the
25 68 absence of transmission after the last detected poliovirus in any given area.
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28 70 As part of the global strategy to manage the risks associated with the oral poliovirus vaccine
29 71 (OPV),^{5,6} and following the certification of serotype 2 wild poliovirus eradication in 2015,⁷
30 72 cessation of attenuated serotype 2-containing OPV occurred in April-May 2016. The virologic
31 73 monitoring of the disappearance of serotype 2 vaccine-related viruses from acute flaccid
32 74 paralysis (AFP) cases and the environment represented an integral activity of the vaccine
33 75 switch.⁸ Even after the eradication of the last circulating wild polioviruses, surveillance will
34 76 remain critical to manage future poliovirus risks. First, certification of wild poliovirus
35 77 eradication and subsequent OPV cessation cannot safely occur without high confidence about the
36 78 absence of transmission. Second, the risk of outbreaks continues to exist after OPV cessation,^{6,9}
37 79 as already demonstrated by circulating vaccine-derived poliovirus outbreaks after serotype 2
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3 80 OPV cessation,¹⁰ virus releases from polio vaccine manufacturing facilities,¹¹ and the existence
4 81 of long-term excretors of immunodeficiency-associated vaccine-derived polioviruses.^{12 13}
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8 83 Established in 1990, the Global Polio Laboratory Network (GPLN) supports poliovirus
9 84 surveillance activities in countries by testing stool samples from patients with AFP (and
10 85 sometimes their contacts) for the presence of polioviruses.¹⁴ AFP may indicate a poliovirus
11 86 infection, but also occurs at a relatively predictable rate due to other causes (e.g., Guillain-Barre
12 87 Syndrome), making the rate of non-polio AFP cases detected a good indicator of the ability of
13 88 the surveillance system to detect AFP caused by poliovirus infection in a population.¹⁵ Currently
14 89 the GPLN analyzes over 200,000 stool samples per year from AFP cases and their contacts. In
15 90 addition to AFP surveillance, which exists in all countries except for 20 high-income countries,
16 91 some GPLN laboratories support supplemental surveillance through testing of environmental
17 92 surveillance (ES) samples (e.g., sewage), or stool collected from non-paralytic individuals (e.g.,
18 93 healthy children surveys or patients with central nervous system diseases such as aseptic
19 94 meningitis). Some laboratories also test for polio antibodies from sera (e.g., from serological
20 95 surveys). The GPLN currently consists of 146 laboratories across 92 countries with different
21 96 roles (i.e., subnational, national, regional reference, and global specialized laboratories) and
22 97 capacities (i.e., sewage concentration, virus isolation, intratypic differentiation (ITD),
23 98 sequencing, and serology testing) that form a comprehensive international referral system to
24 99 ensure testing of any specimen for the presence of poliovirus and sequencing of specific
25 100 polioviruses (e.g., suspected wild or vaccine-derived polioviruses).
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29 102 The GPEI systematically tracks its resource requirements for the GLPN, which estimated a
30 103 budget of \$16.4 million for 2017 (compared to \$79 million for “surveillance and running costs”
31 104 in the field, and \$1.1 billion for all GPEI activities).¹⁴ However, no mechanism exists to
32 105 systematically track the contributions by the countries hosting GPLN laboratories. A survey of
33 106 GPLN laboratories conducted in 2003 found that external GPEI funds accounted for only 34% of
34 107 the reported GLPN costs, with 47% coming from internal (i.e., national) funds and 13% from
35 108 bilateral cooperation funds not included in the GPEI budget.¹⁵ The analysis estimated total
36 109 GPLN costs of \$21 million (2002 USD dollars, equal to \$28 million in 2016 US dollars),
37 110 including \$9 million for various coordinating and supporting activities by the GPEI and the
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3 111 global specialized laboratories. Since the 2003 survey, the number of countries dealing with
4 polio outbreaks decreased significantly, the poliovirus detection and characterization algorithms
5 changed, and the GPEI significantly increased its ES activities. Analysis of ES samples involves
6 a concentration step not needed for AFP samples, requires a separate work space, and impacts
7 laboratory workloads and workflows.^{16 17} Given these changes and questions about the financial
8 resources required to sustain poliovirus surveillance during the polio endgame, we conducted a
9 survey following the same general approach as the 2003 survey¹⁵ to update the full laboratory
10 cost estimates and better understand the extent and costs of poliovirus ES activities.
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120 Methods

121 Survey instrument

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

138 139 Process

140 We piloted the survey among all WHO regional coordinators of the GPLN and a small subset of
141 laboratories before launching the revised, final instrument online and in PDF form in July 2017,

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3 142 in English, Chinese, and Russian. We targeted all 145 active GPLN laboratories (we excluded
4 one laboratory considered dormant) and 3 non-GPLN laboratories recently established to
5 facilitate ES in countries with no easy access to a GPLN laboratory for sewage sample
6 concentration and processing (i.e., concentration-only laboratories). We followed up with
7 responding laboratories to resolve any ambiguities or apparent inconsistencies in the responses
8 (see appendix A2 for a list of the responding laboratories). We reached out four times to non-
9 responding laboratories to increase the response rate through November 2017 and closed the
10 online survey instrument at the end of 2017.
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19 151 *Processing and analysis of results*
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21 152 We collected all original responses directly from the online survey instrument and manually
22 entered any changes indicated by respondents during the follow-up. For rare instances in which
23 a laboratory provided a range of costs for a category, we used the midpoint. Some respondents
24 noted that they reported costs for consumable supplies or shared consumable supplies on a per-
25 sample basis rather than as an annual total, which prompted us to systematically convert
26 consumable supply costs to annual totals when we suspected responses per sample (see appendix
27 A3). We converted all monetary estimates to 2016 US dollars (\$) using publicly available
28 exchange rates from July 1, 2016.¹⁸ We classified the income levels of laboratories based on the
29 2016 World Bank income levels of their host countries.¹⁹ Unless otherwise noted, all results
30 represent the annual totals for 2016.
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41 163 To account for missing cost responses from responding laboratories, we interpreted unanswered
42 or zero responses differently depending on the cost category. We assumed that all laboratories
43 incur costs under the six cost categories of personnel, equipment, durable supplies, consumable
44 supplies, operations, and shipping/transport (i.e., non-zero categories, NZCs). In contrast, we
45 assume that some laboratories may truly not incur any costs for the five categories of training,
46 shared consumable supplies, donated supplies, technical support, and other (i.e., possible zero
47 categories, PZCs). Furthermore, we pre-processed some of the cost data before further analysis
48 because some respondents indicated challenges in separating costs between analysis of AFP and
49 ES samples and others explicitly indicated that they reported only the combined costs.
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3 173 algorithm (i.e., three times as many cell cultures),¹⁶ more often yields viruses that require ITD
4 testing or sequencing (i.e., because an ES sample represents a composite sample from many
5 individuals), and requires about four times the processing time by trained staff.²⁰ The type and
6 nature of adjustment depended on the nature of the missing data (see appendix A3)
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9
10 178 To account for non-responding laboratories, we considered variables that we could obtain
11 outside of the survey for all laboratories from the web-based GPLN management system,
12 including number of employee full-time equivalents (FTEs) employed for poliovirus
13 surveillance, and number of virus isolation tests, ITD tests, and sequences performed on AFP
14 samples. Based on differences between laboratories and descriptive analysis of relationships by
15 WHO region, income level, and laboratory role, we grouped the laboratories by income level and
16 capacity (i.e., virus isolation only, ITD and virus isolation but no sequencing, and sequencing
17 (with or without ITD capacity)) for regression analyses. Within each group, we used univariate
18 linear regression on the number of samples processed for virus isolation to estimate missing
19 costs. In the event of negative intercepts or slopes in a given cost category and group, we forced
20 the intercept to 0, thus effectively reverting to estimation based on the simple average cost per
21 sample processed for virus isolation for the given cost category and group. We also considered
22 linear regression on the number of FTEs, multilinear regression on all variables, and different
23 grouping approaches, but found no substantial improvement or differences in the totals.
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29 193 *Other cost assumptions*
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33 195 To estimate the costs of analysis of serum samples, we assume costs of \$10 per sample for
34 consumables and equipment. For the personnel costs, we multiply the reported average
35 personnel costs per FTE in upper middle- and high-income countries (since these countries test
36 most of the reported serum samples) by the reported number of FTEs for processing of serum
37 samples. We estimate the costs of research and development activities based on extrapolation of
38 data from the largest global specialized laboratory (i.e., the U.S. Centers for Disease Control and
39 Prevention laboratory in Atlanta, GA) (MAP,MSO). We estimate the global overhead costs for
40 coordination, training, and technical support not incurred by individual laboratories based on
41 WHO surveillance budgets (OMD).
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205 *Patient and Public Involvement*206
207 This survey did not involve patients or public opportunities for engagement.208
209 **Results**210
211 *Overall survey response and grouping*212
213 We received responses from 132 of 149 (89%) surveyed laboratories, which included one
214 concentration-only laboratory. Figure 1 provides the breakdown of the response rate by
215 laboratory role, region, and income level, which shows a response rate of at least 78% for all
216 breakdowns, except for the 3 concentration-only laboratories, from which we received only 1
217 response (i.e., response rate 33%). Based on the reported capacities, we grouped the 131
218 responding GPLN laboratories into 30 (23%) laboratories with virus isolation capacity only, 67
219 (50%) laboratories with virus isolation and ITD capacity, and 35 (27%) laboratories with
220 sequencing capacity (regardless of virus isolation and ITD capacity), with the concentration-only
221 laboratory equipped with neither of those capacities. For the estimation of costs to process AFP
222 samples, we further grouped the laboratories by income level into low- and lower middle-income
223 vs. upper middle- and high-income to allow more appropriate cost extrapolation while
224 maintaining sufficient numbers of laboratories in each group. For the estimation of costs to
225 process ES samples, we did not stratify by income level because of the smaller numbers of
226 laboratories in this group.227
228 *AFP sample processing costs*229
230 Table 1 (top) summarizes the breakdown in the laboratory types and the numbers of laboratories
231 in each category. The reported costs to process samples from AFP cases and contacts for each
232 individual cost category reflect different response rates for the various categories (Table 1,
233 numbers in parenthesis next to the reported costs show the percent of laboratories reporting).
234 The reported costs for each category remained markedly lower than the overall survey response

