Availability of Over-the-Counter Diagnostic Tests for STDs with a Focus on Chlamydia and Gonorrhea: A Public Health Perspective

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Microbiology Devices Panel of the Food and Drug Administration
Medical Devices Advisory Committee
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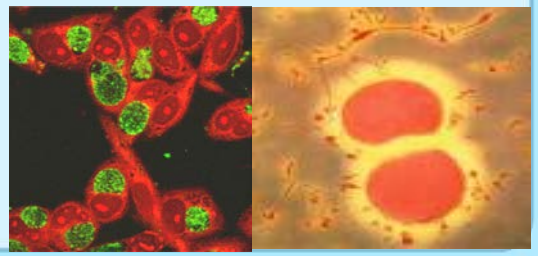
No conflicts of interest

Overview

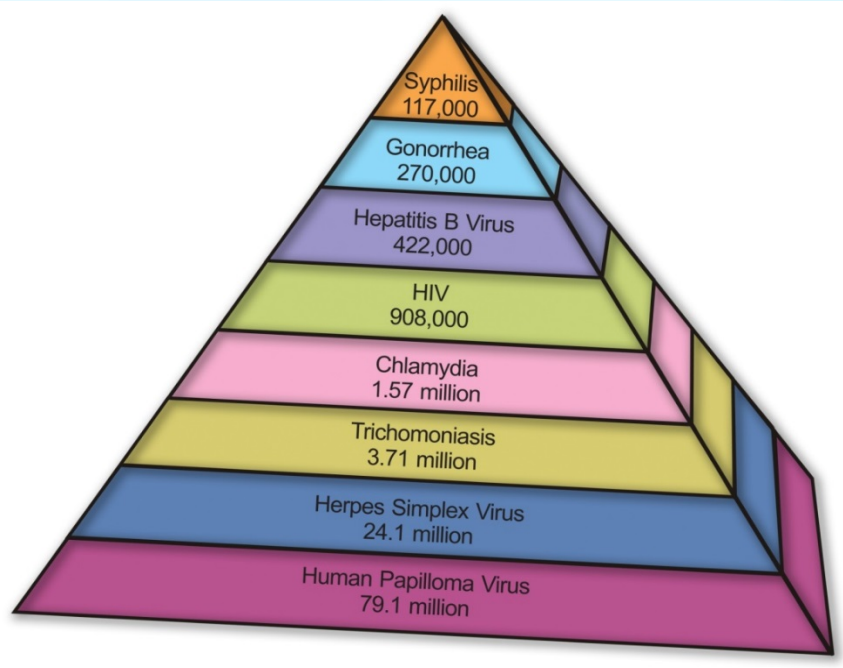
- Chlamydia/gonorrhea epidemiology and surveillance
  - The Hidden Epidemic
  - Limitations of current case-based surveillance system
- Strategies and approaches for STD prevention and control
  - Screening principles and recommendations
  - Supply, demand and patient adherence
- Interventions to increase CT/GC screening and treatment
  - What have we learned from outreach settings
- Over-the counter STIs tests for home testing
  - Acceptable testing performance criteria
  - Potential public health benefit and risks questions

Chlamydia and Gonorrhea – The Hidden Epidemic

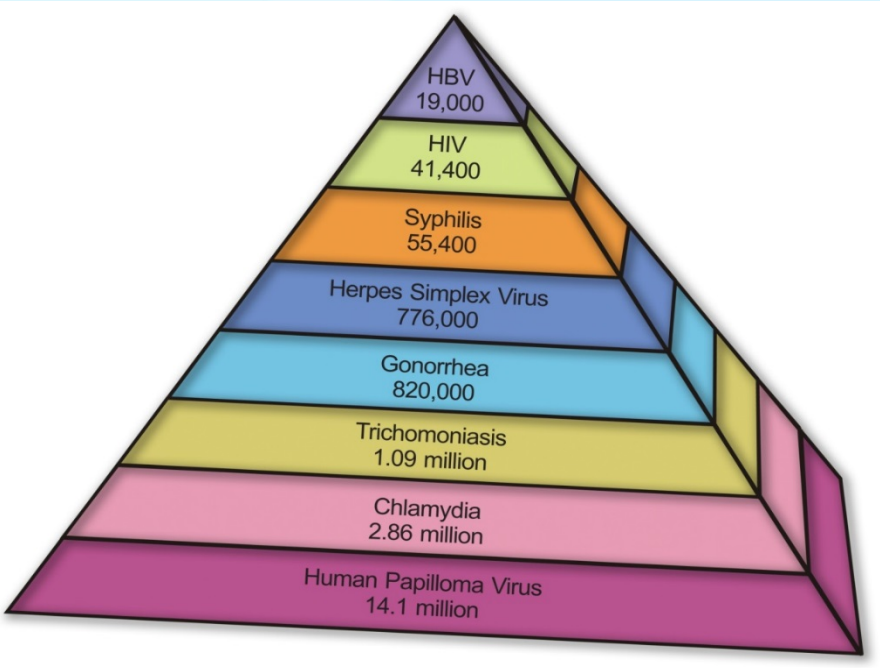
- Most infections are asymptomatic
- 63% of infections are among young sexually active people 15-24 years old
- Also common among sexual and racial/ethnic minorities
- Adverse health outcomes in women include PID, chronic pelvic pain, ectopic pregnancy and infertility
- Facilitates HIV transmission
- Account for 85% of all reported conditions in the US



