The Current Status of HIV Testing

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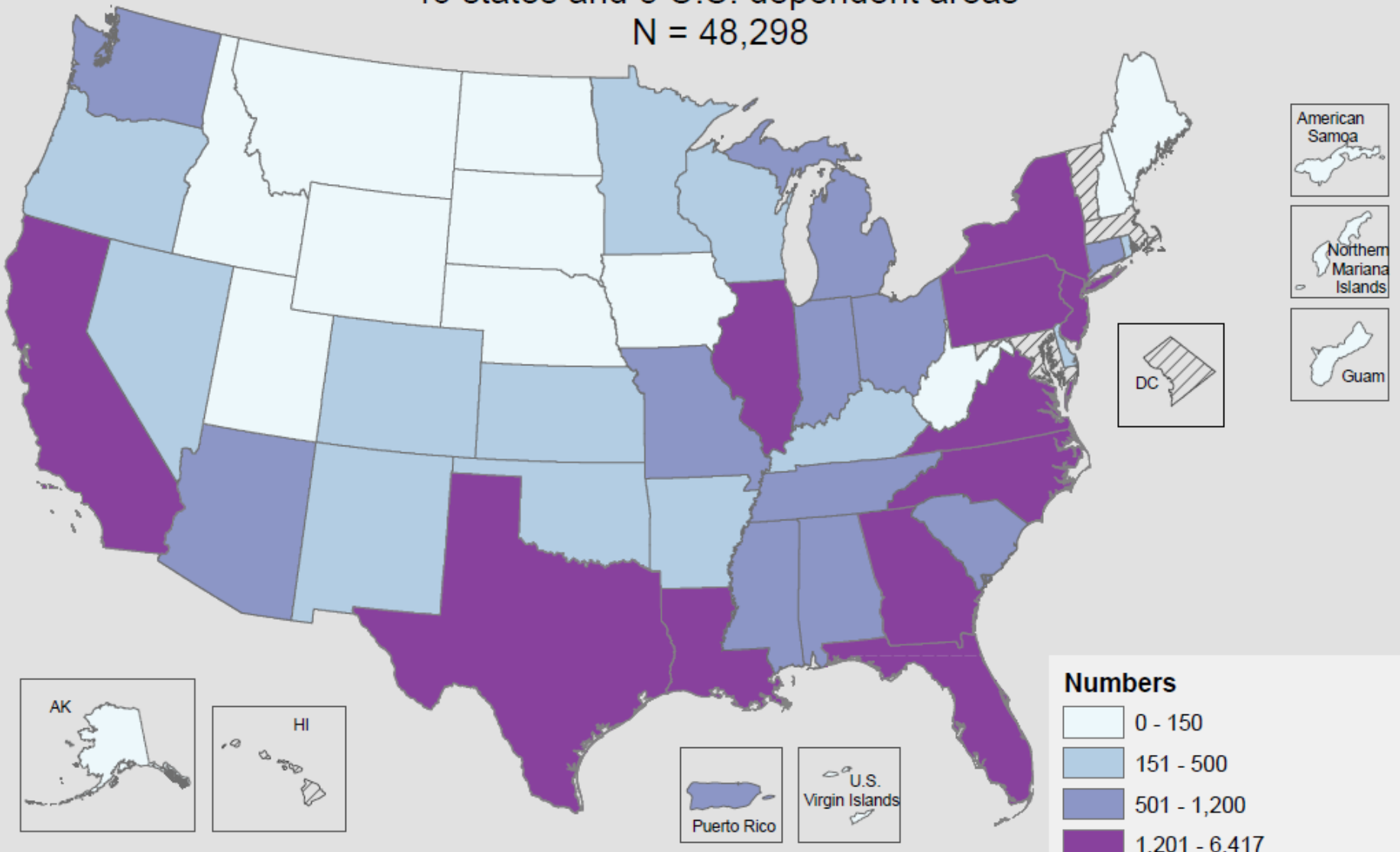
Director of Scientific Affairs

Learning Objectives

- Define the current state of the HIV epidemic and trends in HIV Diagnosis
- Cite the CDC & Medical Organization recommendations for routine HIV testing
- Understand the importance of routine HIV testing in the POL setting and clinics
- Describe the strategies for HIV Testing in Clinic & POL Settings

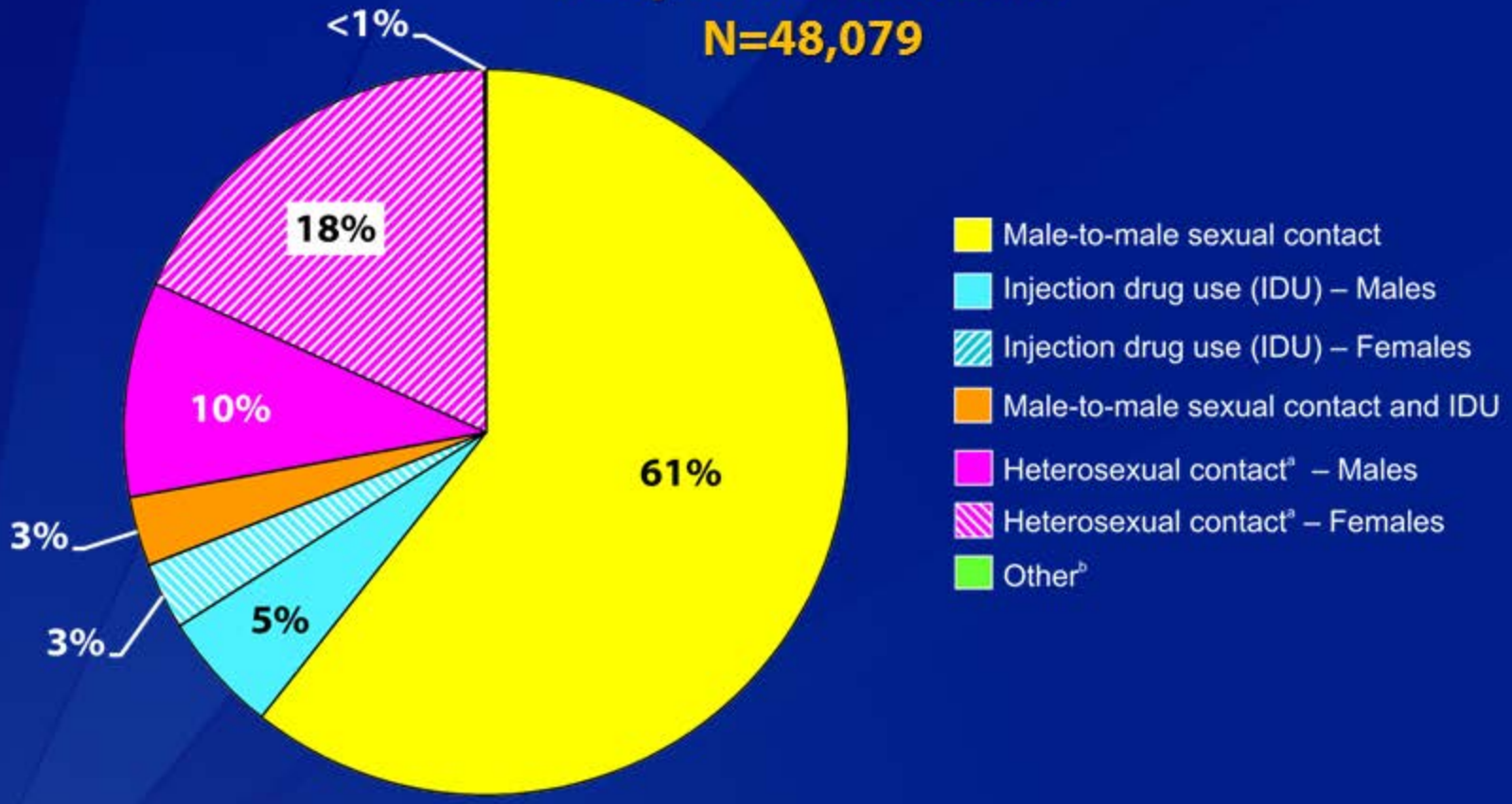
Diagnoses of HIV infection, 2010 - 46 states and 5 U.S. dependent areas N = 48,298



Notes. Data include persons with a diagnosis of HIV infection regardless of the stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
Data source: http://www.cdc.gov/hiv/surveillance/resources/reports/2010report/index.htm
Inset maps not to scale. Map colors based on www.colorbrewer2.org.

Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2010—46 States and 5 U.S. Dependent Areas

N=48,079

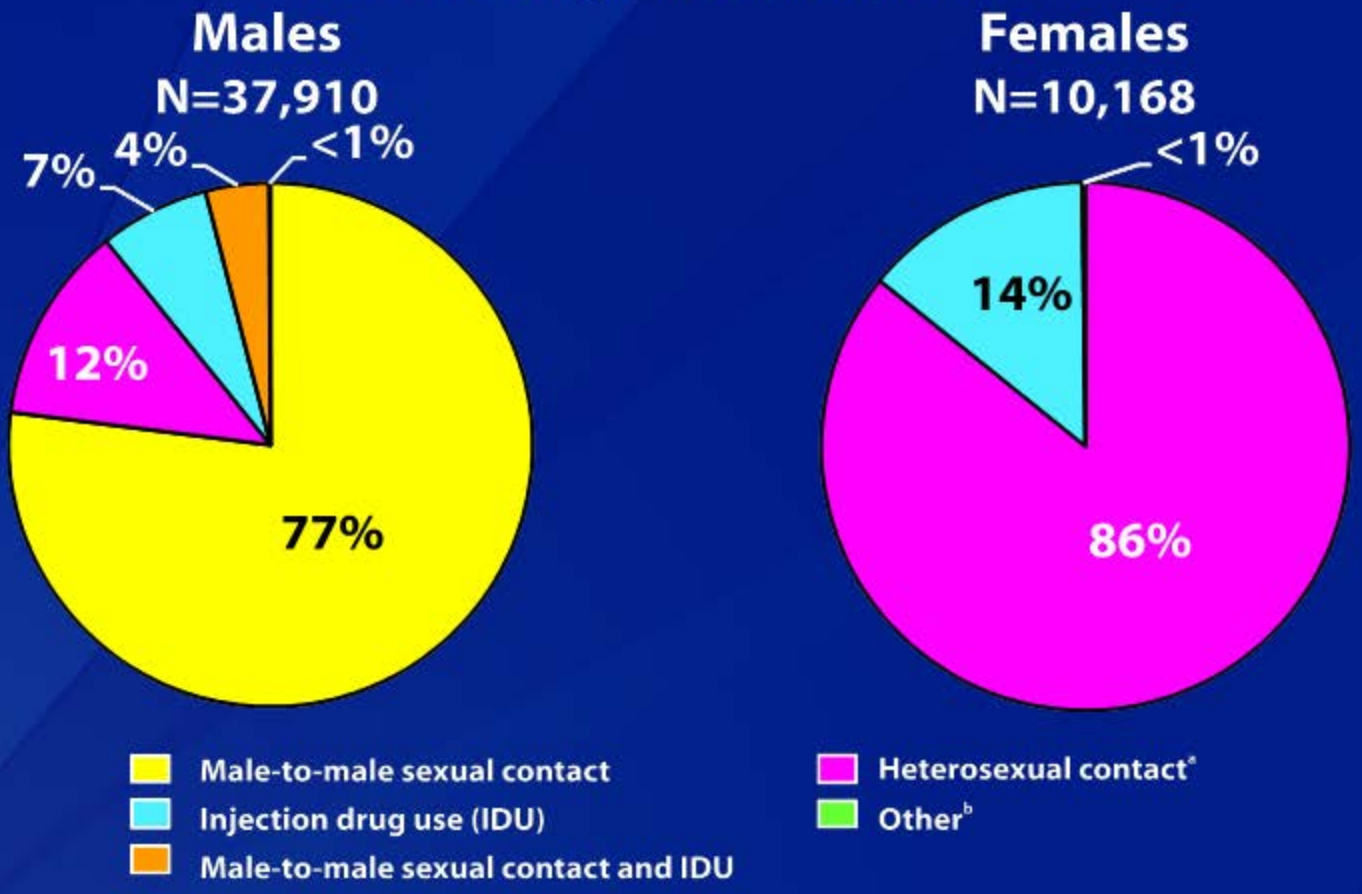


Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing risk-factor information, but not for incomplete reporting.

[a] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

[b] Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.

Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Transmission Category, 2010—46 States and 5 U.S. Dependent Areas

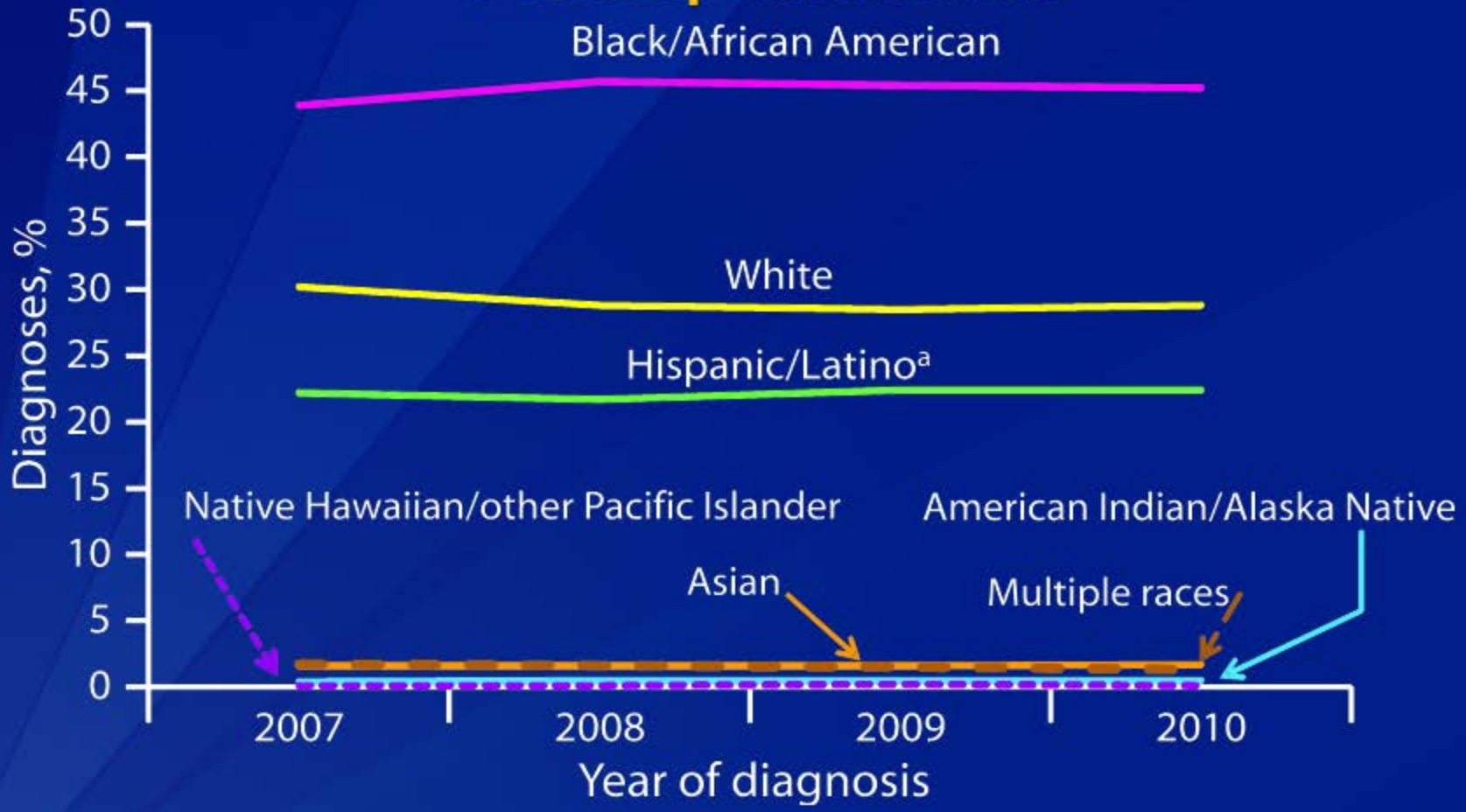


Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing risk-factor information, but not for incomplete reporting.

[a] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

[b] Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.

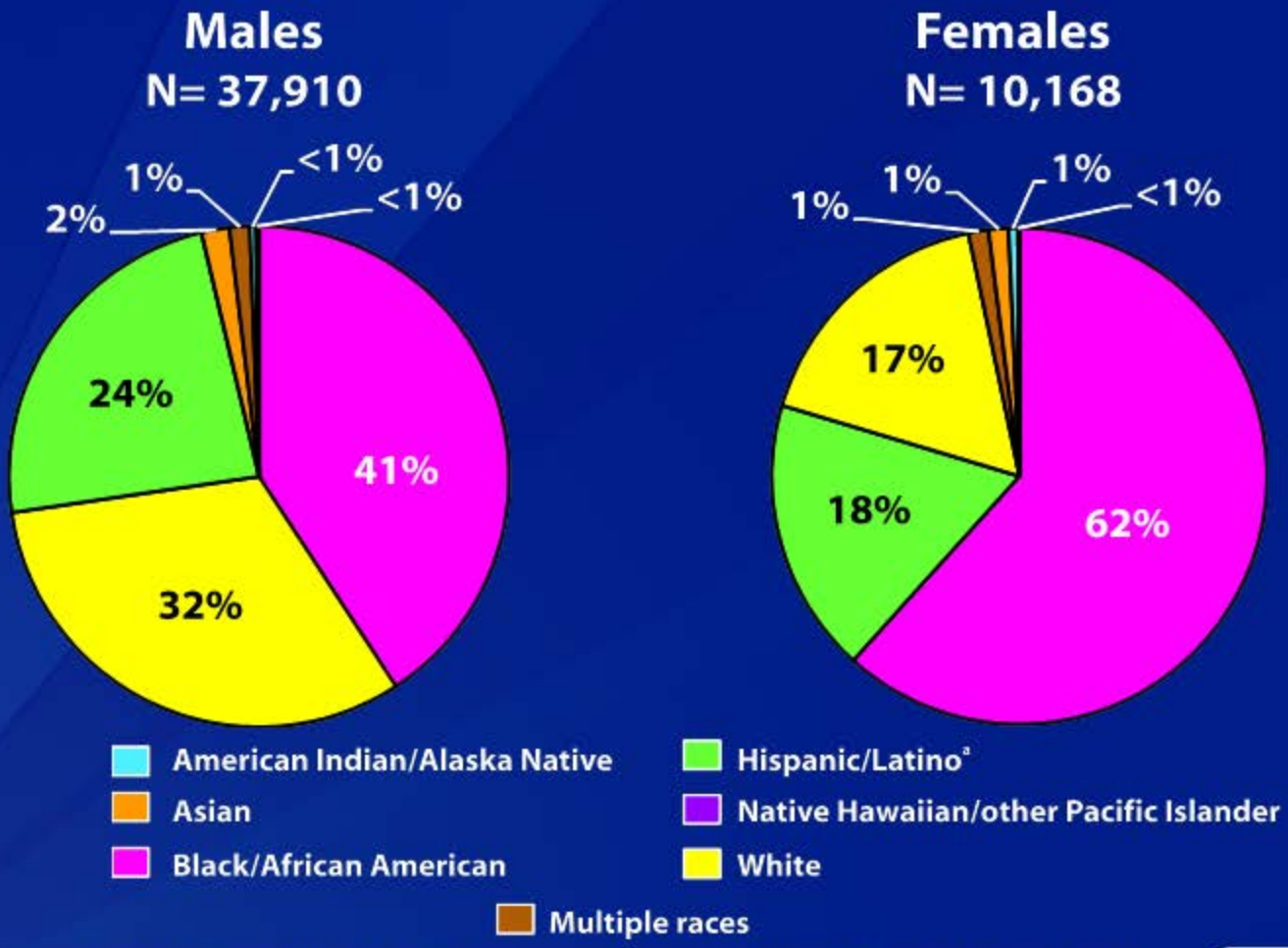
Diagnoses of HIV Infection among Adults and Adolescents, by Race/Ethnicity, 2007–2010—46 States and 5 U.S. Dependent Areas



Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.

[a] Hispanics/Latinos can be of any race.

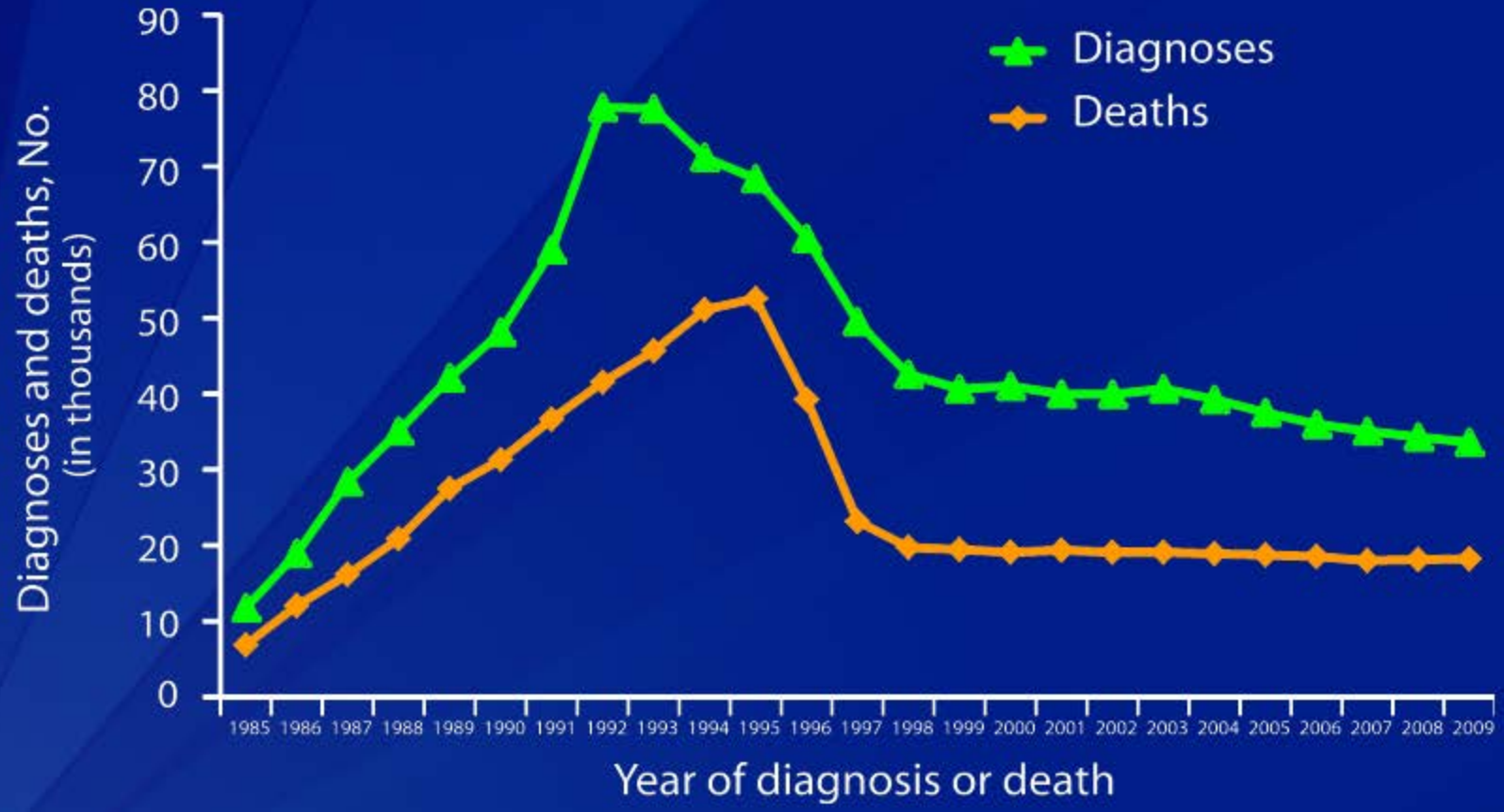
Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Race/Ethnicity, 2010—46 States and 5 U.S. Dependent Areas



Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.

[a] Hispanics/Latinos can be of any race.

