OPEN ACCESS

Epidemiology of herpes simplex virus type 2 in Latin America and the Caribbean: systematic review, meta-analyses and metaregressions

Manale Harfouche,[1,2] Haifa Maalmi,[3] Laith J Abu-Raddad [1,2,4]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/sextrans-2021-054972).

For numbered affiliations see end of article.

Correspondence to
Professor Laith J Abu-Raddad, WHO Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis, Weill Cornell Medicine—Qatar, Cornell University, Qatar Foundation—Education City, Doha, Qatar; lja2002@qatar-med.cornell.edu

Received 15 January 2021
Revised 14 March 2021
Accepted 8 April 2021
Published Online First
4 June 2021

Check for updates

To cite: Harfouche M, Maalmi H, Abu-Raddad LJ. *Sex Transm Infect* 2021;**97**:490–500.

ABSTRACT

Objective To characterise epidemiology of herpes simplex virus type 2 (HSV-2) in Latin America and the Caribbean.

Methods HSV-2 reports were systematically reviewed and synthesised, and findings were reported following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Meta-analyses and metaregressions were conducted.

Finding 102 relevant reports were identified including 13 overall incidence measures, 163 overall (and 402 stratified) seroprevalence measures, and 7 and 10 proportions of virus detection in genital ulcer disease and in genital herpes, respectively. Pooled mean seroprevalence was 20.6% (95% CI 18.7% to 22.5%) in general populations, 33.3% (95% CI 26.0% to 41.0%) in intermediate-risk populations, 74.8% (95% CI 70.6% to 78.8%) in female sex workers, and 54.6% (95% CI 47.4% to 61.7%) in male sex workers, men who have sex with men and transgender people. In general populations, seroprevalence increased from 9.6% (95% CI 7.1% to 12.4%) in those aged <20 years to 17.9% (95% CI 13.6% to 22.5%) in those aged 20–30, 27.6% (95% CI 21.4% to 34.2%) in those aged 30–40 and 38.4% (95% CI 32.8% to 44.2%) in those aged >40. Compared with women, men had lower seroprevalence with an adjusted risk ratio (ARR) of 0.68 (95% CI 0.60 to 0.76). Seroprevalence declined by 2% per year over the last three decades (ARR of 0.98, 95% CI 0.97 to 0.99). Pooled mean proportions of HSV-2 detection in GUD and genital herpes were 41.4% (95% CI 18.9% to 67.0%) and 91.1% (95% CI 82.7% to 97.2%), respectively.

Conclusions One in five adults is HSV-2 infected, a higher level than other world regions, but seroprevalence is declining. Despite this decline, HSV-2 persists as the aetiological cause of nearly half of GUD cases and almost all of genital herpes cases.

INTRODUCTION

With an estimated 24 million incident infections every year, herpes simplex virus type 2 (HSV-2) is an STI of global concern.[1] Unlike common bacterial STIs, HSV-2 is a chronic and incurable infection that is characterised by frequent subclinical shedding and reactivation.[2–6] When symptomatic, HSV-2 infection manifests in the form of painful recurrent genital ulcers that are associated with sexual and psychosocial morbidities and adverse impact on quality of life.[7–10] HSV-2 can also be passed vertically from mother to child, thus causing neonatal herpes, a rare but highly disabling and sometimes fatal outcome in newborns.[9 11] Though with some debate,[12] evidence suggests that HSV-2 increases the risk of HIV acquisition and transmission and may have contributed to driving larger HIV epidemics especially in Africa.[2 13–15]

With the disease burden of STIs, and per the United Nations Sustainable Development Goals,[16] the WHO formulated the 'Global Health Sector Strategy on STIs',[17] which focused on integrating preventive and control measures aimed at eliminating STIs as a main public health concern by 2030. While controlling HSV-2 infection is a main pillar of the global effort to address the population's sexual and reproductive health needs,[18 19] current prevention modalities are inadequate to control transmission and there are no specific programmes for HSV-2 prevention and control even in high-income countries.[20–22] This highlights the critical need for HSV-2 vaccination as a strategic approach to control transmission and to reduce if not eliminate the clinical, psychosexual and economic burden of this infection.[18 23–26]

Against this context, the WHO is spearheading a multisectorial effort to establish the business case and return on investment for HSV-2 vaccines.[18 19 27 28] To inform this effort, this study aims to characterise HSV-2 epidemiology in Latin America and the Caribbean by delineating HSV-2 incidence and antibody prevalence (seroprevalence) levels, estimating pooled mean HSV-2 seroprevalence in the different at-risk populations, identifying predictors of high seroprevalence, and estimating the pooled means for the proportion of HSV-2 detection in genital ulcer disease (GUD) and the proportion of HSV-2 detection in genital herpes.

METHODS

The methods for this study were adapted from our previous systematic reviews characterising HSV-2 epidemiology in Africa[29] and HSV-1 epidemiology in Latin America and the Caribbean.[30] The study methods are described in table 1.

Data sources and search strategy

This systematic review was informed by the *Cochrane Collaboration Handbook*,[31] and its findings were reported per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (online supplemental table S1).[32] Forty-seven countries were included in the study and classified into subregions based on the

Table 1 Description of the methodology for this study

Methodology	Detailed description
Data source and search strategy	► Search conducted on 12 March 2020 in PubMed, Embase and Literatura Latino Americana em Ciências daSaúde (LILACS). ► Search strategies included exploded MeSH/Emtree terms and broad terms with no language or time restrictions. ► The definition of Latin America and the Caribbean included 47 countries classified into three subregions: – Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama. – South America: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Peru, Surinam, Uruguay, Venezuela. – Caribbean: Anguilla, Antigua and Barbuda, Aruba, Bahamas, Barbados, Bermuda, British Virgin Islands, Cayman Islands, Cuba, Curacao, Dominica, Dominican Republic, Grenada, Guadeloupe, Haiti, Jamaica, Martinique, Montserrat, Puerto Rico, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, St. Barthelemy, St. Martin, Trinidad and Tobago, Turks and Caicos.
Study selection and inclusion and exclusion criteria	► Search results were imported into the reference manager EndNote (Thomson Reuters, USA). ► Screening was performed in four stages: 1. Duplicate publications were identified and excluded. 2. Titles and abstracts were screened for relevant and potentially relevant publications. 3. Full texts of relevant and potentially relevant publications were retrieved and screened for relevance. 4. Bibliographies of relevant publications and reviews were checked for additional potentially relevant publications. ► Inclusion criteria were any publication, including a study with a minimum sample size of 10, reporting primary data on any of the following outcome measures: 1. HSV-2 antibody incidence as detected by a type-specific diagnostic assay. 2. HSV-2 antibody prevalence (seroprevalence) as detected by a type-specific diagnostic assay. 3. Proportion of HSV-2 in GUD as detected by standard viral detection and subtyping methods. 4. Proportion of HSV-2 in genital herpes (as opposed to HSV-1), as detected by standard viral detection and subtyping methods. ► Exclusion criteria were – Case reports, case series, reviews, editorials, commentaries and qualitative studies. – Measures reporting seroprevalence in infants <6 months old as their antibodies can be maternal in origin. ► In this study, the term 'publication' refers to a document reporting one or several outcome measures. 'Study' or 'measure' refers to a specific outcome measure and its details.
Data extraction and data synthesis	► Extracted variables included author(s), publication title, year(s) of data collection, publication year, country of origin, country of survey, city, study site, study design, study sampling procedure, study population and its characteristics (eg, sex and age), sample size, HSV-2 outcome measures, and diagnostic assay. ► Overall outcome measure and their stratified measures were extracted, provided the sample size in each stratum is ≥10. ► For studies including overall sample size, but no individual strata sample sizes, the sample size of each stratum was assumed equal to overall sample size divided by the number of strata in the study. ► Stratification hierarchy for incidence and seroprevalence in descending order of preference were 1. Population type as defined in online supplemental box S1. 2. Sex. 3. Age group classified as (groups optimised to best fit reported data): – <20 years old. – 20–30 years old. – 30–40 years old. – >40 years old. ► Stratification hierarchy for GUD and genital herpes included genital herpes episode status and study site: 1. Genital herpes episode status classified as – First episode genital herpes. – Recurrent genital herpes. 2. Study site stratification classified as – Hospital. – STD clinic. ► Measures reporting any HSV-2 outcome among children <15 years old were only reported but not included in the analyses.
Quality assessment	The Cochrane's approach for ROB assessment included ► Study's precision classification into low versus high based on the sample size (<200 vs ≥200). ► Study's appraisal into low vs high ROB was determined using two quality domains: – Sampling method: probability-based *vs* non-probability based. – Response rate: ≥80% vs <80% or unclear.
Meta-analyses	► Meta-analyses were conducted using DerSimonian-Laird random-effects models with inverse variance weighting. The variance of each outcome measure was stabilised using the Freeman-Tukey arcsine square-root transformation. ► Pooled mean HSV-2 seroprevalence was estimated for each population type by sex, and for general populations by country, subregion, year of data collection range and year of publication range. ► Pooled proportions of HSV-2 detection in GUD and in genital herpes cases were estimated. ► Heterogeneity assessment was based on three complementary metrics: – Cochran's Q statistic to assess existence of heterogeneity in effect size (p value of <0.1 indicated heterogeneity). – I^2 heterogeneity measure to assess the percentage of between-study variation in effect size that is due to actual differences in effect size rather than chance. – Prediction interval to describe the distribution of true outcome measures around the pooled mean.
Metaregressions	► Univariable and multivariable random-effects meta-regression analyses using log-transformed proportions were carried out to identify predictors of HSV-2 seroprevalence. ► Factors in the univariable model with a p value of <0.1 were included in the multivariable analysis. ► Factors in the multivariable model with a p value of ≤0.05 were deemed to be significant predictors. ► Variables included in the univariable metaregression model for HSV-2 seroprevalence were – Population type. – Age group. – Sex. – Country. – Subregion. – Country's income: LIC, LMIC, UMIC, and HIC according the World Bank classification. – Assay type (western blot, ELISA, and monoclonal antibody). – Sample size. – Sampling method. – Response rate. – Year of data collection. – Year of publication. – Year of data collection category (<2000, 2000–2010, >2010). – Year of publication category (<2000, 2000–2010, >2010). ► The year of data collection had a few missing variables that were imputed by adjusting the year of publication using the median difference with the year of data collection.

This methodology was adapted from a previously conducted systematic review characterising the epidemiology of HSV-1 in Europe.[88]
GUD, genital ulcer disease; HIC, high-income country; HSV-1, herpes simplex virus type 1; HSV-2, herpes simplex virus type 2; LIC, low-income country; LMIC, lower-income to middle-income country; ROB, risk of bias; UMIC, upper-income to middle-income country.

WHO and United Nations definitions for Latin America and the Caribbean (table 1).[33 34] Search strategies are in online supplemental table S2.

Study selection and inclusion and exclusion criteria

Screening and double screening were conducted by HM and MH, respectively. Screening steps and eligibility criteria are detailed in table 1.

Data extraction and synthesis

Extraction and double extraction of relevant publications were performed by MH and HM. The list of extracted variables is found in table 1.

Quality assessment

Given documented limitations in HSV-2 assays,[35 36] assessment of assays' reliability and validity was conducted with the assistance of Professor Rhoda Ashley-Morrow of the University of Washington, a leading expert in HSV-2 serology. Only studies with reliable and valid assays were included in the systematic review, and each study was subsequently assessed for precision and risk of bias (ROB) as informed by the Cochrane approach.[31] Details of the quality assessment are in table 1.

Meta-analyses

To account for sampling variation and heterogeneity in effect sizes, meta-analyses were conducted using DerSimonian-Laird random-effects models[37] with the variance stabilised using the Freeman-Tukey double arcsine transformation.[38] These analyses were conducted in R V.3.4.1[39] using the 'meta' package[40] (table 1).

Metaregressions

To identify possible predictors of HSV-2 seroprevalence and sources of between-study heterogeneity, log-transformed seroprevalence measures were regressed in STATA/SE V.13[41] using the 'metareg' package[42] (table 1).

RESULTS

Search results and scope of evidence

Study selection process following the PRISMA guidelines is detailed in figure 1. Overall, 4371 citations were identified. After deduplication and title and abstract screening, full text of 631 unique citations were retrieved for further screening. This step identified 95 relevant publications, and their bibliography

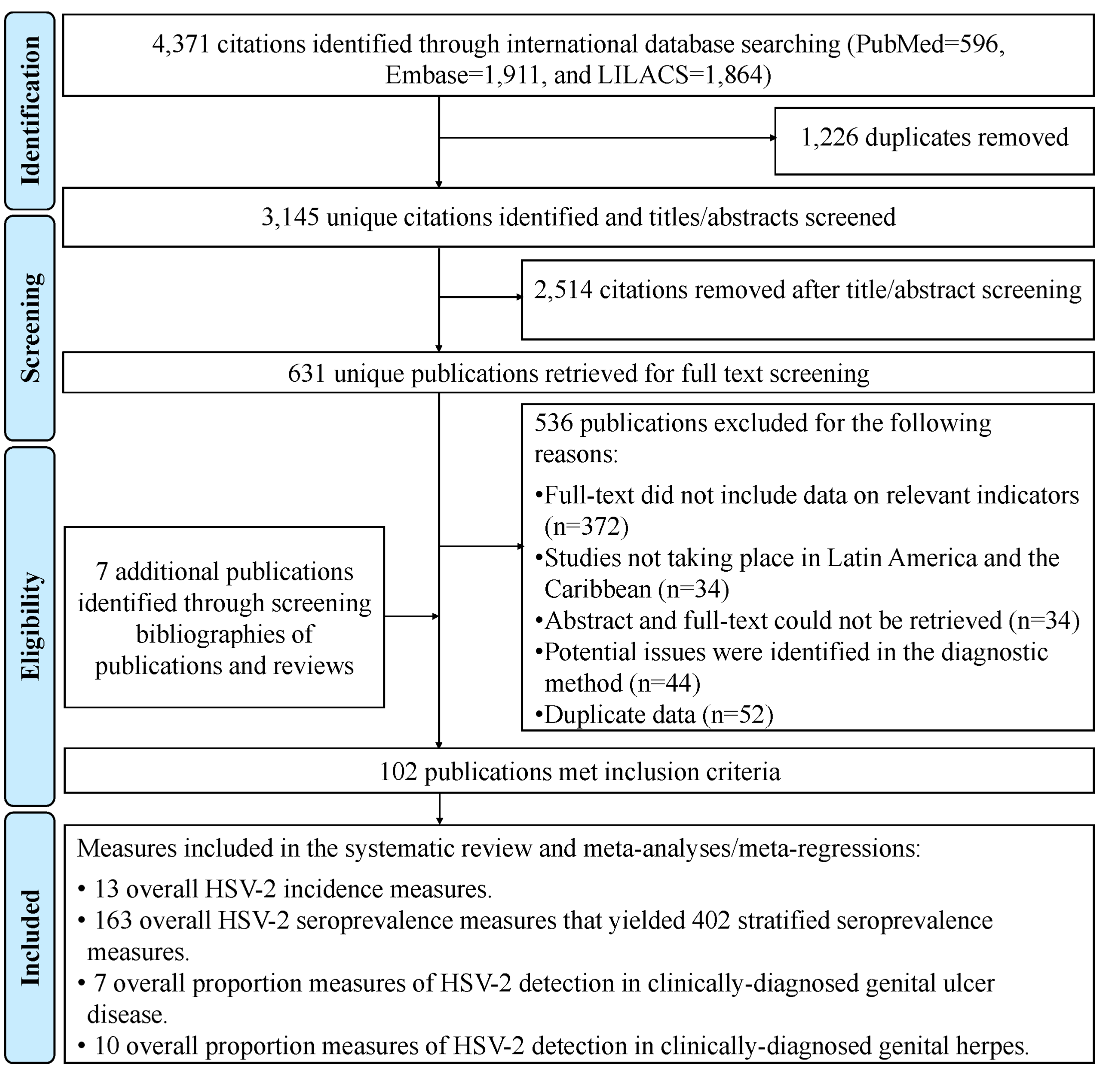


Figure 1 Flowchart of article selection for the systematic review of HSV-2 infection in Latin America and the Caribbean, per the PRISMA guidelines.[32] HSV-2, herpes simplex virus type 2; LILACS, Literatura Latino Americana em Ciências daSaúde, PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 2 Pooled mean estimates for HSV-2 seroprevalence among the different at-risk populations in Latin America and the Caribbean

	Outcome measures	Samples	HSV-2 seroprevalence (%)		Pooled mean HSV-2 seroprevalence	Heterogeneity measures		
Population type	Total N	Total N	Range	Median	Mean (%) (95% CI)	Q* (P value)	I²† (%) (95% CI)	Prediction interval‡ (%)
General populations	236	56 457	0.0–71.4	19.6	20.6 (18.7 to 22.5)	6495.1 (<0.001)	96.(96.1 to 96.6)	1.4–52.5
Women	139	23 959	0.0–71.4	23.9	25.2 (22.5 to 28.0)	2940.6 (<0.001)	95.3 (94.8 to 95.8)	2.7–59.2
Men	85	16 446	0.0–64.3	10.9	14.2 (11.6 to 17.0)	1914.1 (<0.001)	95.6 (95.0 to 96.1)	0.0–44.8
Mixed sexes	12	16 052	2.2–35.8	15.0	16.8 (11.7 to 22.6)	689.2 (<0.001)	98.4 (98.0 to 98.8)	1.7–42.4
Intermediate-risk populations	24	6775	3.4–79.2	32.2	33.3 (26.0 to 41.0)	817.4 (<0.001)	97.2 (96.5 to 97.7)	4.1–72.6
Women	9	1255	22.2–79.2	43.5	49.3 (38.9 to 60.8)	102.5 (<0.001)	92.2 (87.4 to 95.2)	13.4–85.6
Men	15	5520	3.4–51.1	26.8	25.6 (19.5 to 32.2)	331.0 (<0.001)	95.8 (94.3 to 96.9)	4.6–55.6
High-risk populations	93	25 344	9.0–100	71.2	66.2 (61.0 to 71.2)	6206.7 (<0.001)	98.5 (98.4 to 98.6)	18.0–99.3
FSWs	56	9023	9.0–100	75.0	74.8 (70.6 to 78.8)	901.6 (<0.001)	93.9 (92.8 to 94.9)	43.2–96.7
MSWs, MSM and transgender people	37	16 321	13.0–39.9	50.9	54.6 (47.4 to 61.7)	2851.4 (<0.001)	98.7 (98.6 to 98.9)	13.9–91.9
STI clinic attendees and symptomatic populations	6	432	38.9–95.0	47.0	49.2 (41.9 to 56.5)	8.2 (0.146)	39.0 (0.0 to 75.8)	31.3–67.1
Mixed sexes	6	432	38.9–95.0	47.0	49.2 (41.9 to 56.5)	8.2 (0.146)	39.0 (0.0 to 75.8)	31.3–67.1
HIV-positive individuals and individuals in HIV discordant couples	19	2840	20.0–88.0	65.6	67.3 (60.0 to 74.2)	264.1 (<0.001)	93.2 (90.7 to 95.0)	33.8–93.2
Women	9	1354	20.0–88.0	65.6	68.9 (56.2 to 78.6)	133.4 (<0.001)	94.0 (90.7 to 96.1)	25.6–97.7
Men	5	1066	42.3–81.1	53.0	60.6 (45.6 to 74.7)	83.9 (<0.001)	95.2 (91.5 to 97.3)	9.4–99.3
Mixed sexes	5	420	61.4–87.0	73.0	71.9 (62.9 to 80.2)	13.9 (0.007)	71.3 (27.4 to 88.7)	40.0–95.0
Other populations§	24	3497	15.1–82.0	56.8	51.1 (43.7 to 58.5)	422.6 (<0.001)	94.6 (93.0 to 95.8)	16.5–85.2
Women	21	3225	45.1–82.0	56.6	52.0 (44.2 to 59.8)	368.7 (<0.001)	94.6 (92.9 to 95.9)	17.4–85.5
Men	2¶	172	59.6–60.8	60.2	60.5 (53.0 to 67.8)	–	–	–
Mixed sexes	1¶	100	–	–	18.0 (11.0 to 26.2)	–	–	–

*Q: the Cochran's Q statistic is a measure assessing the existence of heterogeneity in seroprevalence.
†I^2: a measure that assesses the magnitude of between-study variation that is due to actual differences in seroprevalence across studies rather than chance.
‡Prediction interval: a measure that estimates the distribution (95% interval) of true seroprevalence around the estimated mean.
§Other populations include populations with an undetermined risk of acquiring HSV-2 infection such as patients with cervical cancer or their spouses.
¶No meta-analysis was done due to the small number of studies (n<3).
FSW, female sex worker; HSV-2, herpes simplex virus type 2; MSM, men who have sex with men; MSW, male sex worker.;

screening identified seven additional relevant publications, including conference posters and abstracts.[43–49]

In total, 102 publications were deemed relevant and extracted. This extraction yielded 13 HSV-2 overall incidence measures, 163 overall (402 stratified) seroprevalence measures, 7 overall proportion measures of HSV-2 detection in GUD and 10 overall proportion measures of HSV-2 detection in genital herpes.

HSV-2 incidence overview

Online supplemental table 3 summarises the extracted seroconversion rates (number of measures (n)=10) and incidence rates (n=6). Study design was either longitudinal cohort (n=8, 61.5%) or randomised controlled trial (n=5, 38.4%), with follow-up durations ranging between 335 days and 2 years. Across all populations, seroconversion rate ranged between 2.0% and 51.1%, and incidence rate ranged between 4.5 and 38.5 per 100 person-years.

HSV-2 seroprevalence overview

Overall extracted seroprevalence measures (n=163) are listed in online supplemental table S4. The earliest study was published in 1989 and the most recent study was published in 2020. Majority of studies were based on convenience sampling (n=96, 58.9%).

Stratified seroprevalence measures varied by population type classification (table 2), with seroprevalence ranging between 0.0% and 71.4% with a median of 19.6% among general populations (n=236), between 3.4% and 79.2% with a median of 32.2% among intermediate-risk populations (n=24), between 9.0% and 100% with a median of 71.2% among high-risk populations (n=93), between 38.9% and 95.0% with a median of 47.0% among STI clinic attendees and symptomatic populations (n=6), and between 20.0% and 88.0% with a median of 65.6% among HIV-positive individuals and individuals in HIV discordant couples (n=19). A detailed summary of seroprevalence measures by sex across the population type classifications is in table 2.

