JOHNS HOPKINS
BLOOMBERG
SCHOOL of PUBLIC HEALTH

New STD Diagnostics: Effect on Population Based Surveillance for STDs

Charlotte Gaydos, MS, MPH, DrPH
Johns Hopkins University

Objectives

1. Review standard methods for diagnosis
2. Review new molecular diagnostic methods
3. Discuss standard and rapid tests
4. Explain the effect new diagnostics has on population based surveillance
5. Future strategies for STD control

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Section A

Review Standard Methods for Diagnosis; Review New Molecular Diagnostic Methods

Requirements for a Diagnostic Assay

- High specificity
- High PPV and NPV for all population types
- Inexpensive, available
- Rapid, simple to perform
- High sensitivity
- Sophisticated equipment not required
- Sample type convenience
- Distinguishes present from past infection

Advantages of Molecular Assays for Diagnosis of STDs

- High sensitivity and specificity
- Useful with noninvasive specimens (urine, self-administered vaginal swabs)
- Relatively rapid results (within 24 hours)
- Stability of specimens vs. culture
- Useful for field settings, screening—no clinic, no clinician required
- Cost-effective despite expense of assays
- Useful for multiple pathogens

Organisms

- Chlamydia trachomatis and neisseria gonorrhoeae
- Trichomonas vaginalis
- Mycoplasma genitalium
- Rapid tests (point of care diagnostics)
  - Chlamydia and gonorrhea
  - Trichomonas
  - Bacterial vaginosis (BV)
  - HSV-1, HSV-2
  - Syphilis
  - HIV

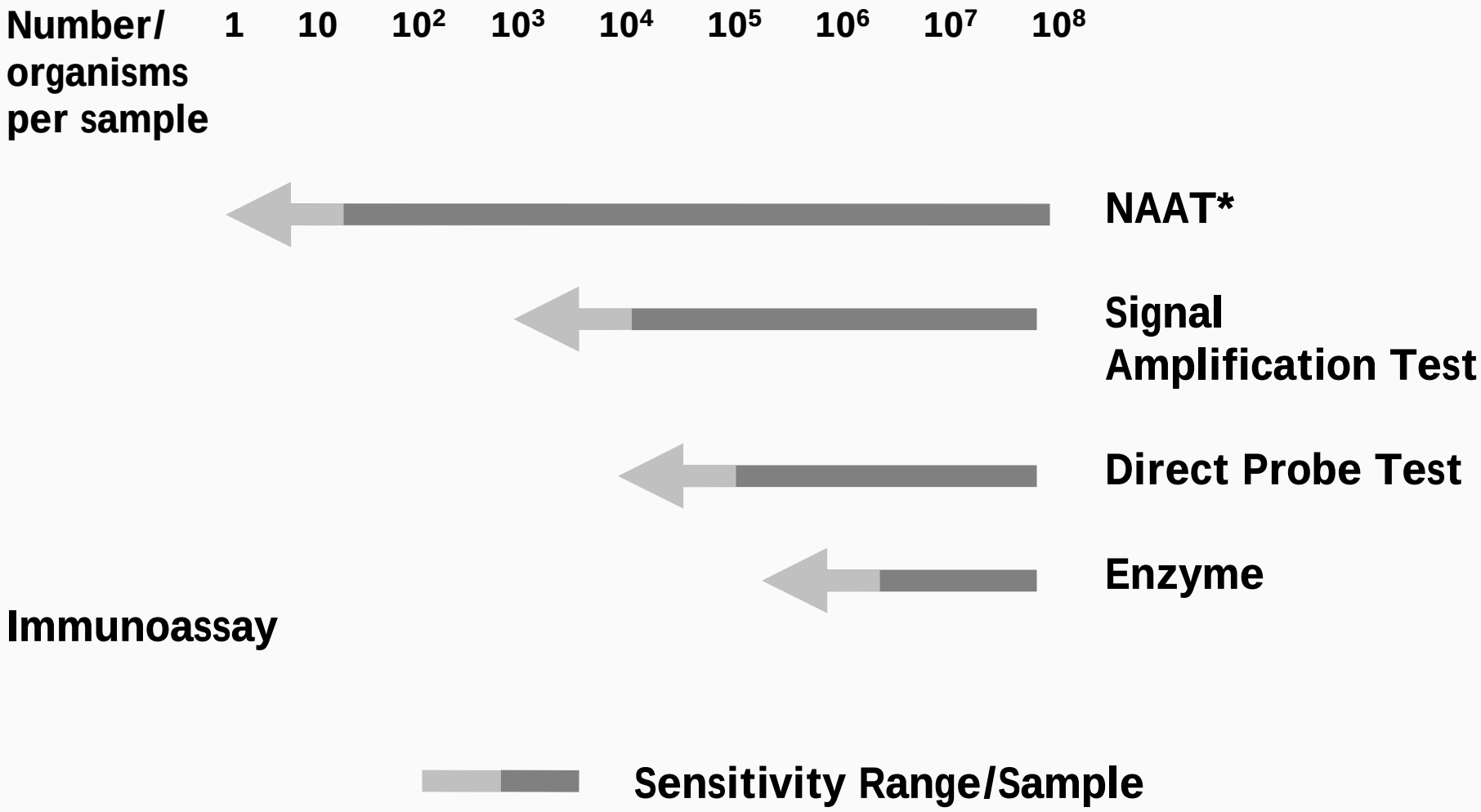
Chlamydia Trachomatis

- DFA stain, tissue culture in McCoy cells
- EIA (enzyme immunoassay)
- Probe Pace 2 (Gen-Probe)
- PCR Amplified DNA (Roche)
- TMA (transcription mediated amplification)
- Amplified RNA (Gen-Probe)
- Amplified Signal (Digene)
- SDA (strand displacement amplification) (Becton Dickinson)
- Robotics
- NAATs (nucleic acid amplification tests)

Neisseria Gonorrhoeae

- Gram stain/culture on Thayer Martin agar
- Probe (Pace 2) (Gen-Probe)
- PCR Amplified DNA (Roche)
- TMA (transcription mediated amplification)
- Amplified RNA (GenProbe)
- Amplified Signal (Digene)
- SDA (strand displacement ampliication) (Becton Dickinson)
- Robotics
- NAATs (nucleic acid amplification tests)

Relative Comparison of Sensitivity of Various Types of Tests for Detection of Chlamydia or Gonorrhea

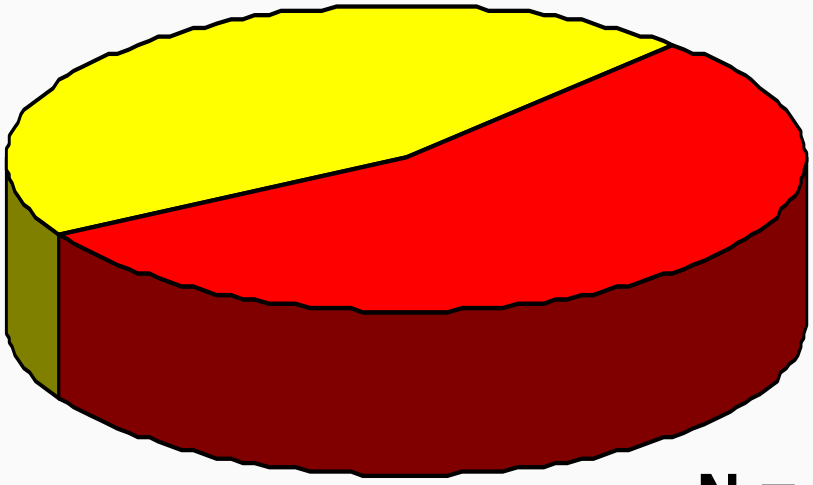


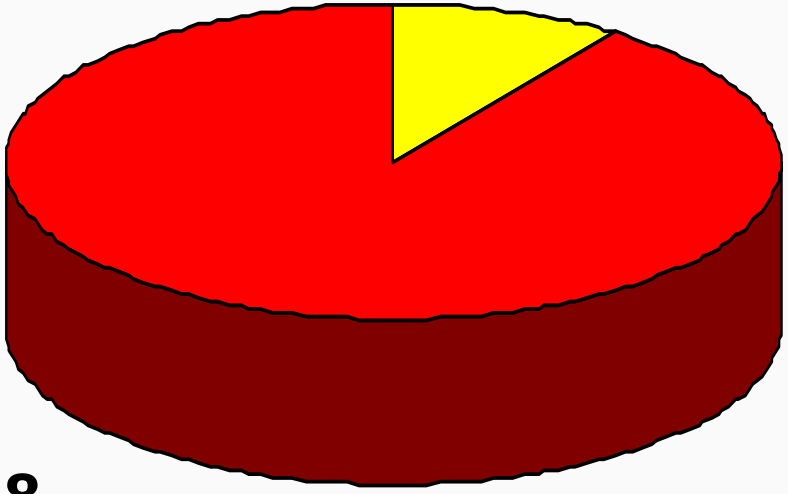
Notes: *Nucleic Acid Amplification Test

Basic Steps in NAATs Nucleic Acid Amplification Tests

- Sample preparation (heat, lysis, extract the DNA or RNA) or extract nucleic acid (NA) robotically
- Thermocycling to amplify DNA x 106 copies
  - Denaturation, annealing, extension
- Detection of amplified DNA product
  - Gel
  - EIA/colorimetric assay, microparticle, hybridization, probe

Sensitivity of Culture and PCR for C. Trachomatis in Men and Women



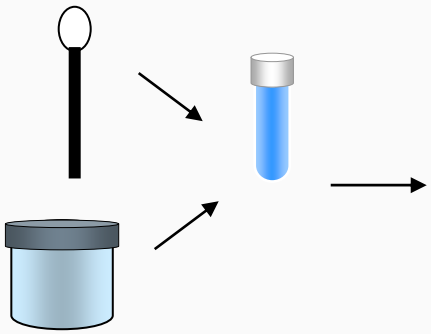


N = 1,238

Pos. 55%
Culture

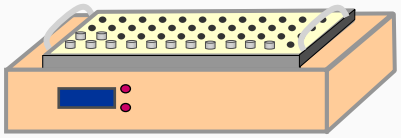
Pos. 90.3%
PCR

BDProbeTec™ ET System (SDA)



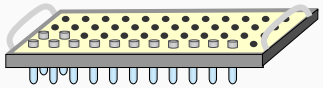
Sample Preparation

30 min



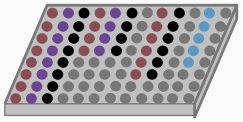
Sample Lysis

15 min

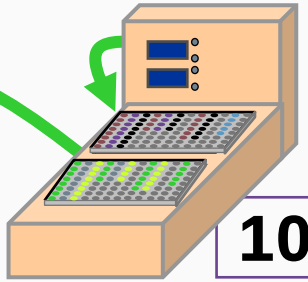


Sample Cooling

20 min

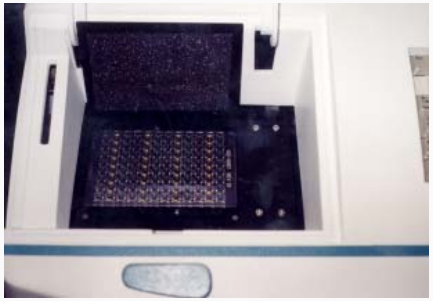


Priming Well Incubation Room Temp



10 min

Priming and Pre-Warm Incubation, Transfer



60 min

Amplification and Detection

APTIMA (TMA)

Target Capture

- Removes inhibitors
  - Amplification targeting ribosomes
- Dual Kinetic Assay (DKA)
  - Simultaneous detection/differentiation CT/GC
- Transport medium allows shipping and storage at 2° to 30° C
- The APTIMA Combo2 is FDA cleared for . . .
  - Male and female swab specimens
  - Male and female urine specimens
  - Symptomatic and asymptomatic patients
  - Self and clinician administered vaginal swabs

Table 1: Sensitivity and Specificity of Diagnostic Tests for the Detection of Chlamydia Trachomatis

Diagnostic Method	Sensitivity	Specificity
Tissue Culture	70-85%	100%
Direct Fluorescent Antibody	80-85%	>99%
Enzyme Immunoassay	53-76%	95%
Hybridization (Pace2)	65-83%	99%
Polymerase Chain Reaction		
Cervical	89.7%	99.4%
Female Urine	89.2%	99.0%
Male Urine	90.3%	98.4%
Strand Displacement Amplif		
Cervical	92.8%	98.1%
Female urine	80.5%	98.4%
Male urine	93.1%	93.8%
Transcription Mediated Amplif		
Cervical	94.2%	97.6%
Female Urine	94.7%	98.9%
Male Urine	97.0%	99.1%
Male Urethral	95.2%	98.2%

Table 2: Sensitivity and Specificity of Diagnostic Tests for the Detection of Neisseria Gonorrhoeae

Diagnostic Method	Sensitivity	Specificity
Culture	80-95%	100%
Gram Stain		
Males-symptomatic	90-95%	95-100%
Males-asymptomatic	50-70%	95-100%
Females	50-70%	95-100%
Hybridization (Pace2)	92.1-96.4%	98.8-99.1%
Polymerase Chain Reaction		
Cervical	92.4%	99.5%
Female Urine	64.8%	99.8%
Male Urine (Symptomatic)	94.1%	99.9%
Strand Displacement Amplif		
Cervical	96.6%	98.0-100%
Female urine	84.9%	99.3-100%
Male urethral	98.5%	91.9-100%
Male urine	97.9%	92.5-100%
Transcription Mediated Amplif		
Cervical	99.2%	98.7%
Female Urine	91.3%	99.3%
Male Urine	97.1%	99.2%
Male Urethral	98.8%	98.2%

Comparison of Three NAATs in Urines for Chlamydia (N = 506)

	Sensitivity	Specificity
ABBOTT LCR	96.0%	99.1%
BD ProbeTec	96.0%	100%
GEN-PROBE Aptima Combo2	100%	98.8%

True positive = 2 positive NAATs

Gaydos, C. JCM (2004); 42: 3041-3045

Trichomonas Vaginalis

- More prevalent than CT or GC
  - Estimates eight million cases annually in the U.S.
  - Not a reportable disease
- Men—may be asymptomatic (>50%), NCNGGU, may cause prostatitis, epididymitis; associated with a significant decrease in sperm motility and viability; isolated from 10% infertile men
- Women—asymptomatic (<50%) or cause frothy discharge, risk for cervical neoplasia, tubal infertility post-hysterectomy infection atypical PID preterm birth, low birth weight
- Risk factor for HIV transmission in men and women (?)
- Sensitivity—wet preparation ~50%; culture ~70%
  - PCR ~90%

Recent Publications

- Soper (2004). *A J Ob Gyn*: Trichomoniasis Review 190: 281-290
- Moodley, et al. (2002). *CID*: TV Associated with PID in HIV+ Women
- Zhang, et al. (1994). *Int J Epidemiol*: TV a Cause of Cervical Neoplasia (24 studies)
- Zhang, et al. (1995). *Ann Epidemiol*: TV and Cervical Cancer: Prospective Study in China
- Sayed El-Ahl, et al. (2002). *J Egypt Soc Parasit:* TV and Cervical Cancer in Egyptian women
- Hobbs, et al. (1999). *STD*: TV Cause Urethritis in Malawian Men
- Hardick, et al. JCM (2006): Cf GP TMA TV with Research PCR

Mycoplasma Genitalium

- Thought to be sexually transmitted
- Associated with NCNGGU in men and cervicitis in women recently
- Possible sequelae
  - Endometritis?
  - PID?
  - Adverse birth outcomes?
- Smallest prokaryote bacteria capable of self-replication; difficult to culture; PCRs described

Recent Publications

- Manhart, et al. (2003). *JID*: M. Gent Assoc with 3.3 Risk MPC
- Mena, at al. (2002). *CID*: M. Gent in 25% of 97 Men Urethritis cf. 7% Asymptomatic p = .006
- Falk, et al. (2004). *STI*: M. Gent+ Men (7%) Had Sym Urethritis More Often than Men Infect with CT (12%), 63% Female PN Infected with M. Gent; 35% of Men w/ Urethritis Had No Agent
- Deguchi, et al. (2004). *STD*: U. Urealyticum in 15.8% Men NGU or Non-CT Urethritis (18%) CF Men without Urethritis (7.8%)
- Jenson, et al. (2004). Urine Better Sample in Men
- Dupin, et al. (2003). *CID*: Real Time PCR 115-kDa Gene, Shift to Decreasing Bacterial Load or Negative PCR after Rx
- Hardick, et al. (2006). *JCM*: Perfm. GP TMA to PCR for MG

