Consultation on Advancing HIV Incidence Surveillance
Summary

Introduction

HIV incidence surveillance (HIS) provides the most representative picture of HIV trends and the impact of HIV on the public's health and related prevention efforts. Data from HIS are critical to assessing the goals of the National HIV/AIDS Strategy and the Division of HIV/AIDS HIV Prevention's Strategic Plan.

Through the case-based National HIV Surveillance System (NHSS), longitudinal data are collected on cases reported in 65 jurisdictions, including the 50 states, the District of Columbia, and U.S. dependencies. Data include demographic, behavioral, laboratory, and clinical information such as CD4 count and viral load testing. Through HIS, results from the serologic testing algorithm for recent HIV seroconversion (STARHS) and HIV testing and treatment history (TTH) information are collected in 25 funded jurisdictions, and through molecular HIV surveillance (MHS) electronically reported HIV genetic sequences are collected in 11 jurisdictions.

Changes to the HIV diagnostic algorithm and novel assays used to determine recent HIV infection may impact the way HIS is conducted and the HIV incidence estimation model. Other methods of HIV incidence estimation using all available data must be considered.

On September 27–28, 2011 CDC hosted a consultation to consider options for HIS and estimation in the United States. Participants were experts with a variety of perspectives including state and local HIS staff, statisticians, researchers, care providers, laboratorians, and representatives from relevant national and international organizations.

Objectives

The objectives of the consultation were to:

- discuss the possible impact of revised HIV testing algorithms on U.S. HIS;
- consider methods to estimate HIV incidence in the United States at national, state, and local levels, considering the data collected through NHSS; and
- discuss alternative ways to estimate HIV incidence in the United States using national surveys.

Synopsis

Consultants received an overview of NHSS including its components and the potential impact that changes to the laboratory and point-of-care testing HIV testing algorithms proposed in March 2010 could have on surveillance. A landscape of HIS including the strengths, limitations, threats, and opportunities of NHSS was presented and the use of novel or different biomarkers and multiple HIV incidence estimation methods were discussed. Consultants participated in one of two breakout sessions focused on approaches to minimize the impact of the new HIV testing algorithm on HIS and on methods to estimate HIV incidence using data collected by the surveillance system.

Highlights from Presentations and Discussion Sessions

New HIV Recency Assays/Multi-assay algorithm

All current assays for recency depend on a mean recency period, are titer-based, and are subject to falsely classifying long-standing infections as recent. Assay performance varies across stages of infection and by test. Multiple new assays that measure a variety of biomarkers are being evaluated and may measure recency of infection more accurately. Multiple assays or approaches can be combined to reduce the false recency rate (FRR) but would require calculation of a combined recency period.

Discussion Highlights:

- Consultants expressed concerns about the length of FDA's approval process for new HIV incidence assays. There may be a shorter FDA approval process if the use of recency assays is not for clinical purposes (and clinicians did express that they did not see a use for it). With no clinical utility, tests of recency would not be reimbursed and funding for recency testing would continue to fall to surveillance

as the user of the test, leading to questions about how to fund the test if it were conducted by multiple laboratories.
- Multiple assay tests or longitudinal methods may require complicated statistical solutions and possibly more blood samples.

Acute HIV infection for HIV incidence estimation

NHSS does not currently collect data on acute HIV infections, but the proposed new HIV disease staging system and new testing algorithm that help to identify acute infections could be used to estimate incidence. Diagnosis of acute HIV infections (AHI) or sub-acute HIV infections (SHI) increased significantly from 2006–2009 in 40 states.

Discussion Highlights:

- Using AHI data to estimate incidence is a good possibility, but its use may be limited due to the brief window period for detection. Changes to eHARS, and reproducibility at the local level must be considered.

Genetic sequence-based methods

Ambiguous base pairs are reported in genetic sequences when there is greater viral diversity within an individual. An ambiguity index (total number of ambiguous bases/total number of bases sequenced) could be used to distinguish between acute and chronic infections because there is a direct correlation between genetic diversity duration of infection.

Discussion Highlights:

- Genetic diversity to determine recency should be explored as standard genotyping data are available. However, this method should be compared with current incidence assays used for incidence estimation.
- Genetic diversity data should not be used as a stand-alone method to determine HIV incidence; the number of incident infections may be underestimated as recent infections can have a high rate of diversity. It could be used in combination with other data and/or in addition to other incidence testing.

HIV incidence in the United States using data from national surveys:

HIV incidence can be estimated with a synthetic cohort method that uses two sequential, nationally representative surveys with the assumption that the survey samples include persons from the same population (though not necessarily the same people) and deaths among persons with HIV can be accurately estimated. Consultants considered the use of the National Health and Nutrition Examination Survey (NHANES) within this method.

