Getting it right: WHO guidance to diagnose correctly 90% of people living with HIV

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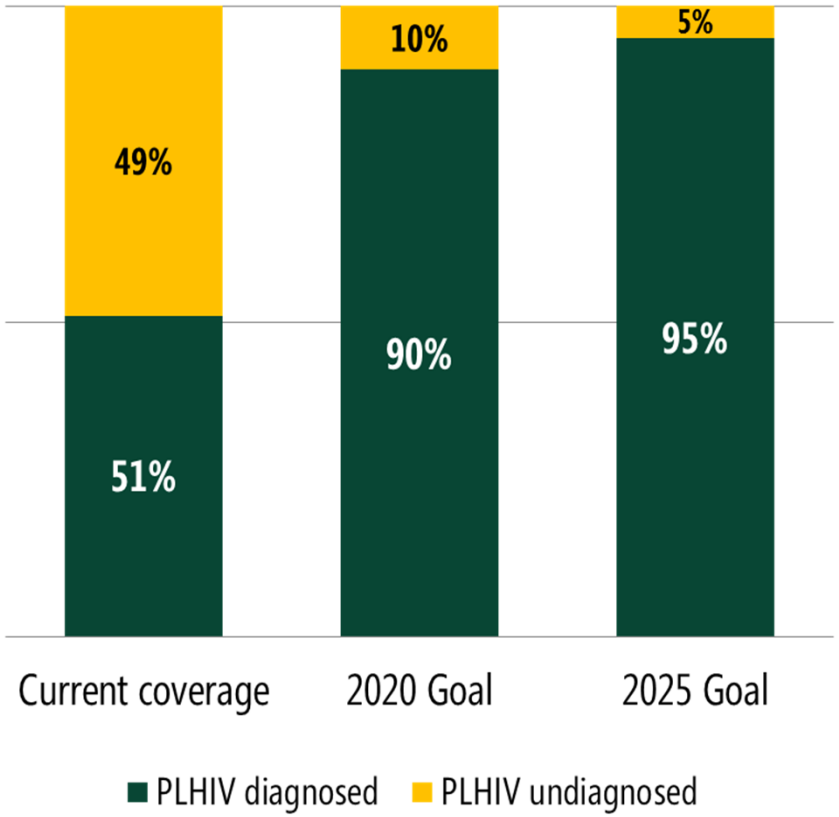
Anita Sands
Prequalification Team – Diagnostics
Essential Medicines and Health Products

World Health Organization

Aims of the new WHO HTS guidelines

- Addressing the testing **gap**
- Getting testing out into **communities**
- Supporting better **linkage**
- Better focus and appropriate **targeting**
- Improving **quality** to prevent misdiagnosis



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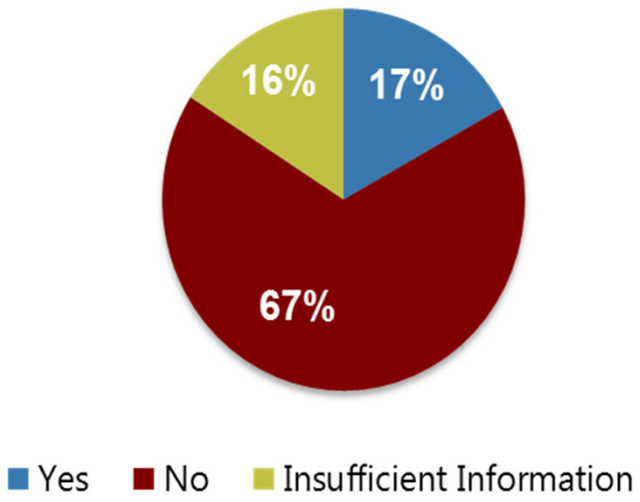
HIV testing quality and misdiagnosis

National testing policies aligned with WHO recommendations 48 countries



Review identified reports of misclassification range from 2.6% to 10.3%[1,2]

Studies (N=44) identified in a literature review, reporting factors related to misdiagnosis