Pooled mean HSV-2 seroprevalence

Table 2 summarises the pooled mean HSV-2 seroprevalence by sex across populations. In general populations, the pooled mean was 25.2% (95% CI 22.5% to 28.0%) among women and 14.2% (95% CI 11.6% to 17.0%) among men. In intermediate-risk populations, the pooled mean was 49.3% (95% CI 38.9% to 60.8%) among women and 25.6% (95% CI 19.5% to 32.2%) among men. In high-risk populations, the pooled mean was 74.8% (95% CI 70.6% to 78.8%) among female sex workers and 54.6% (95% CI 47.4% to 61.7%) among male sex workers, men who have sex with men and transgender people. In STI clinic attendees and symptomatic populations (mixed population of women and men), the pooled mean was 49.2% (95% CI

Table 3 Pooled mean estimates for HSV-2 seroprevalence among the general population in Latin America and the Caribbean

Population classification	Outcome measures	Sample size	HSV-2 seroprevalence (%)		Pooled mean HSV-2 seroprevalence	Heterogeneity measures		
	Total N	Total N	Range	Median	Mean (%) (95% CI)	Q* (P value)	I²† (%) (95% CI)	Prediction interval‡ (%)
Countries								
Brazil	79	22 671	0.0–71.4	28.0	25.5 (22.2 to 28.9)	2049.9 (<0.001)	96.2 (95.7 to 96.6)	3.8–56.9
Colombia	14	1633	1.7–67.3	37.7	35.9 (23.9 to 48.7)	351.6 (<0.001)	96.3 (95.0 to 97.3)	0.5–86.6
Costa Rica	11	1800	17.7–58.8	44.6	41.7 (34.2 to 49.4)	108.8 (<0.001)	90.8 (85.6 to 94.1)	15.7–70.4
Mexico	53	19 574	0.0–45.0	10.9	13.4 (10.8 to 16.2)	1392.9 (<0.001)	96.3 (95.7 to 96.8)	0.6–37.1
Peru	65	6896	0.0–38.0	9.0	11.7 (9.5 to 14.1)	500.3 (<0.001)	87.2 (84.4 to 89.5)	0.0–33.1
Other countries§	14	3883	11.8–65.0	39.6	41.2 (32.6 to 50.1)	378.4 (<0.001)	96.6 (95.4 to 97.4)	10.0–77.0
Subregions								
Central America	68	22 688	0.0–59.9	14.9	18.4 (15.1 to 21.9)	2694.7 (<0.001)	97.5 (97.2 to 97.8)	0.5–51.4
South America	164	32 590	0.0–71.4	21.3	21.1 (18.8 to 23.4)	3632.7 (<0.001)	95.5 (95.1 to 95.9)	1.5–53.3
Caribbean	4	1179	30.5–54.0	37.2	38.7 (29.9 to 47.9)	20.9 (0.001)	85.7 (64.9 to 94.2)	5.9–79.0
Age group								
<20 years	28	5194	0.0–29.0	9.0	9.6 (7.1 to 12.4)	229.1 (<0.001)	88.2 (84.1 to 91.2)	0.5–26.4
20–30 years	30	4453	0.0–47.4	20.8	17.9 (13.6 to 22.5)	379.7 (<0.001)	92.4 (90.2 to 94.1)	1.1–46.4
30–40 years	17	1983	9.6–56.0	28.3	27.6 (21.4 to 34.2)	157.2 (<0.001)	89.8 (95.3 to 93.1)	5.6–57.8
>40 years	34	5029	10.9–71.4	40.3	38.4 (32.8 to 44.2)	561.6 (<0.001)	94.1 (92.7 to 95.3)	10.0–72.0
Mixed	127	39 798	0.0–67.3	17.0	18.7 (16.4 to 21.2)	4188.3 (<0.001)	997.0 (96.7 to 97.3)	0.9–49.5
Year of publication category								
<2000	21	2901	5.0–67.3	36.0	34.1 (26.2 to 42.5)	406.4 (<0.001)	95.1 (93.6 to 96.2)	4.0–74.2
2000–2010	132	28 618	0.0–71.4	23.1	22.8 (20.3 to 25.5)	3336.4 (<0.001)	96.1 (95.7 to 96.4)	2.1–55.6
>2010	83	24 938	0.0–65.0	10.9	14.3 (12.1 to 16.8)	1812.0 (<0.001)	94.9 (94.9 to 96.0)	0.7–39.1
Year of data collection category								
<2000	83	9229	0.0–71.4	30.8	31.1 (27.4 to 34.9)	1173.1 (<0.001)	93.0 (91.9 to 94.0)	5.3–65.7
2000–2010	143	33 565	0.0–59.9	12.0	15.0 (13.1 to 17.1)	3450.4 (<0.001)	95.9 (95.5 to 96.3)	0.3–43.4
>2010	12	13 835	10.4–65.0	29.3	30.7 (24.5 to 38.4)	649.0 (<0.001)	98.3 (97.8 to 98.7)	6.9–61.9
All studies	238	56 628	0.0–71.4	20.0	20.8 (19.0 to 22.8)	6630.7 (<0.001)	96.4 (96.2 to 96.7)	1.4–53.1

*Q: the Cochran's Q statistic is a measure assessing the existence of heterogeneity in seroprevalence.
†I^2: a measure that assesses the magnitude of between-study variation that is due to actual differences in seroprevalence across studies rather than chance.
‡Prediction interval: a measure that estimates the distribution (95% interval) of true seroprevalence around the estimated mean.
§Other countries include Argentina, Barbados, Bolivia, Haiti, Honduras and Panama.
HSV-2, herpes simplex virus type 2.

41.9% to 56.5%). In HIV-positive individuals and individuals in HIV discordant couples, the pooled mean was 68.9% (95% CI 56.2% to 78.6%) among women and 60.6% (95% CI 45.6% to 74.7%) among men. Forest plots of these meta-analyses are in online supplemental figure S1.

Table 3 summarises pooled mean seroprevalence estimates in general populations for different subpopulation categorisations. By country, the pooled mean was lowest at 11.7% (95% CI 9.5% to 14.1%) in Peru and was higher at 13.4% (95% CI 10.8% to 16.2%) in Mexico, 25.5% (95% CI 22.2% to 28.9%) in Brazil, 35.9% (95% CI 23.9% to 48.7%) in Colombia and 41.7% (95% CI 34.2%–49.4%) in Costa Rica. Across age groups, pooled mean seroprevalence increased steadily starting at 9.6% (95% CI 7.1% to 12.4%) in <20-year-old individuals, then at 17.9% (95% CI 13.6% to 22.5%) in individuals aged 20–30 years, 27.6% (95% CI 21.4% to 34.2%) in individuals aged 30–40 years and reaching 38.4% (95% CI 32.8% to 44.2%) in >40-year-old individuals.

Predictors of HSV-2 seroprevalence

Results of the metaregression analyses are shown in table 4 (online supplemental tables S5 and S6). In the univariable analysis, 12 variables were found eligible for inclusion in the multivariable model (p<0.1). Two sets of multivariable models were conducted to account for the collinearity between the year of publication and the year of data collection.

Each conducted multivariable model explained about 69% of seroprevalence variation and included population type, age group, sex, subregion, country's income, sample size, sampling method and response rate, in addition to year of publication or year of data collection. The 'country' and 'country's income' variables were not included in the multivariable models due to collinearity with subregion. However, they did not add notable new results when they were included in sensitivity analyses instead of subregion (online supplemental table S5).

In the model including year of publication as a categorical variable (table 4) and compared with the general populations, HSV-2 seroprevalence was higher by 1.55-fold (95% CI 1.22 to 1.96) in intermediate-risk populations, 3.09-fold (95% CI 2.67 to 3.57) in high-risk populations, 2.40-fold (95% CI 1.48 to 3.90) in STI clinic attendees and symptomatic populations, and 3.06-fold (95% CI:2.37 to 3.95) in HIV-positive individuals and individuals in HIV discordant couples.

Compared with women, men had a 0.68-fold (95% CI 0.60 to 0.76) lower seroprevalence. Compared with those <20 years old, seroprevalence was higher by 1.63-fold (95% CI 1.27 to 2.09) in individuals aged 20–30 years old, 2.24-fold (95% CI 1.68 to 2.99) in individuals aged 30–40 years old individuals,

Table 4 Univariable and multivariable metaregression analyses for HSV-2 seroprevalence among different at-risk populations in Latin America and the Caribbean using the year of publication as the temporal variable

			Outcome measures	Sample size	Univariable analysis				Multivariable analysis*			
									Model 1†		Model 2‡	
			Total n	Total N	RR (95% CI)	p value	LR test P value	Adjusted R^2 (%)	ARR (95% CI)	P value	ARR (95% CI)	P value
Population characteristics	Population type	General populations	236	56 457	1.00	–	<0.001	45.98	1.00	–	1.00	–
		Intermediate-risk populations	24	6775	1.52 (1.16 to 2.00)	0.002			1.55 (1.22 to 1.96)	<0.001	1.54 (1.22 to 1.96)	<0.001
		High-risk populations	93	25 344	3.09 (2.64 to 3.61)	<0.001			3.09 (2.67 to 3.57)	<0.001	3.08 (2.66 to 3.57)	<0.001
		STI clinic attendees and symptomatic populations	6	432	2.49 (1.47 to 4.22)	0.001			2.40 (1.48 to 3.90)	<0.001	2.35 (1.45 to 3.81)	0.001
		HIV-positive individuals and individuals in HIV discordant couples	19	2840	3.21 (2.38 to 4.32)	<0.001			3.06 (2.37 to 3.95)	<0.001	3.02 (2.34 to 3.89)	<0.001
		Other populations§	24	3497	2.42 (1.85 to 3.16)	<0.001			1.56 (1.24 to 1.97)	<0.001	1.53 (1.21 to 1.94)	<0.001
	Age group	<20 years	35	6538	1.00	–	<0.001	10.26	1.00	–	1.00	–
		20–30 years	47	7751	2.05 (1.40 to 3.00)	<0.001			1.63 (1.27 to 2.09)	<0.001	1.62 (1.26 to 2.09)	<0.001
		30–40 years	22	2933	2.58 (1.64 to 4.04)	<0.001			2.24 (1.68 to 2.99)	<0.001	2.22 (1.66 to 2.97)	<0.001
		>40 years	39	5940	2.84 (1.92 to 4.18)	<0.001			3.22 (2.50 to 4.14)	<0.001	3.08 (2.40 to 3.96)	<0.001
		Mixed ages	259	72 183	2.49 (1.82 to 3.41)	<0.001			1.79 (1.44 to 2.21)	<0.001	1.71 (1.39 to 2.11)	<0.001
	Sex	Women	234	38 816	1.00	–	0.001	4.82	1.00	–	1.00	–
		Men	144	39 525	0.67 (0.56 to 0.80)	<0.001			0.68 (0.60 to 0.76)	<0.001	0.69 (0.61 to 0.77)	<0.001
		Mixed sexes	24	17 004	0.81 (0.57 to 1.16)	0.267			0.59 (0.46 to 0.77)	<0.001	0.62 (0.48 to 0.80)	<0.001
	Countries	Brazil	106	25 766	1.00	–	<0.001‡	12.58	–	–	–	–
		Colombia	19	2247	1.36 (0.91 to 2.01)	0.125			–	–	–	–
		Costa Rica	13	2364	1.46 (0.92 to 2.30)	0.102			–	–	–	–
		Mexico	76	23 437	0.71 (0.56 to 0.91)	0.008			–	–	–	–
		Panama	15	3334	1.81 (1.18 to 2.78)	0.006			–	–	–	–
		Peru	131	24 976	0.92 (0.74 to 1.14)	0.476			–	–	–	–
		Other¶	42	13 221	1.84 (1.39 to 2.45)	<0.001			–	–	–	–
	Subregions	Central America	124	38 103	1.00	–	0.065	0.82	1.00	–	1.00	–
		South America	264	54 798	0.95 (0.79 to 1.14)	0.606			1.13 (1.00 to 1.27)	0.047	1.12 (0.99 to 1.27)	0.053
		Caribbean	14	2444	1.62 (1.02 to 2.58)	0.040			1.17 (0.87 to 1.57)	0.281	1.17 (0.87 to 1.56)	0.287
	Country's income	LIC and LMIC	29	9846	1.00	–	<0.001‡	9.07	–	–	–	–
		UMIC	354	81 539	0.45 (0.33 to 0.62)	<0.001			–	–	–	–
		HIC	19	3960	0.86 (0.54 to 1.36)	0.528			–	–	–	–

Continued

Table 4 Continued

			Outcome measures	Sample size	Univariable analysis				Multivariable analysis*			
									Model 1†		Model 2‡	
			Total n	Total N	RR (95% CI)	p value	LR test P value	Adjusted R^2 (%)	ARR (95% CI)	P value	ARR (95% CI)	P value
Study methodology characteristics	Assay type	Western blot	94	11 898	1.00	–	0.432	0.00	–	–	–	–
		ELISA	304	82 744	0.89 (0.73 to 1.09)	0.280			–	–	–	–
		Monoclonal antibody	4	703	1.24 (0.53 to 2.87)	0.614			–	–	–	–
	Sample size**	<200	81	7542	1.00	–	<0.001	7.27	1.00	–	1.00	–
		>200	321	87 803	0.58 (0.47 to 0.71)	<0.001			0.75 (0.64 to 0.87)	<0.001	0.74 (0.64 to 0.87)	<0.001
	Sampling method	Probability-based	151	47 471	1.00	–	<0.001	18.05	1.00	–	1.00	–
		Non-probability-based	251	47 874	2.08 (1.76 to 2.44)	<0.001			1.16 (1.00 to 1.35)	0.037	1.17 (1.01 to 1.35)	0.033
	Response rate	≥80%	194	48 220	1.00	–	0.002	5.52	1.00	–	1.00	–
		<80%	32	6062	0.59 (0.42 to 0.82)	0.002			0.79 (0.63 to 0.99)	0.044	0.77 (0.62 to 0.96)	0.025
		Unclear	176	41 063	1.25 (1.05 to 1.49)	0.010			1.07 (0.94 to 1.22)	0.262	1.09 (0.96 to 1.24)	0.169
Temporal variables	Year of publication category	<2000	49	7244	1.00	–	<0.001	4.39	1.00	–	–	–
		2000–2010	206	51 983	0.61 (0.47 to 0.79)	<0.001			0.88 (0.75 to 1.05)	0.166	–	–
		>2010	147	31 118	0.56 (0.42 to 0.73)	<0.001			0.74 (0.61 to 0.89)	0.002	–	–
	Year of publication		402	95 345	0.97 (0.96 to 0.98)	<0.001	<0.001	2.98	–	–	0.98 (0.97 to 0.99)	0.002

The analysis using year of data collection as the temporal variable is found in online supplemental table S6.
*Countries and country's income were not included in the multivariable models due to collinearity with the variable subregions.
†Variance explained by multivariable model 1 (adjusted R^2)=68.85%.
‡Variance explained by multivariable model 2 (adjusted R^2)=68.99%.
§Other populations include populations with an undetermined risk of acquiring HSV-2 infection such as patients with cervical cancer or their spouses.
¶Other countries include Argentina, Barbados, Bolivia, Chile, Dominican Republic, El Salvador, Guatemala, Haiti, Honduras, Jamaica and Nicaragua.
**Sample size denotes the sample size of each study population found in the original publication.
ARR, adjusted risk ratio; HIC, high-income country; HSV-2, herpes simplex virus type 2; LIC, low-income country; LMIC, lower-income to middle-income country; LR, likelihood ratio; RR, risk ratio; UMIC, upper-income to middle-income country.

Table 5 Pooled mean proportions of HSV-2 virus isolation in clinically diagnosed GUD and in clinically diagnosed genital herpes in Latin America and the Caribbean

	Outcome measures	Samples	Proportion of HSV-2 isolation (%)		Pooled proportion of HSV-2 isolation (%)	Heterogeneity measures		
Population type	Total N	Total N	Range	Median	Mean (95% CI)	Q*(P value)	I²† (%) (95% CI)	Prediction interval‡ (%)
Patients with GUD	7	603	0.0–77.7	50.9	41.4 (18.9 to 67.0)	184.5 (<0.001)	96.7 (95.0 to 97.9)	0.0–100
Patients with genital herpes	10	278	71.5–100	90.1	91.1 (82.7 to 97.2)	31.3 (<0.001)	71.2 (45.2 to 84.9)	58.3–100

*Q: the Cochran's Q statistic is a measure assessing the existence of heterogeneity in pooled outcome measures, here proportions of HSV-2 virus isolation in GUD and in genital herpes.
†I² a measure assessing the magnitude of between-study variation that is due to true differences in proportions of HSV-2 virus isolation across studies rather than sampling variation.
‡Prediction interval: a measure quantifying the distribution 95% interval of true proportions of HSV-2 virus isolation around the estimated pooled mean.
GUD, genital ulcer disease; HSV-2, herpes simplex virus type 2.

and 3.22-fold (95% CI 2.50 to 4.14) in >40-year-old individuals. Seroprevalence was 1.13-fold (95% CI 1.00 to 1.27) higher in South America compared with Central America.

Small-study effect was identified—seroprevalence was 0.75-fold (95% CI 0.64 to 0.87) lower in studies with a sample size of >200 compared with those with a sample size of <200. Seroprevalence was 1.16-fold (95% CI 1.00 to 1.35) higher in studies using non-probability-based sampling compared with studies using probability-based sampling. Seroprevalence was 0.79-fold (95% CI 0.63 to 0.99) lower in studies with low response rate (<80%) compared with studies with high response rate (>80%). No effect was found for assay type on observed seroprevalence.

Compared with studies published before the year 2000, those published after 2010 had 0.74-fold (95% CI 0.61 to 0.89) lower seroprevalence. When year of publication was included as a linear term instead of a categorical variable, seroprevalence was found declining by 0.98-fold (95% CI 0.97 to 0.99) per year. Similar results were found when the year of data collection was used in the metaregressions instead of the year of publication (online supplemental table S6). Year of publication was used in the main analysis as its data were more complete than those for year of data collection.

HSV-2 isolation in GUD and in genital herpes

Online supplemental table S7 summarises the studies reporting proportions of HSV-2 detection in GUD or in genital herpes, while table 5 shows the pooled means for these proportions. Proportion of HSV-2 detection in GUD (n=7) ranged between 0.0% and 77.7% with a median of 50.9% and a pooled proportion of 41.4% (95% CI 18.9% to 67.0%). The proportion of HSV-2 detection in genital herpes (n=10) ranged between 71.5% and 100% with a median of 90.1% and a pooled proportion of 91.1% (95% CI 82.7% to 97.2%). Forest plots of the meta-analyses are in online supplemental figure S2.

Quality assessment

The results of the quality assessment are summarised in online supplemental table S8. In total, 82.2% of studies had high precision; 28.8% had low ROB in the sampling method domain; and 35.6% had low ROB in the response rate domain. Only 2.4% of studies had high ROB in both quality domains.

DISCUSSION

Based on a large volume of data that powered a variety of analyses, the epidemiology of HSV-2 infection in Latin America and the Caribbean was comprehensively investigated. With about 20% of adults being seropositive (table 2), this region harbours one of the highest seroprevalence levels worldwide,[1 50–52] second only to sub-Saharan Africa.[1] Nonetheless and remarkably, this region is witnessing a rapidly declining seroprevalence at a rate of about 2% per year (table 4), for reasons that are not yet clear. Curiously, such declines have been also observed in the USA[26 53–56] and more recently in sub-Saharan Africa.[29] Since HSV-2 seroprevalence has been shown to be an objective biomarker of a population's sexual risk behaviour and risk of HIV infection,[57–62] seroprevalence declines could be suggestive of declines in risky sex, possibly in response to the threat of HIV infection.[63–66] Other factors may have also contributed, such as the global expansion of HIV/STI response, including primary prevention interventions,[67 68] STI awareness that encouraged engagement in safer sexual practices[69] and, possibly, socioeconomic development that has changed the structure of sexual networks towards a structure that is less conducive for STI transmission. In concordance with these declines for HSV-2 seroprevalence, evidence suggests declines in the prevalence of other STIs across world regions, such as of HIV[66 70] and syphilis.[71] It remains to be seen whether these declines are localised to some regions or subregions, or global in nature.

The results of the present study confirmed key classic attributes of HSV-2 epidemiology, and importantly established *effect sizes* for these attributes (table 4), thereby providing parameter inputs and adjustment cofactors for future STI burden estimations using mathematical modelling. There was strong hierarchy in seroprevalence based on sexual risk behaviour classification that explained alone 44% of the seroprevalence variation (table 4). This hierarchy was also consistent with that found recently for sub-Saharan Africa.[29] Seroprevalence reached high levels that exceeded 60% in populations at high risk, such as female sex workers and men who have sex with men (table 2).

Compared with women, men had 0.68-fold lower HSV-2 seroprevalence (table 4), providing further support for a higher bioanatomical susceptibility to the infection among women.[9 52 72] Consistent with existing evidence,[1 52 72 73] age played a critical role in exposure to this infection. Seroprevalence grew steadily with age right after sexual debut (tables 3 and 4). However, unlike in sub-Saharan Africa where it plateaued by mid-30s,[29] seroprevalence continued to grow with age in Latin America and the Caribbean even for those >40 years of age.

The results have shown some evidence for subregion and country variability in HSV-2 seroprevalence (tables 3 and 4). There was also evidence for higher seroprevalence in countries with lower income (tables 3 and 4) that are suggestive of lower socioeconomic status being conducive to higher risk of exposure to this infection, as observed elsewhere.[50 74 75]

The results further show that HSV-2 infection is the aetiological cause of nearly half of GUD cases in this region (table 5), confirming the disproportional role for this infection in this disease outcome. The role of HSV-2 in GUD may continue at this high level for decades to come despite the declining seroprevalence, as other causes of GUD, such as syphilis,[71 76] could also be declining at the same time. HSV-2 infection (as opposed to HSV-1 infection) was also the aetiological cause of >90% of genital herpes cases (table 5). This finding is in line with a recent assessment of HSV-1 infection in Latin America and the Caribbean, indicating that HSV-1 is still mainly acquired orally in a context of slow transitioning epidemiology and limited contribution for HSV-1 in genital herpes.[30] While this finding is consistent with what is observed in sub-Saharan Africa and possibly the Middle East and North Africa,[77–79] it contrasts with what is observed in North America, Europe, and Asia, where the role of HSV-1 in genital herpes has been increasing, and in some settings and populations even reaching the point of being the leading cause of this disease outcome.[80–88]

This study has limitations. HSV-2 epidemiological data were mainly available for the large countries of Latin America and the Caribbean region that constitute most of its population, but there were no data available for 27 out of the 47 (mostly small) countries constituting this part of the world. There were also less data for GUD and genital herpes than for seroprevalence. There was evidence for a small-study effect and somewhat varying seroprevalence by sampling method and response rate (table 4), which may have biased assessed seroprevalence. Studies differed in the employed diagnostic assays (online supplemental table S4), with possibly different sensitivity and specificity profiles.[35 36 89] However, no effect was found for assay type on estimated seroprevalence (table 4). Measured seroprevalence can be affected by the choice of ELISA optical density cut-off for positivity.[35 51 90 91] Studies were excluded if clearly an inappropriate cut-off was used. Still, variation in the use of optical density cutoffs across studies could have influenced estimated seroprevalence.[35 51 90 91] There was high heterogeneity in seroprevalence (tables 2 and 3), but strikingly most of this heterogeneity was subsequently explained by the 'classic' attributes driving variation in HSV-2 seroprevalence, including sexual risk behaviour, sex and age (table 4). On balance, these limitations may have had inconsequential impact on the results and findings of the present study.

CONCLUSIONS

One in five adults in Latin America and the Caribbean is chronically infected with HSV-2, a higher level than that found in most other world regions, but seroprevalence is rapidly declining at a rate of about 2% per year, possibly reflecting changes in sexual behaviour and patterns, sexual networks or use of protective measures, such as condoms, over the last three decades. Despite this decline, HSV-2 infection persists as the aetiological cause of nearly half of GUD cases in this region, and almost all of genital herpes cases. These findings highlight the importance of HSV-2 seroprevalence monitoring and surveillance and demonstrate the need for prophylactic and therapeutic vaccines to alleviate this disease burden. They also advocate for increased momentum and support to the slowly progressing efforts of vaccine development.

Key messages

- ► Herpes simplex virus type 2 (HSV-2) infection is a highly prevalent STI worldwide, and results in a sizeable disease burden.
- ► One in five adults in Latin America and the Caribbean is chronically infected with HSV-2, a higher level than in other regions.
- ► However, this region is witnessing a rapidly declining seroprevalence at a rate of 2% per year.
- ► HSV-2 is the aetiological cause of nearly half of GUD cases and almost all of genital herpes cases in this region.
- ► The findings highlights the need for seroprevalence monitoring, GUD/genital herpes aetiological surveillance, and an HSV-2 vaccine to control transmission and alleviate the disease burden.

