

Supplementary Material for *BMJ Open*

Title: Associations between excessive adiposity and seroprevalence of herpes simplex virus type 1 and type 2 among US adults: a population-based age-period-cohort analysis

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Content: Supplementary Figures S1-6, Tables S1-6

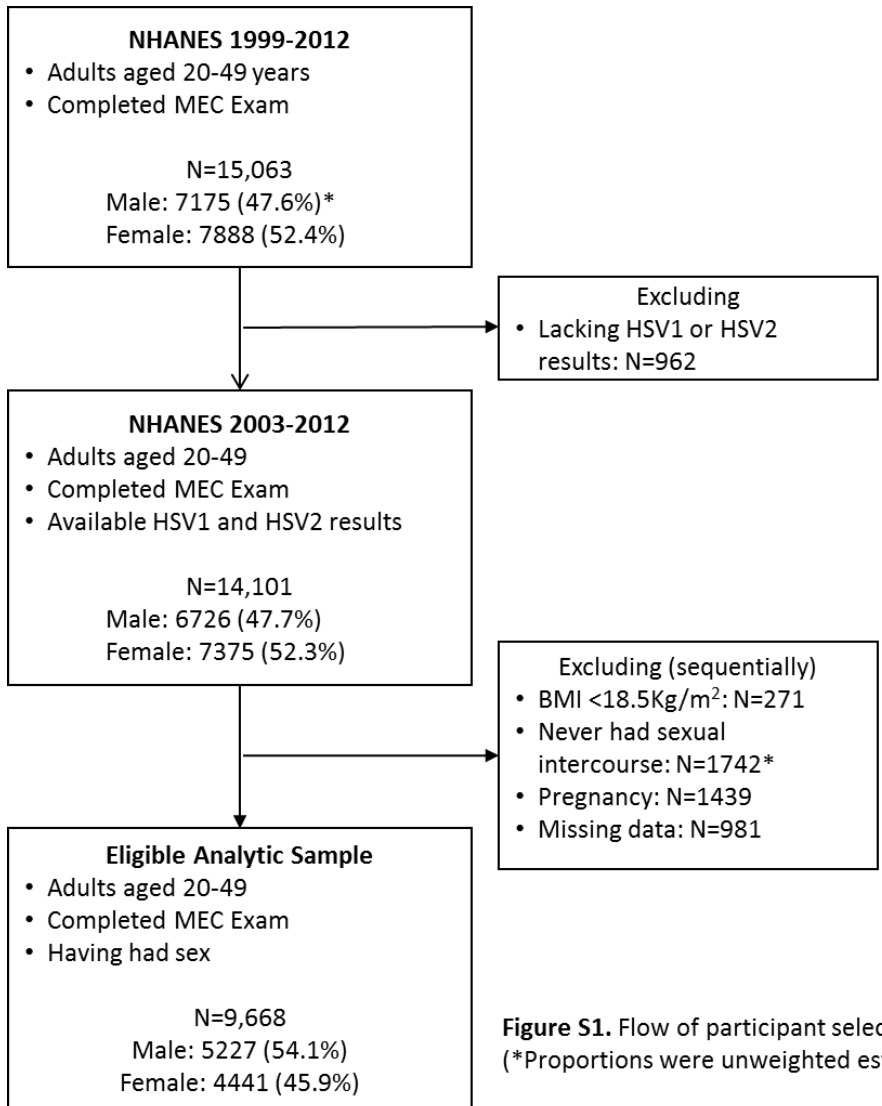


Figure S1. Flow of participant selection for the current analysis (*Proportions were unweighted estimates)