Estimates of Sexually Transmitted Infections in the United States



Estimated Prevalence of Sexually Transmitted Infections in the U.S. (Total 110,197,000)



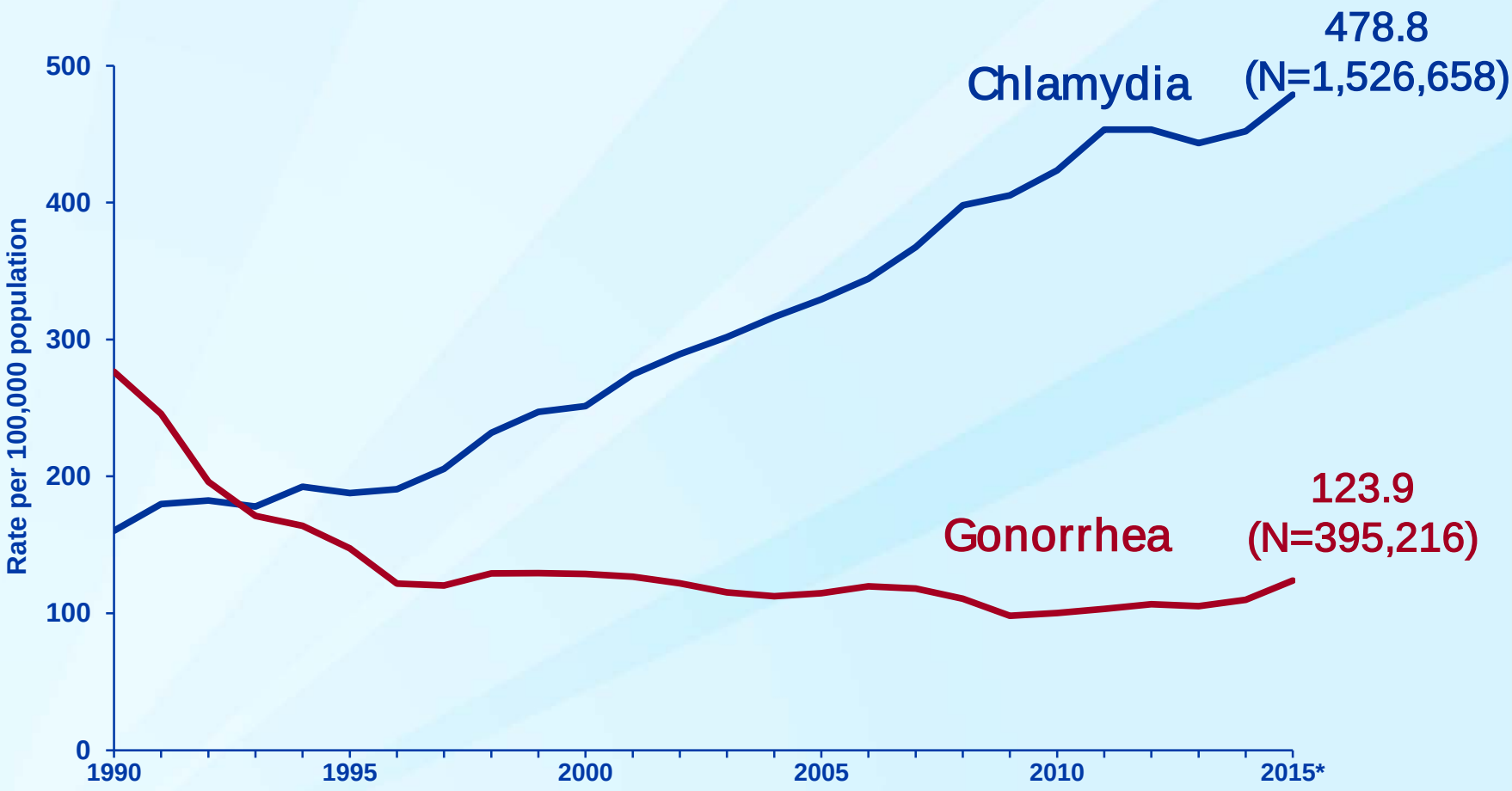
Estimated Incidence of Sexually Transmitted Infections in the U.S. (Total 19,738,800/Year)

Satterwhite CL et al. Sexually Transmitted Diseases 2013;40:187-93.