Author affiliations
[1]Infectious Disease Epidemiology Group, Weill Cornell Medicine—Qatar, Cornell University, Qatar Foundation—Education City, Doha, Qatar
[2]WHO Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis, Weill Cornell Medicine—Qatar, Cornell University, Qatar Foundation—Education City, Doha, Qatar
[3]Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University Düsseldorf, Dusseldorf, Germany
[4]Department of Population Health Sciences, Weill Cornell Medicine, Cornell University, New York, New York, USA

Handling editor Jason J Ong

Acknowledgements The authors gratefully acknowledge Professor Emeritus Rhoda Ashley Morrow from the University of Washington, for her support in assessing the quality of study diagnostic methods. The authors are also grateful for Ms Adona Canlas for administrative support. This publication was made possible by NPRP grant number 9-040-3-008 from the Qatar National Research Fund (a member of Qatar Foundation). The findings achieved herein are solely the responsibility of the authors. The authors are also grateful for pilot funding by the Biomedical Research Programme and infrastructure support provided by the Biostatistics, Epidemiology, and Biomathematics Research Core, both at Weill Cornell Medicine in Qatar.

Contributors MH and HM conducted the systematic search, data extraction and data analysis. MH wrote the first draft of the paper. LJA-R conceived the study and led the data extraction and analyses and interpretation of the results. All authors contributed to drafting and revising the manuscript.

Funding This work was supported by the Qatar National Research Fund (NPRP 9-040-3-008) and through pilot funding by the Biomedical Research Program at Weill Cornell Medicine in Qatar.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Laith J Abu-Raddad http://orcid.org/0000-0003-0790-0506

REFERENCES

1 James C, Harfouche M, Welton NJ, *et al*. Herpes simplex virus: global infection prevalence and incidence estimates, 2016. *Bull World Health Organ* 2020;98:315–29.
2 Abu-Raddad LJ, Magaret AS, Celum C, *et al*. Genital herpes has played a more important role than any other sexually transmitted infection in driving HIV prevalence in Africa. *PLoS One* 2008;3:e2230.

3 Benedetti J, Corey L, Ashley R. Recurrence rates in genital herpes after symptomatic first-episode infection. *Ann Intern Med* 1994;121:847–54.
4 Wald A, Krantz E, Selke S, *et al*. Knowledge of partners' genital herpes protects against herpes simplex virus type 2 acquisition. *J Infect Dis* 2006;194:42–52.
5 Wald A, Langenberg AG, Link K, *et al*. Effect of condoms on reducing the transmission of herpes simplex virus type 2 from men to women. *JAMA* 2001;285:3100–6.
6 Wald A, Zeh J, Selke S, *et al*. Reactivation of genital herpes simplex virus type 2 infection in asymptomatic seropositive persons. *N Engl J Med* 2000;342:844–50.
7 Mindel A, Marks C. Psychological symptoms associated with genital herpes virus infections: epidemiology and approaches to management. *CNS Drugs* 2005;19:303–12.
8 Mark H, Gilbert L, Nanda J. Psychosocial well-being and quality of life among women newly diagnosed with genital herpes. *J Obstet Gynecol Neonatal Nurs* 2009;38:320–6.
9 Gupta R, Warren T, Wald A. Genital herpes. *Lancet* 2007;370:2127–37.
10 Fisman DN. Health related quality of life in genital herpes: a pilot comparison of measures. *Sex Transm Infect* 2005;81:267–70.
11 Looker KJ, Magaret AS, May MT, *et al*. First estimates of the global and regional incidence of neonatal herpes infection. *Lancet Glob Health* 2017;5:e300–9.
12 Omori R, Nagelkerke N, Abu-Raddad LJ. HIV and herpes simplex virus type 2 epidemiological synergy: misguided observational evidence? A modelling study. *Sex Transm Infect* 2018;94:372–6.
13 Freeman EE, Weiss HA, Glynn JR, *et al*. 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.
14 Looker KJ, Elmes JAR, Gottlieb SL, *et al*. Effect of HSV-2 infection on subsequent HIV acquisition: an updated systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:1303–16.
15 Looker KJ, Welton NJ, Sabin KM, *et al*. Global and regional estimates of the contribution of herpes simplex virus type 2 infection to HIV incidence: a population attributable fraction analysis using published epidemiological data. *Lancet Infect Dis* 2020;20:240–9.
16 United Nations. *Transforming our world: the 2030 agenda for sustainable development*, 2016.
17 World Health Organization. *Global health sector strategy on sexually transmitted infections 2016-2021: toward ending STIs*. World Health Organization, 2016.
18 Gottlieb SL, Giersing BK, Hickling J, *et al*. Meeting report: initial World Health organization consultation on herpes simplex virus (HSV) vaccine preferred product characteristics, March 2017. *Vaccine* 2019;37:7408–18.
19 Gottlieb SL, Giersing B, Boily M-C, *et al*. Modelling efforts needed to advance herpes simplex virus (HSV) vaccine development: key findings from the world Health organization consultation on HSV vaccine impact modelling. *Vaccine* 2019;37:7336–45.
20 Fanfair RN, Zaidi A, Taylor LD, *et al*. Trends in seroprevalence of herpes simplex virus type 2 among non-Hispanic blacks and non-Hispanic whites aged 14 to 49 years--United States, 1988 to 2010. *Sex Transm Dis* 2013;40:860–4.
21 Douglas JM, Berman SM. Screening for HSV-2 infection in STD clinics and beyond: a few answers but more questions. *Sex Transm Dis* 2009;36:729–31.
22 Johnston C, Corey L. Current concepts for genital herpes simplex virus infection: diagnostics and pathogenesis of genital tract shedding. *Clin Microbiol Rev* 2016;29:149–61.
23 Giersing BK, Vekemans J, Nava S, *et al*. Report from the world Health organization's third product development for vaccines Advisory Committee (PDVAC) meeting, Geneva, 8-10th June 2016. *Vaccine* 2019;37:7315–27.
24 Gottlieb SL, Deal CD, Giersing B, *et al*. The global roadmap for advancing development of vaccines against sexually transmitted infections: update and next steps. *Vaccine* 2016;34:2939–47.
25 World Health Organization. *World Health organization preferred product characteristics for herpes 1 simplex virus vaccines*, 2018.
26 Ayoub HH, Chemaitelly H, Abu-Raddad LJ. Epidemiological impact of novel preventive and therapeutic HSV-2 vaccination in the United States: mathematical modeling analyses. *Vaccines* 2020;8. doi:10.3390/vaccines8030366. [Epub ahead of print: 08 Jul 2020].
27 World Health Organization. World Health Organization preferred product characteristics for herpes 2 simplex virus vaccines, 2019. Available: https://www.who.int/immunization/research/ppc-tpp/HSV_Vaccine_PPCs_for_Public_Comment.pdf [Accessed 3 Feb 2020].
28 Spicknall IH, Looker KJ, Gottlieb SL, *et al*. Review of mathematical models of HSV-2 vaccination: implications for vaccine development. *Vaccine* 2019;37:7396–407.
29 Harfouche M, Chemaitelly H, Abu-Raddad LJ. Herpes simplex virus type 1 epidemiology in Africa: systematic review, meta-analyses, and meta-regressions. *J Infect* 2019;79:289–99.
30 Sukik L, Alyafei M, Harfouche M, *et al*. Herpes simplex virus type 1 epidemiology in Latin America and the Caribbean: systematic review and meta-analytics. *PLoS One* 2019;14:e0215487.
31 Higgins J, Green S. *Cochrane handbook for systematic reviews of interventions*. John Wiley & Sons, 2011.
32 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
33 World Health Organization. WHO regional offices, 2017. Available: http://www.who.int/about/regions/en/ [Accessed Sep 2019].
34 United Nations-Department of Economic and Social Affairs. Standard country or area codes for statistical use. Available: https://unstats.un.org/unsd/methodology/m49/ [Accessed Apr 2020].
35 Ashley-Morrow R, Nollkamper J, Robinson NJ, *et al*. Performance of focus ELISA tests for herpes simplex virus type 1 (HSV-1) and HSV-2 antibodies among women in ten diverse geographical locations. *Clin Microbiol Infect* 2004;10:530–6.
36 Ashley RL. Performance and use of HSV type-specific serology test kits. *Herpes* 2002;9:38–45.
37 Borenstein MH, Higgins JPT, Rothstein HR. *Introduction to meta-analysis Chichester*. UK: John Wiley & Sons, Ltd, 2009.
38 Freeman MF, Tukey JW. Transformations related to the angular and the square root. *Ann Math Stat* 1950;21:607–11.
39 RStudio Team. *RStudio: integrated development for R*. Boston, MA: RStudio, Inc, 2015. http://www.rstudio.com/
40 Schwarzer G. Meta: an R package for meta-analysis. *R news* 2007;7:40–5.
41 StataCorp. *Stata statistical software: release 14*. College Station, TX: StataCorp LP, 2015.
42 Harbord RM, Higgins JPT. Meta-regression in Stata. *Stata Journal* 2008;8:493–519.
43 Balachandran N, Frame B, Chernesky M, *et al*. Identification and typing of herpes simplex viruses with monoclonal antibodies. *J Clin Microbiol* 1982;16:205–8.
44 HIV, STD and risk behaviors among female sex worker in El Salvador. Poster CDC0622. International AIDS Conference, Vienna, Austria, 2010.
45 do Nascimento MC, Sumita LM, de Souza VA, *et al*. Detection and direct typing of herpes simplex virus in perianal ulcers of patients with AIDS by PCR. *J Clin Microbiol* 1998;36:848–9.
46 Morales-Miranda S, Paredes M, Arambu N. HIV, STD and risk behaviors among men who have sex with men, female sex workers, and indigenous Garífuna population in Honduras. WEAX0305 In: International AIDS Conference Mexico, Mexico, 2008.
47 Sánchez J, Gotuzzo E, Escamilla J, *et al*. Sexually transmitted infections in female sex workers: reduced by condom use but not by a limited periodic examination program. *Sex Transm Dis* 1998;25:82–9.
48 Smith JS, Herrero R, Bosetti C, *et al*. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. *J Natl Cancer Inst* 2002;94:1604–13.
49 Vaccarella S, Franceschi S, Herrero R, *et al*. Sexual behavior, condom use, and human papillomavirus: pooled analysis of the IARC human papillomavirus prevalence surveys. *Cancer Epidemiol Biomarkers Prev* 2006;15:326–33.
50 Smith JS, Robinson NJ. Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. *J Infect Dis* 2002;186(Suppl 1):S3–28.
51 Dargham SR, Nasrallah GK, Al-Absi ES, *et al*. Herpes simplex virus type 2 seroprevalence among different national populations of middle East and North African men. *Sex Transm Dis* 2018;45:482–7.
52 Weiss H. Epidemiology of herpes simplex virus type 2 infection in the developing world. *Herpes* 2004;11(Suppl 1):24A–35.
53 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.
54 McQuillan G, Kruszon-Moran D, Flagg EW, *et al*. Prevalence of herpes simplex virus type 1 and type 2 in persons aged 14-49: United States, 2015-2016. *NCHS Data Brief* 2018;304:1–8.
55 Chemaitelly H, Nagelkerke N, Omori R, *et al*. Characterizing herpes simplex virus type 1 and type 2 seroprevalence declines and epidemiological association in the United States. *PLoS One* 2019;14:e0214151.
56 Ayoub HH, Amara I, Awad SF. Analytic characterization of the herpes simplex virus type 2 epidemic in the United States, 1950-2050. under review.
57 Abu-Raddad LJ, Schiffer JT, Ashley R, *et al*. HSV-2 serology can be predictive of HIV epidemic potential and hidden sexual risk behavior in the middle East and North Africa. *Epidemics* 2010;2:173–82.
58 Omori R, Abu-Raddad LJ. Sexual network drivers of HIV and herpes simplex virus type 2 transmission. *AIDS* 2017;31:1721–32.
59 van de Laar MJ, Termorshuizen F, Slomka MJ, *et al*. Prevalence and correlates of herpes simplex virus type 2 infection: evaluation of behavioural risk factors. *Int J Epidemiol* 1998;27:127–34.
60 Cowan FM, Johnson AM, Ashley R, *et al*. Antibody to herpes simplex virus type 2 as serological marker of sexual lifestyle in populations. *BMJ* 1994;309:1325–9.
61 Obasi A, Mosha F, Quigley M, *et al*. Antibody to herpes simplex virus type 2 as a marker of sexual risk behavior in rural Tanzania. *J Infect Dis* 1999;179:16–24.
62 Kouyoumjian SP, Heijnen M, Chaabna K, *et al*. Global population-level association between herpes simplex virus 2 prevalence and HIV prevalence. *AIDS* 2018;32:1343–52.
63 Hallett TB, Gregson S, Mugurungi O, *et al*. Assessing evidence for behaviour change affecting the course of HIV epidemics: a new mathematical modelling approach and application to data from Zimbabwe. *Epidemics* 2009;1:108–17.

64 Hallett TB, Aberle-Grasse J, Bello G, *et al*. Declines in HIV prevalence can be associated with changing sexual behaviour in Uganda, urban Kenya, Zimbabwe, and urban Haiti. *Sex Transm Infect* 2006;82(Suppl 1):i1–8.
65 Kilian AH, Gregson S, Ndyanabangi B, *et al*. Reductions in risk behaviour provide the most consistent explanation for declining HIV-1 prevalence in Uganda. *AIDS* 1999;13:391–8.
66 Awad SF, Abu-Raddad LJ. Could there have been substantial declines in sexual risk behavior across sub-Saharan Africa in the mid-1990s? *Epidemics* 2014;8:9–17.
67 Wijesooriya NS, Rochat RW, Kamb ML, *et al*. Global burden of maternal and congenital syphilis in 2008 and 2012: a health systems modelling study. *Lancet Glob Health* 2016;4:e525–33.
68 World Health Organization. *Global health sector strategy on sexually transmitted infections 2016–2021: towards ending STIs*. Geneva, 2016.
69 Gayet C, Juarez F, Bozon M. *Sexual practices of Latin America and the Caribbean*. International handbook on the demography of sexuality: Springer, 2013: 67–90.
70 UNAIDS. Global HIV & AIDS statistics — 2019 fact sheet 2019. Available: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf [Accessed Mar 2020].
71 Smolak A, Rowley J, Nagelkerke N, *et al*. Trends and predictors of syphilis prevalence in the general population: global pooled analyses of 1103 prevalence measures including 136 million syphilis tests. *Clin Infect Dis* 2018;66:1184–91.
72 Wald A, Corey L, Arvin A. Persistence in the population: epidemiology, transmission. In: Arvin A, Fiume GC, Mocarski E, *et al*, eds. *Human herpesviruses: biology, therapy, and immunoprophylaxis*. Cambridge: Cambridge University Press, 2007.
73 Looker KJ, Magaret AS, Turner KME, *et al*. Global estimates of prevalent and incident herpes simplex virus type 2 infections in 2012. *PLoS One* 2015;10:e114989.
74 Bradley H, Markowitz LE, Gibson T, *et al*. Seroprevalence of herpes simplex virus types 1 and 2--United States, 1999-2010. *J Infect Dis* 2014;209:325–33.
75 Dévieux JG, Rosenberg R, Saint-Jean G, *et al*. The continuing challenge of reducing HIV risk among Haitian youth: the need for intervention. *J Int Assoc Provid AIDS Care* 2015;14:217–23.
76 Korenromp EL, Mahiané SG, Nagelkerke N, *et al*. Syphilis prevalence trends in adult women in 132 countries - estimations using the Spectrum Sexually Transmitted Infections model. *Sci Rep* 2018;8:11503.
77 Nasrallah GK, Dargham SR, Mohammed LI, *et al*. Estimating seroprevalence of herpes simplex virus type 1 among different middle East and North African male populations residing in Qatar. *J Med Virol* 2018;90:184–90.
78 Chaabane S, Harfouche M, Chemaitelly H, *et al*. Herpes simplex virus type 1 epidemiology in the middle East and North Africa: systematic review, meta-analyses, and meta-regressions. *Sci Rep* 2019;9:1–11.
79 Harfouche M, Chemaitelly H, Abu-Raddad LJ. Herpes simplex virus type 1 epidemiology in Africa: systematic review, meta-analyses, and meta-regressions. *J Infect* 2019;79:289–99.
80 Ayoub HH, Chemaitelly H, Abu-Raddad LJ. Characterizing the transitioning epidemiology of herpes simplex virus type 1 in the USA: model-based predictions. *BMC Med* 2019;17:57.
81 Bernstein DI, Bellamy AR, Hook EW, *et al*. Epidemiology, clinical presentation, and antibody response to primary infection with herpes simplex virus type 1 and type 2 in young women. *Clin Infect Dis* 2013;56:344–51.
82 Löwhagen GB, Tunbäck P, Andersson K, *et al*. First episodes of genital herpes in a Swedish STD population: a study of epidemiology and transmission by the use of herpes simplex virus (HSV) typing and specific serology. *Sex Transm Infect* 2000;76:179–82.
83 Nilsen A, Myrmel H. Changing trends in genital herpes simplex virus infection in Bergen, Norway. *Acta Obstet Gynecol Scand* 2000;79:693–6.
84 Samra Z, Scherf E, Dan M. Herpes simplex virus type 1 is the prevailing cause of genital herpes in the Tel Aviv area, Israel. *Sex Transm Dis* 2003;30:794–6.
85 Gilbert M, Li X, Petric M, *et al*. Using centralized laboratory data to monitor trends in herpes simplex virus type 1 and 2 infection in British Columbia and the changing etiology of genital herpes. *Can J Public Health* 2011;102:225–9.
86 Roberts CM, Pfister JR, Spear SJ. Increasing proportion of herpes simplex virus type 1 as a cause of genital herpes infection in college students. *Sex Transm Dis* 2003;30:797–800.
87 Khadr L, Harfouche M, Omori R, *et al*. The epidemiology of herpes simplex virus type 1 in Asia: systematic review, meta-analyses, and meta-regressions. *Clinical Infectious Diseases* 2019;68:757–72.
88 Yousuf W, Ibrahim H, Harfouche M, *et al*. Herpes simplex virus type 1 in Europe: systematic review, meta-analyses and meta-regressions. *BMJ Glob Health* 2020;5:e002388.
89 Nasrallah GK, Dargham SR, Sahara AS, *et al*. Performance of four diagnostic assays for detecting herpes simplex virus type 2 antibodies in the middle East and North Africa. *J Clin Virol* 2019;111:33–8.
90 Delany-Moretlwe S, Jentsch U, Weiss H, *et al*. Comparison of focus HerpesSelect and Kalon HSV-2 gG2 ELISA serological assays to detect herpes simplex virus type 2 antibodies in a South African population. *Sex Transm Infect* 2010;86:46–50.
91 Mujugira A, Morrow RA, Celum C, *et al*. Performance of the focus HerpeSelect-2 enzyme immunoassay for the detection of herpes simplex virus type 2 antibodies in seven African countries. *Sex Transm Infect* 2011;87:238–41.

Web extra material

Epidemiology of herpes simplex virus type 2 in Latin America and the Caribbean: systematic review, meta-analyses, and meta-regressions

Manale Harfouche MPH[a,b], Haifa Maalmi PhD[a,c], and Laith J. Abu-Raddad PhD[a,b,d]

[a] *Infectious Disease Epidemiology Group, Weill Cornell Medicine-Qatar, Cornell University, Qatar Foundation - Education City, Doha, Qatar*

[b] *World Health Organization Collaborating Centre for Disease Epidemiology Analytics on HIV/AIDS, Sexually Transmitted Infections, and Viral Hepatitis, Weill Cornell Medicine–Qatar, Cornell University, Qatar Foundation – Education City, Doha, Qatar*

[c] *Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Dusseldorf, Dusseldorf, Germany;*

[d] *Department of Population Health Sciences, Weill Cornell Medicine, Cornell University, New York, New York, US*

Table of Contents

Table S1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist.[1]

Section/topic	#	Checklist item	Reported in main text on
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	p.1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	p. 2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	p. 5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	p. 5-6
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	p. 6; Box 1
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	p. 6; Box 1
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Table S2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	p. 6; Box 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	p. 6; Box 1
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Box 1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	p. 7; Box 1
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	p. 7; Box 1
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	p. 7; Box 1
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	p. 7; Box 1
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating	p. 7; Box 1

		which were pre-specified.	
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p. 7-8; Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	p. 8 and p. 11; Tables S3, S4, and S7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	p. 11; Table S8
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	p. 7-11; Tables 1, 2, and 3; Figures S1 and S2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	p. 9-10; Tables 1, 2, and 4; Figures S1 and S2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	p. 11; Table S8
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	p. 9-10; Table 3; Tables S5 and S6
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	p. 12-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	p. 14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	p. 14-15
funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	p. 3

Abbreviations: NA = Not applicable, p = page

Table S2. Data sources and search criteria for systematically reviewing HSV-2 epidemiology in Latin America and the Caribbean.

