Published in final edited form as:
AIDS. 2009 April 27; 23(7): 835–843. doi:10.1097/QAD.0b013e328326f55e.

Targeted Testing for Acute HIV Infection in North Carolina

William C. Miller, M.D., Ph.D., M.P.H.[1,2], **Peter A. Leone, M.D.**[1,2,3], **Sandra McCoy, Ph.D., M.P.H.**[2], **Trang Q. Nguyen, Ph.D., M.P.H.**[4], **Del Williams, Ph.D.**[3], and **Christopher D. Pilcher, M.D.**[5]

[1]Division of Infectious Diseases, Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC

[2]Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC

[3]HIV/STD Prevention and Care Branch, North Carolina Department of Health and Human Services, Raleigh, NC

[4]Bureau of Communicable Disease, New York City Department of Health and Mental Hygiene, New York, NY

[5]HIV/AIDS Division, University of California San Francisco, San Francisco, CA

Abstract

Background—Persons with acute HIV infection contribute disproportionately to HIV transmission. Identification of these persons is a critical public health challenge. We developed targeted approaches to detect HIV RNA in persons with negative serological tests.

Methods—Persons undergoing publicly funded HIV testing in North Carolina between October, 2002 and April, 2005 were included in this cross-sectional study. We used logistic regression to develop targeted testing approaches. We also assessed simple approaches based on clinic type and geography. Algorithm development used persons with recent HIV infection, determined by a detuned ELISA. Validation used persons with acute HIV infection, identified with an HIV RNA pooling procedure.

Results—Among 215,528 eligible persons, 232 persons had recent HIV infection and 44 acute HIV infection. A combination of five indicators (testing site, sexual preference, sex with a person with HIV infection, county HIV incidence, and race) identified 92% of recent infections when testing 50% of the population. In validation among persons with acute HIV infection, this indicator combination had sensitivities of 98% in years 1 & 2 and 88% in year 3. A simple combination of testing site and county performed nearly as well (Development (recent infections): Sensitivity = 95%; Validation (acute infections): Sensitivity = 86% in years 1 & 2; 81% in year 3; cutoff established for testing 50% of population.)

Contact Information: William C. Miller, MD, PhD, MPH, Division of Infectious Diseases, CB #7030, 130 Manning Drive, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599-7435, Telephone: 919-966-9407; Fax: 919-966-6714, bill_miller@unc.edu.

Authors' Contributions

William Miller contributed to the study design and implementation, conducted the data analyses, and drafted the manuscript.
Peter Leone contributed to the study design, oversaw the development and implementation of the STAT program, and edited the manuscript.
Sandra McCoy assisted with implementation of the study, data management, and edited the manuscript.
Trang Nguyen assisted with study implementation, data management, data analyses, and edited the manuscript.
Del Williams contributed to study design, implementation, data collection, and reviewed the manuscript.
Christopher Pilcher contributed to study design and implementation and drafted and edited the manuscript

Conclusions—Acute HIV infection can be identified accurately using targeted testing. Simple approaches to identify the types of clinics and geographical areas where infections are concentrated may be logistically feasible and cost-efficient.

Introduction

Persons with acute HIV infection (AHI) contribute disproportionately to the transmission of HIV.[1,2] During the period of acute HIV infection prior to seroconversion, persons with newly acquired HIV infection develop high concentrations of virus in blood and genital secretions [3,4] and are likely to continue high risk behaviors.[5] High viral concentrations and risky behavior combine to increase transmission risk.[6]

Despite the public health importance of AHI, this syndrome is rarely recognized. Many persons with AHI develop symptoms consistent with acute retroviral syndrome,[7] but these symptoms are non-specific and often do not prompt medical care. Furthermore, when testing is performed during AHI, routine serological testing for HIV will be considered negative or indeterminate. Still, many persons with AHI undergo HIV testing during the acute period.[3,8-13] Identifying this group should be a priority. The addition of an HIV RNA screening step for HIV antibody negative specimens is an accurate, feasible approach to identifying persons with AHI.[8,9, 12]

To date, however, North Carolina (NC) remains the only state in the United States to use a comprehensive testing strategy including HIV RNA testing through a standardized pooling algorithm.[12,14] Many states might consider the costs of implementing this program to be prohibitive, particularly in light of calls for greatly expanding testing of low-risk persons by the CDC.[15] One approach to reducing costs is to reduce the number of tests required by targeting the testing to persons with the highest likelihood of infection.[16] To address this issue, we used data from the NC Screening and Tracing Acute HIV Transmission (STAT) program to develop a risk assessment model at the individual level. We also examined performance of models based on simple criteria (geography and clinic type), which would be easier to implement in testing programs. The models were developed using recently infected persons and validated in the population with AHI.

Methods

Study Design

This cross-sectional study was designed to develop and evaluate targeted testing criteria to detect AHI using program data collected by NC's HIV testing program. We included data from all publicly funded counseling and testing centers in NC.