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3 235 rates (compare Figure 1 with Table 1), and show the highest reporting percentages for personnel
4 and consumable supplies. The responding laboratories reported approximately \$16 million in
5 236 total AFP-related costs (Table 1), which does not include \$510,000 in reported AFP-related costs
6 237 from 12 laboratories that we re-allocated to processing of ES samples. Personnel accounted for
7 238 44% of all reported costs, followed by consumable supplies (21%) and equipment (20%).
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29 260 *ES sample processing costs*
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3 266 to the absence of numbers of ES samples processed for virus isolation needed for inclusion in the
4 regression. Seven non-responding GPLN laboratories support ES according to unpublished
5 WHO data, leading to a total of 65 (45%) GPLN laboratories supporting ES activities in 2016.
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9 270 Table 2 shows the reported and estimated recurring costs for ES based on the variable response
10 rates for each cost category. The responding laboratories reported approximately \$3.2 million in
11 total recurring ES-related costs, which includes \$510,000 in AFP costs that we attributed to ES.
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13 272 Varying the ratio of ES processing cost per sample to the AFP processing cost per sample from 3
14 to 10 changed the AFP processing costs attributed to ES processing from \$340,000 to \$590,000,
15 respectively. Thus, the impact of this assumption on overall costs remains modest, because it
16 only affects 12 laboratories with ambiguity about whether reported AFP processing costs
17 included ES processing costs. The breakdown by cost category remained similar to the costs for
18 processing of AFP samples, and similarly the sequencing laboratories accounted for a large
19 portion (58%) of all reported recurring ES costs.
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24 281 Figure 2b shows the breakdown by cost category and funding source for the reported costs in
25 Table 2, which shows a similar breakdown as for AFP sample processing costs. Overall, 65%,
26 22%, 0.3%, and 12% of all reported recurring ES costs came from internal, external, bilateral,
27 and unspecified funds, respectively.
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31 286 The bottom half of Table 2 shows the extrapolated costs estimated in each group and for each
32 cost category. The resulting total recurring ES costs equal approximately \$5.3 million. Table 2
33 does not factor in the relatively small costs from the one concentration-only laboratory that
34 responded to the survey, which reported only some internally-funded recurring ES costs for
35 personnel with other costs captured in the ES set-up costs or unquantified because they paid for
36 by external resources.
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40 293 Of the 59 laboratories (i.e., 58 GPLN laboratories and 1 concentration-only laboratory) that
41 reported supporting ES activities, 35 (59%) reported that they recently (i.e., between 2010 and
42 2016) set-up or significantly expanded their ES capacity. Of these 35 laboratories, 25 (71%)
43 provided set-up cost estimates for at least one cost category, leading to total reported set-up costs
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3 297 of approximately \$1.8 million. This includes estimates from 16 ITD laboratories, 6 sequencing
4 laboratories, 2 virus isolation laboratories, and 1 concentration-only laboratory. Only 6 of the 25
5 (24%) laboratories reported becoming fully operational during 2016, which suggests that most of
6 the reported set-up costs did occurred sometime between 2010 and 2015. Figure 3 shows the
7 breakdown of the \$1.8 million of reported ES set-up costs, with the legend also showing the
8 response rates for each set-up cost category. New equipment for concentration represented the
9 largest contributor to all reported set-up cost (38%), followed by new equipment for expanded
10 poliovirus processing capacity (12%), new personnel (12%), new consumable supplies (11%)
11 and facility costs (10%). These results suggest that establishing new ES capacity in a laboratory
12 costs approximately \$75,000.
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16 308 *Other findings*
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20 310 We explored the breakdown of reported staff time spent on polio and non-polio diseases by
21 WHO region for staff supported by funding for polio (see appendix A4). We also characterized
22 the reported number of samples or isolates processed in the context of different activities (see
23 appendix A4), with the approximately 250,000 samples from AFP cases and their contacts
24 processed for virus isolation dominating the results and reflecting the primary focus of the GPLN
25 on supporting AFP surveillance. Given the current prevalence of wild polioviruses and level of
26 OPV use, roughly 4.5% of stool samples from AFP cases grow in the L20B cells used for virus
27 isolation. Of these, approximately 7% appear as possible wild or vaccine-derived poliovirus,
28 which then undergo sequencing. In contrast, ES accounted for only 12,000 samples processed
29 for virus isolation originating from 8,200 environmental sample concentrates, 67% of which
30 were concentrated using the WHO-recommended two-phase method.¹⁶ The difference between
31 the number of concentrates and the number of isolates probably comes from laboratories that
32 (re)tested samples already concentrated by another laboratory, including third-party laboratories
33 not part of the GPLN.
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37 325 *Estimated overall GPLN costs*
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3 327 Table 3 estimates the full polio laboratory costs for 2016 based on the results of the survey
4 328 complemented with data from the WHO and the CDC global specialized laboratory in Atlanta,
5 329 GA. Using the results from Tables 1 and 2, we estimate the total laboratory-specific costs to
6 330 support AFP surveillance and ES at approximately \$33 million. This does not include the
7 331 reported recent ES set-up costs of \$1.8 million, which represents only a fraction of the WHO-
8 332 supported ES set-up costs for 2016, or the costs for the analysis of serum samples. For 2016, we
9 333 estimate total costs of serology of approximately \$1 million, total costs of research and
10 334 development activities of approximately \$3 million, and global overhead costs for coordination,
11 335 training, technical of approximately \$6 million. The resulting estimated total poliovirus
12 336 laboratory costs for 2016 equal to \$43.3 million.

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337 338 339 **Discussion** 340

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27 341 This study confirms the important contributions of both GPEI and internal funds to the
28 342 maintenance of a well-functioning poliovirus surveillance laboratories.¹⁵ For comparison, the
29 343 2003 survey estimated substantially lower total costs of \$28 million per year (i.e., 21 million in
30 344 year 2002 US dollars). This estimate broke down as: (1) \$16 million of AFP-related costs for the
31 345 (sub)-national and regional reference laboratories, (2) \$8 million for all polio-related activities by
32 346 global specialized laboratories, including limited ES conducted at the time, and (3) \$4 million in
33 347 global coordination costs.¹⁵ In this study, the corresponding AFP-related costs for the (sub)-
34 348 national and regional reference laboratories equals approximately \$25 million. The total
35 349 estimated AFP and recurring ES costs for the global specialized laboratories equals only \$3.5
36 350 million, but increases to over \$7 million if we add the estimated research and development,
37 351 serology, coordination, training, and technical support costs.

