ADVANCING EXCELLENCE IN SEXUAL AND GENDER MINORITY HEALTH

Sexually Transmitted Infection Prevention and Treatment

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NATIONAL LGBT HEALTH EDUCATION CENTER
A PROGRAM OF THE FENWAY INSTITUTE

HARVARD MEDICAL SCHOOL

Disclosures

I have no financial disclosures.

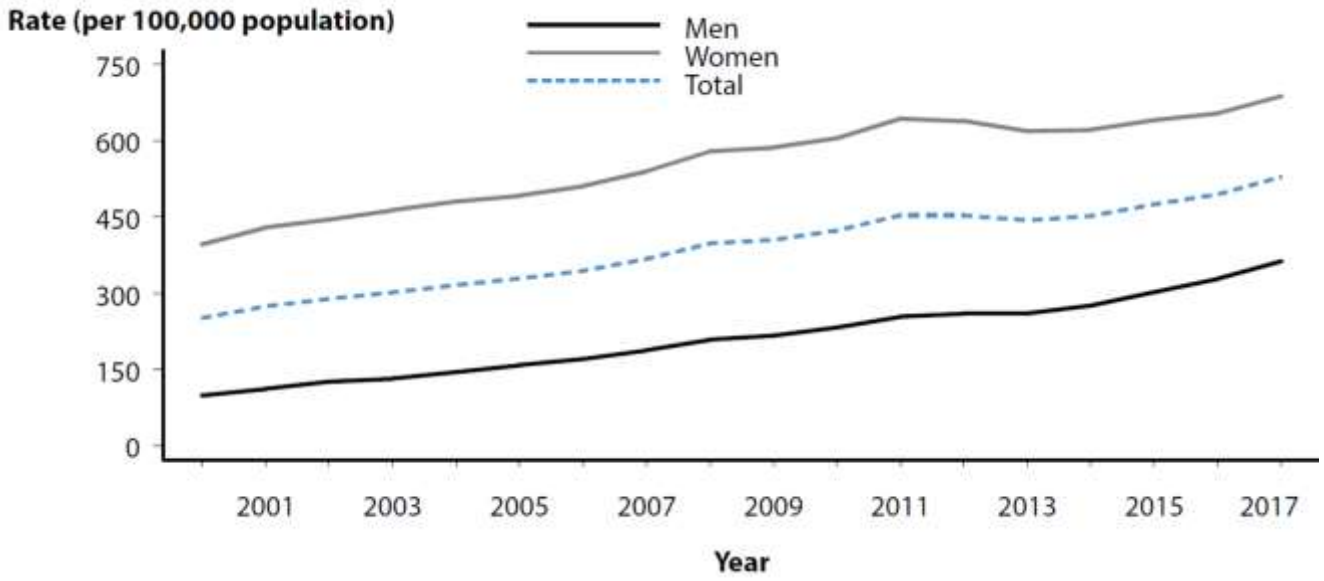
Learning objectives

1. Describe the epidemiology of syphilis, chlamydia, gonorrhea, and other STIs among LGBTQ+ populations
2. Summarize optimal screening strategies for STIs.
3. Outline approaches to STI control that can be integrated into primary care.

Caveats

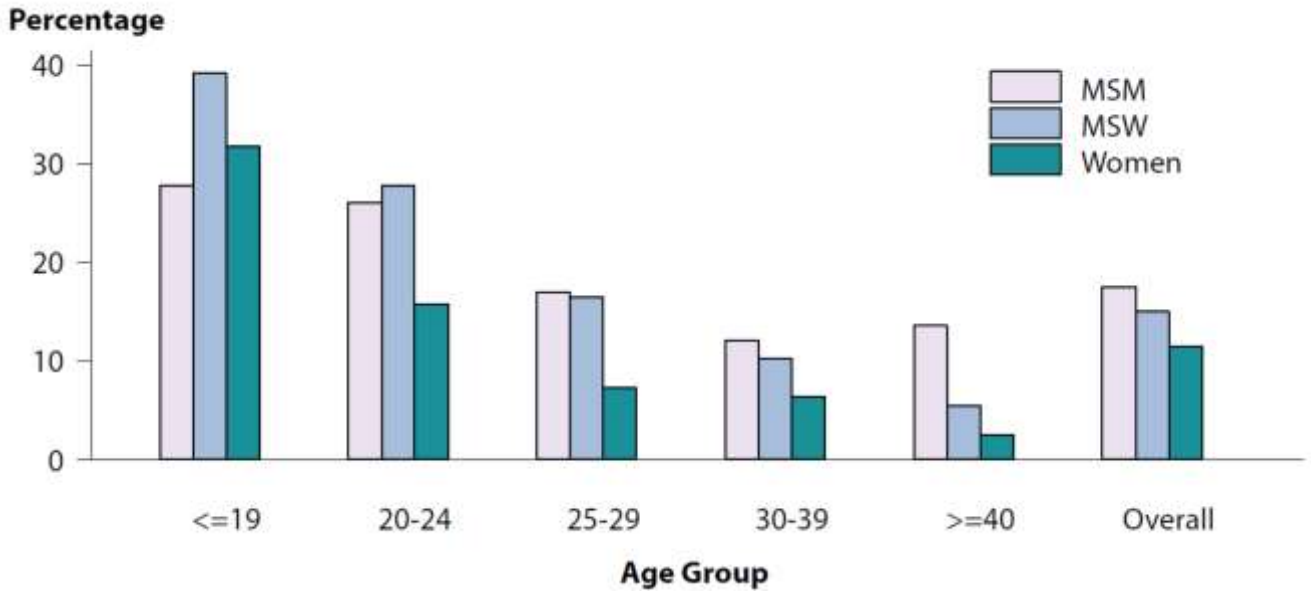
- Many (most?) LGBTQ+ people do not face a high risk of STIs.
- Clinical care must be individualized, not based on group risk.
- Data about STIs among cisgender WSW and transgender/gender non-conforming people are limited.
- Terms that describe identity and behavior are imperfect and change over time.

The rate of chlamydia diagnosis is increasing.



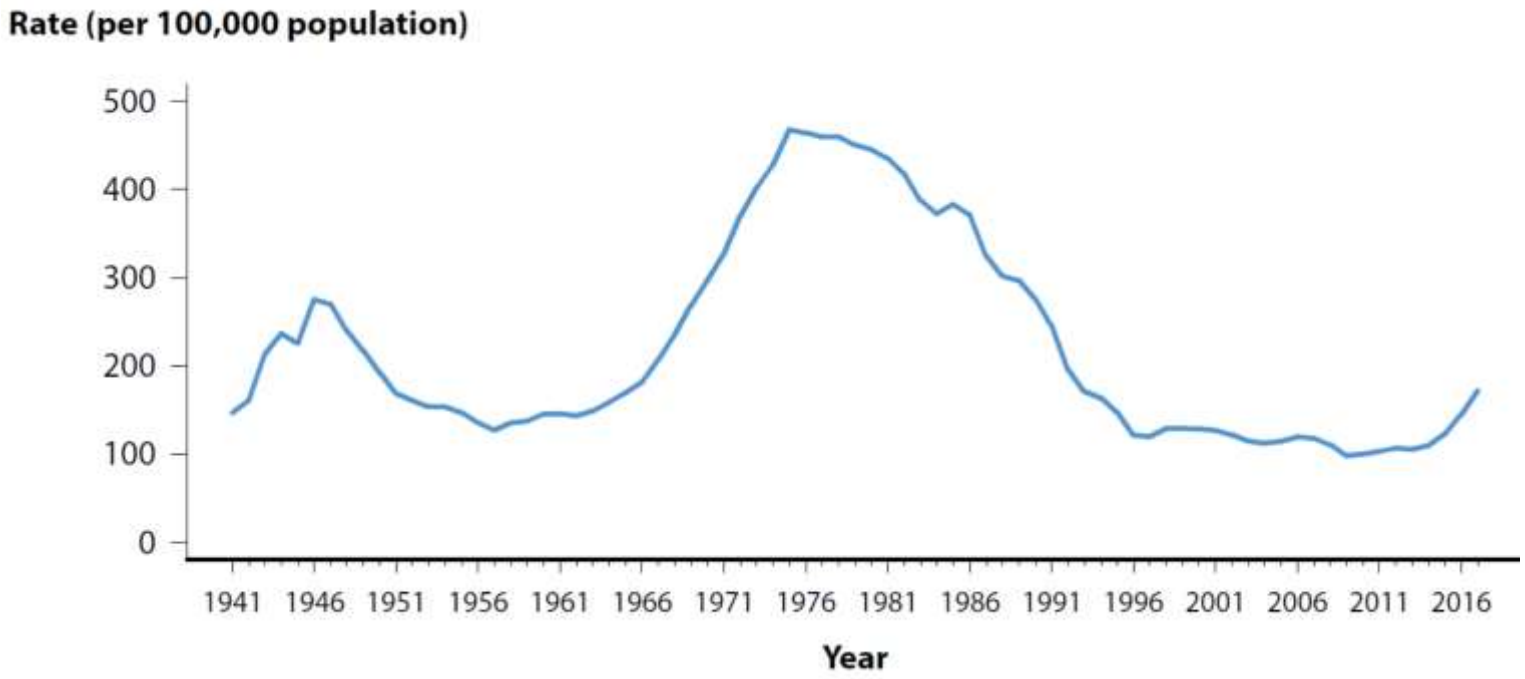
Sexually Transmitted Disease Surveillance 2017, CDC

