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

Kath O'Reilly
Kathleen.oreilly@lshtm.ac.uk
Assoc Prof, LSHTM
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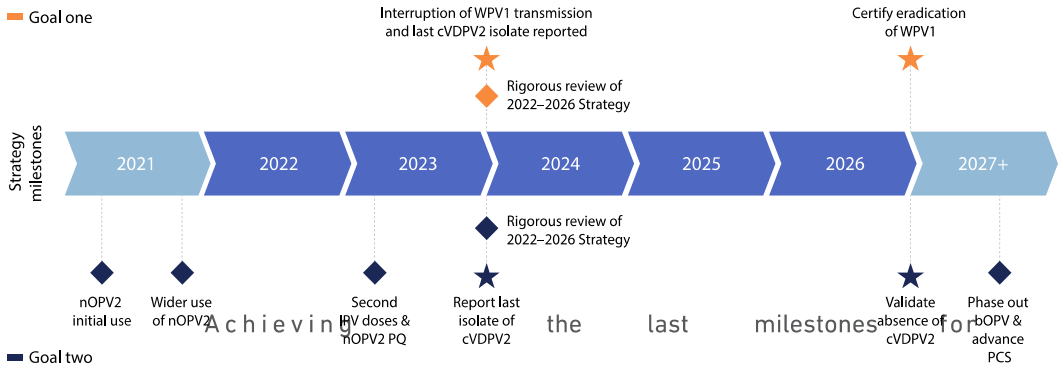
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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 21st GCC report

Where did the 3 years wait come from?

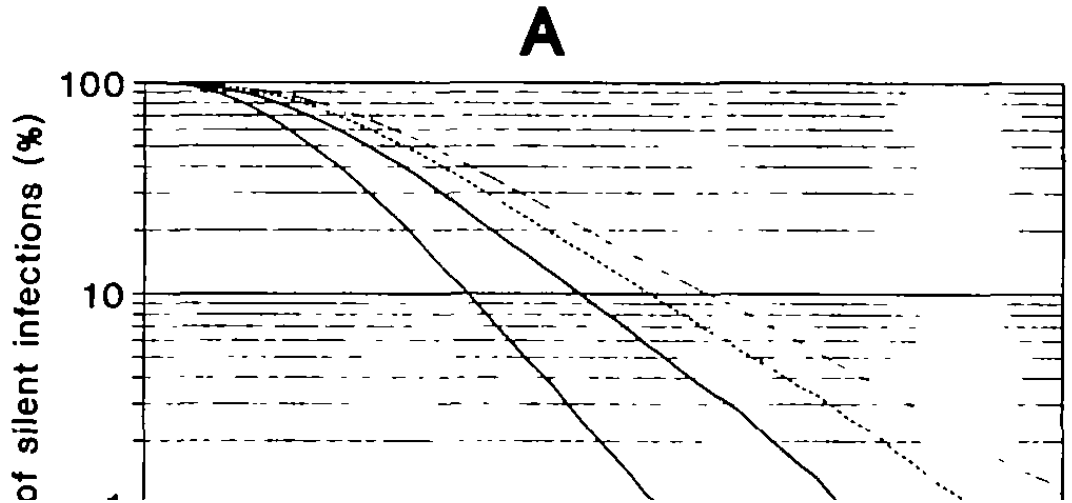
Modelling! "Eradication of poliomyelitis: when can one be sure that polio virus transmission has been terminated?" ***Eichner & Dietz Am J Epi 1996***

"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[1]
- Waiting 3 years provides no incentives to improve surveillance

for 2 years, silent infections are still present in up to 20 percent of the simulations (figure 1) if one of 200 infections leads to paralysis. Only after at least 4 years without paralytic cases is local extinction likely, with