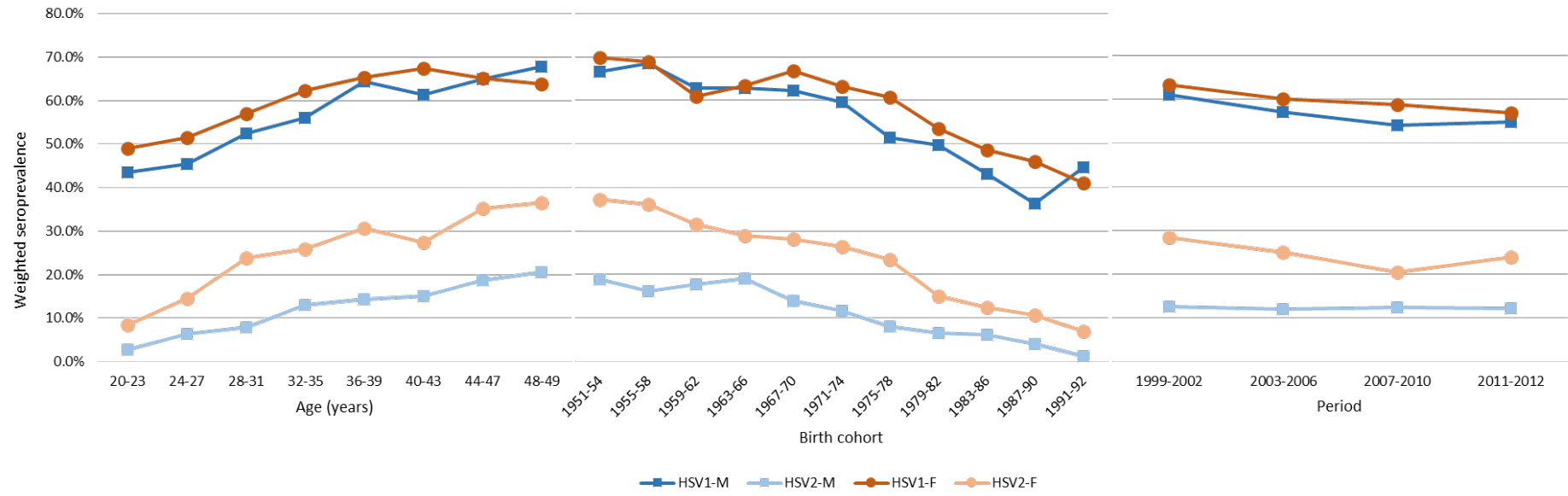


Figure S2. Weighted seroprevalence of HSV1 and HSV2 by age, birth cohort and time period, adult men and women in NHANES 1999-2012