Proportion of STI clinic patients testing positive for chlamydia



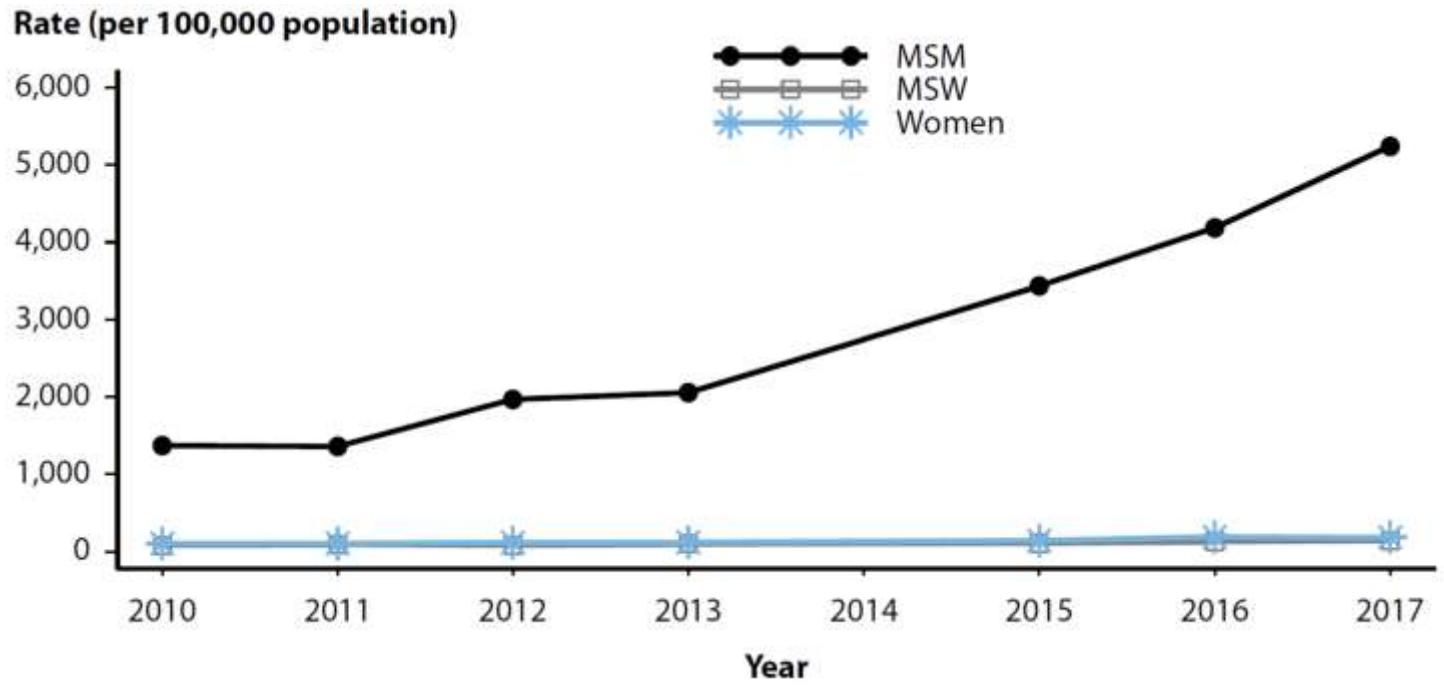
Sexually Transmitted Disease Surveillance 2017, CDC

The rate of gonorrhea diagnosis is increasing.



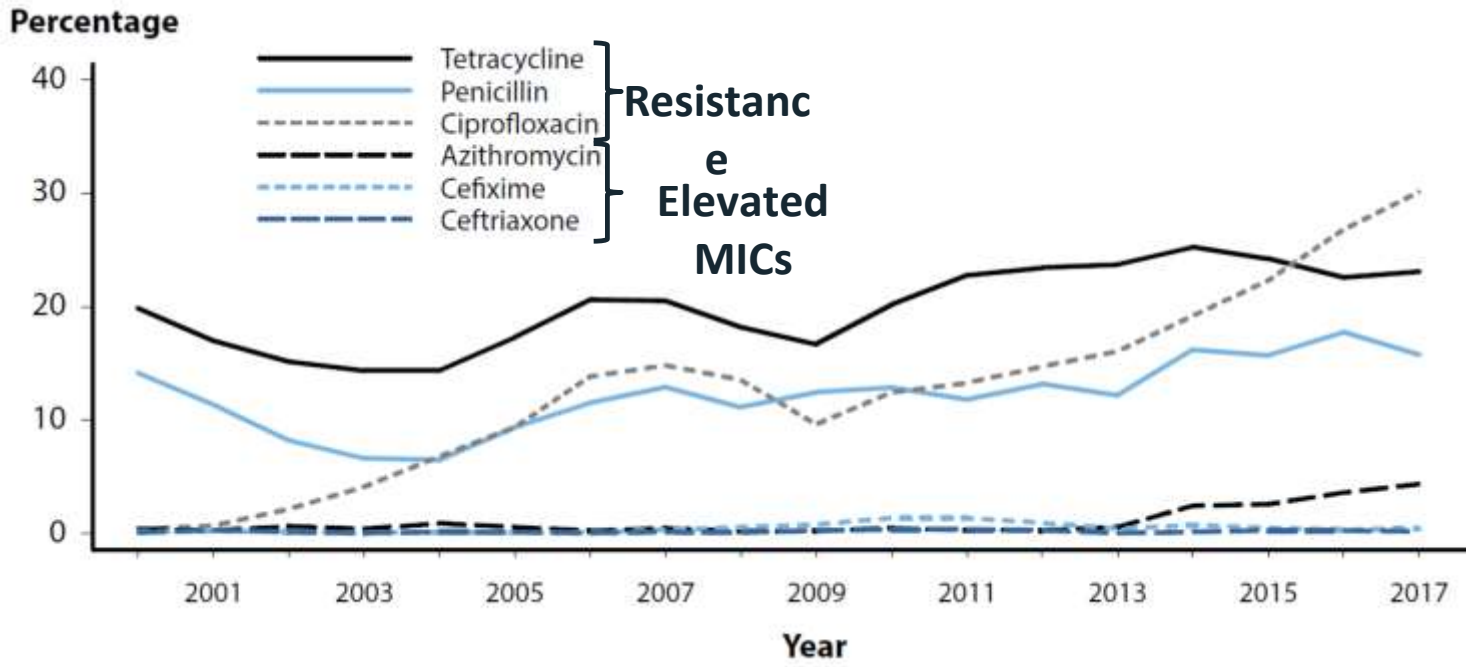
Sexually Transmitted Disease Surveillance 2017, CDC

MSM face an increasing disparity in the rate of gonorrhea.



Sexually Transmitted Disease Surveillance 2017, CDC

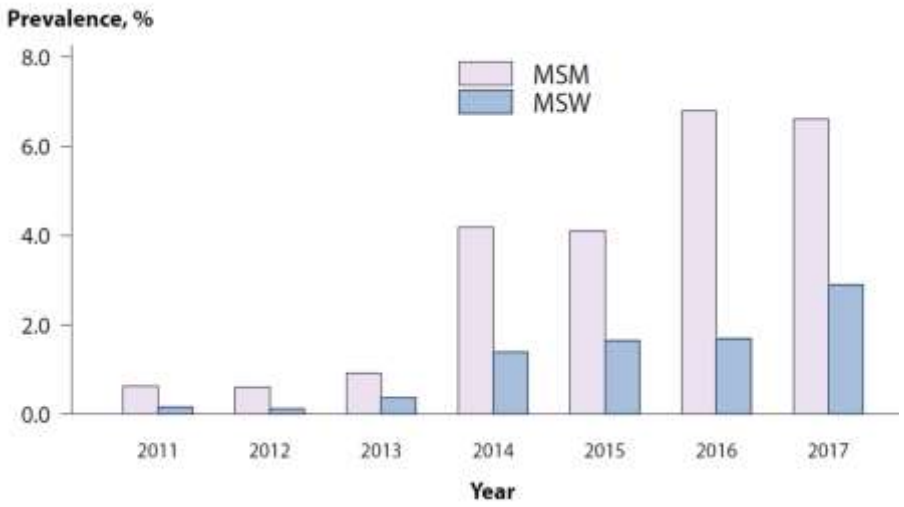
Antimicrobial resistance in gonorrhea is increasing.