Microbial Etiology Study Methods: CT,GC, TV, MG

- Men (290) and women (325) attending STD clinics
- Urethritis and cervicitis was dx'd; multiple samples
- Routine tests—GenProbe Combo2 tests for CT and GC
- Trichomonas research PCR*
  - B tubulin gene; RT-PCR Roche Light Cycler
- Mycoplasma research PCR**
  - Two targets in a diplex assay; MgPa adhesion gene
  - 16S rRNA gene; 7900 ABI Prism system
  - APTIMA TMA*** also performed for trichomonas (AMP-TV) and for mycoplasma genitalium (AMP-MG)

Sources: *Hardick., J., et al. (2003). *JCM*; **Hardick, J., et al. (2006). JCM; *** Hardick, A., et al.(2006). JCM

Microbial Etiology Study Results: N = 325 Females, 290 Males

Females: %

CT*	11.4
GC*	4.3
TV*	14.9
MG*	24.6

*Patient Infected Status

TV B-TUB FRET	15.7
TMA-TV	19.0
MG MLRT PCR	20.9**
TMA MG	21.9**

**Based on Resolved MG results

Males: %

CT*	20.3
GC*	12.8
TV*	3.9
MG*	15.2

*Patient Infected Status

TV B-TUB FRET	3.8
TMA-TV	4.5
MG MLRT PCR	15.7**
TMA MG	17.5**

**Based on Resolved MG results

Results: N = 325 Females, 290 Males

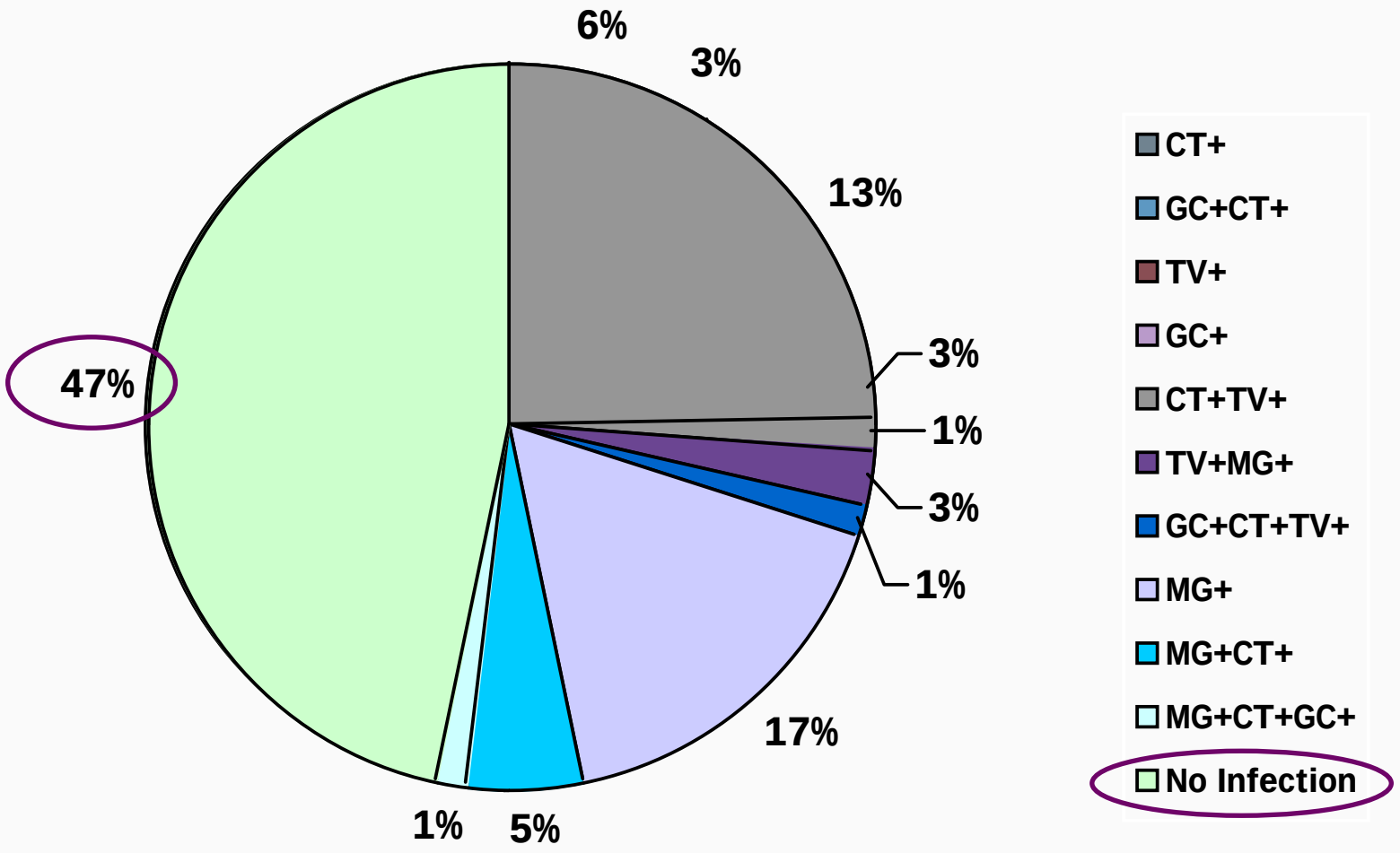
Females:	**N = 77** **Cervicitis**	**N = 248** **No Cervicitis**
CT	18.2% (14/77)	9.3% (23/248)
GC	7.8% (6/77)	3.2% (8/248)
TV	18.2% (14/77)	13.2% (34/246)*
MG	26.0% (20/77)	17.5% (43/246)*

* 2 tests not done

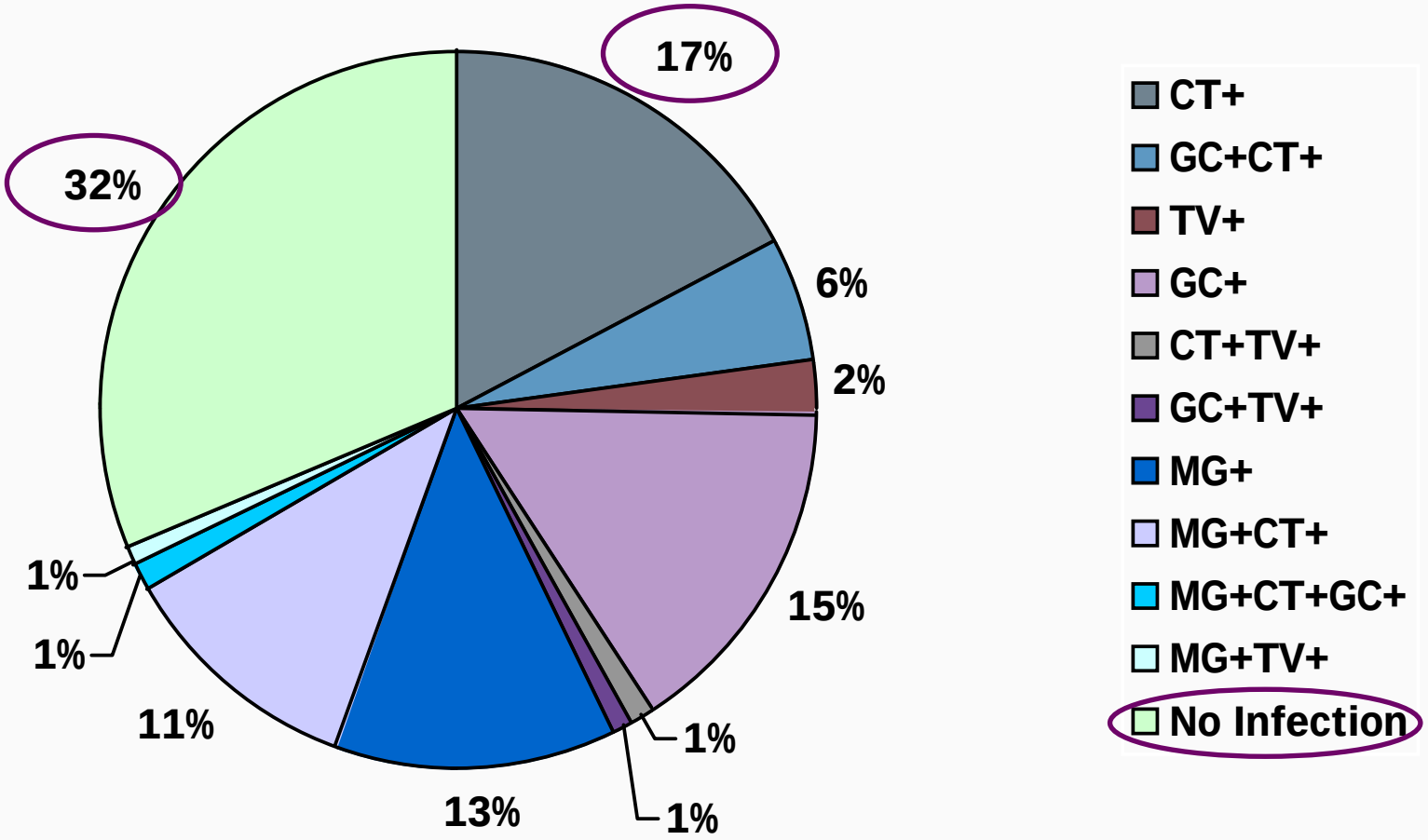
Males:	**N= 153** **Urethritis**	**N=137** **No Urethritis**
CT	32.7% (50/153)	6.6% (9/137)
GC	24.2% (37/153)	0% (0/137)
TV	5.2% (8/153)	2.2% (3/137)
MG	21.7% (31/152)**	8.0% (11/137)

** 1 test not done

Results: Females with Cervicitis (n = 77)



Results Males with Urethritis (n = 153)



Association with Cervicitis

	Univariate		Multivar Model 1		Model 2	
	OR	**p value**	**OR**	**p**	**OR**	**p**
CT	1.95	0.058	1.60	0.250	1.58	0.078
NG	1.69	0.316	1.01	0.983	0.93	0.911
TV	1.61	0.126	1.59	0.146	1.56	0.174
MG	2.64	0.0006	**2.42**	**0.0026**	**1.56**	**0.0028**
Age < 25 Years	1.42	0.140			1.21	0.467
Contact	0.62	0.323			0.47	0.858

Association with Urethritis

	Univariate		Multivariate Model 1	
	OR	**p value**	**OR**	**p**
CT	6.9	< 0.0001	6.92	< 0.0001
NG*	88.5	< 0.0001	----*	
TV	3.72	0.1087	4.29	0.08
MG	3.66	0.000	3.67	0.000
Age < 25 yr	1.1	0.69		
Contact	1.97	0.05		

Notes: * NG could not be fit into the multivariate model due to collinearity between NG and urethritis that caused the model not to fit

Conclusions

- Urethritis and cervicitis cause significant morbidity world wide
- Common agents are gonorrhea and chlamydia, but non-chlamydial-non-gonoococcal ureth/cx common
- Use of newer tests such as Gen-Probe AMPTIMA for trichomonas and mycoplasma or PCR will allow better etiologic diagnostic capability in future studies
- It appears that even with increased diagnostic capability, a significant proportion of urethritis and cervicitis cases yield no etiologic agent
- Reasons—other agents such as HSV, ureplasma, *m. hominis*, un-discovered organisms, *atopobium vaginae*? Others?

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Section B

Standard and Rapid Tests

Summary of New Molecular Tests for CT, GC, TV, MG

- All appear to have superior sensitivity and specificity cf. to older traditional tests
- Expense is an issue
- They are cost effective and C-E analyses can guide choices
- They allow for use of non-invasive specimens and non-traditional venues

Standard and Rapid Tests for STDs

- CT/GC
- Trichomonas
- BV
- Syphilis
- HSV
- HIV

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

CT

- Optical immunoassay (OIA) (formerly Biostar)
- Sensitivity 66-73% cf. culture

GC

- OIA
  - Sensitivity 93.2% for symptomatic male urine
  - Sensitivity 70.7% for female cervical

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

Trichomonas

- Range of sensitivity and specificity of rapid tests for trichomonas vaginalis in women

Test Assay	Sensitivity (%)	Specificity (%)
Wet Preparation*	50-72	100
Culture*	70-78	100
OSOM**	83-99	100
XenoStrip**	77-90	93-99
Affirm VPIII**	80	98

- * Compared to nucleic acid amplification tests (NAATs)
- ** Compared to culture

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

- BV (bacterial vaginosis) Syndrome associated with adverse pregnancy outcomes
- Not exclusively considered an STD (transmitted sexually)
- Characterized by a disturbance of the normal vaginal flora, with a loss of H2O2-producing lactobacillus spp.
- Increase in the numbers of gram-variable coccobacilli (gardnerella and bacteroides spp.), anaerobic organisms (mobiluncus spp., fusobacterium spp., prevotella spp., peptostreptococcus spp.), genital mycoplasmas, BVA organisms
- Rise in the vaginal pH and increased levels of production of proteolytic enzymes, organic acids, and volatile amines
- Diagnosis
  - Amsel—presence of three of four clinical features (a characteristic homogeneous white adherent vaginal discharge, a vaginal fluid pH >4.5, a positive amine test, and “clue cells”)
  - Nugent gram stain method based on points

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

BV (Bacterial Vaginosis)

- Range of sensitivity and specificity

Test Assay	Comparison Criterion	Sensitivity (%)	Specificity (%)
BV Blue	Nugent	88-91	95
	Amsel	50-88	91-100
Fem Exam	Nugent	91	62
	Nugent		
	pH	88-94	57-64
	Amine	41	91
	pH or Amine	89	61
	pH and Amine	40-59	92-95

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

BV (Bacterial Vaginosis)

- Range of sensitivity and specificity of rapid tests for diagnosis of BV compared to Nugent or Amsel criteria

Test Assay	Comparison Criterion	Sensitivity (%)	Specificity (%)
Osmetech	Nugent	82	76
	Amsel	83	77
Affirm VPIII	Nugent	73	97
	"Clue cells"	90	97
	G. vaginalis (10^5 CFU/ml)*	95	100

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

Syphilis Treponema Palladium

- Darkfield microscopy; DFA-treponema pallidum
- Serology—VDRL, RPR, FTA-absorb, MHA-Tp (microhemagglutination) (t. pallidum adsorbed to erythrocytes, TP-PA (particulate gelatin/latex)
- Rapid Tests: ~20 companies manufacture rapid simple treponemal tests (use whole blood, serum, or plasma)
- Immunochromogenic strips coated with treponemal antigens
- Reactions show up as colored lines of a spot on the membrane
- Some use a format similar to the RPR test using tp.coated latex particles
- Use reagents stable at RT, require minimal training, are very cheap, and use only three to four steps with results being available in eight to twenty minutes
- Used in developing countries but are not FDA approved

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs

HSV-1-2 (Western Blot Is Reference Standard)

- Serology Antibody to HSV-2, HerpeSelect 2 ELISA IgG test (focus diagnostics, 96-100% sensitivity and 96-97% specificity)
- Antibody to HSV-1, HerpeSelect 1 ELISA 91-96% sensitivity and specificity of 92-95%
- Kalon EIA—not FDA cleared; UK manufactured; sensitivity 96.4%, specificity 99.1%
- Biokit HSV-2 USA, Inc (formally POCkit HSV-2) is a rapid point-of-care test using capillary blood has sensitivity of 93-100%
- Sensitivity and specificity compared to western blot are 86-100% and 59-96.8%
- Organism PCR assay for HSV1/2 that is available as an analyte specific reagent (ASR), (not FDA cleared but can be validated by an individual laboratory) (cepheid) (culture is ref method)
- Similar assay which can type the HSV as HSV-1 or HSV-2 (cepheid)

Standard and Rapid Tests for STDs

HIV: Serology—EIA, Western Blot Is Reference Method

- Virus Detection: Viral Load—Viral RNA Amplification Methods

Rapid Tests

- FDA cleared
  - OraQuick Rapid HIV-1/2 Antibody Test
  - Reveal G2 Rapid HIV-1 Antibody Test
  - Uni-Gold Recombigen HIV Antibody Test

NOT FDA Cleared

- Determine HIV-1/2/0, Genie II HIV-1/2, Genie II HIV-1/2, OraQuick, Serodia HIV-1/2, HIV SPOT-1/2, Entebe HIV Dipstick, HIV Tri-Dot, DoubleCheck HIV-1/2, HIVCHEK System 3, Hema-Strip HIV-1/2, Sero-Strip HIV-1/2, Capillus HIV-1/2, Quix HIV- 1/2/O