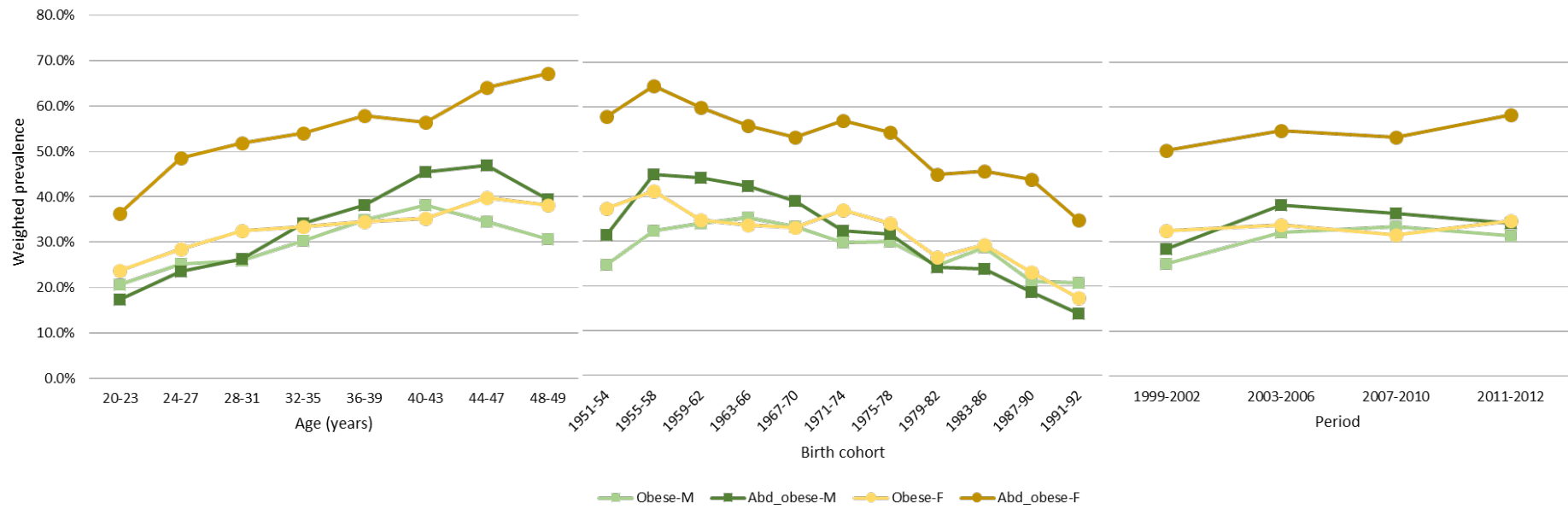


Figure S3. Weighted prevalence of obesity and central obesity by age, birth cohort and time period, adult men and women in NHANES 1999-2012

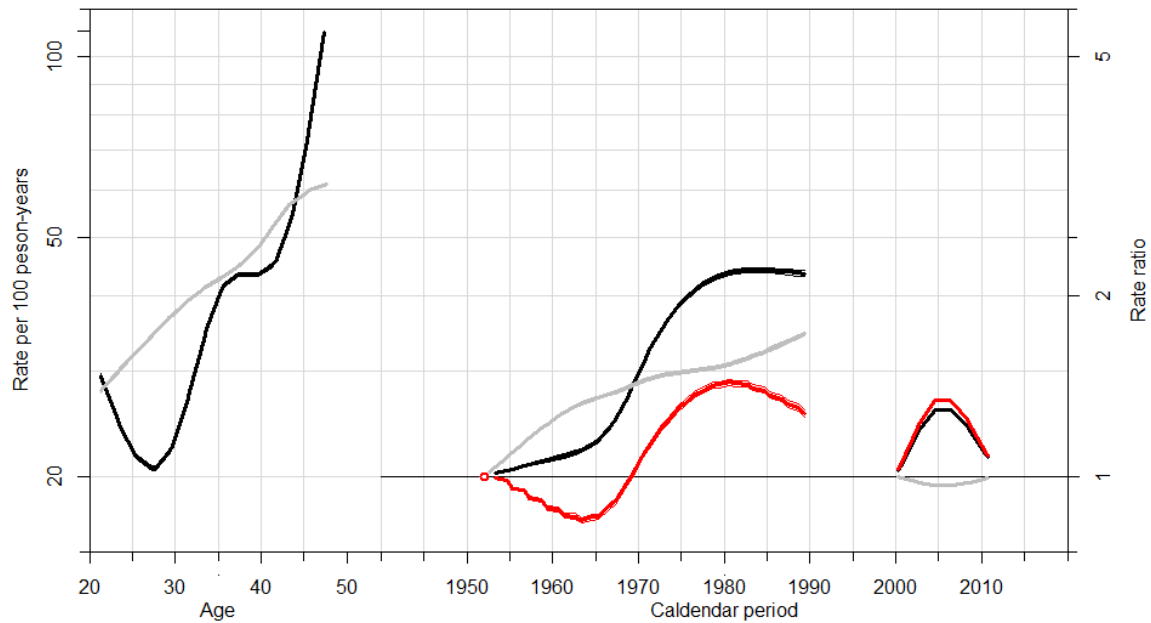


Figure S4. Results of age-period-cohort models on seroprevalence of HSV1 in obese and non-obese women in NHANES 1999-2012. The left panel show the age-specific seroprevalence rates for obese (in black) and nonobese (in gray) women in the reference cohort (1952). The middle panel shows the rate ratio of HSV1 seroprevalence in different cohorts relative to the reference cohort for obese (in black) and non-obese (in gray) women. Meanwhile, the red curve depicts the relative rate ratio comparing cohort effects between obese and nonobese women. The right panel displays the relative change in HSV1 seroprevalence in calendar time with respect to the reference period (1999-2000). The overall slope of period effects was also assumed to be zero, showing that period effects were less significant than cohort effects for non-obese women. However, for obese women, period effects were statistically stronger than the cohort effects (both $P_s < .001$).