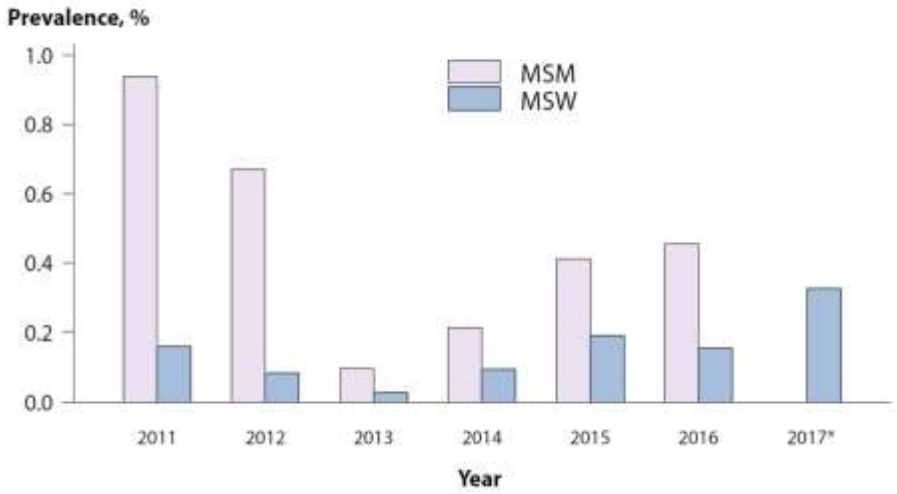
Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2017*. Atlanta: U.S. Department of Health and Human Services; 2018.

Neisseria gonorrhoeae — Percentage of Urethral Isolates with Elevated Azithromycin Minimum Inhibitory Concentrations (MICs) (≥2.0 µg/ml) and Elevated Ceftriaxone MICs (≥0.125 µg/ml) by Reported Sex of Sex Partners, Gonococcal Isolate Surveillance Project (GISP), 2011–2017

A. Azithromycin

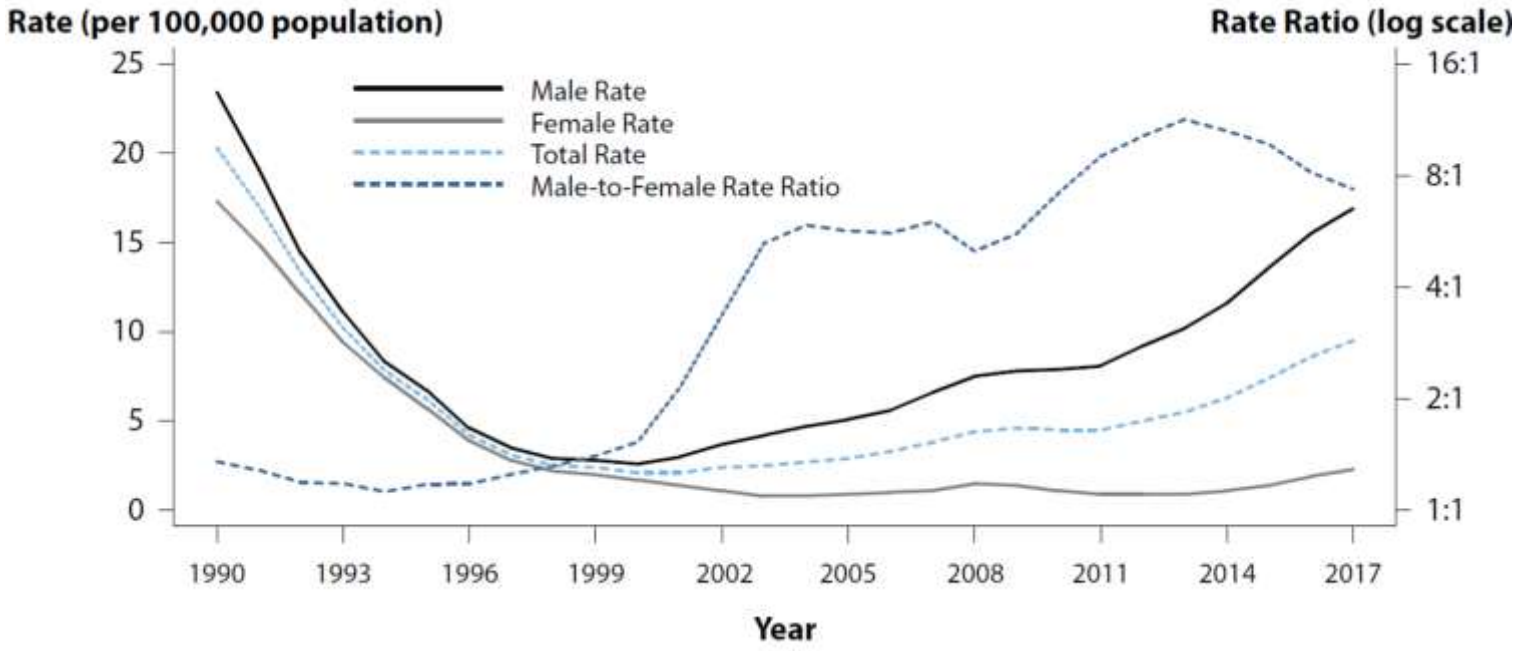


B. Ceftriaxone



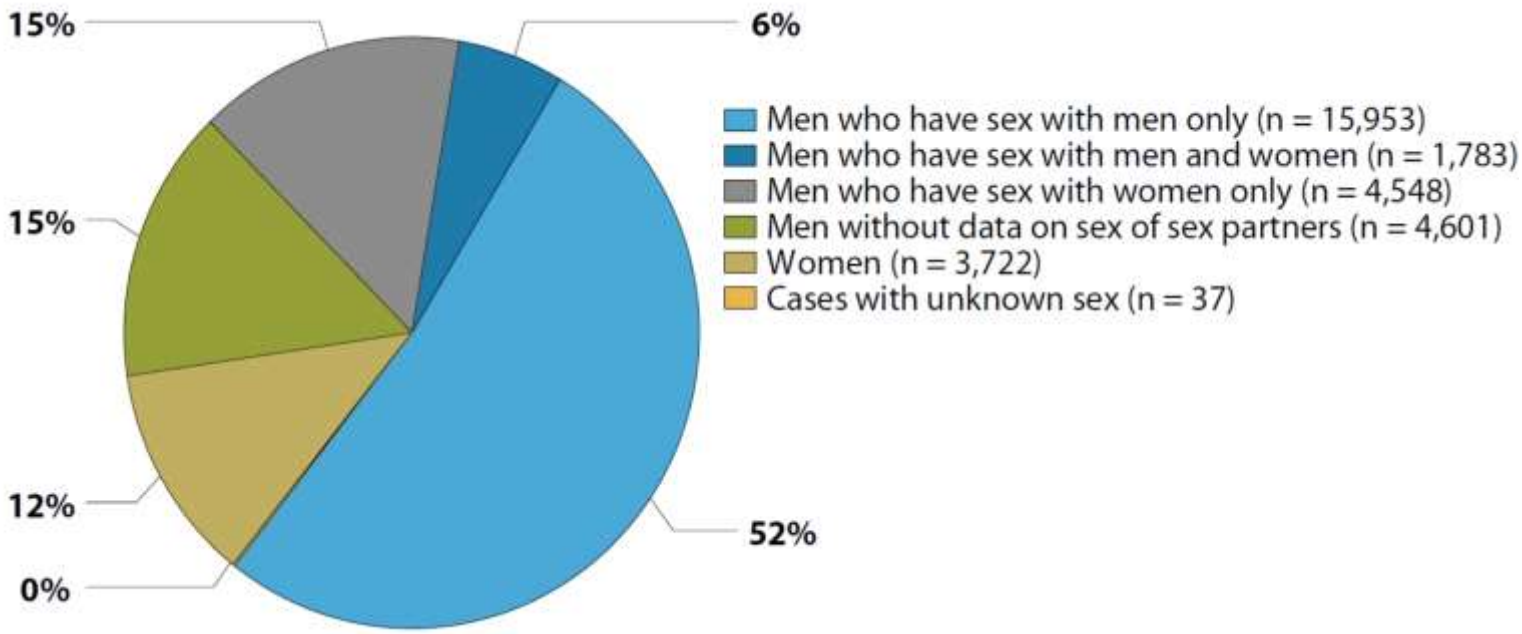
* No cases of elevated ceftriaxone MICs were reported among MSM in 2017.
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.