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48 353 While direct comparison of the absolute costs in 2016 to those in the 2003 study¹⁵ remains
49 354 somewhat challenging due to differences in the specific cost requested, this study finds an
50 355 apparent increase in the proportion of costs paid for by internal funds from 53% in 2003¹⁵ to
51 356 62% in 2016. This may reflect increasing self-funding of the laboratory component of polio
52 357 surveillance activities by polio-free countries no longer at a high risk of outbreaks. In addition,

358 after largely externally-funded capital investments helped to set up laboratories with the capacity
359 to apply molecular methods in many countries, the more often internally-funded personnel costs
360 now represent a relatively larger share of the total costs.

361 The investments in capital costs may also have reduced the recurring costs compared to the 2003
362 survey, despite the increase from approximately 85,000 AFP samples tested in 2002 to almost
363 250,000 in 2016. Nevertheless, with 50% or more of GPLN laboratories in the African, Eastern
364 Mediterranean, and Southeast Asian WHO regions depending on external GPEI funds for at least
365 half of their budgets for AFP sample analysis, planning for financing after the GPEI resources
366 decline post-certification remains of critical importance. In this context, we note that the GPEI
367 budget for 2017 for the GPLN of \$16.4 million reflects only 17% of the GPEI budget for all
368 surveillance activities (i.e., costs associated with the field components of AFP surveillance
369 dominate the costs in the GPLN budget for surveillance) and 1.5% of the overall GPEI budget
370 for 2017.¹⁴

372
373 This study further documents the significant contributions made by poliovirus laboratories to a
374 large number of other disease surveillance efforts, with 30% of all polio-supported staff time
375 reportedly used for surveillance of other diseases. Thus, we hope that this study highlights both
376 the importance of contributions that countries make to poliovirus surveillance and the need to
377 sustain funding to support laboratories worldwide in their surveillance efforts for poliovirus and
378 other diseases. As global population immunity to poliovirus transmission decreases after OPV
379 cessation,²¹ successfully controlling any future outbreaks will require continued vigilance and a
380 rapid immunization response.²² However, questions remain after the certification of eradication
381 about the long-term financial sustainability of poliovirus surveillance and the functions of the
382 GPLN, because of the expected transition of key GPEI responsibilities and resources to other
383 programs.

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385 Based on our results, the poliovirus laboratory costs to support ES remain relatively small
386 compared to the AFP costs. This reflects the reality that despite the ongoing global ES
387 expansion, ES remains limited to parts of some countries, while the global AFP surveillance
388 system remains (nearly) universal. With the first phase of ES expansion continuing during 2017

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3 389 and 2018, we expect both increased set-up costs during those years and higher recurring ES costs
4 going forward compared to the ES costs estimated for 2016. With significant further expansion,
5 the poliovirus laboratory costs for ES could exceed those for AFP, particularly if AFP
6 surveillance declines, although we urge careful consideration of the costs and effectiveness of
7 allowing AFP surveillance to decline.²³
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12 395 This survey relied on self-reported estimates of laboratory costs. While we attempted to
13 formulate the questions unambiguously and provided translations of the survey instrument and
14 during follow up where possible, we cannot rule out possible differences in interpretation of the
15 questions. As described above, some respondents reported difficulties separating costs between
16 categories and activities or amortizing costs of equipment purchased long ago. Although we
17 achieved a high overall response rate of 89%, the response rates for individual cost categories
18 remained variable. Therefore, we relied on estimation based on regression of relatively sparse
19 data to characterize missing values, which may have introduced biases. For example,
20 laboratories receiving funding from the GPEI may be more likely to have omitted estimates for
21 individual cost categories, potentially leading to relatively greater errors in the estimation of the
22 external cost. In addition, laboratories may not have accounted for all equipment, supplies, and
23 operations cost (e.g., utilities, building maintenance) paid for by their hosting institutions,
24 potentially leading to underestimation of the share of costs funded by internal sources. We also
25 did not consider alternative data collection methods, which might have yielded different results
26 (e.g., instead of asking the entire population of laboratories to report annual estimates based on
27 available data and recall we could have attempted to visit a sample of laboratories and observed
28 activities and costs over some period of time and then extrapolated to the full year and full
29 population).

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34 414 Despite its limitations, we hope this study provides valuable insights regarding poliovirus
35 laboratory costs and the cost structure of the GPLN. Future research to inform global long-term
36 poliovirus and broader surveillance may include detailed cost studies of the field component of
37 AFP surveillance and economic analyses of the value of AFP surveillance and ES.

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41 419 **Conclusions**
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4 421 Although countries contribute significantly to poliovirus laboratory finances, many laboratories
5 currently depend on GPEI funds, and these laboratories also support the laboratory component of
6 surveillance activities for other diseases. Sustaining critical global surveillance for polioviruses
7 and other diseases will require continued funding as GPEI resources decline, particularly after
8 global certification. Paying the costs to sustain surveillance represents an essential element for
9 securing a polio-free world, and offers the opportunity to transition at least some of the current
10 poliovirus laboratory resources to control/eliminate other vaccine-preventable or emerging/re-
11 emerging communicable diseases.²⁴
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31 430 **List of abbreviations**
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36 432 AFP, acute flaccid paralysis; ES, poliovirus environmental surveillance; GPEI, Global Polio
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433 **List of abbreviations**

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

437 **DECLARATIONS**

438 **Authors' contributions**

439 All authors (RDT, DMO, MAP, MSO, KMT) contributed to the study design, survey instrument
440 development, interpretation of data, manuscript writing, and revisions. The first author (RDT)
441 performed the data analysis, the last author (KMT) coded and administered the survey instrument
442 in Survey Monkey™, the second author (DMO) contacted the laboratories, the first and second
443 authors (RDT, DMO) recruited participants and followed up with respondents on any questions.
444

445 **Ethics approval and consent to participate**

446 Not applicable

448 **Consent to publish**

449 Not applicable

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3 451 **Competing interests**
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5 452 None
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9 454 **Funding**
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11 455 This publication was supported by Cooperative Agreement Number 5NU2RGH001913-02-00
12 funded by the Centers for Disease Control and Prevention. Its contents are solely the
13 responsibility of the authors and do not necessarily represent the official views of the Centers for
14 Disease Control and Prevention or the Department of Health and Human Services.
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18 460 **Acknowledgments**
19
20 461 The authors thank all GPLN and concentration-only laboratory personnel for providing valuable
21 responses to the survey; Humayun Asghar, Cara Burns, Evgeniy Gavrilin, Varja Grabovac,
22 Nicksy Gumede-Moeletsi, Sirima Pattamadilok, Gloria Rey, and Yan Zhang for helpful feedback
23 on the survey instrument; Evgeniy Gavrilin and Zhu Shuangli for highly valuable help in
24 translating the survey questionnaire into Russian and Chinese, respectively; and Patrick Briand,
25 Stephen Cochi, Lee Hampton, Maria Iakovenko, Fem Paladin, Everardo Vega, Steven Wassilak,
26 and Marita Zimmermann for input at various stages of the process.
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36 470 **Data sharing statement**
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38 471 Technical appendix available on request from the authors.
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3 547 **Table 1: Reported and estimated costs to process acute flaccid paralysis samples, based on regression of reported total number**
4 548 **stool samples processed for virus isolation for the number of laboratories (N) in the category (excluding the costs for the**
5 549 **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) |
| <i>All cost categories</i> | 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 |

| | | | | | | | | |
|---|----------------------------|-----------|-----------|-----------|-----------|-----------|-----------|------------|
| 1 | Consumable supplies | 150,000 | 280,000 | 1,400,000 | 810,000 | 1,500,000 | 450,000 | 4,600,000 |
| 2 | Shared consumable supplies | 8,400 | 63,000 | 87,000 | 230,000 | 290,000 | 110,000 | 790,000 |
| 3 | Donated supplies | 4,600 | 15,000 | 6,200 | 830 | 0 | 600 | 27,000 |
| 4 | Operations | 540,000 | 550,000 | 330,000 | 250,000 | 1,000,000 | 440,000 | 3,100,000 |
| 5 | Shipping/transport | 150,000 | 40,000 | 57,000 | 55,000 | 600 | 170,000 | 470,000 |
| 6 | Technical support | 230 | 21,000 | 40,000 | 46,000 | 200 | 20,000 | 130,000 |
| 7 | Other | 0 | 11,000 | 8,200 | 1,500 | 0 | 2,200 | 23,000 |
| 8 | <i>All cost categories</i> | 5,300,000 | 2,800,000 | 5,700,000 | 4,500,000 | 3,600,000 | 6,000,000 | 28,000,000 |