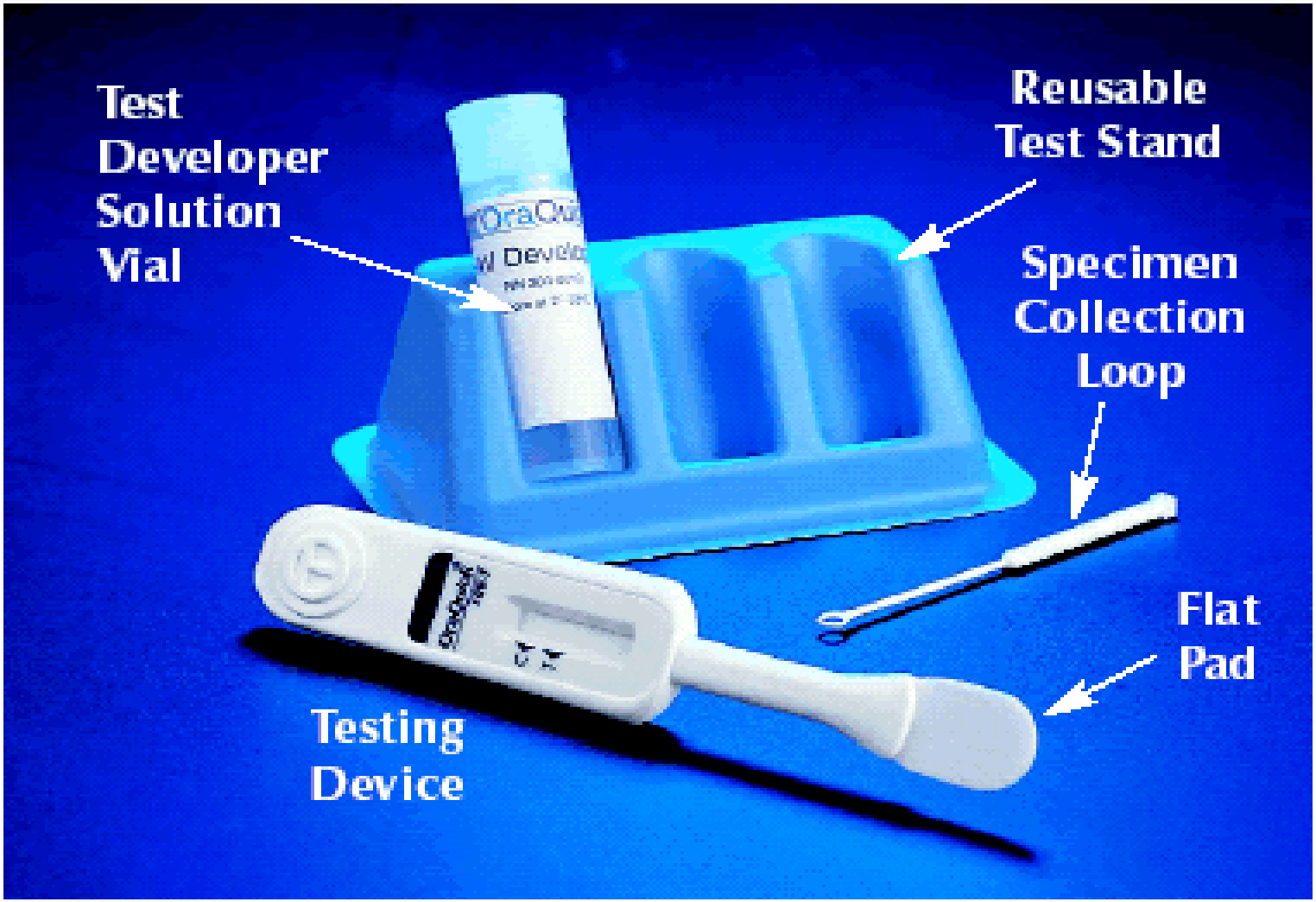
Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

Standard and Rapid Tests for STDs: HIV

Test Kit Name	Manufacturer	Specimen Type	CLIA Category	Equipment Required*	Sensitivity, % (95% C.I.)	Specificity, % (95% C.I.)
OraQuick Advance Rapid HIV-1/2 Antibody Test	Orasure Technologies,Inc. http://www.orasure.com/	Whole blood, Oral Fluid Plasma	Waived Moderate Complexity	Timer	99.6 (98.5-99.9)	100 (99.7-100)
Reveal G2 Rapid HIV-1 Antibody Test	MedMira, Inc. http://www.medmira.com/	Serum, plasma	Moderate Complexity	Centrifuge	99.8 (99.2-100)	99.1 (98.4-99.4)
Uni-Gold Recombigen HIV Test	Trinity BioTech, plc http://www.unigoldhiv.com/	Whole blood Serum, plasma	Waived Moderate Complexity	Timer	100 (99.5-100)	99.7 (99.0-100)

Source: Gaydos, C. (2006). Rapid Tests for STDs, *Current Infect Dis Reports*; 8: 115-124

OraQuick Test



Source: http://www.cdc.gov/hiv/pubs/rt/OraQuick_Test.gif

Reveal Test

Source: http://www.cdc.gov/hiv/pubs/rt/Reveal.jpg

Trinity Test

Source: http://www.cdc.gov/hiv/pubs/Unigold-kit.jpg

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Section C

Epidemiology: Effect of New Diagnostics and New Specimen Types on Population Based Surveillance for STDs

New Specimen Types for Amplification Technologies for STD Diagnosis

- Urine
- Vaginal swabs
  - Self-collected
  - Clinician collected
- Self collected penile swabs

Noninvasive Screening for STDS: Advantages

- Acceptability to the patient, accurate
- Avoids bias in screening only clinic-based populations
- Identifies asymptomatic infections resulting in early treatment and prevention
- Cost-effective and cost savings (pooling)
- Improves outreach to underserved populations
- Utilizes highly sensitive and specific NAAT

Populations and Venues Where Self Sampling Has Been Used

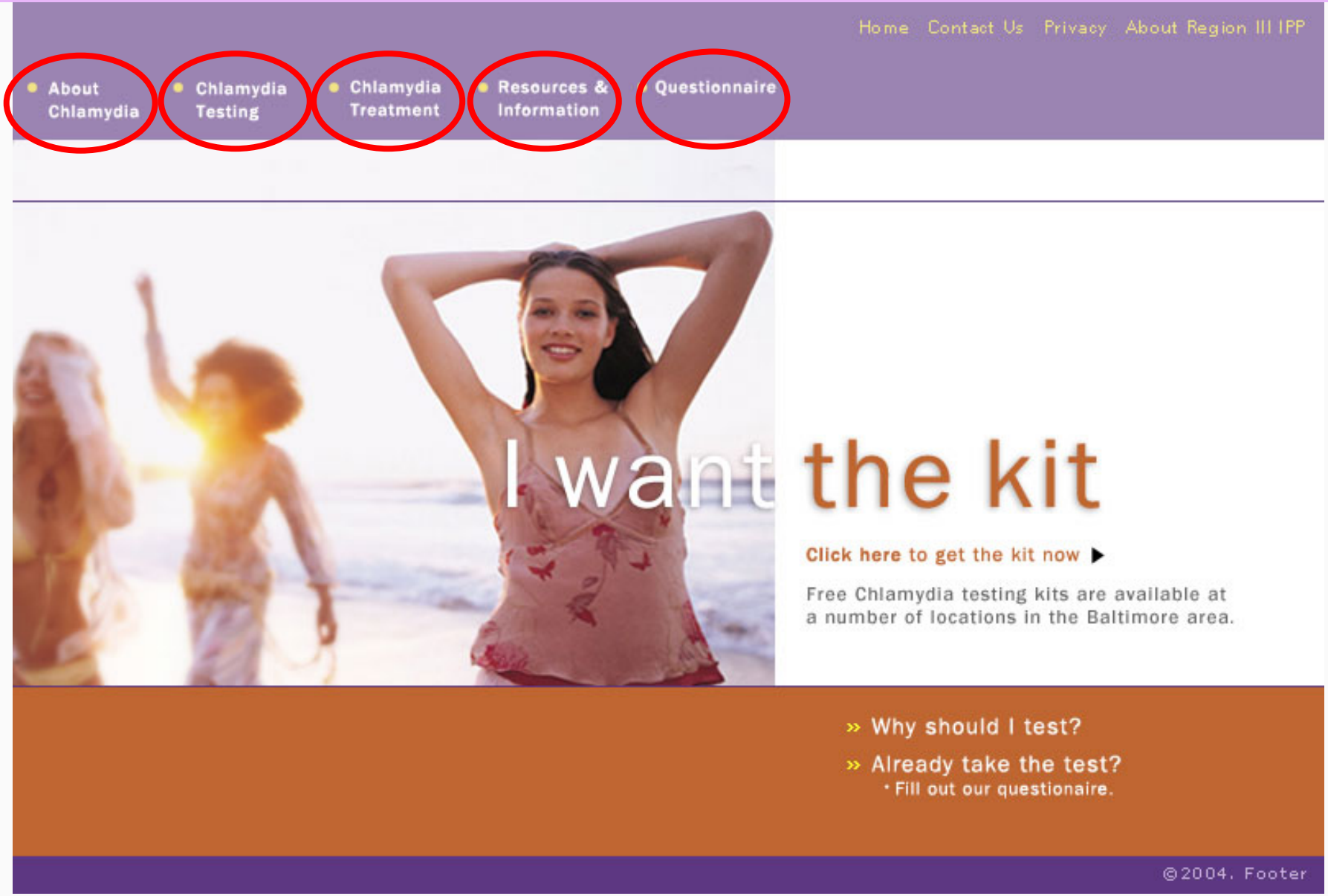
- Groups
  - **Military**
  - **Schools**
  - **Detention/jails**
  - Job corps
- Outreach
  - **Street/home**
  - Drug Rx clinics
  - Homeless shelters
  - Recreation centers
  - Shopping centers
- Other clinics
  - **Emergency departments**
  - Family planning
  - Teen clinics
  - HMOs
- Other countries
  - **Czech/Slovak Republic**
  - **Uganda, Zimbabwe**
  - **Peru**
  - **China, India**

Vaginal Swabs Are Appropriate Specimens for Diagnosis of Genital Tract Infection with C. Trachomatis

- NAAT sensitivity
  - Vaginal swabs 93%
  - Cervical swabs 91%
  - FVU 80.6%
- Culture sensitivity 83.5%
- Specificities (all specimens) >99%
  - GenProbe APTIMA COMBO2 now FDA cleared for vaginal swabs

Source: Schachter, et al. (2003). *JCM*; 41: 3784-3789

Chlamydia Testing Kits



Chlamydia Testing Kits

Home Contact Us Privacy About Region III IPP

About Chlamydia | Chlamydia Testing | Chlamydia Treatment | Resources & Information | Questionnaire

» Why should I test?
» Already take the test?
• Fill out our questionnaire.

• Why test? • How to get a free test • How to test at home

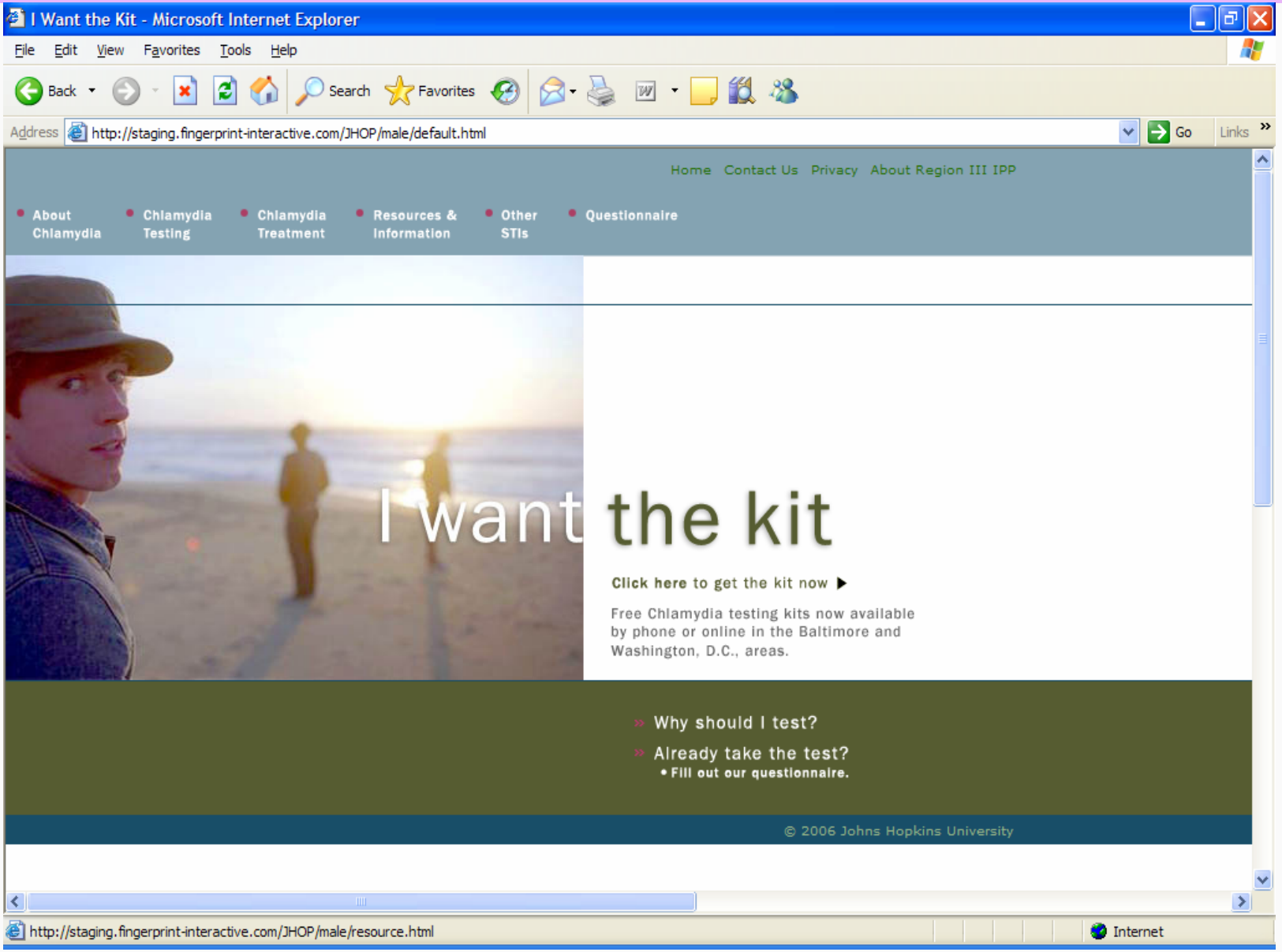
I want the kit

Chlamydia Testing

The Kit is a **free chlamydia test** that you can take in the comfort of your own home. **Use the resources on this site to get one**. It's the first step in protecting yourself from the long-term health problems that can be caused by untreated chlamydia.

- You can use the swab in The Kit to collect a vaginal sample **in the privacy of your own home** by following the easy directions. Then mail the swab directly to our testing lab in the free, stamped, pre-addressed envelope included in The Kit.
- **Testing for chlamydia is done in our laboratory.** We will also test your sample for gonorrhea, a similar infection to chlamydia. Our certified laboratory has skilled technicians who use the most up-to-date, state of the art testing methods available.
- You can get your **confidential test results** within a week or two by calling us using your Kit's unique ID number and a private password that you supply when you mail your sample in for analysis.
- If you are infected and need treatment, you can receive it **free and confidentially** from a local clinic near you, or you can ask us to send the test results to the healthcare provider of your choice.