The rate of syphilis diagnosis is increasing.



Sexually Transmitted Disease Surveillance 2017, CDC

A majority of new syphilis infections occur in MSM.



Sexually Transmitted Disease Surveillance 2017, CDC

Some transgender people face a high burden of STIs.

- **United States systematic review:**
  - STI lifetime prevalence = 21.1%, greater in MTF than FTM people
- **Prospective study of 230 MTF people New York City:**
  - Syphilis incidence 3.6% per year
  - Gonorrhea incidence 4.2% per year
  - Chlamydia incidence 4.5% per year
- **Retrospective study of 145 young people in Boston:**
  - Prevalence of syphilis 2.8%
  - Prevalence of gonorrhea and chlamydia 2.1% each

1. Herbst JH, Jacobs ED, Finlayson TJ, et al. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. AIDS Behav. 2008;12(1):1.
2. Nuttbrock L, Bockting W, Rosenblum A, et al. Gender abuse, depressive symptoms, and HIV and other sexually transmitted infections among male-to-female transgender persons: a three-year prospective study. Am J Public Health. 2013;103(2):300.
3. Reisner SL, Vetters R, White JM, et al. Laboratory-confirmed HIV and sexually transmitted infection seropositivity and risk behavior among sexually-active transgender patients at an adolescent and young adult urban community health center. AIDS Care. 2015;27(8):1031.

STIs are more than the “big three.”

- *Entamoeba histolytica* (Escola-Verge L, Euro Surveill, 2017)
- Lymphogranuloma venereum (De Baetselier I, BMC Infect Dis, 2018)
- Antibiotic-resistant *Shigella* species (Mook P, Emerg Infect Dis, 2016)
- Meningococcus (Folaranmi TA, Clin Infec Dis, 2017)
- Hepatitis C (Price JC, J Infect Dis, 2018)
- Zika (Rosenberg ES, J Infect Dis, 2018)

Mycoplasma genitalium

- First identified in men with non-gonococcal urethritis (NGU) in 1980
- Major cause of NGU; more common than gonorrhea but less common than chlamydia
- Diagnosed by nucleic acid detection; culture challenging
- Treatment can be difficult:
  - Intrinsically resistant to beta-lactams
  - Doxycycline ineffective
  - Azithromycin increasingly ineffective
  - Moxifloxacin usually effective

Horner PJ, Martin DH. Mycoplasma genitalium infection in men. J Infect Dis. 2017;216(Suppl 2):S396-S405.
Workowski KA, Bolan G. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(3).

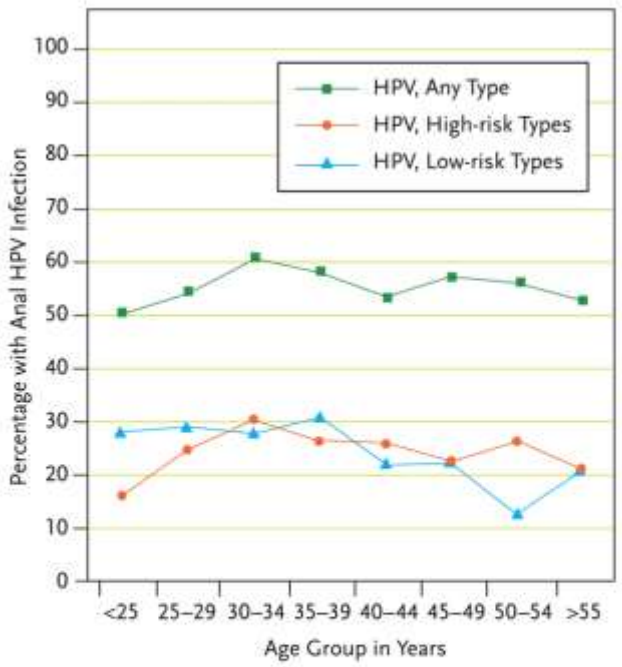
Bacterial vaginosis is more common among WSW than other women.

- Among WSW, risk of BV is increased by:
  - Greater number of sexual partners (recent and lifetime)
  - BV in a partner
- Female partners often share identical Lactobacillus strains.
- Routine BV screening is not recommended for WSW.
- Empiric treatment for female partners of patients with BV is not formally recommended.

Vodstrcil, Clin Infect Dis, 2015; Forcey, PLoS One, 2015; Marrazzo, J Infect Dis, 2009; 2015 STD Treatment Guidelines

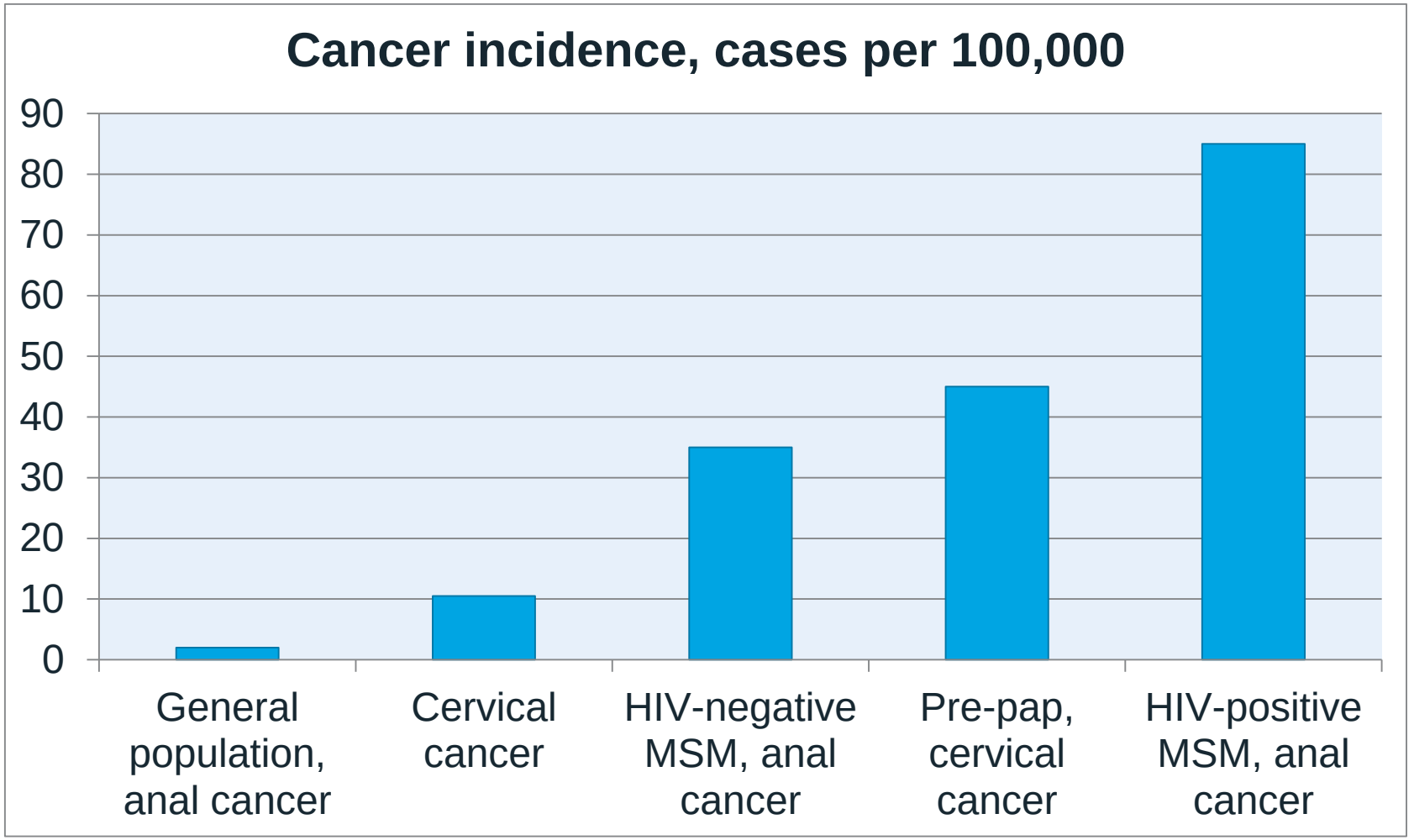
HPV and anal cancer among MSM

Figure 5. Anal HPV Infection by Age Group in Sexually Active HIV-negative MSM



Prevalence of human papillomavirus (HPV) DNA in the anal canals of HIV-negative men who have sex with men (MSM), by age group and by cancer-associated risk type. High-risk (HR) types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, and 73; low-risk types include 6, 11, 53-56, 66, Pap 155, and Pap 291.

