

Sexually Transmitted Diseases: Why should we bother?

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Biographical information:

Arti Barnes is an Assistant Professor of Medicine, Division of Infectious Diseases at UT Southwestern Medical Center. She has an interest in international HIV through her work with OVCs (Orphans and Vulnerable Children) in Uganda, Zambia and Tanzania. She was faculty at the University of Mississippi Medical Center from 2010 to 2013 and worked as the Director of the Cervical Dysplasia Screening Clinic at the Mississippi State Health Department. During her time there, she was a co-PI for the state of Mississippi for two CDC HIV surveillance projects- the MMP and CSBS projects and currently serves as the Clinical Director for the South Central AIDS Education and Training Centers for HRSA Region 6. Dr. Barnes is part of the cervical cancer research group through the Parkland-UTSW PROSPR project.

Her research interests include HIV, STDs, international health, HPV screening and LGBT care.

Purpose and overview:

Sexually transmitted infections or diseases (STIs or STDs) cause a heavy and avoidable burden on the United States health care system, especially emergency departments. 19 million STIs are diagnosed every year in the United States and cost the economy 16 billion dollars with HIV and HPV responsible for the heaviest cost burden. They also cause a heavy burden on the socio-economically disadvantaged and ethno-racial minorities with African Americans and Hispanics having a much higher risk of acquiring STIs such as chlamydia, gonorrhea, syphilis and HPV related cancers like cervical and anal cancer. The clinical significance of STIs is greater than HIV alone. This significance extends to HPV related cancers, mortality from congenital syphilis, and infertility from chlamydia and gonorrhea. This presentation will focus on the factors driving the disparities seen in rates of STIs, the most evidenced based strategies to address these epidemics, and will use data from the Dallas-Forth Worth Hospital Council Emergency Rooms (ER) to demonstrate heavy patterns of STI testing in the ER. Data from the Parkland- UTSW PROSPR Cervical Cancer cohort will also be used to demonstrate health care delivery gaps in cervical cancer screening for women, which impacts the high rates of cervical cancer diagnosed every year at Parkland.

Educational objectives:

1. Increase awareness of the epidemiology of STIs in the US and Texas
2. Improve understanding of the social and economic impact of STIs
3. Advance knowledge of optimization of screening strategies and the factors affecting use of screening services: especially HPV

BACKGROUND

Sexually transmitted infections (STIs) place a significant economic strain on the U.S. healthcare system with 19-20 million¹ new infections including about 40,000 new cases of HIV (Human Immunodeficiency Virus) each year². Over 110 million people in the U.S. have a prevalent STI with HPV (Human Papilloma Virus) infections being the most prevalent and affecting 79.1 million individuals in the U.S. The CDC conservatively estimates that the lifetime cost of treating eight of the most common STIs contracted is 15.6 billion dollars³. Most of these direct lifetime costs are attributed to two conditions- HIV (12 billion dollars) and HPV (1.7 billion dollars). However, the annual cost of curable STIs like gonorrhea, chlamydia and syphilis is also substantial at 742 million dollars (per 2008 estimates)³.

In spite of these costs to the United States health system, federal funding towards STI (non HIV) prevention remains low compared to that for HIV prevention. While the incidence of HIV infections is slowly decreasing, the rates of new infections for curable STIs are now on the rise.¹ After a historic low in syphilis rates in 2000-2001, the rates of primary and secondary syphilis have been steadily climbing with a staggering 19% increase between 2014 and 2015. Gonorrhea rates went up 12.8 and chlamydia rates increased by 5.9% in that same period.¹

A greater cause for concern remains the wide socioeconomic, racial and ethnic disparity in those who are extremely vulnerable to STIs. This review attempts to explore the factors that may be contributing to this epidemic.

1. THE NUMBERS

The current STI epidemics in the US are concentrated in the South, according to the CDC's 2015 STD surveillance report¹. In the case of gonorrhea and chlamydia, the highest number of cases are in the south. (Fig 1 and 2). The syphilis epidemic is distributed slightly differently, being more concentrated in the west, followed by the south (Fig 3). This epidemic follows the new HIV diagnoses more closely than the gonorrhea and chlamydia epidemics.