PubMed (last searched: March 12, 2020)
(Simplexvirus[MeSH] OR Herpes Simplex[MeSH] OR Herpes Genitalis[MeSH] OR Herpes Hominis[Text] OR HSV type-2[Text] OR HSV type 2[Text] OR HSV2[Text] OR HSV-2[Text] OR HSV [Text] OR Human herpes virus[Text] OR Herpes simplex virus type 2[Text] OR Herpes simplex virus type-2[Text] OR herpes simplex virus 2[Text] OR herpes simplex virus-2[Text] OR herpes simplex type 2[Text] OR herpes simplex type-2[Text] OR herpes simplex 2[Text] OR herpes simplex-2[Text] OR Herpesvirus type 2[Text] OR Herpesvirus type-2[Text] OR Herpesvirus 2[Text] OR Herpesvirus-2[Text] OR Herpes virus type 2[Text] OR Herpes virus type-[Text] OR Herpes virus [Text] OR Herpes virus-2[Text] OR genital herpes[Text] OR Herpes Genitalis[Text] OR Stomatitis Herpetic[Text] OR Herpes Labialis[Text]) AND (“Latin America”[MeSH] OR “Central America"[MeSH] OR “South America”[Mesh] OR “Caribbean Region”[MeSH] OR “Mexico”[MeSH]) OR (Anguilla*[Text] OR Aruba*[Text] OR Antigua and Barbuda[Text] OR Argentin*[Text] OR Bahamas*[Text] OR Barbados*[Text] OR Beliz*[Text] OR Bermuda*[Text] OR Bolivia*[Text] OR Brazil*[text] OR “British Virgin Islands”[Text] OR Latin America[Text] OR Latin American*[Text] OR Caribbean*[Text] OR Cayman Islands[Text] OR Chile*[Text] OR Colombia*[Text] OR Costa Rica*[Text] OR Cuba*[Text] OR Curacao*[Text] OR Central America[Text] OR Central American*[text] OR Dominica*[Text] OR Dominican republic[Text] OR Ecuador*[Text] OR El Salvador[Text] OR French Guiana[Text] OR Grenad*[Text] OR Guadeloup*[Text] OR Guatemal*[Text] OR Guyan*[Text] OR Haiti*[Text] OR Honduras*[Text] OR Jamaic*[Text] OR Martiniqu*[Text] OR Montserrat*[Text] OR Mexic*[Text] OR Nicaragua*[Text] OR Panama*[Text] OR Paraguay*[Text] OR Peru*[Text] OR Puerto Rico[Text] OR Puerto Rica*[text] OR Saint Kitts and Nevis[Text] OR Saint Lucia[Text] OR Saint Vincent and the Grenadines[Text] OR Suriname*[Text] OR Saint Martin[Text] OR Sint Maarten[Text] OR South America[Text] OR South American*[Text] OR Trinidad and Tobago[Text] OR Turks and Caicos[Text] OR Uruguay*[Text] OR United States Virgin Islands[Text] OR Venezuel*[Text])
Embase (last searched: March 12, 2020)
(exp Herpes simplex/ or exp Herpesviridae/) OR (Herpes simplex or Herpes simplex virus or HSV type-2 or HSV type 2 or HSV2 or HSV-2 or HSV 2 or human herpes virus or Herpes simplex virus type 2 or Herpes simplex virus type-2 or herpes simplex virus 2 or herpes simplex virus-2 or herpes simplex type 2 or herpes simplex type-2 or herpes simplex 2 or herpes simplex-2 or Herpesvirus type 2 or Herpesvirus type-2 or Herpesvirus 2 or Herpesvirus-2 or Herpes virus type 2 or Herpes virus type-2 or Herpes virus 2 or Herpes virus-2 or genital herpes or Herpes Genitalis or herpes labialis or herpetic stomatitis).mp.) AND (exp "Antigua and Barbuda"/ or exp Argentina/ or exp Aruba/ or exp Bahamas/ or exp Barbados/ or exp Belize/ or exp Bolivia/ or exp Brazil/ or exp "Virgin Islands (British)"/ or exp Cayman Islands/ or exp Chile/ or exp Colombia/ or exp Costa Rica/ or exp Cuba/ or exp Curacao/ or exp Dominica/ or exp Dominican Republic/ or exp Ecuador/ or exp El Salvador/ or exp French Guiana/ or exp Grenada/ or exp Guadeloupe/ or exp Guatemala/ or exp Guyana/ or exp Haiti/ or exp Honduras/ or exp Jamaica/ or exp Martinique/ or exp Mexico/ or exp Montserrat/ or exp Nicaragua/ or exp Panama/ or exp Paraguay/ or exp Peru/ or exp Puerto Rico/ or exp Saint Lucia/ or exp "saint martin (dutch)"/ or exp "saint martin (french)"/ or exp Suriname/) or (exp "Trinidad and Tobago"/ or exp "Virgin Islands (U.S.)"/ or exp Uruguay/ or exp Venezuela/ or exp South America/ or exp Central America/ or exp Caribbean/ or exp "Caribbean (person)"/ or exp Caribbean Netherlands/ or exp Caribbean Islands/ or exp South American/ or exp Central American/ or exp Latin America/) or (Antigua or Argentina or Argentinian or Aruba or Aruban or Bahamas or Belize or belizian or Bolivia or Bolivian or Brazil or Brazilian or British virgin islands or Cayman islands or Chile or Chilean or Colombia or Colombian or Costa Rica or costa Rican or Cuba or Cuban or Curacao or Dominica or Dominican or Dominican republic or Ecuador or Ecuadorian or el Salvador

or el Salvadorian).mp. or (French Guiana or Grenada or Guadeloupe or Guatemala or Guatemalan or Guyana or Haitian or Honduras or Honduran or Jamaica or Jamaican or Martinique or Mexico or Mexican or Montserrat or Nicaragua or Nicaraguan or panama or Panamanian or Paraguay or Paraguayans or Peru or Peruvian* or Puerto Rico or Puerto Ricans or saint Lucia or saint Lucian or Latin America* or south American* or central American*).mp. or ((Turks and caicos) or (saint Vincents and the grenadines) or (saint kitts and the nevis)).mp.
LILACS (last searched: March 12, 2020)
((tw:(herpes)) OR (tw:(herpesvirus 2)) OR (tw:(herpes simplex)) OR (tw:(hsv type-2)) OR (tw:(hsv type 1)) OR (tw:(hsv2)) OR (tw:(hsv-2)) OR (tw:(hsv 2)) OR (tw:(human herpes virus)) OR (tw:(herpes simplex virus type 2)) OR (tw:(herpes simplex virus type-2)) OR (tw:(herpes simplex virus 2)) OR (tw:(herpes simplex virus-2)) OR (tw:(herpes simplex type 2)) OR (tw:(herpes simplex type-2)) OR (tw:(herpes simplex 2)) OR (tw:(herpes simplex-2)) OR (tw:(herpesvirus type 2)) OR (tw:(herpesvirus type-2)) OR (tw:(herpesvirus 2)) OR (tw:(herpesvirus-2)) OR (tw:(herpes virus type 2)) OR (tw:(herpes virus type-2)) OR (tw:(herpes virus 2)) OR (tw:(herpes virus-2)) OR (tw:(genital herpes)) OR (tw:(herpes genitalis)) OR (tw:(stomatitis herpetic))) **AND** (pais_assunto:("america do sul" OR "brasil" OR "oceania" OR "mexico" OR "argentina" OR "caribe ingles" OR "caribe" OR "chile" OR "america central" OR "colombia" OR "venezuela" OR "jamaica" OR "peru" OR "cuba" OR "costa rica" OR "puerto rico" OR "panama" OR "bolivia" OR "haiti" OR "ecuador" OR "guyana francesa" OR "guyana" OR "barbados" OR "trinidad y tobago" OR "uruguay" OR "honduras" OR "el salvador" OR "guatemala" OR "paraguay" OR "nicaragua" OR "republica dominicana" OR "dominica" OR "bahamas" OR "grenada" OR "martinica" OR "santa lucia" OR "suriname"))

Abbreviations: HSV-2 = Herpes simplex virus type 2.

Box S1. Definitions of population type classifications[a].

1. **General populations** (populations at low risk): these include populations at lower risk of exposure to HSV-2, such as antenatal clinic attendees, blood donors, and pregnant women, among others.
2. **Intermediate-risk populations**: these include populations who presumably have frequent sexual contacts with populations engaging in high sexual risk behavior, and have therefore a higher risk of exposure to HSV-2 than the general population. These comprise prisoners, people who inject drugs, and truck drivers, among others.
3. **High-risk populations**: these include populations at high risk of exposure to HSV-2 as a consequence of specific sexual risk behaviors such as female sex workers, men who have sex with men, male sex workers, and transgender populations, among others.
4. **HIV positive individuals and individuals in HIV discordant couples**: these include populations who are HIV positive or are in a spousal relationship with an HIV positive individual.
5. **STI clinic attendees and symptomatic populations**: these include patients attending STI clinics, or have clinical manifestations related to an STI.
6. **Other populations**: these include populations not satisfying above definitions, or populations with an undetermined risk of acquiring HSV-2 infection such as cervical cancer patients and their spouses.

[a] These population types were selected based on our understanding of HIV/STI epidemiology and the variability of risk of exposure in different population types, as informed by existing literature on HIV and STIs.[2-6]

Abbreviations: HSV-2 Herpes simplex virus type 2, STI = Sexually transmitted infection, HIV = Human immunodeficiency virus.

Table S3. Studies reporting HSV-2 seroconversion rate or incidence rate in Latin America and the Caribbean.

Author, year	Year(s) of data collection	Country	Original study design	Population characteristics	HSV-2 serological assay	Sample size	Follow-up duration	Person-years of follow-up	HSV-2 Seroconversion rate (%)	HSV-2 Incidence rate (per 100 person-years)
General populations										
Lupi, 2011 [7]	1996-97	Brazil	Cohort	Blood donors	ELISA	110	1 year	-	2.0	-
Sánchez-Alemán, 2010 [8]	2001-05	Mexico	Cohort	Female students	ELISA	376	-	466.2	5.6	4.5
Sánchez-Alemán, 2010 [8]	2001-05	Mexico	Cohort	Male students	ELISA	128	-	203.0	5.5	4.5
Intermediate-risk populations										
Konda, 2013 [9]	2001-03	Peru	RCT	Men engaging in risky behaviors	ELISA	1,741	2 years	-	3.4	-
High-risk populations										
Castillo, 2015 [10]	2009-11	Peru	RCT	Transgender women	ELISA	40	18 months	-	-	12.2
Castillo, 2015 [10]	2009-11	Peru	RCT	MSM	ELISA	217	18 months	-	-	17.9
Konda, 2013 [9]	2001-03	Peru	RCT	Bisexual men	ELISA	311	2 years	-	4.6	-
Konda, 2013[9]	2001-03	Peru	RCT	MSM	ELISA	93	2 years	-	13.4	-
Lupi, 2011 [7]	1996-97	Brazil	Cohort	MSM	ELISA	103	1 year	-	8.00	-
Sanchez, 2009 [11]	1998-00	Peru	Cohort	MSM	WB	55	335 days	-	-	10.4
Sanchez, 2009 [11]	1998-00	Peru	Cohort	HIV negative MSM	WB	42	335 days	-	11.9	-
HIV positive individuals and individuals in HIV discordant couples										
Sanchez, 2009 [11]	1998-00	Peru	Cohort	HIV positive MSM	WB	13	335 days	-	30.8	-
Yanez Alvarez, 2011 [12]	2003-05	Mexico	Cohort	People living with HIV	ELISA	131	1.5 years	174.0	51.1	38.5

Abbreviations: ELISA = Enzyme-linked immunosorbent assay, HIV = Human immunodeficiency virus, HSV-2 = Herpes simplex virus type 2, MSM = Men who have sex with men, RCT = Randomized controlled trial, WB = Western blot.

Harfouche M, *et al. Sex Transm Infect* 2021;0:1–11. doi: 10.1136/sextrans-2021-054972

Table S4. Studies reporting HSV-2 seroprevalence in Latin America and the Caribbean by population type.

Author, year	Year(s) of data collection	Country	Study site	Original study design*	Sampling method	Population	HSV-2 serological assay	Sample size	HSV-2 seroprevalence (%)
General populations									
Abraham, 2003 [13]	2000	Mexico	Community	CS	CRS	Male students	WB	517	4.1
Abraham, 2003 [13]	2000	Mexico	Community	CS	CRS	Female students	WB	381	7.9
Alberts, 2013 [14]	2005-09	Mexico	Community	CS	Conv	Mexican men	ELISA	1,312	8.8
Alberts, 2013 [14]	2005-09	Brazil	Community	CS	Conv	Brazilian men	ELISA	1,388	38.4
Almeida, 2017 [15]	2011-14	Brazil	Outpatient clinic	CS	Conv	Patients with benign nodules	ELISA	83	28.0
Ashley-Morrow, 2004 [16]	2000-01	Mexico	Community	CS	Conv	Mexican women	WB	94	44.6
Ashley-Morrow, 2004 [16]	2000-01	Costa Rica	Community	CS	Conv	Costa Rican women	WB	94	42.5
Ashley-Morrow, 2004 [16]	2000-01	Argentina	Community	CS	Conv	Argentinian women	WB	97	39.1
Boulos, 1992 [17]	1986-88	Haiti	Community	CS	Conv	Pregnant Haitian women	ELISA	89	54.0
Cárcamo, 2012 [18]	2002	Peru	Community	CS	CRS	18-29 years old women	ELISA	1,486	13.6
Cárcamo, 2012 [18]	2002	Peru	Community	CS	CRS	18-29 years old men	ELISA	1,176	13.5
Carvalho, 1999 [19]	1993-97	Brazil	Outpatient clinic	CS	Conv	Pregnant women	WB	102	22.6
Carvalho, 1999 [19]	1993-97	Brazil	Community	CS	Conv	College students	WB	101	6.9
Clark, 2008 [20]	2003-04	Peru	Community	CS	Conv	Healthy men	ELISA	1,797	16.0
Clemens, 2010 [21]	1996-97	Brazil	Community	CS	CRS	General population in Brazil	ELISA	1,090	11.3
Conde-Glez, 2013 [22]	2005-06	Mexico	Community	CS	MSCS	General population in Mexico	ELISA	3,616	9.9
Conde-Gonzalez, 2003 [23]	2000-00	Mexico	Community	CS	CRS	Women from the general population	WB	730	29.3
Cowan, 2003 [24]	1992-00	Brazil	Community	CS	Conv	Male blood donors	ELISA	398	25.9
Cowan, 2003 [24]	1992-00	Brazil	Community	CS	Conv	Female blood donors	ELISA	84	42.9
Cowan, 2003 [24]	1992-00	Brazil	Community	CS	Conv	Antenatal clinic attendees	ELISA	399	29.3
Cowan, 2003 [24]	1992-00	Brazil	Community	CS	Conv	1-15 years old children	ELISA	697	2.4
Da-Rosa santos, 1996 [25]	1994-94	Brazil	Community	CS	Conv	Blood donors	ELISA	155	29.1
De Sanjose, 1994 [26]	1985-88	Colombia	Community	CC	RS	Healthy women	ELISA	237	49.8
Domercant, 2017 [27]	2012-12	Haiti	Outpatient clinic	CS	Conv	Pregnant women	ELISA	784	30.5
Gabster, 2019 [28]	2018-18	Panama	Community	CS	CRS	Female students	ELISA	273	10.2
Gabster, 2019 [28]	2018-18	Panama	Community	CS	CRS	Male student	ELISA	286	15.7
Goncalez, 2006 [29]	2004-04	Brazil	Community	CS	CRS	Blood donors	ELISA	1,600	15.6
Goncalez, 2015 [30]	2012-13	Brazil	Community	RCT	CRS	Blood donors in the intervention arm	ELISA	6,298	10.4
Goncalez, 2015 [30]	2012-13	Brazil	Community	RCT	CRS	Blood donors in the control arm	ELISA	5,569	11.1
Gutierrez, 2006 [31]	-	Mexico	Community	CS	MSCS	Mexican adolescents in poor urban areas	ELISA	753	12.0
Gutierrez, 2007 [32]	2002-03	Mexico	Community	CS	CRS	School students	ELISA	1,429	18.9
Herrera-Ortiz, 2013 [33]	2006-09	Mexico	Outpatient clinic	CS	Conv	Pregnant women	ELISA	2,300	14.5
Juarez-Figueroa, 1997 [34]	1992-92	Mexico	Community	CS	Conv	Men getting tested for HIV	WB	538	28.8
Konda, 2005 [35]	2000-02	Peru	Community	CS	CRS	Women from the general population	EIA	965	20.0
Konda, 2005 [35]	2000-02	Peru	Community	CS	CRS	Men from the general population	EIA	670	7.0
Lazcano-Ponce, 2001 [36]	1994-96	Mexico	Community	CS	CRS	Women from Mexico	WB	730	29.8
Levett, 2005 [37]	-	Barbados	Outpatient clinic	CS	Conv	Pregnant women	ELISA	122	40.2
Levett, 2005 [37]	-	Barbados	Community	CS	Conv	Blood donors	ELISA	184	34.2
Lupi, 2011 [7]	1996-97	Brazil	Community	Cohort	Conv	Male blood donors	ELISA	155	29.0
Moreira, 2018 [38]	2015-16	Brazil	Hospital	CC	Conv	Mothers of children without congenital malformation	ELISA	160	47.1
Moreira, 2018 [38]	2015-16	Brazil	Hospital	CC	Conv	Mothers of children with congenital malformation	ELISA	32	28.1
Munoz, 1995 [39]	1985-88	Colombia	Outpatient clinic	CC	Conv	Healthy women	ELISA	141	67.3
Munoz, 1995 [39]	1985-88	Colombia	Outpatient clinic	CC	Conv	Healthy men	ELISA	126	64.3
Munoz, 1995 [39]	1985-88	Colombia	Outpatient clinic	CC	Conv	Healthy men	ELISA	73	56.2
Nascimento, 2007 [40]	1995-03	Brazil	Outpatient clinic	CS	Conv	1-2 years old children	WB	249	1.6
Nascimento, 2008 [41]	2003-03	Brazil	Community	CS	Conv	Blood donors in Brazil	ELISA	3,493	26.4
Nascimento, 2009 [42]	2003-04	Brazil	Community	CS	Conv	Non-Amerindian population	ELISA	181	29.8
Nascimento, 2009 [42]	2003-04	Brazil	Community	CS	Conv	Blood donors	ELISA	1,121	35.8

Nascimento, 2009 [42]	2003-04	Brazil	Community	CS	Conv	Amerindian population	ELISA	339	7.4
Oberle, 1989 [43]	1984-85	Costa Rica	Community	CS	CRS	Healthy women	Monoclonal antibody	766	39.4
Patnaik, 2007 [44]	1995-97	Peru	Hospital	CS	Conv	Middle-aged women in Peru	WB	171	35.7
Patnaik, 2007 [44]	1995-97	Colombia	Community	CS	Conv	Middle-aged women in Colombia	WB	65	56.9
Patzi-Churqui, 2020 [45]	2015-19	Bolivia	Community	CS	Conv	Healthy women	WB	389	53.0
Paz-Bailey, 2009 [46]	2006-06	Honduras	Community	CS	MSCS	Honduran-Garifuna participants	ELISA	791	51.1
Rodrıguez, 2003 [47]	1993-94	Costa Rica	Community	Cohort	CRS	Women from the Guanacaste cohort	ELISA	1,100	38.4
Sanchez, 1996 [48]	1991-92	Peru	Outpatient clinic	CS	CRS	>18 years old women	WB	201	21.5
Sanchez, 1996 [48]	1991-92	Peru	Outpatient clinic	CS	CRS	>18 years old men	WB	281	7.7
Sanchez-Aleman, 2005 [49]	2000-01	Mexico	Community	CS	Conv	Students from Mexico	WB	340	5.9
Sánchez-Alemán, 2008 [50]	2001-03	Mexico	Community	CS	Conv	University students	WB	711	4.0
Sánchez-Alemán, 2010 [8]	2003-05	Mexico	Community	CS	Conv	University students	ELISA	592	2.2
Sierra, 2011 [51]	2002-03	Colombia	Community	CS	CRS	Sexual active women	ELISA	869	19.1
Sierra, 2011 [51]	2002-03	Colombia	Community	CS	CRS	Not sexually active women	ELISA	57	1.7
Smith, 2001 [52]	1990-91	Brazil	Outpatient clinic	CC	Conv	Middle-aged women	ELISA	181	42.0
Smith, 2002 [53]	-	Peru	Hospital	CC	Conv	Peruvian women	WB	171	35.7
Smith, 2002 [53]	-	Colombia	Community	CC	Conv	Colombian women	WB	65	56.9
Uribe-Salas, 2009 [54]	2000-00	Mexico	Community	CS	MSCS	Adults in Mexico	ELISA	6,156	17.3
Vaccarella, 2006 [55]	1997-00	Argentina	Community	CS	RS	Healthy women	ELISA	907	37.0
Weinberg, 1993 [56]	1988-89	Brazil	Hospital	CS	Conv	Pregnant women of low socioeconomic status	WB	60	46.0
Weinberg, 1993 [56]	1988-89	Brazil	Hospital	CS	Conv	Pregnant women of middle socioeconomic status	WB	94	36.0
Zamilpa-Mejía, 2003 [57]	1994-95	Mexico	Outpatient clinic	CS	Conv	Women in Mexico city	WB	448	18.1
Zamilpa-Mejía, 2003 [57]	1994-95	Mexico	Outpatient clinic	CS	Conv	Women in Cuernavaca city	WB	388	28.3
Intermediate-risk populations									
Benzaken, 2012 [58]	2009	Brazil	Community	CS	Conv	Individuals attending the leisure circuit	ELISA	585	62.1
Celentano, 2010 [59]	2001-01	Peru	Community	CS	Conv	Promiscuous women	ELISA	294	43.5
Celentano, 2010 [59]	2001-01	Peru	Community	CS	Conv	Promiscuous men	ELISA	2,645	24.4
Clark, 2009 [60]	2003-05	Peru	Community	CS	CRS	Women in slums	ELISA	320	40.6
Couture, 2008 [61]	2006-07	Haiti	Community	CS	Conv	Clients of FSWs in Haiti	ELISA	351	22.0
Konda, 2005 [35]	2000-02	Peru	Community	CS	TLS	Men from a socially marginalized population	EIA	919	20.7
Konda, 2005 [35]	2000-02	Peru	Community	CS	TLS	Women from a socially marginalized population	EIA	108	42.6
Pinho, 2011 [62]	2003-05	Brazil	Community	CS	Conv	Brazilian truck drivers	ELISA	799	26.6
Sabidó, 2011 [63]	2008-09	Guatemala	Community	CS	Conv	Clients of FSWs	ELISA	351	3.4
Uribe-Salas, 1995 [64]	1993-93	Mexico	Community	CS	Conv	Men working in bars	WB	171	32.4
Villarroel-Torrico, 2018 [65]	2013-13	Bolivia	Prison	CS	Conv	>16 years old female prisoners	ELISA	219	62.6
High-risk populations									
Brito, 2015 [66]	2013	Dominican Republic	Community	CS	SS	MSM and transgender women	ELISA	100	38.0
Cárcamo, 2012 [18]	2002-03	Peru	Community	CS	CRS	18-29 years old FSWs	ELISA	381	67.0
Castillo, 2015 [10]	2009-11	Peru	Community	RCT	SS	Transgender men	ELISA	208	80.7
Castillo, 2015 [10]	2009-11	Peru	Community	RCT	SS	25-35 years old MSM	ELISA	510	65.0
Clark, 2009 [60]	2003-05	Peru	Community	CS	CRS	Male sex workers	ELISA	2,424	13.0
Clark, 2009 [60]	2003-05	Peru	Community	CS	CRS	MSM	ELISA	541	69.0
Conde-Glez, 1999 [67]	1992-92	Mexico	Outpatient clinic	CS	Conv	FSWs in Mexico	WB	997	60.8
Creswell, 2010 [68]	2008	El Salvador	Community	CS	RDS	FSWs	ELISA	663	82.6
Da-Rosa santos, 1996 [25]	1994-94	Brazil	Community	CS	Conv	FSWs in Brazil	ELISA	20	75.0
Gotuzzo, 1994 [69]	1991-92	Peru	Outpatient clinic	CS	Conv	FSWs in Peru	WB	400	82.2
Hakre, 2013 [70]	2009-11	Panama	Community	CS	TLS	FSWs in Panama	ELISA	999	74.2
Hakre, 2014 [71]	2011-12	Panama	Community	CS	RDS	MSM in David city	ELISA	203	38.4
Hakre, 2014 [71]	2011-12	Panama	Community	CS	RDS	MSM in Panama city	ELISA	305	62.6
Hakre, 2014 [71]	2011-12	Panama	Community	CS	RDS	MSM in Colon	ELISA	91	72.9
Hernandez, 2011 [72]	2009-10	Nicaragua	Community	CS	RDS	MSM	ELISA	632	39.9
Konda, 2005 [35]	2000-02	Peru	Community	CS	TLS	MSM	EIA	167	72.5
Lama, 2006 [73]	2002-03	Peru	Community	CS	SS	MSM	ELISA	3,280	46.3

