



Statistical Response to the Surveillance of HIV Drug Resistance in the Population Initiating ART

Natalie Exner & Marcello Pagano

Department of Biostatistics

Harvard University School of Public Health



Acknowledgments

Work done in consultation with

- Silvia Bertagnolio – World Health Organization
- Michael Jordan – Tufts University Medical Center



II. HIVDR Surveillance in Population Initiating Treatment

Goal:

- Produce a nationally representative estimate of the prevalence of HIVDR in the population initiating treatment
 - Includes individuals who may have had prior exposure to antiretrovirals



II. HIVDR Surveillance in Population Initiating Treatment

Primary Outcome:

- Estimated prevalence of HIVDR mutations by drug class among patients initiating therapy
- Associated 95% confidence interval
 - Proposed survey is designed for a ***confidence interval width of $\pm 4\%$***



II. HIVDR Surveillance in Population Initiating Treatment

Proposed Survey:

Two-stage cluster survey where countries randomly sample

- 1. 10-20 clinics from a list of all clinics in the country, and
- 2. consecutive eligible patients within clinics during a ***predefined three-month period***

Presented plan can involve stratification on clinic type, region, or urban/rural location if desired



II. HIVDR Surveillance in Population Initiating Treatment

Sampling Clinics:

- For the optimal design (smallest confidence interval width for a given sample size), clinics are sampled proportionally to the # of treatment initiators observed at that clinic
 - Information from a prior time period can be used
- If information on treatment initiators is unavailable, clinics can be sampled proportionally to the total # of patients on ART at each clinic



II. HIVDR Surveillance in Population Initiating Treatment

Extremely Small Clinics:

- Countries may have some clinics with extremely small patient populations
 - The definition of small will be country-specific
 - If less than 10% of the patient population attends extremely small clinics, these clinics can be ignored without incurring too much bias
 - Otherwise, countries should take a small representative sample of these clinics



II. HIVDR Surveillance in Population Initiating Treatment

Sampling Clinics – Strategies:

- *Probability Proportional to Size (PPS) Sampling*
 - Sample clinics proportional to the # of treatment initiators at each clinic
- *Probability Proportional to Proxy Size (PPPS) Sampling*
 - Sample clinics proportional to total # of patients on ART at each clinic



II. HIVDR Surveillance in Population Initiating Treatment

Sampling Patients from Clinics:

- Clearly define enrollment period, such as a *three-month period*
- Screen consecutive patients for eligibility at each sampled site
- Eligible patients are sampled until the patient quota is achieved or the enrollment period ends



II. HIVDR Surveillance in Population Initiating Treatment

Sample Size Calculations:

Probability Proportional to Size (PPS) Sampling,
Confidence Interval Width $\pm 4\%$, HIVDR Prevalence 10%

Number of clinics	Patients per clinic	Total # patients
10	42	420
15	24	360
20	15	300

*Sample size calculations have already been
inflated for 15% genotyping failure rate



II. HIVDR Surveillance in Population Initiating Treatment

Sample Size Calculations:

Confidence Interval Width $\pm 4\%$, HIVDR Prevalence 10%

Sampling Method	Number of clinics	Patients per clinic	Total # patients
PPS (Use # of treatment initiators to construct sampling weights)	10	42	420
PPPS " <i>Proxy</i> " (Use total # on ART to construct sampling weights)	10	59	590

*Sample size calculations have already been inflated for 15% genotyping failure rate



II. HIVDR Surveillance in Population Initiating Treatment

- The calculations described are for a country with a large number of clinics
- We have ignored a statistical concept called the **Finite Population Correction (FPC)**
 - Sampling 50% of the clinics in a country is different from sampling 1% of the clinics
 - For countries with fewer clinics, we can achieve the same confidence interval width with a smaller sample size



II. HIVDR Surveillance in Population Initiating Treatment

Finite Population Correction Example #1:

- Country X has 15 clinics

Name	Size	Name	Size	Name	Size
Clinic A	500	Clinic F	150	Clinic K	40
Clinic B	500	Clinic G	100	Clinic L	10
Clinic C	400	Clinic H	80	Clinic M	10
Clinic D	150	Clinic I	80	Clinic N	5
Clinic E	150	Clinic J	40	Clinic O	5



II. HIVDR Surveillance in Population Initiating Treatment

Finite Population Correction Example #1:

- Country X has 15 clinics

Name	Size	Name	Size	Name	Size
Clinic A	500	Clinic F	150	Clinic K	40
Clinic B	500	Clinic G	100	Clinic L	10
Clinic C	400	Clinic H	80	Clinic M	10
Clinic D	150	Clinic I	80	Clinic N	5
Clinic E	150	Clinic J	40	Clinic O	5

- Could choose to ignore four smallest clinics because they represent <2% of the eligible patient population



II. HIVDR Surveillance in Population Initiating Treatment

Finite Population Correction Example #1:

- Country X has 15 clinics, and 11 are included in the sampling frame

Sampling Method	Number of clinics	Patients per clinic	Total # patients
Without Finite Population Correction	10	42	420
With Finite Population Correction	7	22	154



II. HIVDR Surveillance in Population Initiating Treatment

Finite Population Correction Example #2:

- Country Y has 5 clinics

Name	Size
Clinic A	400
Clinic B	100
Clinic C	40
Clinic D	10
Clinic E	5



II. HIVDR Surveillance in Population Initiating Treatment

Finite Population Correction Example #2:

- Country Y has 5 clinics

Name	Size
Clinic A	400
Clinic B	100
Clinic C	40
Clinic D	10
Clinic E	5

- Could choose to ignore two smallest clinics because they represent <2% of the eligible patient population



II. HIVDR Surveillance in Population Initiating Treatment

Finite Population Correction Example #2:

- Country Y has 5 clinics, and 3 are included in the sampling frame
- We would recommend collecting samples from all 3 clinics
- Country Y would not need to sample *all* eligible patients at each clinic
 - Instead, they could take a *sample* of patients from each clinic
 - To keep the sample proportional, Country Y should collect the most samples from the largest clinic, and the fewest samples from the smallest clinic



II. HIVDR Surveillance in Population Initiating Treatment

Conclusions:

- Goal is to construct a nationally representative estimate of the prevalence of HIVDR in population initiating ART
- Countries with few clinics can adjust their sample size requirements to reflect the total eligible population size



II. HIVDR Surveillance in Population Initiating Treatment

Thank you.

Questions?