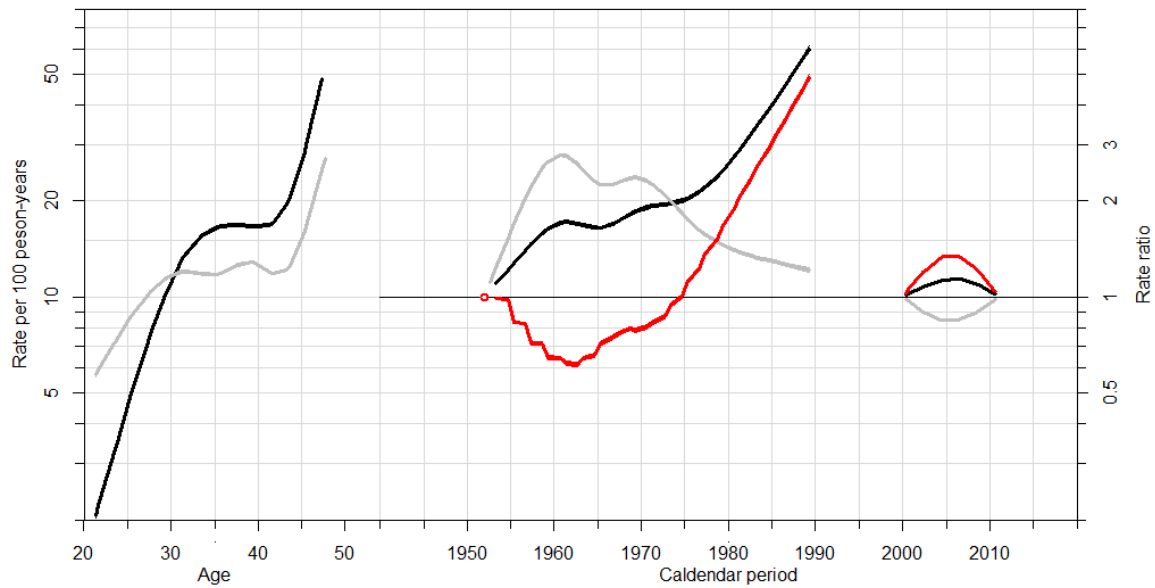


Figure S5. Results of age-period-cohort models on seroprevalence of HSV2 in obese and non-obese women in NHANES 1999-2012. The left panel show the age-specific seroprevalence rates for obese (in black) and nonobese (in gray) women in the reference cohort (1952). The middle panel shows the rate ratio of HSV1 seroprevalence in different cohorts relative to the reference cohort for obese (in black) and non-obese (in gray) women. Meanwhile, the red curve shows the relative rate ratio comparing cohort effects between obese and nonobese women; the cohort effects were stronger (<1) for early cohorts of nonobese women and recent cohorts of obese women (>1). The right panel displays the relative change in HSV1 seroprevalence in calendar time with respect to the reference period (1999-2000) in the two groups. The overall slope of period effects was also assumed to be zero for both comparison groups.