Lupi, 2011 [7]	1996-97	Brazil	Community	Cohort	Conv	MSM	ELISA	170	39.4
Morales-Miranda, 2008 [74]	2006	Honduras	Community	CS	RDS	FSWs	ELISA	808	61.4
Nascimento, 2007 [40]	1995-03	Brazil	Outpatient clinic	CS	Conv	MSM	WB	29	45.0
Perez-Brumer, 2013 [75]	2007-07	Peru	Outpatient clinic	CS	Conv	MSM in Lima	ELISA	560	55.4
Perla, 2012 [76]	2002-03	Peru	Community	CS	SS	FSWs in Peru	ELISA	211	80.1
Rodrigues, 2009 [77]	1994-98	Brazil	Community	CS	Conv	MSM	ELISA	403	45.7
Sanchez, 1998 [78]	1991-92	Peru	Outpatient clinic	CS	Conv	FSWs registered for routine examination	WB	283	82.0
Sanchez, 1998 [78]	1991-92	Peru	Outpatient clinic	CS	Conv	FSWs not registered for routine examination	WB	116	82.8
Sanchez, 2007 [79]	2002-02	Peru	Community	CS	SS	MSM	ELISA	1,328	51.0
Sanchez, 2009 [11]	1998-00	Peru	Outpatient clinic	Cohort	SS	MSM	WB	82	41.5
Shah, 2014 [80]	2008-08	El Salvador	Community	CS	RDS	MSM	ELISA	703	48.1
Shah, 2014 [80]	2008-08	El Salvador	Community	CS	RDS	FSWs	ELISA	768	82.3
Silva-Santisteban, 2012 [81]	2009-09	Peru	Community	CS	RDS	Transgender women in Lima	ELISA	436	79.4
Soto, 2007 [82]	2001-02	El Salvador	Outpatient clinic	CS	MSCS	FSWs from El Salvador	ELISA	136	95.7
Soto, 2007 [82]	2001-02	El Salvador	Community	CS	TLS	MSM from El Salvador	ELISA	81	56.5
Soto, 2007 [82]	2001-02	Guatemala	Outpatient clinic	CS	MSCS	FSWs from Guatemala	ELISA	589	88.6
Soto, 2007 [82]	2001-02	Guatemala	Community	CS	TLS	MSM from Guatemala	ELISA	362	43.3
Soto, 2007 [82]	2001-02	Honduras	Outpatient clinic	CS	MSCS	FSWs from Honduras	ELISA	457	91.1
Soto, 2007 [82]	2001-02	Honduras	Community	CS	TLS	MSM from Honduras	ELISA	316	50.9
Soto, 2007 [82]	2001-02	Nicaragua	Outpatient clinic	CS	MSCS	FSWs from Nicaragua	ELISA	553	82.1
Soto, 2007 [82]	2001-02	Nicaragua	Community	CS	TLS	MSM from Nicaragua	ELISA	269	53.8
Soto, 2007 [82]	2001-02	Panama	Outpatient clinic	CS	MSCS	FSWs from Panama	ELISA	560	73.0
Soto, 2007 [82]	2001-02	Panama	Community	CS	TLS	MSM from Panama	ELISA	515	44.3
Uribe-Salas, 1999 [83]	1992-93	Mexico	Community	CS	TLS	FSWs in Mexico city	WB	757	65.1
Uribe-Salas, 2003 [84]	1998-98	Mexico	Community	CS	Conv	FSWs in Mexico	WB	468	85.7
Zunt, 2006 [85]	-	Peru	Community	CS	SS	HTLV-II seronegative MSM	ELISA	2,621	44.9
Zunt, 2006 [85]	-	Peru	Community	CS	SS	HTLV-II seropositive MSM	ELISA	33	93.9
STI clinic attendees and symptomatic populations									
Carvalho, 1999 [19]	1993-97	Brazil	Outpatient clinic	CS	Conv	STI clinic attendees	WB	96	53.1
Martinez, 2005 [86]	2003-03	Chile	Outpatient clinic	CS	Conv	STI clinic attendees	ELISA	200	43.0
Nascimento, 2007 [40]	1995-03	Brazil	Outpatient clinic	CS	Conv	STI clinic attendees	WB	137	51.0
HIV positive populations and HIV sero-discordant couples									
Batista, 2009 [87]	2002	Brazil	Community	Cohort	Conv	HIV positive patients	ELISA	145	61.4
Boulos, 1992 [17]	1986-88	Haiti	Community	CS	Conv	HIV positive pregnant Haitian women	ELISA	95	88.0
Da-Rosa Santos, 1996 [25]	1994-94	Brazil	Community	CS	Conv	HIV positive patients	ELISA	85	73.0
Domercant, 2017 [27]	2012-12	Haiti	Outpatient clinic	CS	Conv	HIV positive women	ELISA	144	71.5
Levett, 2005 [37]	-	Barbados	Outpatient clinic	CS	Conv	HIV positive adults	ELISA	120	77.5
Lima, 2018 [88]	2005-08	Brazil	Outpatient clinic	Cohort	Conv	Pregnant women with HIV	ELISA	134	59.7
Nascimento, 2007 [40]	1995-03	Brazil	Outpatient clinic	CS	Conv	HIV patients with GUD	WB	30	87.0
Nascimento, 2007 [40]	1995-03	Brazil	Outpatient clinic	CS	Conv	HIV positive patients	WB	40	62.0
Paz-Bailey, 2012a [89]	2006-06	Honduras	Outpatient clinic	CS	Conv	HIV positive patients	ELISA	810	77.9
Paz-Bailey, 2012b [90]	2008-08	El Salvador	Outpatient clinic	CS	Conv	HIV positive patients	ELISA	760	84.5
Sanchez, 2009 [11]	1998-00	Peru	Outpatient clinic	Cohort	SS	MSM who seroconverted to HIV	WB	26	42.3
Santos, 2006 [91]	2001-02	Brazil	Outpatient clinic	CS	Conv	HIV positive patients	ELISA	150	52.0
Yanez Alvarez, 2011 [12]	2003-05	Mexico	Outpatient clinic	Cohort	Conv	HIV positive patients	ELISA	301	48.5
Other populations[b]									
Almeida, 2017 [15]	2011-14	Brazil	Outpatient clinic	CS	Conv	Patients with malignant nodules	ELISA	100	18.0
Bahena-Roman, 2020 [92]	2008-11	Mexico	Outpatient clinic	CS	Conv	Women with cervical related diseases	ELISA	644	25.0
Boulos, 1992 [17]	1986-88	Haiti	Community	CS	Conv	HTLV-I seropositive pregnant Haitian women	ELISA	45	82.0
Calderon, 2018 [93]	2014-15	Peru	Outpatient clinic	CS	Conv	Women with cancer	ELISA	44	36.4
Castle, 2003 [94]	1993-97	Jamaica	Outpatient clinic	CC	Conv	Women with low grade cervical neoplasia	ELISA	201	60.9
Castle, 2003 [94]	1993-97	Jamaica	Outpatient clinic	CC	Conv	Women with cervical neoplasia grade 2	ELISA	117	61.6
Castle, 2003 [94]	1993-97	Jamaica	Outpatient clinic	CC	Conv	Women with cervical neoplasia grade 3	ELISA	92	73.5
Conde-Gonzalez, 2003 [23]	2000-00	Mexico	Community	CS	CRS	Women with cervical cancer	WB	408	46.8
Conde-Gonzalez, 2003 [23]	2000-00	Mexico	Community	CS	CRS	Women with cancer	WB	128	22.6

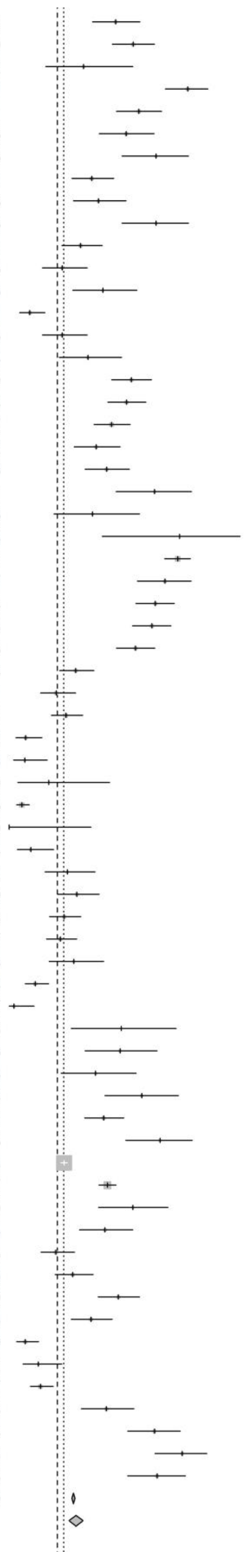
De Sanjose, 1994 [26]	1985-88	Colombia	Outpatient clinic	CC	Conv	Women with CIN III	ELISA	243	60.8
DeBritton, 1993 [95]	1986-87	Panama	Hospital	CS	Conv	Women with cervical cancer	WB	189	57.0
Munoz, 1995 [39]	1985-88	Colombia	Outpatient clinic	CC	Conv	Women with invasive cancer	ELISA	121	75.2
Munoz, 1995 [39]	1985-88	Colombia	Outpatient clinic	CC	Conv	Husbands of women with invasive cancer	ELISA	52	59.6
Munoz, 1995 [39]	1985-88	Colombia	Outpatient clinic	CC	Conv	Husbands of women with CIN III	ELISA	120	60.8
Smith, 2002 [53]	-	Brazil	Outpatient clinic	CC	Conv	Brazilian women with squamous-cell carcinoma	WB	145	55.2
Smith, 2002 [53]	-	Brazil	Outpatient clinic	CC	Conv	Brazilian women with adeno- or adenosquamous carcinoma	WB	16	43.8
Smith, 2002 [53]	-	Colombia	Outpatient clinic	CC	Conv	Colombian women with squamous-cell carcinoma	WB	78	61.5
Smith, 2002 [53]	-	Peru	Outpatient clinic	CC	Conv	Peruvian women with squamous-cell carcinoma	WB	166	56.6
Smith, 2002 [53]	-	Peru	Outpatient clinic	CC	Conv	Peruvian women with adeno- or adenosquamous carcinoma	WB	24	66.7
Stone, 1995 [96]	1982-84	Costa Rica	Community	CC	Conv	Women with cervical carcinoma	WB	415	54.7
Stone, 1995 [96]	1982-84	Costa Rica	Community	CC	Conv	Women with invasive cervical cancer	WB	149	57.8

[a] The reported study design is the original study design (case control, cross sectional, cohort, or randomized controlled trial). The included seroprevalence measures are those for the baseline measures at the beginning of the study.
[b] Other populations include populations with an undetermined risk of acquiring HSV-2 infection such as patients with cervical cancer or their spouses.
Abbreviations: CC = Case control, Conv = Convenience, CIN = Cervical intraepithelial neoplasia, CRS = Cluster random sampling, CS = Cross sectional, EIA = Enzyme immunosorbent assay, ELISA = Enzyme-linked immunosorbent assay, FSWs = Female sex workers, GUD = Genital ulcer disease, HIV = Human immunodeficiency virus, HSV-2 = Herpes simplex virus type 2, HTLV = Human T- cell leukemia virus, MSCS = Multiple stage cluster sampling, MSM = Men who have sex with men, RCT = Randomized controlled trial, RDS = Response driven sampling, RS = Random sampling, SS = Snowball sampling, STI = Sexually transmitted infection, TLS = Time-location sampling, VCT = Voluntary counselling and testing, WB = Western blot.

Figure S1. Forest plots presenting the outcomes of the pooled mean herpes simplex virus type 2 (HSV-2) seroprevalence among the different at risk populations in Latin America and the Caribbean.

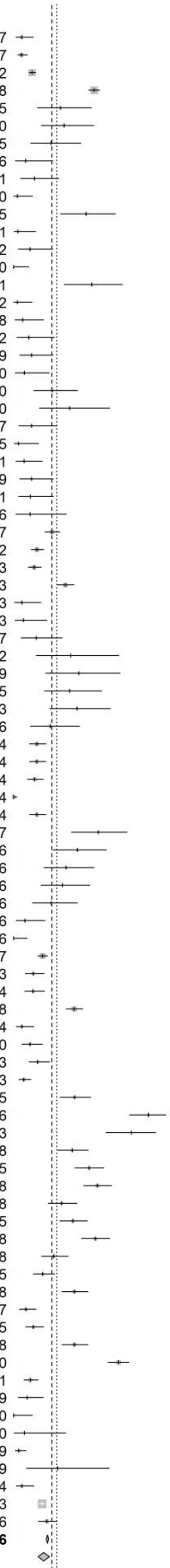
A) General populations

Author, Year	HSV-2 positive	Sample size	Events per 100 observations	W(Random)	Prev(%)	95%CI
Females						
Abraham, 2003	6	98		0.4%	6.1	[2.3; 12.9]
Abraham, 2003	15	192		0.4%	7.8	[4.4; 12.6]
Ashley-Morrow, 2004	42	94		0.4%	44.7	[34.4; 55.3]
Ashley-Morrow, 2004	40	94		0.4%	42.6	[32.4; 53.2]
Ashley-Morrow, 2004	38	97		0.4%	39.2	[29.4; 49.6]
Boulos, 1992	48	89		0.4%	53.9	[43.0; 64.6]
Cárcamo, 2012	12	72		0.4%	16.7	[8.9; 27.3]
Cárcamo, 2012	15	91		0.4%	16.5	[9.5; 25.7]
Cárcamo, 2012	7	67		0.4%	10.4	[4.3; 20.3]
Cárcamo, 2012	7	51		0.4%	13.7	[5.7; 26.3]
Cárcamo, 2012	9	64		0.4%	14.1	[6.6; 25.0]
Cárcamo, 2012	3	64		0.4%	4.7	[1.0; 13.1]
Cárcamo, 2012	22	67		0.4%	32.8	[21.8; 45.4]
Cárcamo, 2012	2	68		0.4%	2.9	[0.4; 10.2]
Cárcamo, 2012	5	61		0.4%	8.2	[2.7; 18.1]
Cárcamo, 2012	1	79		0.4%	1.3	[0.0; 6.9]
Cárcamo, 2012	24	66		0.4%	36.4	[24.9; 49.1]
Cárcamo, 2012	4	68		0.4%	5.9	[1.6; 14.4]
Cárcamo, 2012	9	49		0.4%	18.4	[8.8; 32.0]
Cárcamo, 2012	3	61		0.4%	4.9	[1.0; 13.7]
Cárcamo, 2012	4	47		0.4%	8.5	[2.4; 20.4]
Cárcamo, 2012	4	49		0.4%	8.2	[2.3; 19.6]
Cárcamo, 2012	1	69		0.4%	1.4	[0.0; 7.8]
Cárcamo, 2012	14	63		0.4%	22.2	[12.7; 34.5]
Cárcamo, 2012	8	52		0.4%	15.4	[6.9; 28.1]
Cárcamo, 2012	8	64		0.4%	12.5	[5.6; 23.2]
Cárcamo, 2012	1	51		0.4%	2.0	[0.0; 10.4]
Cárcamo, 2012	2	55		0.4%	3.6	[0.4; 12.5]
Cárcamo, 2012	5	60		0.4%	8.3	[2.8; 18.4]
Cárcamo, 2012	4	48		0.4%	8.3	[2.3; 20.0]
Carvalho, 1999	9	19		0.3%	47.4	[24.4; 71.1]
Carvalho, 1999	5	21		0.3%	23.8	[8.2; 47.2]
Carvalho, 1999	5	27		0.4%	18.5	[6.3; 38.1]
Carvalho, 1999	4	35		0.4%	11.4	[3.2; 26.7]
Clemens, 2010	5	55		0.4%	9.1	[3.0; 20.0]
Clemens, 2010	5	47		0.4%	10.6	[3.5; 23.1]
Clemens, 2010	11	52		0.4%	21.2	[11.1; 34.7]
Clemens, 2010	8	31		0.4%	25.8	[11.9; 44.6]
Clemens, 2010	6	33		0.4%	18.2	[7.0; 35.5]
Clemens, 2010	11	51		0.4%	21.6	[11.3; 35.3]
Clemens, 2010	17	51		0.4%	33.3	[20.8; 47.9]
Clemens, 2010	9	42		0.4%	21.4	[10.3; 36.8]
Conde-Glez, 2013	76	208		0.5%	36.5	[30.0; 43.5]
Conde-Glez, 2013	43	208		0.5%	20.7	[15.4; 26.8]
Conde-Glez, 2013	20	208		0.5%	9.6	[6.0; 14.5]
Conde-Glez, 2013	11	208		0.5%	5.3	[2.7; 9.3]
Conde-Glez, 2013	76	208		0.5%	36.5	[30.0; 43.5]
Conde-Gonzalez, 2003	40	196		0.4%	20.4	[15.0; 26.7]
Conde-Gonzalez, 2003	160	404		0.5%	39.6	[34.8; 44.6]
Conde-Gonzalez, 2003	14	130		0.4%	10.8	[6.0; 17.4]
Cowan, 2003	49	69		0.4%	71.0	[58.8; 81.3]
Cowan, 2003	46	69		0.4%	66.7	[54.3; 77.6]
Cowan, 2003	20	69		0.4%	29.0	[18.7; 41.2]
Cowan, 2003	24	69		0.4%	34.8	[23.7; 47.2]
Cowan, 2003	27	69		0.4%	39.1	[27.6; 51.6]
Cowan, 2003	20	69		0.4%	29.0	[18.7; 41.2]
Cowan, 2003	8	69		0.4%	11.6	[5.1; 21.6]
De Sanjose, 1994	118	237		0.5%	49.8	[43.3; 56.3]
Domercant, 2017	239	784		0.5%	30.5	[27.3; 33.8]
Goncalez, 2006	135	763		0.5%	17.7	[15.0; 20.6]
Gutierrez, 2006	49	258		0.5%	19.0	[14.4; 24.3]
Gutierrez, 2006	6	148		0.4%	4.1	[1.5; 8.6]
Herrera-Ortiz, 2013	166	1163		0.5%	14.3	[12.3; 16.4]
Herrera-Ortiz, 2013	103	390		0.5%	26.4	[22.1; 31.1]
Herrera-Ortiz, 2013	64	747		0.5%	8.6	[6.7; 10.8]
Konda, 2005	73	257		0.5%	28.4	[23.0; 34.3]
Konda, 2005	49	226		0.5%	21.7	[16.5; 27.6]
Konda, 2005	32	232		0.5%	13.8	[9.6; 18.9]
Konda, 2005	42	250		0.5%	16.8	[12.4; 22.0]
Lazcano-Ponce, 2001	59	145		0.4%	40.7	[32.6; 49.2]
Lazcano-Ponce, 2001	51	210		0.5%	24.3	[18.6; 30.7]
Lazcano-Ponce, 2001	72	160		0.4%	45.0	[37.1; 53.1]
Lazcano-Ponce, 2001	32	215		0.5%	14.9	[10.4; 20.4]



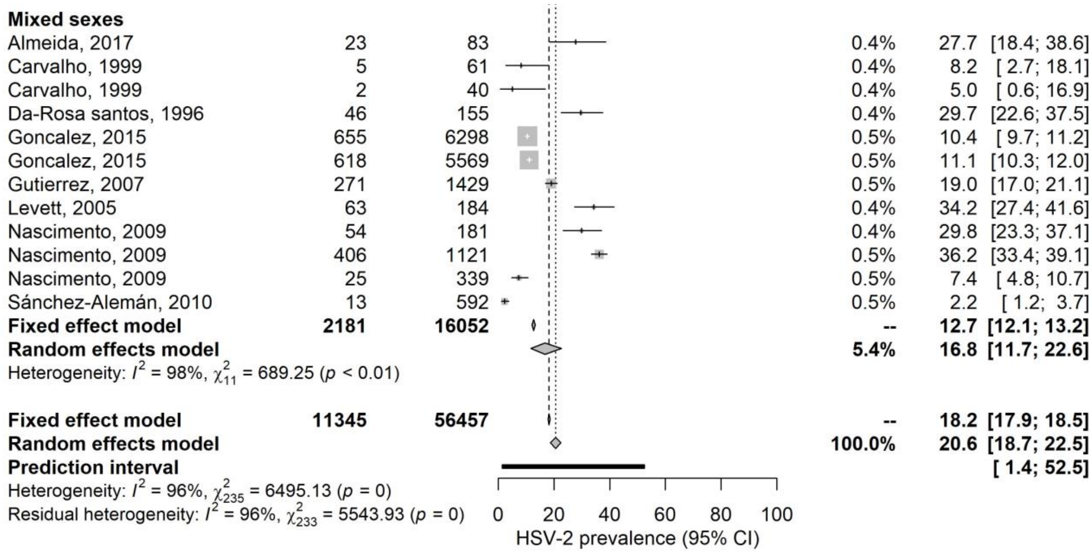
Levett, 2005	49	122	0.4%	40.2	[31.4; 49.4]
Moreira, 2018	75	160	0.4%	46.9	[39.0; 54.9]
Moreira, 2018	9	32	0.4%	28.1	[13.7; 46.7]
Munoz, 1995	95	141	0.4%	67.4	[59.0; 75.0]
Nascimento, 2008	69	141	0.4%	48.9	[40.4; 57.5]
Nascimento, 2008	42	95	0.4%	44.2	[34.0; 54.8]
Nascimento, 2008	36	65	0.4%	55.4	[42.5; 67.7]
Nascimento, 2008	44	141	0.4%	31.2	[23.7; 39.5]
Nascimento, 2008	32	95	0.4%	33.7	[24.3; 44.1]
Nascimento, 2008	36	65	0.4%	55.4	[42.5; 67.7]
Nascimento, 2008	38	141	0.4%	27.0	[19.8; 35.1]
Nascimento, 2008	19	95	0.4%	20.0	[12.5; 29.5]
Nascimento, 2008	23	65	0.4%	35.4	[23.9; 48.2]
Nascimento, 2008	11	141	0.4%	7.8	[4.0; 13.5]
Nascimento, 2008	19	95	0.4%	20.0	[12.5; 29.5]
Nascimento, 2008	19	64	0.4%	29.7	[18.9; 42.4]
Oberle, 1989	83	180	0.4%	46.1	[38.7; 53.7]
Oberle, 1989	86	194	0.4%	44.3	[37.2; 51.6]
Oberle, 1989	80	207	0.5%	38.6	[32.0; 45.6]
Oberle, 1989	40	122	0.4%	32.8	[24.6; 41.9]
Patnaik, 2007	50	136	0.4%	36.8	[28.7; 45.5]
Patnaik, 2007	28	51	0.4%	54.9	[40.3; 68.9]
Patnaik, 2007	11	35	0.4%	31.4	[16.9; 49.3]
Patnaik, 2007	9	14	0.3%	64.3	[35.1; 87.2]
Paz-Bailey, 2009	249	391	0.5%	63.7	[58.7; 68.5]
Rodrıguez, 2003	57	97	0.4%	58.8	[48.3; 68.7]
Rodrıguez, 2003	107	194	0.4%	55.2	[47.9; 62.3]
Rodrıguez, 2003	104	193	0.4%	53.9	[46.6; 61.1]
Rodrıguez, 2003	93	195	0.4%	47.7	[40.5; 54.9]
Rodrıguez, 2003	46	183	0.4%	25.1	[19.0; 32.1]
Rodrıguez, 2003	25	141	0.4%	17.7	[11.8; 25.1]
Sanchez, 1996	43	201	0.4%	21.4	[15.9; 27.7]
Sanchez-Aleman, 2005	7	112	0.4%	6.2	[2.5; 12.5]
Sanchez-Aleman, 2005	4	68	0.4%	5.9	[1.6; 14.4]
Sanchez-Aleman, 2005	3	20	0.3%	15.0	[3.2; 37.9]
Sánchez-Alemán, 2008	16	335	0.5%	4.8	[2.8; 7.6]
Sánchez-Alemán, 2008	0	10	0.3%	0.0	[0.0; 30.8]
Sánchez-Alemán, 2008	6	74	0.4%	8.1	[3.0; 16.8]
Sierra, 2011	18	82	0.4%	22.0	[13.6; 32.5]
Sierra, 2011	33	129	0.4%	25.6	[18.3; 34.0]
Sierra, 2011	40	193	0.4%	20.7	[15.2; 27.1]
Sierra, 2011	38	197	0.4%	19.3	[14.0; 25.5]
Sierra, 2011	18	74	0.4%	24.3	[15.1; 35.7]
Sierra, 2011	19	194	0.4%	9.8	[6.0; 14.9]
Sierra, 2011	1	57	0.4%	1.8	[0.0; 9.4]
Smith, 2001	11	26	0.4%	42.3	[23.4; 63.1]
Smith, 2001	23	55	0.4%	41.8	[28.7; 55.9]
Smith, 2001	15	46	0.4%	32.6	[19.5; 48.0]
Smith, 2001	27	54	0.4%	50.0	[36.1; 63.9]
Smith, 2002	61	171	0.4%	35.7	[28.5; 43.3]
Smith, 2002	37	65	0.4%	56.9	[44.0; 69.2]
Uribe-Salas, 2009	876	4233	0.5%	20.7	[19.5; 21.9]
Vaccarella, 2006	336	907	0.5%	37.0	[33.9; 40.3]
Weinberg, 1993	28	60	0.4%	46.7	[33.7; 60.0]
Weinberg, 1993	34	94	0.4%	36.2	[26.5; 46.7]
Zamilpa-Mejía, 2003	27	153	0.4%	17.6	[12.0; 24.6]
Zamilpa-Mejía, 2003	35	146	0.4%	24.0	[17.3; 31.7]
Zamilpa-Mejía, 2003	66	160	0.4%	41.2	[33.5; 49.3]
Zamilpa-Mejía, 2003	45	146	0.4%	30.8	[23.5; 39.0]
Zamilpa-Mejía, 2003	9	149	0.4%	6.0	[2.8; 11.2]
Zamilpa-Mejía, 2003	9	82	0.4%	11.0	[5.1; 19.8]
Gabster, 2019	28	237	0.5%	11.8	[8.0; 16.6]
Patzi-Churqui, 2020	36	98	0.4%	36.7	[27.2; 47.1]
Patzi-Churqui, 2020	57	104	0.4%	54.8	[44.7; 64.6]
Patzi-Churqui, 2020	64	98	0.4%	65.3	[55.0; 74.6]
Patzi-Churqui, 2020	48	86	0.4%	55.8	[44.7; 66.5]
Fixed effect model	**6184**	**23959**	**--**	**24.2**	**[23.7; 24.8]**
Random effects model			**58.8%**	**25.2**	**[22.6; 28.0]**