STD Case-based Surveillance

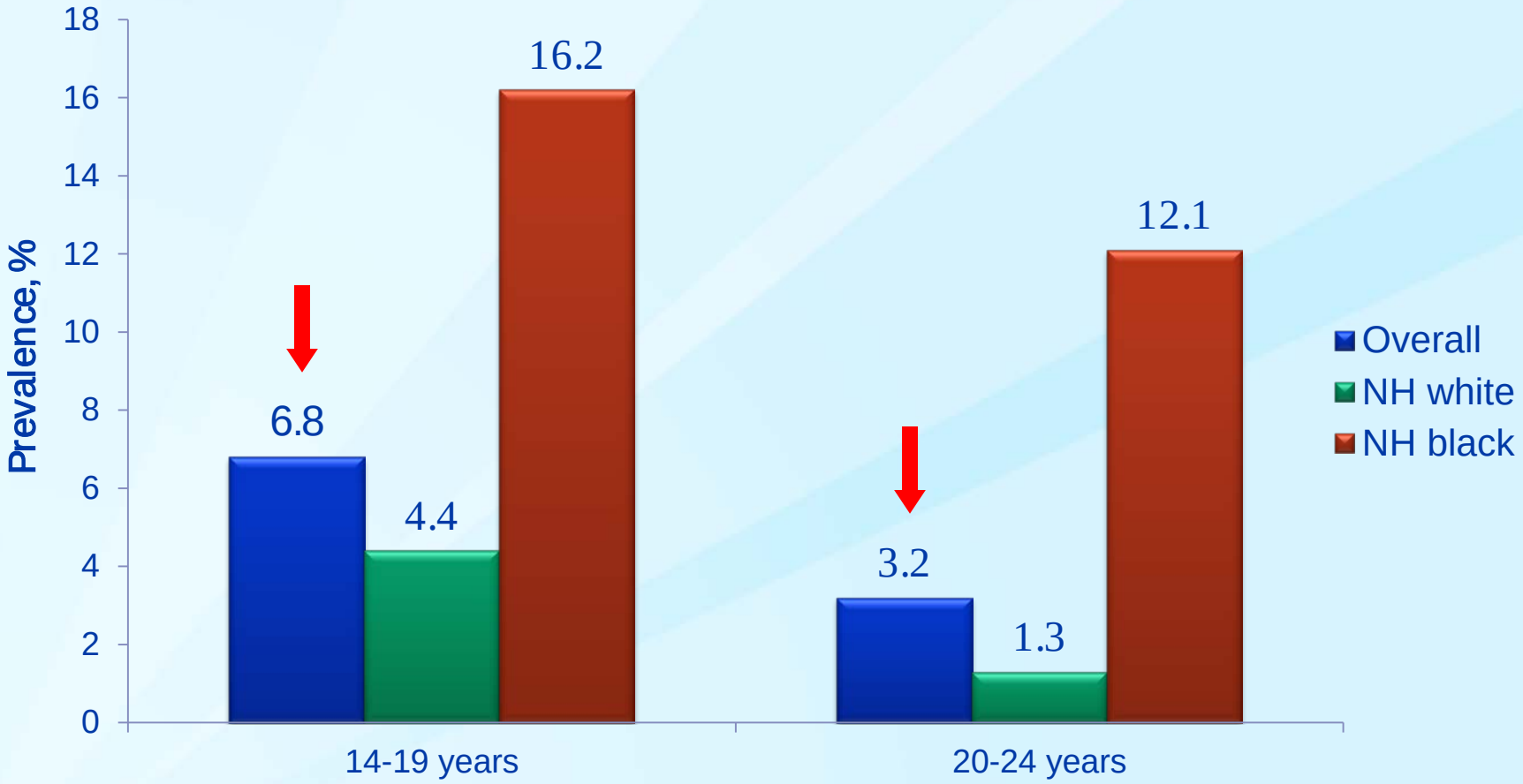
- Core function and backbone of public health
- Population case-based CT/GC infection data used for public health action to reduce morbidity and improve population health
- Authorized by state legislators and carried out by public health officials
- Reportable CT/GC meets public health importance criteria
- Data are used for aligning STD funds with burden of infections and targeting prevention interventions
  - STD prevention program funding formula:
    - 50% of funds: # of cases (80% cases, 20% infection rates)
    - 50% of funds: at-risk population (15-44 years of age)

Chlamydia and Gonorrhea, 1990–2015*



*2015 data are preliminary

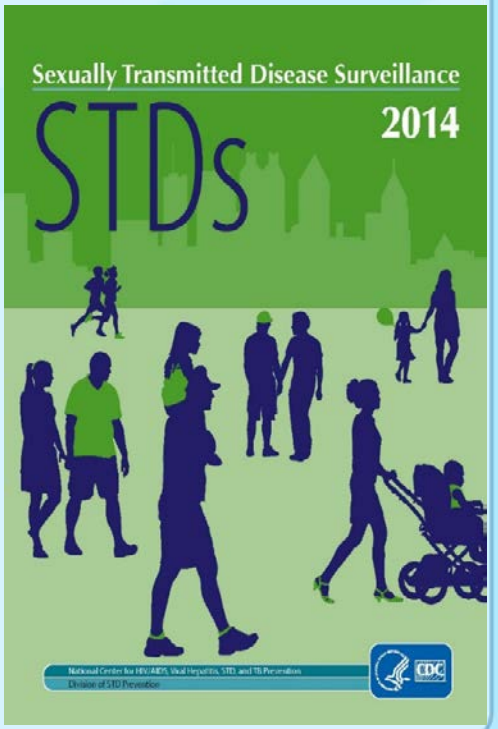
Chlamydia Prevalence in Sexually Active Females Aged 14-24 in the United States

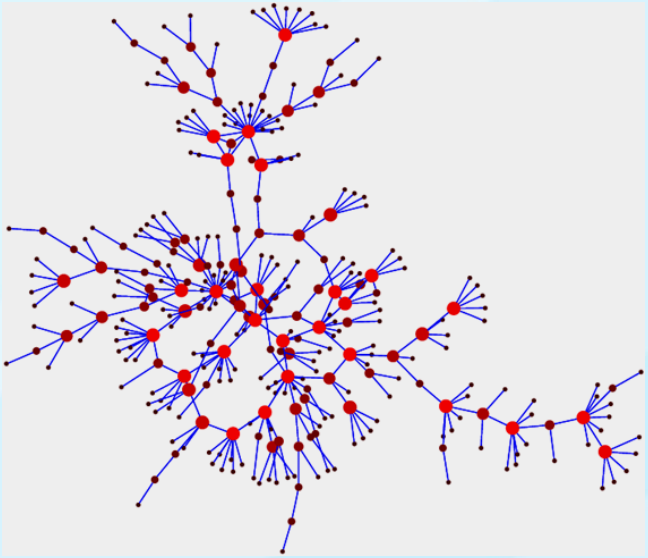


NHANES, National Health and Nutrition Examination Survey, 1999-2008
Sexual activity ="yes" response to "Have you ever had sex?"
Sex = vaginal, anal, or oral sex