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3 552 **Table 2: Reported and estimated recurring costs to process environmental samples, based on regression by reported total
4 number of environmental samples processed for virus isolation (results exclude costs from concentration-only laboratories).**
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| 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) |
| <i>All cost categories</i> | 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 |

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|--|----------------------------|---------|-----------|-----------|-----------|
| | <i>All cost categories</i> | 540,000 | 1,400,000 | 3,400,000 | 5,300,000 |
|--|----------------------------|---------|-----------|-----------|-----------|

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556 **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

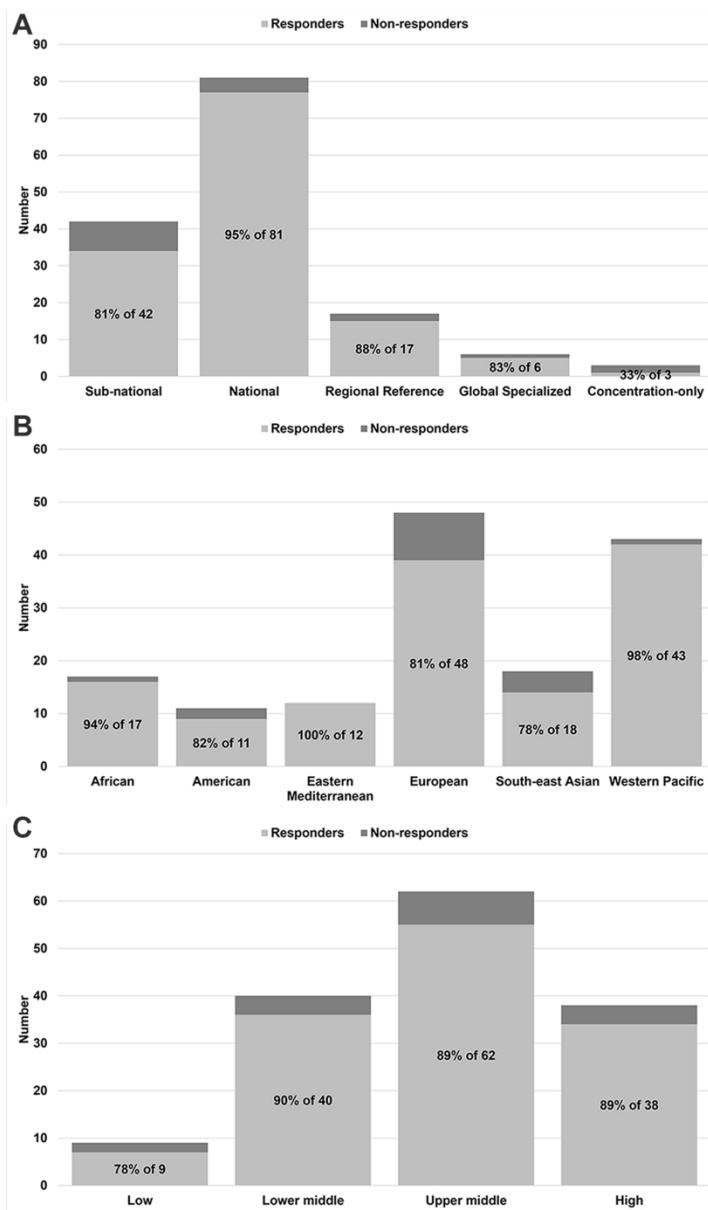
Figure 2: Reported costs by cost category and source of funding

(a) Costs to process acute flaccid paralysis samples

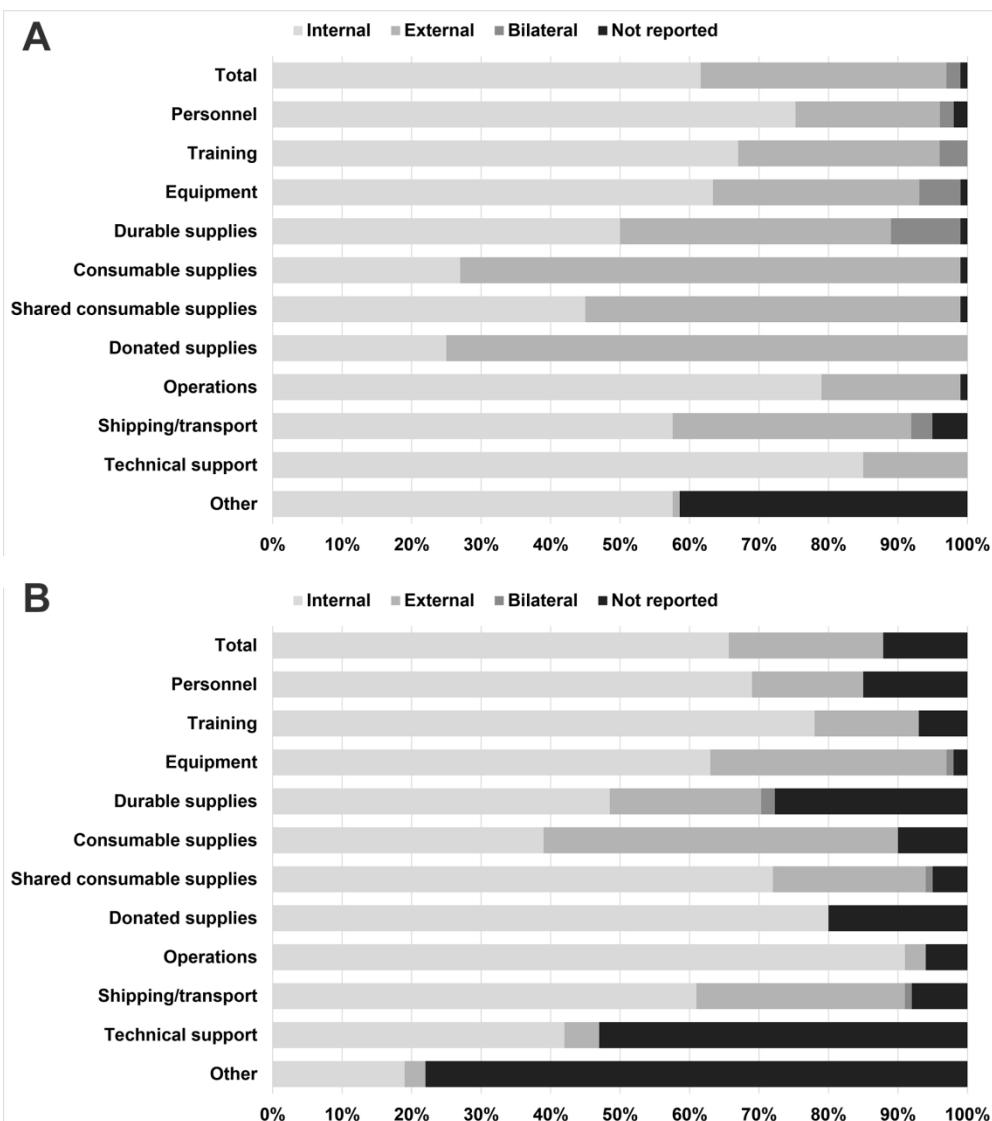
(b) Costs to process environmental samples

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.