Study Population

The study population comprised all persons undergoing HIV testing at publicly funded testing sites during the study period, October 22, 2002 to April 30, 2005. Testing was confidential and linked to patient information using a system of unique identifiers according to state public health statutes. Persons provided informed consent for HIV testing according to the state protocol. All persons identified to have HIV infection were contacted by Disease Intervention Specialists and partner tracing was routinely performed. The procedures of this study were approved by the University of North Carolina Institutional Review Board.

The study population was restricted to persons older than 10 years of age. For analyses, the following persons were excluded: 1) county of residence or zip code outside of NC, 2) established HIV infection, or 3) missing demographic information.

Data Collection – Patient Information

Persons presenting for HIV testing in NC routinely provide personal information during pre-test counseling. This information includes age, sex, race, insurance, reason for visit, and HIV risk category. The type of testing site, residential county and residential zip code were also recorded. The location of the testing site was not considered during model development.

In addition to the routinely collected data from the testing centers, we used reported HIV case surveillance data to estimate HIV disease burden in each county of residence.[17] Both number of cases and incidence rate were used for the two years preceding the date of testing.

Data Collection – HIV Testing

Sera submitted for HIV testing were processed centrally at the NC State Laboratory of Public Health and maintained at -70°C. A standard Vironostika HIV-1 EIA (bioMerieux, Durham NC) and western blot (BioRad, Hercules, CA) were used for antibody screening. Specimens with negative or indeterminate antibody test results were tested with PCR for the presence of RNA using a specimen pooling algorithm to increase specificity and reduce costs.[12,13] Persons with antibody negative-RNA positive results indicative of AHI were contacted by specialists in disease intervention, interviewed and asked to provide additional samples for confirmatory testing.

In addition to these standard testing procedures, we sought to identify persons with recent HIV infection among those with positive sera. During early HIV infection, antibodies are typically of low titer and avidity. We used a de-tuned antibody testing procedure (a “less-sensitive” HIV antibody EIA that remains negative for an average of 170 days after a standard “sensitive” antibody EIA becomes positive) to identify recent infections.[18] For this study, sera that were positive by the standard antibody EIA/western blot were made anonymous by recoding unique identifiers and then re-tested by a CDC-certified laboratory using a less-sensitive HIV antibody EIA based on the Vironostika kit.[18]

HIV Outcome Definitions

We defined *HIV negative* as a person with negative HIV ELISA and negative HIV RNA nucleic acid amplification test (NAAT) at initial or subsequent testing. We defined *acute HIV infection* as a person with a negative or indeterminate HIV antibody result and a positive HIV RNA test. We defined *recent HIV infection* as a person with positive HIV antibody result using routine HIV ELISA and western blot, but with a negative less-sensitive de-tuned ELISA, suggesting recent seroconversion. We defined *established HIV infection* as a person with positive ELISA, western blot and de-tuned ELISA.

Statistical Analyses

We performed all analyses using Stata SE, version 8.2 (StataCorp, College Station, TX). After initial examination of frequencies and distributions, the analyses proceeded in two stages – development and validation.

The study population was divided into two groups based on the period of data collection and infection status. To develop risk assessment strategies, we used data collected during the first two years of the program, and restricted the population to persons with recent HIV infection or no HIV infection. Validation of the sensitivity of the risk assessment strategies was initially performed using acute infections identified during this two year period. Further validation of sensitivity for detection of AHI and validation of specificity and the proportion of the population tested was performed with data collected during the first 6 months of the third year of data collection.

We developed the risk assessment procedure using the population comprising persons with recent HIV infection or no infection. We used recent HIV infection as the outcome because the number of persons with AHI was small, thereby limiting model stability. We initially examined the bivariable relationship between each candidate predictor variable and the outcome. For continuous variables, both continuous and categorical representations were evaluated. In each case, performance was comparable and only categorical representations are presented here. We excluded candidate predictor variables with small cell sizes in the bivariable analyses (cell size < 10 observations) from further analyses, including referrals for symptoms; client referral; referrals from drug treatment, family planning, prenatal, tuberculosis, court, immigration, or occupational settings; and the following reported risks – child of a woman with HIV, hemophilia, and health care exposure. Two variables, sex with a male and sex with a female, were excluded from multivariable models because of collinearity with the gender/sexual preference variable.

We used multiple logistic regression to develop a model-based individual risk assessment procedure. We identified candidate predictor variables in bivariable analyses using simple logistic regression. Prevalence odds ratios (OR) with 95% confidence intervals were estimated. Those variables associated with recent HIV infection with $p<0.20$ in bivariable analyses were included in the full logistic model.[19] In initial models, we examined continuous variables in continuous form with a linear term and assessed the gain in prediction obtained with quadratic spline terms. Given, however, that the goal of the model building was easily implementable risk assessment at the clinic level, continuous variables were categorized prior to model reduction. We used a manual backward elimination procedure based on likelihood ratio tests to reduce the model to a parsimonious form. After elimination of each variable, the area under the receiver operating characteristic (ROC) curve was assessed to evaluate model accuracy. Model reduction was discontinued when $p < 0.05$ for all remaining variables. In addition to the stopping criteria based on p-value, we examined Akaike's Information Criterion and the Bayesian Information Criterion with similar results. Goodness of fit was examined with the Hosmer-Lemeshow test.