Reprinted with permission from The University of Chicago Press.[22]

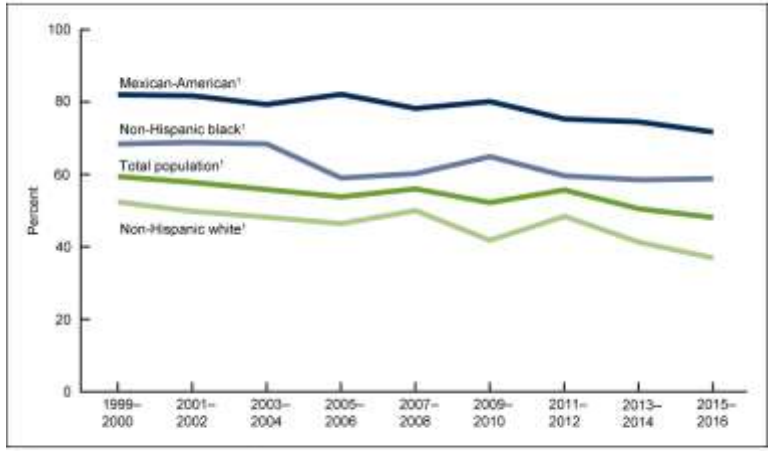


Chin-Hong PV, J Infect Dis, 2004
D'Souza G, J Acquir Immune Defic Syndr, 2008

Herpes simplex virus

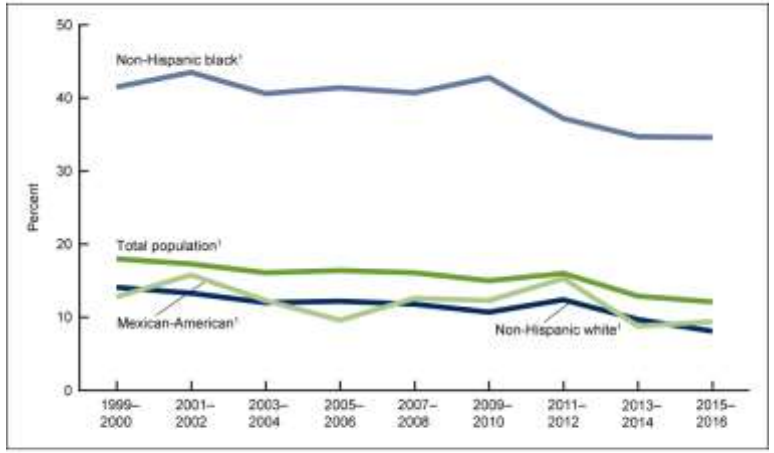
- HSV-2 not clearly more common among MSM than other men in the United States.
- Anogenital herpes is often due to HSV-1 among MSM.
- HSV-1 and HSV-2 are becoming less common in the United States.

Figure 2. Trends in age-adjusted prevalence of herpes simplex virus type 1 among persons aged 14–49, for the total population and by race and Hispanic origin: United States, 1999–2000 through 2015–2016



¹Significant decreasing linear trend over time, $p < 0.05$.
NOTES: Age adjusted by the direct method to the 2000 U.S. Census population, using age groups 14–19, 20–29, 30–39, and 40–49 years. Total population includes all race and Hispanic-origin groups including those not shown separately. Data for the Asian subpopulation are only available since 2011, so this subpopulation is not shown separately, but included in the total population. Access data table for Figure 2 at: https://www.cdc.gov/nchs/data/databriefs/db304_table.pdf#2.
SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2016.

Figure 4. Trends in age-adjusted prevalence of herpes simplex virus type 2 among persons aged 14–49, for the total population and by race and Hispanic origin: United States, 1999–2000 through 2015–2016



¹Significant decreasing linear trend over time, $p < 0.05$.
NOTES: Age adjusted by the direct method to the 2000 U.S. Census population, using age groups 14–19, 20–29, 30–39, and 40–49 years. Total population includes all race and Hispanic-origin groups including those not shown separately. Data for the Asian subpopulation are only available since 2011, so this subpopulation is not shown separately, but included in the total population. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db304_table.pdf#4.
SOURCE: NCHS, National Health and Nutrition Examination Survey, 1999–2016.

Xu F, Sex Transm Dis, 2010; Durukan D, Sex Transm Infect, 2018; McQuillan G, CDC, 2018

Why are STI diagnoses increasing?

Increased detection

Affordable Care Act (2010, 2014)

Extragenital gonorrhea and chlamydia testing

Increased transmission

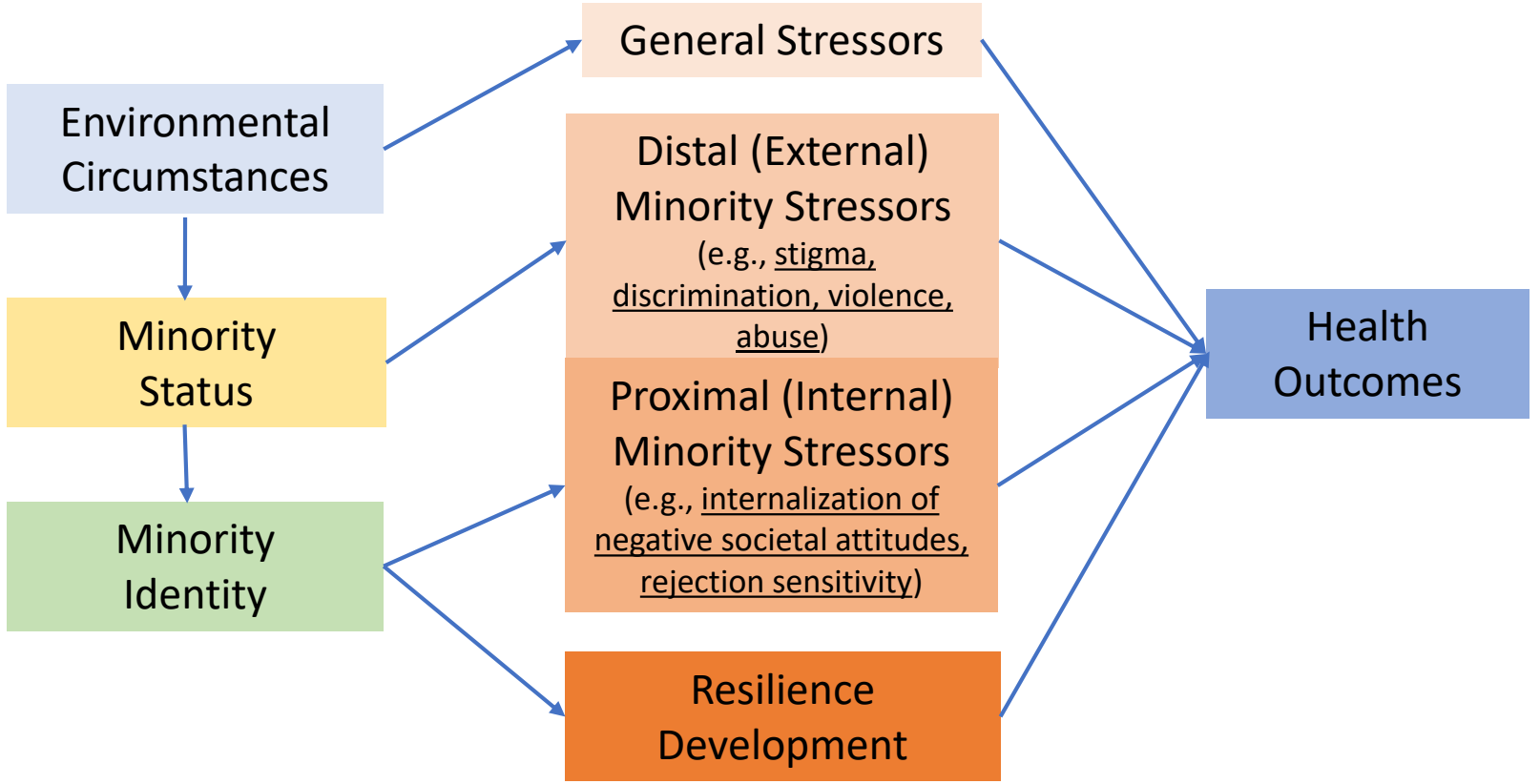
Smartphones and geosocial networking apps