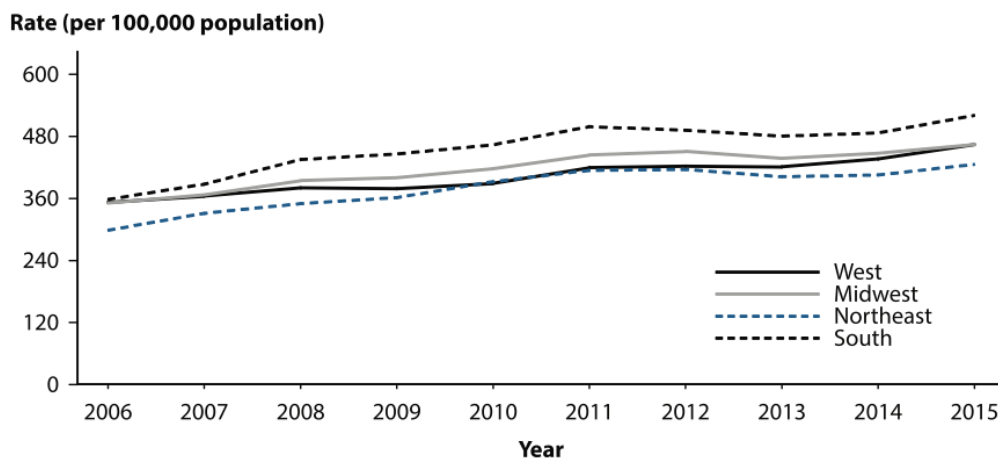
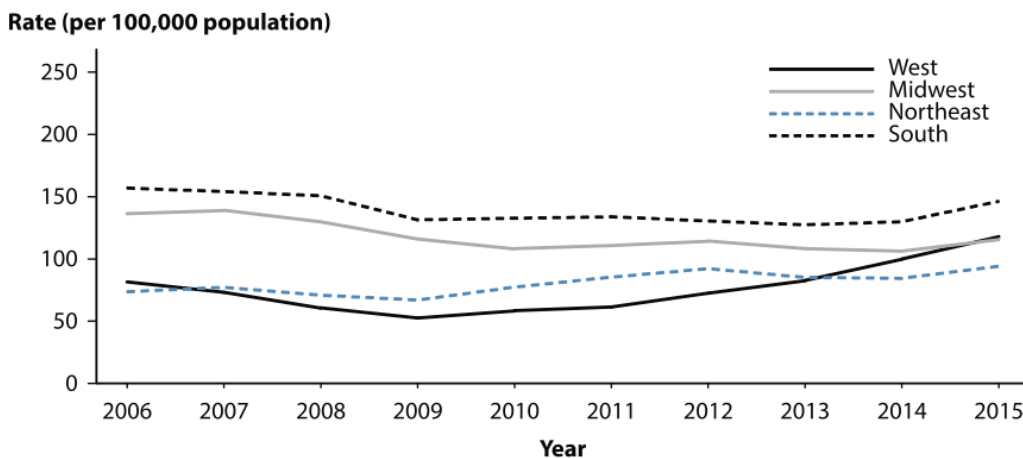


Fig 1: Chlamydia- Rates of Reported cases by Region- United States, 2006-2015. Source: 2015 CDC STI Surveillance Report



Figure

2: Gonorrhea- Rates of Reported cases by Region- United States, 2006-2015 Source: 2015 CDC STI Surveillance Report