The principal goal in the development of the risk assessment strategies was to reduce the number of persons referred for pooled HIV RNA testing. Consequently, the principal results of interest are the sensitivity and the proportion of the population that would be tested with a given strategy. For multivariable models, we determined cutoffs from the predicted probabilities derived from each unique combination of variables. We then identified those cutoffs that would limit the population tested to 70% or 50% of the total population. We also examined a cutoff that would yield sensitivity ≥ 90%.

In addition to the model-based individual risk-assessment, we developed simple criteria using information that would be readily available to a health agency. These criteria were based on clinic-type and geographical area to provide a simple strategy for implementation at a central testing laboratory.

Results

During the first two years of the project (development phase), 227162 persons underwent testing in public NC testing centers. Of these, 3045 (1.3%) reported home addresses out of NC. Among the remaining 224117 persons, 224087 (99.99%) had valid county or zip code information.

Using our definitions of HIV status, we identified 875 (0.39%) persons with newly diagnosed but established HIV infection, who were excluded from further analyses. Recent HIV infection

was identified in 237 (0.11%) and AHI in 44 (0.02%). The remaining population (n=222931, 99.48%) were considered HIV negative by serology and pooled HIV RNA screening.

To develop risk assessment strategies, we restricted the population to persons with recent or no HIV infection and complete demographic and behavioral information (n=215528). Persons with AHI were used in the validation phase. This complete case dataset excluded 5 (2.1%) persons with recent HIV infection and 7679 (3.4%) persons without HIV infection who were missing demographic or behavioral information.

Testing was performed in an STD setting most frequently (41.5%; Table 1). Nearly half of the population was African American (45.4%). Two-thirds of the population was female (66.3%), with 30.2% heterosexual men and 3.5% men who have sex with men.

Model Development

In bivariable (unadjusted) models, MSM were much more likely than women to have recent HIV infection (OR 24.5, 95% CI: 18.0-33.3). Heterosexual men were about twice as likely as women to have recent HIV infection (Table 1). The most important reported risk factors were sexual intercourse with an HIV-infected person (OR 19.1, 95% CI: 14.0-26.0) and sexual intercourse with MSM (OR 15.6, 95% CI: 11.8-20.6). However, a small proportion of the population reported these risks (1.5% and 2.9%, respectively). Persons living in counties with more than 200 reported cases of HIV infection during the 2 years prior to testing were also more likely to have recent HIV infection (OR 4.7, 95% CI: 2.6-8.4), compared to persons living in counties with 0-10 cases. Testing site was also strongly associated with infection status. Several testing sites, including family planning, tuberculosis, antenatal, drug treatment, and community health centers, had particularly low prevalence of recent infection (0.014%).

In multivariable models, demographics including sexual preference, testing site, and geographical location were important predictors of recent HIV infection (Table 2). Sexual intercourse with an HIV-infected person was the only reported risk behavior associated with infection status. In the full model, the overall accuracy was reasonably high (ROC area 0.867). Reduction of the model had minimal effect on overall accuracy (ROC area 0.861).

Model Performance

Both the full and reduced model showed reasonable performance. In each case, a cutoff chosen to test 50% of the population would have identified ~92% of persons with recent HIV infection (Table 3). Testing 70% of the population would have identified ~98% of infections. Identification of 90% of persons with recent infection would require testing 40-43% of the population using the reduced or full model.

Model Validation

We validated model performance in two groups. First, we examined the sensitivity of the models for detecting persons with AHI during Years 1 & 2. Note that the models were developed using persons with recent infection, excluding those with acute infection. The sensitivity of the full and reduced models for AHI was >90% in all cases, comparable to the sensitivity in model development (Table 4).

We also examined the performance of the models in the first half of Year 3, evaluating sensitivity in a limited population of persons with AHI, specificity and proportion of the population tested. In both the full and reduced model, testing ~70% of the population would have detected 94% of the persons with AHI. Using the cutoffs for 50% of the population led to identification of 87.5% of the cases. Using the cutoff for sensitivity >90% also identified 87.5%, but resulted in only ~40% of the population undergoing testing.

Simple Criteria

To provide alternative simple criteria, we examined the potential of targeting testing based on the type of testing site and geographical location. These group level variables provide a more feasible strategy for implementation.

Limiting testing to single types of testing sites (e.g. STD clinics) was inadequate. In the development period (Years 1 & 2), restricting testing to STD clinics only identified ~40% of recent infections, while testing about 40% of the population (Table 3), indicating little enrichment for recent infections in the STD clinics as compared to the full population. Testing in the Counseling and Testing Sites (CTS) yielded 34% of the infections, but represented only 10% of the population.

Several types of testing sites yielded very few infections. If testing for recent infection was limited to CTS, STD, prison/jail, field visits, and “other”, while excluding family planning, tuberculosis, antenatal, drug treatment and community health centers, 95% of recent infections would have been detected, but only 64% of the population would have been tested.

By combining the site type information and the geographical region of the state, we could improve performance substantially. If testing was restricted to counties with >1 case over the two years, and simultaneously limited to the higher risk testing sites (CTS, STD, prison/jail, field visits, and other), 95% of the recent infections would have been identified while testing 53% of the population. This performance is comparable to the model-based criteria.

