Surveillance of Transmitted HIV Drug Resistance

Michael R. Jordan MD MPH

Consultant, WHO

Tufts University School of Medicine,
Boston, USA

Surveillance of Transmitted HIV Drug Resistance (TDR)

- This work done by Natalie Exner and Marcello Pagano, Harvard School of Public Health
- In collaboration with Michael Jordan, Tufts University School of Medicine and Silvia Bertagnolio, WHO

Surveillance of TDR

Goal:

- Estimate the national prevalence of drug resistance in a recently infected population by integrating drug resistance testing into a pre-existing HIV surveillance system or routine diagnostic testing

Strategy:

- Use epidemiologic criteria (such as age and parity) to enrich population with recently infected samples
- For countries performing CD4 testing, further enrich population by excluding specimens with CD4 count <500 which likely represent late-stage infections
- Consider use of laboratory assays (MAA or LAg), if available, to identify recent infections

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Examples of Sampling Frames:

1. Primigravida women <25 years of age included in antenatal care (ANC) surveys
2. Individuals <25 years of age newly diagnosed with HIV at voluntary counseling & testing (VCT) sites (if women, no previous pregnancies)
3. Community-based or facility-based bio-behavioral surveys (BBS) of key populations (MSM, IDU/DU, SW, transgender) <25 years of age
4. HIV case reporting (if centralized): <25 yrs and/or CD4 >500 and no previous pregnancies if female

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Sampling Frame Considerations:

- **Option 1:** integrate TDR surveillance into routine HIV sentinel surveillance (ANC, VCT or BBS survey)

Sample Size:

- Countries with low prevalence and/or concentrated epidemics may consider testing all available specimens meeting criteria for "recent infection"

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Sampling Frame Considerations:

- **Option 2**: select specimens meeting predefined epidemiological and/or laboratory criteria at the level of the diagnostic laboratory(s)

Sample Size:

- Countries with many samples available may identify a target sample size after considering testing costs and desired precision for public health policy

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		Observed Prevalence of Drug Resistance 95% Wilson Confidence Interval	
		3%[A]	**10%[B]**
Survey Sample Size	**n=25**	(0.4%,18.1%)	(3.2%,27.5%)
	n=50	(0.7%,12.0%)	(4.3%,21.4%)
	n=100	(1.0%,8.5%)	(5.5%,17.4%)
	n=150	(1.2%,7.1%)	(6.2%,15.8%)
	n=200	**(1.4%,6.4%)**	**(6.6%,14.9%)**
	n=250	(1.5%,5.9%)	(6.9%,14.3%)
	n=300	(1.6%,5.6%)	(7.1%,13.9%)

A: Estimated TDR Prevalence from 2012 WHO HIVDR Report

B: Example of a higher observed TDR Prevalence from 2012 WHO HIVDR Report

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Primary Analysis of the Survey:

- Calculate a point prevalence
  - Proportion of genotyped samples with HIVDR
    - NUM: HIV+ eligible individuals with resistance
    - DEN: HIV+ eligible individuals recruited **over a 3 months**
- Calculate a 95% confidence interval
  - Recommend the Wilson (score) interval

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Generalizability of Results:

- Will depend on population sampled
- TDR survey results generated by a study with representative sampling of the population of interest is ideal; however, this may not always be possible
- TDR survey results derived from sentinel systems have inherent biases; nonetheless, results are valuable for public health planning

Surveillance of TDR: International Benchmarks Reporting of TDR

HIGH	(>15%)
MODERATE	(5-15%)
LOW	(<5%)

- Reporting of data must take into account confidence intervals

Surveillance of TDR: Reporting of Data

Confidence Interval	Reporting
(1.0% , 4.0%)	LOW
(6.0%, 11.0%)	MODERATE
(16.0% , 25.0%)	HIGH
(3.0%, 11.0%)	LOW/MODERATE
(8.0%, 18.0%)	MODERATE/HIGH
(4.0%, 18.0%)	NO CLASSIFICATION

Surveillance of TDR: Public Health Actions

- Based on individual country cost effectiveness modeling
- Actions may include:
  - More frequent VL monitoring
  - Enhanced focus on Early Warning Indicators of HIVDR
  - Optimization of prevention messaging for HIV-positives in care
  - Enhanced l HIV prevention messaging/awareness

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Questions?