Chlamydia Testing Kits



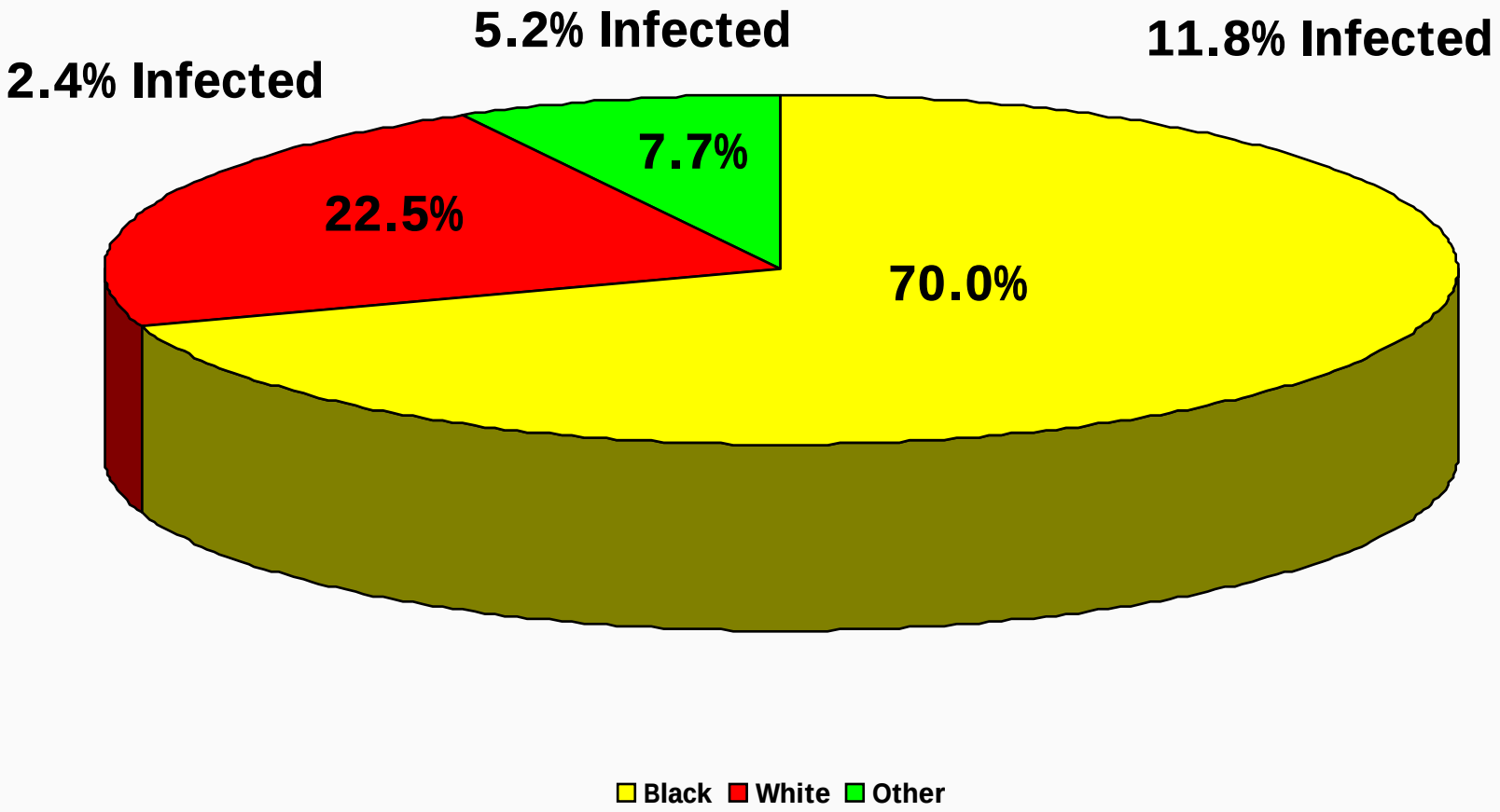
Internet SAS Progress: Analysis of Vaginal Swabs Received the Most Internet Requested

Of 778 Tested

- 71 (9.1%) CT positives*
- 12 (1.3%) GC
- Trichomonas 13/115 (11.3%)
  - * Of 500 tested by all three NAAT assays . . .
    - ProbeTec sensitivity 82.6%
    - Amplicor PCR sensitivity 100%
    - APTIMA Combo2 sensitivity 100%
  - Specificity 100% for all assays

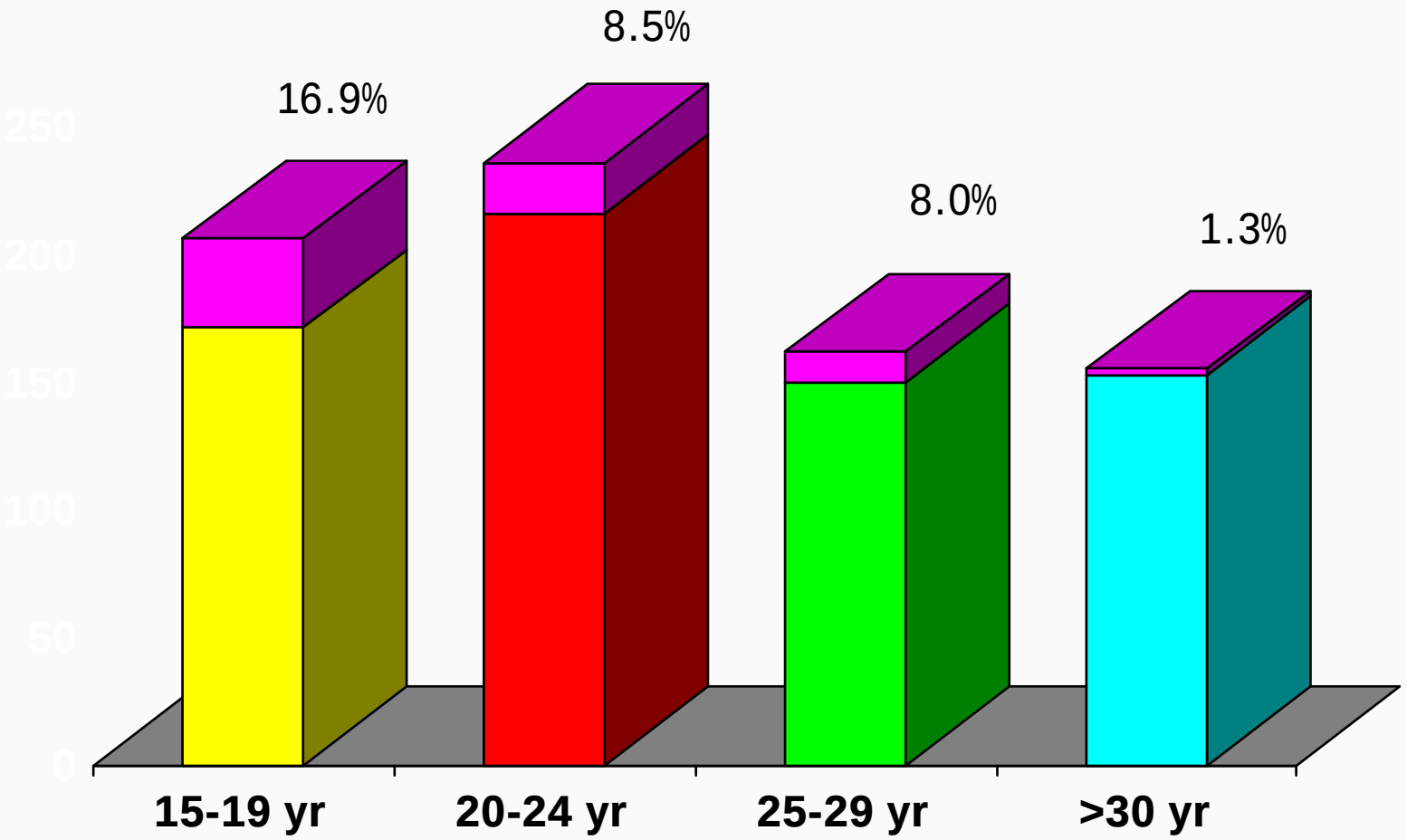
Source: www.iwantthekit.org

CT Prevalence: Results by Race (n = 752*)



Notes: * Eight did not report race: Black race vs. all others, p = 0.0003;
Of 69 total positives: Black: 62 (90%), White: 4 (5.8%), Other: 3 (4.3%)

CT Prevalence: Results by Age (n = 756*)



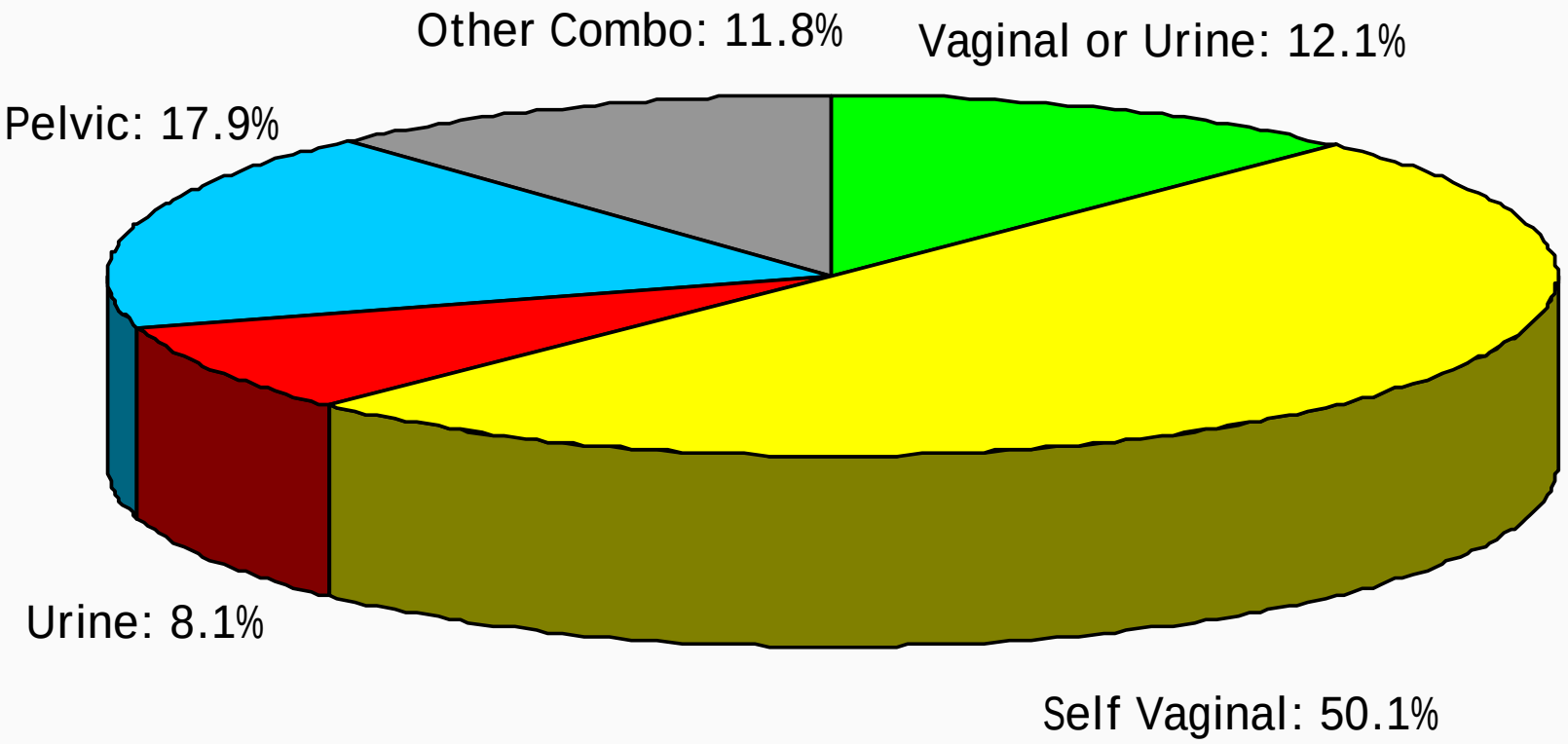
Notes: * Four did not report age; there were nine women 14 years old, all were chlamydia negative

Multivariate Logistic Regression of Demographics and Risk Factors

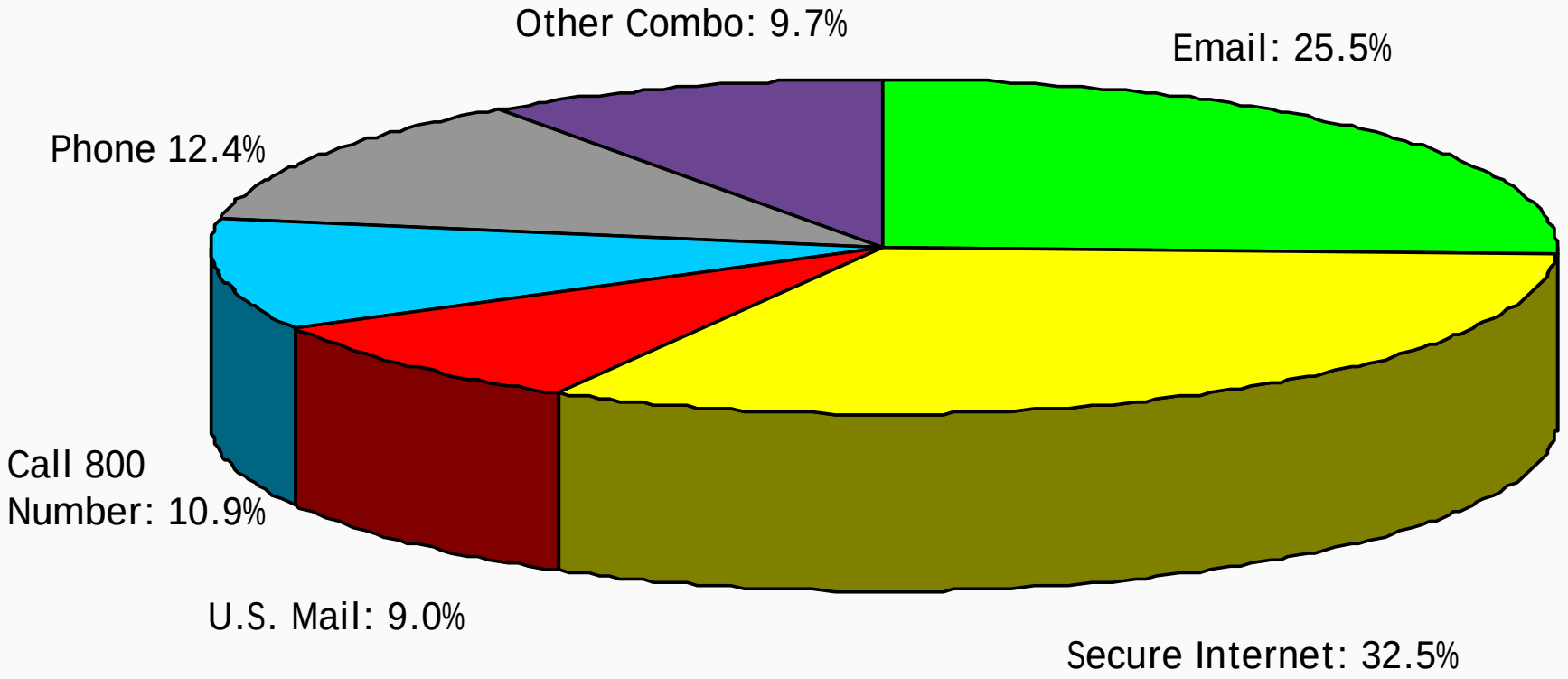
	O.R. (95% C.I.)
Black Race (ref. White)	5.8 (2.0, 16.6)
Age	2.7 (1.4, 5.2)
Birth Control	1.8 (1.05, 3.2)
Non-Consensual Sex	0.4 (0.2, 0.9)
Multiple Partners	2.2 (1.2, 4.0)

Variables: Race, age, multiple partners, prior CT, prior GC, oral/anal sex, birth control, non-consensual sex. Hosmer–Lemeshow Goodness of fit test = 0.77