1 O'Reilly et al (2015) BMC ID DOI: 10.1186/s12879-018-3070-4

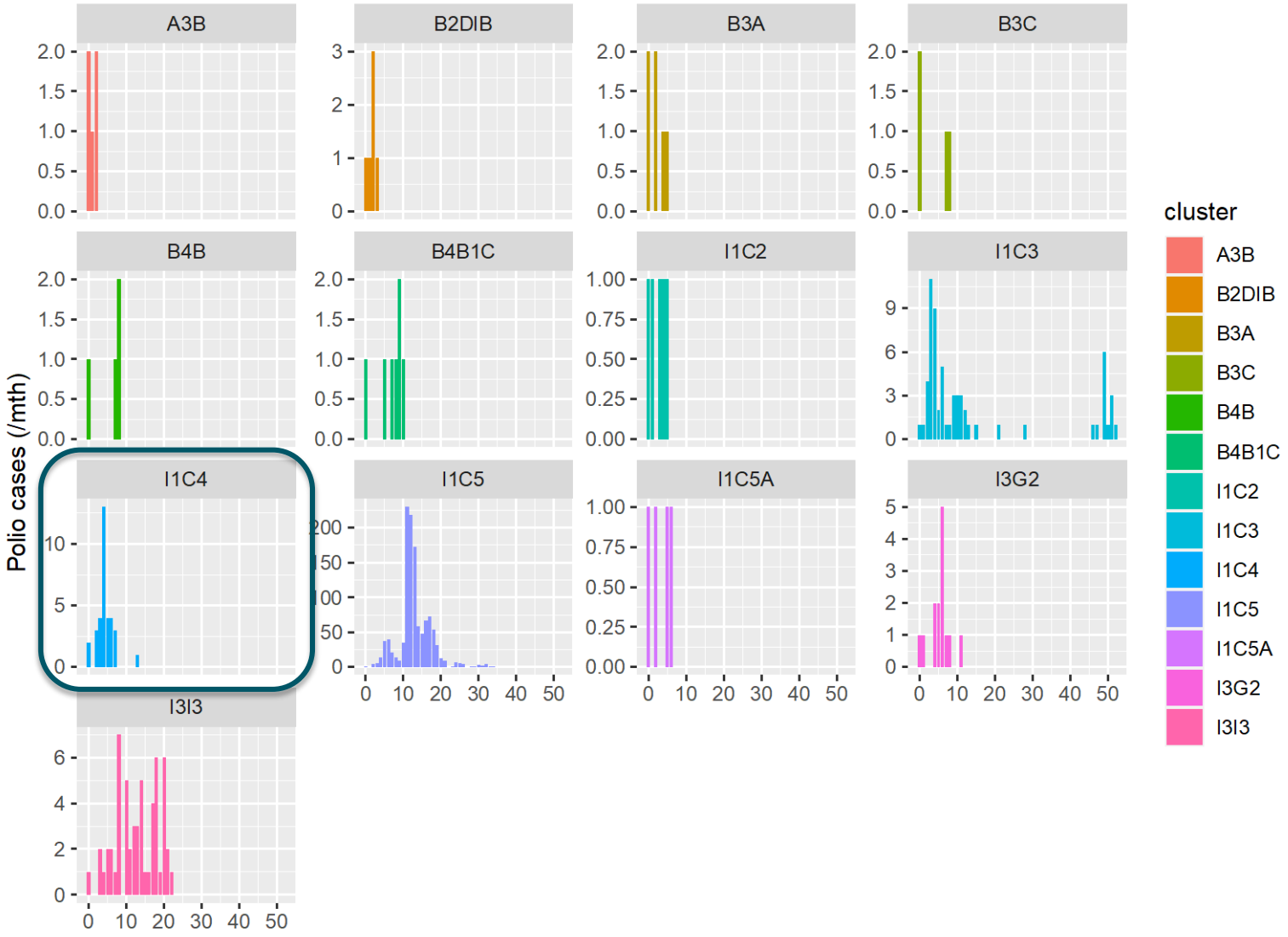
Overview

- 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

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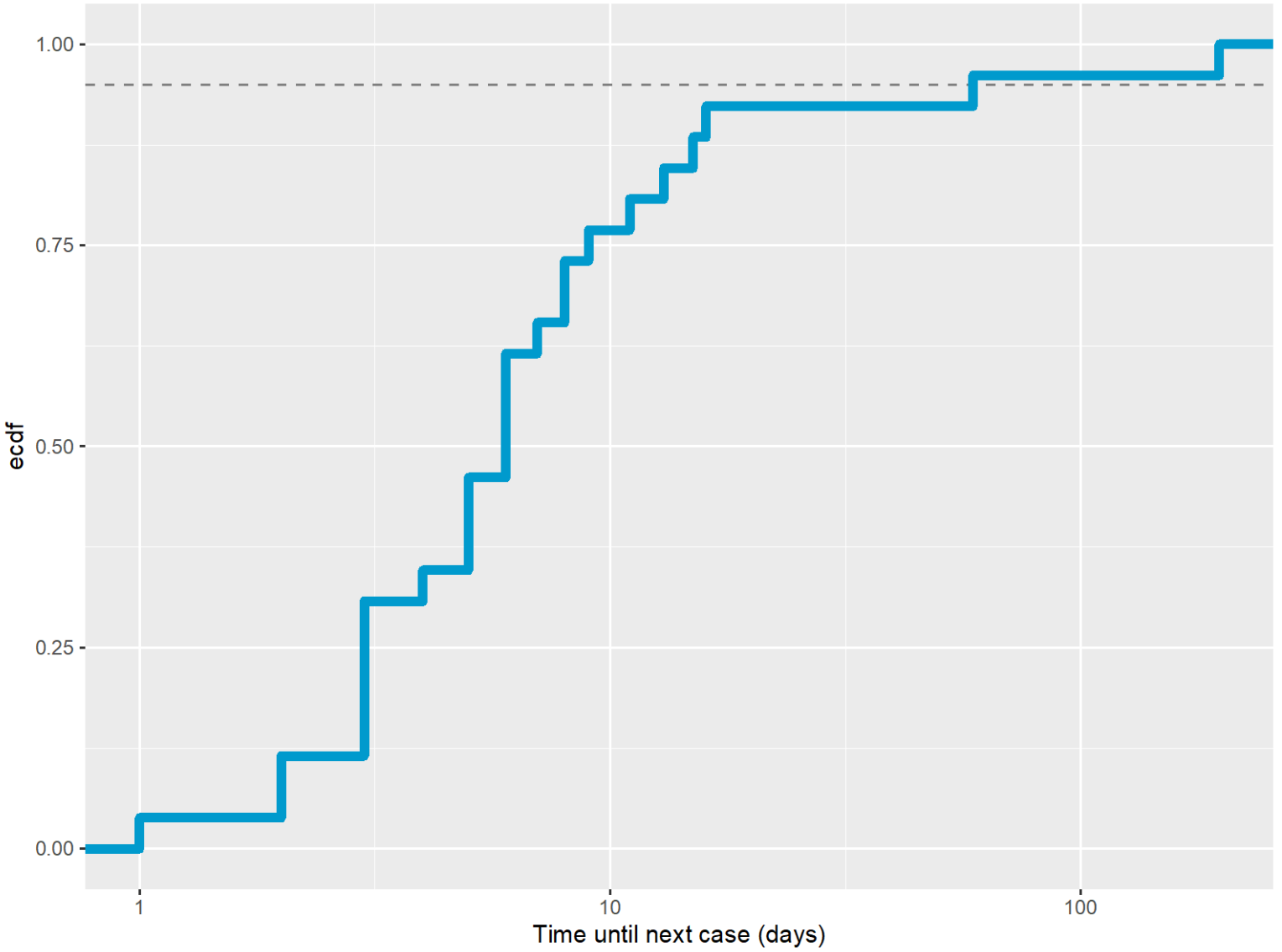
Cluster "I1C4"