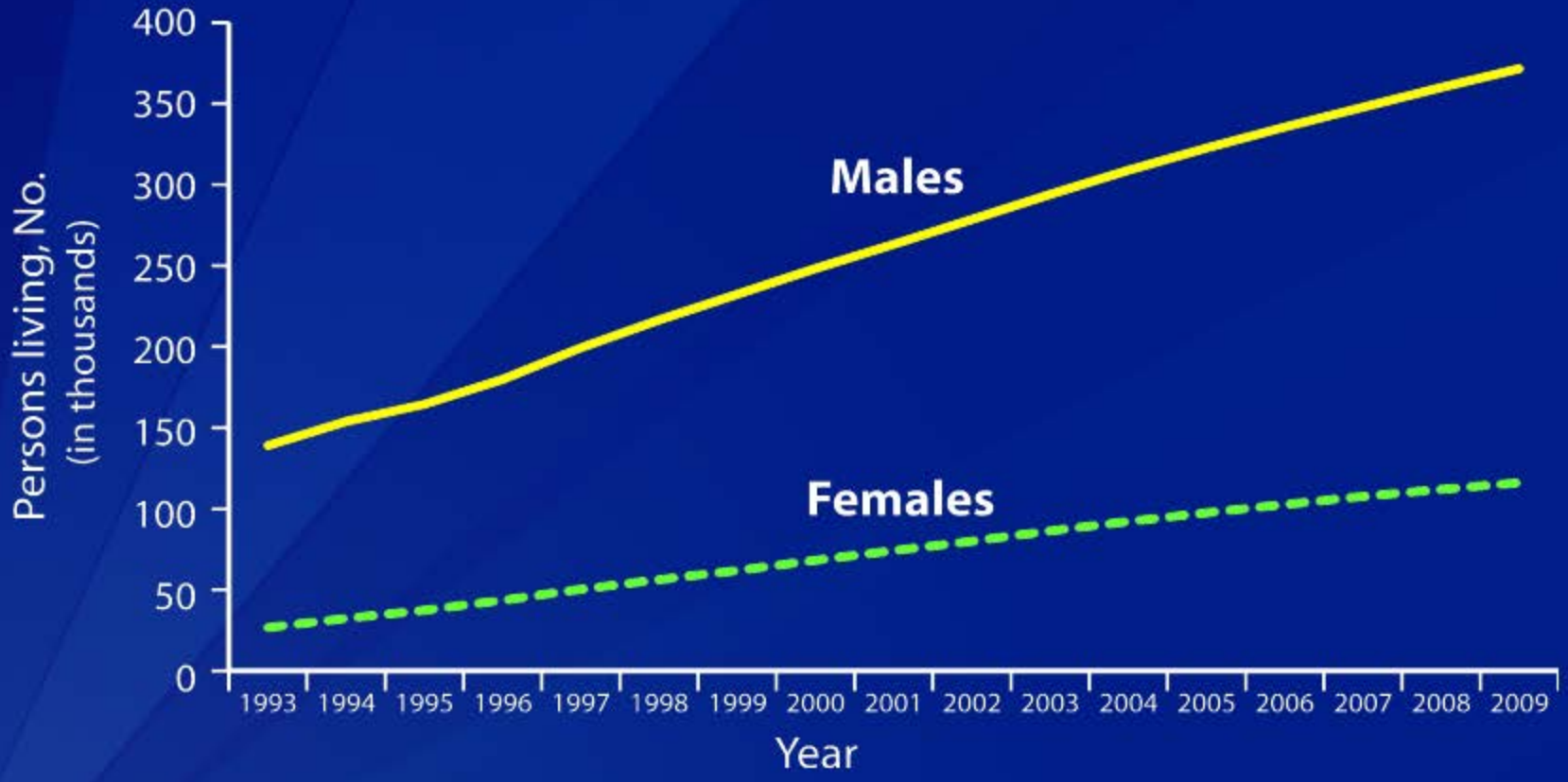
AIDS Diagnoses and Deaths of Adults and Adolescents with AIDS, 1985–2009—United States and 6 U.S. Dependent Areas



Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Deaths of persons with an AIDS diagnosis may be due to any cause.

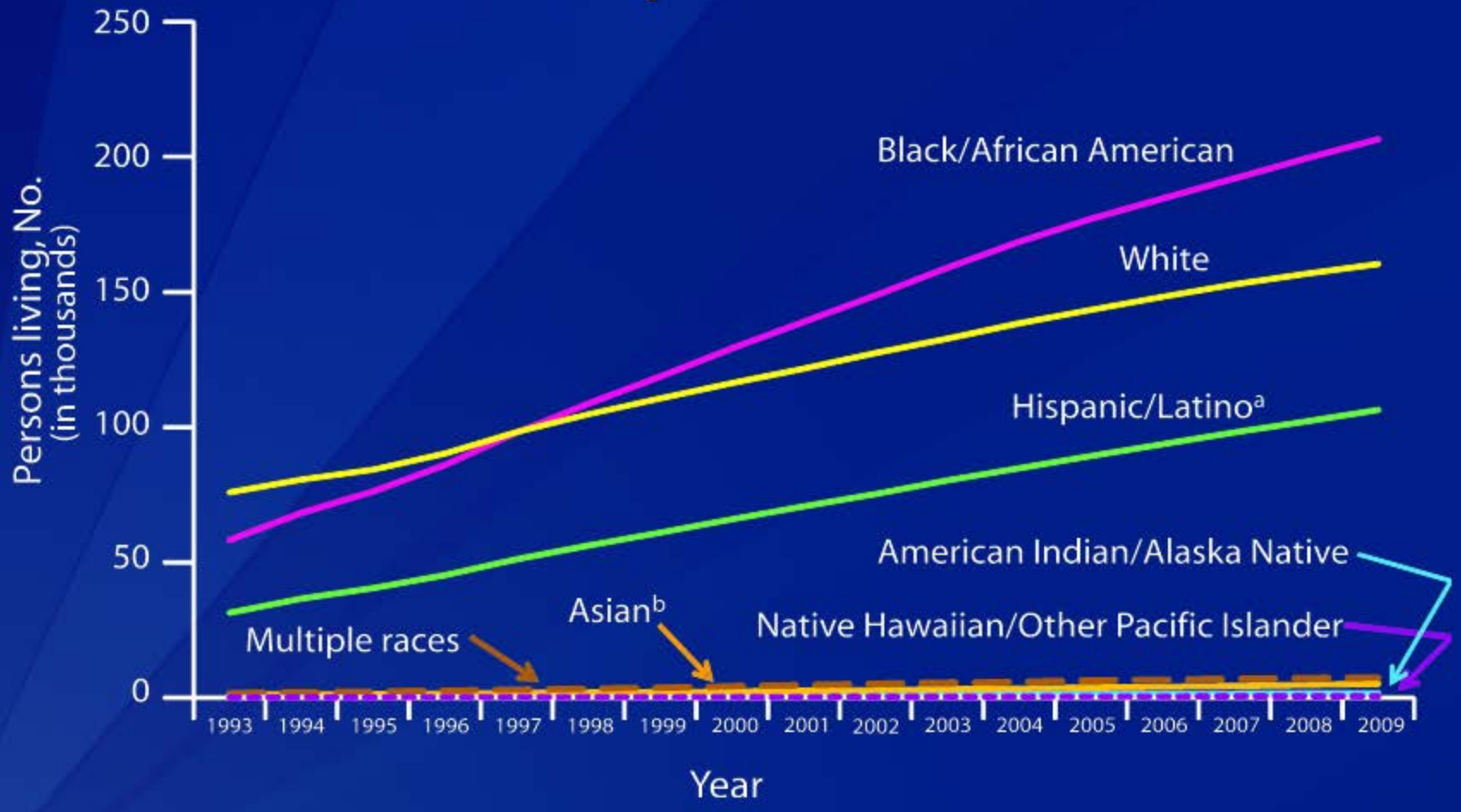
CDC

Adults and Adolescents Living with an AIDS Diagnosis, by Sex, 1993–2009—United States and 6 U.S. Dependent Areas



Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.

Persons Living with an AIDS Diagnosis, by Race/Ethnicity, 1993-2009—United States and 6 U.S. Dependent Areas



Note. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.

[a] Hispanics/Latinos can be of any race.

[b] Includes Asian/Pacific Islander legacy cases.

CDC & Medical Organization recommendations for routine HIV testing

Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings

MMWR 2006;55 (No. RR-14):1-17

Published September 22, 2006

http://www.cdc.gov/mmwr/pdf/rr/rr5514.pdf

Revised Recommendations Adults and Adolescents - I

Routine, voluntary HIV screening for all persons 13-64 in health care settings, not based on risk

All patients with TB, or seeking treatment for STDs, should be screened for HIV

Repeat HIV screening of persons with known risk at least annually

Revised Recommendations Adults and Adolescents - II

When acute retroviral infection is a possibility, use an RNA test in conjunction with an HIV antibody test

Settings with low or unknown prevalence:

- Initiate screening
- If yield from screening is less than 1 per 1000, continued screening is not warranted

Revised Recommendations Adults and Adolescents - III

- Opt-out HIV screening with the opportunity to ask questions and the option to decline testing
- Separate signed informed consent should not be required
- Prevention counseling in conjunction with HIV screening in health care settings should not be required

Revised Recommendations Adults and Adolescents - IV

Screening is voluntary

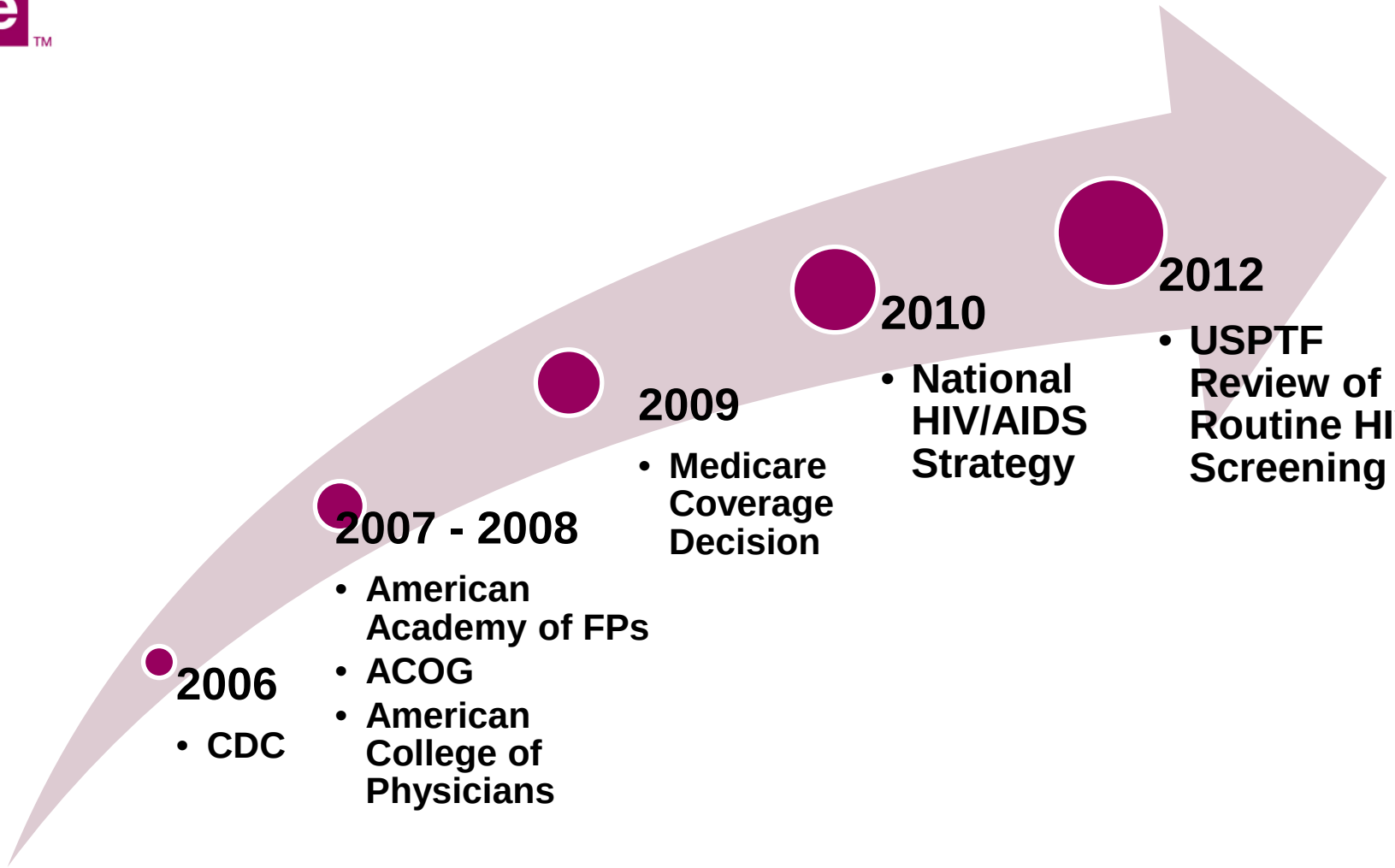
Inform patients orally, or in writing, that HIV testing will be performed unless they decline.

