A Framework to Assess Poliovirus Elimination from Clinical and Environmental Surveillance Data

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Background

• Polio modellers & other stakeholders focus where cases and ES\(^1\) detections are
  • Vaccine effectiveness & strategies to reduce transmission

• We will explore “the other side”...pathways to eradication

• How it works (endemic countries):\(^2\)
  • “Interruption of transmission”, ie no cases or ES detections for 3 years*
  • Data reviewed by certification committees: National, Regional, Global
  • Certification
  • Cessation process starts, ie. removal of OPV

\(^1\) Environmental surveillance  \(^2\) GPEI Strategic Plan 2022-26  * Stated in 21\(^{st}\) GCC report
Where did the 3 years wait come from?

Modelling! “Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated?”


“The case-free period must exceed 3 years before one can be 95% certain that there has been local extinction of the wild polio virus infection”

Further 21st century considerations:
• Perfect surveillance for cases was assumed, this might not reflect reality
• ES has likely improved surveillance for polioviruses
• Waiting 3 years provides no incentives to improve surveillance

Overview

• Empirical approaches to inform on time between cases

• Statistical model for estimating surveillance sensitivity and probability of elimination

• Informing policy
Empirical approaches

Previous WPV1 outbreaks (2000-2011)
- Outbreaks defined by viral genotype & cluster
- Fully observed
- N = 34, with 13 of size > 3 polio cases
- All have ‘tails’ and some have resurgence...
- If all cases in outbreak are $Y_1 \ldots Y_f$, what is the distribution of time between cases?
- Note: no ES during this time*

* Not much, and not included in this analysis
Empirical approaches

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Cluster “I1C4”
- N = 34, affecting YEM, CAF, CAE
- Longest wait, 197 days (median, 5 days)
Empirical approaches

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Cluster “I1C4”
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• Longest wait, **197 days** (median, 5 days)

All Clusters
• A lot of variability in how long is worth waiting...many influencing factors...
• Longest wait, **537 days**
• Also, Nigeria near elimination in 2016...Adamu et al. (2019) MMWR
Start with a positive null hypothesis:

\[ H_0: \text{Poliovirus is present in the population above a pre-determined threshold (design prevalence)} \]

Aim of the analysis is to dis-prove this hypothesis, using evidence from data

The framework provides as outputs;
1. Surveillance sensitivity (for AFP and ES, at design prevalence)
2. Poliovirus transmission risk
3. Probability of being infection free, at time \( t \) after the last detection
4. Scenarios of surveillance and how this affects sensitivity & \( \text{Pr(} \text{infection free}) \)

See O’Reilly et al. (2020) Epidemiology and Infection DOI: 10.1017/S0950268820001004. for application of methods to UK polio surveillance
2. Surveillance Pathways

AFP and ES surveillance pathways are defined
- Each step has a probability of detection, estimated from data
- Sensitivity of each system is estimated

Account for variability in transmission risk
- Immunity
- Previous cases and ES detections
2a. AFP Surveillance

Sensitivity of detecting at least 1 infection from AFP surveillance is low (<1%)

- We know this, estimate largely here for comparison

Caveats in current analysis

- Have not (yet) included impact of district variability in AFP notification and stool data
- Impact of conflict not included, such as...
  - Increased poliovirus risk (reduction in immunity, increase in movement)
  - Reduced probability of AFP notification, stool samples

<table>
<thead>
<tr>
<th>SurveillanceNode</th>
<th>Estimates</th>
<th>Should this vary by district?</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFPCase (inf ratio)</td>
<td>190 (250-150)</td>
<td>No</td>
</tr>
<tr>
<td>AFPnotified</td>
<td>0.9 (0.6-0.999)</td>
<td>Yes</td>
</tr>
<tr>
<td>AFPStool</td>
<td>0.8 (0.5-0.95)</td>
<td>Yes</td>
</tr>
<tr>
<td>AFPTest</td>
<td>0.97 (0.95-0.999)</td>
<td>Yes</td>
</tr>
<tr>
<td>AFPSens</td>
<td>0.00315 (0.00173-0.00476)</td>
<td></td>
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</tbody>
</table>
Current ES data

- 150 ‘regular’ sites in Pakistan and Afghanistan

Data that informs the model

- Catchment sizes ($ESCatch$)
  - Catchment covered avg 58% (80% CI 1-100%) of the population based on watershed
  - Detection per mth was 47% (80% CI 1-72%) based on stats model