- N = 34, affecting YEM, CAF, CAE
- Longest wait, 197 days (median, 5 days)



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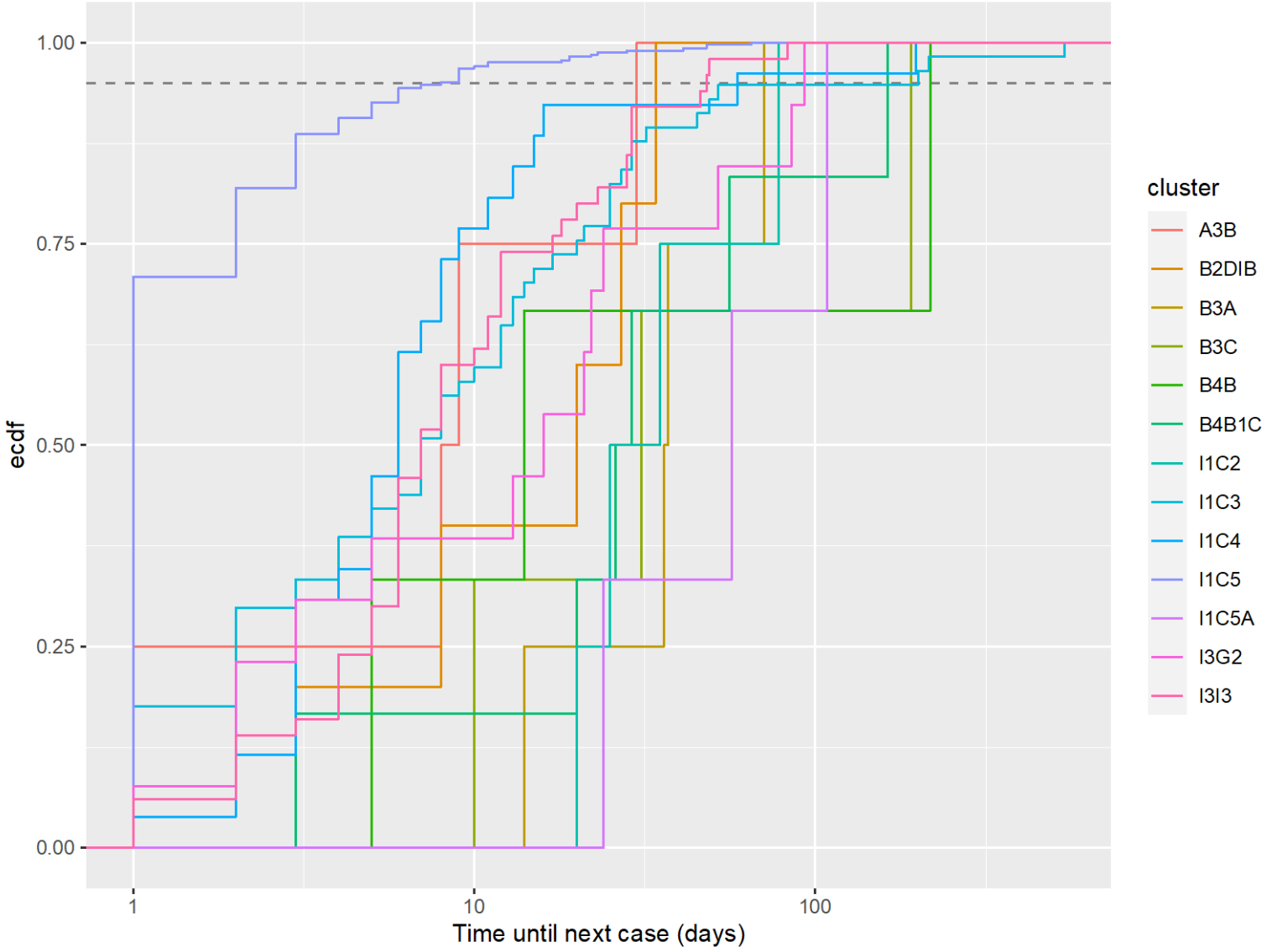
All Clusters

- 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**



“Infection Free” Methods

Start with a positive null hypothesis:

H_0: 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 & Pr(infection free)