Category	#	%
Clerical/technical errors (e.g. mis-labelling, poor recordkeeping, clerical mistakes)	14	32%
User error (e.g. errors performing RDT or interpreting results, misapplication of buffer, inaccurate reading time and other human errors)	11	48%
Cross-reactivity (e.g. antibodies from inter-current infection, environmental exposure to test components, HIV subtype, or late-stage AIDS)	8	18%
Incorrect / suboptimal testing strategy or algorithm (e.g. tiebreaker testing strategy)	22	50%
Poor management and supervision (work load stress, staff shortages, lack of training, poor adherence to testing strategy or testing algorithm, substandard operating procedures, testing in window period)	20	45%

Source: 1. Shanks PLoS One 2013; 2. Klarkowski PLoS One 2009; WHO 2015 forthcoming

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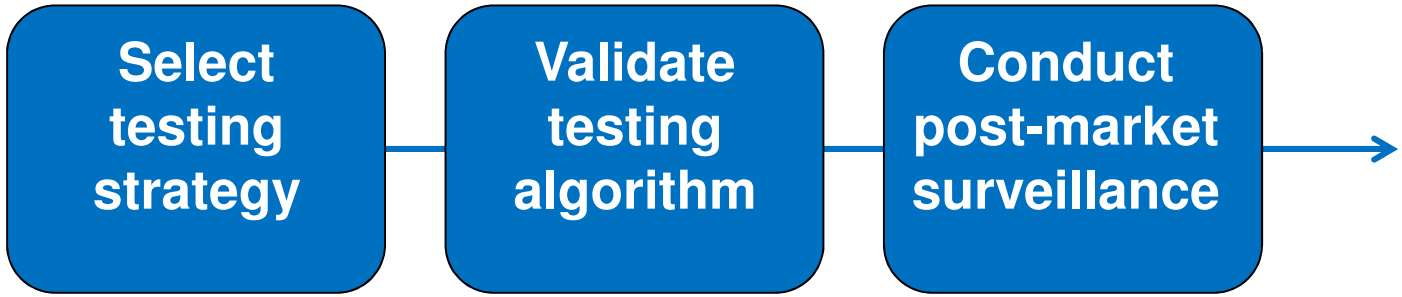
Assuring quality of diagnostics



Key points

1. Chose a **testing strategy** (high or low prevalence)
2. Select products and validate the **testing algorithm**
3. Ensure **post-market surveillance** of products used

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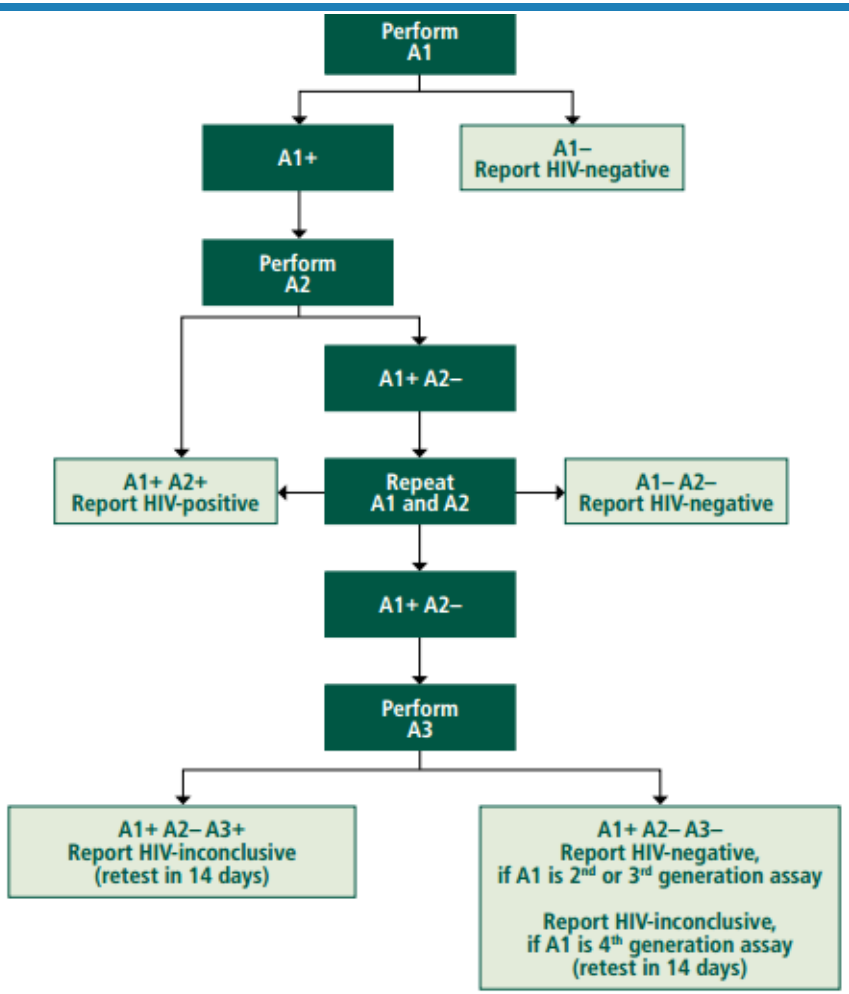
HIV testing definitions