HIV treatment as prevention

PrEP

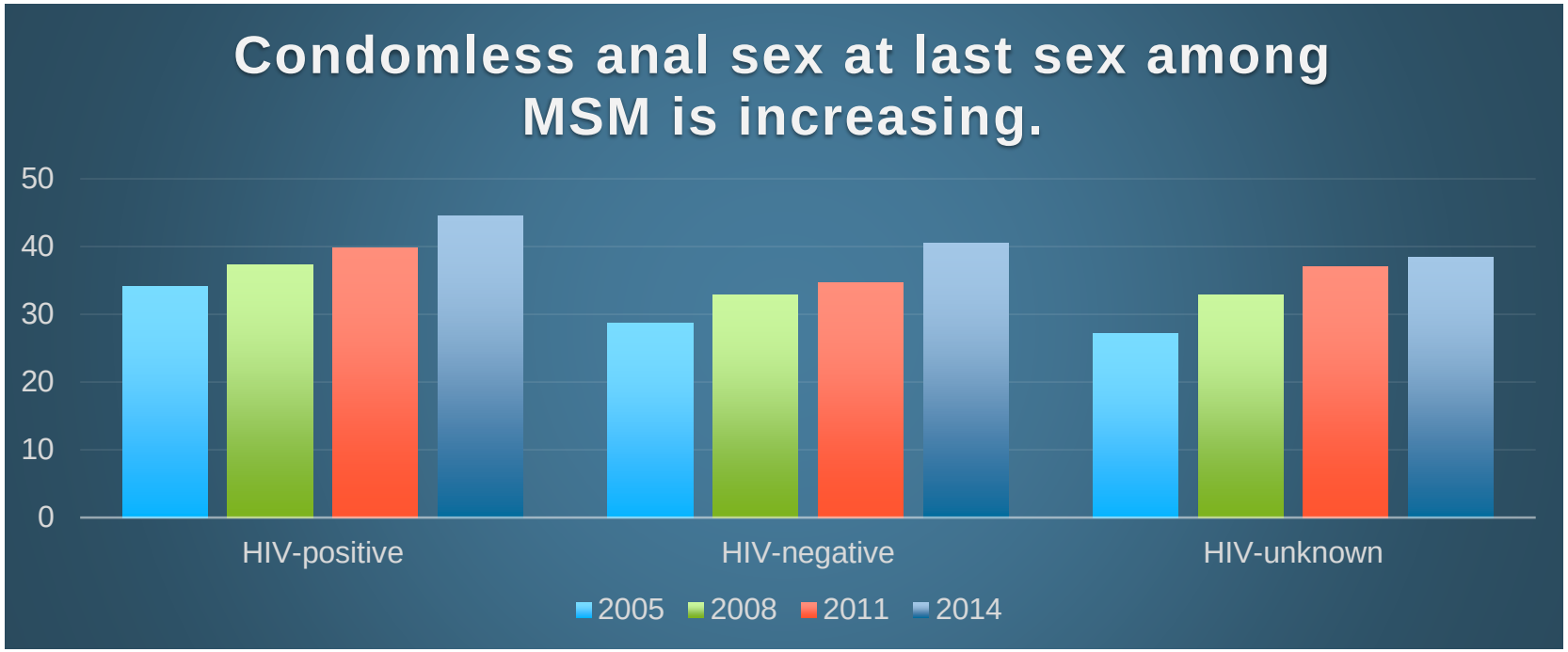
Schillinger JA. The intersection of PrEP and sexually-transmitted infections. Conference on Retroviruses and Opportunistic Infections, Boston, MA. 2018. Abstract 105.

Minority Stress Model (adapted from Meyer)



Slide courtesy of Dr. Alex Keuroghlian

Condom use is falling among MSM.



Paz-Bailey G, AIDS, 2016

Sexual histories should be routine and free of assumptions.

STI prevention for LGBTQ+ people

1. Addressing socioeconomic factors that increase vulnerability
2. Vaccines – HAV, HBV, HPV
3. Condoms and risk-reduction counseling
4. PrEP for those at risk for HIV
5. STI screening and treatment – interrupting transmission prevents future infections

What do we say about condoms in 2019?

- One item on a menu of options for HIV/STI prevention
- Condom counseling must adapt to the era of biobehavioral HIV prevention
- Advantages and disadvantages:
  - Protect against a wide range of STIs
  - Widely available; not a medical intervention
  - Use is apparent to partners
  - Efficacy is imperfect (as with all strategies); 70% effective at preventing HIV among MSM
  - Consistent condom use is rare
  - Some patients are unlikely to benefit from condoms (e.g., mutually monogamous serodifferent couple in which the partner living with HIV is virologically suppressed)

Smith DK, J Acquir Immune Defic Syndr, 2015
Paz-Bailey G, AIDS, 2016

CDC's screening recommendations for MSM

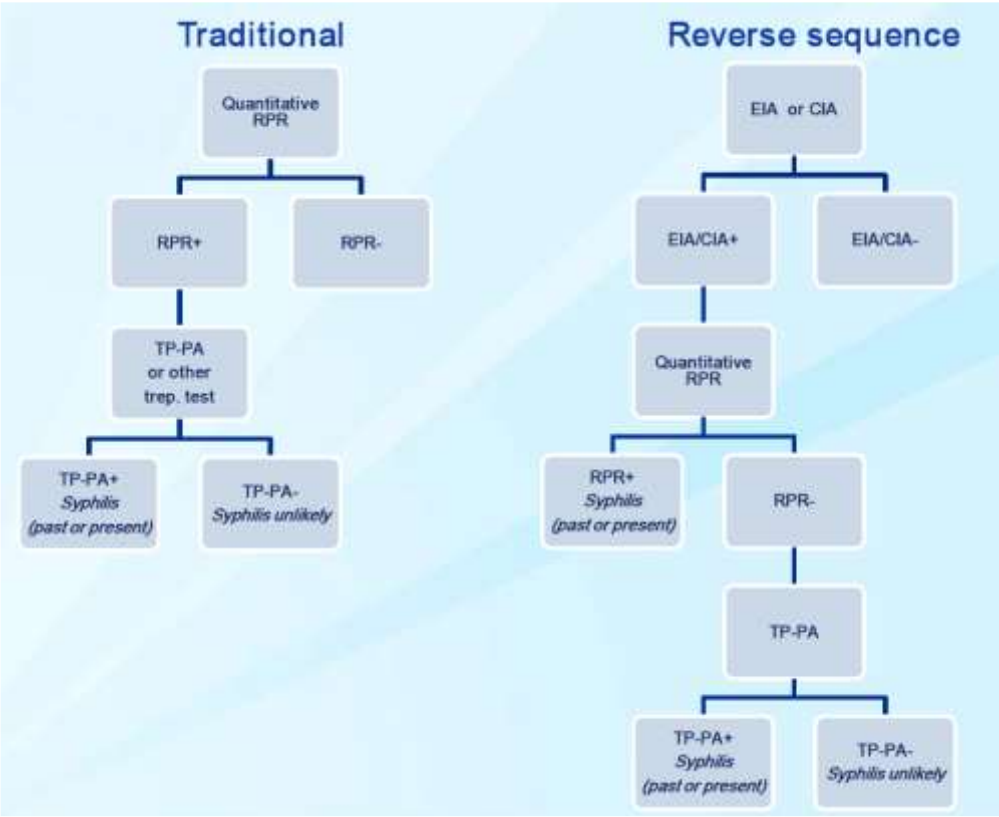
- HIV antibody/antigen assay
- Syphilis serology
- NAAT for *N. gonorrhoeae* and *C. trachomatis*
  - From the urethra/urine and rectum for both, if exposed
  - From the pharynx for *N. gonorrhoeae* only
- At least once: Hepatitis B surface antigen
- Yearly, if living with HIV: HCV antibody assays

2015 STD Treatment Guidelines

Screening for transgender people and sexual minority women is based on risk assessment.

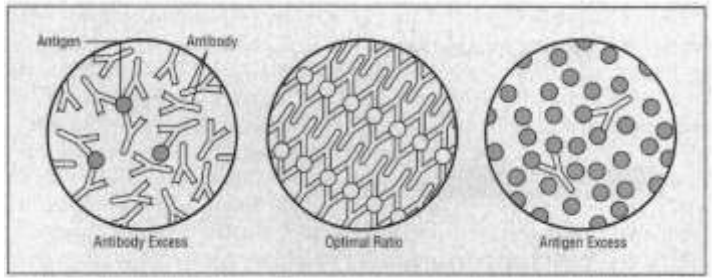
"Clinicians should assess STD- and HIV-related risks for their transgender patients **based on current anatomy and sexual behaviors**. Because of the diversity of transgender persons regarding surgical affirming procedures, hormone use, and their patterns of sexual behavior, providers must remain aware of symptoms consistent with common STDs and screen for asymptomatic STDs on the basis of behavioral history and sexual practices."

Syphilis testing follows a “traditional” or “reverse” testing algorithm.



Causes of discordant syphilis test results in the “reverse” algorithm?

