Potential Effect of Alternative HIV Testing Algorithms on HIV Case Surveillance

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The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Outline

- Background
  - Current HIV surveillance case definition
  - New algorithms in the 2009 Status Report
- Reasons for and against revising the case definition in response to new algorithms
- Surveillance implications
  - Diagnostic scenarios for reporting results
- Timeline for changes to HIV surveillance

Background (1)

- The “HIV Testing Algorithms: 2009 Status Report” describes HIV testing algorithms that have the potential to augment and provide alternatives to the algorithm currently used to diagnose HIV infection.
- Any change in the way clinicians diagnose HIV infection may impact the way national HIV case surveillance is conducted.
- Surveillance Principles:
  - Case definition is only intended for public health surveillance
    - Primary use of surveillance data is for monitoring the epidemic and planning on a population level
  - Case definition should not act as a guide for clinical diagnosis.
    - Surveillance is intended to follow clinical guidelines, not set the standard of care

Background (2)

- CDC's HIV Incidence and Case Surveillance Branch convened a workgroup to explore:
  - How the new algorithms may affect the surveillance case definition
  - If the case definition needs to be revised in response to the new algorithms
  - How surveillance system should be modified if changes to the case definition are necessary

Current Surveillance Case Definition for HIV Infection

- *"Revised Surveillance Case Definition for HIV Infection"* — United States, 2008. MMWR 2008; 57(No. RR-10).
- Single unified case definition for *HIV infection* that includes all persons infected with HIV regardless of their stage of disease (i.e., AIDS)
- Laboratory-confirmed evidence of HIV infection is required for HIV infection

Case Definition - Laboratory Evidence

Laboratory Criteria

1. Positive result from an HIV antibody screening test (e.g., reactive enzyme immunoassay) confirmed by a positive result from a supplemental HIV antibody test (e.g., Western blot or immunofluorescence antibody test)

   OR

2. Positive result or report of a detectable quantity from any of the following HIV virologic (i.e., non-antibody) tests:
   - HIV nucleic acid (DNA or RNA) detection test (e.g., polymerase chain reaction [PCR])
   - HIV p24 antigen test, including neutralization assay
   - HIV isolation (viral culture)

New Algorithms in the 2009 Status Report

- Dual immunoassay algorithms (e.g., rapid-rapid, rapid-EIA)
- Whether the new algorithms require a new surveillance case definition depends on whether they:
    1. Provide an enhanced screening step that must still be confirmed by one of the tests currently accepted by the surveillance case definition *OR*
    2. Are interpreted as replacing the confirmatory antibody test (WB or IFA) with the second immunoassay in a dual-immunoassay screening algorithm

✓ If the first statement is true, the current case definition is sufficient. The remainder of this presentation is based on the assumption that the second statement is the more realistic.

What are the reasons for revising the case definition? (1)

1. If the sensitivity and specificity of the dual algorithm are as high as those of the EIA + WB algorithms currently accepted, the dual algorithm should be acceptable for a clinical diagnosis and included in the case definition.
    - The Positive Predictive Value (PPV) should also be considered, as low prevalence settings could have higher false positive rates.
2. If clinical recommendations promoting the use of a dual immunoassay algorithm as a substitute for the WB or NAAT are published, surveillance should be flexible and adapt to the standard of clinical care.

What are the reasons for revising the case definition? (2)

3. Cases based on new algorithms (without confirmation by WB or NAAT) would not meet the current surveillance case definition and would go unreported.
   - Surveillance case counts would artificially drop, particularly if patients diagnosed in the new way did not promptly have a detectable VL reported to surveillance.
   - The artificial decrease would be more significant if a large percent of patients were lost to follow-up after being referred elsewhere for care by a screening center.

What are the reasons for *NOT* revising the case definition? (1)

1. If positive results on the dual-immunoassay algorithm are interpreted as providing only a **presumptive** diagnosis of HIV infection, rather than a **definitive** diagnosis, it may be inappropriate for patients to be counted as surveillance cases
   - Surveillance data collected could become less accurate (with more false positives)
   - Some clinicians might incorrectly take CDC's surveillance case definition as clinical guidelines, and stop doing the more specific confirmatory tests, which could lead to deterioration in the quality of clinical care.

What are the reasons for *NOT* revising the case definition? (2)

2. Acceptance of the dual immunoassay could be harmful to the patient if discordant results on the second immunoassay are misinterpreted as meaning that the patient is not infected.
   - Discordant results should lead to follow-up for further testing to rule out early HIV infection or infection with an atypical viral strain, such as HIV-2.