Discussion Highlights:

- NHANES does not represent all populations at risk because it is a household and no other surveys would be useful for this purpose. However, there could be potential to explore the use of NHANES for incidence estimation in high-risk populations such as MSM.
- CDC should explore the applicability of the synthetic cohort method to National HIV Behavioral Surveillance data.

Highlights from Breakout Sessions:

New HIV testing algorithm (securing samples and improving data completeness)

- The new diagnostic algorithm is not a threat to HIV incidence surveillance; however, widespread transition to point-of-care testing (facilitated by a new algorithm) *would* be a threat—especially if newly diagnosed patients do not enter care immediately.
- CDC should provide recommendations to health departments regarding the data/specimens that should be collected in association with rapid testing.
- CDC should explore the use of dried fluid spots (DFS) collected at point-of-care or in laboratories.
- Surveillance areas should integrate electronic laboratory reporting (ELR) and eHARS data to allow the conduct of HIV surveillance in real time and successful collection of viral load specimens for STARHS testing before they are discarded by testing laboratories.

- If the price were decreased sufficiently, a test for recent infection could be run as part of routine HIV screening on all confirmed HIV positive specimens.
- CDC should consider how the regionalization of incidence testing might improve data completeness. It was suggested that a regional testing approach could facilitate specimen tracking due to increased accessibility of patient information.
- CDC should facilitate access to specimens from large private/commercial laboratories.
- CDC should communicate with laboratories about the new testing algorithm and revised reporting recommendations so that both providers and surveillance staff can identify the "supplemental" results that provide diagnostic confirmation.
- CDC should advise jurisdictions to use all available data sources to obtain TTH data including data from the AIDS Drug Assistance Program, Ryan White Clinics, STD*MIS, etc.
- CDC should increase the number of sites conducting incidence surveillance.

Methods to estimate HIV incidence in the United States, at the national and local/state level, considering mixed methods/combining information available for estimation

- It is feasible to combine information on BED, CD4, and viral load to reduce the FRR. However, those data are not missing at random and the current estimation model will require adjustments.
- Reduce the contribution of BED to the overall model by supplementing with AHI.
- Genetic diversity data
    - Should not be used as a stand-alone method to determine HIV incidence. It could be used in combination with other data and/or in addition to other incidence testing.
    - Aspects to consider when using genetic diversity data for incidence estimation should include:
        - How to apply genetic diversity methods to population based sequences; and
        - How to ensure that data are analyzed and reported in a uniform fashion.

Summary

After consideration of all presentations, discussions and commentary, consultants expressed that the impact of a revised HIV diagnostic algorithm seemed to be less problematic to current estimation methods than CDC had anticipated, and that blood specimens for recency testing would continue to be available. However, they did acknowledge that specimen collection could be more difficult in the context of "point-ofcare HIV testing" and that surveillance programs would likely have to find alternative means of specimen collection. No single alternative to the current approach to incidence estimation emerged from the consultation.

General Comments and Recommendations

- Smaller confidence intervals (CIs) are needed to measure the National HIV/AIDS Strategy goals. CDC should investigate the improvements needed and the factors that affect variation.
- The recency period distribution, mean recency period and FRR have an important role in determining CIs. CDC should investigate whether a longer mean recency period that reduces FRR would improve incidence estimates.
- Consider the impact of transitioning from BED to another HIV recency assay on incidence estimates.
- CDC should explore the implications and bias that re-classification of acute HIV infections as "recent" at an individual-level may cause to the incidence estimation model which is based on a population-level assay.
- FDA should participate in future discussions about the potential clinical or other uses of tests for recent infection and provide input on the FDA requirements. .
- Surveillance should include other types of HIV tests (e.g., multi-spot assay) in reporting regulations.
- The ability to produce local estimates, in addition to national, is an important means of evaluating prevention efforts.

Next Steps

- Develop a protocol that evaluates the impact of another assay on incidence estimates upon transition from BED, including an option that uses both tests on samples for a year to compare differences in estimates.

- Develop a model/protocol that explores the use of viral load and CD4 data to reduce false recency rates and recalculate the recency period.
- Assess the feasibility of conducting recency analysis based on genetic data using longitudinal vaccine study data for recent seroconverters and AIDS cases.
- Explore incorporating acute HIV infections into existent estimation model.
- Explore combination approaches for incidence estimation with different amounts of data for each case (BED, acute HIV, viral load, CD4 counts, genetic sequences, and no BED).