Simple Criteria – Validation Period

Generally, performance of the simple criteria in the validation samples was comparable to that in the development period with a few exceptions (Table 4). Restricting to the higher risk clinics only would have detected 97.7% of AHI in Years 1&2, but only 87.5% of infections in Year 3. These clinics represented 64% of the population. Adding the restriction of counties with at least 1 recent case reduced the population tested to 54%, but only 81% of AHI in Year 3 would have been identified.

Antenatal Clinics

Pregnant women represent a special group because of the potential to prevent HIV infection in their infants. We examined the effect of adding the antenatal clinics to the simple criteria described above. Adding the antenatal (OB) clinics to the higher risk testing sites increased sensitivity slightly, but led to substantially more of the population being tested (Table 3). These changes were consistent in the validation groups (Table 4).

Discussion

In an effort to assist programs to identify persons with AHI efficiently, we examined both model-based and simple criteria for predicting persons with higher likelihood of AHI. Our primary goal was to reduce the number of persons requiring special testing to identify AHI while simultaneously identifying a large proportion of persons with AHI. Using simple criteria (testing site and county of residence), we were able to identify 80-95% of persons with AHI while testing ~54% of the population. More complex, model-based criteria performed similarly.

In the development phase, we used recent HIV infection as our primary outcome, rather than AHI. We made this decision for three reasons. First, the number of persons with AHI was small (~5% of the total number of persons with HIV infection in our sample), thereby reducing the stability of model estimates. Second, excluding AHI in Years 1 & 2 gave us a separate study

sample to validate the sensitivity of the risk assessment criteria. Finally, and perhaps most importantly, we recognized that most jurisdictions are not currently using the pooled testing algorithm for AHI, but might have access, or could gain access, to data regarding recent HIV infections using CDC- and WHO-endorsed tests for recent infection. These data can be obtained through standard surveillance procedures with the addition of "detuned" ELISA testing. Therefore, by demonstrating that this process yielded a reasonable risk assessment strategy, we believe other areas could replicate our efforts locally.

Model-based strategies for risk assessment included a limited number of predictors for HIV infection. Reduction of the model had relatively little effect on model accuracy. Consequently, five variables, sexual preference, testing site, county, race, and sexual exposure to a person with HIV infection were sufficient to predict recent (and acute) HIV infection with reasonable accuracy. In particular, men who have sex with men had a substantially greater likelihood of infection than heterosexual men or women.

Despite the reasonable accuracy of the model-based strategies, individual-level risk assessment would be challenging programmatically. The individual strategy would require each specimen to be sorted, adding to data management and technician costs. In contrast, the strategies using simple criteria could be sorted as a group (e.g., by using separate forms distributed to targeted clinics), reducing the work required. Given that performance of the simple strategies was reasonably comparable to the model-based strategies, we feel that from a programmatic perspective, this approach is preferable.

AHI testing is not without cost, but is likely to be highly cost-effective. In our previous work, we found that pooled RNA testing added $3.63 to the cost of testing each specimen in North Carolina (nearly doubling the per-specimen testing cost in this moderate-prevalence state).[12] From a societal perspective, though, these costs were largely offset by the downstream costs associated with transmission by acutely infected clients.[20,21] Identifying AHI in pregnant women may be particularly cost-effective,[20] due to the lifetime of costs associated with transmission to an infant. However, women attending antenatal clinics are at very low risk for AHI. In the present study, testing women attending antenatal clinics had minimal effects on the sensitivity of the risk assessment, but increased the number of women referred for testing. From a purely programmatic perspective, testing for these women might not be warranted. However, from a societal perspective considering cost-effectiveness, identification of even a small number of pregnant women with AHI could be critically important. Ultimately, programs will need to determine the level of cost that can be incurred to detect AHI. Future efforts must also consider the potential utility of standard tests with greater sensitivity to detect HIV.

This tension between the programmatic cost and societal cost-effectiveness is highly germane in the current era, where HIV testing in the US is being expanded to include low-risk groups (e.g., clients routine primary health care[15] that would be expected to have a much lower risk of AHI than groups that are currently offered voluntary counseling and testing at most public testing sites. Formal cost-effectiveness analyses assessing both universal and targeted testing scenarios, as well as the use of alternative initial testing strategies, could be a valuable tool in assessing optimal local strategies for acute HIV testing.[21]

Identifying persons with AHI is a laudable public health goal. Persons with AHI have high viral loads in both blood and genital secretions, facilitating transmission.[3,4] Identifying and intervening with persons with AHI has the potential to reduce onward transmission. Furthermore, identifying persons at the earliest possible point in their course of HIV infection provides an opportunity to engage these persons in HIV care and potentially diminish transmission throughout the course of their disease. In NC, implementation of this program has provided key insights into an ongoing HIV outbreak among young African American men

who have sex with men.[22] The identification of this outbreak has led to several new initiatives to address transmission with this group.