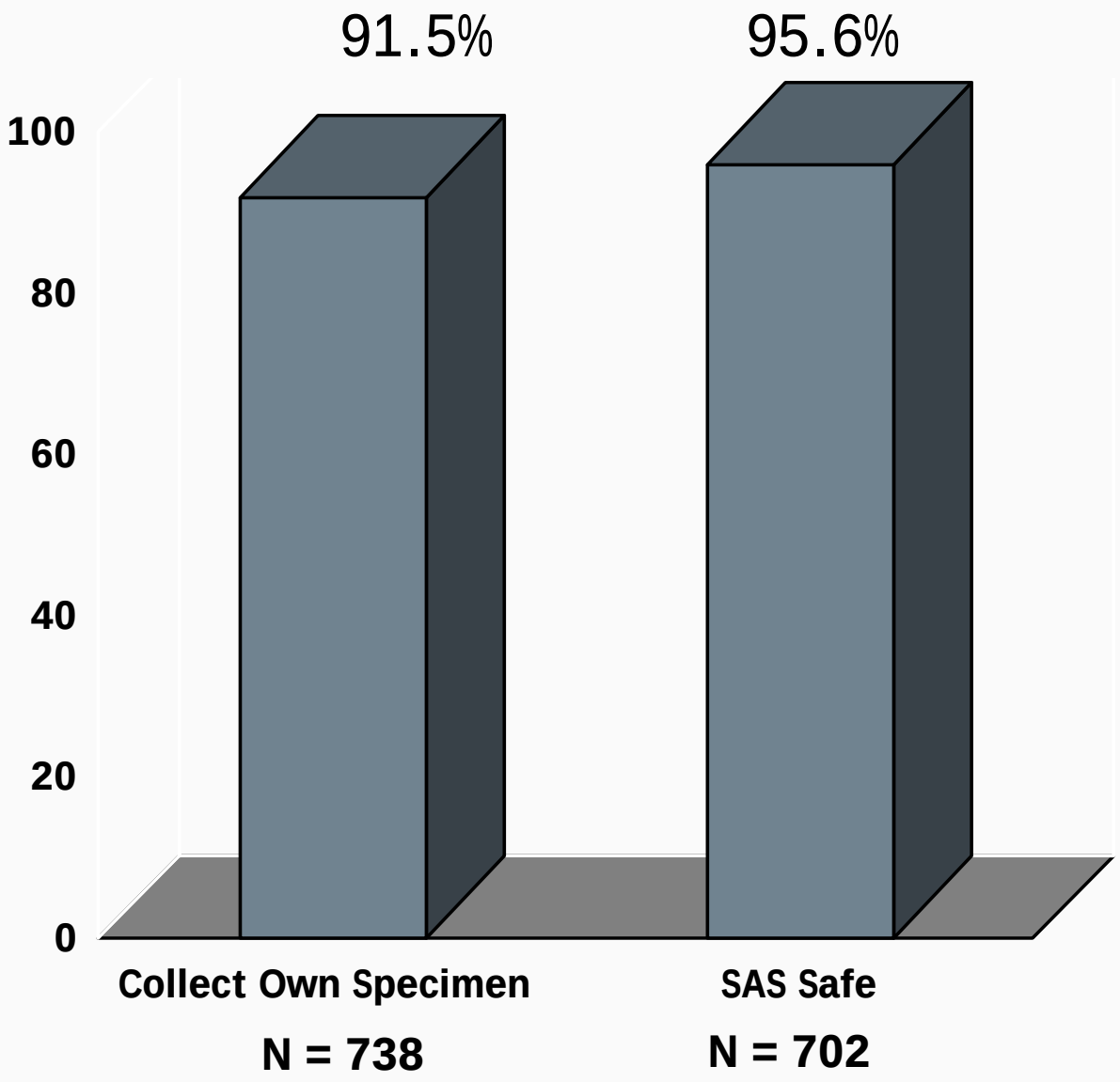
Questionnaire Results: Preference for Sample Type (N = 745)



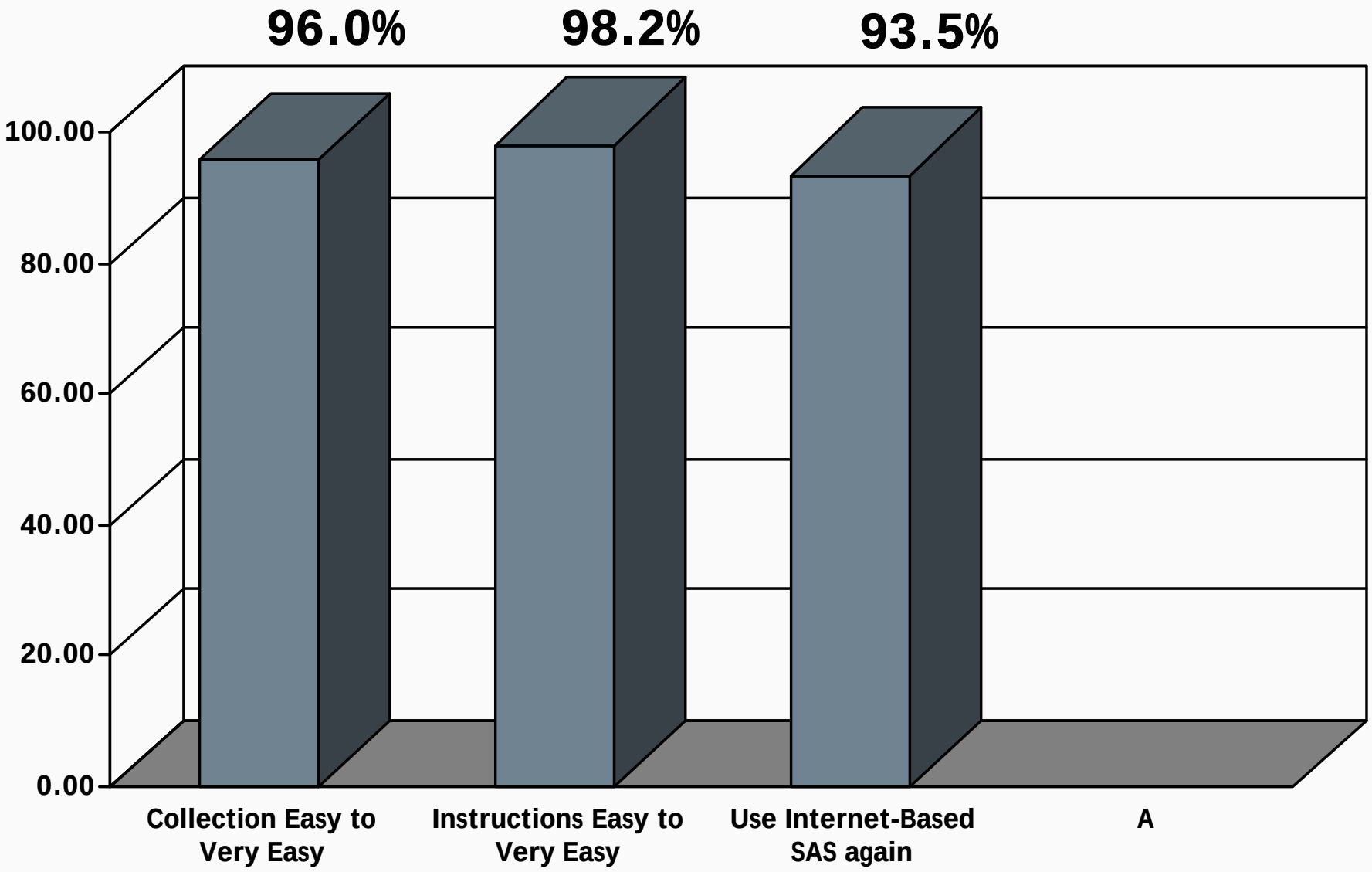
Questionnaire Results: Preference for Receiving Results (N = 744)



Questionnaire Results: Self Collection

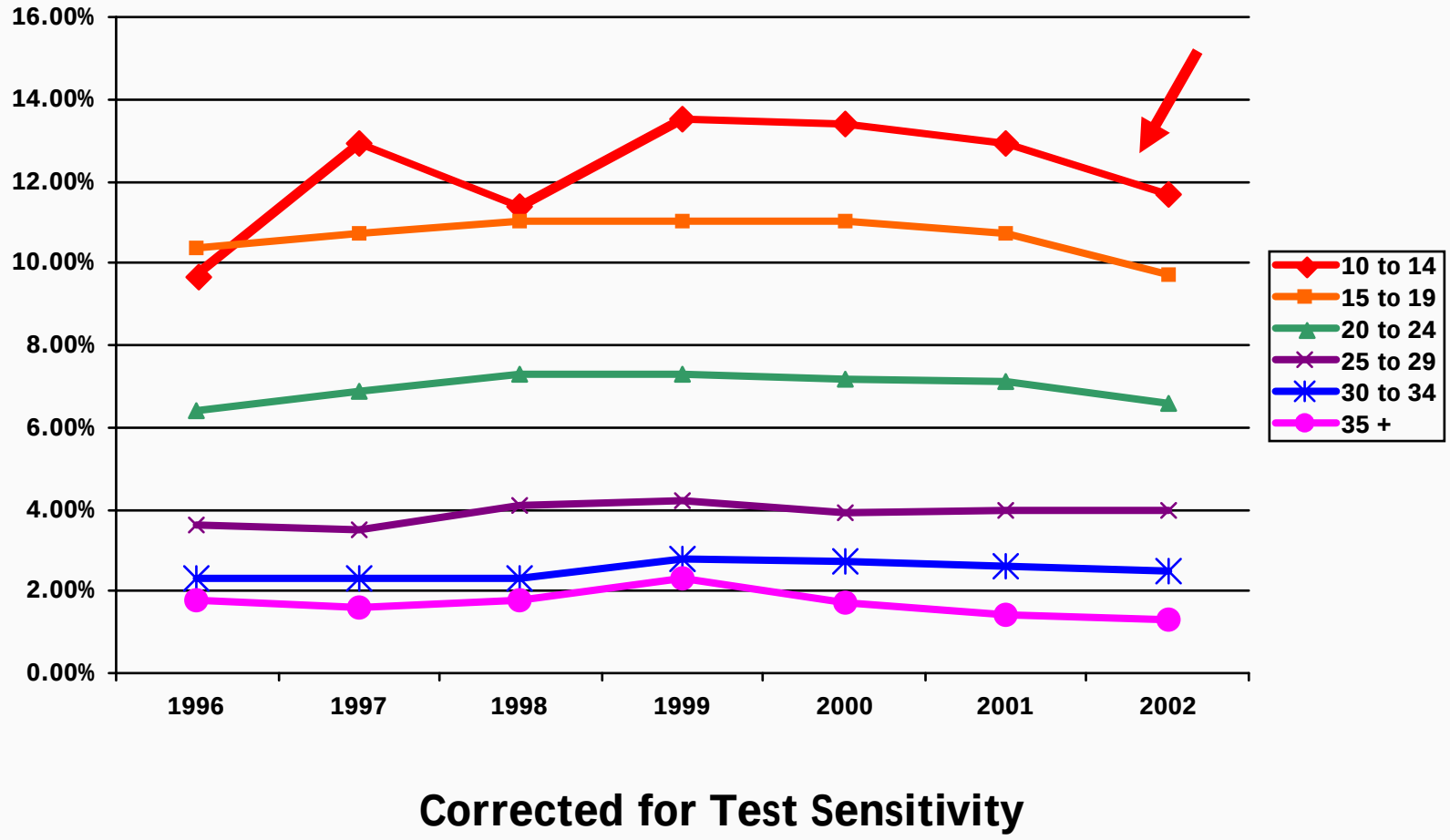


Questionnaire Results SAS Collection (N >700)



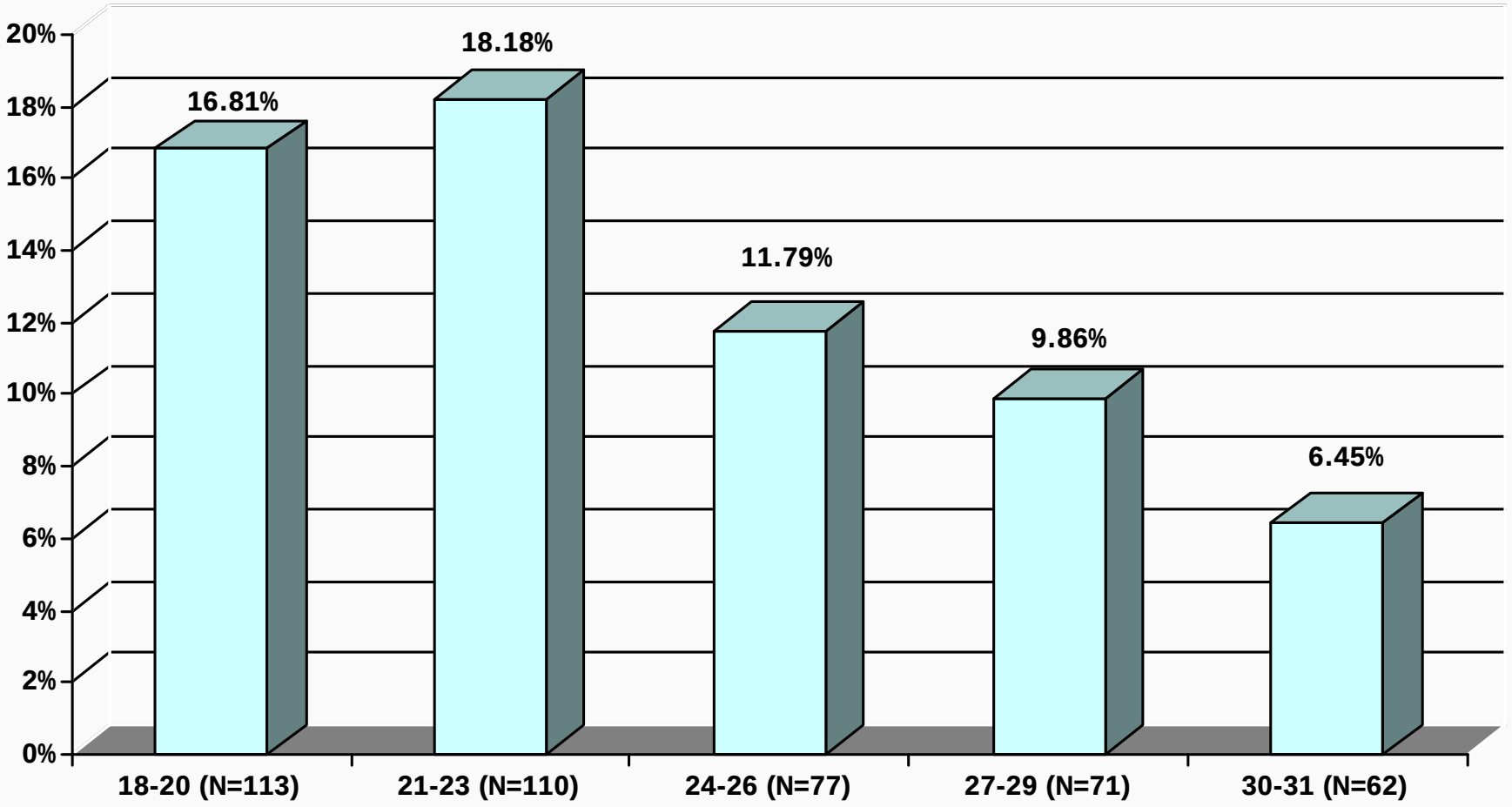
Region III: Chlamydia Positivity by Age, All Sites, 1996-2002

- Age is a risk factor!!!