45 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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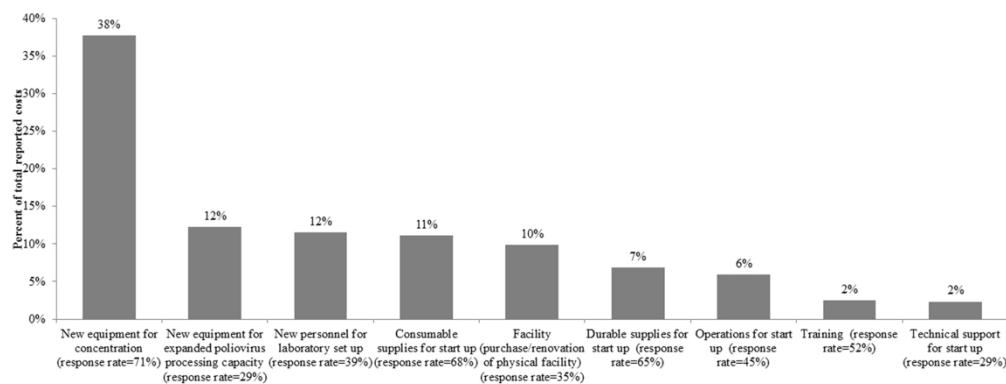


Figure 3: Breakdown by cost categories of reported environmental surveillance set-up costs. Response rates for each cost category represent percentages among 30 laboratories that reported having set-up or significantly expanded poliovirus environmental surveillance capacity between 2010 and 2016. The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

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2 **APPENDIX for Duintjer Tebbens et al., "Characterizing the costs of the Global Polio**
3 **Laboratory Network: A survey-based analysis"**
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6 **A1. Survey instrument**
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9 Introduction: Poliovirus Laboratory Survey
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12 The World Health Organization (WHO)-led Global Polio Laboratory Network (GPLN) continues
13 to play an essential role in global polio eradication, and periodic efforts to quantify its overall
14 value provide important information that helps to motivate financial support for GPLN
15 laboratories. Assessing the value of the GPLN is of utmost importance at this stage of the GPEI,
16 as the partners discuss the strategies to maintain polio laboratory functions pre- and post-
17 certification of wild poliovirus eradication and global containment of live polioviruses. This
18 GPLN survey aims to collect data on activities and costs of all of the GPLN laboratories to
19 support an overall synthesis. The objectives of this survey include to: (1) update estimates of the
20 total costs of the GPLN reported based on a similar 2003 survey, (2) better understand the
21 different cost components, including environmental surveillance, and (3) characterize the extent
22 to which the GPLN contributes to surveillance of other diseases. The survey form should take
23 approximately 60 minutes to complete, and we expect that collecting data and calculating some
24 of the costs may take an additional 1-4 hours, depending on the size and complexity of the
25 laboratory. Please start the survey as soon as possible, so if you have any questions or if you
26 need to compile data, you will have time to do so. The survey includes questions about acute
27 flaccid paralysis (AFP) surveillance (i.e., stool samples from AFP cases and contacts) and
28 environmental surveillance (i.e., sewage samples).
29
30

31 Please note:
32
33 · we pre-filled some answers based on data collected in GPLNMS annual reports for 2016 as of
34 June 2017, and we ask that you please check the pre-filled answers carefully and correct the
35 information as appropriate.
36
37 · please do not leave any answers blank, because we cannot interpret these correctly, so please
38 enter "0" for zero, "unknown" for unknown, "not applicable" for not applicable, or "data not
39 available" or other appropriate text. If you find any question too difficult to answer, please do not
40 quit the entire question or survey, but instead reply with "unable to answer" and please add any
41 information that can help us understand the reason.
42
43

44 We provided a glossary to promote consistent interpretation of survey language. If you have any
45 questions, please contact Dr. Radboud Duintjer Tebbens (Kid Risk) and Dr. Ousmane Diop
46 (WHO). Thank you very much for your time and effort to respond to the survey. We look
47 forward to hearing from you - please complete your response by September 1, 2017. We will
48 share the results with all polio laboratory directors for dissemination once they become available.
49
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51 1. Please provide information about how to contact you and about your laboratory
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53 Laboratory Name:
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55 Your Name:
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57 Phone number:
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59 Email address:
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3 47 City:
4 48 Country:
5 49 WHO Region:
6 50 * Total employee full-time equivalents (FTEs) for poliovirus surveillance employed by the
7 laboratory:
8 52 Please enter the percent (between 0-100, without the % sign) of FTEs reported for the line with
9 the * above supported by National/internal funds:
10 54 Please enter the percent (between 0-100, without the % sign) of FTEs reported for the line with
11 the * above supported by GPEI external funds:
12 56 Please enter the percent (between 0-100, without the % sign) of FTEs reported for the line with
13 the * above supported by Other external funds (non GPEI-external funds, including bi-lateral
14 support) - This line should total 100 minus the percents on the prior 2 lines.
15 58
16 59
17 60 2. What role did your laboratory play in the global polio laboratory network in 2016?
18 61 Subnational
19 62 National
20 63 Regional reference
21 64 Specialized
22 65 Other (please specify)
23 66
24 67 3. Please list the geographic areas (country, state, region) that your laboratory served in 2016 for
25 each laboratory capacity (enter "None" for any you do not do and please note any special
26 activities by including the word "Special" after the name of the geographic area indicated, for
27 example to help with overflow from another lab, if applicable for 2016):
28 71 Virus isolation:
29 72 Intratypic differentiation (ITD):
30 73 Sequencing:
31 74 Serology:
32 75 Environmental surveillance:
33 76
34 77 4. Please estimate what percentages (without including the "%" sign) of polio-supported staff
35 time and equipment your laboratory spends on poliovirus surveillance and research activities
36 (including methods development, serology, clinical trials, next generation or complete genome
37 sequencing, etc.) versus surveillance and research activities for other diseases.
38 81 Poliovirus activities (indicate 100 here and 0 on all other answers if your lab supports poliovirus
39 surveillance activities exclusively):
40 83 Non-polio enteroviruses:
41 84 Measles and/or rubella viruses:
42 85 Rotavirus:
43 86 Influenza:
44 87 Japanese encephalitis:
45 88 Yellow fever:
46 89 Other arboviruses (e.g., Zika, dengue) or hemorrhagic fever viruses:
47 90 Other (please provide percentage here and details about what this includes in Question 9):
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3 92 5. Did your laboratory perform the following for poliovirus environmental surveillance in 2016
4 93 (if none indicate no for all)?
5 94 Site selection: Y/N
6 95 Sample collection: Y/N
7 96 Sample transportation: Y/N
8 97 Concentration: Y/N
9 98 Virus isolation: Y/N
10 99 Intratypic differentiation: Y/N
11 100 Sequencing: Y/N
12 101 Other (please specify): Y/N
13 102

14 103 6. Please tell us about any poliovirus serology testing you did in 2016 (if none, then enter "None"
15 104 for this question).

16 105 How many serum samples did you test for poliovirus antibodies in 2016?
17 106 Approximately how many employee hours did your laboratory spend in 2016 for poliovirus
18 107 serum sample processing?

19 108 What laboratory method do you use for poliovirus serology testing?
20 109 Please indicate the purpose(s) for the poliovirus serology sampling (e.g., seroprevalence
21 110 assessment, support for vaccine trials, etc.)

22 111 7. Please tell us the number of samples your laboratory processed in 2016 related to other
23 112 activities (i.e., non-AFP, non-poliovirus environmental surveillance, and non-poliovirus serology
24 113 activities) for the following (please specify details about the methods used and your role in
25 114 sample collection in Question 9)

26 115 Non-polio enterovirus surveillance:

27 116 Healthy children / adult surveys (e.g., stool surveys) that are not part of AFP surveillance:
28 117 Clinical trial support:

29 118 Other (please specify the nature of these samples in Question 9):

30 119 8. What currency do you use to track laboratory costs and will you use to report costs in this
31 120 survey?

32 121 9. Please specify details here if you answered "other" for Question 4 and/or 7, please also
33 122 describe any research activities conducted by your laboratory in 2016 related to polioviruses, and
34 123 please use this space to enter any other comments you would like to make related to the
35 124 questions on this page.

36 125 10. How many samples/isolates from AFP cases and their contacts did you process in 2016?

37 126 Acute flaccid paralysis (AFP) surveillance:

38 127 Virus isolation:

39 128 Intratypic differentiation:

40 129 Sequencing:

41 130 Other (please enter the number here and specify the type of processing in Question 14):

42 131 11. How many people (full-time equivalents) worked on the different steps of processing AFP
43 132 samples in 2016?

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2
3 138 Cell culture:
4 139 Virus isolation:
5 140 Intratypic differentiation:
6 141 Sequencing:

7
8 142 Management (including supervisors, data management, analytics, recording, and reporting):
9 143 Other (please enter number here and specify the type of processing in Question 14):
10 144

11 145 12. How much did your laboratory spend (in the currency you specified in Question 8) for
12 analysis of AFP samples in 2016 for each cost category?

