Attachment M. Statistical Consultation Summary

HIV Incidence Estimation Consultation
June 15–16, 2006
Corporate Square, Building 8, Conference Room 1 B/C
Meeting Notes

June 15

Welcome

Introductions — Tim Green

Charge to the Group — Tim Green

Main Objectives

1. Examine the validity of the HIV incidence estimation method proposed by Karon, Song, Kaplan, and Brookmeyer, if the necessary information can be gathered, with respect to
   a. Stochastic uncertainty
   b. Bias (violation of assumptions)
   c. Performance characteristics of the assay
2. Identify other methods of HIV incidence estimation.
3. Determine what sort of an estimate can be produced by December 2006 for calendar year 2005.

Overview of Estimation Procedure — John Karon

1. Background
2. Sample survey approach
3. Potential problems and points for discussion
4. Assumptions about procedure

Discussion of Karon model

1. Stochastic uncertainty
   a. Variances have been worked out for several of the terms that involve uncertainty (e.g., I_o, I_1, I_B).
   b. One big source of variability is the uncertainty in the multiplier in equation 5 of the *Statistics in Medicine* submission (i.e., the coefficient of variation of φ). The estimate is very sensitive to the estimate of the mean window period.
2. Bias and assumptions
   a. Incidence and testing patterns (i.e., hazard, or instantaneous risk, of being tested) remain constant during AIDS incubation period (steady state).
      Problem: These assumptions are quite strong.
      Question: On the basis of these assumptions, can we use simpler models to arrive at a similar estimate?

b. All data are complete and accurate (including results of the assay and all responses to supplemental questions about testing history).

Problem: Realistically, we can only expect about 50% of assay results and an even smaller proportion of data on testing history. Missing data could be a big problem and needs further evaluation.

c. The window period distribution is valid.

Problem: The window period distribution for the BED assay hasn't been fully validated.

d. Testing characteristics of persons who avoid testing (i.e., test-resistant) differ from all others at risk for testing and must be stratified accordingly.

Problem: Conscious delay of testing may not be an accurate reflection of infection, especially if motivation *for* testing is not related to infection (i.e., we must assume a rational motive in both directions: early [soon after person becomes infected] and delayed testing).

3. Testing history information

a. We do not currently use motivation to classify individuals. Supporting information and justification is available from HICSB on request. We will test the sensitivity of the estimate to this assumption.

b. We do not need individual-level information on testing frequency.

c. We can obtain subgroup information from NHBS to determine the intertest distribution.

Problem: NHBS surveys only populations at high risk.

Question: Is it possible to survey HIV-negative persons who receive HIV counseling and testing services (CTS)?

d. We will consider incorporating into simulations the increased risk of testing soon after infection.

e. We have not resolved whether it is necessary to stratify according to whether individuals consciously delay testing.

i. The proportion of persons with AIDS who have not had a previous HIV test seems to be stable. A proportion of this population might be test-resistant.

ii. It may be possible to evaluate test-resistance by using testing frequency information from various populations (e.g., incidence data, NHBS, HITS, SHAS, BRFSS, NHANES, NHIS). We need to investigate whether these data sets are useful for us based on the available data variables and sample sizes.

4. General criticism

a. The group seemed to consider the mathematics valid but to believe that some of the steady state assumptions may be too strong.

b. Some participants felt that because of the steady state assumptions, this approach uses a sophisticated weighting scheme to essentially produce an estimate of the total number of new diagnoses—information that could be obtained more directly from surveillance data.

Status of Implementation

1. Data collection — Maria Rangel
2. Data completeness — Rick Song
    a. Dr. Rangel highlighted the collection of data on testing history and the collection of blood specimens for BED testing.
    b. Dr. Song presented preliminary surveillance data, with emphasis on completeness of data collected during 2005. Of the roughly 29,000 new cases diagnosed during 2005,
        i. More than 80% of reports of cases of HIV infection (not AIDS) were missing data on the most recent negative test result.
        ii. Only 13% of cases of HIV infection were BED tested.
        iii. 24% of cases of HIV infection received a diagnosis of AIDS within 1 month after receiving a diagnosis of HIV infection.
    c. In response to a request, Dr. Rangel presented the testing frequency distribution among cases diagnosed during 2005.

Review of Estimators — John Karon

1. Estimators for persons with a previous negative test result of known date
2. Estimators for persons not previously tested
3. Estimators for persons whose BED test was delayed
4. Extension of estimators to persons for whom data were missing
    a. Stratification
    b. Propensity scores
    c. Incorporation of patterns of missing data into simulations

June 16

Other Estimators and Supplemental Approaches

1. Naïve estimator: Number of newly diagnosed cases scaled to the national population (accounting for persons who will never get tested)

   Problem: Assumes that new diagnoses = new infections.

