



Statistical Response to the Surveillance of Acquired HIV Drug Resistance in Populations Receiving ART (ADR)

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Acknowledgments

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



III. Surveillance of ADR

Goals:

- Measure nationally representative outcomes relating to viral load suppression and HIVDR
- Viral load suppression outcome will inform programme functioning
- Observed HIVDR will support selection of second-line ART
- Population of interest is all patients on ART for more than 6 months



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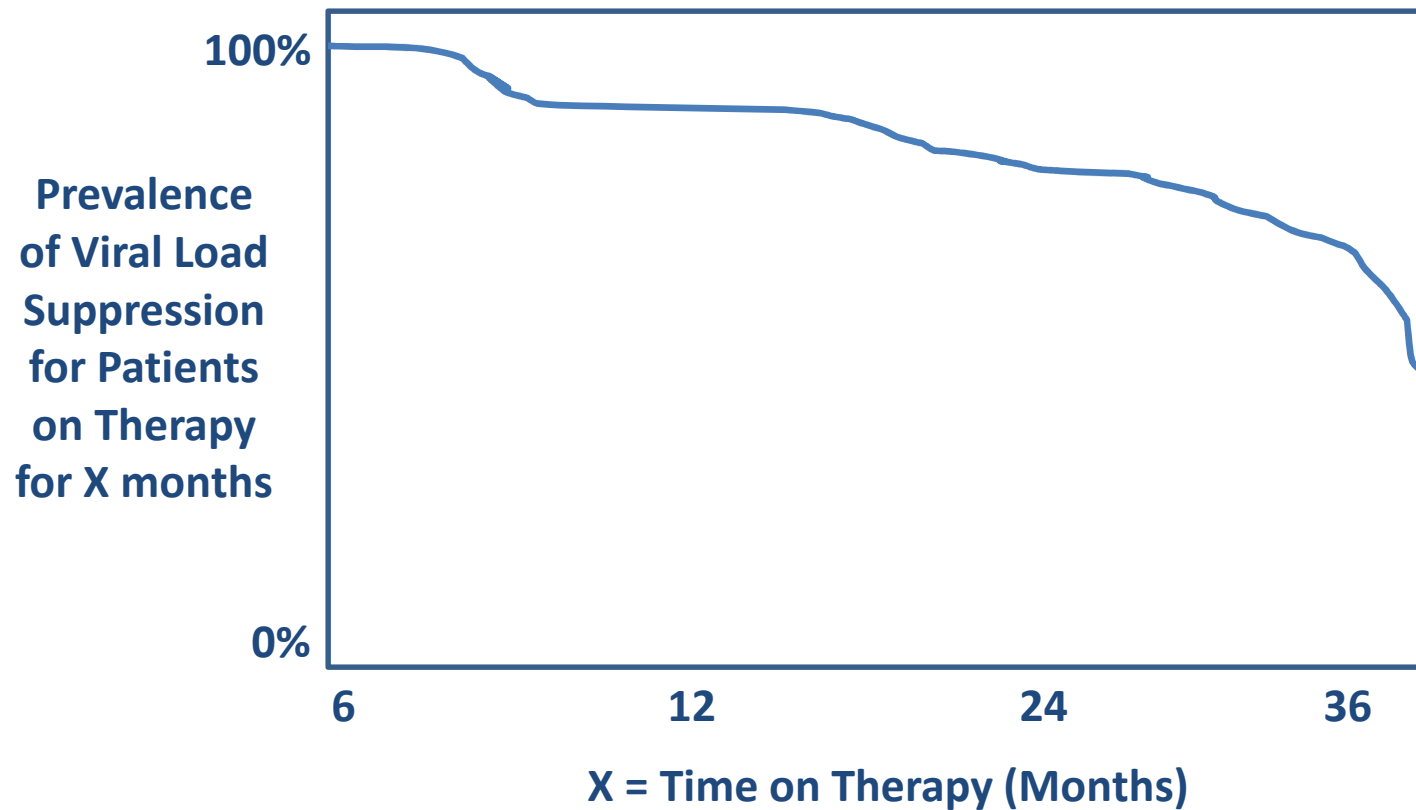
Primary Outcome #1:

- Using cross-sectional data from patients on therapy for more than 6 months, describe the prevalence of viral load suppression as a function of the length of time on ART



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Primary Outcome #1:

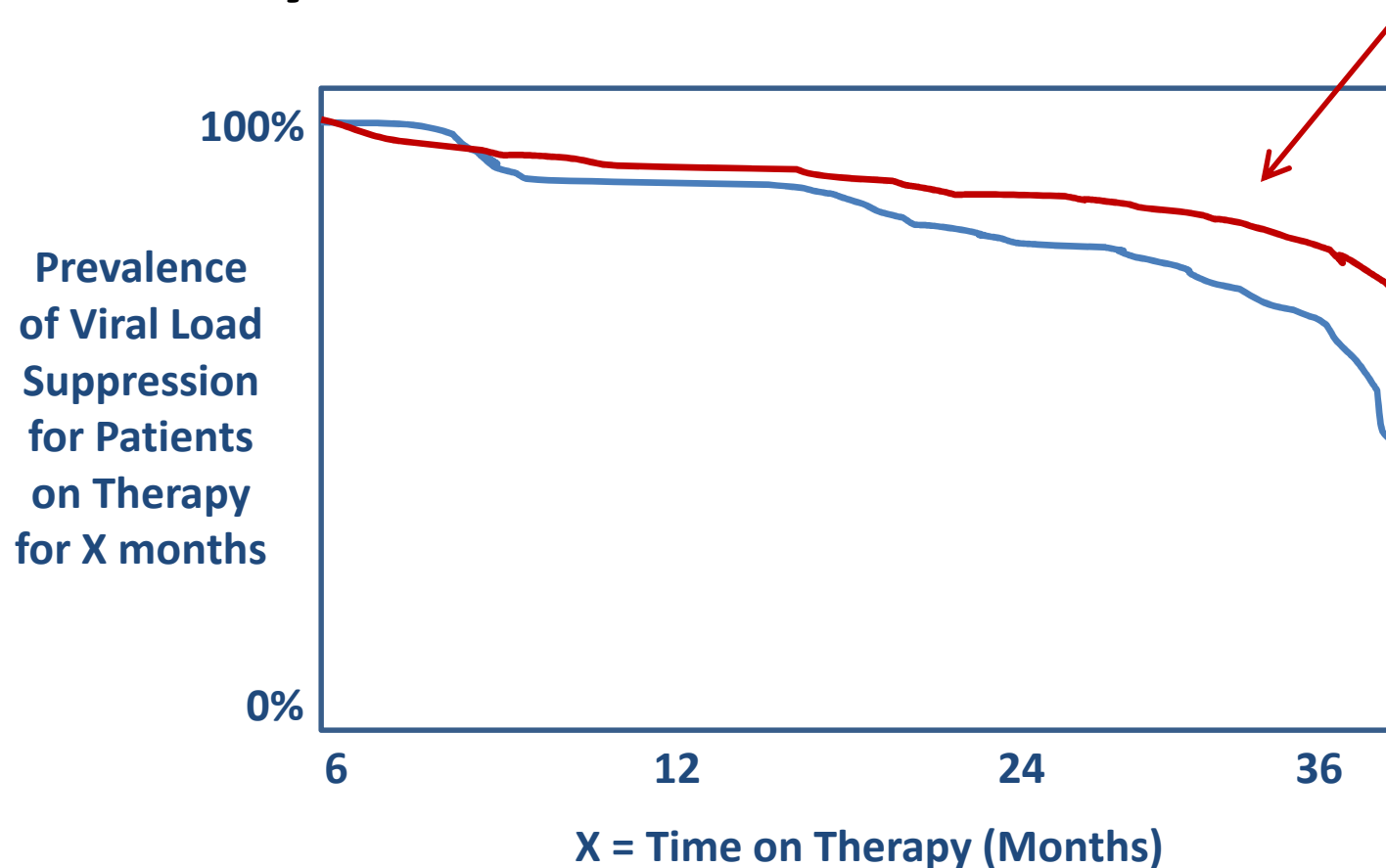




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Primary Outcome #1:

Normative Threshold





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Primary Outcome #2:

- Produce a nationally representative estimate of the prevalence of viral load failure and HIVDR in the population on ART for >6 mos

Patients with Viral Load Suppression (Defined as VL < 1000 copies/ml)	Patients with Viral Load Failure and HIVDR	Patients with Viral Load Failure and no HIVDR
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Primary Outcome #2:

- Produce a nationally representative estimate of the prevalence of viral load failure and HIVDR in the population on ART for >6 mos

Patients with Viral Load Suppression (Defined as VL < 1000 copies/ml)	Patients with Viral Load Failure and HIVDR	Patients with Viral Load Failure and no HIVDR
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Numerator = # of Patients with Viral Load Failure and HIV DR

Denominator = # of Patients with Viral Load Measured



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Primary Outcome #2:

- Produce a nationally representative estimate of the prevalence of viral load failure and HIVDR in the population on ART for >6 mos
- Calculate associated 95% confidence interval
 - Proposed survey is designed for a ***confidence interval width of $\pm 5\%$***



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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



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- Countries with routine viral load testing can use existing data to construct ***Primary Outcome #1 – Viral Load Suppression Curve***
- Countries with routine genotyping among patients with viral load failure can use existing data to construct ***Primary Outcome #2 – Prevalence of HIVDR/Viral Load Failure***
- We will provide responsible frameworks for analyzing both outcomes



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Sampling Clinics:

- Sampling proceeds in the same manner described for the pre-treatment survey
 - List all clinics in the country
 - Identify extremely small clinics and determine if these clinics can be excluded from the sampling frame
 - Construct weights using information about # of patients on ART at each clinic



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Sample Size Calculations for Primary Outcome #2:

Prevalence of HIVDR and Viral Load Failure

Probability Proportional to Proxy Size (PPPS) Sampling,
Confidence Interval Width $\pm 5\%$, HIVDR/VL Failure 14%

Number of clinics	Patients per clinic	Total # patients
10	51	510
15	25	375
20	16	320

Sample size calculations inflated for 15% viral load testing failure



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Sample Size Calculations for Primary Outcome #2:

Prevalence of HIVDR and Viral Load Failure

- Countries with few clinics can use the finite population correction to adjust sample size calculations



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Sample Size Calculations for Primary Outcome #1:

Viral Load Suppression Curve

- Sample size calculations are pending available data
- In countries using existing databases with viral load measurements, use all available data



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Clinic-Level Statements:

- If countries want to make clinic-level statements about viral load suppression, they can calculate a clinic-specific curve
- Power to make clinic-level statements increases with the number of patients sampled per clinic



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Relationship to Pre-Treatment Survey:

- Countries may choose to sample or analyze data from the same clinics for the pre-treatment and ADR surveys



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Pediatric Population:

- Surveillance of ADR can also be conducted in each country's pediatric population
 - Definition of pediatric is country-specific
- Survey would follow same framework as described for the adult population
- Sampling frame is a list of all sites in the country providing pediatric ART



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Thank you.

Questions?