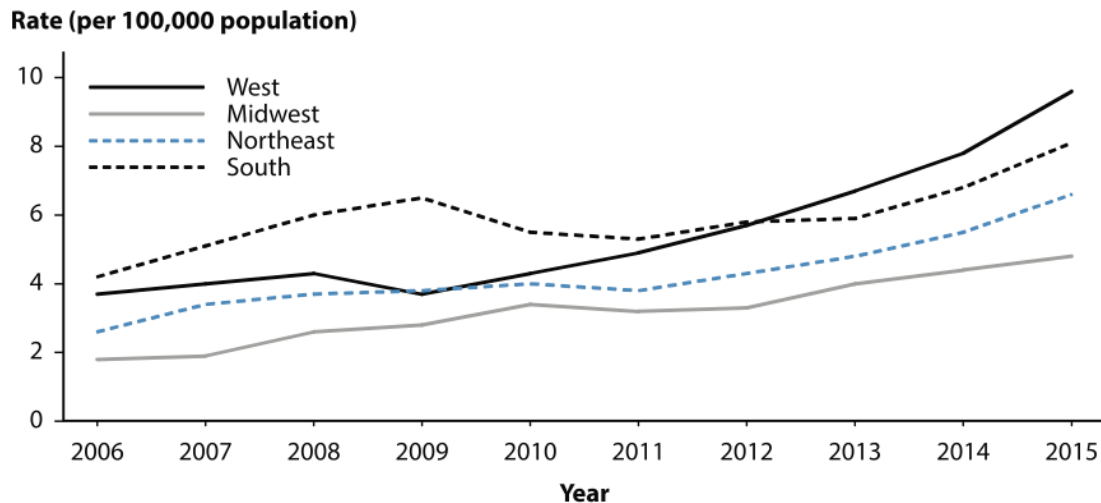


Figure 3: Syphilis Rates of Reported cases by Region- United States, 2006-2015 Source: 2015 CDC STI Surveillance Report

Among the southern states, Texas has higher than the national average for gonorrhea and chlamydia. Specifically, for chlamydia the incident rate was 523.6 per 100,000 persons (compared to 428.8 per 100,000 persons nationally). Dallas county further outnumbered the entire state at 649.2 per 100,000 persons in 2015.¹

Interestingly, Texas does have lower than the national average rates of primary and secondary syphilis, however it has the 3rd highest rate of congenital syphilis in the nation with 75 newborns with this condition in 2015⁵. It is unclear what explains the disconnect between the rising rates of congenital syphilis in Texas in the setting of slightly decreasing overall syphilis rates the state. One explanation is the difference in the demographic distribution of the disease. Gonorrhea and chlamydia diagnoses are driven by national guidelines requiring all sexually active women under 25 years to get tested⁴, whereas syphilis testing in women is only required at the first pre-natal visit.

A CDC report⁵ addressing the rise of congenital syphilis nationally determined that of the 458 congenital syphilis cases in 2014, 314 mothers had received at least one prenatal visit. However 43% of them received no treatment. This included those who acquired syphilis after their initial syphilis test and those who were never tested at all. Of the

314 mothers, 30% received inadequate treatment (a nonpenicillin or inappropriate dose for the stage of syphilis). This exposes a need for providers to understand the importance of screening and improve knowledge of treatment options.

The other gap that is exposed in the fight against STIs is the huge funding gap between HIV and non-HIV STI prevention funding. The overall federal budget for HIV in 2015 was over 3.2 billion dollars with the CDC contributing over 555 million dollars towards prevention funding⁶. Comparatively, the entire CDC's STI prevention budget for 2015 was only 94 million dollars.⁶ While Texas gets a steady proportion from both these funding sources, the amount of federal dollars attributed to prevent one new case of HIV in Texas in 2015 was over 8000 dollars per case (an increase from 2014). Whereas the money attributed to prevent all other STIs including chlamydia, gonorrhea and syphilis was 33 cents per case in Texas in 2015 (a decrease from 2014). It may be intuitive that efforts towards preventing one STI (i.e. HIV) would prevent all others. However, the epidemiological trends reveal otherwise with a slight decrease in the new cases of HIV in Texas corresponding with a rise in gonorrhea and chlamydia rates. One explanation could be that prevention efforts towards HIV effectively target certain risk groups like men who have sex with men (MSM) but women and men who have sex with women (MSW) are not uniformly exposed to the same prevention efforts. Testing bias may also account for some of these rates as more women are screened for chlamydia and gonorrhea than for HIV or syphilis. However, it is worth examining whether the disparity in prevention funding between HIV and STIs is an effective strategy towards combating these inter-dependent epidemics.

2. DISEASE AND DISPARITY

Health disparities are prevalent in almost every disease condition in the U.S. This unfortunate paradigm involves the STI epidemic too, with the ethnic, gender and sexual minorities being the most vulnerable to these diseases.