Notes: Region III: DE, MD, PA, WV, VA, DC, Baltimore, Philadelphia

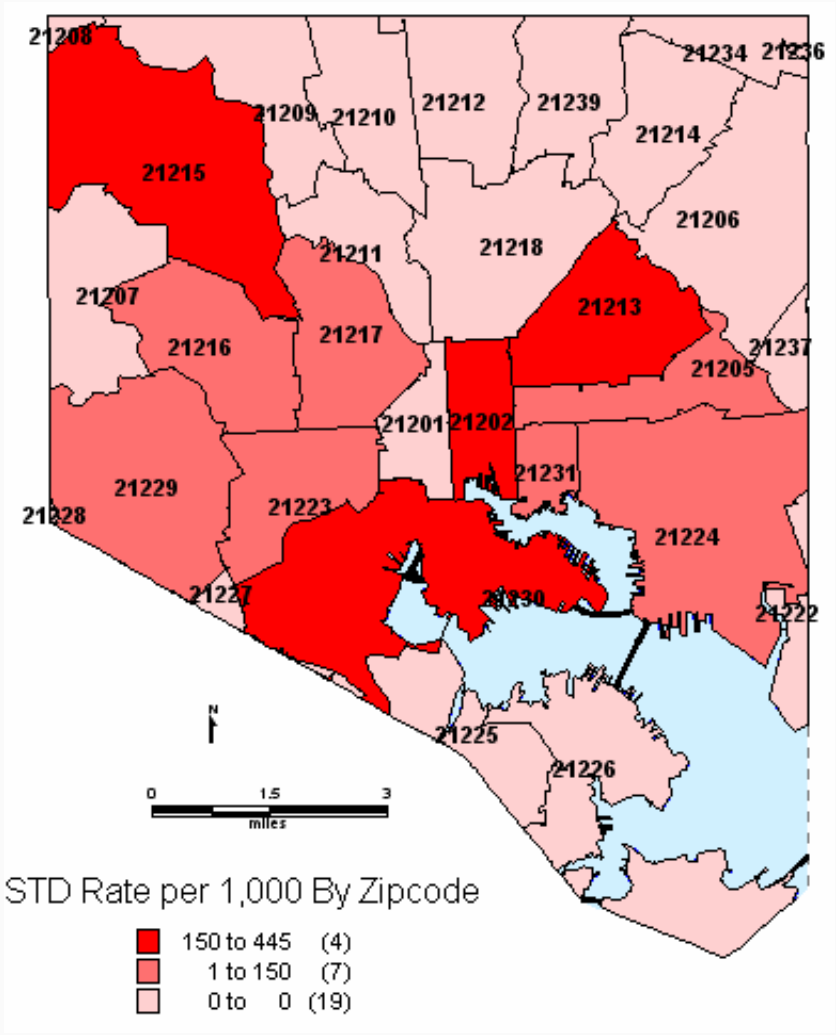
Chlamydia or Gonorrhea (13.6%) ED



- 22% had more than one sex partner in the past 90 days; 37% male, volume rate 77%; 28% had a new sex partner in the past 90 days; 76% of infections were undetected by clinicians at initial ED visit

Source: Mehta, S.D., et al. (2001). *Sex Transm Dis*; 28: 33

Chlamydia Outreach Testing—Pregnant Females (N = 1171): Mapping and Geocoding



Street	Site ID	Rate/1,000
Caroline	1	134.3
Chester	2	73.5
Carey	3	119.6

CT—9.6% GC—2.8%

CT co-infection with GC: 11.5%

GC co-infection with CT: 39/4%

Source: Hardick, et al. (2003). ISSTDR

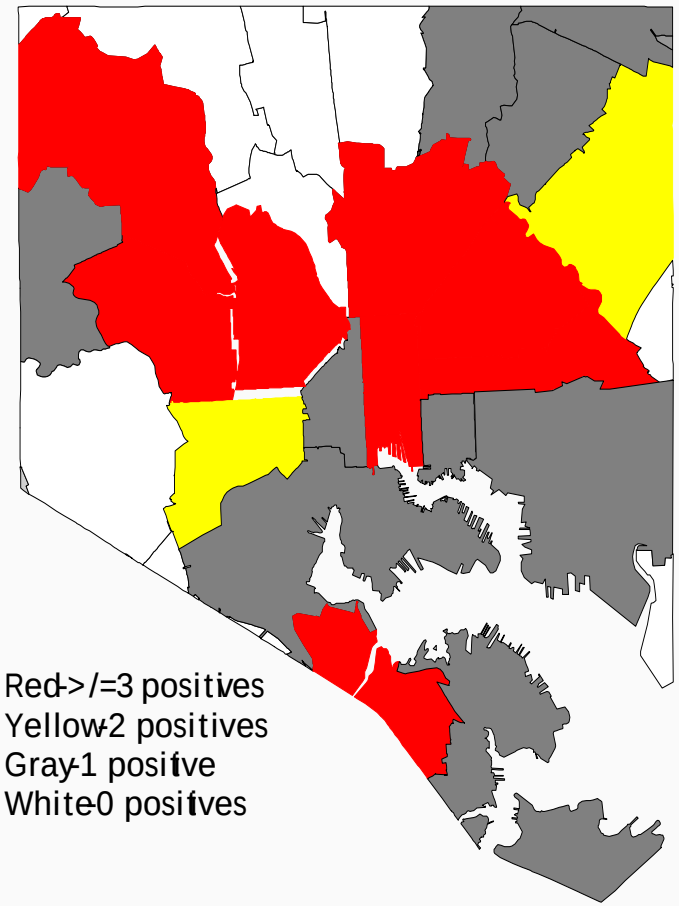
Women in Detention: Analysis by Age (N = 1858)

Age Group	CT Positives	GC Positives
<25 (n=244)	16.4% (40/244)	8.2% (20/244)
25-34 (n=860)	5.7% (49/860)	3.5% (30/860)
>34 (n=753)	2.7% (20/753)	1.7% (13/753)

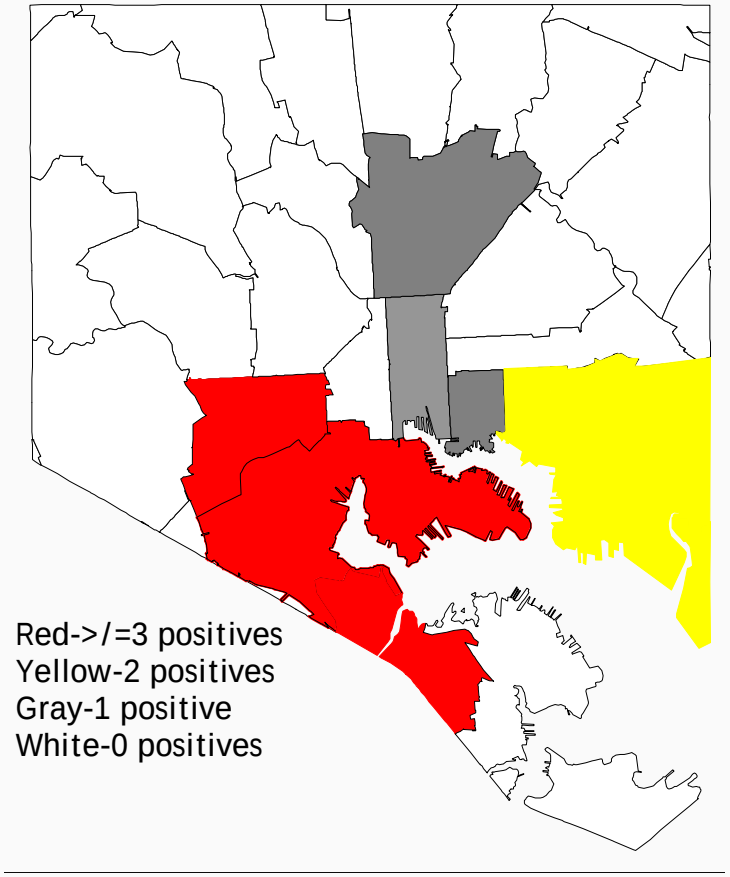
- CT prevalence—5.9%; O.R. 6.8; GC prevalence—3.4%; O.R. 4.6

Source: Hardick, J. et al. (2003). Surveillance of C. Trachomatis and N. Gonorrhoeae Infections in Women in Detention in Baltimore, MD. *STD*; 30: 64-70.

Results: CT Positives

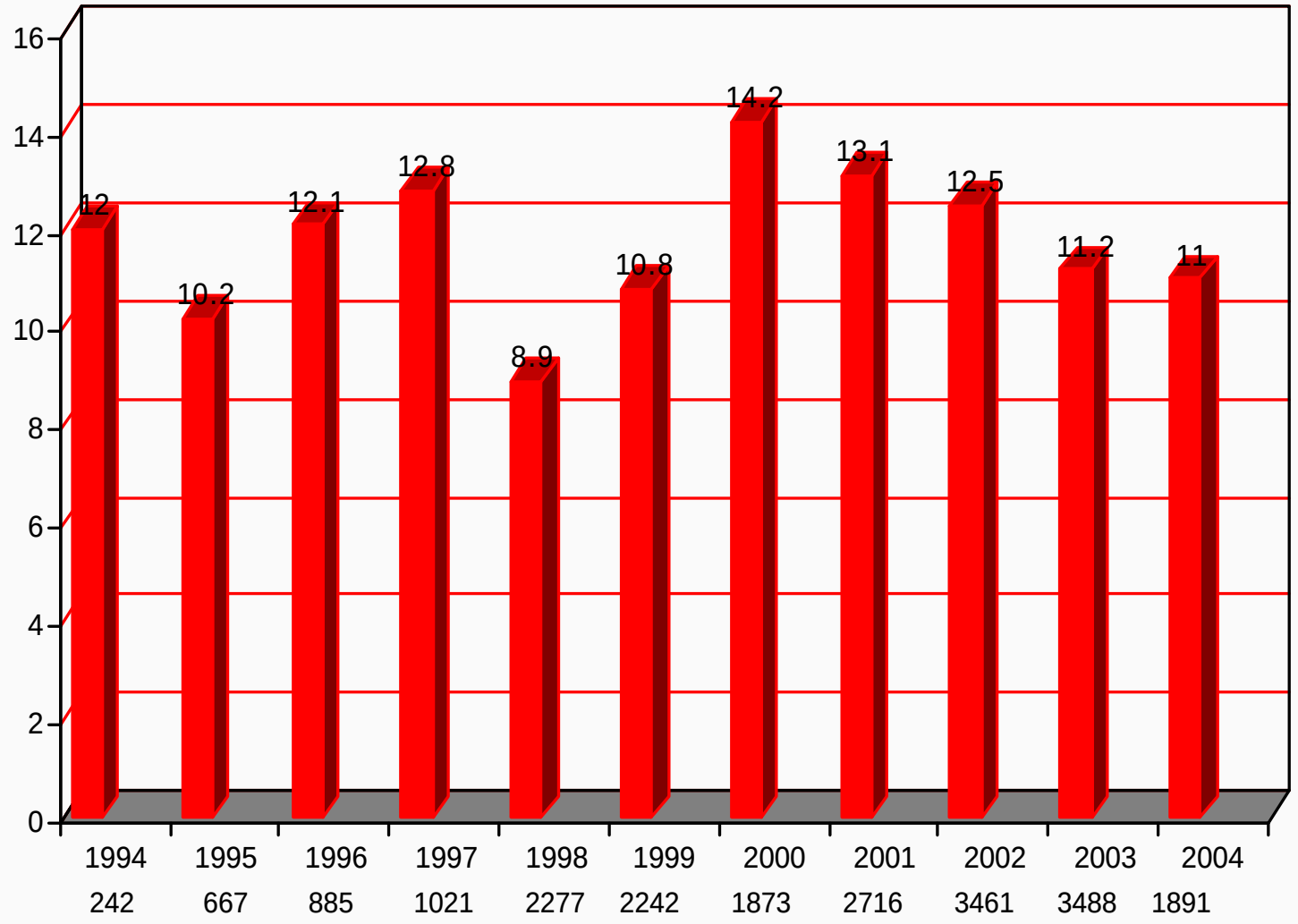


African American



Caucasian

Baltimore Chlamydia Prevalence by Year: High and Middle School Females

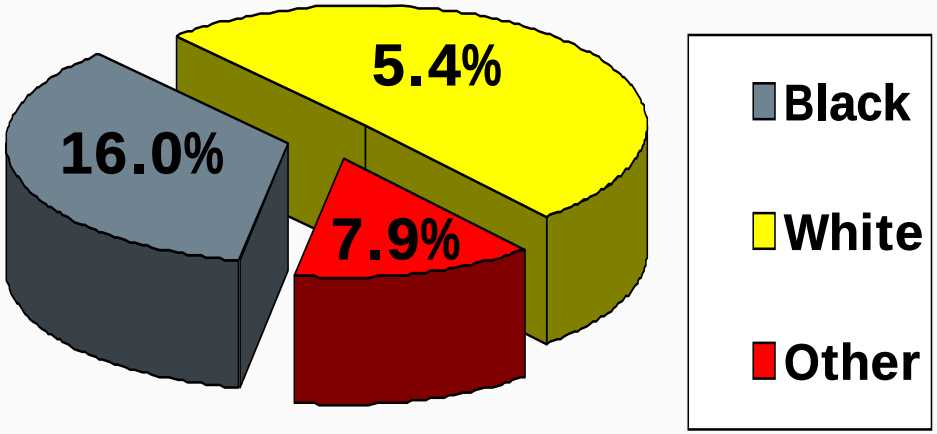


Region III Data

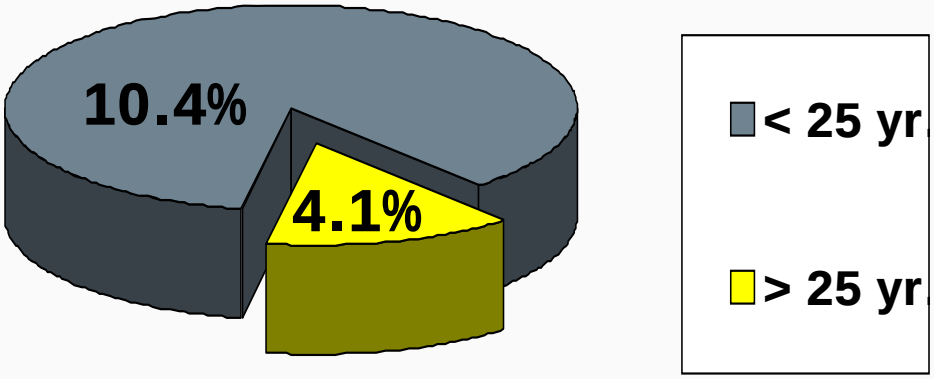
Sustained High Prevalence of Chlamydia Infections in Female Army Recruits

- 23,010 non-health care seeking females
- Urine-based NAAT
- Fort Jackson, SC
- Acceptance rate—80%
- Prevalence—9.5%
- Tested within three days of joining (brought chlamydia with them)

Female U.S. Army Recruits: Results

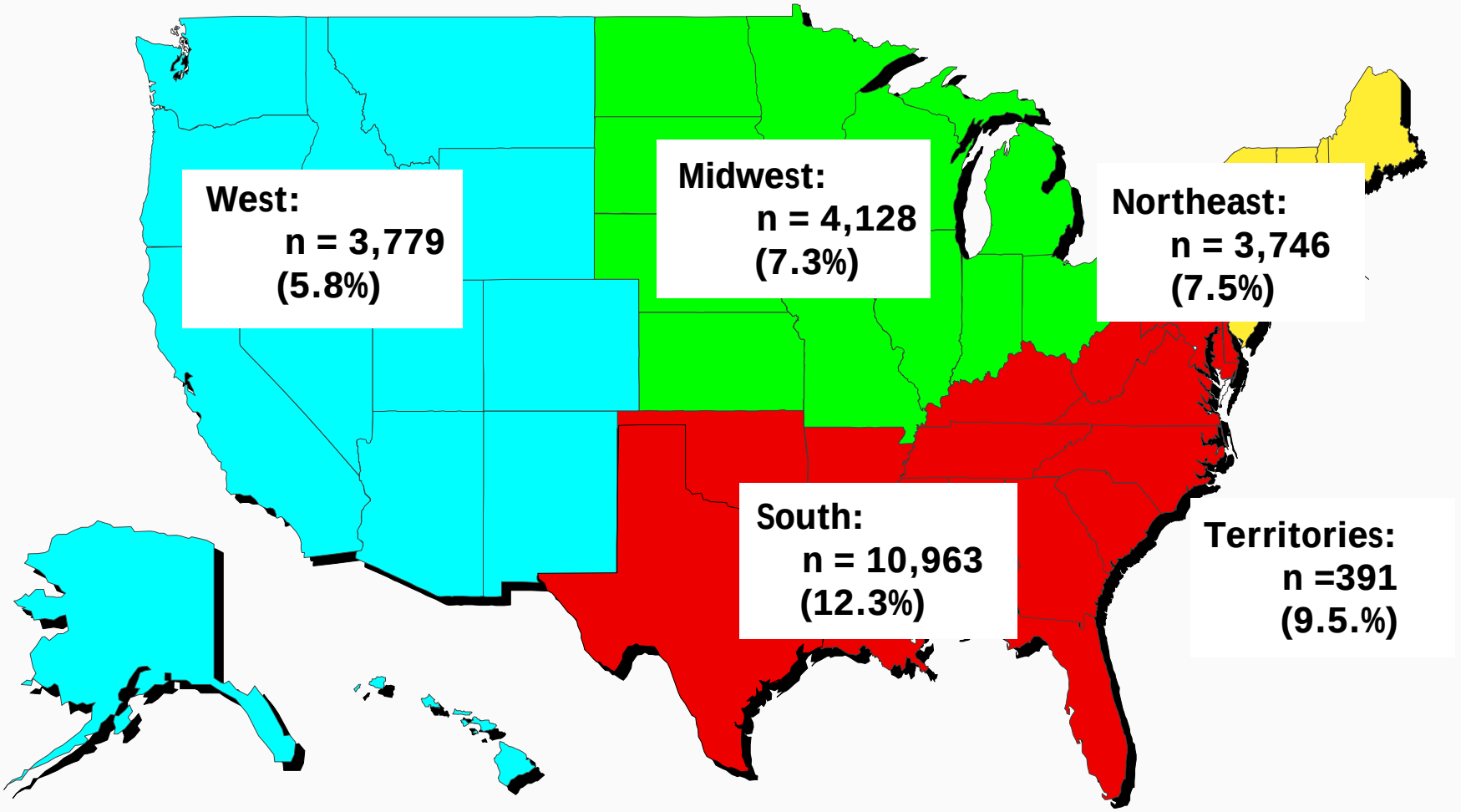


- Mean Age: 20.6 years. OR 2.8 (proportion <25 yr = 85.8%)
  - 1996: 8.51%
  - 1997: 9.68%
  - 1998: 9.90%
  - 1999: 9.92%
- p = 0.018, using 1996 as referent



Source: Gaydos, et al. (2003) *STD* 30: 539-544

Female U.S. Army Recruits: 1996-1999
Chlamydia Prevalence, by Urine LCR (n=23,007)



Notes: CDC Reporting Region—Northeast, South, Midwest, West, Territories
(three individuals missing region assignment)

Independent Predictors of Chlamydia Infection in Female Army Recruits

Age < 25	OR 2.7
African-American	OR 2.9
More than one sex partner/90 days	OR 1.6
Lack of condom use	OR 0.8
Southern residence	OR 1.9
Year three and four of study	OR 1.2

NAAT and Self Samples Help Define Repeat C. Trachomatis Infections

- 15 Studies have assessed risk of reinfection—high risk
- 5% of women treated for CT again tested positive in four weeks
- 10% (range 7-13%) of women diagnosed with CT again in four months
- Reasons—new partner, non-treated regular partner, persistence, antibiotic resistance?
- Recommendation—re-screen infected women at 10-16 weeks

Source: Golden, M.R. and Handsfield, H.H. (2003), *Medscape Infect.* Dis 5(2).