Limitations of STD Case-based Surveillance Systems

- Problems with underreporting of cases.
- Problems with presumptive treatment without testing.
- Most infections are asymptomatic so individuals do not access care or providers do not screen according to recommendations.
- Cases only reflect those who access care, get tested and are reported to public health.
- Limited epidemiologic and clinical data





STRATEGIES AND APPROACHES FOR STD PREVENTION AND CONTROL

STD Prevention and Control Strategies

- Prevent
  - Health Education and Promotion
  - Behavioral Interventions
  - Vaccination
- Detect and Link to Care
  - Screening of Asymptomatic Persons
  - Diagnosis of Symptomatic Persons
- Treat
  - Patients and Partners
- Report cases to public health

STD Prevention and Control Approaches

- Increase Supply
  - In the health care system for at-risk populations
  - In the public health outreach to at-risk populations
  - Other- OTC home testing of at-risk/intended use population?
- Increase Demand
  - By health care and public health providers of at-risk populations
  - By at-risk/intended use population
- Increase Adherence
  - Screening → Earlier diagnosis → More timely treatment of patient and their sexual partners to improve health outcomes and reduce community transmission
- Report cases to public health

SCREENING PRINCIPLES

Screening vs. Diagnostic Testing

Screening

- **Goal:** test apparently healthy people to find those who are infected
  - **Patient is asymptomatic!**

Diagnostic Testing

- **Goal:** assess signs, symptoms, and patient complaints

Uses and Abuses of Screening Tests

- Screening tests are ubiquitous in clinical practice
- Principles of screening are widely misunderstood
- *Goal of screening is to test apparently well people to find those at increased risk of a disease or disorder*
- Inappropriate screening is harmful
  - Injurious to one's health
  - Stigmatizing
  - Costly

Grimes, D et al, Lancet 2002

When Earlier Diagnosis is Worth the Cost

- If improves survival or quality of life
- If the clinician has the time to manage the diagnosis before symptoms/disease develop
- If the patient with an earlier diagnosis will comply with intervention
- If the screening program effectiveness has been established
- If the test/intervention cost, accuracy/effectiveness and acceptability are acceptable to the patient and society

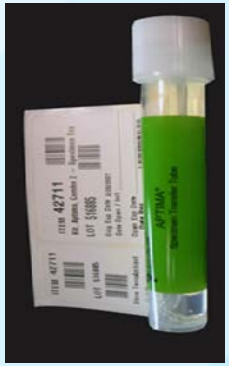
Sackett, Clinical Epidemiology: a basic science for clinical medicine

Cost-effective Screening Programs Depend On…..

- Prevalence of disease in population
- Sensitivity and specificity of screening criteria
- Test performance characteristics of diagnostic test
- Cost of test
- Cost of treatment and complications

Ideal Screening Programs

- Right population
  - High prevalence
- Right infection
  - High-morbidity disease
  - Likely to be asymptomatic
  - Early detection and treatment reduces complications and improves health
- Right test
  - Non-invasive, inexpensive and acceptable to patients
  - Easy collection, transport and lab procedure
  - Highly sensitive and specific
- Overall cost-effective in terms of population health



POPULATION-BASED SCREENING RECOMMENDATIONS

Chlamydia and Gonorrhea Screening for Non-pregnant Women and MSM

- **Sexually active adolescents & women < age 25**
  - ✓ Annual chlamydia and gonorrhea screening
- **Sexually active women > age 24**
  - ✓ If increased chlamydia or gonorrhea risk:
    - New or multiple sex partners, partner with concurrent partners, or partner with an STI
  - ✓ If increased chlamydia or gonorrhea clinic or community prevalence
- **Sexually active gay, bisexual and other MSM**
  - ✓ At least annual chlamydia and gonorrhea screening and more frequently (every 3-6 months) if risk
    - Urine GC and CT
    - Rectal GC and CT (receptive anal sex)
    - Pharyngeal GC (receptive oral sex)

CDC 2015 STD Tx Guidelines and USPSTF 2014

What About Screening Heterosexual Men?

- Screening heterosexual men
  - Not recommended for chlamydia or gonorrhea
  - No documented substantial secondary prevention in women
  - Costly
  - Consider in certain venues with high prevalence such as corrections, STD clinics, teen clinics
- Highest risk heterosexual men:
  - Partners of chlamydia and gonorrhea-infected females
  - Focus is on partner services