- Previously treated syphilis
- Old, untreated syphilis
- Very early syphilis (in a “window period” between treponemal antibody and RPR positivity, or the prozone phenomenon)



2015 Sexually Transmitted Disease Treatment Guidelines. CDC. Available at: www.cdc.gov/std/tg2015/default.htm
Jurado RL, Arch Intern Med, 1993

What we know about gonorrhea and chlamydia testing in cisgender people

CIS WOMEN

- NAATs are preferred.
- Sensitivity of first-catch urine is 10% less than a vaginal swab.
- A self-collected vaginal swab performs as well as a clinician-collected swab.
- Vaginal swabs perform as well as endocervical swabs.

CIS MEN

- NAATs are preferred.
- Sensitivity of first-catch urine is the same as a urethral swab.

Papp JR, et al. Recommendations for the laboratory-based detection of Chlamydia trachomatis and Neisseria gonorrhoeae – 2014. MMWR. March 14, 2014/63(RR02);1.

Unanswered questions in STI screening for transgender people

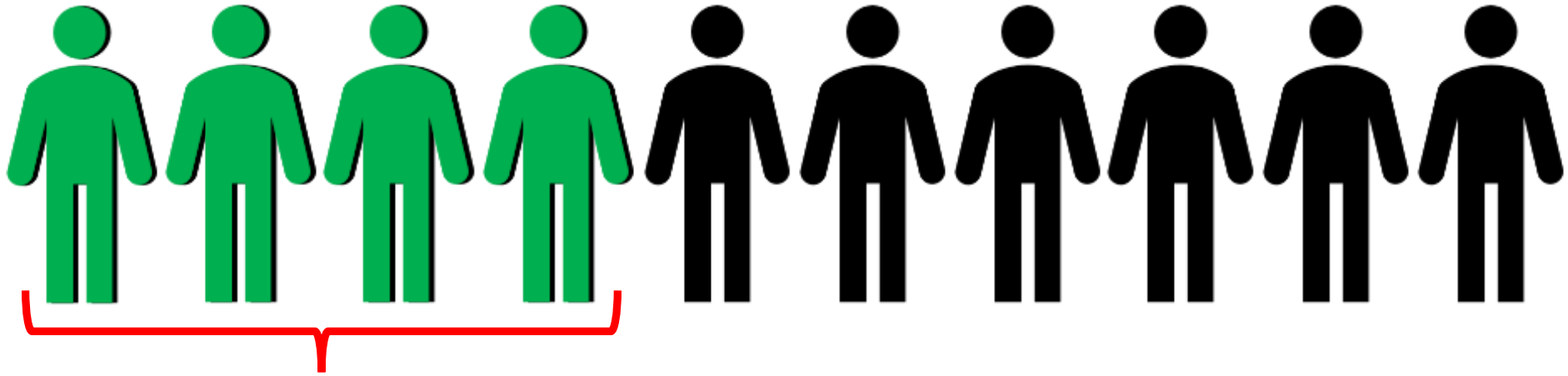
- What is the risk of STIs in surgically-constructed vaginas and penises?
  - **Vaginoplasty techniques may involve urethral or colorectal mucosa, which is presumably susceptible to infection.**

- What is the optimal screening strategy for gonorrhea/chlamydia in the setting of genital reconstruction?
  - **Urine NAAT versus vaginal/urethral NAAT in vaginoplasty/phalloplasty**
  - **Some experts consider urine NAAT preferred.**

- Do STIs present differently in reconstructed tissue?
  - **Case report of neovaginal gonorrhea presenting as coital bleeding**

1. Poteat T. Transgender people and sexually transmitted infections. UCSF Center for Excellence in Transgender Health. 2018. Available at: http://transhealth.ucsf.edu/trans?page=guidelines-stis.
2. Van der Sluis WB, Bouman MB, Gijs L, van Bodegraven AA. Gonorrhoea of the sigmoid neovagina in a male-to-female transgender. Int J STD AIDS. 2015;26(8):595.

PrEP may be an STI control intervention among MSM.



On PrEP,
Reduce condom use by 40%

42% of gonorrhea and 40% of chlamydia infections prevented over 10 years

Jenness SM, Weiss K, Goodreau S, et al. Incidence of gonorrhea and chlamydia following human immunodeficiency virus preexposure prophylaxis among men who have sex with men: A modeling study. Clin Infect Dis. 2017;65(5):712-718.

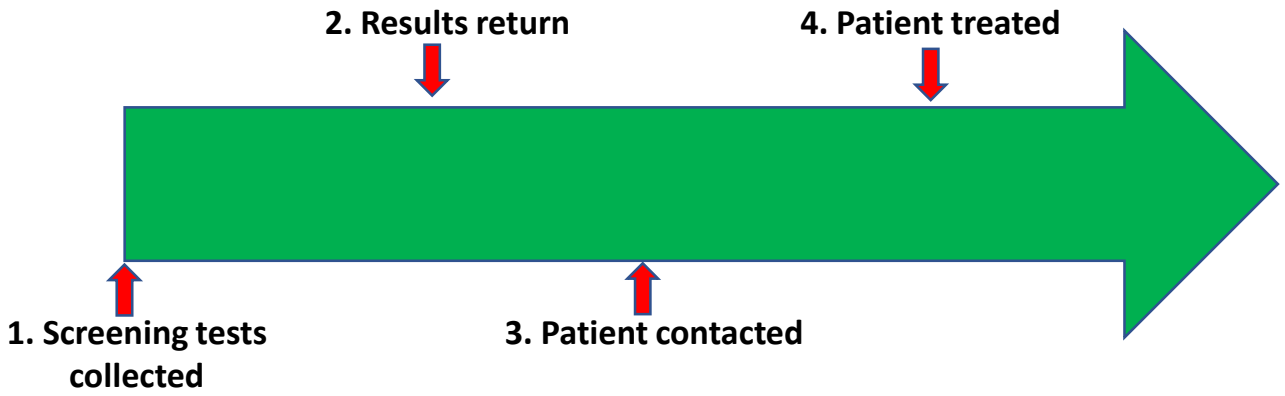
SUMMARY OF THE 2015 CDC SEXUALLY TRANSMITTED DISEASE (STD) TREATMENT GUIDELINES
MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH (MDPH) – DIVISION OF STD PREVENTION (DSTDP)

These guidelines for treatment of STDs reflect recommendations of the **MDPH DSTDP** and of the **CDC STD Treatment Guidelines**. These guidelines focus on STDs encountered in outpatient settings and are not an exhaustive list of effective treatments. Please refer to the complete CDC document for more information or call the DSTDP. Clinical and epidemiological services are available through the DSTDP including staff to assist healthcare providers with confidential notification of sexual partners of patients with STDs and/or HIV infection. Please call the DSTDP for assistance at (617) 983-6940.

DISEASE	RECOMMENDED TREATMENT	ALTERNATIVES (use only if recommended regimens are contraindicated)
SYPHILIS		
ADULTS Primary, Secondary or Early Latent (<1 Year)	• Benzathine penicillin G 2.4 million units IM once	(For penicillin-allergic non-pregnant patients only) • Doxycycline 100 mg orally 2 times a day for 14 days ***OR*** • Tetracycline 500 mg orally 4 times a day for 14 days
ADULTS Late Latent (>1 Year) or Latent Of Unknown Duration	• Benzathine penicillin G 2.4 million units IM for 3 doses at 1 week intervals (total 7.2 million units)	(For penicillin-allergic non-pregnant patients only) • Doxycycline 100 mg orally 2 times a day for 28 days ***OR*** • Tetracycline 500 mg orally 4 times a day for 28 days
All Suspect Syphilis Cases: Call the STD Program at (617) 983-6940 for past titers and treatment. **NEUROSYPHILIS including OCULAR SYPHILIS**	• Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days[1]	• Procaine penicillin G 2.4 million units IM once daily **PLUS** probenecid 500 mg orally 4 times a day, both for 10-14 days
CHILDREN Primary, Secondary or Early Latent (<1 Year)	• Benzathine penicillin G 50,000 units/kg IM once, up to adult dose of 2.4 million units	No specific alternative regimens exist.
CHILDREN Late Latent (>1 Year) or Latent Of Unknown Duration	• Benzathine penicillin G 50,000 units/kg IM (up to adult dose of 2.4 million units) for 3 doses at 1 week intervals (up to total adult dose of 7.2 million units)	
CONGENITAL SYPHILIS	See complete CDC guidelines.	
HIV INFECTION	Same stage-specific recommendations as for HIV-negative persons.	
PREGNANCY	Penicillin is the only recommended treatment for syphilis during pregnancy. Women who are allergic should be desensitized and treated with penicillin. Treatment is the same as in non-pregnant patients for each stage of syphilis.[2]	
GONOCOCCAL INFECTIONS		
ADULTS, ADOLESCENTS and CHILDREN >45 kg Pharyngeal, Urogenital, Rectal	• Ceftriaxone 250 mg IM once **PLUS**[3] • Azithromycin 1 g orally once	***Note:*** **Use of an alternative regimen for pharyngeal gonorrhea should be followed by a test-of-cure 14 days after treatment.**[4] **For urogenital or rectal infections ONLY, and ONLY if ceftriaxone is *not* available:** • Cefixime 400mg orally once **PLUS**[3] • Azithromycin 1 g orally once **OR in case of azithromycin allergy** • Doxycycline 100 mg orally 2 times a day for 7 days **For azithromycin allergy:** ♦ Ceftriaxone 250 mg IM once **PLUS**[3] ♦ Doxycycline 100 mg orally 2 times a day for 7 days **For cephalosporin allergy or IgE-mediated penicillin allergy:** ♦ Gemifloxacin 320 mg orally once ***OR*** ♦ Gentamicin 240 mg IM once **PLUS**[3] ♦ Azithromycin 2 g orally once

https://www.mass.gov/files/documents/2016/07/sz/ma-std-tx-guidelines-2016.pdf

Point-of-care testing for STIs may decrease transmission but shortening duration of infectivity.