3. Expanding the surveillance case definition in this way should be done *only* if necessary, because it will require a massive change in how surveillance is done, placing a much greater work load on surveillance staff.

Implications of expanding the case definition (1)

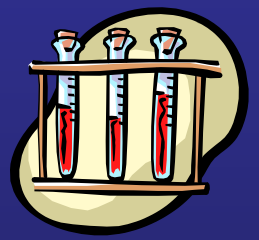
Changing Reporting Laws

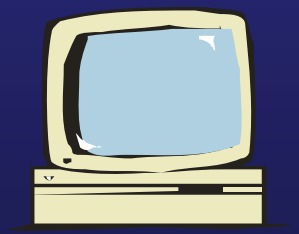
- Many state laws or regulations would need to be revised to mandate or at least permit reporting of positive results of HIV immunoassays

- Immunoassays for screening are currently not reported in some states, because reporting is required only for confirmatory tests.
- Timeline for changes: months to years, depending on the state

Implications of expanding the case definition (2)

Shift from Passive to more Active Surveillance System





Current system: Heavily dependent on passive reporting of electronic laboratory results

Post shift: Much more dependent on active surveillance methods to identify new diagnoses

Implications of expanding the case definition (3)

Linking Immunoassay results

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#1: Result of screening immunoassay

#2: Result of confirmatory immunoassay

Implications of expanding the case definition (4)

Training Staff & Monitoring Case Reporting

- Staff at Point of Care (POC) facilities (e.g., screening sites, STD clinics, providers' offices) would need to be trained to report the results to the health department on a case report form (in addition to the form currently used to monitor testing programs)
- Surveillance programs would also be tasked with developing a system to monitor the reporting of results and to ensure compliance at POC sites.

Implications of expanding the case definition (5)

Changes to Surveillance Software (eHARS)*

- eHARS does not currently count persons that receive a clinical diagnosis of HIV based on the new algorithms as cases.

- eHARS would need to be modified to collect data on tests and supplemental information related to the new algorithms.

* *eHARS = HIV/AIDS Reporting System*

Implications of expanding the case definition (6a)

HIV Incidence Surveillance (HIS)

- The BED assay, used for HIS to determine recent versus long-term infection at the population level, requires a confirmed specimen from the earliest diagnosis *OR* from an HIV-related test collected within 3 months after the earliest diagnosis.
- This specimen would not be collected with rapid testing alone
- There is a substantial decrease in the probability that a specimen drawn at a later date from a person recently infected with HIV at the time of diagnosis would be classified recent on the BED assay.

Implications of expanding the case definition (6b)

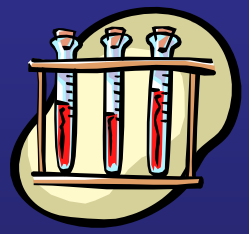
HIV Incidence Surveillance (HIS)

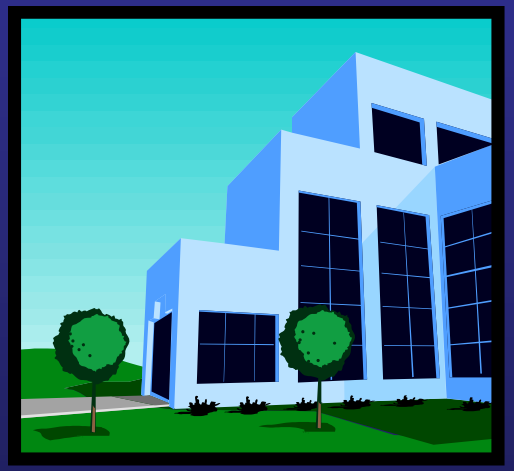
- A larger proportion of the specimens tested for HIS with the BED assay come from public health labs, which largely service Counseling and Testing Sites (CTS), than from commercial labs.

- If the proportion of specimens collected at screening centers is reduced, necessitating the collection of specimens at a later date than the earliest possible diagnosis, this could create a potential systematic bias toward long-term infections that could lead to a bias in the estimation of HIV incidence.