Despite the importance of AHI, efforts to identify persons with acute infection have not been given high priority by national or global public health authorities, primarily because of perceived and real costs. Using a rational approach to targeting acute infection testing to those at greater risk, we have demonstrated that one could reduce the number of specimens requiring acute HIV testing by about 50% while still detecting 80-90% of infections. Based on these data, we propose that careful assessment of the testing sites that are responsible for the majority of recent infections in a public health jurisdiction could provide a useful mechanism to implement a testing strategy for AHI. If the identification of persons with AHI can be targeted to clinical settings where it is most likely to be detected on a wide scale, the potential to reduce the burden of HIV disease in this country is substantial.

Acknowledgments

We are indebted to the staff of the North Carolina State Laboratory of Public Health Serology/Virology Laboratory for all antibody testing and nucleic acid amplification testing for the North Carolina Department of Health and Human Services Screening and Tracing Active Transmission program, the University of North Carolina Center for AIDS Research Retrovirology Core Laboratory, and to the Disease Intervention Specialists of the HIV/STD Prevention and Care Branch of the North Carolina Department of Health and Human Services. We are also indebted to Evelyn Foust and Dr. Steve Cline for leadership within the North Carolina Department of Health and Human Services.

Grant Support: Supported by the National Institutes of Health (NIMH-R01 068686).

References

1. Brenner BG, Roger M, Routy JP, et al. High rates of forward transmission events after acute/early HIV-1 infection. J Infect Dis 2007;195:951–959. [PubMed: 17330784]
2. Wawer MJ, Gray RH, Sewankambo NK, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. J Infect Dis 2005;191:1403–1409. [PubMed: 15809897]
3. Pilcher CD, Joaki G, Hoffman IF, et al. Amplified transmission of HIV-1: comparison of HIV-1 concentrations in semen and blood during acute and chronic infection. AIDS 2007;21:1723–1730. [PubMed: 17690570]
4. Pilcher CD, Eron JJ Jr, Galvin S, Gay C, Cohen MS. Acute HIV revisited: new opportunities for treatment and prevention. J Clin Invest 2004;113:937–945. [PubMed: 15057296]
5. Colfax GN, Buchbinder SP, Cornelisse PG, Vittinghoff E, Mayer K, Celum C. Sexual risk behaviors and implications for secondary HIV transmission during and after HIV seroconversion. AIDS 2002;16:1529–1535. [PubMed: 12131191]
6. Koopman JS, Jacquez JA, Welch GW, et al. The role of early HIV infection in the spread of HIV through populations. J Acquir Immune Defic Syndr Hum Retrovirol 1997;14:249–258. [PubMed: 9117458]
7. Kelley CF, Barbour JD, Hecht FM. The relation between symptoms, viral load, and viral load set point in primary HIV infection. J Acquir Immune Defic Syndr 2007;45:445–448. [PubMed: 17514014]
8. Priddy FH, Pilcher CD, Moore RH, et al. Detection of acute HIV infections in an urban HIV counseling and testing population in the United States. J Acquir Immune Defic Syndr 2007;44:196–202. [PubMed: 17312561]
9. Patel P, Klausner JD, Bacon OM, et al. Detection of acute HIV infections in high-risk patients in California. J Acquir Immune Defic Syndr 2006;42:75–79. [PubMed: 16763493]
10. Pincus JM, Crosby SS, Losina E, King ER, LaBelle C, Freedberg KA. Acute human immunodeficiency virus infection in patients presenting to an urban urgent care center. Clin Infect Dis 2003;37:1699–1704. [PubMed: 14689354]
11. Stekler J, Swenson PD, Wood RW, Handsfield HH, Golden MR. Targeted screening for primary HIV infection through pooled HIV-RNA testing in men who have sex with men. AIDS 2005;19:1323–1325. [PubMed: 16052089]

12. Pilcher CD, Fiscus SA, Nguyen TQ, et al. Detection of acute infections during HIV testing in North Carolina. N Engl J Med 2005;352:1873–1883. [PubMed: 15872202]

13. Pilcher CD, McPherson JT, Leone PA, et al. Real-time, universal screening for acute HIV infection in a routine HIV counseling and testing population. JAMA 2002;288:216–221. [PubMed: 12095386]

14. Sherlock M, Zetola NM, Klausner JD. Routine detection of acute HIV infection through RNA pooling: survey of current practice in the United States. Sex Transm Dis 2007;34:314–316. [PubMed: 17483725]

15. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep 2006;55:1–17. [PubMed: 16988643]

16. Busch MP, Hecht FM. Nucleic acid amplification testing for diagnosis of acute HIV infection: has the time come? AIDS 2005;19:1317–1319. [PubMed: 16052087]

17. Epidemiology & Special Studies Unit. Raleigh, NC: HIV/STD Prevention and Care Branch, North Carolina Department of Health and Human Services; 2006 [06/03/2008]. North Carolina 2005 HIV/STD Surveillance Report. http://www.epi.state.nc.us/epi/hiv/pdf/std05rpt.pdf

18. Janssen RS, Satten GA, Stramer SL, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. JAMA 1998;280:42–48. [PubMed: 9660362]

19. Sun GW, Shook T, Kay G. Inappropriate use of bivariable analysis to screen risk factors for use in multivariable analysis. Journal of Clinical Epidemiology 1996;49:907–916. [PubMed: 8699212]

20. Patterson KB, Leone PA, Fiscus SA, et al. Frequent detection of acute HIV infection in pregnant women. AIDS 2007;21:2303–2308. [PubMed: 18090278]

21. Simpson, K.; Biddle, A.; Leone, P., et al.. Cost Effectiveness of Screening for Acute HIV Infection: The North Carolina STAT Program. Conference on Retroviruses and Opportunistic Infections; Denver, CO. 2006.