Arrange access to care, prevention, and support services for patients with positive HIV test results

Rationale for Revising CDC Recommendations

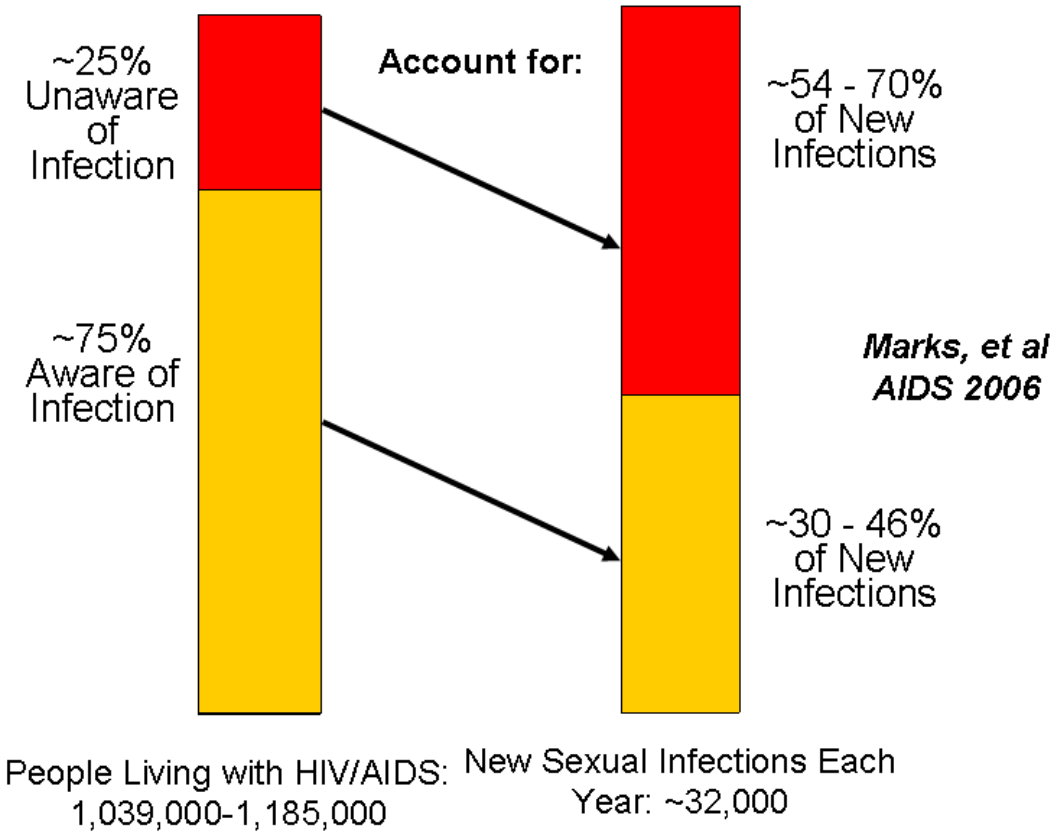
- Many HIV-infected persons access health care but are not tested for HIV until symptomatic
- Effective treatment available
- Awareness of HIV infection leads to substantial reductions in high-risk sexual behavior
- Inconclusive evidence about prevention benefits from typical counseling for persons who test negative
- Great deal of experience with HIV testing, including rapid tests

Progression to Routine Testing



Importance of Routine HIV Testing in POLs and clinics

Awareness of Serostatus Among People with HIV and Estimates of Transmission

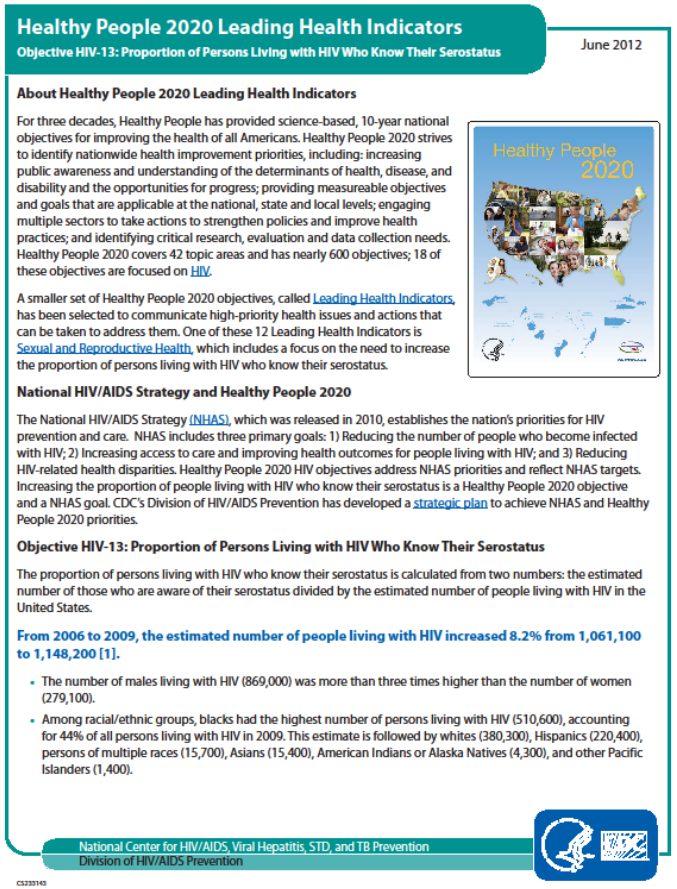


HIV Prevalence in the United States

	Total persons living with HIV infection		Persons whose HIV infection was undiagnosed		
Characteristic	No.	(95% CI)	No.	(95% CI)	Rate (%)
Total	1,178,350	(1,128,350 – 1,228,500)	236,400	(224,900 – 247,900)	20.1

HIV prevalence in the United States: CDC. HIV surveillance— United States, 1981-2008. *MMWR. 2011;60:689-693.*

Healthy People 2020



Healthy People 2020 Leading Health Indicators

Objective HIV-13: Proportion of Persons Living with HIV Who Know Their Serostatus

June 2012

About Healthy People 2020 Leading Health Indicators

For three decades, Healthy People has provided science-based, 10-year national objectives for improving the health of all Americans. Healthy People 2020 strives to identify nationwide health improvement priorities, including: increasing public awareness and understanding of the determinants of health, disease, and disability and the opportunities for progress; providing measureable objectives and goals that are applicable at the national, state and local levels; engaging multiple sectors to take actions to strengthen policies and improve health practices; and identifying critical research, evaluation and data collection needs. Healthy People 2020 covers 42 topic areas and has nearly 600 objectives; 18 of these objectives are focused on HIV.

A smaller set of Healthy People 2020 objectives, called Leading Health Indicators, has been selected to communicate high-priority health issues and actions that can be taken to address them. One of these 12 Leading Health Indicators is Sexual and Reproductive Health, which includes a focus on the need to increase the proportion of persons living with HIV who know their serostatus.

National HIV/AIDS Strategy and Healthy People 2020

The National HIV/AIDS Strategy (NHAS), which was released in 2010, establishes the nation's priorities for HIV prevention and care. NHAS includes three primary goals: 1) Reducing the number of people who become infected with HIV; 2) Increasing access to care and improving health outcomes for people living with HIV; and 3) Reducing HIV-related health disparities. Healthy People 2020 HIV objectives address NHAS priorities and reflect NHAS targets. Increasing the proportion of people living with HIV who know their serostatus is a Healthy People 2020 objective and a NHAS goal. CDC's Division of HIV/AIDS Prevention has developed a strategic plan to achieve NHAS and Healthy People 2020 priorities.

Objective HIV-13: Proportion of Persons Living with HIV Who Know Their Serostatus

The proportion of persons living with HIV who know their serostatus is calculated from two numbers: the estimated number of those who are aware of their serostatus divided by the estimated number of people living with HIV in the United States.

From 2006 to 2009, the estimated number of people living with HIV increased 8.2% from 1,061,100 to 1,148,200 [1].

- The number of males living with HIV (869,000) was more than three times higher than the number of women (279,100).
- Among racial/ethnic groups, blacks had the highest number of persons living with HIV (510,600), accounting for 44% of all persons living with HIV in 2009. This estimate is followed by whites (380,300), Hispanics (220,400), persons of multiple races (15,700), Asians (15,400), American Indians or Alaska Natives (4,300), and other Pacific Islanders (1,400).

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention

CS233143

Objective HIV-13: Proportion of Persons Living with HIV Who Know Their Serostatus

Target: 90.0 %

Baseline: 79.0 %of persons aged 13 years and older living with HIV were aware of their HIV infection in 2006.

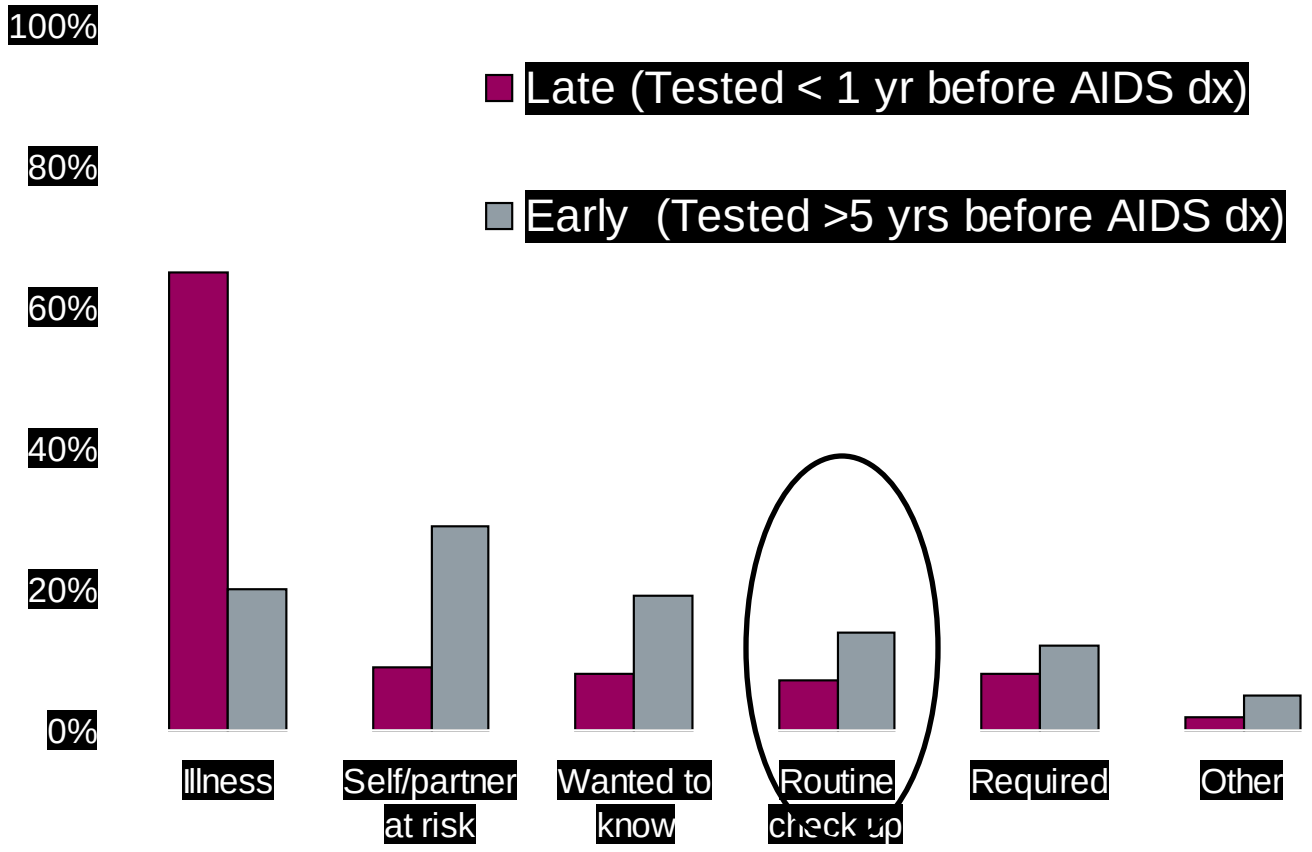
Target setting method: Consistent with the National HIV/AIDS Strategy.

Data source: HIV Surveillance System, CDC, NCHHSTP.