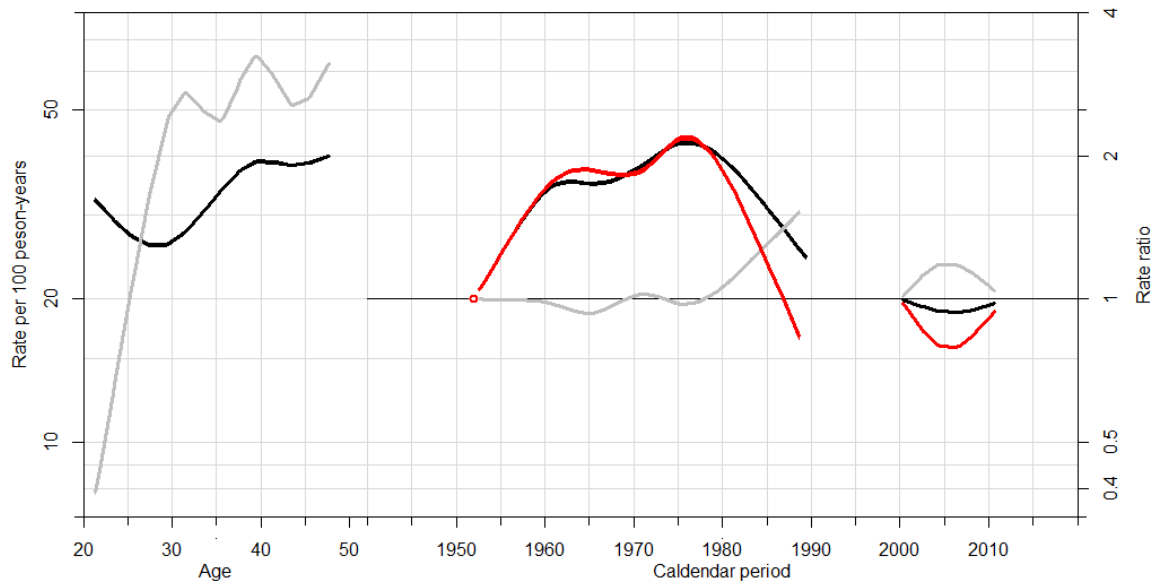


Figure S6. Results of age-period-cohort models on seroprevalence of HSV1 in obese and non-obese men in NHANES 1999-2012. The left panel shows the age-specific seroprevalence rates for obese (in black) and nonobese (in gray) men in the reference cohort (1952). The middle panel shows the rate ratio of HSV1 seroprevalence in different cohorts relative to the reference cohort for obese (in black) and non-obese (in gray) males. The red curve depicts the relative rate ratio comparing cohort effects between the two comparison groups, indicating a consistent, stronger (relative rate ratio > 1) cohort effects in the obese than in the non-obese men (relative to the reference cohort). The right panel displays the relative change in HSV1 seroprevalence in calendar time with respect to the reference period (1999-2000); the overall temporal change was assumed to be zero as suggested by results of deviance analysis. The only exception was for non-obese men: among whom, period effects were no less significant than cohort effects on the changes in the HSV1 seroprevalence (both P s < 0.001).

Table S1. Weighted seroprevalence of HSV1 and HSV2 by age, birth cohort and calendar period in adults aged 20-49 years, NHANES 1999-2012

	HSV1						HSV2					
	All		Men		Women		All		Men		Women	
	%	p-value*	%	p-value*	%	p-value*	%	p-value*	%	p-value*	%	p-value*
Overall	58.4%		56.9%		60.2%		17.8%		12.2%		24.5%	
Age												
20-23	46.1%	<0.001	43.5%	<0.001	49.0%	<0.001	5.5%	<0.001	2.8%	<0.001	8.4%	<0.001
24-27	48.2%		45.4%		51.6%		10.1%		6.4%		14.4%	
28-31	54.6%		52.4%		56.9%		15.4%		8.0%		23.8%	
32-35	59.1%		56.1%		62.4%		19.2%		13.1%		26.0%	
36-39	64.9%		64.4%		65.4%		22.1%		14.3%		30.7%	
40-43	64.3%		61.3%		67.5%		21.0%		15.1%		27.4%	
44-47	65.0%		64.9%		65.1%		25.3%		18.6%		35.2%	
48-49	66.6%		67.9%		63.9%		25.6%		20.5%		36.5%	
Period												
1999-2002	62.2%	0.007	61.1%	0.011	63.4%	0.049	20.1%	0.017	12.5%	0.886	28.3%	0.003
2003-2006	58.5%		57.1%		60.0%		18.1%		11.9%		24.9%	
2007-2010	56.1%		54.1%		58.8%		15.8%		12.2%		20.4%	
2011-2012	55.7%		54.9%		56.9%		16.9%		12.1%		23.9%	
Cohort												
1951-1954	68.3%	<0.001	66.6%	<0.001	69.8%	<0.001	28.3%	<0.001	18.9%	<0.001	37.2%	<0.001
1955-1958	68.7%		68.5%		68.8%		25.8%		16.2%		36.0%	