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

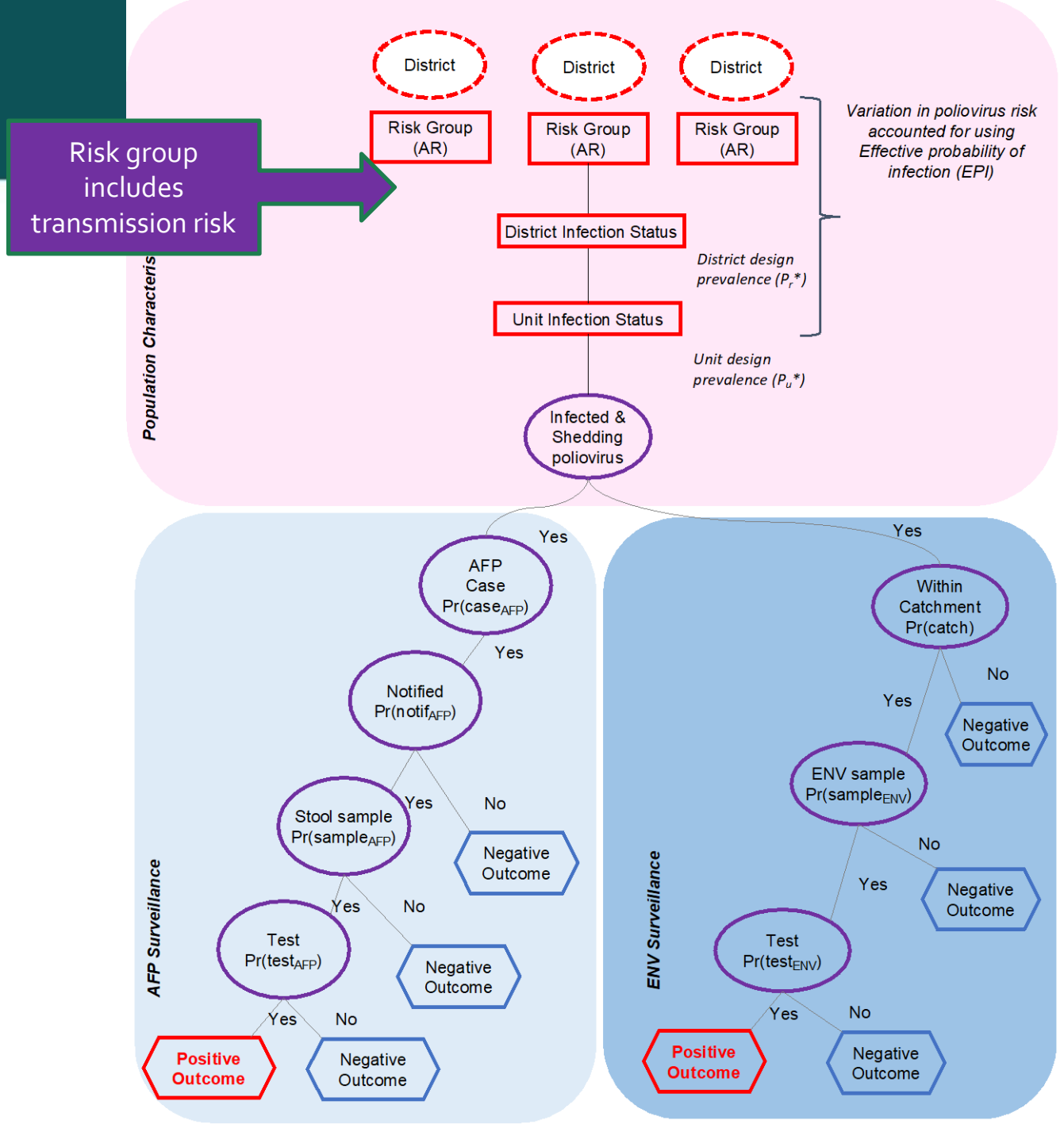
2. Surveillance Pathways

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

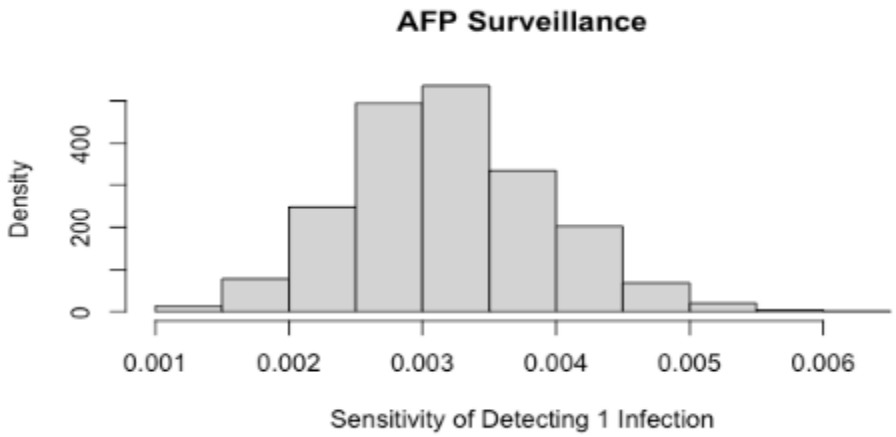
Sensitivity of detecting at least 1 infection from AFP surveillance is low (<1%)

- 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

SurveillanceNode	Estimates	Should this vary by district?
AFPcase (inf ratio)	190 (250-150)	No
AFPnotified	0.9 (0.6-0.999)	Yes
AFPStool	0.8 (0.5-0.95)	Yes
AFPTest	0.97 (0.95-0.999)	Yes
AFPSens	**0.00315 (0.00173-0.00476)**	



Environmental Surveillance (1)

Current ES data

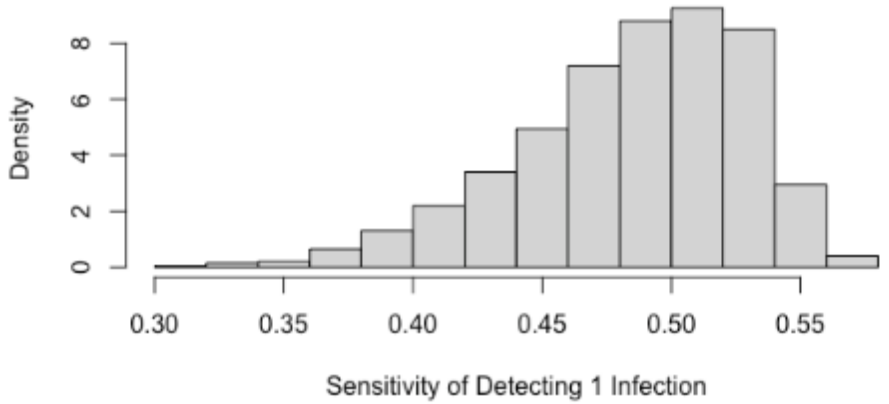
- 150 'regular' sites in Pakistan and Afghanistan

Data that informs the model

- Catchment sizes (*ESCatch*)
  - Catchment covered avg 58% (80% CI 1-100%) of the population based on watershed [1]
  - Detection per mth was 47% (80% CI 1-72%) based on stats model [1]
- Sampling frequency (*ESSample*)
  - monthly-fortnightly sampling
  - Fortnightly sampling Pr(capture) ~ 99%
  - Monthly Pr(capture) ~ 46%