Chlamydia Re-Infection in Baltimore: High and Middle School Students

- Reinfection rates (1996-2003): 3,703 students tested
- CT—957 positive with at least one positive test and 2nd
- Re-infection defined as 2nd pos 30-365 days after 1st
  - 248 with 2nd pos test
  - Reinfection rate—**25.9%** (248/957)
  - Females—26.3% (males 20%)
- Females > 15 year more likely reinfected (p = 0.013)
- Median time to re-infection 180.2 days
  - Females 181.3, males 157.2 days

What about Male Screening?

- Screening and treating males for CT and GC may help lower prevalence in women and prevent sequelae
- Few large nat'l studies screening males
- Cecil (2001). Military recruits—CT 5.3%; GC: 0.6%
- Arcari (2004). Military recruits—CT 4.7%; GC: 0.4%
- Miller (2004). Adol. Health—CT 4.19%; GC: 0.4%
- CDC Job Corps data; STD (2006)
- NHANES III—White NH CT 0.9%; Black NH CT 6.3%

Source: Cecil, *JID* (2001); 184: 1216; Arcari, *STD* (2004); 31: 443; Miller, *JAMA* (2004) 291: 2229
Mertz, *STD* (1998); 25: 225

Male Chlamydia Prevalence in Military Recruits: 4.7%

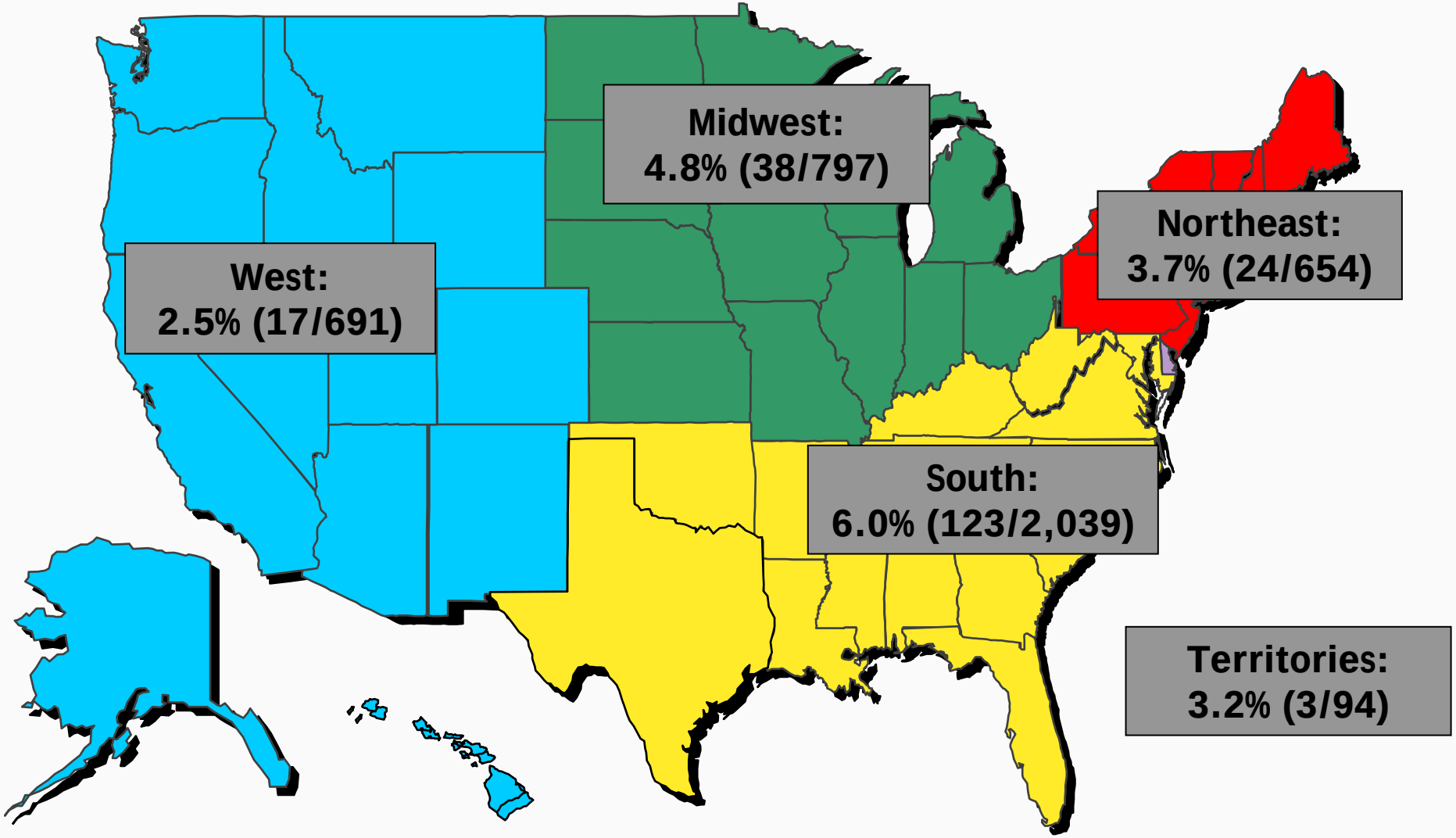
- 4,602 male recruits (90.0% volunteer) screened by LCR
- 3,911 had complete demographic and lab results

Age (yr):	< 20	4.1%	OR 2.2
	20-24	6.5%	OR 3.5
	> 25	1.8%	
Race:	Black	10.7%	OR 3.9
	White	2.4%	
	Hispanic	5.1%	OR 2.1
Risk Factors	> 2 PN	9.2%	OR 2.3
	Ever Sex	5.15	OR 9.6

- Independent predictors—age < 25; African-American; > one sex partner/90 days; lack of condom use

Source: Arcari, et al. (2004) *STD*, 31: 443-447

CDC* Reporting Region: Male Chlamydia Prevalence Northeast, South, Midwest, West, Territories



Source: Arcari, (2004). *STD*; 31: 443.

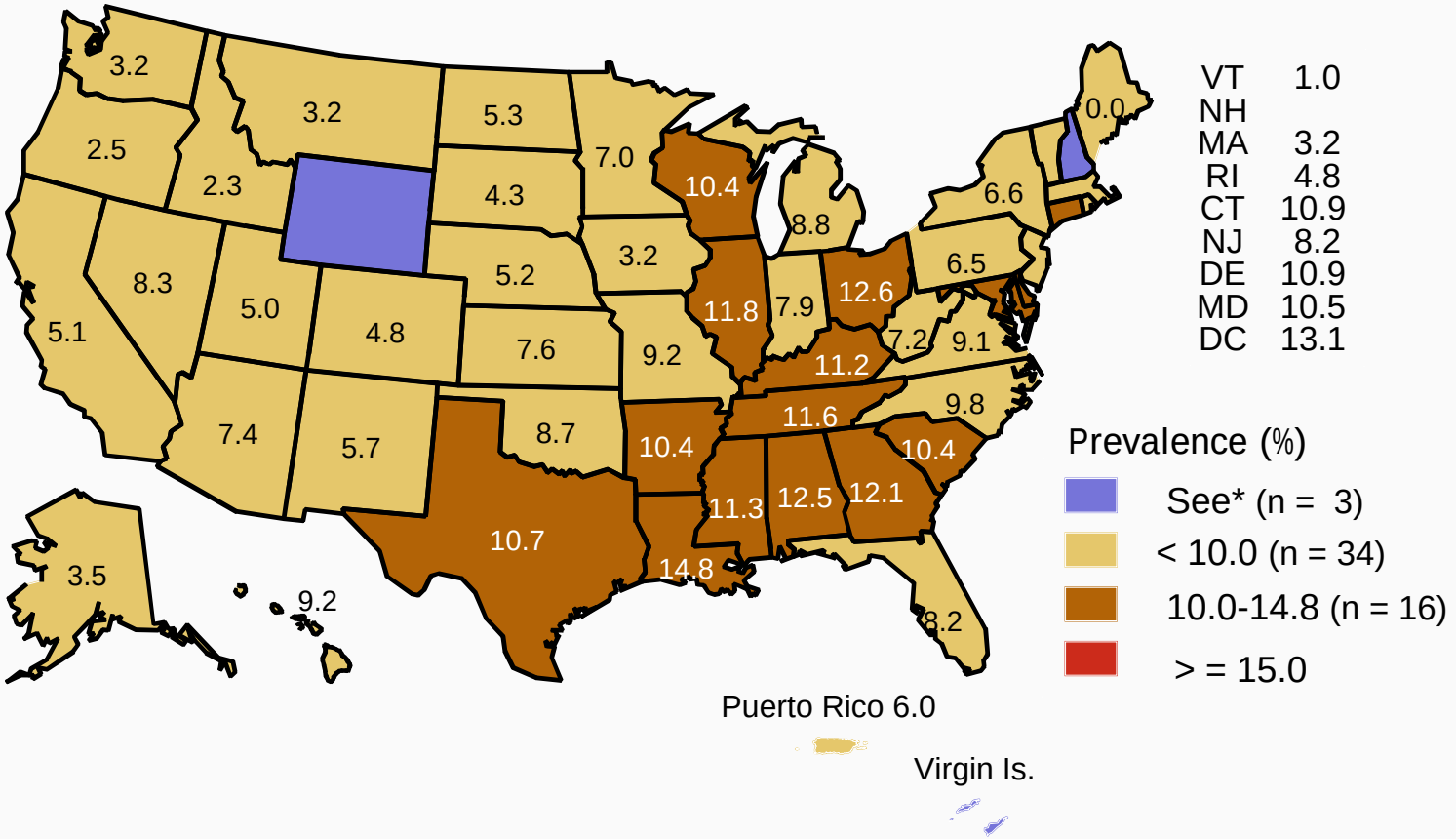
Prevalence of CT and GC Infections among Young Adults in the U.S

N = 12,548 Wave III Add Health Participants—2001-2002
(66.3% the 18,924 Wave I 1994-5 participants); 80 HS, 52 MS

CT	4.19%	South	5.39%
		N. East	2.39%
Female	4.74%	Black	13.95%
		White	2.52%
Male	3.67%	Black	11.12%
		White	1.39%
GC			0.43%

Source: Miller, et al. *JAMA* (2004); 291: 229-2236

Chlamydia—Prevalence among 16- to 24-Year-Old Men Entering the National Job Training Program by State of Residence



- * Fewer than 100 men residing in these states/areas and entering the National Job Training Program were screened for chlamydia in 2005
  - Note: The median state-specific chlamydia prevalence among male students entering the National Job Training Program in 2005 was 8.1% (range 0.0% to 14.8%)

Source: Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance* (2005)

Objectives: CDC Male Screening Study

- Four cities—Baltimore, Denver, San Francisco, and Seattle
- To measure the prevalence of chlamydia and gonorrhea in males in clinical and non-clinical settings (chlamydia focus on asymptomatic-96%)
- To inform guidance regarding male CT screening for those wanting to implement male screening
- To measure feasibility and acceptability of urine-based screening

Source: Schillinger, (2005). *STD*; 32: 74-77. Gaydos (2006). *STD*; 33: 314-319. Marrazzo *STD*; 2007 (in press).

Results: Chlamydia—Male Screening

- Over 23,000 men screened for CT in 3.5 years
- Prevalence was 7% (range 1-12%)
  - Baltimore n = 3129 (12%)
  - Denver n = 3516 (10%)
  - San Francisco n = 16,097 (5%)
  - Seattle n = 765 (1%)
- Race
  - White 3%
  - Black 9%
  - Hispanic 6%
  - Asian/Pacific 4%
  - Multi-race 4%
  - Other/Native Am. 4%

Source: Schillinger (2005). *STD*; 32: 74-77.

Results: Chlamydia—Male Screening

- Total prevalence—7%
  - Symptomatic—22%
  - **Asymptomatic**—6%
- By venue for **asymptomatic**:
  - Adolescent primary care 12%
  - Adult primary care 6%
  - Juvenile detention 5%
  - Adult detention 6%
  - School clinic 8%
  - Community-based 11%
  - Street outreach 3%
  - College clinics 3%
  - School health fair 1%
  - Drug treatment 4%

Source: Schillinger (2005). *STD*; 32: 74-77.

Results: Gonorrhea—Male Screening

- Over 17,717 men screened for GC in 3.5 years
- Of 16,850 asymptomatic men prevalence was 1.4% (range 0-1.5%)
  - Baltimore n = 2593 (1.2%) Denver n = 2942 (1.4%)
  - San Francisco n = 11,054 (1.5%) Seattle n = 261 (0%)
- Race
  - White 1.0%
  - Black 2.0%
  - Hispanic 1.1%
  - Other 1.1%
- Age
  - < 19 1.3%
  - 20-24 1.8%
  - 25-29 1.0%
  - >30 1.5%
- 862 symptomatic men (prevalence was 20.4%; range 0-28.3%)

Source: Gaydos (2006). *STD*; 33: 314-319

Conclusions: Asymptomatic Male Screening

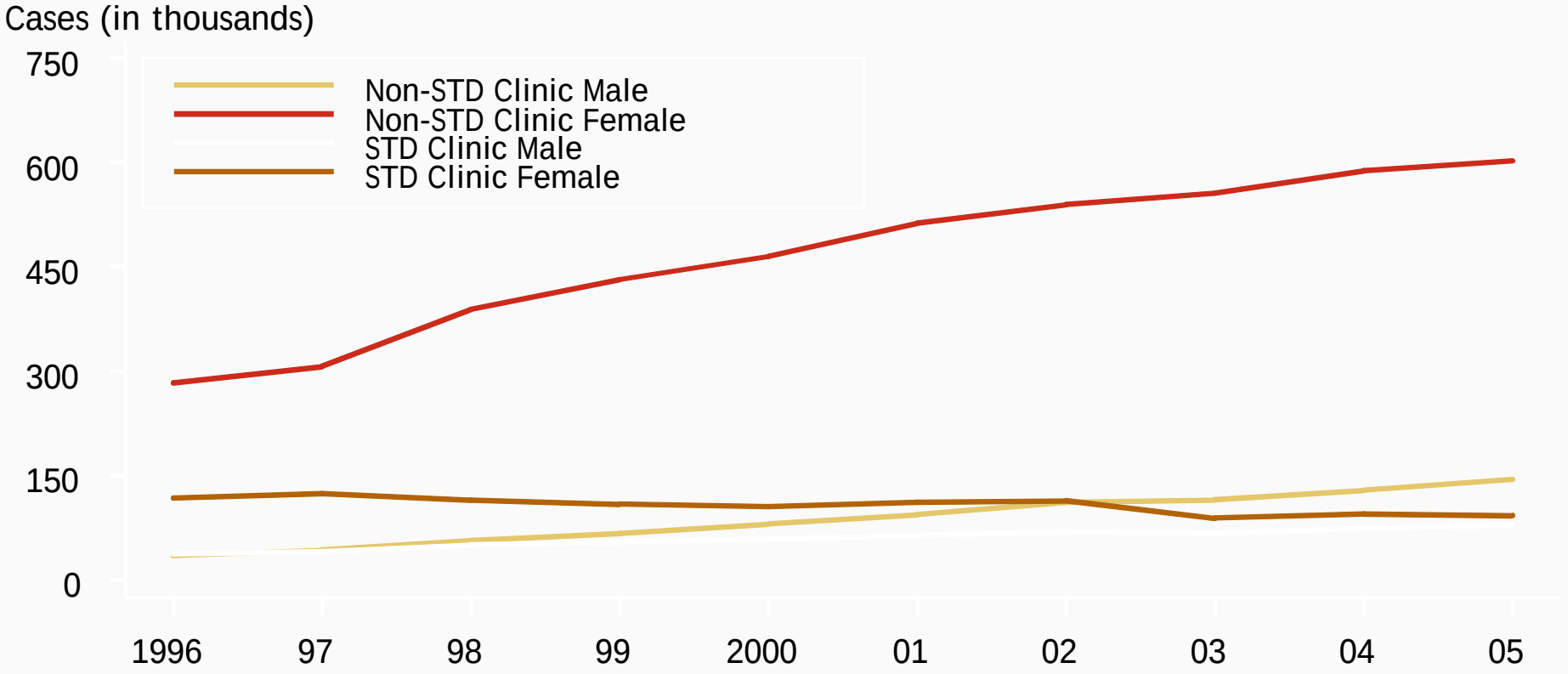
- Asymptomatic prevalence of CT is moderate and may support screening, in specific venues; CDC guidance/recommendations pending
- High prevalence CT/GC in symptomatic men supports diagnostic testing
- Prevalence of GC in asymptomatic men is low
- Routine GC screening cannot be recommended when screening for CT, unless substantial local prevalence is documented in targeted venues/groups

Source: Schillinger (2005). *STD*; 32: 74-77; Gaydos (2006). *STD*; 33: 314-319.