1959-1962	62.1%	62.9%	61.0%	23.3%	17.6%	31.6%
1963-1966	63.1%	62.8%	63.4%	23.1%	19.1%	28.9%
1967-1970	64.4%	62.3%	66.8%	20.5%	13.9%	28.2%
1971-1974	61.4%	59.7%	63.3%	18.5%	11.5%	26.4%
1975-1978	55.7%	51.5%	60.7%	14.9%	7.9%	23.4%
1979-1982	51.4%	49.7%	53.5%	10.5%	6.5%	15.1%
1983-1986	45.8%	43.1%	48.7%	9.1%	6.0%	12.4%
1987-1990	41.1%	36.3%	46.0%	7.3%	4.0%	10.7%
1991-1992	43.2%	44.7%	41.1%	3.4%	1.1%	6.9%

* P-value for trend in univariate Poisson regression models

Table S2. Weighted prevalence of obesity and abdominal obesity by age, birth cohort and calendar period in adults aged 20-49 years, NHANES 1999-2012

	Obesity						Abdominal Obesity					
	All		Men		Women		All		Men		Women	
	%	p-value*	%	p-value*	%	p-value*	%	p-value*	%	p-value*	%	p-value*
Overall	31.5%		30.4%		32.9%		43.0%		34.3%		53.5%	
Age												
20-23	22.1%	<0.001	20.6%	<0.001	23.8%	<0.001	26.4%	<0.001	17.3%	<0.001	36.4%	<0.001
24-27	26.8%		25.3%		28.5%		35.0%		23.6%		48.6%	
28-31	29.0%		25.9%		32.5%		38.3%		26.2%		51.9%	
32-35	31.8%		30.4%		33.4%		43.6%		34.1%		54.1%	
36-39	34.7%		34.9%		34.5%		47.5%		38.1%		57.9%	
40-43	36.8%		38.2%		35.3%		50.7%		45.5%		56.3%	
44-47	36.6%		34.5%		39.8%		53.9%		47.0%		64.1%	
48-49	33.1%		30.7%		38.2%		48.3%		39.5%		67.1%	
Period												
1999-2002	28.6%	0.042	25.0%	0.004	32.5%	0.806	38.9%	0.054	28.4%	0.022	50.2%	0.060
2003-2006	32.8%		31.9%		33.8%		46.1%		38.1%		54.7%	
2007-2010	32.5%		33.3%		31.5%		43.6%		36.2%		53.3%	
2011-2012	32.7%		31.3%		34.7%		43.9%		34.0%		58.3%	
Cohort												
1951-1954	31.3%	<0.001	24.8%	<0.001	37.3%	<0.001	45.1%	<0.001	31.5%	<0.001	58.0%	<0.001
1955-1958	36.6%		32.3%		41.2%		54.5%		44.9%		64.7%	