- A **testing strategy** describes an approach for a specific testing purpose considering presumed HIV prevalence in the **population being tested**
- A **testing algorithm** describes the products (brands) of HIV assays to used within a given HIV testing strategy
- **Positive predicative value** determines the probability that the test result obtained reflects the true result
- An **assay** is a procedure for measuring the presence of a given analyte, e.g. antibodies to HIV-1/2

Diagnosis - high prevalence (above 5%)

- A1- = negative
- A1+; A2+ = positive
- A1+; A2-; A3- = negative
- **A1+; A2-; A3+ = inconclusive**



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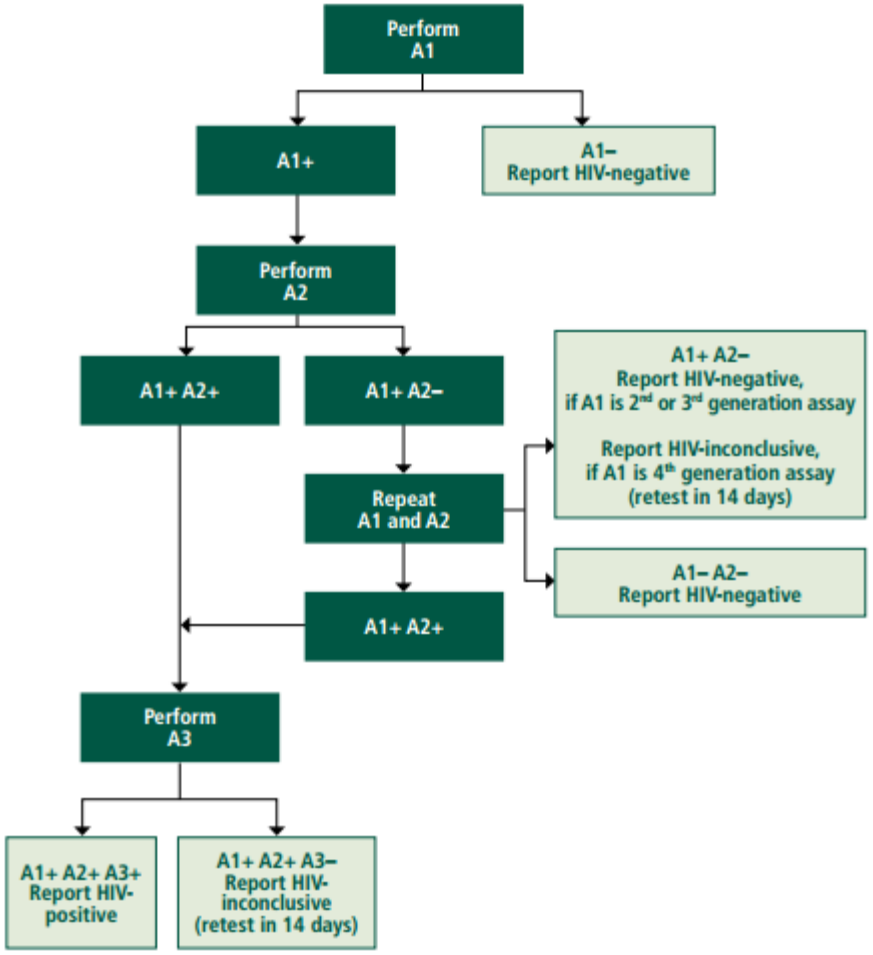
Diagnosis - low prevalence (below 5%)