Amsterdam STI clinic modelling study:

- 35% of MSM had sexual contexts in the time between testing and treatment (23% of whom had CAS)
- POC testing for all MSM anticipated to decrease gonorrhea prevalence by 11% over 5 years

Bartelsman M, Sex Transm Infect, 2017

What about anal cytology?

YES

- Anal cancer is HPV-associated and exhibits biology similar to that of cervical cancer
- Rates of anal cancer are high in MSM, especially in those with HIV
- Recommended for all HIV-infected MSM

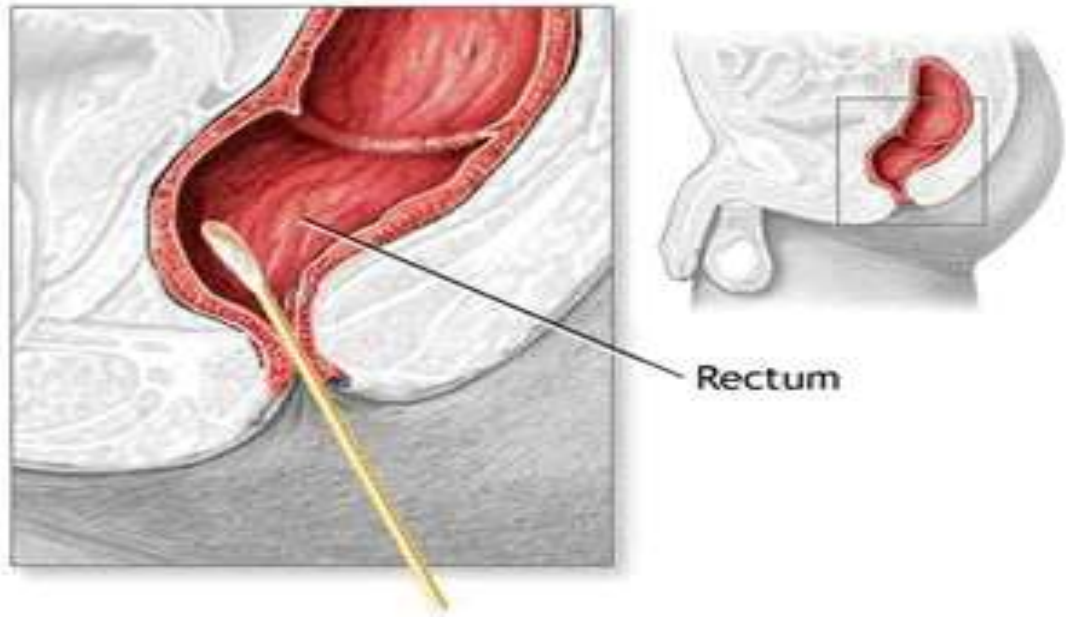
NO

- As of yet, no randomized trials have been performed to assess the benefits of screening
- Whom to screen, how often, and when to start/stop screening are unclear

1. Silverberg MJ, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. Clin Infect Dis. 2012;54(7):1026-1034.
2. Aberg JA, et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Disease Society of America. 2014;58(1):1-10.

How to obtain anal cytology

- Place the patient in the lateral recumbent position.
- Insert a Dacron swab 5-6 cm into the anus.
- Apply lateral pressure and, while withdrawing the swab, rotate it.
- Submit the specimen as you would cervical cytology.



1. Knight D. Procedural advice for performing anal pap smears. Am Fam Physician. 2005;71(10):1874-1879.
2. Image available from: www.hivandhepatitis.com

1. Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. MMWR. 2010;59:RR-12.
2. FDA licensure of quadrivalent human papillomavirus vaccine (HPV4, Gardasil) for use in males and guidance from the Advisory Committee on Immunization Practices (ACIP). MMWR. 2010;59(20):630-632.

HEALTH

The New York Times

GIFT THE TIMES

HPV Vaccine Expanded for People Ages 27 to 45

About 14 million women and men become infected with the human papillomavirus each year in the United States, according to the Centers for Disease Control and Prevention.

Keith Bedford/The Boston Globe, via Getty Images

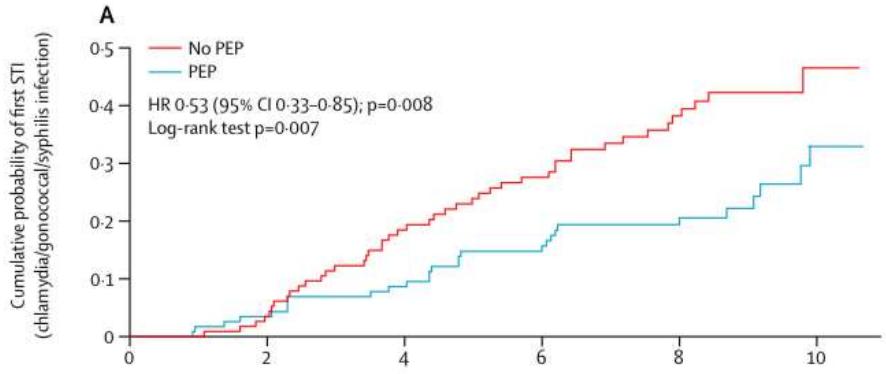
Group B OMV meningococcal vaccine prevents gonorrhea infection.

- Mass vaccination against meningococcal group B infection in New Zealand from 2004-2008 (81% coverage of people < 20 years)
- Case control study of people ages 15-30 in sexual health clinics
  - Cases = Confirmed gonorrhea
  - Controls = Confirmed chlamydia
  - Exposure = Group B OMV meningococcal vaccination
- Vaccine effectiveness against gonorrhea = 31% (95% CI 21-39)

Petousis-Harris H, et al. Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhea in New Zealand: a retrospective case-control study. Lancet. 2017;390(10102):1603-1610.

Doxycycline PEP prevents syphilis and chlamydia among MSM.

- 232 MSM in a trial of open-label, on-demand PrEP with TDF-FTC
- Randomized to doxycycline within 24 hours of sex or no PEP
- Doxycycline reduced chlamydia and syphilis infections but not gonorrhea



Molina JM, Lancet Infect Dis, 2018

PEP with doxycycline is generally well-tolerated.

	PEP (n=116)	No PEP (n=116)	p value
Any adverse events	106 (91%)	104 (90%)	0·65
Any serious adverse events	5 (4%)	10 (9%)	0·18
Any grade 3 or 4 events	4 (3%)	8 (9%)	0·24
Treatment discontinuation because of adverse events	8 (7%)	NA	..
Gastrointestinal adverse events	62 (53%)	47 (41%)	0·05
Drug-related gastrointestinal adverse events	29 (25%)	16 (14%)	0·03
Nausea or vomiting	10 (9%)	3 (3%)	..
Abdominal pain	14 (12%)	5 (4%)	..
Diarrhoea	6 (5%)	9 (8%)	..
Other gastrointestinal disorders	5 (4%)	1 (1%)	..

Molina JM, Lancet Infect Dis, 2018

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ORIGINAL ARTICLE

Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

Stephanie N. Taylor, M.D., Jeanne Marrazzo, M.D., M.P.H., Byron E. Batteiger, M.D., Edward W. Hook, III, M.D., Arlene C. Seña, M.D., M.P.H., Jill Long, M.D., M.P.H., Michael R. Wierzbicki, Ph.D., Hannah Kwak, M.H.S., Shacondra M. Johnson, B.S.P.H., Kenneth Lawrence, Pharm.D., and John Mueller, Ph.D.

Recap

- Provide LGBTQ+-affirming care
- Make the sexual history part of routine care
- Screen frequently, if the history indicates the need
- Vaccinate
- Consider doxycycline for MSM who have a high risk of STIs