Diagnostic Scenario 1

Tests performed at the POC site and lab



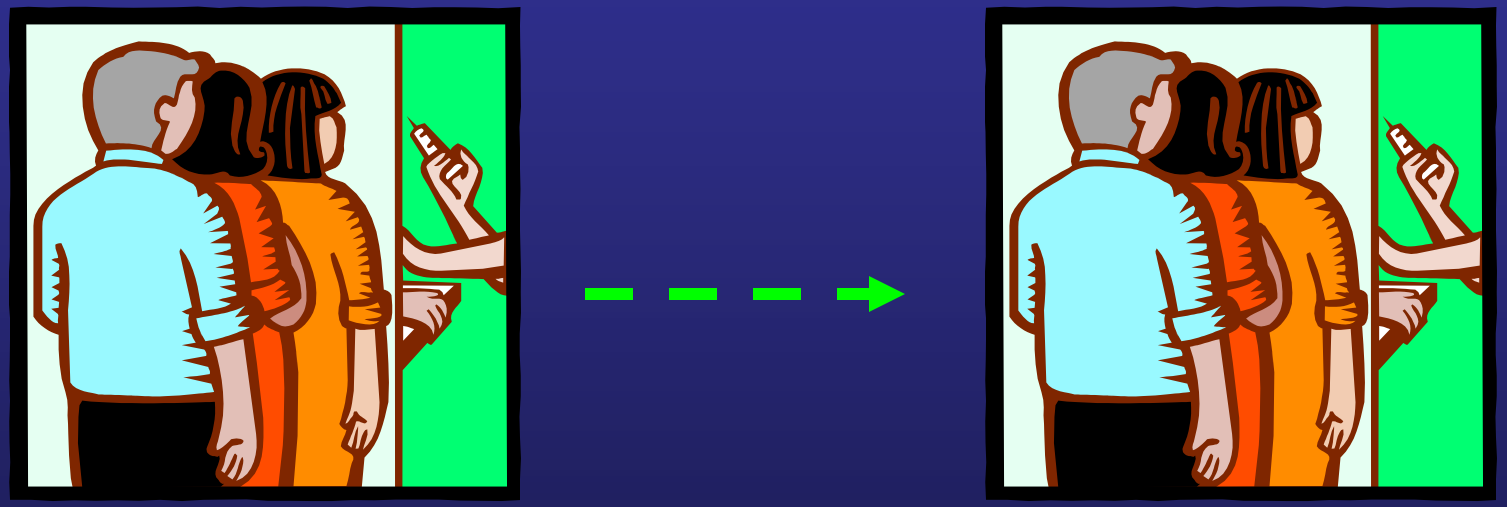


Challenges:

- Linking the screening and diagnostic test results
- Test results will have to be reported by the POC and the lab

Diagnostic Scenario 2

Both tests performed at the POC site

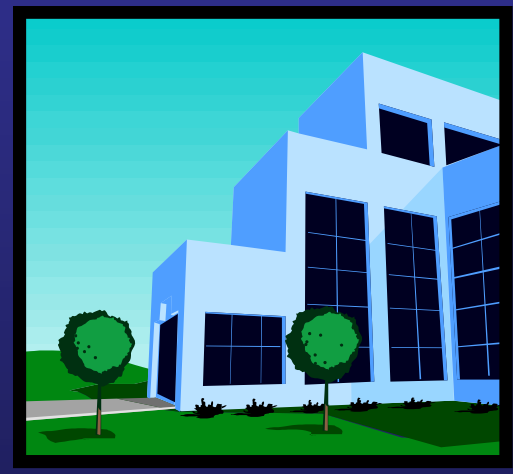


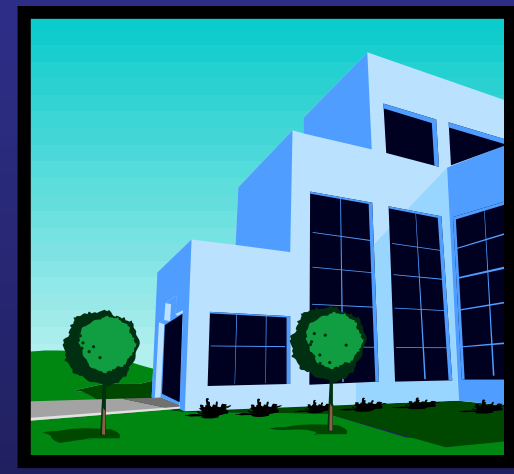
Challenges:

- No lab involvement = no requirement for electronic reporting
- 100% case report form compliance from providers or staff at screening centers

Diagnostic Scenario 3

Both tests performed at the laboratory





Challenges:

- Labs would have to ensure that results from a dual testing algorithm were not reported as duplicates
- Labs would ideally report results to the health department only after two tests were done

What is the timeline for revising the case definition?

- Surveillance should not drive clinical practice or run the risk of setting the standard of care.
- Surveillance should wait until national recommendations are published to accept a dual immunoassay algorithm as a basis for definitive, rather than presumptive, diagnosis, before expanding the case definition.
- In the meantime, CDC and surveillance programs should begin to prepare for the large-scale shift in surveillance practices at both the state and national levels.

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Questions/Comments?

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