22. Hightow LB, MacDonald PD, Pilcher CD, et al. The unexpected movement of the HIV epidemic in the Southeastern United States: transmission among college students. J Acquir Immune Defic Syndr 2005;38:531–537. [PubMed: 15793362]

Table 1

Characteristics, prevalence and associations with recent HIV infection among persons undergoing HIV testing in North Carolina (Development Data; n = 215,484)

Characteristic	N	(%)	Prev (%)	OR	(95%CI)	p-value
Age						
> 40 years	30208	(14.0)	0.199	2.1	(1.6 - 2.9)	<0.001
≤ 40 years	185276	(86.0)	0.093	Ref		
Race						
African American	97818	(45.4)	0.156	2.3	(1.8 - 3.1)	<0.001
White/Other	117666	(54.6)	0.067	Ref		
Gender/Sexual Preference						
MSM	7495	(3.5)	1.254	24.5	(18.0 - 33.3)	<0.001
Heterosexual Male	65179	(30.2)	0.098	1.9	(1.4 - 2.6)	<0.001
Female	142810	(66.3)	0.052	Ref		
Test Site						
CTS	22193	(10.3)	0.360	25.8	(13.7 - 48.4)	<0.001
STD	89429	(41.5)	0.102	7.3	(3.9 - 13.6)	<0.001
Prison/Jail	5550	(2.6)	0.162	11.6	(4.8 - 27.9)	<0.001
Field	5250	(2.4)	0.324	23.1	(10.8 - 49.4)	<0.001
Other	14728	(6.8)	0.163	11.6	(5.7 - 23.7)	<0.001
FP/TB/OB/Drug treatment/CHC	78334	(36.4)	0.014	Ref		
HIV Cases (Surveillance)						
> 200	64921	(30.1)	0.173	4.7	(2.6 - 8.4)	<0.001
51-200	45454	(21.1)	0.106	2.8	(1.5 - 5.4)	0.001
11-50	72791	(33.8)	0.082	2.2	(1.2 - 4.1)	0.012
0-10	32318	(15.0)	0.037	Ref		
Risk - Sex with HIV(+) Person						
Yes	3336	(1.5)	1.589	19.1	(14.0 - 26.0)	<0.001
No	212148	(98.5)	0.084	Ref		
Risk - Exchange Sex						
Yes	7362	(3.4)	0.231	2.2	(1.4 - 3.7)	0.001
No	208122	(96.6)	0.103	Ref		

Characteristic	N	(%)	Prev (%)	OR	(95%CI)	p-value
Risk - Sex with IDU						
Yes	5992	(2.8)	0.184	1.7	(1.0 - 3.2)	0.073
No	209492	(97.2)	0.105	Ref		
Risk - Assault Victim						
Yes	11778	(5.5)	0.153	1.5	(0.9 - 2.4)	0.127
No	203706	(94.5)	0.105	Ref		
Risk - IDU						
Yes	4893	(2.3)	0.266	2.6	(1.5 - 4.5)	0.001
No	210591	(97.7)	0.104	Ref		
Risk - Sex with MSM						
Yes	6355	(2.9)	1.164	15.6	(11.8 - 20.6)	<0.001
No	209129	(97.1)	0.076	Ref		
Risk - Other						
Yes	38503	(17.9)	0.148	1.5	(1.1 - 2.0)	0.008
No	176981	(82.1)	0.099	Ref		
Reason for Test - STD						
Yes	13762	(6.4)	0.153	1.5	(0.9 - 2.3)	0.099
No	201722	(93.6)	0.105	Ref		
Reason for Test - Retest						
Yes	12105	(5.6)	0.173	1.7	(1.1 - 2.6)	0.025
No	203379	(94.4)	0.104	Ref		
Reason for Test - Request Test						
Yes	101494	(47.1)	0.160	2.6	(2.0 - 3.4)	<0.001
No	113990	(52.9)	0.061	Ref		
Provider Referral						
Yes	3938	(1.8)	0.279	2.7	(1.5 - 4.9)	0.001
No	211546	(98.2)	0.104	Ref		
Risk - STD Diagnosis						
Yes	62290	(28.9)	0.111	1.0	(0.8 - 1.4)	0.779
No	153194	(71.1)	0.106	Ref		
Risk - Non-injection Drug Use						
Yes	41377	(19.2)	0.114	1.1	(0.8 - 1.5)	0.683

AIDS. Author manuscript; available in PMC 2010 April 27.