1959-1962	34.3%	34.0%	34.7%	50.6%	44.2%	60.0%
1963-1966	34.7%	35.4%	33.7%	47.9%	42.3%	55.8%
1967-1970	33.3%	33.4%	33.1%	45.7%	39.0%	53.3%
1971-1974	33.2%	29.8%	37.0%	43.8%	32.3%	57.0%
1975-1978	31.8%	30.0%	33.9%	41.8%	31.5%	54.4%
1979-1982	25.5%	24.6%	26.5%	33.9%	24.2%	45.0%
1983-1986	28.9%	28.7%	29.3%	34.2%	23.9%	45.7%
1987-1990	22.0%	21.0%	23.1%	31.1%	18.7%	43.8%
1991-1992	19.4%	20.8%	17.4%	22.2%	13.8%	34.7%

* P-value for trend in univariate Poisson regression models

Table S3. Weighted seroprevalence of HSV1 and HSV2 by selected characteristics in 9668 adults aged 20-49 years, NHANES 1999-2012

Characteristics	HSV1		HSV2	
	%	p-value	%	p-value
Overall	58.4%		17.80%	
Anthropometrics				
Abdominal obesity (WC>88 or 102cm)				
No	55.0%	<0.001	14.7%	<0.001
Yes	62.9%		21.9%	
Obesity (BMI≥30)				
No	56.17%	<0.001	16.5%	<0.001
Yes	63.27%		20.6%	
BMI category				
18.5-24.9	54.2%	<0.001	15.3%	<0.001
25-29.9	58.2%		17.8%	
30-34.9	63.2%		19.0%	
≥35	63.4%		22.8%	
Demographics				
Race				
Non-Hispanic White	52.5%	<0.001	13.8%	<0.001
Non-Hispanic Black	64.6%		45.7%	
Mex. American and others	75.6%		16.9%	
Education ≥ College				
No	62.8%	<0.001	20.3%	<0.001
Yes	47.2%		11.3%	
Marital status				
Married	60.3%	0.003	15.3%	<0.001
Single or divorced	55.4%		20.6%	
Living with a partner	58.5%		21.0%	
Annual household income level				
PIR<2.5	64.7%	<0.001	21.5%	<0.001
PIR≥2.5	53.7%		15.0%	
Coverage by health insurance				
No	65.7%	<0.001	20.4%	0.001
Yes	56.1%		16.9%	
Risk factors				
Hypertension history				
No	57.2%	<0.001	17.2%	0.026
Yes	64.2%		20.3%	
Diabetes history				
No	58.0%	0.003	17.5%	0.001

Yes	69.8%		25.9%	
Recent drinking history (≥ 12 drinks in previous 12 mo.)	n=9660		n=9660	
No	63.8%	<0.001	18.7%	0.431
Yes	57.2%		17.6%	
Lifetime smoking history (≥ 100 pieces)				
No	55.9%	<0.001	14.4%	<0.001
Yes	61.4%		21.7%	
Lifetime sex partners ≥ 5				
No	55.4%	<0.001	10.5%	<0.001
Yes	60.3%		22.3%	
Recent sex partners ≥ 5 in prior 12 mo.				
No	58.4%	0.940	17.5%	0.002
Yes	58.6%		24.8%	
Ever having genital herpes				
No	58.8%	0.007	15.5%	<0.001
Yes	49.8%		74.4%	
Sex debut before age 16	n=9658		n=9658	
No	62.6%	<0.001	24.5%	<0.001
Yes	56.6%		14.8%	
Using condom	n=6512		n=6512	
Not always	56.9%	0.475	20.0%	0.043
Always	55.4%		17.2%	

Abbreviations: BMI, body mass index; HSV, herpes simplex virus; mo., months; PIR, poverty index ratio; WC, waist circumference

Table S4. Results of age- and cohort (AC)-adjusted multivariable Poisson regression on seropositivity of HSV1 by obesity or abdominal obesity for adult men, NHANES 1999-2012

	Obesity					Abdominal obesity			
	N	aPR ^a	LL	UL		N	aPR ^a	LL	UL
Overall	5227	1.06	1.00	1.13	Overall	5227	1.07	1.01	1.13
Age (years)					Age (years)				
24-27 or 48-49 ^b	976	0.89	0.77	1.03	24-27, 40-43 or 48-49 ^c	1723	0.93	0.85	1.02
Other age groups	4251	1.10	1.02	1.18	Other age groups	3504	1.12	1.04	1.20