13 147 Personnel (costs should correspond to number of people in Question 11 plus any staff not on
14 payroll):
15 149 Training (please exclude any costs counted in the personnel row above):
16 150 Equipment, please estimate the amortized annual cost, see Excel worksheet:
17 151 Durable supplies, please estimate the amortized annual cost, see Excel worksheet:
18 152 Consumable supplies attributable to each sample:
19 153 Shared consumable supplies purchased by laboratory not easily attributable to each sample:
20 154 Donated supplies provided by your lab to other labs (please specify the other labs you provide
21 these to in Question 14):
22 155

23 156 Operations:
24 157 Shipping/transport:
25 158 Technical support (not otherwise captured):
26 159 Other (please specify in Question 14):
27 160

28 161 13. Please indicate the approximate percents of the amounts spent in Question 12 for each cost
29 category by contribution type: 1. National/internal; 2. GPEI external; and 3. Bilateral and non-
30 GPEI external. For example, if all support came from national sources then indicate "100; 0; 0"
31 OR if all contributions came from the GPEI indicate "0; 100; 0" OR if approximately equal
32 support came from each indicate "33.4; 33.3; 33.3" and please verify that the totals of all three
33 components of the answer for each row add to 100)
34 166

35 167 Personnel

36 168 Training

37 169 Equipment

38 170 Durable supplies

39 171 Consumable supplies

40 172 Shared consumable supplies

41 173 Donated supplies

42 174 Operations

43 175 Shipping/transport

44 176 Technical support

45 177 Other

46 178

47 179 14. Please specify details here about Questions 10-13 for which you answered "other" or enter
48 any comments you would like to make related to the questions on this page.
49 180

50 181 15. Did your laboratory support any poliovirus environmental surveillance or research activities
51 in 2016 (please verify)?
52 182
53 183
54 184

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3 184 No
4 185 Yes
5 186
6 187 16. Did your laboratory first establish its capacity to process poliovirus environmental samples
7 between 2010 and 2016 (i.e., relatively recently)? (If yes, the survey will ask you to estimate set
8 up costs. If your laboratory established its capacity to process environmental samples before
9 2010, but made significant investments in 2016 to expand its capacity, then answer yes and
10 estimate the costs for expanding the capacity in 2016 in Question 18).
11 192 No
12 193 Yes
13 194
14 195 17. Please enter the dates your laboratory first began to develop the capacity to support
15 poliovirus environmental surveillance efforts and became fully operational (if exact date
16 unknown, please estimate month and enter "14" for day)?
17 Date laboratory began to develop the poliovirus ES capacity: MM/DD/YYYY
18 Date your lab became fully operational to support poliovirus environmental surveillance:
19 MM/DD/YYYY
20
21
22
23 202 Environmental surveillance SET UP questions (for capacity established AFTER 2009 OR
24 expanded during 2016 ONLY):
25
26
27 205 18. Please estimate the costs your laboratory spent to SET UP poliovirus ES capacity between
28 the dates you reported in Question 17 (in the currency you specified in Question 8) for each cost
29 category.
30 Facility (purchase/renovation of physical facility)
31 New personnel for laboratory set up
32 Training
33 New equipment for concentration (e.g., centrifuge, refrigerators, funnels, filtration devices, etc.)
34 New equipment for expanded poliovirus processing capacity
35 Durable supplies for start up
36 Consumable supplies for start up
37 Operations for start up
38 Technical support for start up
39 Other (please specify in Question 20)
40
41
42 219 19. If you included estimates of SET UP costs in Question 18, please indicate the approximate
43 percents of the amounts for each cost category by contribution type: 1. National/internal; 2. GPEI
44 external; and 3. Bilateral and non-GPEI external. For example, if all support came from national
45 sources then indicate "100; 0; 0" OR if all contributions came from the GPEI indicate "0; 100; 0"
46 OR if approximately equal support came from each indicate "33.4; 33.3; 33.3" and please verify
47 that the totals of all three components of the answer for each row add to 100)
48 Facility
49 New personnel for laboratory set up
50 Training for start up
51 New equipment for concentration
52 New equipment for expanded poliovirus processing capacity
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3 230 Durable supplies for start up
4 231 Consumable supplies for start up
5 232 Operations for start up
6 233 Technical support for start up
7 234 Other (please specify in Question 20)
8 235
9
10 236 20. Please specify details here about Questions 18-19 for which you answered "other" or enter
11 any comments you would like to make related to the questions on this page.
12 238
13 239 21. Which organization(s) collect the poliovirus environmental samples that your laboratory
14 receives?
15 241
16 242 22. Please enter the total number of environmental samples your laboratory received in 2016
17 from each of the following types of water source(s) sampled (if known). If only unknown water
18 source(s) sampled, then please indicate the total number of environmental samples for 2016 in
19 the second-to-last row.
20 246 Wastewater treatment plant
21 247 Pumping station
22 248 Open drains or canals
23 249 Streams, rivers, or other flowing surface water
24 250 Lakes, ponds or other standing surface water
25 251 Access point from sewage system
26 252 Unknown
27 253 Other (please indicate type in Question 27)
28 254
29 255 23. Please enter the number of environmental samples for which your laboratory took the
30 indicated number of days between the time of sample collection and starting the process of virus
31 isolation. Your internal data for all poliovirus ES samples should provide the sample collection
32 date and the date your lab started sample processing.
33 259 Less than 2 days
34 260 3 to 5 days
35 261 6 to 10 days
36 262 11 to 15 days
37 263 16 to 20 days
38 264 21 to 25 days
39 265 26 to 30 days
40 266 31 to 35 days
41 267 More than 35 days
42 268
43 269 24. How many environmental samples did your laboratory process in 2016 for each of the
44 following?
45 271 Concentration using
46 272 WHO-recommended two-phase separation
47 273 Concentration using other methods (please specify method(s) used in Question 27)
48 274 Virus isolation
49 275 Intratypic differentiation
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3 276 Sequencing
4 277 Research
5 278 Direct detection
6 279 Other (please specify type of processing in the comment field at the bottom of this page in
7 280 Question 27)
8 281
9 282 25. How much did your laboratory spend (in the currency you specified in Question 8) for
10 analysis of environmental samples in 2016 (excluding any costs for SET UP that occurred in
11 2016, which you should have reported in Question 18) and excluding any costs already reported
12 in Question 12 related to AFP processing that applied to processing environmental samples.
13 285 Personnel (FTEs for environmental surveillance activities)
14 286
15 287 Training
16 288 Equipment, please estimate the amortized annual cost, see Excel worksheet
17 289 Durable supplies, please estimate the amortized annual cost, see Excel worksheet
18 290 Consumable supplies
19 291 Shared consumable supplies
20 292 Donated supplies (please specify the other labs you provide these to in Question 27)
21 293 Operations
22 294 Shipping/transport
23 295 Technical support
24 296 Other (please specify in Question 27)
25 297
26 298 26. Please indicate the approximate percent of the amounts spent in Question 25 for each cost
27 category by contribution type: 1. National/internal; 2. GPEI external; and 3. Other external. For
28 example, if all support came from national sources then indicate "100; 0; 0" OR if all
29 contributions came from the GPEI indicate "0; 100; 0" OR if approximately equal support came
30 from each indicate "33.4; 33.3; 33.3" and please verify that the totals of all three components of
31 the answer for each row add to 100)
32 304 Personnel
33 305 Training
34 306 Equipment
35 307 Durable supplies
36 308 Consumable supplies
37 309 Shared consumable supplies
38 310 Donated supplies
39 311 Operations
40 312 Shipping/transport
41 313 Technical support
42 314 Other (please specify in Question 27)
43 315
44 316 27. Please specify details here about Questions 21-26 for which you answered "other" or enter
45 any comments you would like to make related to the questions on this page.
46 317
47 318
48 319 28. Please list and indicate the nature and source of all in-kind contributions your laboratory
49 receives that support AFP and/or ES sample processing (please provide a brief description that
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3 321 includes the amount, source, and purpose of the in-kind support). If your laboratory provides in-
4 kind support to other laboratories, please provide details about this.
5
6 323 No
7 324 Yes (please specify)
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9 325
10 326 29. Did your laboratory experience any significant changes in its workload/workflow in 2016
11 compared to 2015, if so please describe reasons (e.g., increased/decreased AFP, contact samples,
12 special surveys, serology or clinical trials, introduction of environmental surveillance,
13 implementation of polio laboratory containment and GAP III requirements or other activities,
14 and impacts of changes in financials support, etc.)?
15 331 No
16 332 Yes (please specify)
17
18 333
19 334 30. Does your laboratory expect to make any significant changes in its workload/workflow in the
20 future compared to 2016, if so please describe reasons (e.g., increased/decreased AFP, contact
21 samples, special surveys, serology or clinical trials, or other activities, introduction of
22 environmental surveillance)?
23 338 No
24 339 Yes (please specify)
25
26 340
27 341 31. What other costs or issues related to poliovirus laboratories do you think we should consider?
28 What questions should we ask that we did not ask? Please use this space to make any final
29 comments on the survey. Thank you very much for your responses.
30
31 344
32 345 32. Are you ready to submit your completed survey?
33 346 No (if not, please make sure to select "Prev" below to go back to the prior questions)
34 347 Yes (if so, and only if so, select "Done" below, because you will not be able to make any
35 changes after selecting "Done")
36
37 350 **A2. Responding laboratories**
38
39 352 We received responses from the following 131 Global Polio Laboratory Network (GPLN)
40 laboratories, organized by World Health Organization (WHO) region, laboratory type, and
41 country of laboratory location:
42
43 356 **African Region (15 of 16)**
44 357 Regional reference laboratories in Central African Republic, Ghana, and South Africa
45 358 National laboratories in Algeria, Cameroon, Cote d'Ivoire (note: this lab also serves as the
46 National lab for Mali, Burkina Faso, Liberia, and Sierra Léone), Democratic Republic of the
47 Congo, Ethiopia, Kenya, Madagascar, Nigeria (2: Ibadan, Maiduguri), Uganda (note: this lab
48 also serves as the National lab for Burundi, Rwanda, and the Republic of Tanzania, South
49 Sudan), Zambia, and Zimbabwe (note: this lab also serves as the National lab for Malawi)
50
51 363
52 364 **Region of the Americas (9 of 11)**
53 365 Global specialized laboratory in the United States of America
54 366 Regional reference laboratory in Brazil
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3 367 National laboratories in Canada, Columbia, Cuba, Mexico, Trinidad and Tobago, and Venezuela
4 368 Subnational laboratory in Brazil
5 369