Heterogeneity: I^2 = 95%, χ^2_{138} = 2940.59 (p = 0)



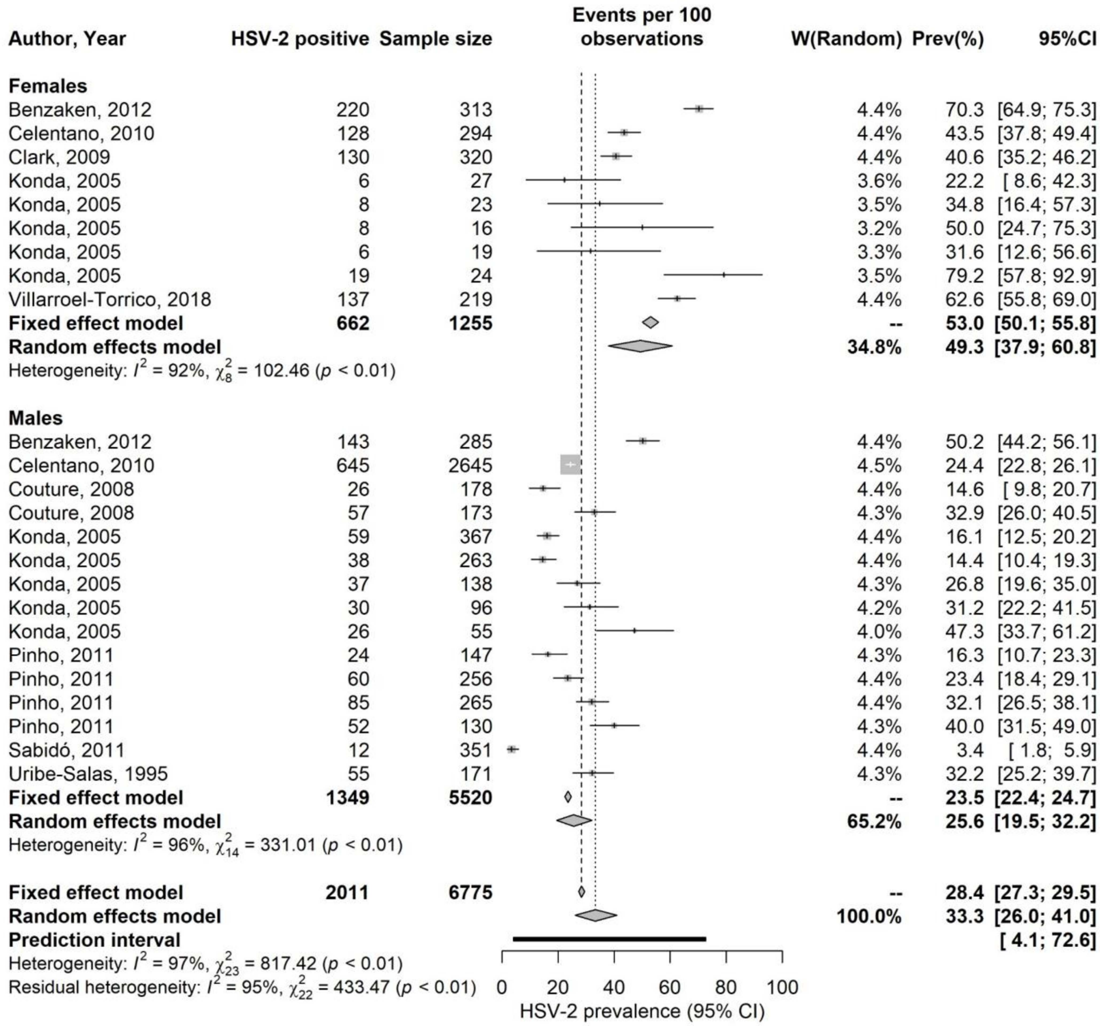
Males					
Abraham, 2003	4	107	0.4%	3.7	[1.0; 9.3]
Abraham, 2003	11	297	0.5%	3.7	[1.9; 6.5]
Alberts, 2013	115	1312	0.5%	8.8	[7.3; 10.4]
Alberts, 2013	533	1388	0.5%	38.4	[35.8; 41.0]
Cárcamo, 2012	10	45	0.4%	22.2	[11.2; 37.1]
Cárcamo, 2012	12	50	0.4%	24.0	[13.1; 38.2]
Cárcamo, 2012	8	45	0.4%	17.8	[8.0; 32.1]
Cárcamo, 2012	2	36	0.4%	5.6	[0.7; 18.7]
Cárcamo, 2012	5	51	0.4%	9.8	[3.3; 21.4]
Cárcamo, 2012	1	60	0.4%	1.7	[0.0; 8.9]
Cárcamo, 2012	19	55	0.4%	34.5	[22.2; 48.6]
Cárcamo, 2012	1	51	0.4%	2.0	[0.0; 10.4]
Cárcamo, 2012	4	52	0.4%	7.7	[2.1; 18.5]
Cárcamo, 2012	0	50	0.4%	0.0	[0.0; 7.1]
Cárcamo, 2012	19	51	0.4%	37.3	[24.1; 51.9]
Cárcamo, 2012	1	62	0.4%	1.6	[0.0; 8.7]
Cárcamo, 2012	2	48	0.4%	4.2	[0.5; 14.3]
Cárcamo, 2012	3	42	0.4%	7.1	[1.5; 19.5]
Cárcamo, 2012	5	59	0.4%	8.5	[2.8; 18.7]
Cárcamo, 2012	2	40	0.4%	5.0	[0.6; 16.9]
Cárcamo, 2012	11	60	0.4%	18.3	[9.5; 30.4]
Cárcamo, 2012	8	30	0.4%	26.7	[12.3; 45.9]
Cárcamo, 2012	4	47	0.4%	8.5	[2.4; 20.4]
Cárcamo, 2012	1	45	0.4%	2.2	[0.1; 11.8]
Cárcamo, 2012	3	61	0.4%	4.9	[1.0; 13.7]
Cárcamo, 2012	5	59	0.4%	8.5	[2.8; 18.7]
Cárcamo, 2012	4	51	0.4%	7.8	[2.2; 18.9]
Cárcamo, 2012	2	26	0.4%	7.7	[0.9; 25.1]
Clark, 2008	85	467	0.5%	18.2	[14.8; 22.0]
Clark, 2008	51	462	0.5%	11.0	[8.3; 14.3]
Clark, 2008	37	383	0.5%	9.7	[6.9; 13.1]
Clark, 2008	114	463	0.5%	24.6	[20.8; 28.8]
Clemens, 2010	2	53	0.4%	3.8	[0.5; 13.0]
Clemens, 2010	2	43	0.4%	4.7	[0.6; 15.8]
Clemens, 2010	5	47	0.4%	10.6	[3.5; 23.1]
Clemens, 2010	6	22	0.3%	27.3	[10.7; 50.2]
Clemens, 2010	9	29	0.4%	31.0	[15.3; 50.8]
Clemens, 2010	12	45	0.4%	26.7	[14.6; 41.9]
Clemens, 2010	13	43	0.4%	30.2	[17.2; 46.1]
Clemens, 2010	8	46	0.4%	17.4	[7.8; 31.4]
Conde-Glez, 2013	29	264	0.5%	11.0	[7.5; 15.4]
Conde-Glez, 2013	29	264	0.5%	11.0	[7.5; 15.4]
Conde-Glez, 2013	26	264	0.5%	9.8	[6.5; 14.1]
Conde-Glez, 2013	0	264	0.5%	0.0	[0.0; 1.4]
Conde-Glez, 2013	29	264	0.5%	11.0	[7.5; 15.4]
Cowan, 2003	23	57	0.4%	40.4	[27.6; 54.2]
Cowan, 2003	17	56	0.4%	30.4	[18.8; 44.1]
Cowan, 2003	14	56	0.4%	25.0	[14.4; 38.4]
Cowan, 2003	13	56	0.4%	23.2	[13.0; 36.4]
Cowan, 2003	10	56	0.4%	17.9	[8.9; 30.4]
Cowan, 2003	3	56	0.4%	5.4	[1.1; 14.9]
Cowan, 2003	0	56	0.4%	0.0	[0.0; 6.4]
Goncalez, 2006	115	837	0.5%	13.7	[11.5; 16.3]
Gutierrez, 2006	17	183	0.4%	9.3	[5.5; 14.5]
Gutierrez, 2006	15	164	0.4%	9.1	[5.2; 14.6]
Juarez-Figueroa, 1997	155	538	0.5%	28.8	[25.0; 32.8]
Konda, 2005	4	104	0.4%	3.8	[1.1; 9.6]
Konda, 2005	10	130	0.4%	7.7	[3.8; 13.7]
Konda, 2005	21	183	0.4%	11.5	[7.2; 17.0]
Konda, 2005	12	253	0.5%	4.7	[2.5; 8.1]
Lupi, 2011	45	155	0.4%	29.0	[22.0; 36.9]
Munoz, 1995	81	126	0.4%	64.3	[55.3; 72.6]
Munoz, 1995	41	73	0.4%	56.2	[44.1; 67.8]
Nascimento, 2008	44	158	0.4%	27.8	[21.0; 35.5]
Nascimento, 2008	70	195	0.4%	35.9	[29.2; 43.1]
Nascimento, 2008	87	218	0.5%	39.9	[33.4; 46.7]
Nascimento, 2008	36	158	0.4%	22.8	[16.5; 30.1]
Nascimento, 2008	55	195	0.4%	28.2	[22.0; 35.1]
Nascimento, 2008	85	218	0.5%	39.0	[32.5; 45.8]
Nascimento, 2008	30	158	0.4%	19.0	[13.2; 26.0]
Nascimento, 2008	27	195	0.4%	13.8	[9.3; 19.5]
Nascimento, 2008	63	218	0.5%	28.9	[23.0; 35.4]
Nascimento, 2008	9	157	0.4%	5.7	[2.7; 10.6]
Nascimento, 2008	18	195	0.4%	9.2	[5.6; 14.2]
Nascimento, 2008	63	218	0.5%	28.9	[23.0; 35.4]
Paz-Bailey, 2009	200	400	0.5%	50.0	[45.0; 55.0]
Sanchez, 1996	22	281	0.5%	7.8	[5.0; 11.6]
Sanchez-Aleman, 2005	5	79	0.4%	6.3	[2.1; 14.2]
Sanchez-Aleman, 2005	0	40	0.4%	0.0	[0.0; 8.8]
Sanchez-Aleman, 2005	1	20	0.3%	5.0	[0.1; 24.9]
Sánchez-Alemán, 2008	4	169	0.4%	2.4	[0.6; 5.9]
Sánchez-Alemán, 2008	4	19	0.3%	21.1	[6.1; 45.6]
Sánchez-Alemán, 2008	4	104	0.4%	3.8	[1.1; 9.6]
Uribe-Salas, 2009	260	1923	0.5%	13.5	[12.0; 15.1]
Gabster, 2019	45	286	0.5%	15.7	[11.7; 20.5]
Fixed effect model	**2980**	**16446**	--	**16.0**	**[15.5; 16.6]**
Random effects model			**35.8%**	**14.2**	**[11.6; 17.0]**

Heterogeneity: $I^2 = 96\%$, $\chi^2_{84} = 1914.09$ ($p = 0$)



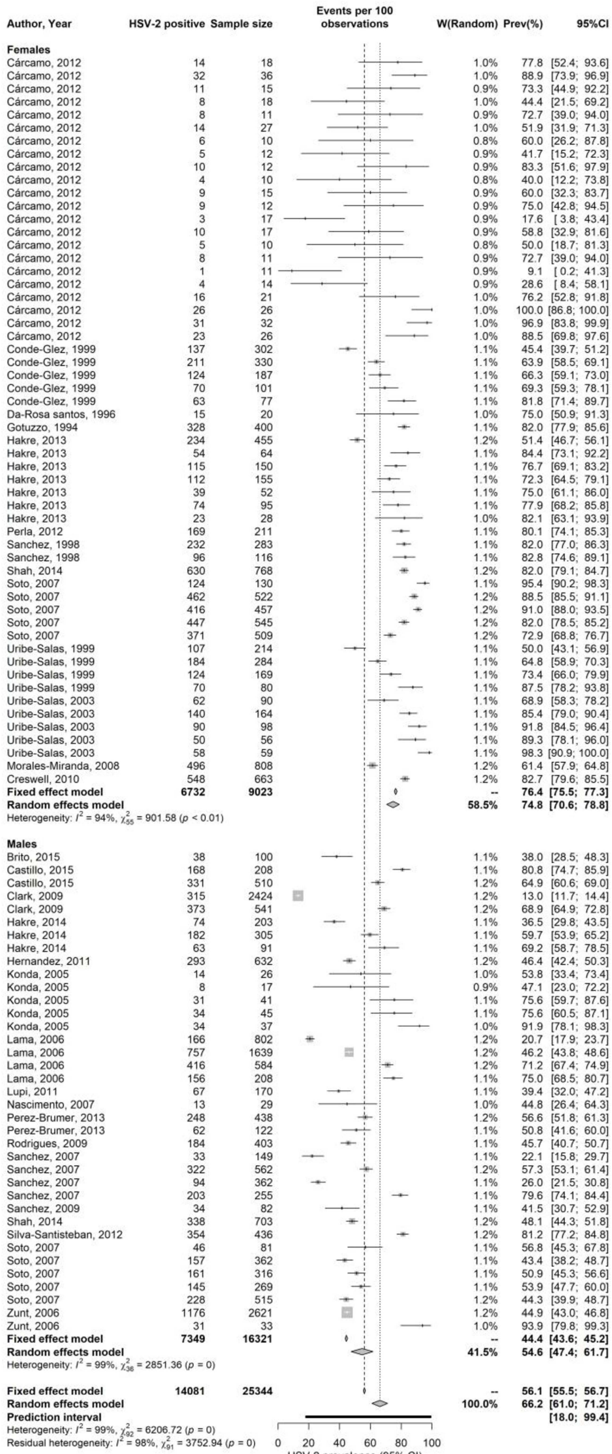
Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2.

B) Intermediate-risk populations



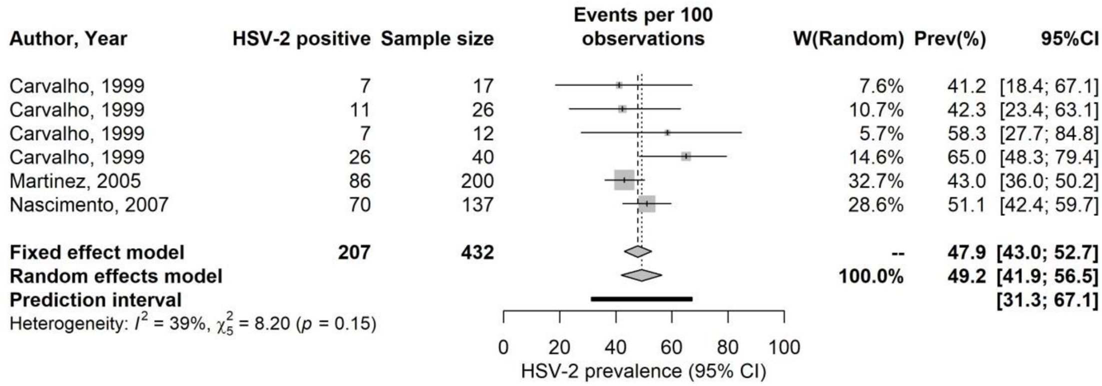
Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2.

C) High-risk populations



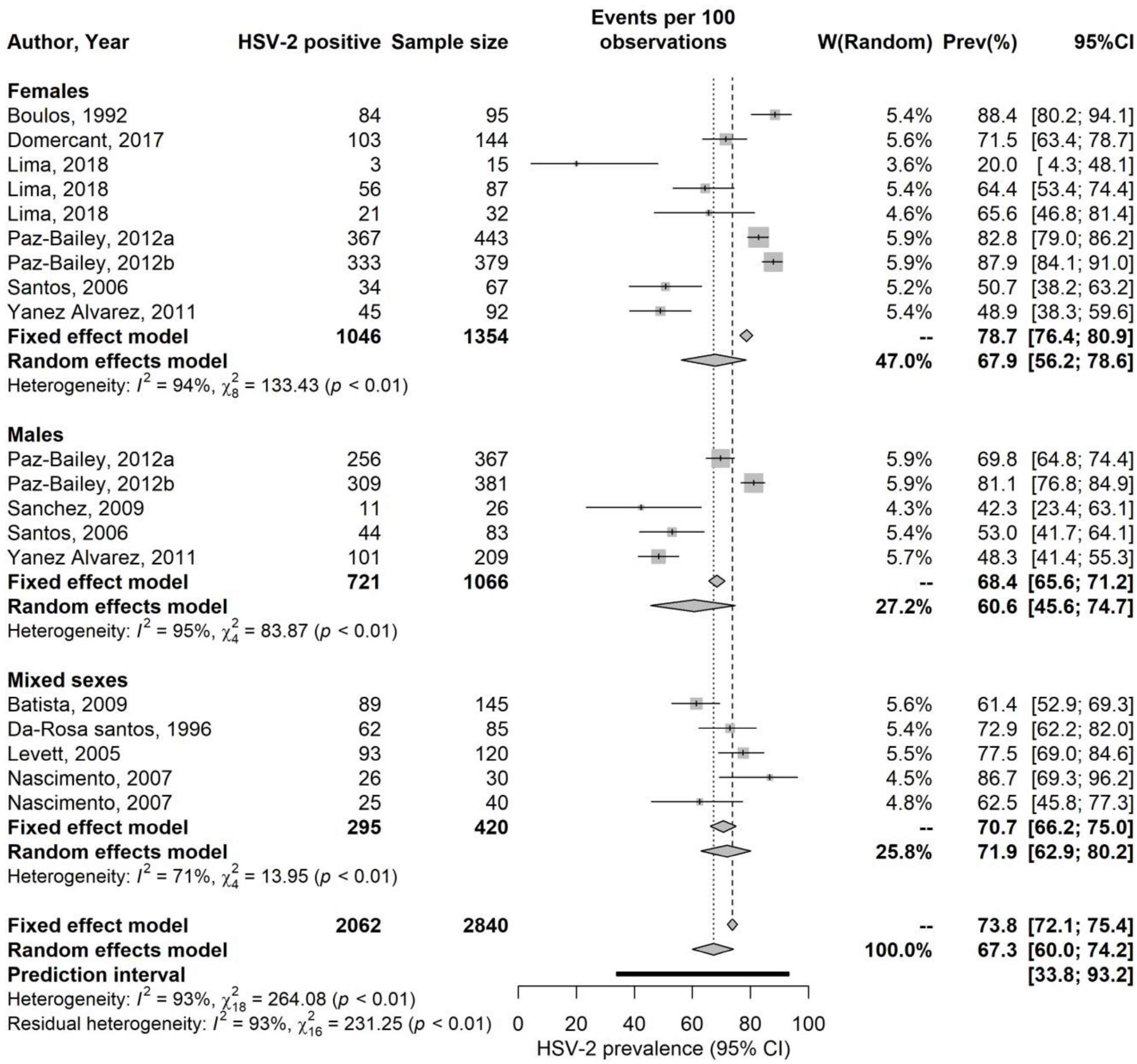
Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2.

D) STI clinic attendees and symptomatic populations (mixed women and men)



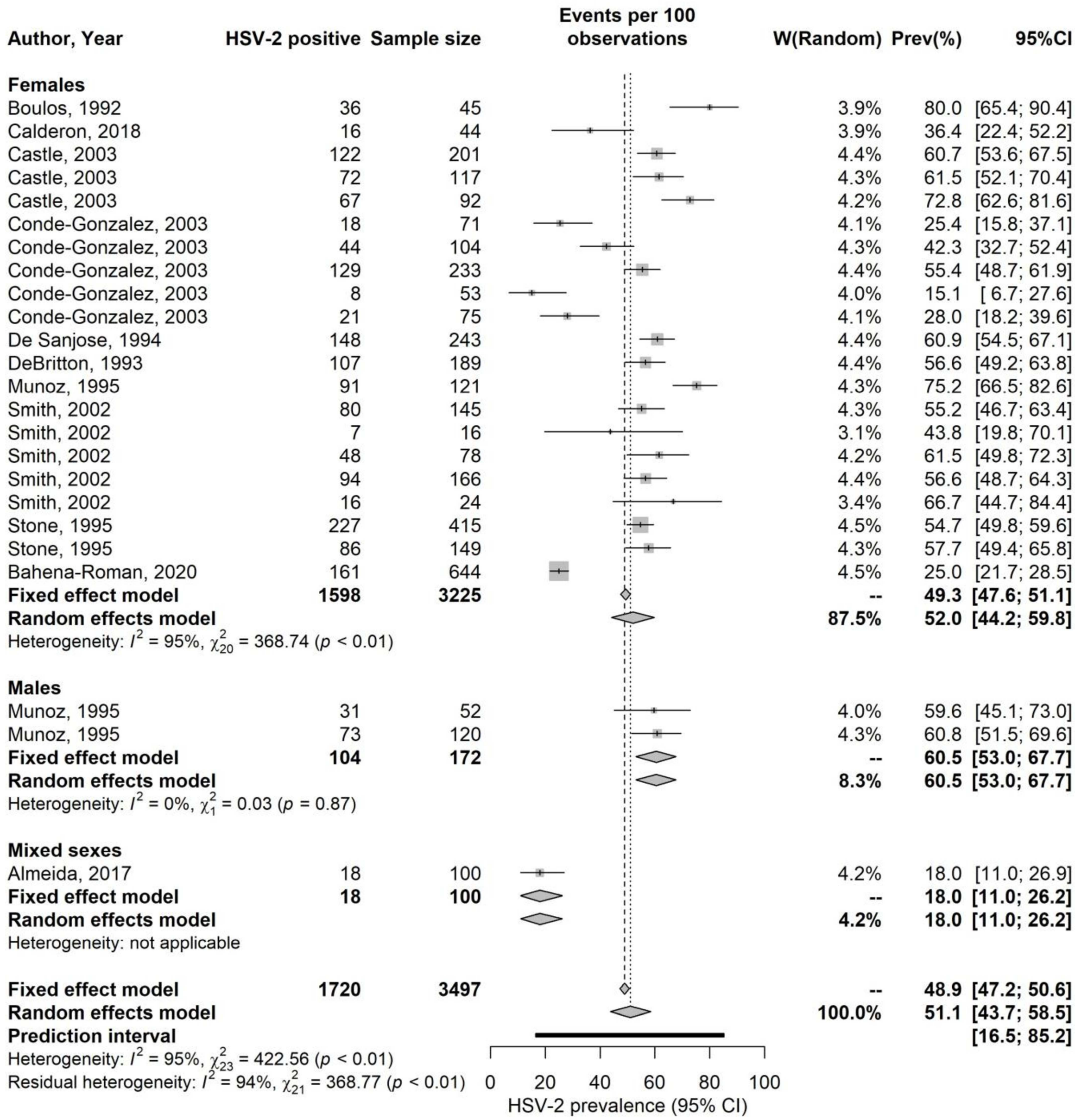
Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2, STI = Sexually transmitted infection.