- Sampling frequency ($ESSample$)
  - monthly-fortnightly sampling
  - Fortnightly sampling $Pr(\text{capture}) \sim 99%$
  - Monthly $Pr(\text{capture}) \sim 46%$

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<tr>
<th>Surveillance Node</th>
<th>Estimates</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$ESCatch$</td>
<td>0.58 (0.01-0.8)</td>
<td>Proportion in catchment</td>
</tr>
<tr>
<td>$ESSample$</td>
<td>0.99 (0.9-0.999)</td>
<td>$Pr(\text{shedder poop caught in ES samples})$ – effect of sampling frequency</td>
</tr>
<tr>
<td>$ESTest$</td>
<td>0.9 (0.7-0.99)</td>
<td>Virus load above LoD – effect of site factors</td>
</tr>
<tr>
<td>$ESSens$</td>
<td>0.491 (0.385 0.552)</td>
<td></td>
</tr>
</tbody>
</table>

Of districts with Environmental Surveillance...

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Poliovirus risk

Circulation Risk Apr-2023
Last 6 months
Detection of Poliovirus Each Month

If poliovirus was present at least at 1 infection per 100,000 in 1 district, what is the probability that it would be detected?

Main Results

National sensitivity per month
- AFP alone 2% (95% 1-4%)
- AFP & ES 19% (95% 18-20%)

Sensitivity varies across districts
- Varying circulation risk
- Presence / absence ES
3. Probability of being infection free

No detections from Mar 2023 onwards – how long should we wait?

*Using a prior chance ~50% of being infection free, each month is updated using the fact that surveillance has happened and nothing is detected*

Main results

**AFP Surveillance**
- Not very informative (national sensitivity ~2%)

**AFP & ES Surveillance**
- $\Pr(\text{infection free})$ improves in time, with good confidence at 2 years. (national sensitivity ~19%)

Caveats

The Prior value of being infection free has a big effect on the result, but is not known
- Could use *Expert Elicitation* to inform prior
Question posed by GCC\(^1\) in July 2021, "**does global certification of WPV\(1\) eradication require a full three years?**"

Presented to GCC in March 2022
- IDM and Kid Risk also presented modelling: different models but similar conclusion
- Alongside review of surveillance tools (genomics, ES)

GCC meeting in July 2022\(^2\)
- "GCC is recommending the adoption of a ‘flexible’ approach to certification"

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\(^1\) GCC - Global Certification Committee 
\(^2\) https://polioeradication.org/news-post/gcc-reviews-global-certification-criteria/
Discussion

• The *infection free* framework is a tool that estimates the sensitivity of detecting poliovirus
  • Also important for cVDPV2 analysis
  • Potential for use in other diseases approaching elimination
• Confidence in elimination can be improved with more information
  – Target more high risk districts
  – Sensitivity of detection can also reduce (emph high quality ES sites)

• This work is on-going...
  – Precise values of sensitivity shouldn’t be taken literally
  – Relative values should be informative, eg. AFP vs. AFP and ES combined, ES sampling options
  – Aiming to improve methods & analysis,
    • “Quality” metrics for ES sites, catchment area analysis, impact of conflict and population mobility
Thank you for listening!

LSHTM colleagues:
W John Edmunds, Megan Auzenbergs, Paul Fine, Neil Pearce, Emily Nightingale
Members of CMMID

IDM & BMGF:
Hil Lyons, Arie Voorman, Corey Peak, Rachel Burke

GPEI stakeholders and group members:
Country partners, GCC members, modellers within the SAM
Options to improve WPV detection...

1. **Improve AFP sensitivity** (eg. increase stool adequacy, etc)
   - Limited impact because of infection:case ratio
   - Could improve to **4% (95% 3-5%) at most**

2. **Increase ES sampling from fortnightly to weekly**
   - Limited impact
     - Fortnightly is likely sufficient due to shedding profile
     - Exception is ‘catching’ shedders from other districts

3. **Increase number of ES sites in high risk districts (from ~90 in 2022)**
   - + 20 sites, sensitivity 31% (95% 30-32%)
   - + 40 sites, sensitivity 37% (95% 35-38%)
   - **Results in a rapid improvement in confidence to within 1 year**
   - **A practical challenge?**
For risk-based surveillance, we want to have better surveillance in places with higher risk.

Transmission risk calculated as:

\[
Risk(i) = 1 - Imm(i) \sum_j Case(j) \cdot Rad(ij)
\]

White squares indicate ES sites returning (WPV) negative samples.