6 370 **Eastern Mediterranean Region (12 of 12)**

7 371 Regional reference laboratories in Egypt, Kuwait, Pakistan, and Tunisia
8 372 National laboratories in Iran, Iraq, Jordan, Morocco, Oman, Saudi Arabia, Sudan, and the Syrian
9 373 Arab Republic
10 374

11 375 **European Region (39 of 48)**

12 376 Global specialized laboratories in France and the Netherlands
13 377 Regional reference laboratories in Finland, Italy, and the Russian Federation
14 378 National laboratories in Albania, Austria, Belarus, Bulgaria, Croatia, Czech Republic, Denmark,
15 379 Estonia, France, Georgia, Greece, Hungary, Ireland, Israel, Kazakhstan, Latvia, Lithuania,
16 380 Moldova, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain,
17 381 Switzerland, Turkey, Ukraine, United Kingdom, and Uzbekistan
18 382 Subnational laboratories in Russian Federation (Khabarovsk), Turkey, and Ukraine (Odessa)
19 383

20 384 Note: At the time of the survey, we did not contact the National lab in the Democratic People's
21 385 Republic of Korea because it was considered dormant (i.e., no active or known contact)
22 386

23 387 **South East Asia Region (14 of 16)**

24 388 Global specialized laboratory in India
25 389 Regional reference laboratories in Sri Lanka and Thailand
26 390 National laboratories in Bangladesh, India (6 – Bangalore, New Delhi, Ahmedabad, Kasauli,
27 391 Kolkata, and Lucknow), Indonesia (3 - Bandung, Jakarta, Surabaya), and Myanmar
28 392

29 393 **Western Pacific Region (42 of 43)**

30 394 Global specialized laboratory in Japan
31 395 Regional reference laboratories in Australia and China
32 396 National laboratories in China (Hong Kong), Malaysia, Mongolia, New Zealand, Philippines,
33 397 Republic of Korea, Singapore, and Viet Nam (2 – Hanoi, Ho Chi Minh)
34 398 Subnational laboratories in China (30 – Anhui, Beijing, Chongqing, Fujian, Gansu, Guangdong,
35 399 Guangxi, Guizhou, Hainan, Hebei, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Jiangxi,
36 400 Jilin, Liaoning, Neimengu, Ningxia, Qinghai, Shaanxi, Shandong, Shanghai, Shanxi,
37 401 Sichuan, Tianjin, Xinjiang, Yunnan, and Zhejiang)
38 402

39 403 In addition to these GPLN laboratories, we received a response from the Concentration-only
40 404 laboratory in Niger.
41 405

42 406 **A3. Technical details for analysis**

43 407 *Adjustment for under-reporting of (shared) consumable costs*

44 408 When both the (shared) consumable supply costs per reported virus isolation test equaled less
45 409 than \$20 and the absolute (shared) consumable supply costs equaled less than \$400, we
46 410 multiplied the reported costs by the reported number of virus isolation tests. The second
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3 413 condition served to ensure no undue multiplication by the number of virus isolation tests for
4 414 some laboratories with very large numbers of reported virus isolation tests but modest reported
5 415 (shared) consumable supplies. This approach resulted in multiplication by the number of virus
6 416 isolation tests of the reported consumable and shared consumable supplies for AFP sample
7 417 processing for 59 and 25 laboratories, respectively. The results remained robust to choices of the
8 418 thresholds of \$20 and \$400. With the exception of two laboratories that clearly reported (shared)
9 419 consumable supplies per sample for ES sample processing, we did not adjust any of the reported
10 420 (shared) consumable supply costs for ES sample processing.
11 421
12 422 *Adjustments to account for missing data*
13 423

15 424 As described in the main text, we separated the cost categories into non-zero categories (NZCs)
16 425 and possible zero categories (PZCs). Some respondents indicated challenges in separating AFP
17 426 and ES sample costs, and others explicitly indicated that they reported only the combined costs.
18 427 This led us to pre-process the data from these laboratories. Based on the average total costs per
19 428 sample processed for virus isolation reported among all laboratories that provided separate costs
20 429 for AFP and ES, we assume that, on average, ES samples require seven times the cost per virus
21 430 isolation test as AFP samples. Specifically, for costs in the NZCs, if a laboratory reported non-
22 431 zero costs for AFP processing and either indicated that they combined AFP and ES costs or
23 432 reported zero recurring or set-up ES costs for the cost category, then we estimated the portion of
24 433 reported AFP costs attributable to ES based on the number of ES samples processed for virus
25 434 isolation times seven, divided by the total samples (i.e., the number of ES samples times seven
26 435 plus the number of AFP samples processed for virus isolation). We then subtracted the estimated
27 436 ES-attributable costs from the reported AFP costs. For PZCs, we estimated and subtracted the
28 437 ES-attributable costs only if the laboratory reported non-zero AFP costs and explicitly indicated
29 438 that they combined ES and AFP costs (i.e., not if they reported 0 ES costs for the category).
30 439 Recognizing uncertainty about the true ratio of costs per sample processed for virus isolation for
31 440 ES compared to AFP samples, we explored the impact of varying this ratio from three to ten.
32 441
33 442 In addition to making assumptions to separate combined cost estimates, we further treated the
34 443 data differently depending on the type of cost category. For NZCs, we interpreted any response
35 444 not corresponding to a positive number as a missing estimate requiring estimation (i.e., even if a
36 445 laboratory responded with 0, we interpreted this as an indication that the laboratories did not
37 446 have access to the data required to estimate the costs). For PZCs, we interpreted zeroes, blanks,
38 447 or any text indicating an inability to estimate the costs (e.g., not applicable, unknown, unable to
39 448 estimate) as a true zero. For these categories, we only estimated costs for non-responding
40 449 laboratories or laboratories that did not provide an estimate for any of the cost categories in the
41 450 corresponding question according to the logic shown in Table A1 for AFP and Table A2 for ES.
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3 453 **Table A1: Logic for interpretation of AFP cost responses (after any subtractions as a result**
4 454 **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 |

20 455 NZC, non-zero (cost) category; PZC, possible zero (cost) category
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3 456 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 |