SurveillanceNode	Estimates	Comments
ESCatch	0.58 (0.01-0.8)	Proportion in catchment
ESSample	0.99 (0.9-0.999)	Pr(shedder poop caught in ES samples) – effect of sampling frequency
ESTest	0.9 (0.7-0.99)	Virus load above LoD – effect of site factors
ESSens	**0.491 (0.385 0.552)**	

Of districts with Environmental Surveillance…



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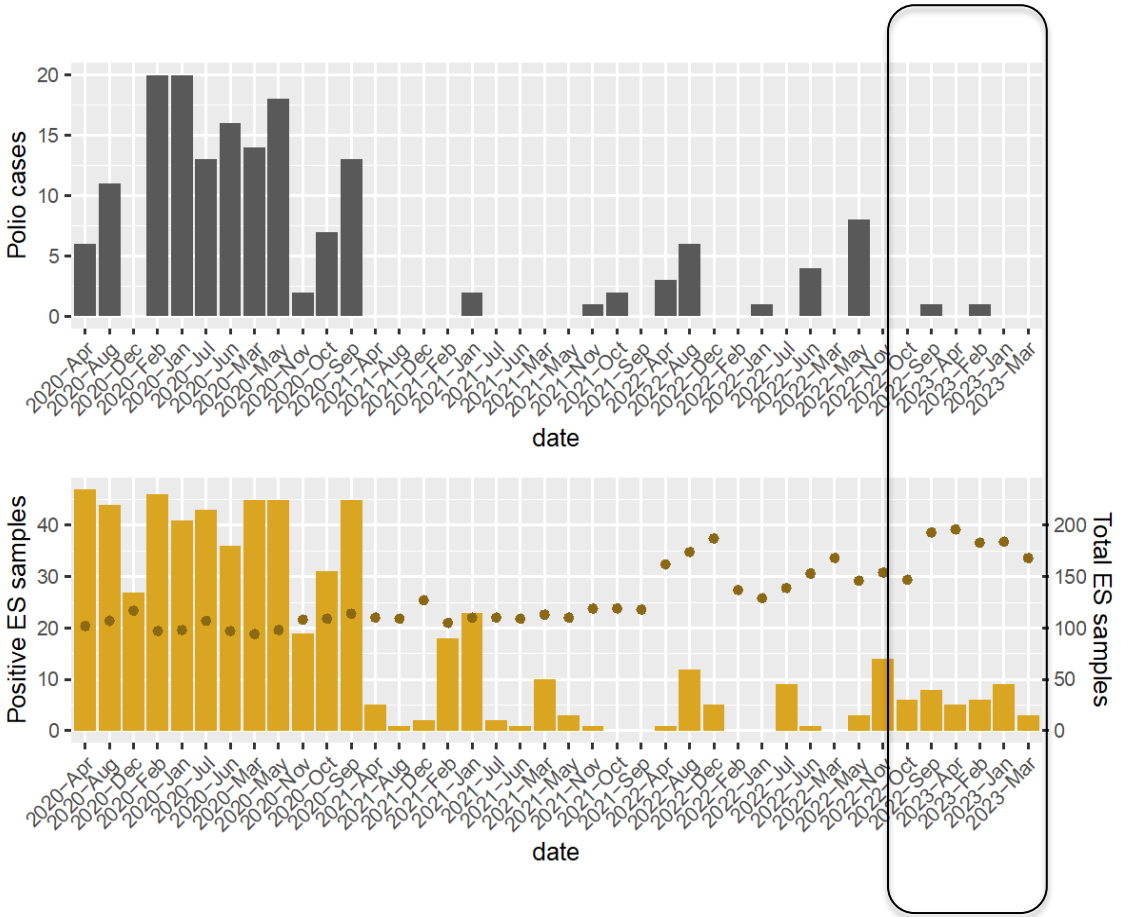
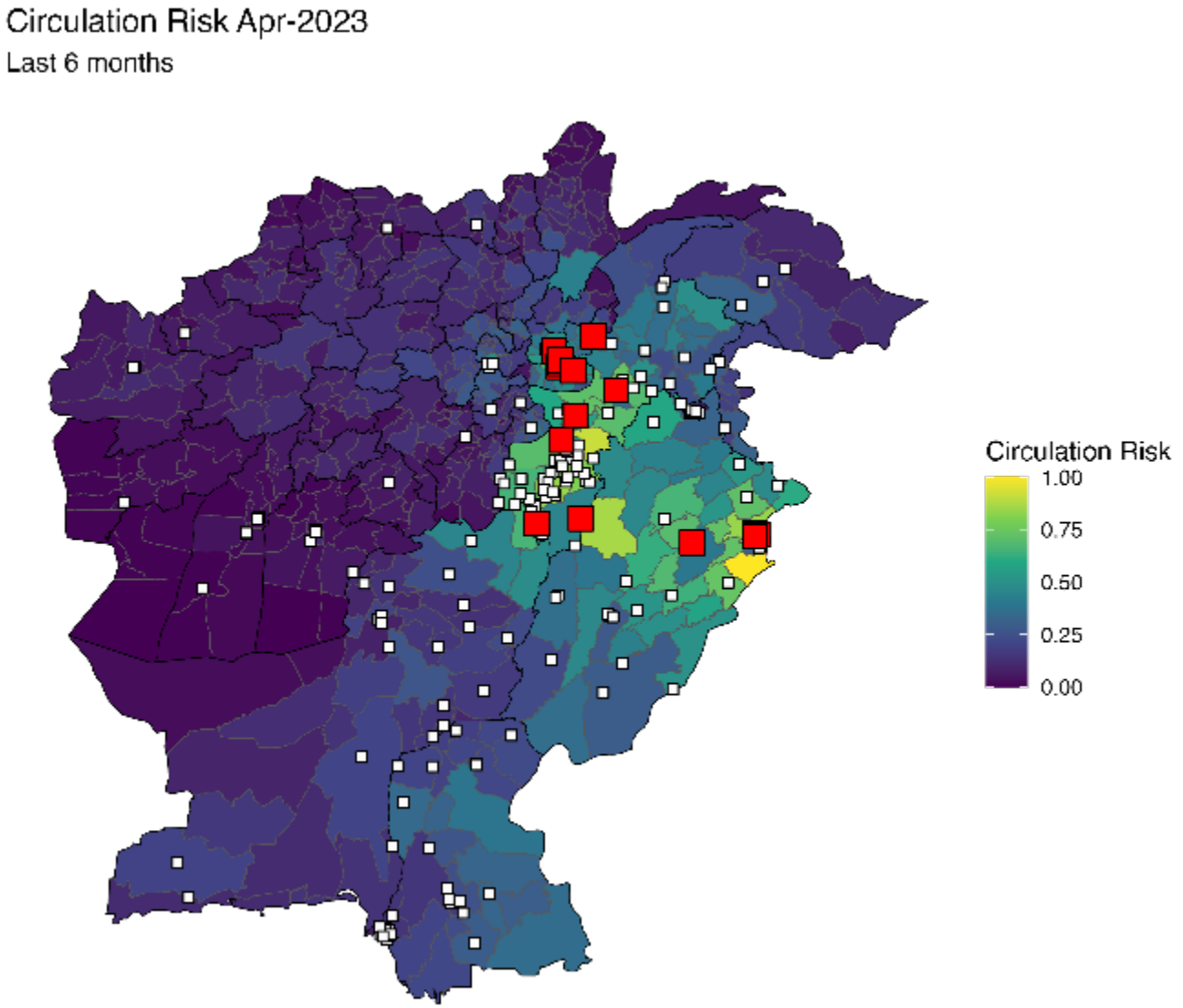
Poliovirus risk





