Paediatric HIV testing in practice

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Case 1

- HIV-exposed baby is seen at 6w at local clinic
- 6w PMTCT PCR is done → PCR positive
- Work-up for urgent ART initiation
- HIV VL undetectable
- Confusion!
- Repeat PCR done → PCR negative
- ???
  - False positive PCR

Case 2

- HIV-exposed baby is seen at 6w at local clinic
- 6w PMTCT PCR is done ⟹ PCR negative
- Baby admitted at 4 months with PCP
- PCR redone ⟹ PCR positive
- HIV VL= 3 million
- On enquiry the mother never breastfed and baby had 6w NVP
- ???
  - False negative PCR

Case 3

- 18m old child brought to HIV clinic by aunt – mom died 1 month ago
- Child on ART since age 8w: ABC + 3TC + Kaletra
- Clinically well, growing well, VL undetectable
- Aunt wants to adopt child. Social worker insisted that children for adoption need HIV-test, so HIV-ELISA was done.
- HIV ELISA negative
- Confusion!
- ???
  - Seroreversion

THE PATIENT
THE TREATMENT
THE TEST
THE EPIDEMIC

The patient

- 12m child admitted with FTT, generalized LA, oral thrush & chronic diarrhoea
- 6m old HIV-exposed child admitted with pneumonia
- 6w old infant from PMTCT programme

⇨ What is the difference between these scenarios?

⇨ Pre-test probability of disease

The treatment

- ART suppresses HIV replication!
  - False negative results
    - PMTCT prophylaxis:
      - Infant NVP
      - Maternal ART in breastmilk
        - False negative or indeterminate PCR results and low VL
    - ART:
      - Seroreversion
        - Negative ELISA in a child on ART

The test

- Sensitivity
  - Proportion of people with positive test among those with disease
- Specificity
  - Proportion of people with negative test among those without disease
- Positive predictive value (PPV)
  - Proportion of people with disease among all those with a positive test
- Negative predictive value (NPV)
  - Proportion of people without disease among those with negative test

PPV and NPV depend on the prevalence of disease in the tested population

Predictive values are key, as they give information on how likely the test result correlates with actual disease

		Condition	
		Present	**Absent**
Test	**Positive**	**True positive** (TP)	**False positive** (FP)
	Negative	**False negative** (FN)	**True negative** (TN)

Positive predictive value = $\frac{TP \ldots.}{(TP + FP)}$

Negative predictive value = $\frac{TN\ldots.}{(FN + TN)}$

Sensitivity = $\frac{TP\ldots}{(TP + FN)}$

Specificity = $\frac{TN\ldots}{(FP + TN)}$

The epidemic

- PMTCT programme since 2002
- Sequential PMTCT improvements – ⇈ ART use

⇨ Rapidly declining HIV-transmission rates

⇨ Rapid changes in Paediatric HIV epidemic

Hypothetical HIV PCR results with predictive values in SA HIV exposed infants at different %MTCT

	HIV transmission rate (% MTCT)							
	30%	25%	20%	15%	10%	5%	3%	1%
Estimated absolute numbers of HIV exposed infants tested using a single HIV DNA PCR								
Nr of True Positive PCR tests	92,863	77,386	61,909	46,432	30,954	15,477	9,286	3,095
Nr of True Negative PCR tests	217,998	233,569	249,140	264,711	280,283	295,854	302,082	308,311

Calculations used HIV PCR test **SENSITIVITY OF 98.8%** and **SPECIFICITY OF 99.4%** and population data for the year 2008 with estimated **313,305 HIV-EXPOSED INFANTS**

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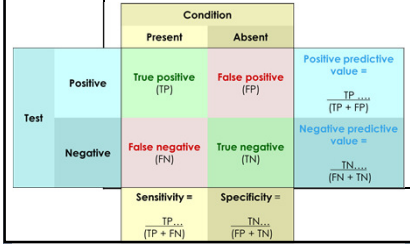

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Predictive values of a single HIV DNA PCR test result								
% False Positive PCR tests	1.4%	1.8%	2.4%	3.3%	5.2%	10.3%	16.4%	37.6%
Positive predictive value (PPV)	98.6%	98.2%	97.6%	96.7%	94.8%	89.7%	83.6%	62.4%

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Predictive values of a single HIV DNA PCR test result								
% False Negative PCR tests	0.5%	0.4%	0.3%	0.2%	0.1%	0.1%	0%	0%
Negative predictive value (NPV)	99.5%	99.6%	99.7%	99.8%	99.9%	99.9%	100%	100%