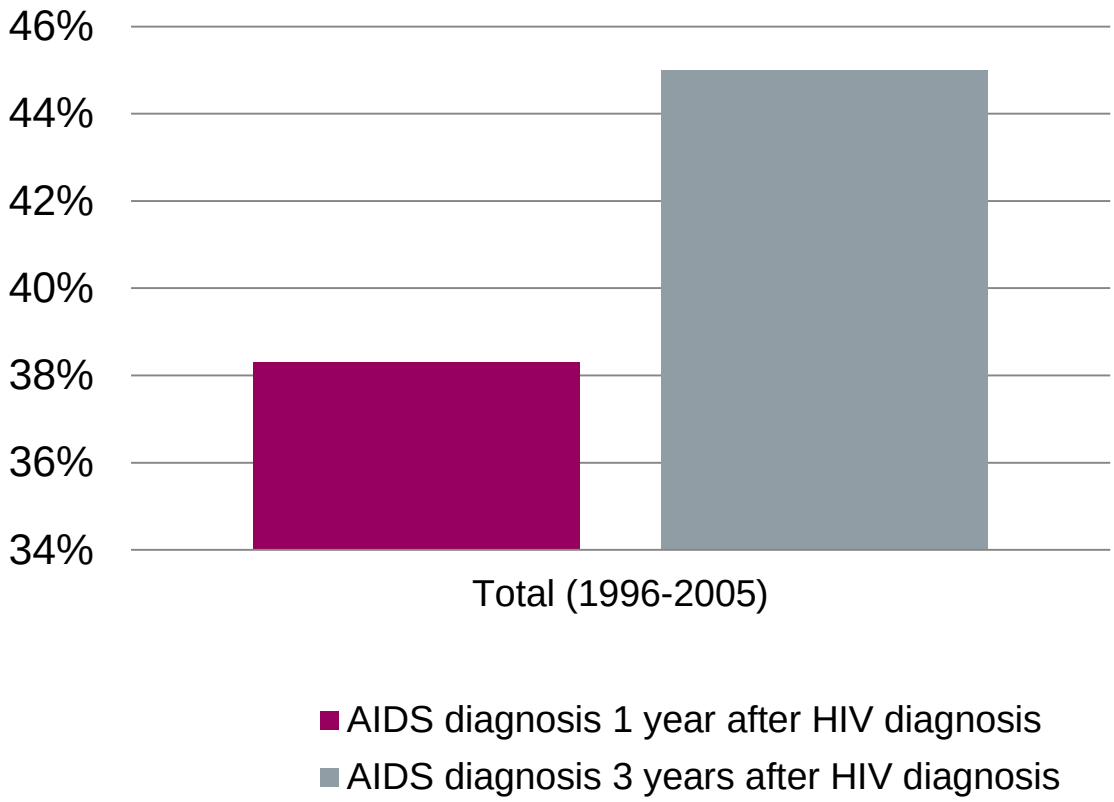
http://www.cdc.gov/hiv/resources/factsheets/PDF/LHI-Factsheet-FINAL-6-26-12.pdf (Last Accessed 9/11/12)
http://healthypeople.gov/2020/topicsobjectives2020/pdfs/HIV.pdf (Last Accessed 9/11/12)

Reasons for Testing: Late versus Early Testers

Supplement to HIV/AIDS Surveillance, 2000-2003



Late HIV Testing, 1996--2005



CDC. Late HIV testing—34 states, 1996–2005. *MMWR. 2009;58:661-665*
. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5824a2.htm#tab

Late Diagnosis of HIV Infection - 2009

Table 10a. Time to an AIDS diagnosis after a diagnosis of HIV infection, by selected characteristics, 2009—46 states with confidential name-based HIV infection reporting

	<12 Months[a]		≥12 Months[b]		Total
	Est. No.	%	Est. No.	%	Est. No.[c]
Age at diagnosis (yr)					
<13	14	7	186	93	200
13–14	8	31	18	69	27
15–19	310	15	1,818	85	2,128
20–24	1,145	17	5,546	83	6,691
25–29	1,561	24	4,990	76	6,551
30–34	1,721	30	3,931	70	5,652
35–39	2,044	36	3,575	64	5,619
40–44	2,310	39	3,601	61	5,910
45–49	2,149	42	3,000	58	5,150
50–54	1,617	45	1,947	55	3,564
55–59	946	45	1,146	55	2,091
60–64	444	46	514	54	958
≥65	418	53	377	47	795
Race/ethnicity					
American Indian/Alaska Native	60	29	148	71	208
Asian	248	34	477	66	724
Black/African American	6,469	31	14,605	69	21,074
Hispanic/Latino[d]	3,456	37	5,950	63	9,406
Native Hawaiian/Other Pacific Islander	25	34	47	66	72
White	4,174	32	8,981	68	13,155
Multiple races	255	37	442	63	697
Transmission category					
Male adult or adolescent					
Male-to-male sexual contact	8,181	31	18,546	69	26,727
Injection drug use	1,085	45	1,326	55	2,411
Male-to-male sexual contact and injection drug use	449	31	993	69	1,442
Heterosexual contact[e]	1,868	42	2,548	58	4,416
Other[f]	26	79	7	21	33
Subtotal	11,611	33	23,419	67	35,030
Female adult or adolescent					
Injection drug use	552	35	1,008	65	1,560
Heterosexual contact[e]	2,492	29	6,035	71	8,527
Other[f]	18	89	2	11	20
Subtotal	3,062	30	7,045	70	10,107
Child (<13 yrs at diagnosis)					
Perinatal	12	7	152	93	164
Other[g]	2	6	33	94	35
Subtotal	14	7	186	93	200
Total[h]	**14,686**	**32**	**30,650**	**68**	**45,336**

Note. Estimated numbers resulted from statistical adjustment that accounted for reporting delays and missing risk-factor information, but not for incomplete reporting.

See Technical Notes for the list of areas that have had laws or regulations requiring confidential name-based HIV infection reporting since at least January 2007 and that have reported these data to CDC since at least June 2007.

Data exclude 32 persons whose month of diagnosis of HIV infection is unknown.

[a] Includes persons whose diagnoses of HIV infection and AIDS were made at the same time.

[b] Includes persons in whom AIDS has not developed.

[c] Because the estimated totals were calculated independently of the corresponding values for each subpopulation, the subpopulation values may not sum to the totals shown here.

[d] Hispanics/Latinos can be of any race.

[e] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

[f] Includes hemophilia, blood transfusion, perinatal exposure, and risk factor not reported or not identified.

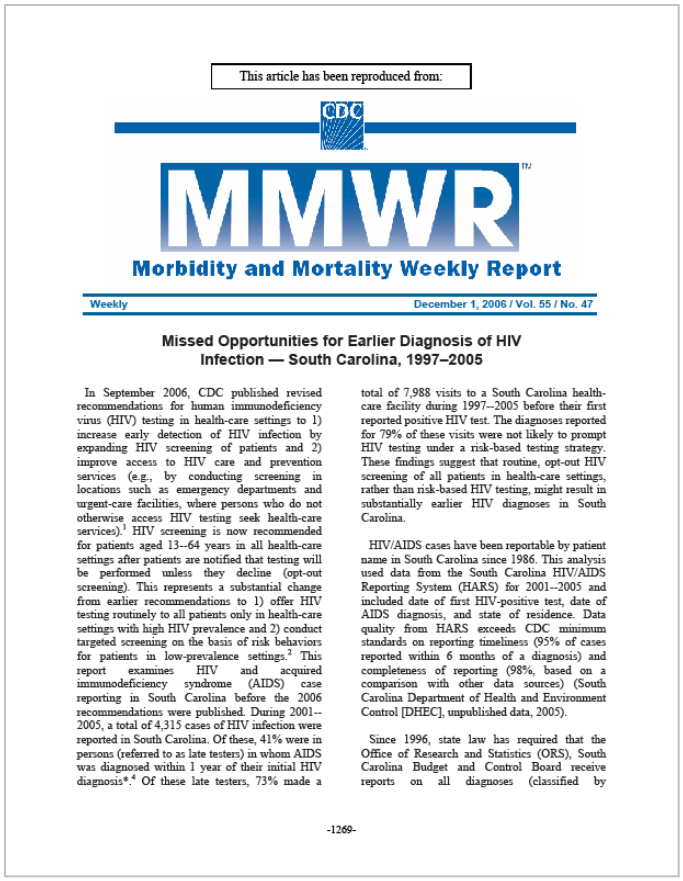
[g] Includes hemophilia, blood transfusion, and risk factor not reported or not identified.

[h] Because column totals for estimated numbers were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total.

Among persons initially diagnosed with HIV infection during 2009, 32% received an AIDS diagnosis within 12 months

CDC. HIV Surveillance Report, 2010; vol.22. *http://www.cdc.gov/hiv/topics/surveillance/resources/reports/*. *Published March 2012. Accessed 9/10/12*

Missed Opportunities for Earlier Diagnosis of HIV Infection



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CDC

MMWR

Morbidity and Mortality Weekly Report

Weekly December 1, 2006 / Vol. 55 / No. 47

Missed Opportunities for Earlier Diagnosis of HIV Infection — South Carolina, 1997–2005

In September 2006, CDC published revised recommendations for human immunodeficiency virus (HIV) testing in health-care settings to 1) increase early detection of HIV infection by expanding HIV screening of patients and 2) improve access to HIV care and prevention services (e.g., by conducting screening in locations such as emergency departments and urgent-care facilities, where persons who do not otherwise access HIV testing seek health-care services).[1] HIV screening is now recommended for patients aged 13--64 years in all health-care settings after patients are notified that testing will be performed unless they decline (opt-out screening). This represents a substantial change from earlier recommendations to 1) offer HIV testing routinely to all patients only in health-care settings with high HIV prevalence and 2) conduct targeted screening on the basis of risk behaviors for patients in low-prevalence settings.[2] This report examines HIV and acquired immunodeficiency syndrome (AIDS) case reporting in South Carolina before the 2006 recommendations were published. During 2001--2005, a total of 4,315 cases of HIV infection were reported in South Carolina. Of these, 41% were in persons (referred to as late testers) in whom AIDS was diagnosed within 1 year of their initial HIV diagnosis*.[4] Of these late testers, 73% made a total of 7,988 visits to a South Carolina health-care facility during 1997--2005 before their first reported positive HIV test. The diagnoses reported for 79% of these visits were not likely to prompt HIV testing under a risk-based testing strategy. These findings suggest that routine, opt-out HIV screening of all patients in health-care settings, rather than risk-based HIV testing, might result in substantially earlier HIV diagnoses in South Carolina.

HIV/AIDS cases have been reportable by patient name in South Carolina since 1986. This analysis used data from the South Carolina HIV/AIDS Reporting System (HARS) for 2001--2005 and included date of first HIV-positive test, date of AIDS diagnosis, and state of residence. Data quality from HARS exceeds CDC minimum standards on reporting timeliness (95% of cases reported within 6 months of a diagnosis) and completeness of reporting (98%, based on a comparison with other data sources) (South Carolina Department of Health and Environment Control [DHEC], unpublished data, 2005).

Since 1996, state law has required that the Office of Research and Statistics (ORS), South Carolina Budget and Control Board receive reports on all diagnoses (classified by

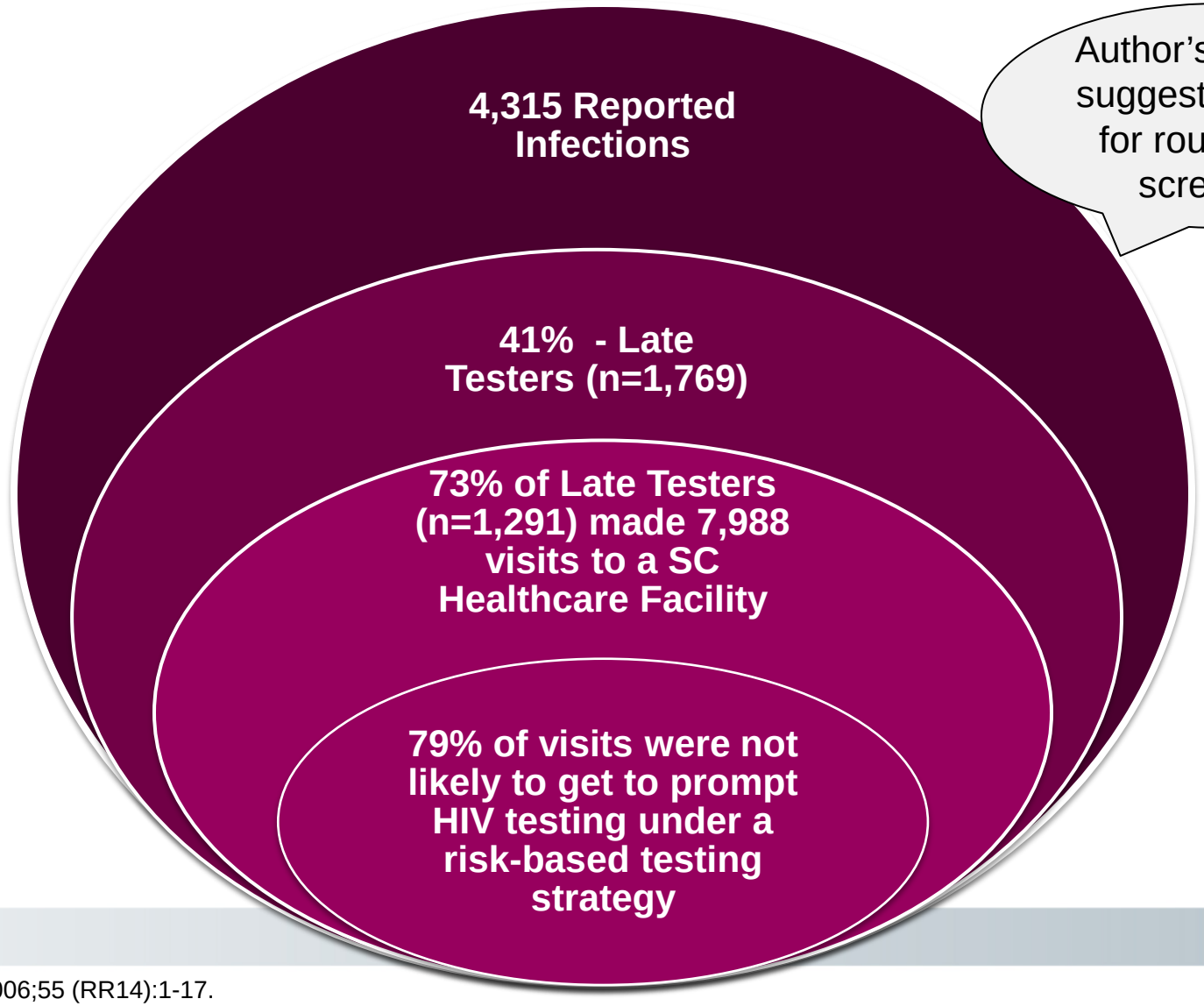
-1269-

KEY POINTS

- Data collected from:
  - 60 Emergency Departments
  - 62 Inpatient Facilities
  - 63 Ambulatory-Care facilities
  - 19 Free medical clinics
- 2001 – ‘05: 4,315 reported cases of HIV infection in SC

CDC. MMWR 2006;55 (RR14):1-17.