CDC 2015 STD Tx Guidelines and USPSTF 2014

Chlamydia & Gonorrhea Diagnostic Tests

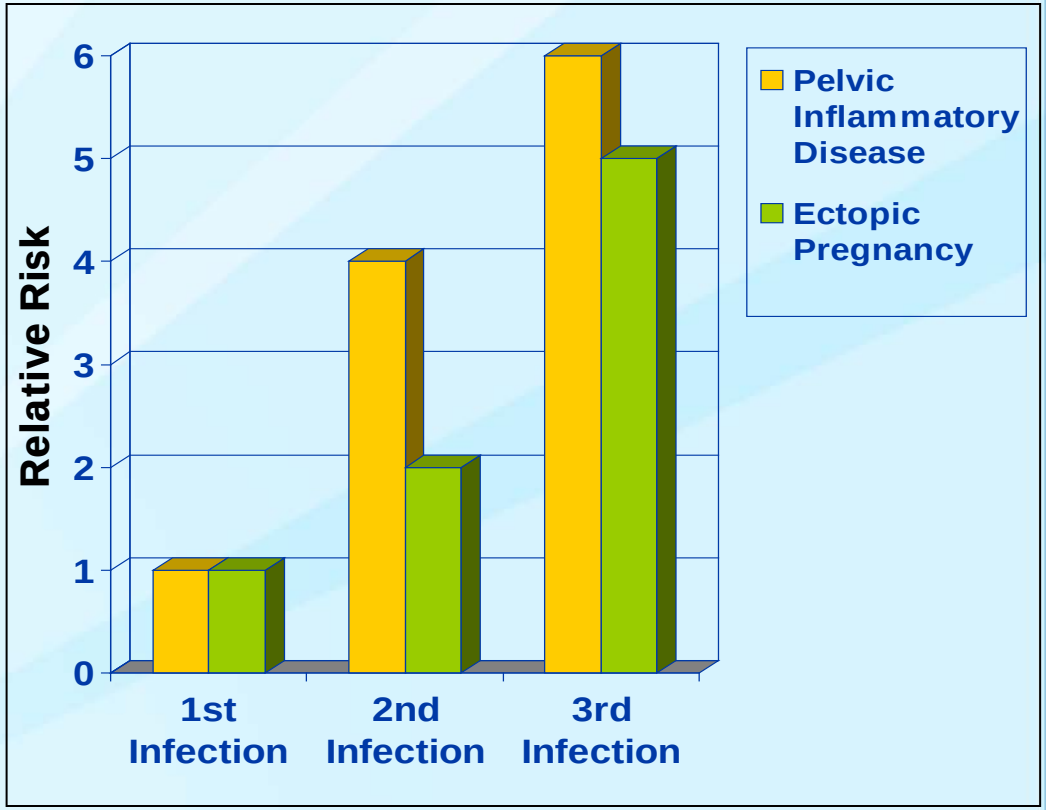
- Nucleic acid amplification tests (NAAT) recommended for men & women.
- Optimal specimen: first-catch urine in men and vaginal swabs in women
- Self-collected vaginal swab in a clinical setting is FDA cleared.
- NAAT optimal for rectal and pharyngeal testing; not FDA cleared but commercially available & validation protocols available for local labs including self-collection.
- Limitations: no GC antibiotic resistance testing with NAAT (need culture).

http://www.cdc.gov/mmwr 2014

TESTING AFTER AN STD INFECTION

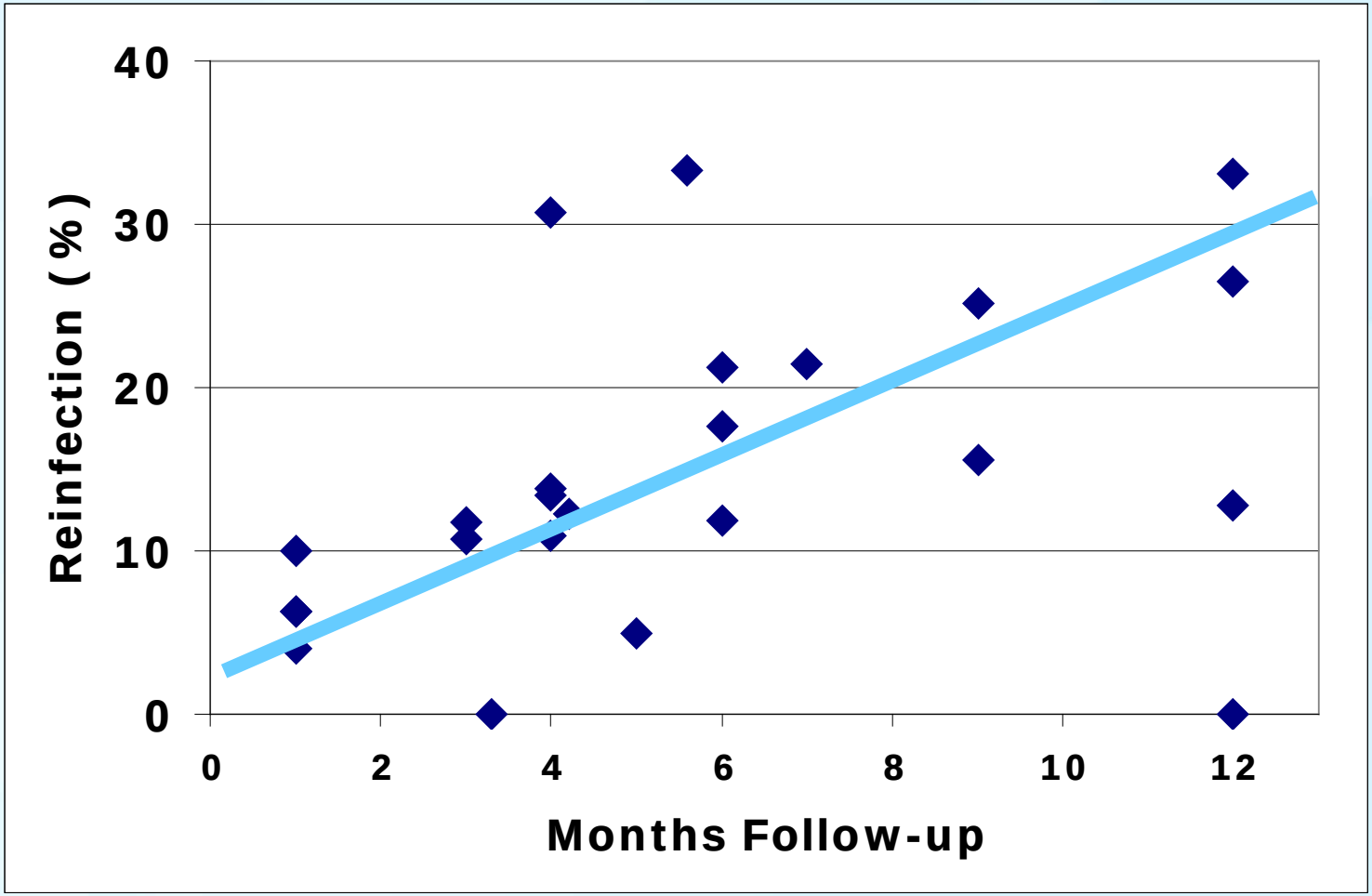
Relative Risk of Complications from Repeat Chlamydia Infections in Females