2.1 RACE AND ETHNICITY

African American women have a 5.4 times higher rate of chlamydia than their White counterparts.¹ African American men have an even higher risk of chlamydia at 6.8 times the rate compared to their white counterparts.¹ Native Americans/American Indians (AI/AN) and native Hawaiians/Pacific Islanders (NHOPI) have a 3.3-3.8 times higher rates than Whites. Hispanics have a two fold higher risk for chlamydia than their Non-Hispanic White counterparts. This contrast is even more stark for gonorrhea with African Americans experiencing a 9.6 times higher rate of infection compared to their white counterparts. Native Americans/American Indians have a 4.4 times higher rate compared to whites. Hispanics have a 1.8 times higher rate compared to non-hispanic whites. Racial disparities have a strong regional preponderance with midwestern African Americans having the highest rate ratios for gonorrhea (Rate ratios are calculated as the rate of reported gonorrhea cases per 100,000 population for a given racial or ethnic minority population divided by the rate of reported gonorrhea cases per 100,000 population for Whites.).

While primary and secondary syphilis cases are highest among African American men, it is African American women who suffer the largest disparity with their rates being 8.8 times that of white women. Among newborns with congenital syphilis, 57% of them were born to African American mothers.

Economic disparities within different minority groups have been determined to be an important determinant for STI transmission. This is evident in counties with a high income disparity between the African American and White households. In such counties there is a higher rate of STIs for African Americans than in counties with lower income disparities⁷ (Figure 4).