Missed Opportunities for Earlier Diagnosis of HIV Infection



Author's Findings suggest the need for routine HIV screening

CDC. MMWR 2006;55 (RR14):1-17.

Criteria that Justify Routine Screening

- Serious health disorder that can be detected before symptoms develop
- Treatment is more beneficial when begun before symptoms develop
- Reliable, inexpensive, acceptable screening test
- Costs of screening are reasonable in relation to anticipated benefits
- Treatment must be accessible

Principles and Practice of Screening for Disease
-WHO Public Health Paper, 1968

Opt-Out Screening

Prenatal HIV testing for pregnant women:

RCT of 4 counseling models with opt-in consent:

- *35% accepted testing*
- *Some women felt accepting an HIV test indicated high risk behavior*

Testing offered as routine, opportunity to decline

- *88% accepted testing*
- *Significantly less anxious about testing*

Simpson W, et al, BMJ June,1999

Cost Effectiveness

Expanded screening for HIV in the U.S. – an analysis of cost effectiveness.

“In all but the lowest-risk populations, routine, voluntary screening for HIV once every 3 to 5 years is justified on both clinical and cost-effectiveness grounds. One-time screening in the general population may also be cost-effective.”

Paltiel AD, et al. NEJM 2005;352:586.

Cost Effectiveness

Prenatal HIV screening	• Averts ~1500 cases of neonatal HIV per year • Cost saving
HIV antibody testing of 15 million blood donations	• Averts ~1500 HIV infections per year • Costs $3,600 per QALY
Pooled RNA screening for HIV and HCV	• Averts 4 HIV and 56 HCV infections per year • Costs $4.3 million per QALY

Cost-Effectiveness of Expanded HIV Screening in the US

One-time HIV screening of low-risk persons coupled with annual screening of high-risk persons could prevent 6.7% of a projected 1.23 million new infections

- Cost $22,382 per QALY gained

Ann Intern Med. 21 December 2010;153(12):778-789

http://annals.org/article.aspx?articleid=746571

Strategies for HIV Testing in Clinic & POL Settings

Role for Rapid HIV Tests

- Increase receipt of test results
- Increase identification of HIV-infected pregnant women so they can receive effective prophylaxis
- Increase feasibility of testing in acute-care settings with same-day results
- Increase number of venues where testing can be offered to high-risk persons

Rapid Lateral Flow Tests

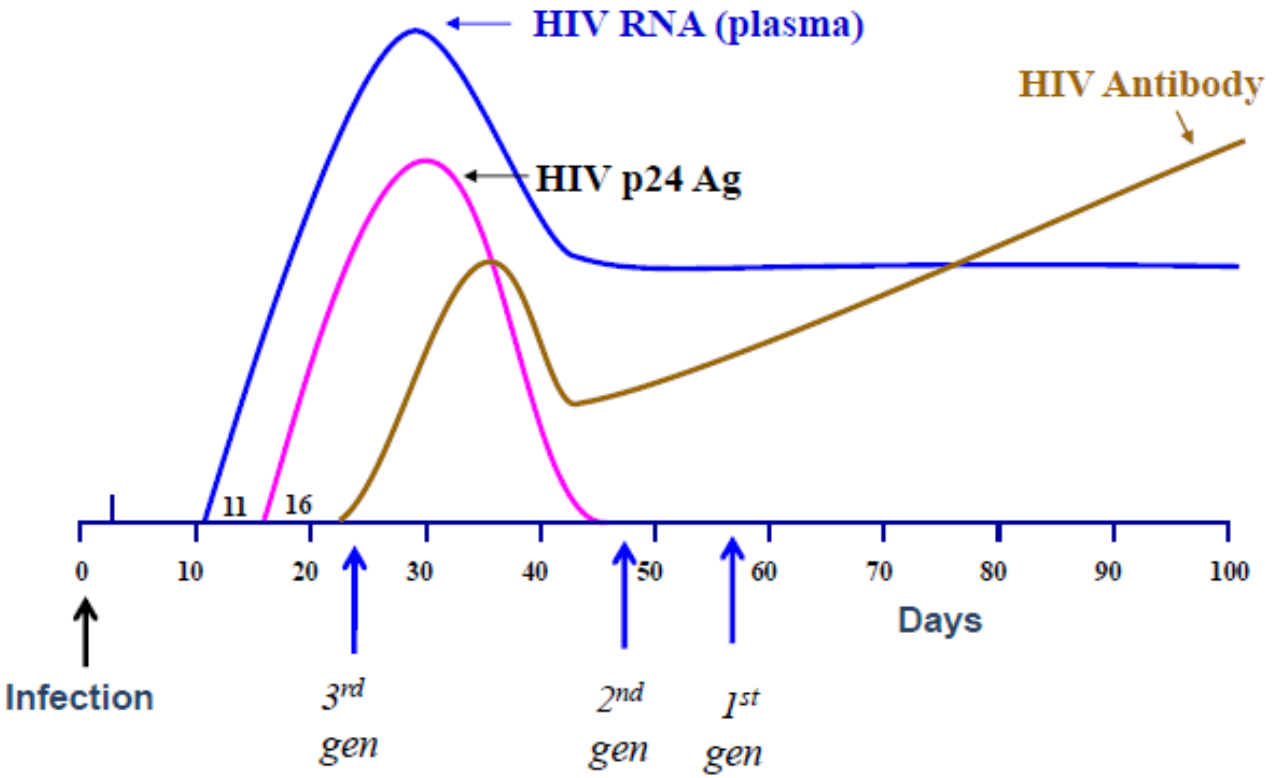
Capture antibody or antigen immobilized as a line on nitrocellulose

Detector antibody or antigen is a gold particle or latex particle

Generations of HIV Tests

- 1st Generation – Detect antibody to HIV with viral lysate
- 2nd Generation – Detect antibody to HIV with recombinant proteins or synthetic peptides
- 3rd Generation – Detect both IgG and IgM antibody to HIV
- 4th Generation – Detect antibody and viral protein

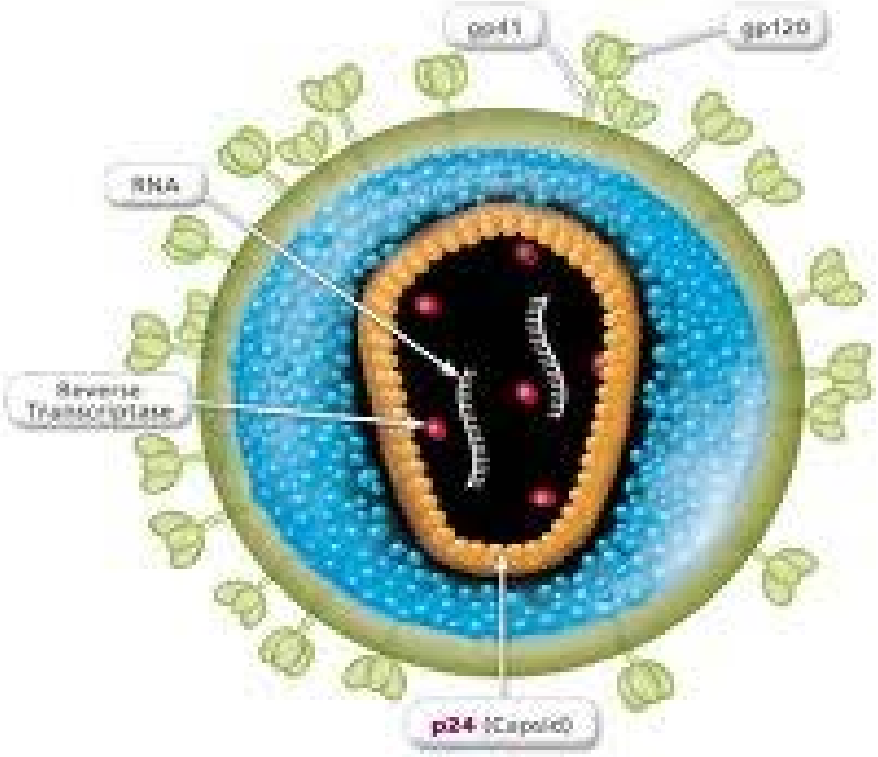
HIV Infection & Laboratory Markers



Modified after Busch et al. Am J Med. 1997

p24 antigen

- p24 antigen is a viral protein that makes up most of the the viral core.

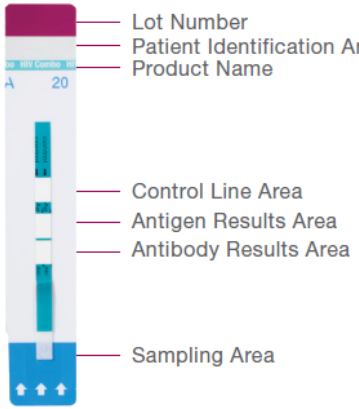


P24 antigen

- Serum concentrations of p24 antigen are high in the first few weeks after infection; tests sensitive to p24 antigen are therefore useful for diagnosing very early infection when antibody levels are not present or are still low.

Rapid HIV Tests (Waived)

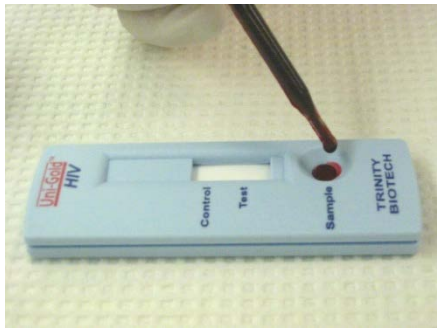
Clearview® HIV 1/2 STAT-PAK®



Determine Combo HIV/AG

Clearview® COMPLETE HIV 1/2

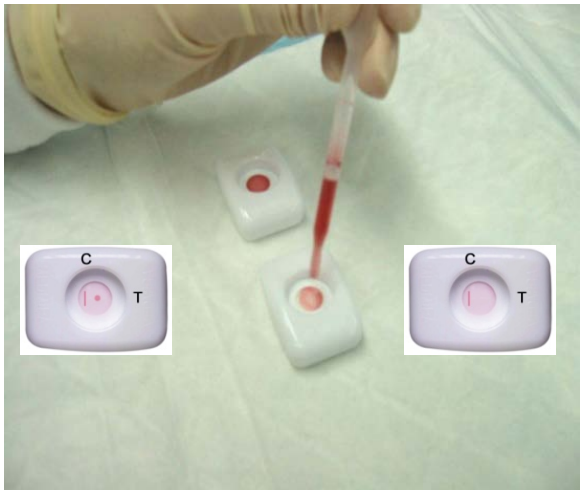
OraQuick Advance®



Uni-Gold Recombigen™

INSTI™ HIV-1 Antibody Test

Rapid HIV Tests (Moderate)



