

Seroprevalence of Herpes Simplex Virus Type 2 in the United States: Results from the National Health and Nutrition Examination Survey (NHANES), 2005–2008

La'Shan D. Taylor, Fujie Xu, Sami Gottlieb, Maya Sternberg, Sara Forhan, Stuart Berman, Lauri E. Markowitz

Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA



Background

- Herpes simplex virus type 2 (HSV-2) infection is one of the most common STIs
 - Main cause of genital herpes and neonatal herpes
- Clinical course and transmission:
 - Lifelong infection, thus seroprevalence best method to estimate HSV-2 prevalence
 - May manifest as recurrent, painful genital lesions, but most infections unrecognized
 - Subclinical viral shedding is frequent and most transmission occurs without symptoms
- Increases risk of HIV acquisition at least 2-fold¹
- Population-based trends since 1976:
 - Decreasing trend in HSV-2 seroprevalence during the last decade found by Xu et al.²
 - 1988–1994 = 21% → 1999–2004 = 17%
 - Unclear if decreasing trend is continuing

Objective

- To determine the seroprevalence of HSV-2 infection using 2005-2008 population-based data

Methods

- Data from National Health and Nutrition Examination Survey (NHANES), 2005-2008
 - Complex probability sampling used to represent the civilian, non-institutionalized U.S. population
 - Adolescents, Mexican-Americans, and non-Hispanic blacks oversampled
 - Participants interviewed, examined, and biologic samples collected
 - Overall examination rate = 88%
- HSV-2 antibodies detected using a type-specific immunodot assay
 - Participants aged 14–49 years (n= 7,293)
- HSV-2 seroprevalence estimated by age, sex, race/ethnicity, and lifetime sex partners
 - Weighted seroprevalence, 95% confidence intervals (CI) generated by SUDAAN® to account for complex survey design
 - Wald chi-square F statistic used to evaluate differences between groups

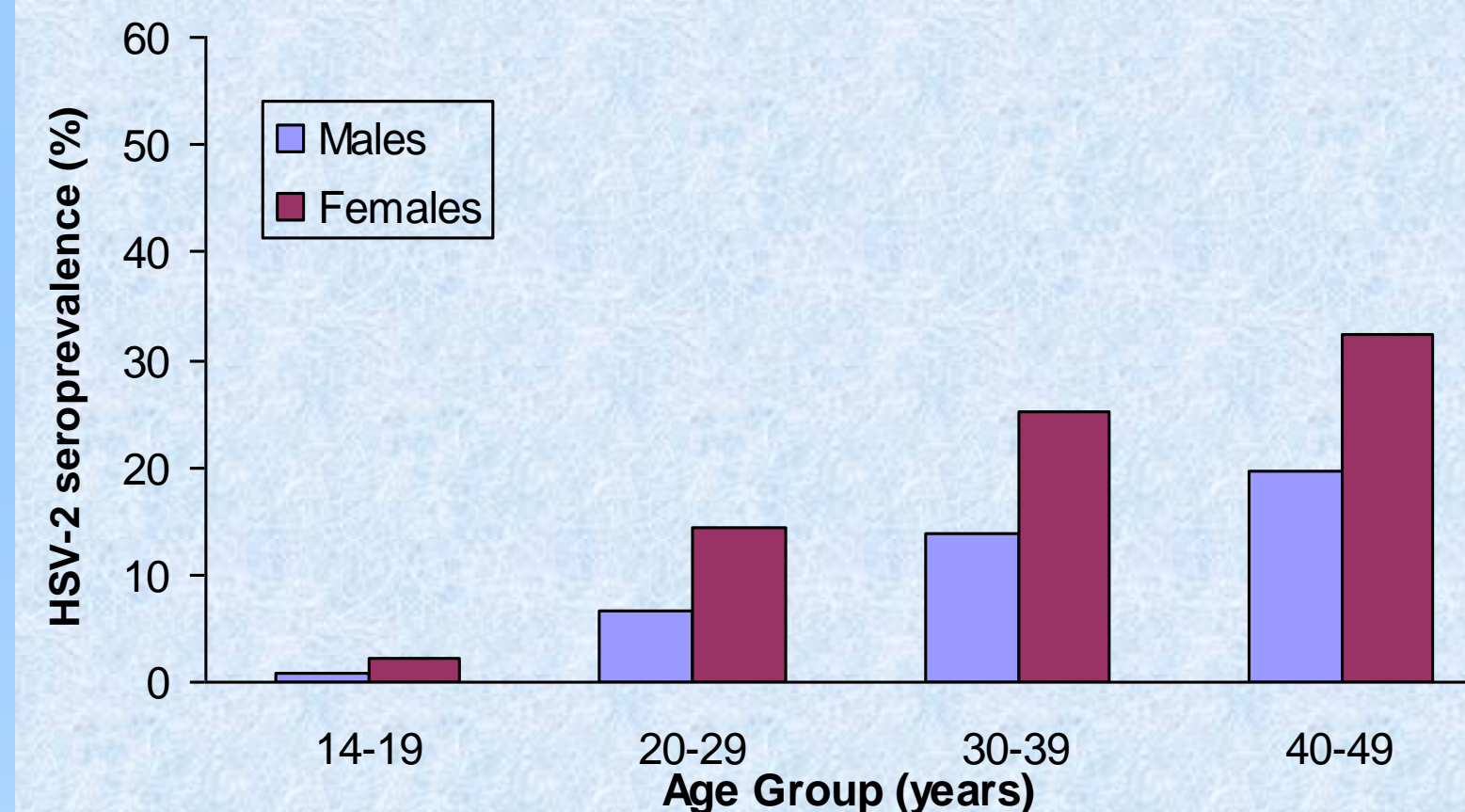
- Overall HSV-2 seroprevalence compared with NHANES 1999-2004 estimate
- Among HSV-2 infected, proportion with undiagnosed infection calculated
 - “Has a doctor or other health care professional ever told you that you had genital herpes?”