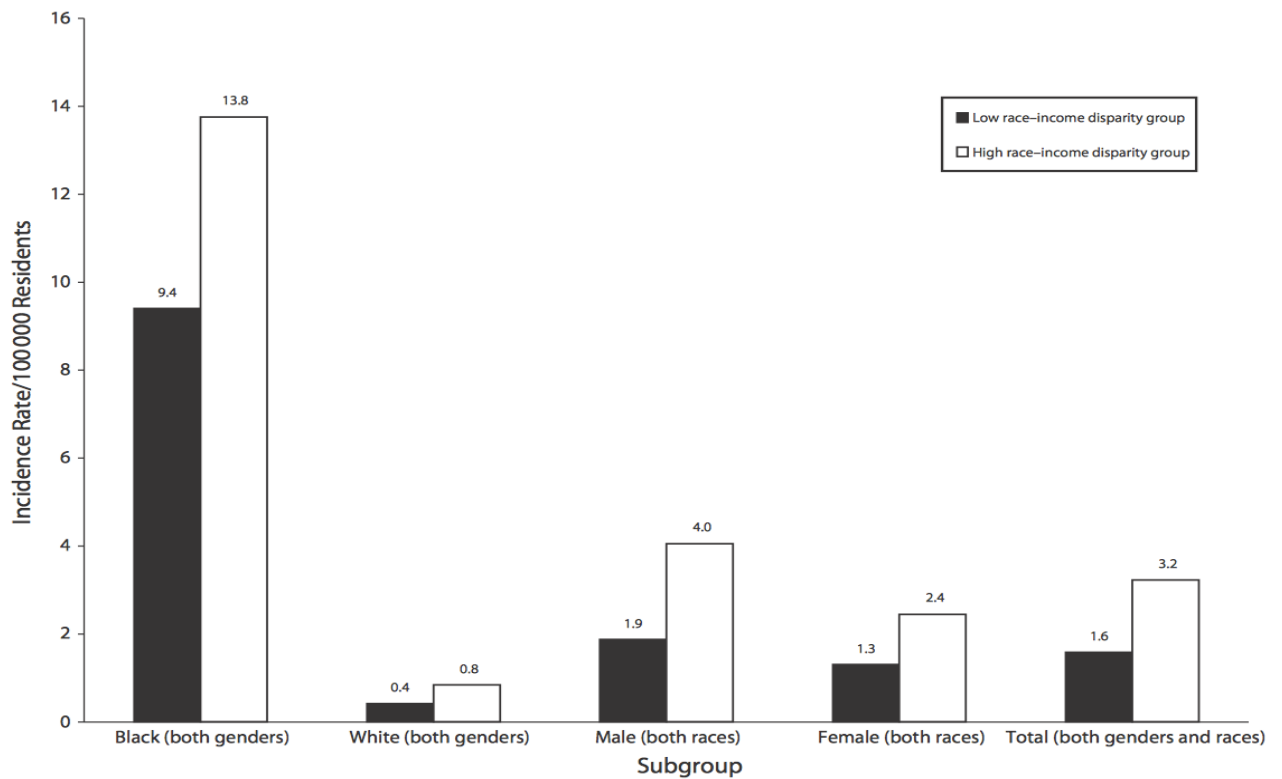


Figure 4: Primary and secondary syphilis incidence rates (per 100 000 residents) for high and low race–income disparity groups by race and gender: United States, 1999–2001.

2.2 GENDER

Women are at unique risk for certain sexually transmitted infections like chlamydia due to cervical ectopy.⁸ Women also face more serious complications from STIs such as like pelvic inflammatory disease, ectopic pregnancy and cervical and anal cancer. These are reflected in the higher cost burden for women for chlamydia, gonorrhea and HPV compared to men (Table 1). There is no obvious disparity in cost or complications in the management of primary and secondary syphilis. But congenital syphilis due to poor antenatal care remains a challenge for women.

	Males	Females
Chlamydia	20	244
Gonorrhea	53	266
<u>Sequelae :</u>		
Epididymitis	144 - 684	
Pelvic inflammatory disease/ectopic pregnancy		1,060 -3,626
Primary/secondary and early latent syphilis	53	53
Neurosyphilis	56,806- 166, 374	56,806- 166, 374
HPV*	45	191

Table 1: Costs in USD per case (in 2000 dollar rates). Source: Chesson H et al, 2004 ⁹ * Source: Owusu-Edusei K et al, 2013 (in 2008 dollar rates)

There are also significant differences in the risk of transmission of various STIs by gender. Gonorrhea and herpes are more easily transmitted from males to females than from females to males^{10,11}.

Infections from HPV (Human Papilloma Virus) are fairly ubiquitous with 60% of the population estimated to be infected at any point in time. Fortunately, it is a self-limited process with high rates (90%) of spontaneous clearance within twelve months ¹². However there are over 38,000 HPV related cancers diagnosed annually with the largest number being oropharyngeal cancers in men (12, 638) and cervical cancers in women (11,771)¹³. Hispanic women have the highest rate of cervical cancer (9.7 per 100,000) in the nation, followed by African American women (9.2 per 100,100). The racial demographic for

oropharyngeal and anal cancers flips with white men having the highest rate of oropharyngeal cancer (8 per 100,000) and white women with the highest rates of anal cancer (1.9 per 100,000)¹³.

3. FACTORS DRIVING TRANSMISSION DYNAMICS

There are several factors that govern STI epidemics including sexual behaviors, sexual networks and public health policies. These in turn are dictated by complex and diverse environmental conditions such as poverty, geography, education, religious and cultural norms and historic precepts that guide an individual's degree of engagement with their health system for both preventative needs as well as treatment for sexually transmitted infections.

3.1 SEXUAL BEHAVIORS AND NETWORKS

Two common theories about sexually transmitted diseases are concurrency patterns and core groups.

Concurrency implies sexual partnerships overlapping in time, which is thought to contribute to the spread of infections. Concurrency can be reactive (i.e. seeking other sexual partners in response to their main partner having other partners), transitional (a period of overlap between two subsequent relationships), experimental or compensatory (i.e. driven by financial or social needs). In a study involving over a thousand attendees to a public STI clinic in the Deep South, 51% of male attendees reported concurrent behaviors. Being bisexual (OR 2.06), having >10 lifetime partners (OR 6.0), weekly heavy drinking (OR 2.8), drug use (OR 3.7) and believing your partner had other partners (OR 7.7) were significantly associated with concurrent behaviors¹⁴.