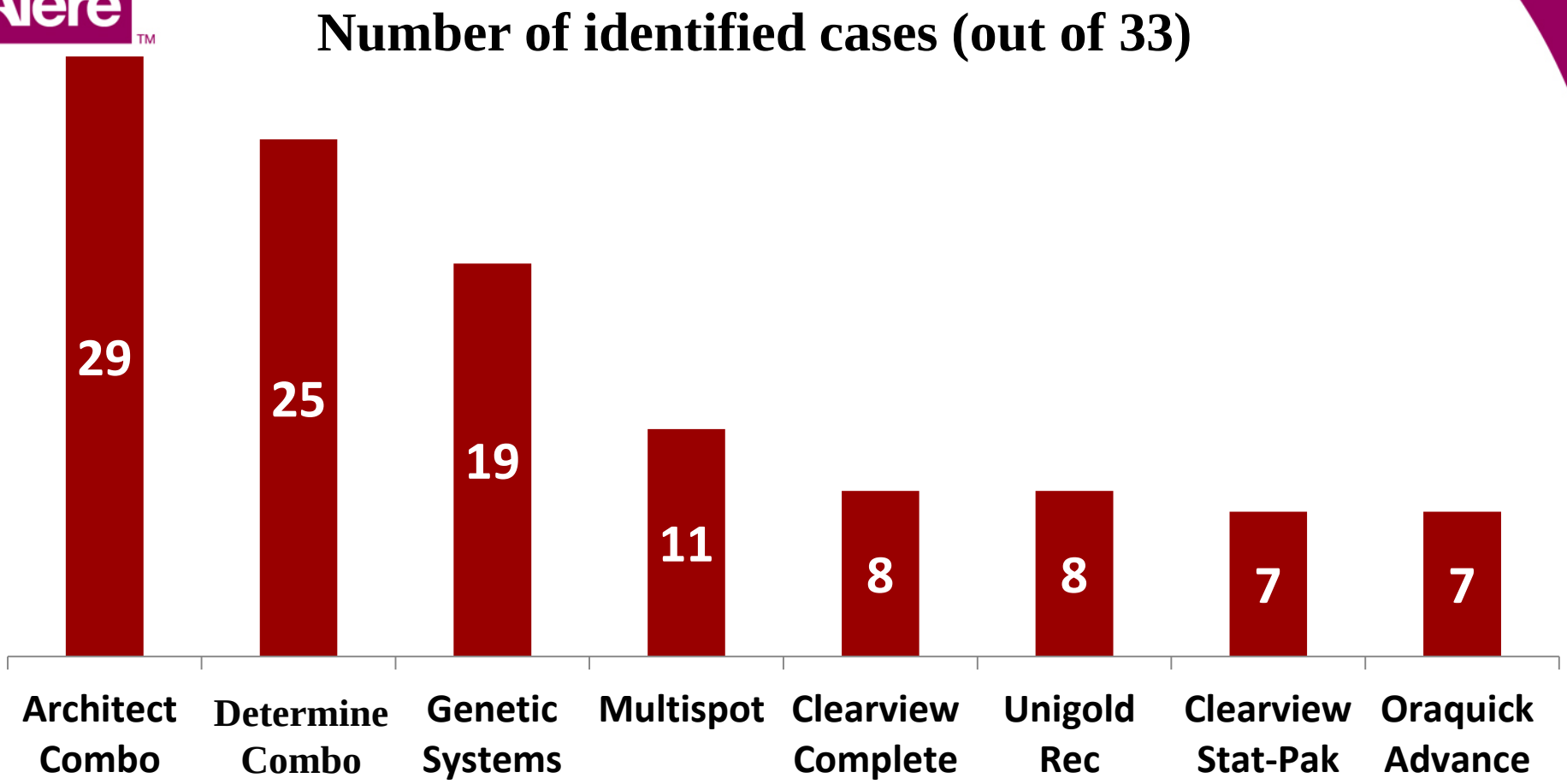
Reveal® G3

Multispot HIV-1/HIV-2

FDA-approved Rapid HIV Tests

	Sensitivity *(95% C.I.)*	Specificity *(95% C.I.)*
Whole blood (F.S.)		
OraQuick Advance®	99.6 *(98.5 – 99.9)*	100 *(99.7 –100)*
Uni-Gold Recombigen™	100 *(99.5 – 100)*	99.7 *(99.0 – 100)*
Clearview® HIV 1/2 STAT-PAK®	99.7 *(98.9 – 100)*	99.9 *(98.6 – 100)*
Clearview® COMPLETE HIV 1/2	99.7 *(98.9 – 100)*	99.9 *(98.6 – 100)*
INSTI® HIV-1 Antibody Test	99.8 *(99.3 – 99.9)*	99.5 *(99.0 – 99.8)*
Determine HIV Combo	*99.9 (99.4-100)*	*99.6 (99.2 – 99.8)*
Serum/plasma		
Reveal® G3	99.8 *(99.2 – 100)*	99.9 *(98.6 – 100)*
Multispot	100 *(99.9 – 100)*	99.9 *(99.8 – 100)*

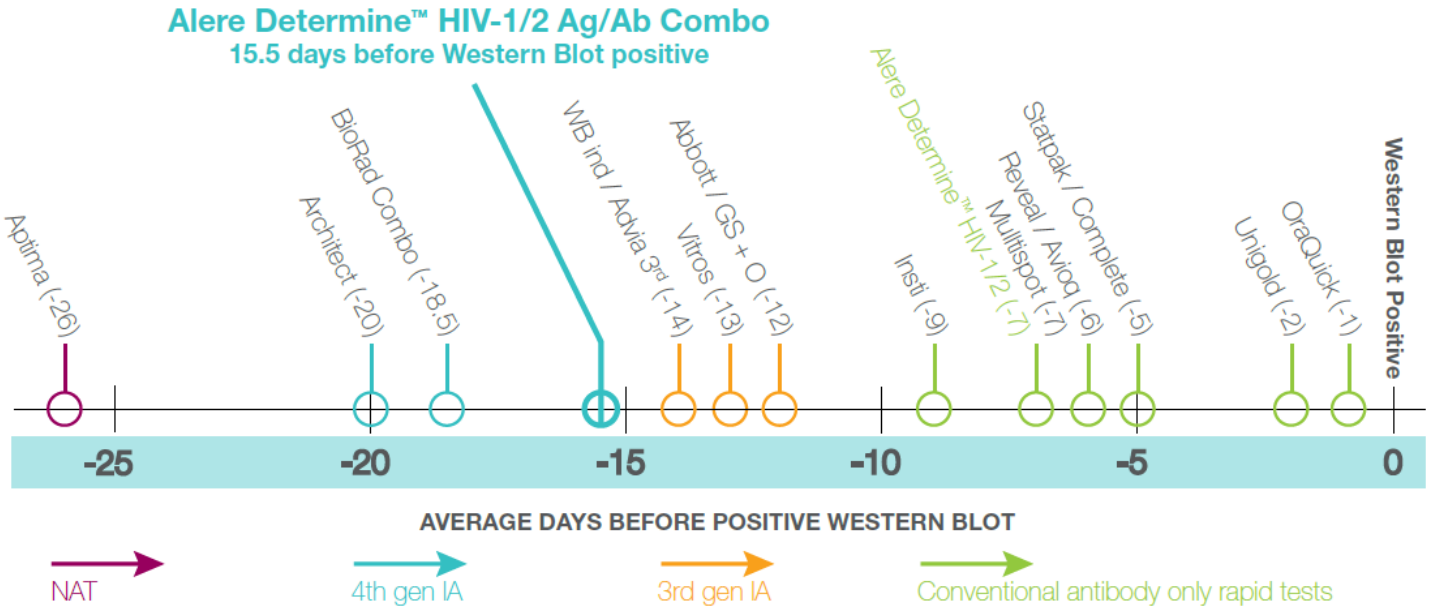
CDC Study: Early HIV screening



Modified from Patel et al. JCV
May 2012

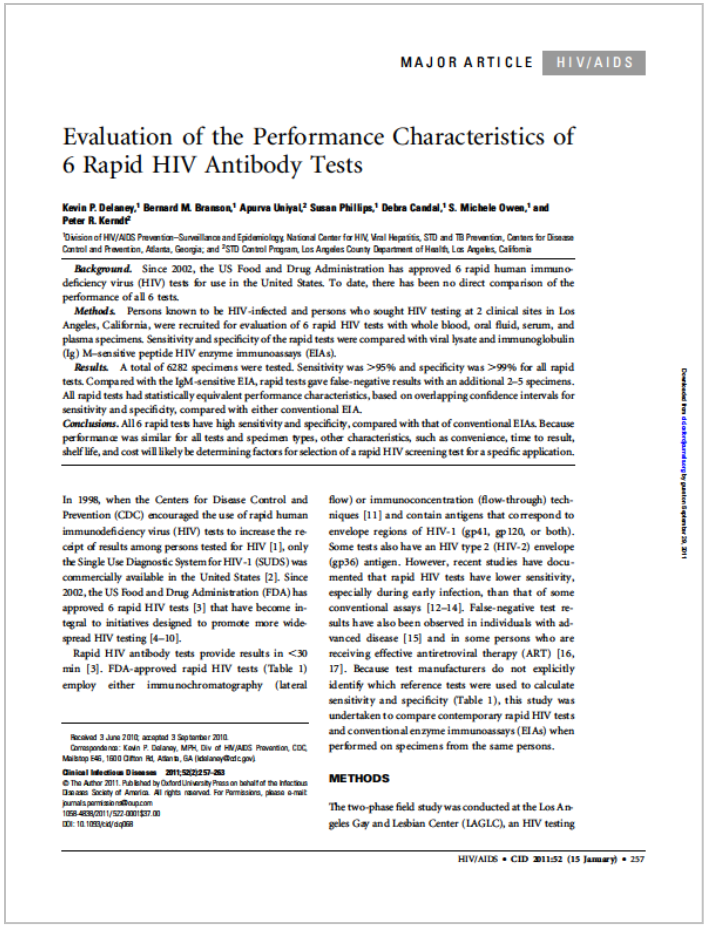
Performance of Alere Determine™ HIV-1/2 Ag/Ab Combo

Sensitivity of assay reactivity during early HIV-1 infections relative to number of days before first positive Western Blot



Masciotra S, et al. Performance of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test with specimens from HIV-1 seroconverters from the US and HIV-2 infected individuals from Ivory Coast. J Clin Virol 2013: Published online 05 August 2013. DOI: 10.1016/j.jcv.2013.07.002

Delaney et al



MAJOR ARTICLE HIV/AIDS

Evaluation of the Performance Characteristics of 6 Rapid HIV Antibody Tests

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Background. Since 2002, the US Food and Drug Administration has approved 6 rapid human immunodeficiency virus (HIV) tests for use in the United States. To date, there has been no direct comparison of the performance of all 6 tests.

Methods. Persons known to be HIV-infected and persons who sought HIV testing at 2 clinical sites in Los Angeles, California, were recruited for evaluation of 6 rapid HIV tests with whole blood, oral fluid, serum, and plasma specimens. Sensitivity and specificity of the rapid tests were compared with viral lysate and immunoglobulin (Ig) M–sensitive peptide HIV enzyme immunoassays (EIAs).

Results. A total of 6282 specimens were tested. Sensitivity was >95% and specificity was >99% for all rapid tests. Compared with the IgM-sensitive EIA, rapid tests gave false-negative results with an additional 2–5 specimens. All rapid tests had statistically equivalent performance characteristics, based on overlapping confidence intervals for sensitivity and specificity, compared with either conventional EIA.

Conclusions. All 6 rapid tests have high sensitivity and specificity, compared with that of conventional EIAs. Because performance was similar for all tests and specimen types, other characteristics, such as convenience, time to result, shelf life, and cost will likely be determining factors for selection of a rapid HIV screening test for a specific application.

In 1998, when the Centers for Disease Control and Prevention (CDC) encouraged the use of rapid human immunodeficiency virus (HIV) tests to increase the receipt of results among persons tested for HIV [1], only the Single Use Diagnostic System for HIV-1 (SUDS) was commercially available in the United States [2]. Since 2002, the US Food and Drug Administration (FDA) has approved 6 rapid HIV tests [3] that have become integral to initiatives designed to promote more widespread HIV testing [4–10].

Rapid HIV antibody tests provide results in <30 min [3]. FDA-approved rapid HIV tests (Table 1) employ either immunochromatography (lateral flow) or immunoconcentration (flow-through) techniques [11] and contain antigens that correspond to envelope regions of HIV-1 (gp41, gp120, or both). Some tests also have an HIV type 2 (HIV-2) envelope (gp36) antigen. However, recent studies have documented that rapid HIV tests have lower sensitivity, especially during early infection, than that of some conventional assays [12–14]. False-negative test results have also been observed in individuals with advanced disease [15] and in some persons who are receiving effective antiretroviral therapy (ART) [16, 17]. Because test manufacturers do not explicitly identify which reference tests were used to calculate sensitivity and specificity (Table 1), this study was undertaken to compare contemporary rapid HIV tests and conventional enzyme immunoassays (EIAs) when performed on specimens from the same persons.