Results

HSV-2 Seroprevalence among 14-49 year-olds, by sex

Sex	%	(95% CI)
Overall	16.2	(14.6-17.9)
Males	11.5	(9.8-13.3)
Females	20.9	(18.9-23.1)

Figure 1. HSV-2 Seroprevalence by Age and Sex



- HSV-2 seroprevalence increases with age (p <.001)
- HSV-2 seroprevalence higher among females after stratifying by age (p <.001)

Figure 2. HSV-2 Seroprevalence by Race/Ethnicity and Sex

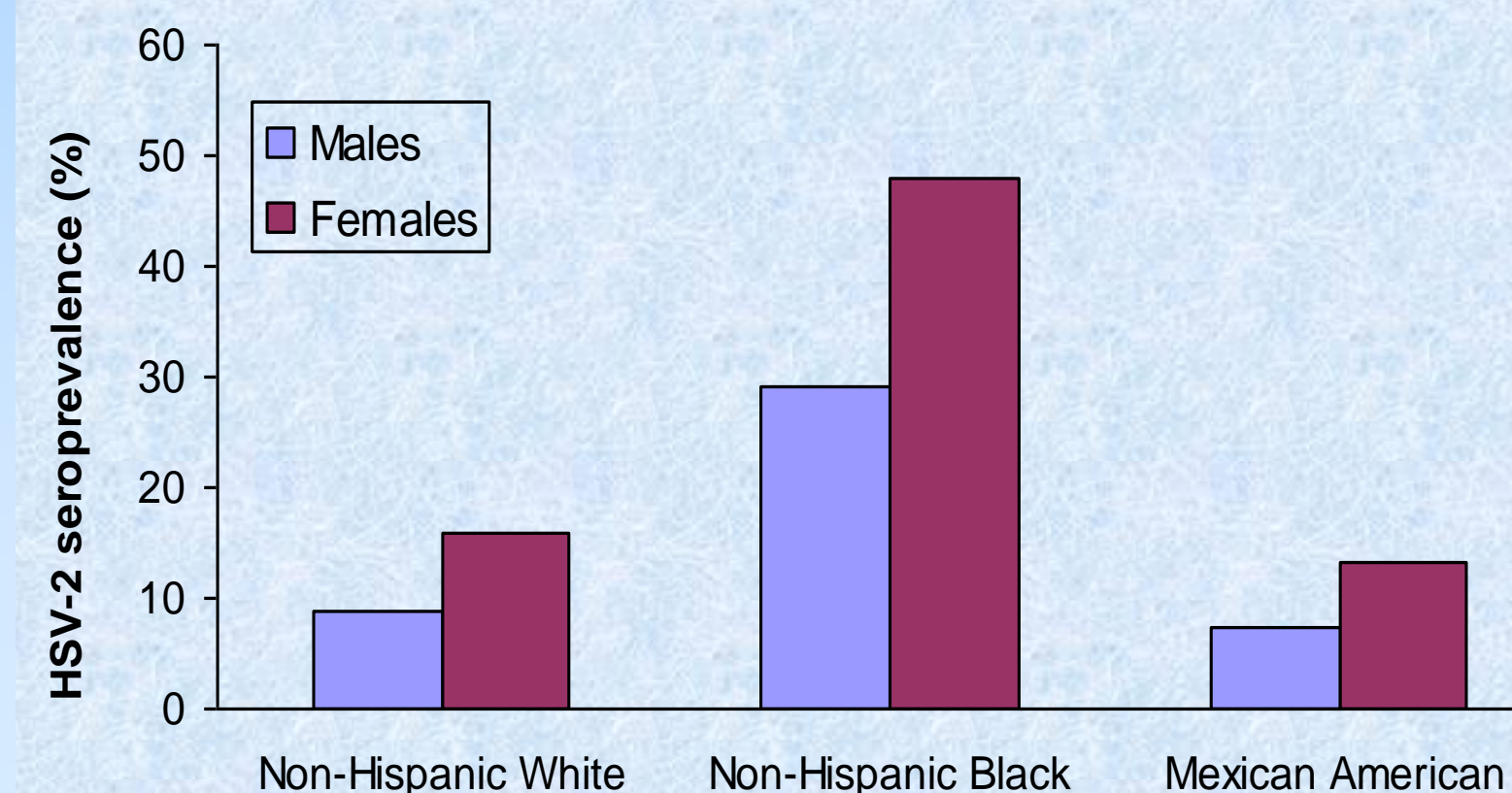
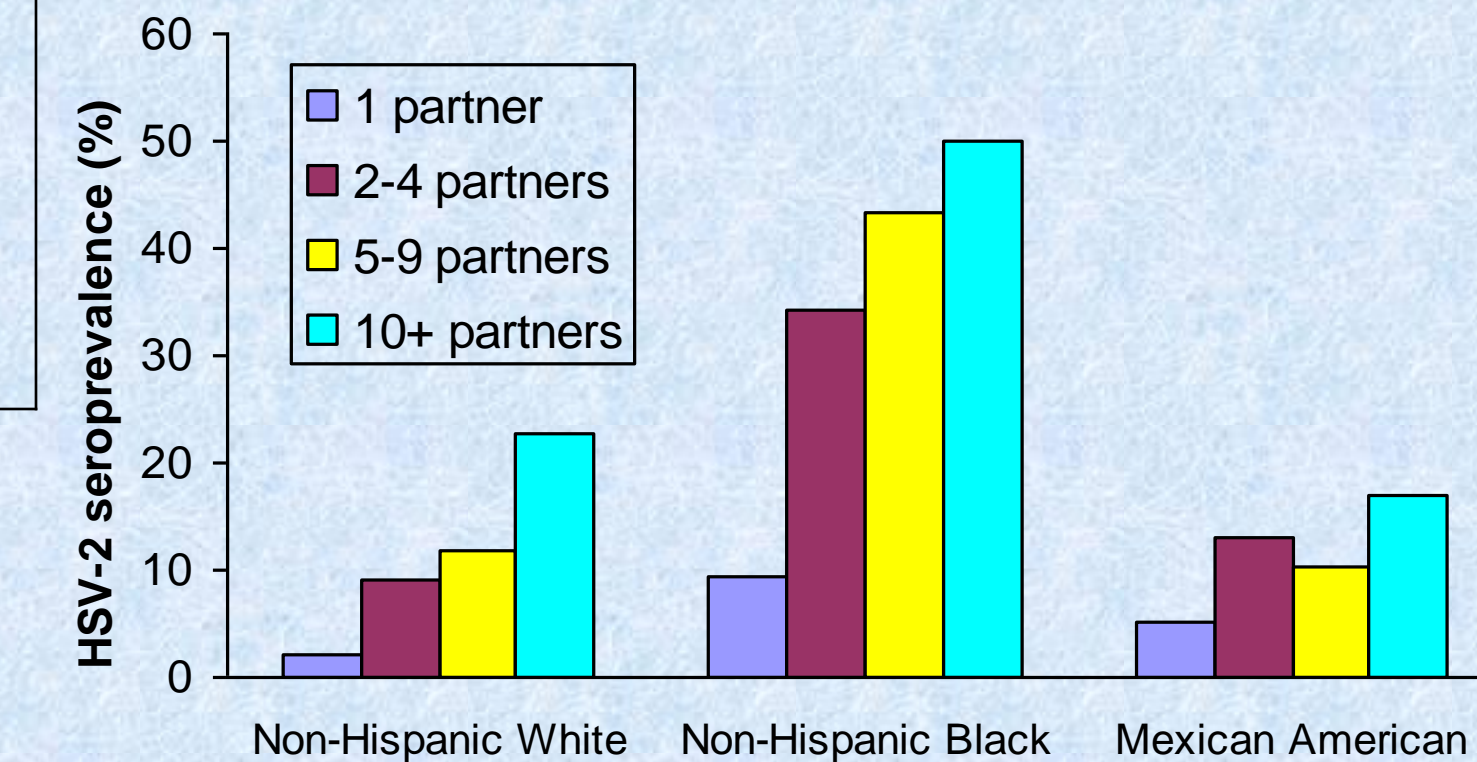