Abbreviations: HSV1, herpes simplex virus 1; aPR, adjusted prevalence ratio; LL, lower limit of 95% CI; UL, upper limit of 95%CI; CI, confidence interval.

a. Adjusted for age, birth cohort, race/ethnicity, college education, marital status, annual household income, health insurance coverage, history of symptomatic genital herpes, cumulative smoking ≥ 100 pieces of cigarettes, number of lifetime sex partners ≥ 5

b. P-value for interaction=0.011

c. P-value for interaction=0.001

Table S5. Results of multivariable-adjusted Poisson regression on seropositivity of HSV1 and HSV2 by obesity or abdominal obesity, adult non-Hispanic white or black women in NHANES 1999-2012

	HSV1 (<i>AP</i> -adjusted models)				HSV2 (<i>PC</i> -adjusted models)				
	N	aPR ^a	LL	UL	N	aPR ^b	LL	UL	
Obesity					Obesity				
Overall	2971	1.04	0.96	1.12	Overall	2971	0.95	0.81	1.1
Period					Period				
1999-2002, 2011-12 ^c	1180	0.94	0.84	1.05	2003-2006 ^e	833	1.27	0.90	1.79
2003-06, 2007-10	1791	1.11	1.00	1.23	Other time periods	2138	0.98	0.84	1.15
Abdominal obesity					Central obesity				
Overall	2971	1.08	1.00	1.16	Overall	2971	1.13	0.98	1.31
Period					Period				
1999-2002 ^d	782	0.89	0.77	1.04	1999-2002 ^f	782	0.96	0.78	1.19
Other time periods	2189	1.18	1.08	1.29	Other time periods	2189	1.27	1.04	1.55

Abbreviations: HSV1, herpes simplex virus 1; aPR, adjusted prevalence ratio; LL, lower limit of 95% CI; UL, upper limit of 95%CI; CI, confidence interval; *AP* models, age-period-adjusted models; *PC* models; period-cohort-adjusted models.

a. Adjusted for age, time period, race/ethnicity, college education, marital status, annual household income, health insurance coverage, history of symptomatic genital herpes, cumulative smoking ≥ 100 pieces of cigarettes, number of lifetime sex partners ≥ 5

b. Adjusted for time period, birth cohort, race/ethnicity, college education, marital status, annual household income, health insurance coverage, history of symptomatic genital herpes, cumulative smoking ≥ 100 pieces of cigarettes, number of lifetime sex partners ≥ 5

c. P for interaction=0.016

d. P for interaction<0.001

e. P for interaction=0.111

f. P for interaction=0.056

Table S6. Results of multivariable-adjusted Poisson regression on seropositivity of HSV2 by obesity or abdominal obesity, adult non-Hispanic white or black men in NHANES 1999-2012

	HSV2 (PC-adjusted models)			
	N	aPR ^a	LL	UL
Obesity				
Overall	3492	0.92	0.76	1.11
Cohort				
1983-86 ^b	280	0.70	0.23	2.16
Other birth cohorts	3212	1.01	0.83	1.22
Abdominal obesity				
Overall	3492	0.96	0.81	1.13
Cohort				
1963-66 or 1975-78 ^c	911	0.76	0.51	1.13
Other birth cohorts	2581	1.31	1.07	1.60

Abbreviations: HSV1, herpes simplex virus 1; aPR, adjusted prevalence ratio; LL, lower limit of 95% CI; UL, upper limit of 95%CI; CI, confidence interval.

a. Adjusted for period, birth cohort, race/ethnicity, college education, marital status, annual household income, health insurance coverage, history of symptomatic genital herpes, cumulative smoking ≥ 100 pieces of cigarettes, number of lifetime sex partners ≥ 5

b. P for interaction=0.153

c. P for interaction=0.011