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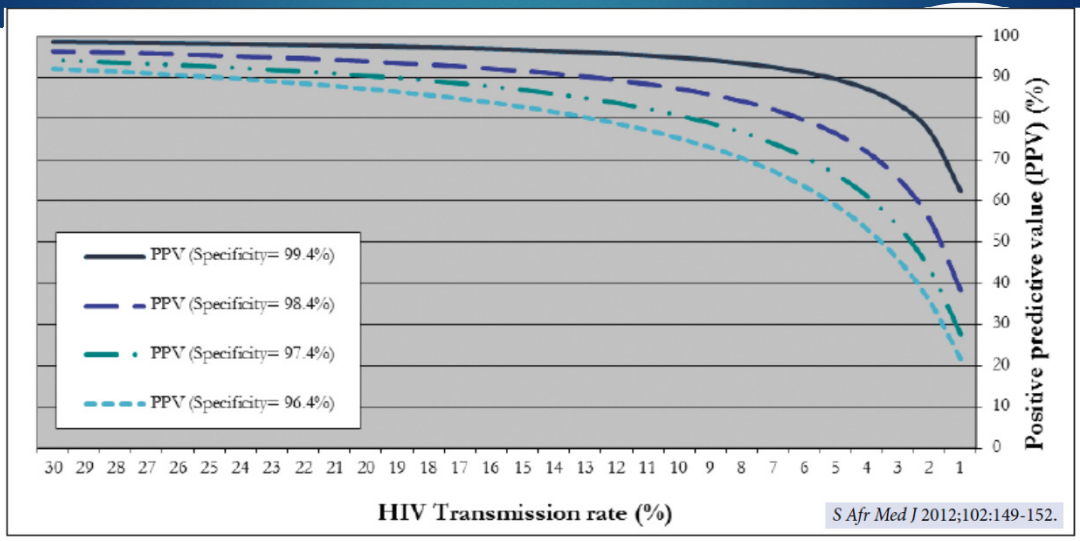
PPV of HIV PCR test at varying test specificities and declining HIV transmission rates



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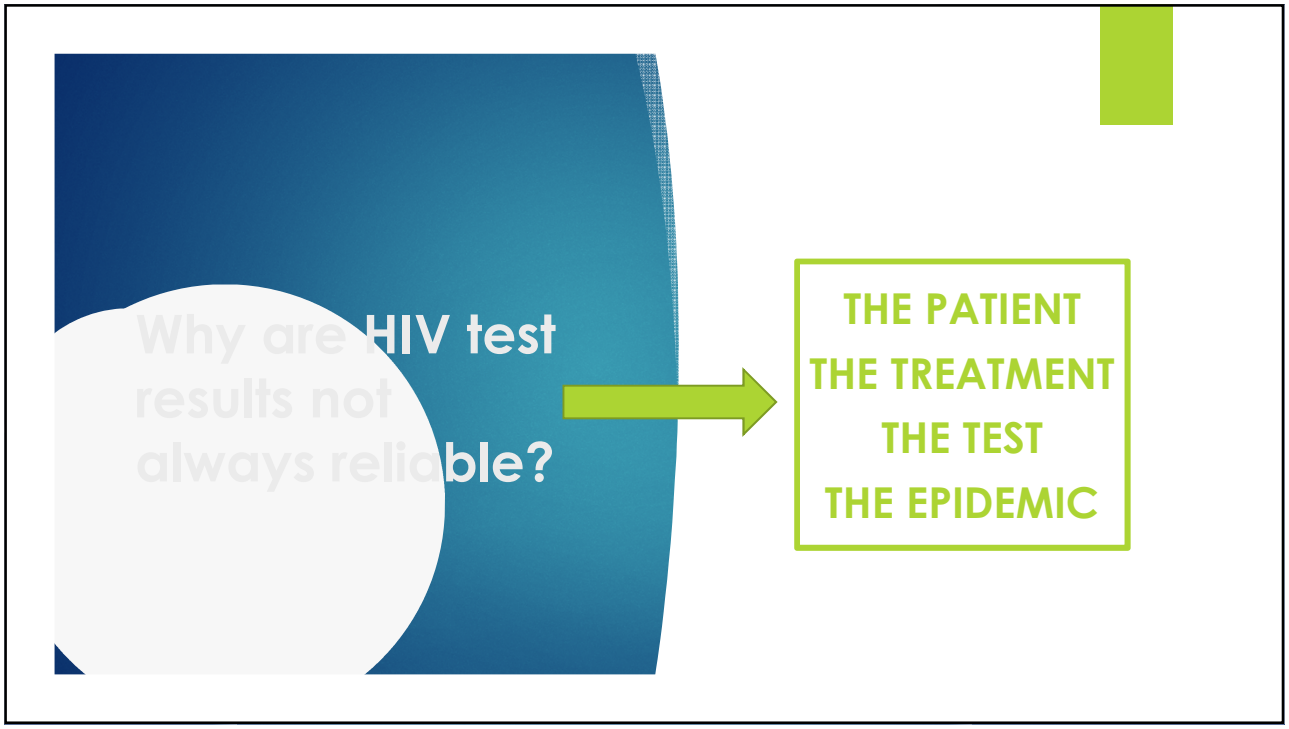
Why are HIV test results not always reliable?
THE PATIENT
THE TREATMENT
THE TEST
THE EPIDEMIC


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THANK YOU!
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