The core group theory was proposed in the 1970s when it was noted that detecting and treating 10% of new gonorrhea infections in women resulted in a 20% decline in incidence over the subsequent years. Thus it was expostulated that a small group of people in a population are

responsible for majority of the spread of a sexually transmitted infection¹⁵. Most sexual network maps have demonstrated empirical evidence of core groups during investigations of STI outbreaks.

Education, especially sex education is an important determinant of future behaviors. While most public schools have some form of sex education, most schools in the Deep South have lower rates than schools in the North East. Rates of sex education in several Southern schools also significantly decreased from 2008 to 2010¹⁶. Texas in particular reported that 92% of its public schools provided specific education to high school students on how to prevent HIV, pregnancies and STIs in 2010. This however includes abstinence only education. There appear to be few educational resources for teenagers who not protected by abstinence only strategies. In comparison to 58% of the schools nationally only 34% of the schools in Texas include education on condom use and efficacy, importance of consistent use and how to obtain them.

3.2 PUBLIC HEALTH POLICIES

Most people seek testing and treatment for STIs in the private sector due to fear of embarrassment and stigma associated with STIs. Unfortunately Public-Private partnerships to strengthen STI services are rare (Figure 5).

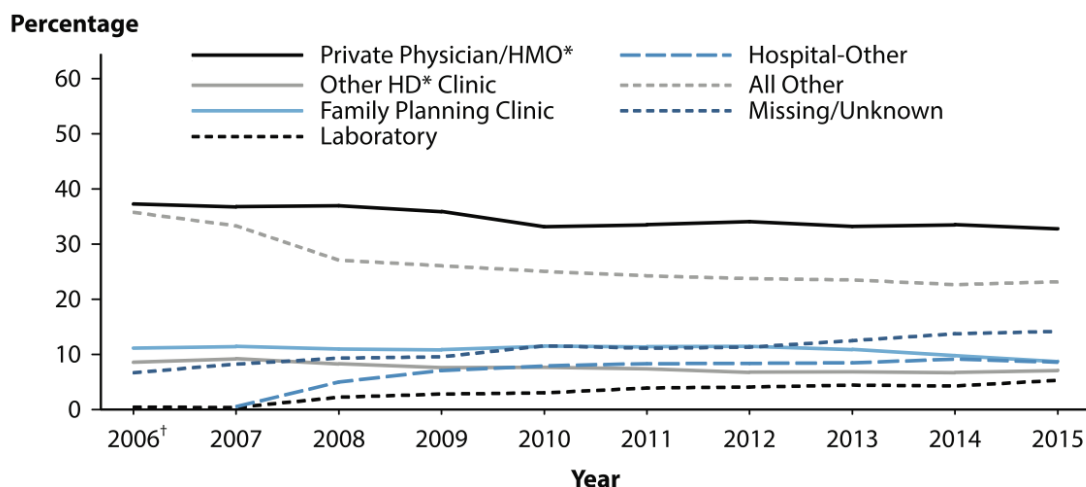


Figure 5 Chlamydia — Reported Cases Among Women by Reporting Source, United States, 2006–2015. Source: 2015 CDC STD Surveillance Report