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?

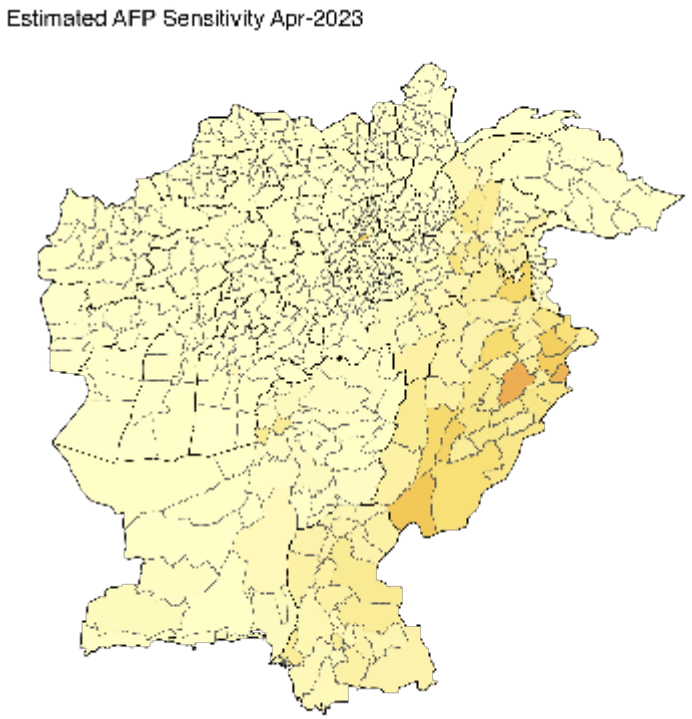
Main Results

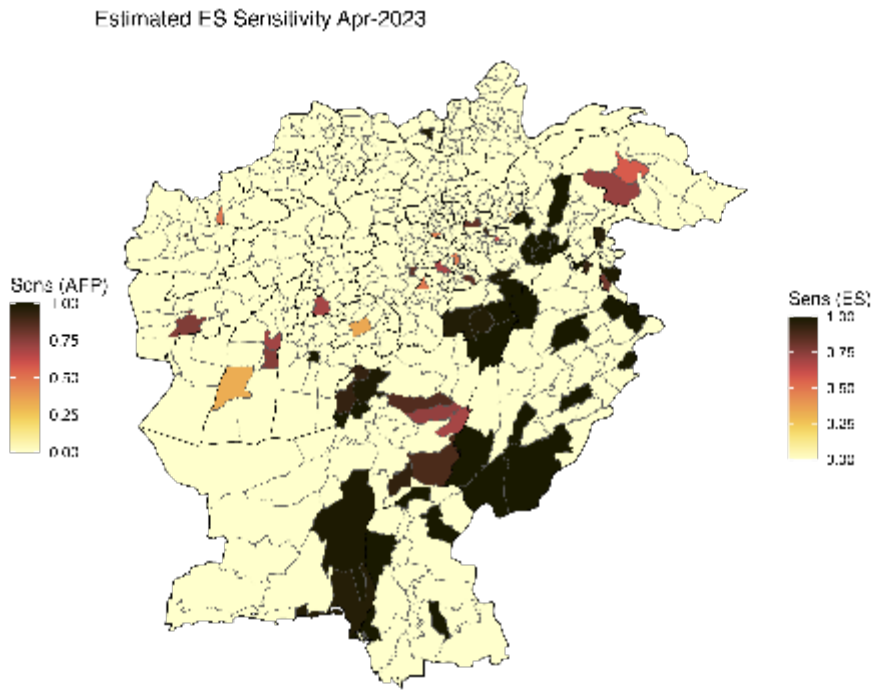
National sensitivity per month

- 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%)