Characteristic	N	(%)	Prev (%)	OR	(95%CI)	p-value
No	174107	(80.8)	0.106	Ref		
Risk - Sex with Male						
Yes	145186	(67.4)	0.114	1.2	(0.9 - 1.6)	0.175
No	70298	(32.6)	0.094	Ref		
Risk - Sex with Female						
Yes	72143	(33.5)	0.147	1.7	(1.3 - 2.2)	<0.001
No	143341	(66.5)	0.088	Ref		

Prev (%) = prevalence of recent HIV infection, expressed as a percentage or the number of cases per 100 persons

FP/TB/OB/Drug treatment/CHC = Testing site was family planning, tuberculosis, antenatal, drug treatment or community health center setting

HIV Cases (surveillance) = Number of newly reported HIV cases in the county of residence over the previous two years

AIDS. Author manuscript; available in PMC 2010 April 27.

Table 2

Full and reduced multivariable predictive models for recent HIV infection among persons undergoing HIV testing in North Carolina (Development Data; n = 215,484)

	Full Model			Reduced Model		
Characteristic	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Age						
> 40 years	1.2	(0.9 - 1.6)	0.275			
≤ 40 years	Ref					
Race						
African American	2.7	(2.0 - 3.6)	<0.001	2.7	(2.0 - 3.5)	<0.001
White/Other	Ref			Ref		
Gender/Sexual Preference						
MSM	8.4	(5.4 - 13.2)	<0.001	10.5	(7.8 - 14.2)	<0.001
Heterosexual Male	1.1	(0.8 - 1.5)	0.711	Ref		
Female	Ref			Ref		
Test Site						
CTS	9.1	(4.5 - 18.3)	<0.001	10.5	(5.5 - 20.1)	<0.001
STD	3.7	(1.9 - 7.2)	<0.001	4.3	(2.3 - 8.0)	<0.001
Prison/Jail	5.7	(2.2 - 14.8)	<0.001	6.7	(2.8 - 16.4)	<0.001
Other	5.5	(2.4 - 12.7)	<0.001	6.7	(3.1 - 14.8)	<0.001
Field	3.9	(1.8 - 8.4)	0.001	4.5	(2.1 - 9.4)	<0.001
FP/TB/OB/Drug treatment/CHC	Ref			Ref		
HIV Cases (Surveillance)						
> 200	2.1	(1.1 - 3.8)	0.019	2.0	(1.1 - 3.7)	0.022
51-200	1.8	(0.9 - 3.3)	0.085	1.7	(0.9 - 3.3)	0.098
11-50	1.9	(1.0 - 3.5)	0.052	1.8	(1.0 - 3.4)	0.060
0-10	Ref			Ref		
Risk - Sex with HIV(+) Person						
Yes	4.2	(2.9 - 6.0)	<0.001	4.7	(3.3 - 6.6)	<0.001
No	Ref			Ref		
Risk - Exchange Sex						

	Full Model			Reduced Model		
Characteristic	**OR**	**(95% CI)**	**p-value**	**OR**	**(95% CI)**	**p-value**
Yes	0.9	(0.5 - 1.5)	0.582			
No	Ref					
Risk - Sex with IDU						
Yes	0.9	(0.4 - 1.7)	0.688			
No	Ref					
Risk - Assault Victim						
Yes	1.4	(0.8 - 2.3)	0.196			
No	Ref					
Risk - IDU						
Yes	1.7	(0.9 - 3.3)	0.100			
No	Ref					
Risk - Sex with MSM						
Yes	1.5	(1.0 - 2.4)	0.075			
No	Ref					
Risk - Other						
Yes	1.1	(0.8 - 1.6)	0.477			
No	Ref					
Reason for Test - STD						
Yes	1.6	(0.9 - 2.6)	0.087			
No	Ref					
Reason for Test - Retest						
Yes	0.8	(0.5 - 1.3)	0.400			
No	Ref					
Reason for Test - Request Test						
Yes	1.1	(0.8 - 1.6)	0.582			
No	Ref					
Provider Referral						
Yes	1.6	(0.8 - 3.1)	0.146			
No	Ref					

AIDS. Author manuscript; available in PMC 2010 April 27.

Ref = Referent

FP/TB/OB/Drug treatment/CHC = Testing site was family planning, tuberculosis, antenatal, drug treatment or community health center setting

HIV Cases (surveillance) = Number of newly reported HIV cases in the county of residence over the previous two years

Table 3

Performance of model-based and simple criteria for detection of recent HIV infection