Policy Implications/Decisions

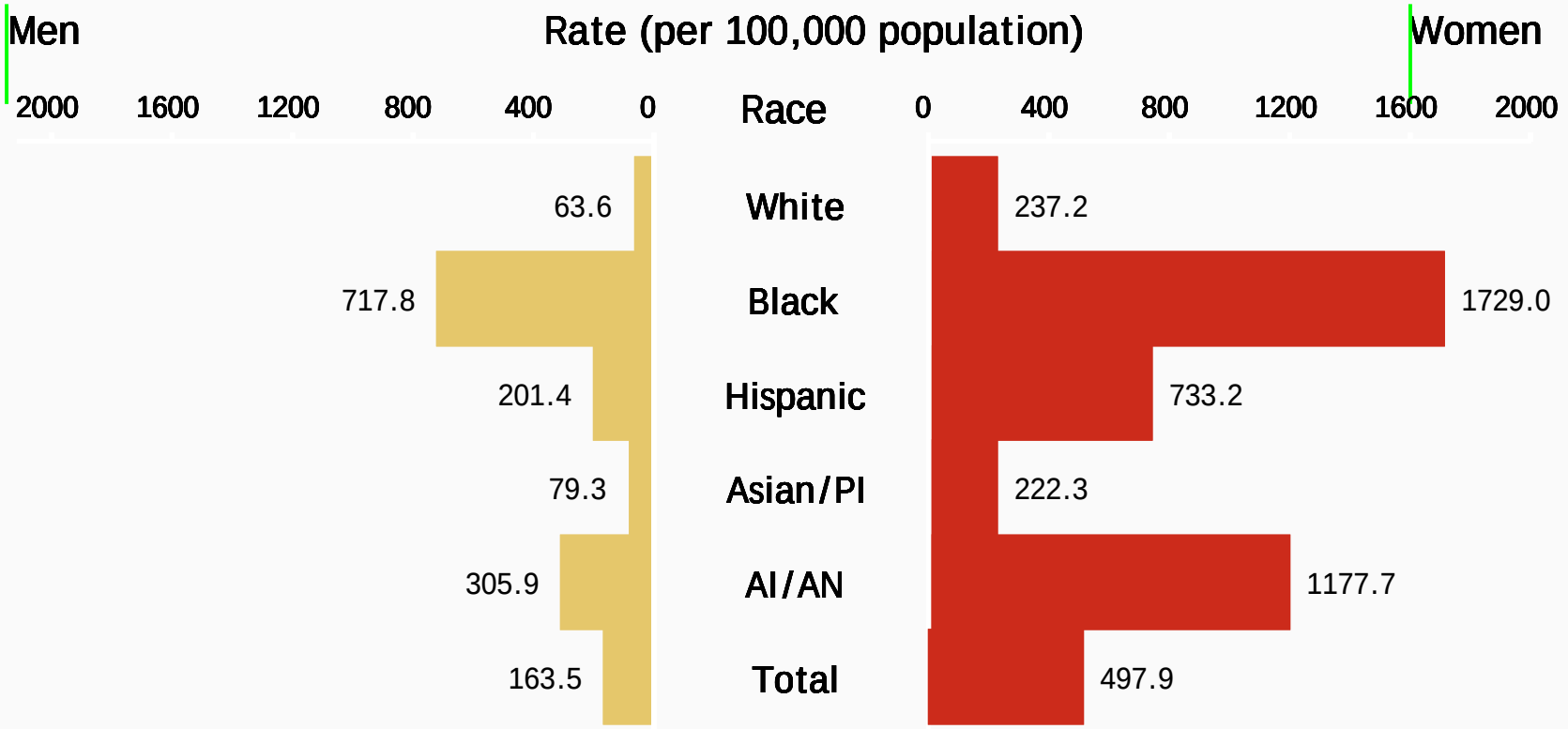
- With limited resources where would you spend your funds?
- Which organisms would you screen for?
- Which tests would you use?
- Who would you screen?
- Screen women?
- Screen men?
- Which venues?
- What ages?

Chlamydia—Cases by Reporting Source and Sex: United States, 1996–2005



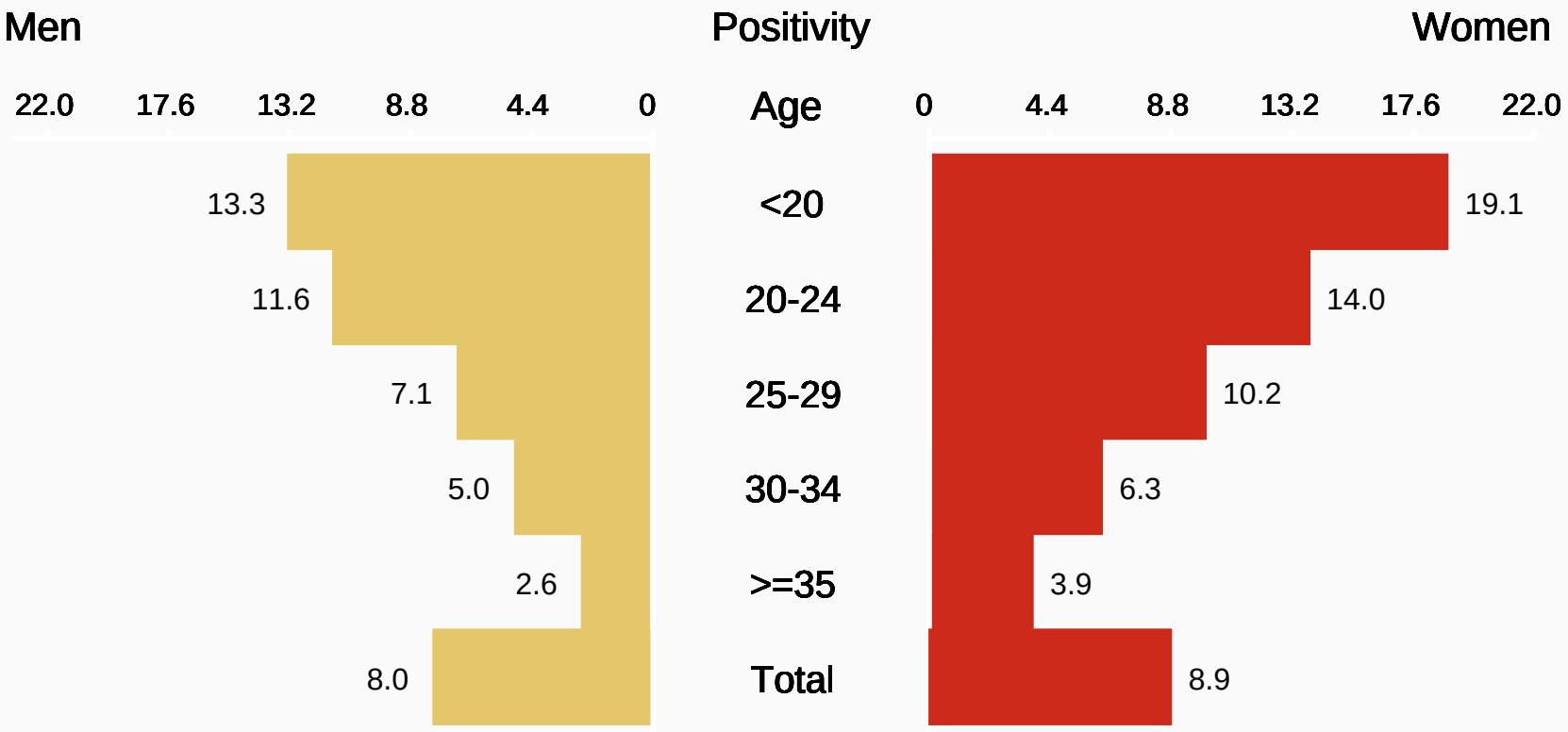
Source: Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance*, 2005

Chlamydia—Rates by Race/Ethnicity and Sex: United States, 2005



Source: Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance (2005)

Chlamydia—Positivity by Age, Adult Corrections Facilities, 2005



Note: Percentage of positivity is presented from facilities reporting > 100 test results.

Source: Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance (2005)

Male Chlamydia Screening Consultation

- March, 2006
- Purpose—using available literature, develop guidance on male CT screening for programs currently implementing, or planning to implement, screening
  - NOT to provide evidence for/against screening men for CT
- Four workgroups
  - Venues and re-infection issues
  - Demographics and behavior
  - Cost effectiveness and partner management
  - Laboratory
- 21 recommendations proposed
  - Quality of evidence
  - Strength of recommendations

Decision/Policy Topics

- Screening men for CT presents challenges to programs
  - Limited resources
  - Lack of knowledge of high prevalence settings
  - Lack of information on the impact of screening men for CT on rates and outcomes in females
- Primary focus—screen women < 26 years of age
- Secondary focus—screen men for CT
  - To prevent CT infection and sequelae among women
- Publish consensus recommendations (colleague letter?)
- Publish topical presentations in a special issue of a peer-reviewed journal

Proposed Recommendations

Recommendation	Average Score (Median)[#]	Quality of the Evidence[*]	Strength of the Recommendation[†]
Males < 30 years of age entering jails should be screened for Ct	4.59 (5) Strong	II	A
Males attending STD clinics should be tested for Ct (including screening asymptomatic men and testing men with symptoms)	4.87 (5) Strong	II	A
Males with Ct infection should be re-screened at three months for repeat Ct	4.42 (5) Strong	II	A
Urine is the specimen of choice for screening asymptomatic men for Ct	5.00 (5) Strong	II	A
NAATs are the test of choice; LET is not recommended for screening males for Ct	5.00 (5) Strong	I	A

[#] Range: 1-5 (5 is strongest)

* I = Good, II = Fair, III = Poor

†A = Strongly recommended, B = Recommended, C = No recommendation for or against, D = Recommended against, I = Insufficient evidence

Proposed Recommendations

Recommendation	Average Score (Median)[#]	Quality of the Evidence[*]	Strength of the Recommendation[†]
Pooling of urine specimens should be considered for Ct testing in low prevalence settings to conserve resources	4.76 (5) Strong	I	A
Self-referral is the most feasible method for managing partners of males with Ct, mounting evidence of efficacy of EPT	4.46 (5) Strong		
Screening men in the National Job Training Program, in the military, and in STD clinics should continue	4.84 (Job Corps), 4.66 (Military), 4.78 (STD clinics) (5 = Median for all) Strong	II/III	A

[#] Range: 1-5 (5 is strongest)

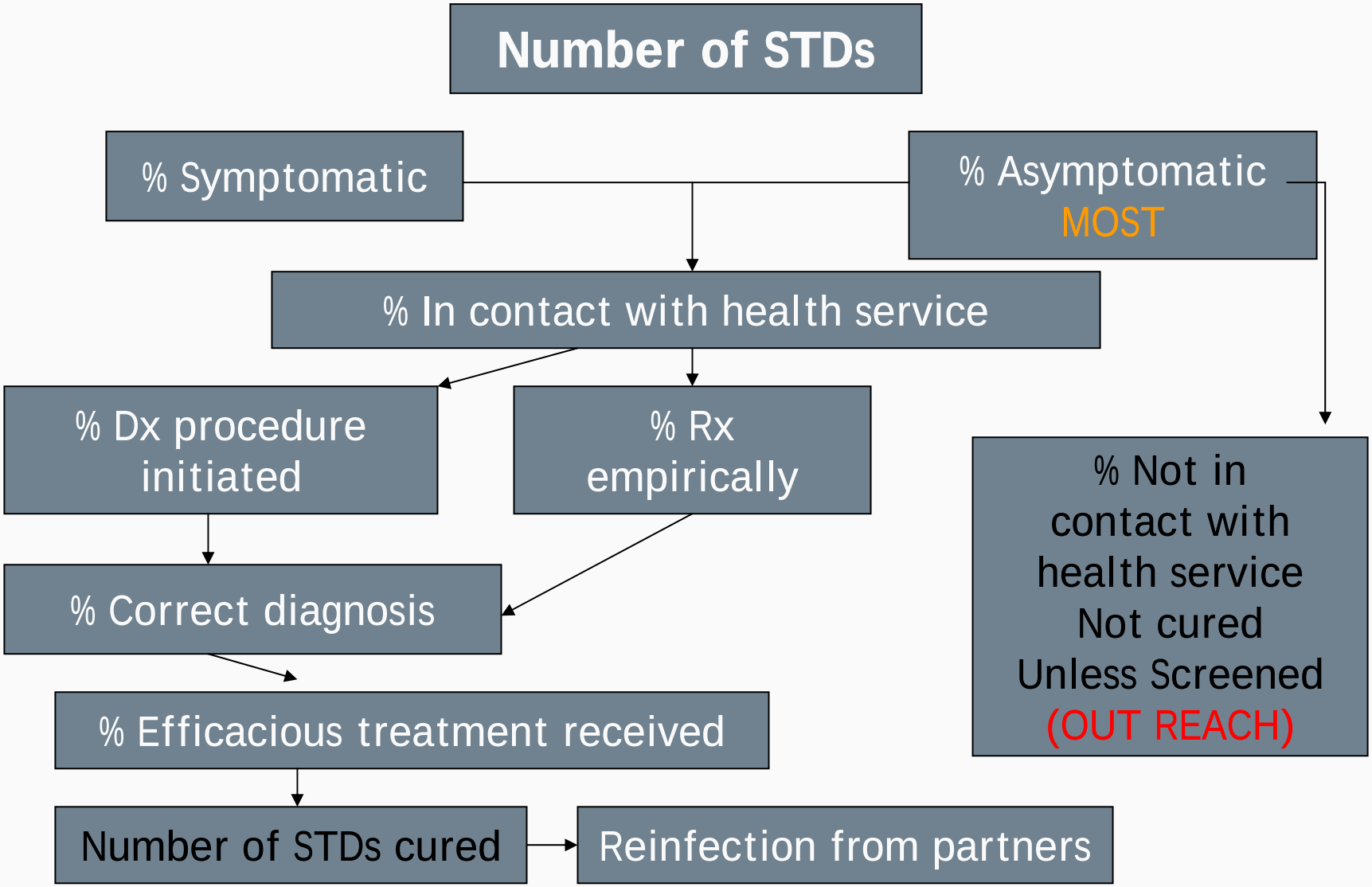
* I = Good, II = Fair, III = Poor

†A = Strongly recommended, B = Recommended, C = No recommendation for or against, D = Recommended against, I = Insufficient evidence

Remaining Policy and Public Health Issues

- Who should pay? Best use of resources?
- Need for increased resources for improved screening in non-clinic based setting
- Partner notification and treatment of both infected partners and their sexual partners
- Internet notification? (www.inSpot.com)

Curing STDs in the Community



Non-Invasive Sampling Methods in Epidemiology Studies Summary:

- Age is a risk factor!
- Traditional risk factors
- Geography is important
- Non-traditional venues possible
- Non-traditional patients possible
- "The more you look the more you find"
- Repeat infections are common
- Self sampling methods are accurate and acceptable
- Home collected samples with mailing might make a difference in reaching those most at risk