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1058-4838/2011/5202-0001$37.00
DOI: 10.1093/cid/ciq068

METHODS

The two-phase field study was conducted at the Los Angeles Gay and Lesbian Center (LAGLC), an HIV testing

Objective: Direct comparison of 6 FDA approved rapid HIV Tests (STAT-PAK, COMPLETE, OraQuick, Uni-Gold, Multispot, and Reveal)

Design:

- Conducted at LA Gay & Lesbian Center, & Altamed Clinic
- 6282 participants that were at high risk for HIV infection

Summary:

All 6 rapid HIV tests demonstrated high sensitivity and specificity compared with conventional EIAs. Other characteristics such as convenience, cost, time to results, shelf life – determining factors for a specific application.

Delaney, K et al. Evaluation of the Performance Characteristics of 6 Rapid HIV Antibody Tests. Clin Infect Dis, 2011;52(2):257-263.

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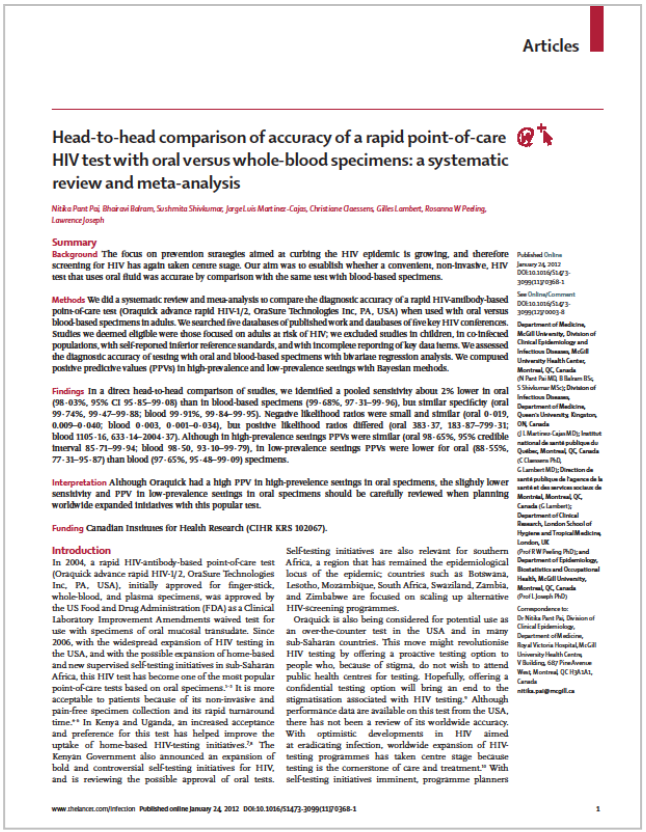

Articles

Head-to-head comparison of accuracy of a rapid point-of-care HIV test with oral versus whole-blood specimens: a systematic review and meta-analysis

Nitika Pant Pai, Bhairavi Balram, Sushmita Shivkumar, Jorge Luis Martinez-Cajas, Christiane Claessens, Gilles Lambert, Rosanna W Peeling, Lawrence Joseph

Summary

Background The focus on prevention strategies aimed at curbing the HIV epidemic is growing, and therefore screening for HIV has again taken centre stage. Our aim was to establish whether a convenient, non-invasive, HIV test that uses oral fluid was accurate by comparison with the same test with blood-based specimens.

Methods We did a systematic review and meta-analysis to compare the diagnostic accuracy of a rapid HIV-antibody-based point-of-care test (Oraquick advance rapid HIV-1/2, OraSure Technologies Inc, PA, USA) when used with oral versus blood-based specimens in adults. We searched five databases of published work and databases of five key HIV conferences. Studies we deemed eligible were those focused on adults at risk of HIV; we excluded studies in children, in co-infected populations, with self-reported inferior reference standards, and with incomplete reporting of key data items. We assessed the diagnostic accuracy of testing with oral and blood-based specimens with bivariate regression analysis. We computed positive predictive values (PPVs) in high-prevalence and low-prevalence settings with Bayesian methods.

Findings In a direct head-to-head comparison of studies, we identified a pooled sensitivity about 2% lower in oral (98·03%, 95% CI 95·85–99·08) than in blood-based specimens (99·68%, 97·31–99·96), but similar specificity (oral 99·74%, 99·47–99·88; blood 99·91%, 99·84–99·95). Negative likelihood ratios were small and similar (oral 0·019, 0·009–0·040; blood 0·003, 0·001–0·034), but positive likelihood ratios differed (oral 383·37, 183·87–799·31; blood 1105·16, 633·14–2004·37). Although in high-prevalence settings PPVs were similar (oral 98·65%, 95% credible interval 85·71–99·94; blood 98·50, 93·10–99·79), in low-prevalence settings PPVs were lower for oral (88·55%, 77·31–95·87) than blood (97·65%, 95·48–99·09) specimens.

Interpretation Although Oraquick had a high PPV in high-prevalence settings in oral specimens, the slightly lower sensitivity and PPV in low-prevalence settings in oral specimens should be carefully reviewed when planning worldwide expanded initiatives with this popular test.

Funding Canadian Institutes for Health Research (CIHR KRS 102067).

Introduction

In 2004, a rapid HIV-antibody-based point-of-care test (Oraquick advance rapid HIV-1/2, OraSure Technologies Inc, PA, USA), initially approved for finger-stick, whole-blood, and plasma specimens, was approved by the US Food and Drug Administration (FDA) as a Clinical Laboratory Improvement Amendments waived test for use with specimens of oral mucosal transudate. Since 2006, with the widespread expansion of HIV testing in the USA, and with the possible expansion of home-based and new supervised self-testing initiatives in sub-Saharan Africa, this HIV test has become one of the most popular point-of-care tests based on oral specimens.[1–3] It is more acceptable to patients because of its non-invasive and pain-free specimen collection and its rapid turnaround time.[4–6] In Kenya and Uganda, an increased acceptance and preference for this test has helped improve the uptake of home-based HIV-testing initiatives.[7,8] The Kenyan Government also announced an expansion of bold and controversial self-testing initiatives for HIV, and is reviewing the possible approval of oral tests. Self-testing initiatives are also relevant for southern Africa, a region that has remained the epidemiological locus of the epidemic; countries such as Botswana, Lesotho, Mozambique, South Africa, Swaziland, Zambia, and Zimbabwe are focused on scaling up alternative HIV-screening programmes.

Oraquick is also being considered for potential use as an over-the-counter test in the USA and in many sub-Saharan countries. This move might revolutionise HIV testing by offering a proactive testing option to people who, because of stigma, do not wish to attend public health centres for testing. Hopefully, offering a confidential testing option will bring an end to the stigmatisation associated with HIV testing.[9] Although performance data are available on this test from the USA, there has not been a review of its worldwide accuracy. With optimistic developments in HIV aimed at eradicating infection, worldwide expansion of HIV-testing programmes has taken centre stage because testing is the cornerstone of care and treatment.[10] With self-testing initiatives imminent, programme planners

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Objectives:

1. Compare diagnostic accuracy of oral fluid vs. whole blood samples
2. Compute Positive Predictive Values in high- and low-prevalence settings

Study Design

- Systematic review & meta-analysis
- Five databases of published work & five key HIV Conferences
- Bayesian Statistical Model

Pai, P. et al. Head-to-head comparison of accuracy of a rapid point-of-care HIV test with oral versus whole-blood specimens: a systematic review and meta-analysis The Lancet D01:10.1016/S1473-3099(11)70368-1

Proof Source – Pai et al

	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Log (diagnostic odds ratio)
Subgroup 1a (oral mucosal transudate within study; n=10)	98·03% (95·85–99·08)	99·74% (99·47–99·88)	383·37 (183·87–799·31)	0·019 (0·009–0·040)	9·87
Subgroup 1b (whole blood within study; n=10)	99·68% (97·31–99·96)	99·91% (99·84–99·95)	1105·16 (633·14–2004·37)	0·003 (0·001–0·034)	12·75
Subgroup 2 (oral mucosal transudate only; n=6)	99·43% (95·28–99·93)	99·86% (99·22–99·98)	721·65 (126·84–4105·76)	0·006 (0·001–0·050)	11·75
Subgroup 3 (whole blood only; n=17)	99·8% (99·07–99·93)	99·78% (99·27–99·93)	466·96 (137·42–1586·76)	0·003 (0·001–0·009)	11·78

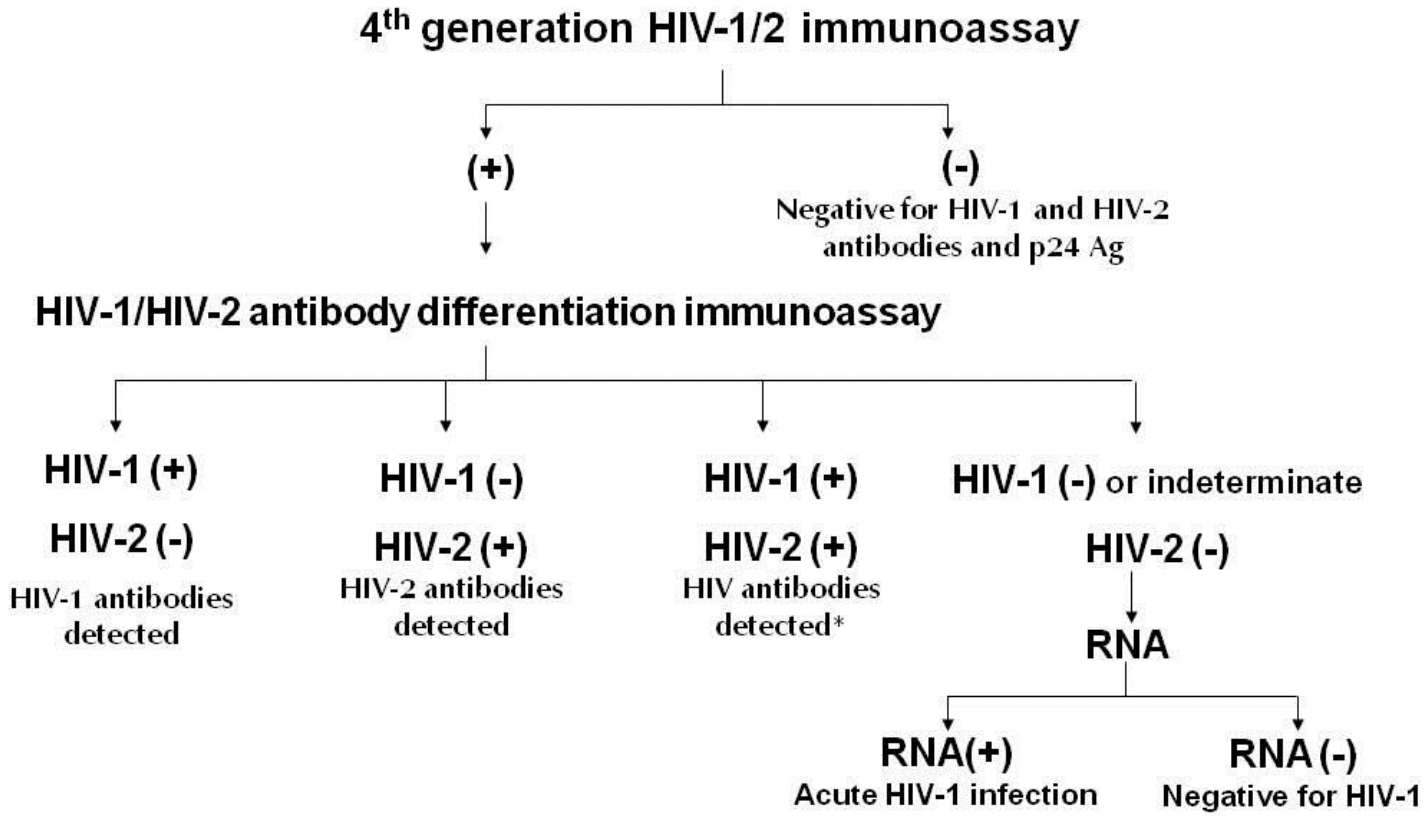
n refers to a datapoint (one set of true positive, false positive, false negative, and true negative).

Table 1: **Pooled estimates of accuracy across studies**

Pooled sensitivity of oral fluid was ~2% lower than FS whole blood

Pai, P. et al. Head-to-head comparison of accuracy of a rapid point-of-care HIV test with oral versus whole-blood specimens: a systematic review and meta-analysis The Lancet D01:10.1016/S1473-3099(11)70368-1

RECOMMENDED CDC GUIDELINES



*Additional testing required to rule out dual infection

How do rapid tests fit into HIV algorithm?

The CDC prefers using the algorithm, but understands that it is not practical in many settings

Rapid tests,

- if negative, no further testing
- If positive, start at beginning of algorithm

Summary

There is an urgent need to increase the proportion of persons who are aware of their HIV-infection status

Expanded, routine, voluntary, opt-out screening in health care settings is needed

Such screening is cost-effective

New CDC guidelines focuses on early infections