F) HIV positive individuals and individuals in HIV discordant couples



Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2, HIV = Human immunodefficency virus.

G) Other populations



Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2.

Table S5. Univariable and multivariable meta-regression analyses for HSV-2 seroprevalence among the different at risk populations in Latin America and the Caribbean using each of country's income and country *instead* of subregion in the multivariable meta-regression.

			Outcome measures	Sample size	Univariable analysis				Multivariable analysis					
									Model 1[a]		Model 2[b]		Model 3[c]	
			Total n	Total N	*RR* (95%CI)	p-value	LR test p-value	Adjusted R^2 (%)	*ARR* (95% CI)	p-value	*ARR* (95% CI)	p-value	*ARR* (95% CI)	p-value
Population characteristics	Population type	General populations	236	56,457	1.00	-	<0.001	45.98	1.00	-	1.00	-	1.00	-
		Intermediate-risk populations	24	6,775	1.52 (1.16-2.00)	0.002			1.55 (1.22-1.96)	<0.001	1.49 (1.18-1.87)	0.001	1.58 (1.26-1.97)	<0.001
		High-risk populations	93	25,344	3.09 (2.64-3.61)	<0.001			3.09 (2.67-3.57)	<0.001	2.81 (2.44-3.23)	<0.001	3.08 (2.66-3.55)	<0.001
		STI clinic attendees and symptomatic populations	6	432	2.49 (1.47-4.22)	0.001			2.40 (1.48-3.90)	<0.001	2.15 (1.34-3.45)	0.002	2.18 (1.38-3.42)	0.001
		HIV positive individuals and individuals in HIV discordant couples	19	2,840	3.21 (2.38-4.32)	<0.001			3.06 (2.37-3.95)	<0.001	2.59 (2.02-3.33)	<0.001	2.77 (2.18-3.51)	<0.001
		Other populations[d]	24	3,497	2.42 (1.85-3.16)	<0.001			1.56 (1.24-1.97)	<0.001	1.55 (1.24-1.94)	<0.001	1.51 (1.22-1.88)	<0.001
	Age group	<20 years	35	6,538	1.00	-	<0.001	10.26	1.00	-	1.00	-	1.00	-
		20-30 years	47	7,751	2.05 (1.40-3.00)	<0.001			1.63 (1.27-2.09)	<0.001	1.70 (1.34-2.17)	<0.001	1.63 (1.29-2.05)	<0.001
		30-40 years	22	2,933	2.58 (1.64-4.04)	<0.001			2.24 (1.68-2.99)	<0.001	2.29 (1.72-3.03)	<0.001	2.11 (1.61-2.77)	<0.001
		>40 years	39	5,940	2.84 (1.92-4.18)	<0.001			3.22 (2.50-4.14)	<0.001	3.20 (2.50-4.09)	<0.001	2.92 (2.30-3.71)	<0.001
		Mixed ages	259	72,183	2.49 (1.82-3.41)	<0.001			1.79 (1.44-2.21)	<0.001	1.72 (1.40-2.12)	<0.001	1.68 (1.37-2.07)	<0.001
	Sex	Women	234	38,816	1.00	-	0.001	4.82	1.00	-	1.00	-	1.00	-
		Men	144	39,525	0.67 (0.56-0.80)	<0.001			0.68 (0.60-0.76)	<0.001	0.70 (0.62-0.78)	<0.001	0.68 (0.61-0.76)	<0.001
		Mixed sexes	24	17,004	0.81 (0.57-1.16)	0.267			0.59 (0.46-0.77)	<0.001	0.65 (0.50-0.83)	0.001	0.62 (0.48-0.80)	<0.001
	Countries	Brazil	106	25,766	1.00	-	<0.001	12.58	-	-	-	-	1.00	-
		Colombia	19	2,247	1.36 (0.91-2.01)	0.125			-	-	-	-	1.20 (0.93-1.55)	0.156
		Costa Rica	13	2,364	1.46 (0.92-2.30)	0.102			-	-	-	-	1.23 (0.92-1.64)	0.157
		Mexico	76	23,437	0.71 (0.56-0.91)	0.008			-	-	-	-	0.66 (0.56-0.78)	<0.001
		Panama	15	3,334	1.81 (1.18-2.78)	0.006			-	-	-	-	1.10 (0.82-1.47)	0.506
		Peru	131	24,976	0.92 (0.74-1.14)	0.476			-	-	-	-	0.87 (0.73-1.02)	0.096
		Other[e]	42	13,221	1.84 (1.39-2.45)	<0.001			-	-	-	-	1.20 (0.99-1.46)	0.050
	Subregions	Central America	124	38,103	1.00	-	0.065	0.82	1.00	-	-	-	-	-
		South America	264	54,798	0.95 (0.79-1.14)	0.606			1.13 (1.00-1.27)	0.047	-	-	-	-
		Caribbean	14	2,444	1.62 (1.02-2.58)	0.040			1.17 (0.87-1.57)	0.281	-	-	-	-
	Country's income	LIC and LMIC	29	9,846	1.00	-	<0.001	9.07	-	-	1.00	-	-	-
		UMIC	354	81,539	0.45 (0.33-0.62)	<0.001			-	-	0.65 (0.54-0.78)	<0.001	-	-
		HIC	19	3,960	0.86 (0.54-1.36)	0.528			-	-	0.83 (0.63-1.11)	0.220	-	-
Study methodology characteristics	Assay type	Western Blot	94	11,898	1.00	-	0.432	0.00	-	-	-	-	-	-
		ELISA	304	82,744	0.89 (0.73-1.09)	0.280			-	-	-	-	-	-
		Monoclonal antibody	4	703	1.24 (0.53-2.87)	0.614			-	-	-	-	-	-
	Sample size[f]	<200	81	7,542	1.00	-	<0.001	7.27	1.00	-	1.00	-	1.00	-
		>200	321	87,803	0.58 (0.47-0.71)	<0.001			0.75 (0.64-0.87)	<0.001	0.75 (0.64-0.86)	<0.001	0.82 (0.71-0.95)	0.010
	Sampling method	Probability based	151	47,471	1.00	-	<0.001	18.05	1.00	-	1.00	-	1.00	-
		Non-probability based	251	47,874	2.08 (1.76-2.44)	<0.001			1.16 (1.00-1.35)	0.037	1.24 (1.08-1.42)	0.002	1.18 (1.03-1.35)	0.013
	Response rate	≥80%	194	48,220	1.00	-	0.002	5.52	1.00	-	1.00	-	1.00	-
		<80%	32	6,062	0.59 (0.42-0.82)	0.002			0.79 (0.63-0.99)	0.044	0.76 (0.62-0.95)	0.016	0.89 (0.72-1.10)	0.300
		Unclear	176	41,063	1.25 (1.05-1.49)	0.010			1.07 (0.94-1.22)	0.262	1.07 (0.94-1.22)	0.260	1.13 (1.00-1.29)	0.046
Temporal variables	Year of publication category	<2000	49	7,244	1.00	-	<0.001	4.39	1.00	-	1.00	-	1.00	-
		2000-2010	206	51,983	0.61 (0.47-0.79)	<0.001			0.88 (0.75-1.05)	0.166	0.88 (0.75-1.04)	0.141	0.90 (0.76-1.06)	0.212
		>2010	147	31,118	0.56 (0.42-0.73)	<0.001			0.74 (0.61-0.89)	0.002	0.74 (0.62-0.89)	0.001	0.76 (0.63-0.91)	0.004

[a] Variance explained by the multivariable model (adjusted R^2) = 68.85%.
[b] Variance explained by the multivariable model (adjusted R^2) = 70.63%.
[c] Variance explained by the multivariable model (adjusted R^2) = 73.85%.
[d] Other populations include populations with an undetermined risk of acquiring HSV-2 infection such as patients with cervical cancer or their spouses.
[e] Other countries include Argentina, Barbados,, Bolivia, Chile, Dominican republic, El Salvador, Guatemala, Haiti, Honduras, Jamaica, and Nicaragua.

[f] Sample size denotes the sample size of each study population found in the original publication.
Abbreviations: *ARR* = Adjusted risk ratio, CI = Confidence interval, ELISA = Enzyme-linked immunosorbent assay, HIC = High-income country HIV = Human immunodeficiency virus, HSV-2 = Herpes simplex virus type 2, LIC = Low-income country, LMIC = Lower-middle-income country, LR = Likelihood ratio, *RR* = Risk ratio, STI = Sexually transmitted infection, UMIC = Upper-middle-income country.

Table S6. Univariable and multivariable meta-regression analyses for HSV-2 seroprevalence among the different at-risk populations in Latin America and the Caribbean using the year of data collection as the temporal variable. The analysis using year of publication as the temporal variable is found in Table 3 of main text.

			Outcome measures	Sample size	Univariable analysis				Multivariable analysis			
									Model 1[a]		Model 2[b]	
			Total n	Total N	*RR* (95%CI)	p-value	LR test p-value	Adjusted R^2 (%)	*ARR* (95% CI)	p-value	*ARR* (95% CI)	p-value
Population characteristics	**Population type**	General populations	236	56,457	1.00	-	<0.001	45.98	1.00	-	1.00	-
		Intermediate-risk populations	24	6,775	1.52 (1.16-2.00)	0.002			1.65 (1.30-2.10)	0.001	1.58 (1.24-2.01)	<0.001
		High-risk populations	93	25,344	3.09 (2.64-3.61)	<0.001			3.13 (2.71-3.62)	<0.001	3.10 (2.67-3.59)	<0.001
		STI clinic attendees and symptomatic populations	6	432	2.49 (1.47-4.22)	0.001			2.47 (1.52-4.00)	<0.001	2.40 (1.47-3.90)	<0.001
		HIV positive individuals and individuals in HIV discordant couples	19	2,840	3.21 (2.38-4.32)	<0.001			3.07 (2.38-3.95)	<0.001	2.95 (2.28-3.81)	<0.001
		Other populations[c]	24	3,497	2.42 (1.85-3.16)	<0.001			1.60 (1.24-2.02)	<0.001	1.56 (1.23-1.97)	<0.001
	Age group	<20 years	35	6,538	1.00	-	<0.001	10.26	1.00	-	1.00	-
		20-30 years	47	7,751	2.05 (1.40-3.00)	<0.001			1.64 (1.29-2.10)	<0.001	1.64 (1.27-2.11)	<0.001
		30-40 years	22	2,933	2.58 (1.64-4.04)	<0.001			2.14 (1.60-2.86)	<0.001	2.23 (1.66-2.98)	<0.001
		>40 years	39	5,940	2.84 (1.92-4.18)	<0.001			3.01 (2.34-3.87)	<0.001	3.08 (2.39-3.97)	<0.001
		Mixed ages	259	72,183	2.49 (1.82-3.41)	<0.001			1.70 (1.38-2.10)	<0.001	1.70 (1.37-2.09)	<0.001
	Sex	Women	234	38,816	1.00	-	0.001	4.82	1.00	-	1.00	
		Men	144	39,525	0.67 (0.56-0.80)	<0.001			0.71 (0.63-0.79)	<0.001	0.69 (0.61-0.77)	<0.001
		Mixed sexes	24	17,004	0.81 (0.57-1.16)	0.267			0.61 (0.47-0.79)	<0.001	0.63 (0.48-0.82)	0.001
	Countries	Brazil	106	25,766	1.00	-	<0.001	12.58	-	-	-	-
		Colombia	19	2,247	1.36 (0.91-2.01)	0.125			-	-	-	-
		Costa Rica	13	2,364	1.46 (0.92-2.30)	0.102			-	-	-	-
		Mexico	76	23,437	0.71 (0.56-0.91)	0.008			-	-	-	-
		Panama	15	3,334	1.81 (1.18-2.78)	0.006			-	-	-	-
		Peru	131	24,976	0.92 (0.74-1.14)	0.476			-	-	-	-
		Other[d]	42	13,221	1.84 (1.39-2.45)	<0.001			-	-	-	-
	Subregions	Central America	124	38,103	1.00	-	0.065	0.82	1.00	-	1.00	-
		South America	264	54,798	0.95 (0.79-1.14)	0.606			1.11 (0.98-1.25)	0.082	1.09 (0.96-1.23)	0.147
		Caribbean	14	2,444	1.62 (1.02-2.58)	0.040			1.10 (0.82-1.47)	0.506	1.16 (0.86-1.56)	0.308
	Country's income	LIC and LMIC	29	9,846	1.00	-	<0.001	9.07	-	-	-	-
		UMIC	354	81,539	0.45 (0.33-0.62)	<0.001			-	-	-	-
		HIC	19	3,960	0.86 (0.54-1.36)	0.528			-	-	-	-
Study methodology characteristics	**Assay type**	Western Blot	94	11,898	1.00	-	0.432	0.00	-	-	-	-
		ELISA	304	82,744	0.89 (0.73-1.09)	0.280			-	-	-	-
		Monoclonal antibody	4	703	1.24 (0.53-2.87)	0.614			-	-	-	-
	Sample size[e]	<200	81	7,542	1.00	-	<0.001	7.27	1.00	-	1.00	-
		>200	321	87,803	0.58 (0.47-0.71)	<0.001			0.79 (0.67-0.93)	0.004	0.73 (0.63-0.85)	<0.001
	Sampling method	Probability based	151	47,471	1.00	-	<0.001	18.05	1.00	-	1.00	-
		Non-probability based	251	47,874	2.08 (1.76-2.44)	<0.001			1.17 (1.01-1.35)	0.030	1.18 (1.02-1.36)	0.026
	Response rate	≥80%	194	48,220	1.00	-	0.002	5.52	1.00	-	1.00	-
		<80%	32	6,062	0.59 (0.42-0.82)	0.002			0.80 (0.64-1.00)	0.053	0.78 (0.62-0.97)	0.030
		Unclear	176	41,063	1.25 (1.05-1.49)	0.010			1.09 (0.96-1.24)	0.189	1.11 (0.97-1.27)	0.104
Temporal variables	**Year of data collection category**	<2000	151	27,266	1.00	-	0.007	1.94	1.00	-	-	-
		2000-2010	231	53,038	0.65 (0.54-0.78)	<0.001			0.77 (0.68-0.88)	<0.001	-	-
		>2010	20	14,041	0.85 (0.58-1.25)	0.429			0.95 (0.75-1.20)	0.683	-	-
	Year of data collection		402	95,345	0.98 (0.97-0.99)	0.024	<0.001	2.98	-	-	0.99 (0.98-0.99)	0.031

[a] Variance explained by the multivariable model (adjusted R^2) = 69.12%.
[b] Variance explained by the multivariable model (adjusted R^2) = 68.45%.
[c] Other populations include populations with an undetermined risk of acquiring HSV-2 infection such as patients with cervical cancer or their spouses.
[d] Other countries include Argentina, Barbados,, Bolivia, Chile, Dominican republic, El Salvador, Guatemala, Haiti, Honduras, Jamaica, and Nicaragua.
[e] Sample size denotes the sample size of each study population found in the original publication.
Abbreviations: *ARR* = Adjusted risk ratio, CI = Confidence interval, ELISA = Enzyme-linked immunosorbent assay, HIC = High-income country HIV = Human immunodeficiency virus, HSV-2 = Herpes simplex virus type 2, LIC = Low-income country, LMIC = Lower-middle-income country, LR = Likelihood ratio, *RR* = Risk ratio, STI = Sexually transmitted infection, UMIC = Upper-middle-income country.

Table S7. Studies reporting proportions of HSV-2 virus isolation in clinically-diagnosed genital ulcer disease and in clinically-diagnosed genital herpes in Latin America and the Caribbean.

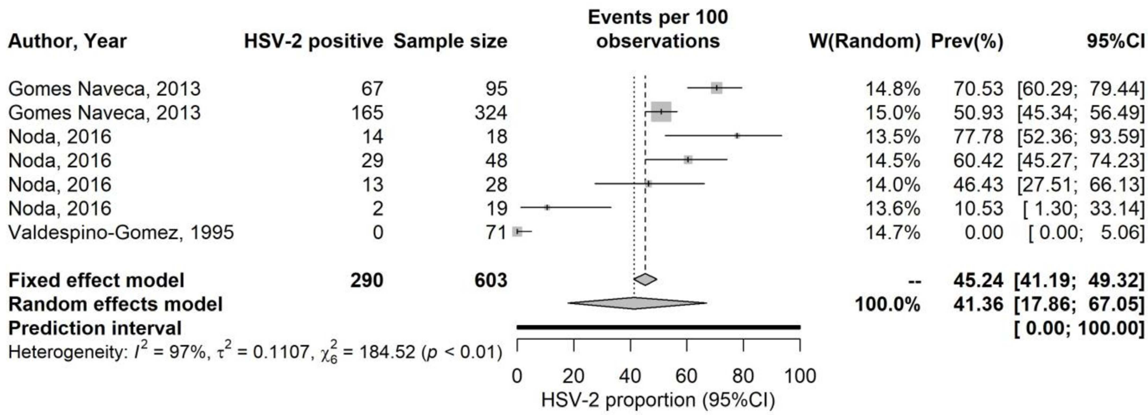
Author, year	Year(s) of data collection	Country	Study site	Original study design*	Sampling method	Population	HSV-2 biological assay	Sample size	Proportion of HSV-2 detection (%)
Patients with clinically-diagnosed GUD									
Gomes Naveca, 2013 [97]	2008-09	Brazil	Outpatient clinic	CS	Conv	Patients with primary GUD	PCR	324	50.9
Gomes Naveca, 2013 [97]	2008-09	Brazil	Outpatient clinic	CS	Conv	Patients with recurring GUD	PCR	95	70.5
Noda, 2016 [98]	2012-15	Cuba	Outpatient clinic	CS	Conv	Male patients with GUD aged 15-20 years	PCR	18	77.8
Noda, 2016 [98]	2012-15	Cuba	Outpatient clinic	CS	Conv	Male patients with GUD aged 21-30 years	PCR	48	60.4
Noda, 2016 [98]	2012-15	Cuba	Outpatient clinic	CS	Conv	Male patients with GUD aged 31-40 years	PCR	28	46.4
Noda, 2016 [98]	2012-15	Cuba	Outpatient clinic	CS	Conv	Male patients with GUD aged >41 years	PCR	19	10.5
Valdespino-Gomez, 1995 [99]	1990	Mexico	Community	CS	Conv	FSWs with GUD	IF	71	0.0
Patients with clinically-diagnosed genital herpes									
Balachandran, 1982 [100]	-	Puerto Rico	Outpatient clinic	CS	Conv	Patients with genital herpes	IF	12	91.6
Belli, 1990 [101]	1982-83	Argentina	Outpatient clinic	CS	Conv	Patients with genital herpes	IF	25	79.0
do Nascimento, 1998 [102]	1995	Brazil	Outpatient clinic	CS	Conv	HIV positive patients with genital herpes	PCR	36	94.4
Hun, 1987 [103]	-	Costa Rica	Outpatient clinic	CS	Conv	STI clinic attendees with genital herpes	Virus isolation	12	75.0
Orozco-Topete, 1997 [104]	-	Mexico	Outpatient clinic	RCT[a]	RS	HIV positive patients with recurrent genital herpes	Culture	45	100
Prabhakar, 1987 [105]	1982-84	Jamaica	Outpatient clinic	CS	Conv	Women with genital herpes	IF	40	100
Schultz, 1994 [106]	1988-90	Chile	Outpatient clinic	CS	Conv	Pregnant women with genital lesions	IF	20	90.0
Suárez, 1988 [107]	1985-86	Chile	Outpatient clinic	CS	Conv	Patients with primary genital herpes	IF	14	71.5
Suárez, 1988 [107]	1985-86	Chile	Outpatient clinic	CS	Conv	Patients with recurrent genital herpes	IF	64	90.2
Suárez, 1989 [108]	1984-86	Chile	Outpatient clinic	CS	Conv	Women with genital herpes	IF	13	76.9

[a] The reported study design is the original study design (case control, cross sectional, longitudinal cohort, or randomized controlled trial). The included seroprevalence measures are those for the baseline measures at the beginning of the study.
Abbreviations: Conv = Convenience, CS = Cross sectional, GUD = Genital ulcer disease, FSWs = Female sex workers HSV-2 = Herpes simplex virus type 2, IF = Immunofluorescence, PCR = Polymerase chain reaction, RCT = Randomized controlled trial, RS = Random sampling. STI = Sexually transmitted infections.

Harfouche M, *et al. Sex Transm Infect* 2021;0:1–11. doi: 10.1136/sextrans-2021-054972

Figure S2. Forest plots presenting the outcomes of the pooled mean proportions of HSV-2 virus isolation in clinically-diagnosed genital ulcer disease and in clinically-diagnosed genital herpes in Latin America and the Caribbean.

A) Patients with GUD

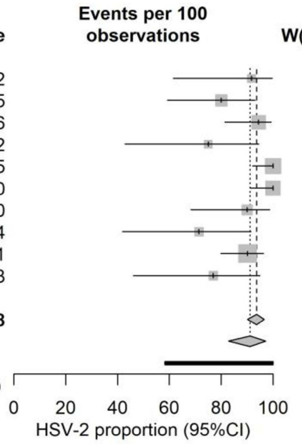


Abbreviations: CI = Confidence interval, GUD = Genital ulcer disease, HSV-2 = Herpes simplex virus type 2.

B) Patients with genital herpes

Author, Year	HSV-2 positive	Sample size	W(Random)	Prev(%)	95%CI
Balachandran, 1982	11	12	7.9%	91.67	[61.52; 99.79]
Belli, 1990	20	25	10.4%	80.00	[59.30; 93.17]
Do Nascimento, 1998	34	36	11.4%	94.44	[81.34; 99.32]
Hun, 1987	9	12	7.9%	75.00	[42.81; 94.51]
Orozco-Topete, 1997	45	45	11.9%	100.00	[92.13; 100.00]
Prabhakar, 1987	40	40	11.7%	100.00	[91.19; 100.00]
Schultz, 1994	18	20	9.7%	90.00	[68.30; 98.77]
Suárez, 1988	10	14	8.4%	71.43	[41.90; 91.61]
Suárez, 1988	55	61	12.6%	90.16	[79.81; 96.30]
Suarez, 1989	10	13	8.2%	76.92	[46.19; 94.96]
Fixed effect model	**252**	**278**	**--**	**93.70**	**[90.10; 96.65]**
Random effects model			**100.0%**	**91.07**	**[82.74; 97.17]**
Prediction interval					**[58.26; 100.00]**

Heterogeneity: $I^2 = 71\%$, $\tau^2 = 0.0227$, $\chi^2_9 = 31.28$ ($p < 0.01$)



Abbreviations: CI = Confidence interval, HSV-2 = Herpes simplex virus type 2.