- Repeat CT infection leads to higher risk of complications: PID, ectopic pregnancy, infertility
- Most infections are asymptomatic



Hillis SD, et al. (1997). Am J Obstet Gynecol 176(1 Pt 1): 103-7.

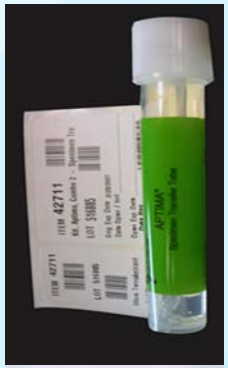
Reinfection of Women with Chlamydia Within 12 Months of Initial Infection



Hosenfeld et al. Review of 17 active cohort studies

Testing after an STD infection

- Women who test positive for chlamydia, gonorrhea, or trichomonas should be rescreened 3 months following treatment.
- Men who test positive for chlamydia or gonorrhea should be rescreened at 3 months following treatment.
- All patients with a bacterial STDs or trichomonas should be tested for other STDs including CT/GC, syphilis, and HIV.
- Role for provider prescribed home test



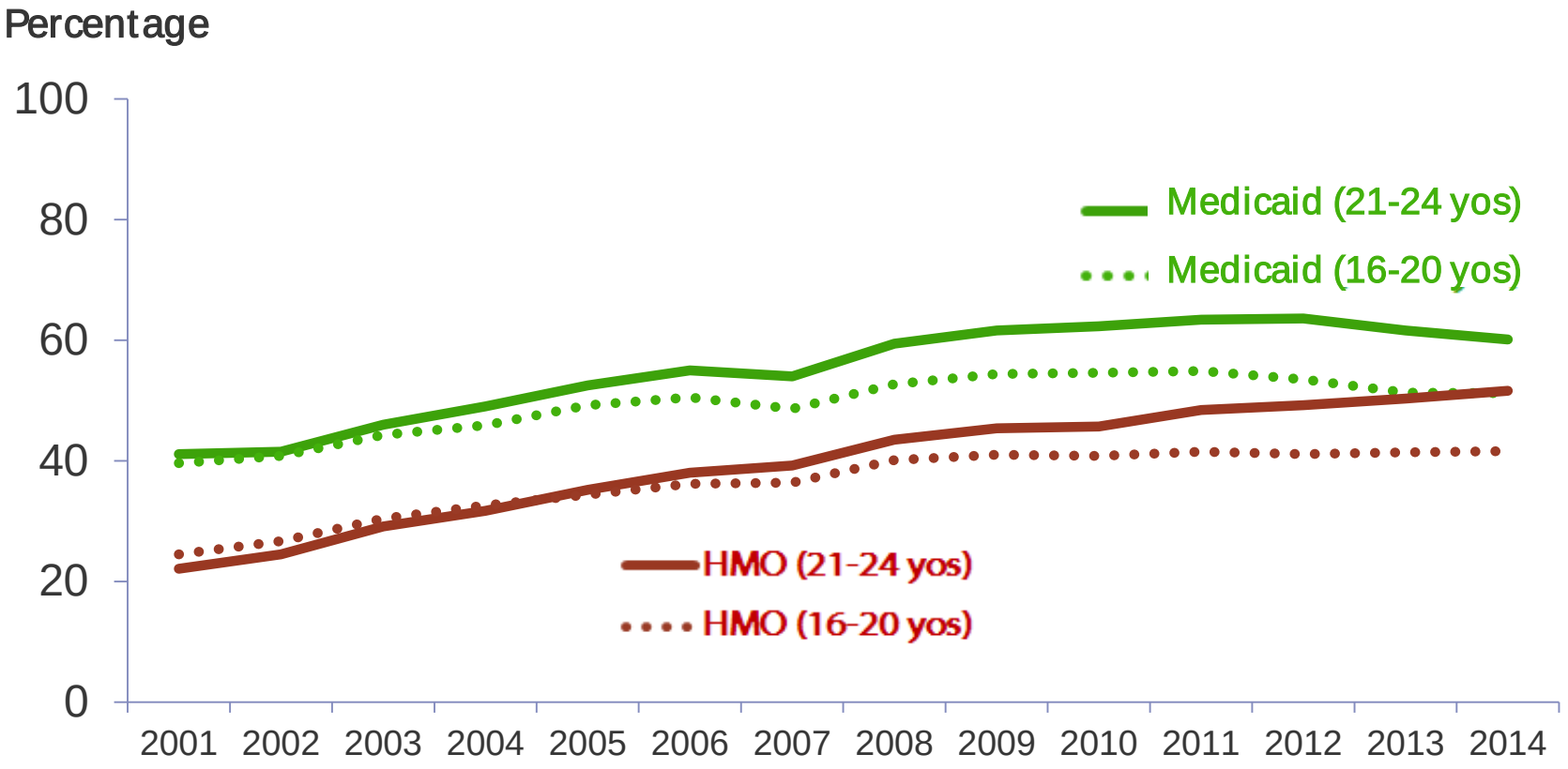
INTERVENTIONS TO INCREASE CHLAMYDIA AND GONORRHEA SCREENING AND TREATMENT:

WHAT HAVE WE LEARNED?

Public Health Interventions to Increase Screening

- Clinical Settings
- Community outreach
  - Mobile vans
  - Venue-based- pharmacies, bars, health fairs, hairs salons etc
  - Field-based through contact tracing programs
- Online internet or smart phone outreach
  - I Want The Kit
  - Internet sites offering STD testing
    - Order online, mail self-collected specimen, test in lab
    - Order online, collect and test at home, instant results
  - E-STD Services for STD diagnosis and treatment
    - E-testing and e-prescriptions
    - For patients and partners

Chlamydia — Screening Coverage Trends Among Sexually-Active Women,* by Age and Plan, HEDIS, 2001–2014



*Among women enrolled in commercial or Medicaid plans who had a visit where they were determined to be sexually active

SOURCE: The State of Healthcare Quality, 2015

Factors that Limit Access to Chlamydia Screening among Adolescent and Young Women

- Provider knowledge and attitudes
  - Lack of information about disease rates in their community
  - Belief that their patients are not at risk/inadequate sexual histories
  - Cannot offer confidential services to adolescents
  - Lack of insurance coverage or adequate reimbursement
  - Believe chlamydia is not an urgent medical condition
  - Limited time
- **Client concerns**
  - **Stigma or embarrassment**
  - **Anxiety related to pelvic examinations**
  - **Confidentiality and EOBs**
  - **High co-pays and deductibles**
- Other Factors
  - Less clinical visits to screen because of:
    - Changes in Pap smear recommendations
    - Increase in LARC use

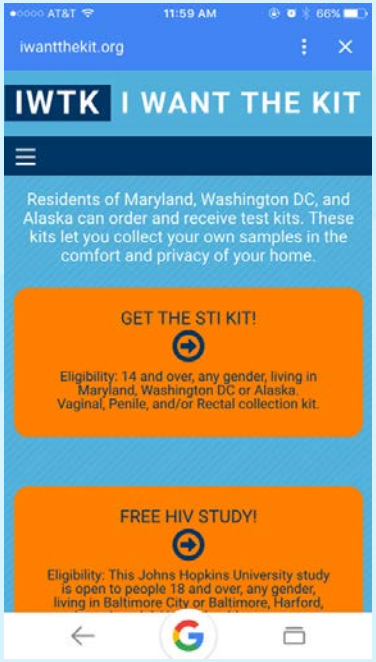
What have we learned about community outreach screening programs

- Mobile vans
- Venue-based- pharmacies, bars, health fairs, hair salons etc
- Field-based through contact tracing programs

- Costly
- Lower prevalence than in clinical settings
- Limited public health DIS workforce
- Limited reach or scale in a given population

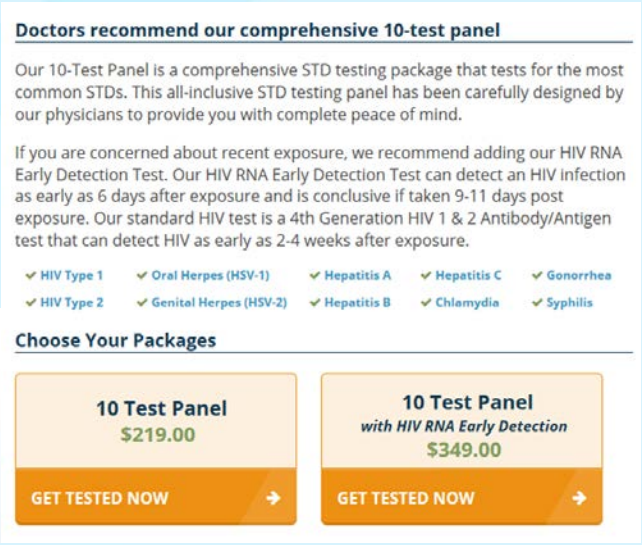
What have we learned about internet outreach screening programs: I Want The Kit*?

- Summary of 5 years of recent experience from 2011-2015
- Limited reach
  - Average annual requests- ~3100
  - Average annual swabs tested- ~1700
- Limited return rates (range 42% to 65%)
- Conducted as research until recently
- Self-collected swabs are acceptable
  - Reported to be easy to collect by women and men
  - Preferred by women
  - Test performance comparable to clinician-collected
- Limited information on treatment



What have we learned about internet outreach screening programs?