Figure 3. HSV-2 Seroprevalence by Number of Lifetime Sex Partners and Race/Ethnicity



- Overall, HSV-2 seroprevalence increases with number of lifetime sex partners for all race/ethnicity groups (p<.001)
- Seroprevalence high among non-Hispanic blacks even with few lifetime sex partners: with only 2-4 partners, seroprevalence 34%

HSV-2 Seroprevalence & Proportion of Infections that are Undiagnosed, 1999-2004 and 2005-2008

Years	%	(95% CI)	% Undiagnosed
1999-2004	17.0	(15.8-18.3)	86.7
2005-2008	16.2	(14.6-17.9)	81.1*

- No evidence of change in overall HSV-2 seroprevalence between 1999-2004 and 2005-2008 (p=0.34)
- *The proportion undiagnosed only includes ages 20-49 years

Summary

- 1 in 6 Americans aged 14–49 years have HSV-2 infection; seroprevalence stable over past decade
- Seroprevalence increases with age and lifetime number of sex partners
- HSV-2 seroprevalence higher among females and non-Hispanic blacks
- Most HSV-2 infections are undiagnosed

Discussion

- Substantial proportion of U.S. population infected with HSV-2
 - Most undiagnosed, but many may have symptoms: need to raise awareness of signs/symptoms among patients/clinicians³
 - Treatment available to reduce symptoms, and daily suppressive therapy can reduce transmission to sex partner by 50%⁴
- Burden of HSV-2 especially important given strong synergy between HSV-2 and HIV infection¹
 - HIV testing and risk-reduction strategies important for those with known HSV-2 infection and those at high risk for HSV-2
- Disparities in HSV-2 infection prominent, probably contribute to disparities in HIV infection
 - Women more susceptible to HSV than men, likely due to biological differences (e.g., greater mucosal surface area)
 - Racial disparities likely perpetuated by higher prevalence in black communities; greater chance of exposure with any sexual encounter
- Prevention: combination of strategies will likely be needed and optimal approach unknown
 - General risk-reduction strategies important, e.g., condom use can reduce risk of HSV-2 acquisition⁵
 - Serologic testing could identify unrecognized HSV-2 infections, but role of screening controversial
 - Limited data on benefits of screening to change behavior and reduce HSV transmission on population level
 - Generalized screening not recommended, but may be useful in selected high-risk populations

Next Steps

- Continued research on HSV-2 prevention strategies including:
 - Evaluating the overall benefit, feasibility, and cost effectiveness of serologic testing to prevent transmission
 - Evaluating the judicious use of suppressive therapy regimens for prevention in various populations
- Continued research into the development of HSV-2 vaccine

References

- Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. *AIDS*. 2006;20:73-83.
 - Xu F, Sternberg MR, Kottiri BJ, et al. Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. *JAMA*. 2006;296:964-73.
 - Langenberg A, Benedetti J, Jenkins J, et al. Development of clinically recognizable genital lesions among women previously identified as having 'asymptomatic' herpes simplex virus type 2 infection. *Ann Intern Med*. 1989;110:882-887.
 - Corey L, Wald A, Patel R, et al. Once-daily valacyclovir to reduce the risk of transmission of genital herpes. Valacyclovir HSV Transmission Study Group. *N Engl J Med*. 2004;350:11-20.3.
 - Martin ET, Krantz E, Gottlieb SL, Magaret AS, Langenberg A, Stanberry L, et al. A pooled analysis of the effect of condoms in preventing HSV-2 acquisition. *Arch Intern Med* 2009;169:13:12331240
- The findings and conclusion in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention. It does not represent and should not be construed to represent any agency determination or policy*