- A1- = negative
- A1+; A2- = negative or inconclusive
- **A1+; A2+; A3+ = positive**
- A1+; A2+; A3- = inconclusive



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Re-testing recommendations

- Retesting means
  - Different specimen, same testing algorithm, different testing site
  - Significant limitations when on ART
- Individuals with **HIV-inconclusive** status should be retested after 14 days
  - To rule in or rule out seroconversion (static vs. evolving results)
  - To rule out operator error, test device error, transcription errors
- **Newly diagnosed HIV-positive** individuals should be retested prior to care and/or treatment

Validation of testing algorithms

- Choose:
  - 6-10 assays from list of prequalified assays
- Conduct:
  - Validation study to identify best combination of assays
- Select:
  - One A1 (and back-up) with **superior sensitivity**
  - One each for A2 and A3 with **superior specificity**

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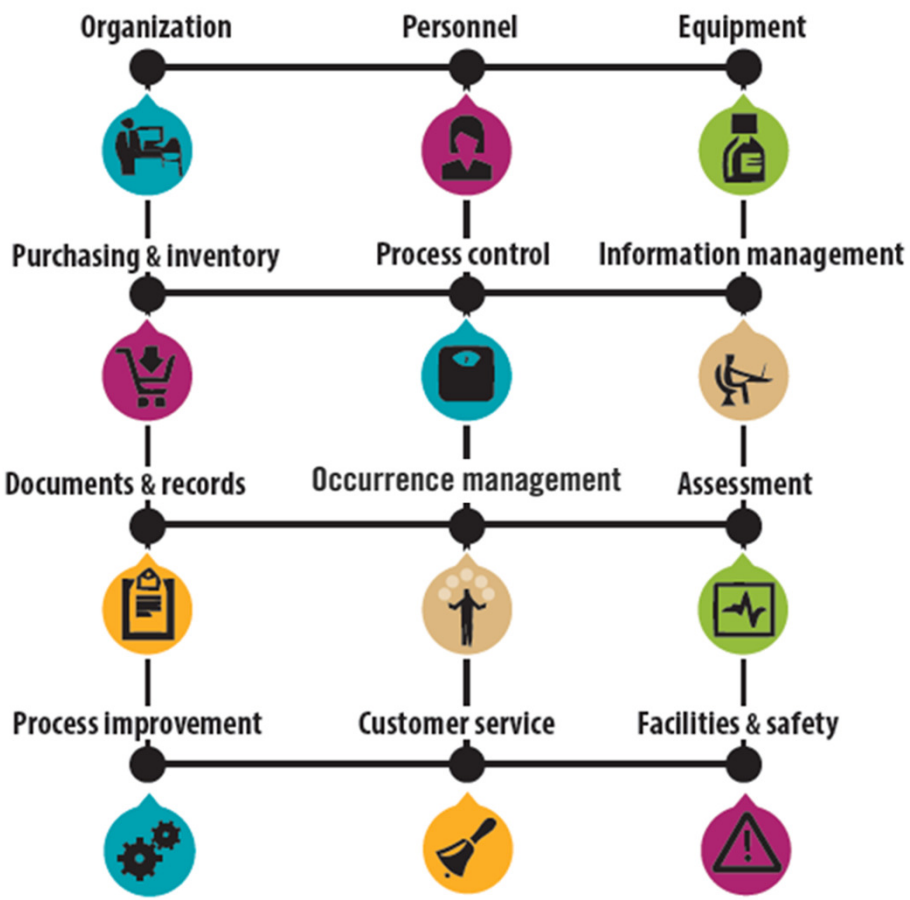
Limitations of certain diagnostics

- Inadequate internal QC
  - Most RDTs don't control for specimen addition
- Assays for detection of HIV-2
  - Up to 57% cross-reactivity observed for "discriminatory" HIV-1/HIV-2 assays
- 4th generation (Ag/Ab) assays
  - Designed for use as A1
  - Current products have limitations for detecting acute infection but good sensitivity for established infection

How to assure quality of HIV testing



- Assessment
  - EQA, supervisory visits
- Process control
  - QC, including storage
- Recordkeeping and documentation
- Personnel
  - Training, support

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