	Recent HIV Infection (n=232)		No HIV Infection (n=215252)		Total Population (n=215484)	
	Sensitivity	**(95% CI)**	**Specificity**	**(95% CI)**	**Proportion Tested**	**(95% CI)**
Model-Based Criteria						
Full Model						
Test <70%	0.987	(0.972 - 1.002)	0.300	(0.298 - 0.302)	0.700	(0.698 - 0.702)
Test <50%	0.927	(0.893 - 0.961)	0.405	(0.402 - 0.407)	0.498	(0.496 - 0.500)
Sens >90%	0.901	(0.862 - 0.940)	0.596	(0.594 - 0.598)	0.404	(0.402 - 0.406)
Reduced Model						
Test <70%	0.983	(0.966 - 1.000)	0.323	(0.321 - 0.325)	0.678	(0.676 - 0.680)
Test <50%	0.922	(0.888 - 0.957)	0.442	(0.439 - 0.444)	0.486	(0.484 - 0.488)
Sens >90%	0.901	(0.862 - 0.940)	0.574	(0.571 - 0.576)	0.427	(0.425 - 0.429)
Simple Criteria						
Testing Site						
CTS Only	0.345	(0.283 - 0.406)	0.897	(0.896 - 0.899)	0.103	(0.102 - 0.104)
STD Only	0.392	(0.329 - 0.456)	0.585	(0.583 - 0.587)	0.415	(0.413 - 0.417)
CTS/STD/Jail/Field/Other	0.953	(0.925 - 0.980)	0.364	(0.362 - 0.366)	0.636	(0.634 - 0.639)
County Cases						
Counties with >1 recent case	1.000	(1.000 - 1.000)	0.201	(0.200 - 0.203)	0.799	(0.797 - 0.800)
Combined Criteria						
County & High Yield Clinic	0.953	(0.925 - 0.980)	0.467	(0.465 - 0.469)	0.533	(0.531 - 0.535)
Incorporating Antenatal Sites						
CTS/STD/Jail/Field/Oth/OB	0.970	(0.948 - 0.992)	0.196	(0.194 - 0.198)	0.804	(0.803 - 0.806)
County & High Yield or OB Clinic	0.970	(0.948 - 0.992)	0.345	(0.343 - 0.347)	0.656	(0.654 - 0.658)

AIDS. Author manuscript; available in PMC 2010 April 27.

AIDS. Author manuscript; available in PMC 2010 April 27.

Table 4

Validation of performance of model-based and simple criteria

	Acute HIV Infection (Years 1 & 2) (n=44)		Acute HIV Infection (6 months, Year 3) (n=16)		No HIV Infection (6 months, Year 3) (n=58674)		Total Population (6 months, Year 3) (n=58690)	
	Sens	**(95% CI)**	**Sens**	**(95% CI)**	**Spec**	**(95% CI)**	**Prop Tested**	**(95% CI)**
Model-Based Criteria								
Full Model[1]								
Test <70%	1.000	(1.000 - 1.000)	0.938	(0.804 - 1.071)	0.300	(0.296 - 0.304)	0.700	(0.696 - 0.704)
Test <50%	0.977	(0.931 - 1.023)	0.875	(0.693 - 1.057)	0.523	(0.519 - 0.527)	0.477	(0.473 - 0.481)
Sensitivity >90%	0.932	(0.854 - 1.009)	0.875	(0.693 - 1.057)	0.602	(0.598 - 0.606)	0.398	(0.394 - 0.402)
Reduced Model[2]								
Test <70%	1.000	(1.000 - 1.000)	0.938	(0.804 - 1.071)	0.321	(0.317 - 0.324)	0.679	(0.676 - 0.683)
Test <50%	0.977	(0.931 - 1.023)	0.875	(0.693 - 1.057)	0.515	(0.511 - 0.519)	0.485	(0.481 - 0.489)
Sensitivity >90%	0.955	(0.890 - 1.019)	0.875	(0.693 - 1.057)	0.576	(0.572 - 0.580)	0.424	(0.420 - 0.428)
Simple Criteria								
Testing Site								
CTS Only	0.205	(0.080 - 0.329)	0.188	-(0.027 - 0.402)	0.907	(0.905 - 0.909)	0.093	(0.091 - 0.096)
STD Only	0.455	(0.301 - 0.608)	0.500	(0.225 - 0.775)	0.577	(0.573 - 0.581)	0.423	(0.419 - 0.427)
CTS/STD/Jail/Field/Other	0.977	(0.931 - 1.023)	0.875	(0.693 - 1.057)	0.363	(0.359 - 0.367)	0.637	(0.633 - 0.641)
County Cases								
Counties with >1 recent case	0.886	(0.789 - 0.984)	0.813	(0.598 - 1.027)	0.193	(0.190 - 0.197)	0.807	(0.803 - 0.810)
Combined Criteria								
County & High Yield Clinic	0.864	(0.758 - 0.969)	0.813	(0.598 - 1.027)	0.462	(0.458 - 0.466)	0.538	(0.534 - 0.542)
Incorporating Antenatal Sites								
CTS/STD/Jail/Field/Oth/OB	1.000	(1.000 - 1.000)	0.938	(0.804 - 1.071)	0.201	(0.198 - 0.204)	0.799	(0.796 - 0.802)
County & High Yield or OB Clinic	0.886	(0.789 - 0.984)	0.813	(0.598 - 1.027)	0.343	(0.339 - 0.347)	0.657	(0.653 - 0.661)

[1] Probability based cutoffs = ≥0.0002097544, ≥0.0003901102, and ≥0.0005905231, respectively

[2] Probability based cutoffs = ≥0.0002338851, ≥0.0004015853, and ≥0.0004757698, respectively

Prop tested = Proportion tested