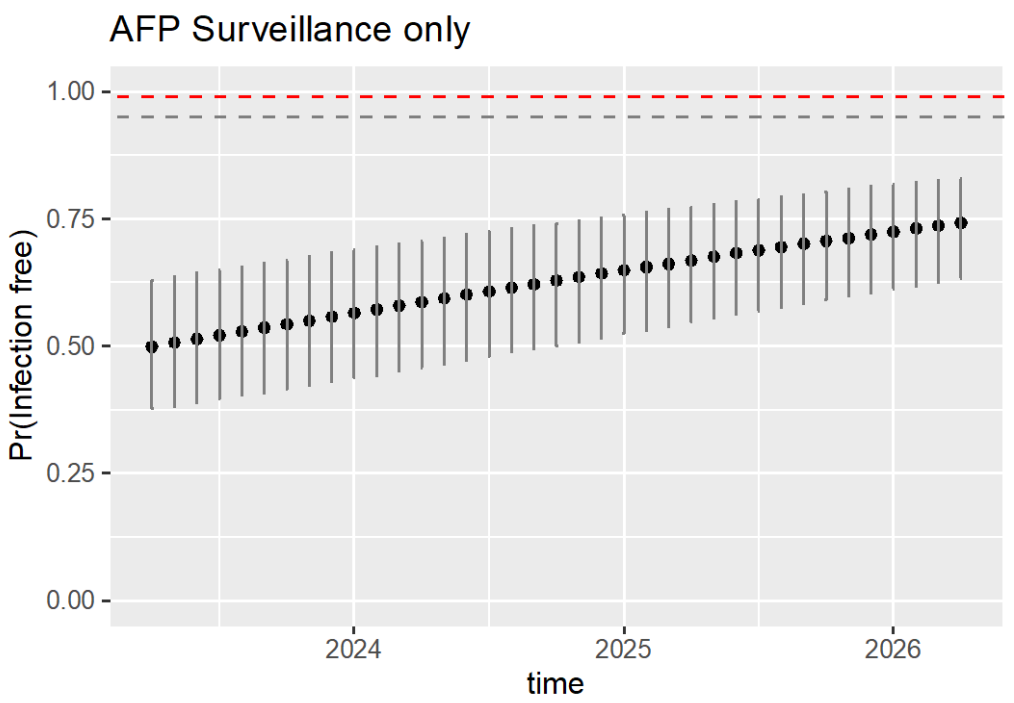
AFP & ES Surveillance

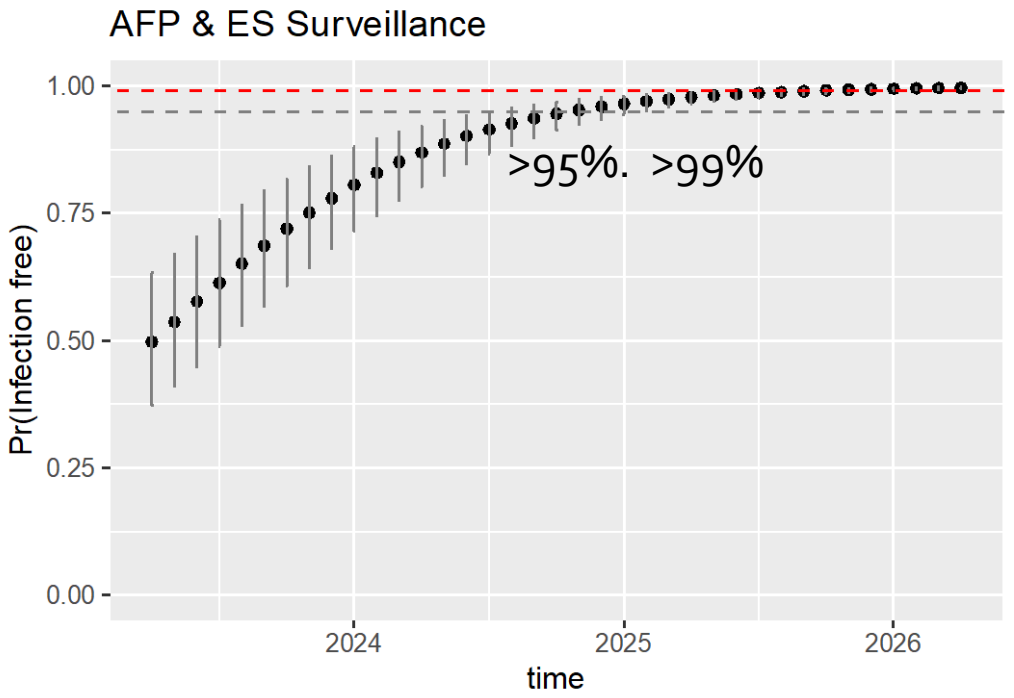
- Pr(infection free) improves in time, with good confidence at 2 years. (national sensitivity ~19%)

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





Informing Policy

Question posed by GCC[1] in July 2021, **"does global certification of WPV1 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"

[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!

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Members of CMMID

IDM & BMGF:

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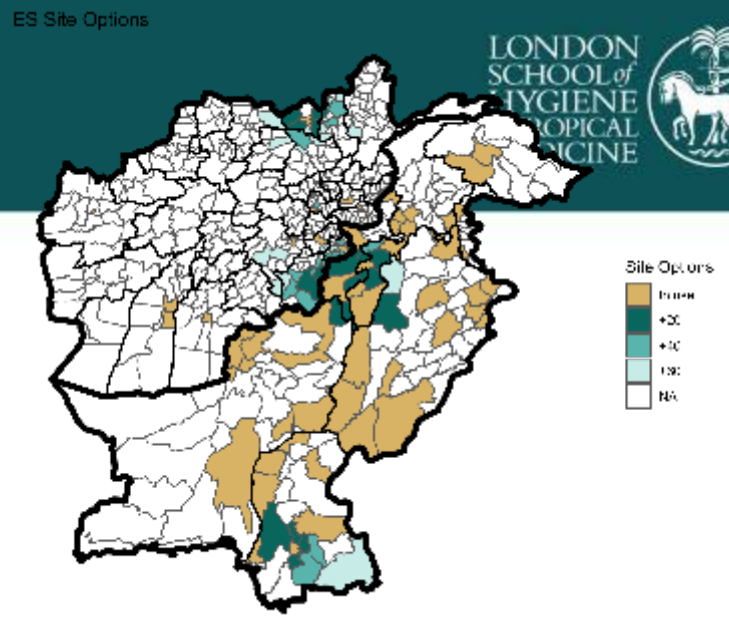
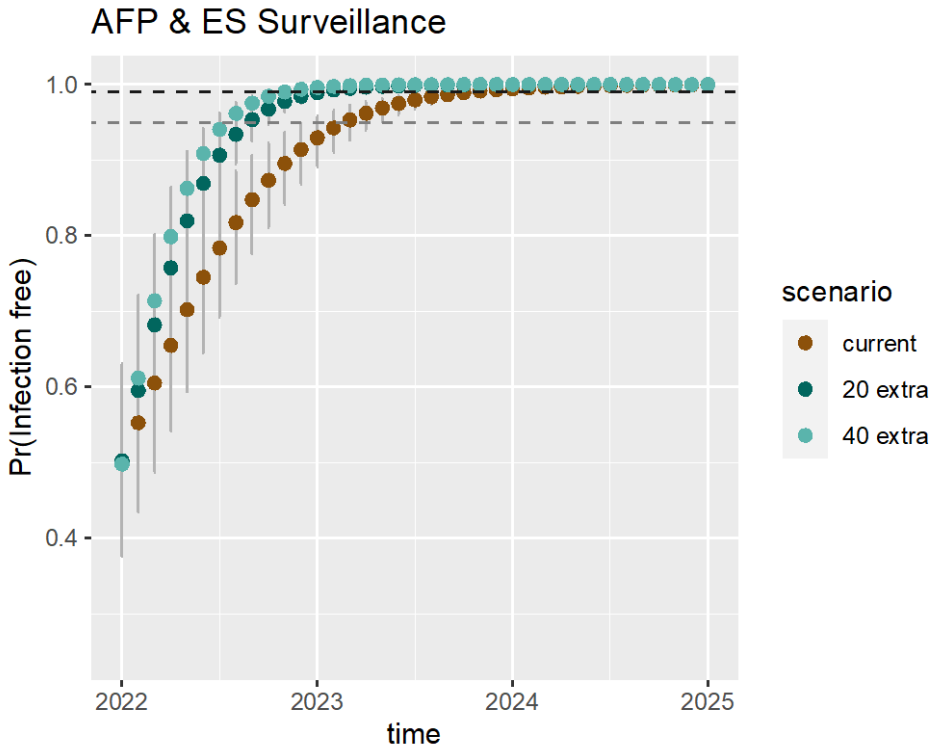
GPEI stakeholders and group members:

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?*



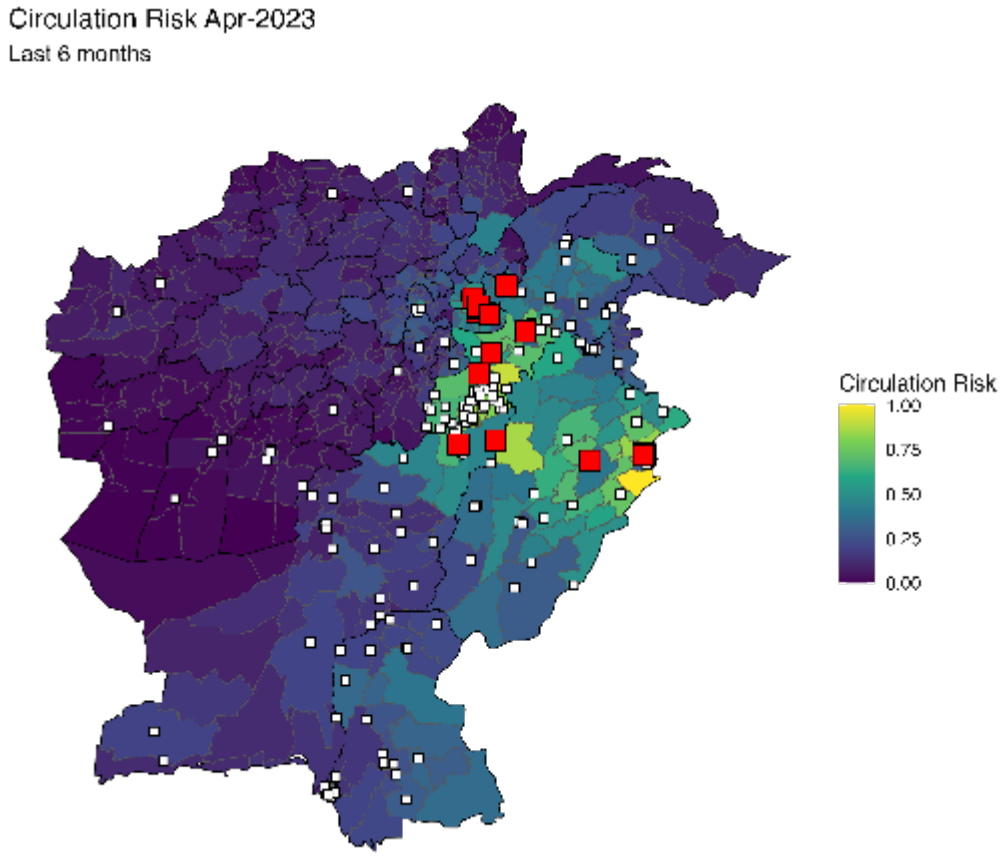


Extra - Poliovirus Transmission Risk

For risk-based surveillance, we want to have better surveillance in places with higher risk

Transmission risk calculated as;

$$Risk(i) = 1 - Imm(i)^{\sum_j Case(j).Rad(ij)}$$



White squares indicate ES sites returning (WPV) negative samples