2. Back-calculation model developed by Rhodes and Glynn

3. Simplified STARHS estimator:

   The following proposal, although less mathematically sophisticated than the Karon et al. proposal, is much simpler. It is based on, but different from, $I_0 + I_B$.

   I_s = (# STARHS-recent) ÷ [P(1)*P(2)*P(3)], where

   P(1) = P(test HIV+ within 1 year | newly HIV infected)

   I.e., the probability that a person will be tested within 1 year after infection (stratified by subgroup).

   P(2) = P(STARHS administered | test result HIV+)

   I.e., the probability that this person receives a STARHS test. This estimate can be obtained from incidence surveillance data (13% for 2005). The number varies, depending on geographic location as well as testing location.

   P(3) = P(detected during window period | STARHS administered within 1 year after HIV infection)

   I.e., the probability the infection will be detected during the window period if STARHS is administered within 1 year after the person becomes infected.

   Discussion:

   a. Local areas may be able to use this estimator to compute local estimates.

   b. Like I_B, the information on testing behavior does not have to be linked to individual test results. Thus, several estimates can be obtained for each component of the estimator and combined to obtain a range of credible estimates for HIV incidence.

   c. Example.

      Number STARHS-recent = 757. This is the current number reported to HIV incidence surveillance for 2005.

      P(1) = 0.48 = 252/527. This is the proportion of newly diagnosed cases with at least 2 HIV tests during the 2 years before diagnosis, based on the data from the pretest questionnaire for incidence surveillance. Because this proportion does not include persons who had never tested before or who did not respond, it is likely to be inflated.

      P(2) = 0.13. This is the proportion of incidence surveillance cases that were STARHS tested in 2005.

      P(3) = 0.42. This is based on the mean window period = 5/12.

   d. Ways to obtain a better estimate of P(1).
      i. Use incidence data to estimate P(1) among HIV+ persons.
      ii. Use NHBS data to estimate P(1) in a population at high risk for infection.
      iii. Use BRFSS or other sources (see list above) to estimate P(1) in a general population.
   e. Seattle data on intertest intervals are linked with results from an incidence assay (probably Abbott).
   f. Try to verify the assumption that P(1) does not actually depend on infection status or how recently one was infected once membership in a population (e.g., MSM, IDU, or heterosexual adults or adolescents at high risk) is accounted for.

4. Direct (back of the envelope) estimator
   a. Use incidence rate and population size data on MSM in NYC.
   b. Scale to all transmission categories and national population.

5. Alternative approaches and issues
   a. To detect trends in incidence, monitor the number of new infections as a proportion of the total number of infections diagnosed over time.
   b. Obtain information on the total number of persons tested during a given period. This would require information on the number of negative test results and an adjustment for repeat testing among both positive and negative individuals—information is generally available only on the number of test kits distributed or the number of tests performed rather than on the number of persons tested.
   c. Obtain the testing frequency in a general population by surveying persons with a negative test result at CTS sites.
   d. Test the independence between the proportion recently tested and the proportion BED tested by site or facility (there should be no association).
   e. Evaluate uncertainty, consistency, and plausibility. Possibly convene an expert working group.
   f. Produce plausible ranges and lower and upper bounds for *N* and for large subgroups.
   g. Compare 2005 estimates with historical estimates for the mid-1990s.
   h. Evaluate window period estimates.
      Questions: Can better estimates of the window period be obtained? Very few data are available on people who have been infected more than 3 years. What about those who remain STARHS-recent even after a long time? Are incidence trends robust to STARHS results that falsely indicate recent infection (i.e., false-recents)?
   i. Investigate whether the probability of being tested within a year after becoming HIV infected is higher than the probability of being tested before infection.
   j. Investigate whether our sample of HIV+ persons whose specimens have been subjected to STARHS is biased because the early implementation of STARHS has been mostly at public testing sites.
   k. Estimate the proportion/number of HIV+ persons determined only by AIDS diagnosis.

l. Investigate what might happen if testing behavior changes.
m. Produce subgroup estimates.
    i. age (young adults 18–25, …)
    ii. sex
    iii. race/ethnicity
    iv. transmission category (male-to-male sexual contact, injection drug use, high-risk heterosexual contact)

Estimates of Window Period Distribution Bob Byers

Need to Adjust for Persons with Very Long Window Periods Meade Morgan

No recommendations were made to adjust the window period or formally incorporate adjustments for false-recents into the BED results.

Next Steps

1. Have draft report of 2005 estimates ready for internal review in 3 months (30 Sep 2006); have final report by 31 Dec 2006.
2. Convene groups to work on each of the estimation methods suggested. Each approach will incorporate data from multiple sources and will account for bias as well as variability.

DHAP Principals

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