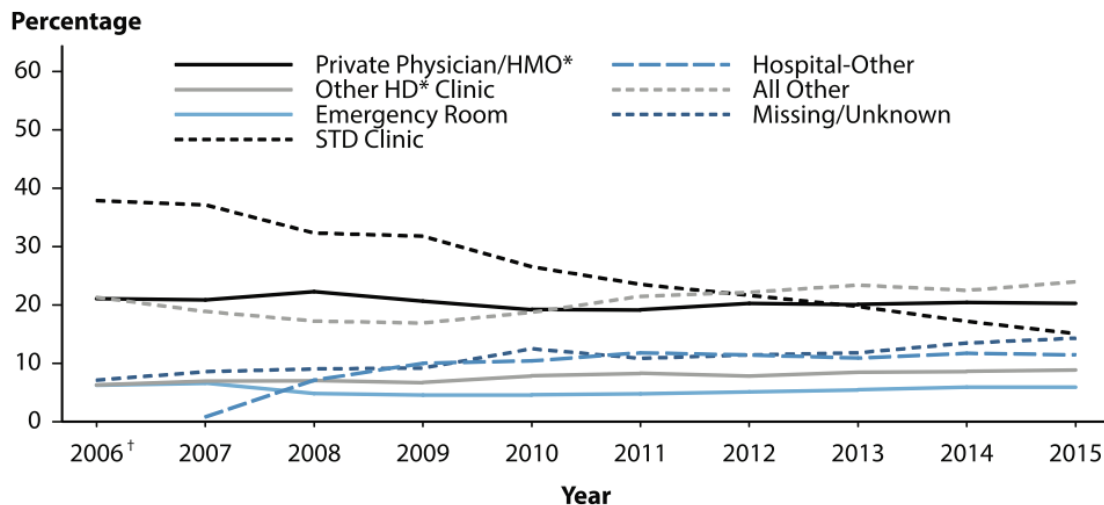


Figure 6: Gonorrhea Reported Cases Among Men by Reporting Source, United States, 2006–2015 Source: 2015 CDC STD Surveillance Report

HMO = health maintenance organization, HD= health department. Other=Drug Treatment, Tuberculosis Clinic, Correctional Facility, Laboratory, Blood Bank, Labor and Delivery, Prenatal Care, National Job Training Program, School-based Clinic, Mental Health Provider, Indian Health Service, Military, Emergency Room, and HIV Counseling and Testing Site.

In the Dallas-Forth Worth region, data from the DFWHC (Dallas Forth Worth Hospital Council) revealed that testing for sexually transmitted diseases occurred in 6% of all the visits to the emergency department (ED) between 2014-2015. Over 90,000 individuals received at least one STI test during their ED visit in this region. However, only 33% of them received testing for more than one STI at a time. This reveals that though providers in the ED may think to screen for one STI, co-testing for any other STI is seldom practiced. The CDC recommends co-testing and repeat syphilis testing especially in pregnant women who may be “at risk”. About 9000 women who received only one STI test during their ED visit had a presenting complaint of “ complications with their pregnancy”. Safety net hospitals delivering mostly indigent care provided the most testing as

well as co-testing in this region. With new imperatives to redirect care to non-ED settings especially for conditions like STIs that can be easily managed in the outpatient clinics, this re-emphasizes the need to enhance STI care delivery towards other venues as well as optimize testing in the ED, when done at that venue. As the most frequent symptom associated with STI testing in the ED included “Genitourinary symptoms”, this could result in substantial cost savings as an ER visit for that condition costs 2598 dollars on average, compared to average of 156 dollars for the same condition at an Urgent Care clinic^{17,18}.

State laws can also impact STI epidemics. A review of the impact of such interventions¹⁹ noted that a raise in beer taxes in a state was associated with decreasing rates of gonorrhea and HIV. Decreases in alcohol outlet density were also associated with decreased gonorrhea rates within those census tracts. Legalization of same sex marriages was associated with decreased syphilis rates but did not have an impact on gonorrhea or HIV rates. This review also noted that tolerance for same sex behaviors was inversely related to HIV rates. It is important to note that most economists acknowledge that causal relationships cannot be demonstrated for any of these findings. Yet, examining the direct and indirect impact of public policies is important if they are to be a tool in the efforts to decrease STI epidemics.

4. SOLUTIONS

Several evidenced based interventions exist that have proven effective in reducing the rates of STIs and their complications. These include expedited partner therapy (EPT) for sexual contacts of people diagnosed with STIs, community embedded Disease Intervention Specialists (CEDIS), vaccination and cancer screening programs for HPV.

4.1 EXPEDITED PARTNER THERAPY

The CDC estimates the proportion of partners who seek evaluation and treatment in response to patient referral ranges from 29% to 59%²⁰. Studies have demonstrated re-infection of treated index subjects by untreated partners accounts for 14% to 30% of incident bacterial STI²¹. Therefore, in 2006, it recommended expedited partner therapy based on data that it had proven effective in reducing rates of chlamydia and gonorrhea in heterosexuals. Note that EPT is not recommended for syphilis and for MSMs due to the risk of missing opportunities for diagnosis and treatment of neurosyphilis and HIV. In addition, EPT for gonorrhea necessitates use of oral cefexime which is not considered optimal in the management of gonorrhea. Therefore it is recommended with caution and if used, it must be followed by test of cure in the partner.