- Internet sites offering STD testing
  - Order online, mail self-collected specimen, test in lab
  - Order online, collect and test at home, instant results
  - Little known about these sites and testing accuracy
  - Offer panels of 8-10 pathogens
  - Expensive



Public Health Interventions to Increase Treatment

- Point of care testing
  - Desired by clinicians and patients
  - Many are not yet accurate enough or able to be performed in a short period of time
  - Theoretical advantages:
    - Faster results and more timely and correct treatment
    - Reduced clinic waiting and follow-up visits
    - Reduced presumptive treatment
    - Less patients lost to follow-up
    - More targeted prevention counseling
    - Decrease community transmission
    - Improve clinical practice efficiency
    - Improve medical outcomes

Needs Assessment of Clinicians: Build Your Own POC Test

- For which organisms do clinicians want a POC test?
  - Most say chlamydia
- How sensitive?
  - Most important factor: 90-99%
- How specific?
  - 99%
- How fast does it have to be?
  - 20 min
- What about cost?
  - Second most important factor: $20
- What about equipment?
  - no or little equipment

Hsieh Y-H et al. Plos One vol 6, issue 4, e19263, 2011.
Hsieh Y-H et al. Point of Care 11:126-129, 2012

WHO "*ASSURED*" Criteria for POC

Affordable: by those at risk of infection

Sensitive: few false negatives

Specific: few false positives

User-friendly and simple to perform: 3-4 steps, minimal training

Rapid and Robust

- rapid: enable treatment at first visit
- robust: no refrigerated storage

Equipment-free: easily collected non-invasive specimens

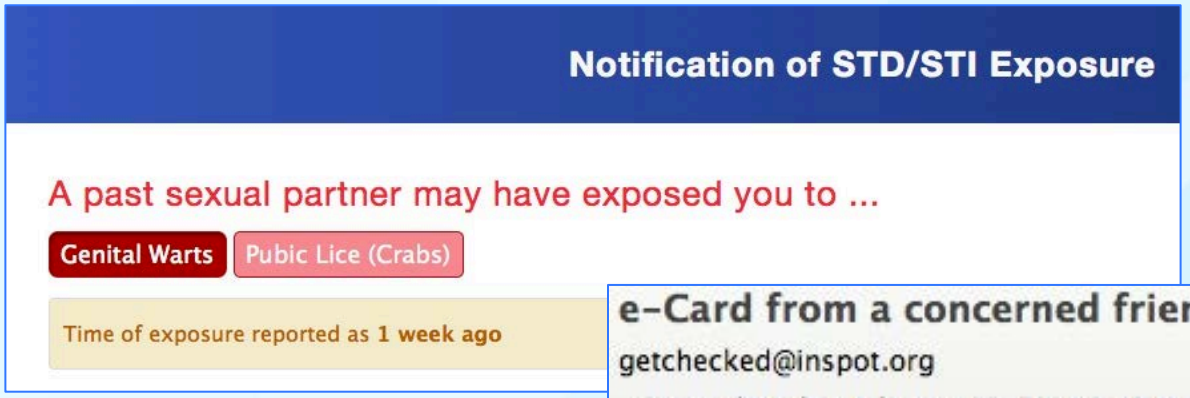
Delivered: delivered to end-users

http://www.who.int/std_diagnostics/about_SDI/priorities.htm

Public Health Interventions to Increase Treatment

- E-STD Services for STD diagnosis and treatment
  - E-testing and e-prescriptions
  - For patients and partners

Internet Partner Services



www.inspot.org
www.dontspreadit.com

OVER-THE-COUNTER TESTS FOR HOME TESTING:

WHAT TO WE KNOW?

Potential Benefits of Over-the Counter Chlamydia and Gonorrhea Testing

[Assuming sensitive and specific, easy to use and interpret, affordable and acceptable to the intended user]

- Increases access to and reach of testing which may result in earlier diagnosis and more timely treatment with improved health outcomes and reduction in further transmission
- Reduces stigma
- Offers privacy and confidentiality
- More convenient and preferred by some

Potential Risks of Over-the Counter Chlamydia and Gonorrhea Testing

- Patient may not seek treatment or inform partners of exposure to a communicable disease and the need for evaluation and treatment
- Unintended users may access testing resulting in more false positive results because of lower positive predictive value in a low prevalence population False positives can cause stigma, emotional distress, relationship issues, unnecessary treatment and other health care costs
- If positive tests are not reported to public health, CT/GC surveillance will be compromised:
  - STD prevention funds may be misaligned
  - Public health action and prevention interventions may be misguided
  - Antimicrobial resistance GC strains may go undetected
  - Economic modeling and network analysis of transmission dynamics may be wrong

Further studies are needed

- Many of the benefits and risks are speculative and need to be studied.
- Acceptability of self collection and home testing in larger and more generalizable populations, stratified by age, gender, SOGI, and race/ethnicity and other cultural factors need to be examined. Plus, the role of a public health reporting requirement on acceptability needs to be evaluated.
- The benefit, risk and cost of unintended users testing is unknown.
- OTC tests need to be developed that are sensitive and specific, easy to use and interpret, affordable and acceptable to the intended user.
- Patient adherence to timely treatment and timely partner treatment after testing needs to be studied as it is not know how many will seek treatment and inform partners after a positive test

Thank you!

Questions?

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For more information please contact Centers for Disease Control and Prevention

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