38 457 NZC, non-zero (cost) category; PZC, possible zero (cost) category

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3 459 **A4. Other findings**
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5 461 *Other diseases*
6 462
7 463 Table A3 show the breakdown of polio-supported staff time spent on polio and non-polio
8 464 diseases by WHO region. Only 1 of 132 (1%) of laboratories that responded to the survey did
9 465 not provide estimates for the total number of polio-supported FTEs or the percentages spent on
10 466 polio and other diseases. Overall, polio-supported staff spent approximately 30% of time
11 467 supporting activities for other diseases or viruses, including non-polio enteroviruses (11%),
12 468 measles and/or rubella viruses (7%), and a wide range of other diseases not specifically asked
13 469 about in the survey (5%). The American (41%) and European (46%) regions reported the lowest
14 470 percentages of staff time spent on polio. The Eastern Mediterranean region (87%), which
15 471 includes one laboratory serving two polio-endemic countries (i.e., Afghanistan and Pakistan),
16 472 reported the highest percentage.
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18 474 Respondent laboratories collectively reported spending 41 FTEs on diseases/conditions not
19 475 specifically listed in Table A3. The laboratories reported that these other diseases/conditions
20 476 included TORCH, exanthemal infections, urogenital, immunology, intestinal and parasitic
21 477 infection groups, human immunodeficiency virus, hepatitis, acute respiratory viral infections,
22 478 teratogenic infections, mycoplasma, chlamydophyll, transgenic organisms control, astrovirus,
23 479 norovirus, sapovirus, adenovirus, rabies, non-influenza respiratory diseases, non-rotavirus acute
24 480 gastroenteritis, herpes group viruses, mumps, rhinovirus, parainfluenza virus, respiratory
25 481 syncytial virus, metapneumovirus, parechovirus, polyomavirus, varicella virus, diphtheria,
26 482 tetanus, pertussis, cytomegalovirus, crystalli, parotitis, severe fever with thrombocytopenia
27 483 syndrome, meningitis, and encephalitis.
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3 488 **Table A1: Staff time spent on polio and non-polio diseases by World Health Organization Region for staff supported by**
4 489 **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 |

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3 491 *Other types of polio laboratory tests*
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5 493 Laboratories reported performing several other types of laboratory tests, including ELISA, PCR,
6 494 RT-PCR, HBsAg, microtitration, genotyping, and serology for numerous viruses and on various
7 495 sample types (i.e., sera, nasopharyngeal washings, blood, feces, urine, urogenital scrapings,
8 496 sectional material, mites, spinal fluid, rectal swab and vomitus from diarrhea and food poisoning
9 497 cases, ice and drinking water, soil) as well as virus isolation on fecal samples from AFP cases
10 498 over age 15, AFP samples from provinces outside of the areas normally served by the laboratory,
11 499 fecal samples from non-AFP patients not part of a survey, and research activities.
12 500

13 501 Table A4 summarizes the reported number of samples or isolates processed in the context of
14 502 different activities. The difference between the number of concentrates and the number of
15 503 isolates for ES probably comes from laboratories that (re)tested samples already concentrated by
16 504 another laboratory, including third-party laboratories not part of the GPLN. A much larger
17 505 fraction of isolates from ES samples compared to AFP samples underwent Intratypic
18 506 differentiation (ITD) testing (54%) and sequencing (15%), probably because ES samples
19 507 comprise a composite from potentially thousands of individuals and they often yield complex
20 508 mixtures of viruses. This results in higher costs on a per-sample basis for ES than AFP, with ES
21 509 sample processing additionally requiring three times as many cell cultures as the AFP sample
22 510 processing. As shown in Table A4, laboratories also reported analyzing almost 2,000 ES
23 511 samples in the context of research activities and 82 ES samples using direct detection methods.
24 512

25 513 Forty responding laboratories further reported analyzing over 50,000 serum samples for the
26 514 presence of antibodies, which they estimated took almost 13,000 employee hours (i.e., 12.7 FTEs
27 515 assuming 2,000 employee hours per year). Laboratories analyzed almost 40,000 samples in the
28 516 context of non-polio enterovirus surveillance and approximately 150,000 other samples,
29 517 reflecting the reality that many GPLN laboratories perform non-polio services (not necessarily
30 518 funded by polio surveillance), particularly in countries with no recent polio outbreaks. While 49
31 519 laboratories reported testing other samples, 3 of these laboratories accounted for 83% of the
32 520 150,000 samples and indicated that their reported numbers included routine diagnostic services.
33 521 Laboratories also reported analyzing approximately 6,900 and 4,300 samples in the context of
34 522 healthy children or adult stool surveys and clinical trials, respectively.
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524 **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 |

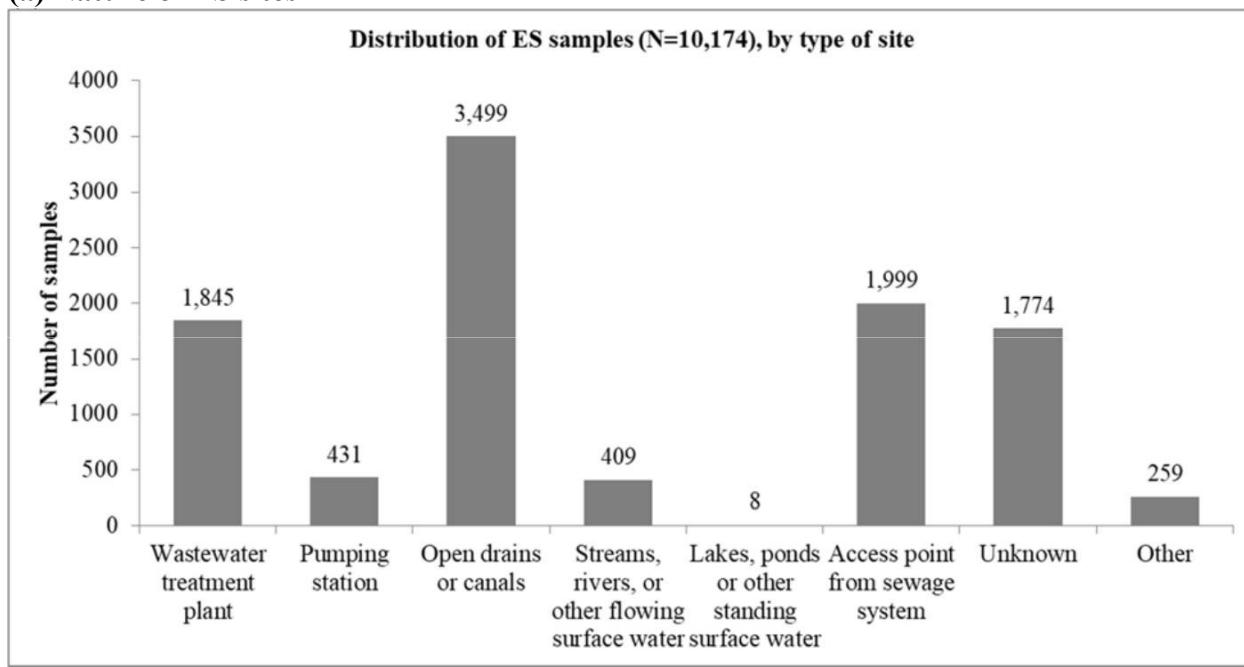
^a Includes serotyping and polymerase chain reaction analysis of non-polio enteroviruses identified in acute flaccid paralysis cases, Sanger sequencing, and next generation sequencing of complete genomes

^b See text

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3 530 *Additional results related to ES sampling*
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5 532 Figure A1 summarizes characteristics of the ES systems based on reported results for
6 533 approximately 10,000 ES samples (the total numbers of samples differ from Table A4 due to
7 534 incomplete responses for some (sub)questions and possible double-counting of samples analyzed
8 535 by multiple laboratories through the referral system). The majority of ES samples came from
9 536 open drains or canals (34%), followed by other access points from sewage systems (19%),
10 537 wastewater treatment plants (18%), and unknown sources (18%). Eighty percent of samples
11 538 started processing for virus isolation within 5 days of sample collection, which likely reflects the
12 539 routine handling of ES samples collected in the context of ongoing ES (see Figure A1b).
13 540 However, the reported 6% of samples taking more than 35 days until virus isolation began
14 541 suggests a long tail of the distribution of transportation and processing delays (Figure A1b). The
15 542 delays may relate to a supply shortage situation during the rapid global expansion of ES, which
16 543 efforts to streamline quality assurance and quality control may limit as the system become more
17 544 established. Moreover, ES conducted in the context of research activities may follow different
18 545 timelines.
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3 548 **Figure A1: Reported results related to the ES systems**
4 549 **(a) Nature of ES sites**



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