In spite of EPT being legally permissible in 38 states including Texas, it is rarely implemented in routine clinical practice. These implementation challenges remain a barrier in the efforts to control rates of STIs.

4.2 VACCINES AND HPV CANCER SCREENING

A powerful tool in the arsenal against the most common STI is the HPV vaccine. The CDC recommended it in 2009 for all individuals ages 9 to 26 years of age. The quadrivalent and nonavalent HPV vaccine are covered by the federal Vaccines for Children (VFC) program till the age of 18 years. Vaccination rates in the US are actually increasing to 63% coverage for girls and 50% coverage for boys with at least 1 dose of the vaccine. This may prove promising for the future of HPV related cancers as a recent review²² revealed that the rate of high grade cervical abnormalities had decreased by 47% in Australia where they have had population level HPV vaccinations since 2007. It also noted a decrease in incidence of low-grade dysplasia in populations in Canada and Denmark. Optimistically, vaccination rates for girls at Parkland hospital have also improved

from 17.9% in 2008 to 41.9% in 2015 due to quality improvement efforts from several groups including the PROSPR (Population-Based Research Optimizing Screening through Personalized Regimens) cervical cancer program.

Unfortunately more than half the girls and boys eligible for vaccination at a safety net setting like Parkland, remain unvaccinated and there are a staggering number of cervical and anal cancer cases diagnosed at Parkland each year. PROSPR data reveals that each year there are about 79 cases of invasive cervical cancer diagnosed at Parkland. Most (89%) of these women presented to the healthcare system with cancer and so had no real opportunities for screening. Of those cases that were already established at Parkland, 77% had missed opportunities for screening.

The other HPV derived cancer whose rates have risen almost 100% nationally, in the last thirty years, is anal cancer. There were about 25 anal cancer cases diagnosed annually at Parkland between 2009 and 2013 in the absence of any screening intervention. In 2015, a screening program for high risk i.e. HIV infected people was initiated at Parkland in order to improve detection rates in this group. Longitudinal multicenter National Cancer Institute studies²³ are underway in order to inform future national guidelines regarding specific screening for anal cancer.

4.3 EDUCATED HEALTH CARE PROVIDERS

Most patients in the U.S. seek STI care in the private sector when possible and pay out of pocket due to privacy issues and concerns for accidental disclosure to their partners through insurance claims. However data from the National Family Growth Survey revealed that private insurance coverage for women seeking STI care is decreasing and Medicaid coverage is increasing over time²⁴. Providers in both the public and private sector will be expected to provide STI services and gaining comfort and competence in this area will be important. Patients have reported that their biggest barrier to revealing their

sexual concerns was the provider and that having the provider ask them about their sexual concerns increased their reporting of such more than six fold.²⁵ Institutionalized heterosexism, poor health care experiences due to sexual identity, perceived adverse effects from disclosure about sexual activities all contribute to a patient's hesitance in discussing their sexual health.

Providers who develop confidence in their ability to discuss these issues as well as understand the importance of co-testing for STIs are at an advantage. Extra-genital testing (oropharyngeal and rectal) testing for gonorrhea and chlamydia is another rarely practiced/offered test. Extragenital infections can be asymptomatic and occur in 50-65% of MSMs attending STI clinics²⁶. In addition, performing only urogenital testing would have missed 30.3% of the gonorrhea and 13.8 % of the chlamydia cases in women.²⁷ Parkland has launched extra-genital nucleic acid amplification testing for Chlamydia and Gonorrhea in 2017 in order to enhance its STI services.

5. CONCLUSIONS

Sexually transmitted infections like chlamydia and gonorrhea are on the rise nationally, as are rates of congenital syphilis. In order to tackle these epidemics, funding gaps and gross health disparities in those most at risk need to be addressed. Increased uptake of vaccination programs for vaccine preventable HPV related cancers could impact rates of cervical cancer and potentially anal and oropharyngeal cancers. Provider competence in STI care delivery, including improvement in co-testing rates and extra-genital testing, will be a key feature in a successful battle against the STI epidemics.

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