Table S8. Summary of the precision assessment and risk of bias assessment for the studies reporting HSV-2 seroprevalence in Latin America and the Caribbean.

Quality assessment	HSV-2 seroprevalence measures	
	Number of studies	**%**
Precision of seroprevalence measures[a]		
Low precision	29	17.8
High precision	134	82.2
Risk of bias quality domain[b]		
Sampling method		
Low risk of bias	47	28.8
High risk of bias	116	71.2
Response rate		
Low risk of bias	58	35.6
High risk of bias	9	5.5
Unclear risk of bias	96	58.9
Summary of the risk of bias assessment		
Low risk of bias		
In at least one quality domain	63	38.6
In both quality domains	30	18.4
High risk of bias		
In at least one quality domain	37	22.7
In both quality domains	4	2.4
Seroprevalence studies where risk of bias assessment was possible	**163**	**100**

[a] Precision was assessed based on the overall sample size (not each stratum subsample size) of the study as reported in the record/publication.
[b] Risk of bias was assessed based on the overall sample size (not each stratum subsample size) of the study as reported in the record/publication.
Abbreviations: HSV-2 = Herpes simplex virus type 2.

Harfouche M, *et al. Sex Transm Infect* 2021;0:1–11. doi: 10.1136/sextrans-2021-054972

References

1. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097
2. Smolak A, Chemaitelly H, Hermez JG, et al. Epidemiology of Chlamydia trachomatis in the Middle East and north Africa: a systematic review, meta-analysis, and meta-regression. *Lancet Glob Health* 2019;7(9):e1197-e225. doi: 10.1016/S2214-109X(19)30279-7 [published Online First: 2019/08/14]
3. Abu-Raddad LJ, Akala FA, Semini I, et al. Characterizing the HIV/AIDS Epidemic in the Middle East and North Africa : Time for Strategic Action. World Bank. © World Bank. https://openknowledge.worldbank.org/handle/10986/2457 License: CC BY 3.0 IGO. 2010
4. Brunham RC, Plummer FA. A general model of sexually transmitted disease epidemiology and its implications for control. *Med Clin North Am* 1990;74(6):1339-52.
5. Low N, Broutet N, Adu-Sarkodie Y, et al. Global control of sexually transmitted infections. *Lancet* 2006;368(9551):2001-16.
6. World Health Organization. Global strategy for the prevention and control of sexually transmitted infections: 2006 - 2015. Breaking the chain of transmission. WHO Press, Geneva, Switzerland. Found at: http://www.who.int/reproductivehealth/publications/rtis/9789241563475/en/. Last accessed April 2012. 2007
7. Lupi O. Prevalence and risk factors for herpes simplex infection among patients at high risk for HIV infection in Brazil. *Int J Dermatol* 2011;50(6):709-13.
8. Sánchez-Alemán MA, Uribe-Salas FJ, Lazcano-Ponce EC, et al. HSV-2 seroincidence among Mexican college students: the delay of sexual debut is not enough to avoid risky sexual behaviours and virus transmission. *Sex Transm Infect* 2010;86(7):565-9.
9. Konda KA, Lescano AG, Celentano DD, et al. In Peru, reporting male sex partners imparts significant risk of incident HIV/sexually transmitted infection: all men Engaging in same-sex behavior need prevention services. *Sex Transm Dis* 2013;40(7):569-74.
10. Castillo R, Konda KA, Leon SR, et al. HIV and Sexually Transmitted Infection Incidence and Associated Risk Factors Among High-Risk MSM and Male-to-Female Transgender Women in Lima, Peru. *J Acquir Immune Defic Syndr* 2015;69(5):567-75.
11. Sanchez J, Lama JR, Peinado J, et al. High HIV and ulcerative sexually transmitted infection incidence estimates among men who have sex with men in Peru: awaiting for an effective preventive intervention. *J Acquir Immune Defic Syndr* 2009;51 Suppl 1:S47-51.
12. Yanez Alvarez I, Martinez Salazar MF, Conde Gonzalez CJ, et al. Herpes simplex virus type 2 seroprevalence and seroincidence among HIV infected persons. *Enfermedades Infecciosas y Microbiologia* 2011;31(3):93-97.
13. Abraham CD, Conde-Glez CJ, Cruz-Valdez A, et al. Sexual and demographic risk factors for herpes simplex virus type 2 according to schooling level among Mexican youths. *Sex Transm Dis* 2003;30(7):549-55.
14. Alberts CJ, Schim van der Loeff MF, Papenfuss MR, et al. Association of Chlamydia trachomatis infection and herpes simplex virus type 2 serostatus with genital human papillomavirus infection in men: the HPV in men study. *Sex Transm Dis* 2013;40(6):508-15.
15. Almeida JFM, Campos AH, Marcello MA, et al. Investigation on the association between thyroid tumorigeneses and herpesviruses. *Journal of endocrinological investigation* 2017;40(8):823-29. doi: 10.1007/s40618-017-0609-y [published Online First: 2017/03/10]
16. Ashley-Morrow R, Nollkamper J, Robinson NJ, et al. Performance of Focus ELISA tests for herpes simplex virus type 1 (HSV-1) and HSV-2 antibodies among women in ten diverse geographical locations. *Clinical Microbiology and Infection* 2004;10(6):530-36. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1111/j.1469-0691.2004.00836.x

17. Boulos R, Ruff AJ, Nahmias A, et al. Herpes simplex virus type 2 infection, syphilis, and hepatitis B virus infection in Haitian women with human immunodeficiency virus type 1 and human T lymphotropic virus type I infections. The Johns Hopkins University (JHU)/Centre pour le Developpement et la Santé (CDS) HIV Study Group. *J Infect Dis* 1992;166(2):418-20.
18. Cárcamo CP, Campos PE, García PJ, et al. Prevalences of sexually transmitted infections in young adults and female sex workers in Peru: a national population-based survey. *Lancet Infect Dis* 2012;12(10):765-73.
19. Carvalho M, De Carvalho S, Pannuti CS, et al. Prevalence of herpes simplex type 2 antibodies and a clinical history of herpes in three different populations in Campinas City, Brazil. *International Journal of Infectious Diseases* 1999;3(2):94-98. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1016/S1201-9712%2899%2990016-4
20. Clark JL, Konda KA, Munayco CV, et al. Prevalence of HIV, herpes simplex virus-2, and syphilis in male sex partners of pregnant women in Peru. *BMC Public Health* 2008;8:65-65.
21. Clemens SAC, Farhat CK. Seroprevalence of herpes simplex 1-2 antibodies in Brazil. *Rev Saude Publica* 2010;44(4):726-34.
22. Conde-Glez C, Lazcano-Ponce E, Rojas R, et al. Seroprevalences of varicella-zoster virus, herpes simplex virus and cytomegalovirus in a cross-sectional study in Mexico. *Vaccine* 2013;31(44):5067-74.
23. Conde-Gonzalez CJ, Lazcano-Ponce E, Hernandez-Giron C, et al. [Seroprevalence of type 2 herpes simplex virus infection in 3 population groups of Mexico City]. *Salud publica de Mexico* 2003;45 Supp 5:S608-16. [published Online First: 2004/02/21]
24. Cowan FM, French RS, Mayaud P, et al. Seroepidemiological study of herpes simplex virus types 1 and 2 in Brazil, Estonia, India, Morocco, and Sri Lanka. *Sex Transm Infect* 2003;79(4):286-90.
25. Da Rosa-Santos OL, Gonçalves Da Silva A, Pereira AC. Herpes simplex virus type 2 in Brazil: seroepidemiologic survey. *Int J Dermatol* 1996;35(11):794-6.
26. De Sanjose S, Munoz N, Bosch F, et al. Sexually transmitted agents and cervical neoplasia in Colombia and Spain. *International Journal of Cancer* 1994;56(3):358-63.
27. Domercant JW, Jean Louis F, Hulland E, et al. Seroprevalence of Herpes Simplex Virus type-2 (HSV-2) among pregnant women who participated in a national HIV surveillance activity in Haiti. *BMC Infect Dis* 2017;17(1):577-77.
28. Gabster A, Pascale JM, Cislaghi B, et al. High Prevalence of Sexually Transmitted Infections, and High-Risk Sexual Behaviors Among Indigenous Adolescents of the Comarca Ngäbe-Buglé, Panama. *Sex Transm Dis* 2019;46(12):780-87.
29. Goncalez TT, Sabino EC, Murphy EL, et al. Human immunodeficiency virus test-seeking motivation in blood donors, São Paulo, Brazil. *Vox Sang* 2006;90(3):170-6.
30. Goncalez TT, Blatyta PF, Santos FM, et al. Does offering human immunodeficiency virus testing at the time of blood donation reduce transfusion transmission risk and increase disclosure counseling? Results of a randomized controlled trial, São Paulo, Brazil. *Transfusion* 2015;55(6):1214-22.
31. Gutierrez J-P, Bertozzi SM, Conde-Glez CJ, et al. Risk behaviors of 15-21 year olds in Mexico lead to a high prevalence of sexually transmitted infections: results of a survey in disadvantaged urban areas. *BMC Public Health* 2006;6:49-49.
32. Gutierrez JP, Conde-González CJ, Walker DM, et al. Herpes simplex virus type 2 among Mexican high school adolescents: prevalence and association with community characteristics. *Arch Med Res* 2007;38(7):774-82.
33. Herrera-Ortiz A, Conde-Glez CJ, Vergara-Ortega DN, et al. Avidity of antibodies against HSV-2 and risk to neonatal transmission among Mexican pregnant women. *Infect Dis Obstet Gynecol* 2013;2013:140142-42.
34. Juarez-Figueroa LA, Uribe-Salas FJ, Conde-Glez CJ, et al. Hepatitis B markers in men seeking human immunodeficiency virus antibody testing in Mexico City. *Sex Transm Dis* 1997;24(4):211-7. [published Online First: 1997/04/01]

35. Konda KA, Klausner JD, Lescano AG, et al. The epidemiology of herpes simplex virus type 2 infection in low-income urban populations in coastal Peru. *Sex Transm Dis* 2005;32(9):534-41.
36. Lazcano-Ponce E, Smith JS, Muñoz N, et al. High prevalence of antibodies to herpes simplex virus type 2 among middle-aged women in Mexico City, Mexico: a population-based study. *Sex Transm Dis* 2001;28(5):270-6.
37. Levett PN. Seroprevalence of HSV-1 and HSV-2 in Barbados. *Med Microbiol Immunol* 2005;194(1-2):105-7.
38. Moreira-Soto A, Cabral R, Pedroso C, et al. Exhaustive TORCH Pathogen Diagnostics Corroborate Zika Virus Etiology of Congenital Malformations in Northeastern Brazil. *mSphere* 2018;3(4) doi: 10.1128/mSphere.00278-18 [published Online First: 2018/08/10]
39. Muñoz N, Kato I, Bosch FX, et al. Cervical cancer and herpes simplex virus type 2: case-control studies in Spain and Colombia, with special reference to immunoglobulin-G sub-classes. *Int J Cancer* 1995;60(4):438-42.
40. Nascimento MC, Ferreira S, Sabino E, et al. Performance of the HerpeSelect (Focus) and Kalon enzyme-linked immunosorbent assays for detection of antibodies against herpes simplex virus type 2 by use of monoclonal antibody-blocking enzyme immunoassay and clinicovirological reference standards in Brazil. *Journal of clinical microbiology* 2007;45(7):2309-11. doi: 10.1128/jcm.00144-07 [published Online First: 2007/05/18]
41. Nascimento MC, De Souza VA, Sumita LM, et al. Prevalence of, and risk factors for Kaposi's sarcoma-associated herpesvirus infection among blood donors in Brazil: A multi-center serosurvey. *Journal of Medical Virology* 2008;80(7):1202-10. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1002/jmv.21188
42. Nascimento MC, Sumita LM, Souza VU, et al. Seroprevalence of Kaposi sarcoma-associated herpesvirus and other serologic markers in the Brazilian Amazon. *Emerging infectious diseases* 2009;15(4):663-7. doi: 10.3201/eid1504.081488 [published Online First: 2009/04/01]
43. Oberle MW, Rosero-Bixby L, Lee FK, et al. Herpes simplex virus type 2 antibodies: high prevalence in monogamous women in Costa Rica. *Am J Trop Med Hyg* 1989;41(2):224-9.
44. Patnaik P, Herrero R, Morrow RA, et al. Type-specific seroprevalence of herpes simplex virus type 2 and associated risk factors in middle-aged women from 6 countries: the IARC multicentric study. *Sex Transm Dis* 2007;34(12):1019-24.
45. Patzi-Churqui M, Terrazas-Aranda K, Liljeqvist JA, et al. Prevalence of viral sexually transmitted infections and HPV high-risk genotypes in women in rural communities in the Department of La Paz, Bolivia. *BMC Infect Dis* 2020;20(1):204. doi: 10.1186/s12879-020-4931-1 [published Online First: 2020/03/08]
46. Paz-Bailey G, Morales-Miranda S, Jacobson JO, et al. High rates of STD and sexual risk behaviors among Garífunas in Honduras. *J Acquir Immune Defic Syndr* 2009;51 Suppl 1:S26-34.
47. Rodríguez AC, Castle PE, Smith JS, et al. A population based study of herpes simplex virus 2 seroprevalence in rural Costa Rica. *Sex Transm Infect* 2003;79(6):460-5.
48. Sánchez J, Gotuzzo E, Escamilla J, et al. Gender differences in sexual practices and sexually transmitted infections among adults in Lima, Peru. *Am J Public Health* 1996;86(8):1098-107.
49. Sánchez-Alemán MA, Conde-Glez CJ, Gayet C, et al. Sexual behavior and herpes simplex virus 2 infection in college students. *Arch Med Res* 2005;36(5):574-80.
50. Sánchez-Alemán MA, Conde-Glez CJ, Uribe-Salas F. Core group approach to identify college students at risk for sexually transmitted infections. *Rev Saude Publica* 2008;42(3):428-36.
51. Sierra CA, Bedoya AM, Paris S, et al. Prevalence of specific herpes simplex virus-2 antibodies and associated factors in women of a rural town of Colombia. *Trans R Soc Trop Med Hyg* 2011;105(4):232-8.
52. Smith JS, Herrero R, Muñoz N, et al. Prevalence and risk factors for herpes simplex virus type 2 infection among middle-age women in Brazil and the Philippines. *Sex Transm Dis* 2001;28(4):187-94.

53. Smith JS, Herrero R, Bosetti C, et al. Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. *Journal of the National Cancer Institute* 2002;94(21):1604-13. [published Online First: 2002/11/07]
54. Uribe-Salas F, Palma-Coca O, Sánchez-Alemán MA, et al. Population-based prevalence of antibodies against herpes simplex virus type 2 and socio-demographic characteristics in Mexico. *Trans R Soc Trop Med Hyg* 2009;103(2):151-8.
55. Vaccarella S, Franceschi S, Herrero R, et al. Sexual behavior, condom use, and human papillomavirus: pooled analysis of the IARC human papillomavirus prevalence surveys. *Cancer Epidemiology and Prevention Biomarkers* 2006;15(2):326-33.
56. Weinberg A, Canto CL, Pannuti CS, et al. Herpes simplex virus type 2 infection in pregnancy: asymptomatic viral excretion at delivery and seroepidemiologic survey of two socioeconomically distinct populations in Sao Paulo, Brazil. *Revista do Instituto de Medicina Tropical de Sao Paulo* 1993;35(3):285-90. [published Online First: 1993/05/01]
57. Zamilpa-Mejía LG, Uribe-Salas F, Juárez-Figueroa L, et al. Prevalencia y factores asociados con sífilis y herpes genital en dos grupos de población femenina. *Salud publica de Mexico* 2003;45 Supp 5:S617-23.
58. Benzaken A, Sabidó M, Galban E, et al. HIV and sexually transmitted infections at the borderlands: situational analysis of sexual health in the Brazilian Amazon. *Sex Transm Infect* 2012;88(4):294-300.
59. Celentano DD, Mayer KH, Pequegnat W, et al. Prevalence of Sexually Transmitted Diseases and Risk Behaviors from the NIMH Collaborative HIV/STD Prevention Trial. *International journal of sexual health : official journal of the World Association for Sexual Health* 2010;22(4):272-84. doi: 10.1080/19317611.2010.494092 [published Online First: 2010/01/01]
60. Clark JL, Lescano AG, Konda KA, et al. Syndromic management and STI control in urban Peru. *PLoS One* 2009;4(9):e7201-e01.
61. Couture M-C, Soto JC, Akom E, et al. Clients of female sex workers in Gonaives and St-Marc, Haiti characteristics, sexually transmitted infection prevalence and risk factors. *Sex Transm Dis* 2008;35(10):849-55.
62. Pinho AA, Chinaglia M, Lippman SA, et al. Prevalence and factors associated with HSV-2 and hepatitis B infections among truck drivers crossing the southern Brazilian border. *Sex Transm Infect* 2011;87(7):553-9.
63. Sabidó M, Lahuerta M, Montoliu A, et al. Human immunodeficiency virus, sexually transmitted infections, and risk behaviors among clients of sex workers in Guatemala: are they a bridge in human immunodeficiency virus transmission? *Sex Transm Dis* 2011;38(8):735-42.
64. Uribe-Salas F, Hernandez-Giron C, Conde-Gonzalez C, et al. Characteristics related to STD/HIV in men working in Mexico City bars where female prostitution takes place. *Salud publica de Mexico* 1995;37(5):385-93.
65. Villarroel-Torrico M, Montano K, Flores-Arispe P, et al. Syphilis, human immunodeficiency virus, herpes genital and hepatitis B in a women's prison in Cochabamba, Bolivia: prevalence and risk factors. *Revista espanola de sanidad penitenciaria* 2018;20(2):47-54. [published Online First: 2018/09/20]
66. Brito MO, Hodge D, Donastorg Y, et al. Risk behaviours and prevalence of sexually transmitted infections and HIV in a group of Dominican gay men, other men who have sex with men and transgender women. *BMJ Open* 2015;5(4):e007747-e47.
67. Conde-Glez CJ, Juárez-Figueroa L, Uribe-Salas F, et al. Analysis of herpes simplex virus 1 and 2 infection in women with high risk sexual behaviour in Mexico. *Int J Epidemiol* 1999;28(3):571-6.
68. HIV, STD and risk behaviors among female sex worker in El Salvador. Poster CDC0622. International AIDS Conference; 2010; Vienna, Austria.
69. Gotuzzo E, Sanchez J, Escamilla J, et al. Human T cell lymphotropic virus type I infection among female sex workers in Peru. *J Infect Dis* 1994;169(4):754-9. [published Online First: 1994/04/01]
70. Hakre S, Arteaga G, Núñez AE, et al. Prevalence of HIV and other sexually transmitted infections and factors associated with syphilis among female sex workers in Panama. *Sex Transm Infect* 2013;89(2):156-64.

71. Hakre S, Arteaga GB, Núñez AE, et al. Prevalence of HIV, syphilis, and other sexually transmitted infections among MSM from three cities in Panama. *J Urban Health* 2014;91(4):793-808.
72. Hernandez F, Arambu N, Alvarez B, et al. High incidence of HIV and low HIV prevention coverage among men who have sex with men in Managua, Nicaragua. *Sexually Transmitted Infections* 2011;87(SUPPL. 1):A146. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1136/sextrans-2011-050108.112
73. Lama JR, Lucchetti A, Suarez L, et al. Association of herpes simplex virus type 2 infection and syphilis with human immunodeficiency virus infection among men who have sex with men in Peru. *J Infect Dis* 2006;194(10):1459-66.
74. Morales-Miranda S, Paredes M, Arambu N, et al. HIV, STD and risk behaviors among men who have sex with men, female sex workers, and indigenous Garífuna population in Honduras. . WEAX0305 In: International AIDS Conference Mexico, Mexico, 2008.
75. Perez-Brumer AG, Konda KA, Salvatierra HJ, et al. Prevalence of HIV, STIs, and risk behaviors in a cross-sectional community- and clinic-based sample of men who have sex with men (MSM) in Lima, Peru. *PLoS One* 2013;8(4):e59072-e72.
76. Perla ME, Ghee AE, Sánchez S, et al. Genital tract infections, bacterial vaginosis, HIV, and reproductive health issues among Lima-based clandestine female sex workers. *Infect Dis Obstet Gynecol* 2012;2012:739624-24.
77. Rodrigues J, Grinsztejn B, Bastos FI, et al. Seroprevalence and factors associated with herpes simplex virus type 2 among HIV-negative high-risk men who have sex with men from Rio de Janeiro, Brazil: a cross-sectional study. *BMC Infect Dis* 2009;9:39-39.
78. Sanchez J, Gotuzzo E, Escamilla J, et al. Sexually transmitted infections in female sex workers: reduced by condom use but not by a limited periodic examination program. *Sex Transm Dis* 1998;25(2):82-9. [published Online First: 1998/03/28]
79. Sanchez J, Lama JR, Kusunoki L, et al. HIV-1, sexually transmitted infections, and sexual behavior trends among men who have sex with men in Lima, Peru. *J Acquir Immune Defic Syndr* 2007;44(5):578-85.
80. Shah NS, Kim E, de Maria Hernández Ayala F, et al. Performance and comparison of self-reported STI symptoms among high-risk populations - MSM, sex workers, persons living with HIV/AIDS - in El Salvador. *Int J STD AIDS* 2014;25(14):984-91.
81. Silva-Santisteban A, Raymond HF, Salazar X, et al. Understanding the HIV/AIDS epidemic in transgender women of Lima, Peru: results from a sero-epidemiologic study using respondent driven sampling. *AIDS Behav* 2012;16(4):872-81.
82. Soto RJ, Ghee AE, Nunez CA, et al. Sentinel surveillance of sexually transmitted infections/HIV and risk behaviors in vulnerable populations in 5 Central American countries. *J Acquir Immune Defic Syndr* 2007;46(1):101-11.
83. Uribe-Salas F, Hernández-Avila M, Juárez-Figueroa L, et al. Risk factors for herpes simplex virus type 2 infection among female commercial sex workers in Mexico City. *Int J STD AIDS* 1999;10(2):105-11.
84. Uribe-Salas F, Conde-Glez CJ, Juarez-Figueroa L, et al. Socio-demographic characteristics and sex practices related to herpes simplex virus type 2 infection in Mexican and Central American female sex workers. *Epidemiol Infect* 2003;131(2):859-65.
85. Zunt JR, La Rosa AM, Peinado J, et al. Risk factors for HTLV-II infection in Peruvian men who have sex with men. *Am J Trop Med Hyg* 2006;74(5):922-5.
86. Martinez MJ, Navarrete N, Santander E, et al. Seroprevalence of herpes simplex virus type 2 (HSV-2) infection in two clinics for sexually transmitted diseases in Santiago, Chile. *Revista medica de Chile* 2005;133(3):302-06.
87. Batista MD, Ferreira S, Sauer MM, et al. High human herpesvirus 8 (HHV-8) prevalence, clinical correlates and high incidence among recently HIV-1-infected subjects in Sao Paulo, Brazil. *PLoS ONE* 2009;4(5):e5613. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1371/journal.pone.0005613
88. Lima LRP, Fernandes LEBC, Villela DAM, et al. Co-infection of human herpesvirus type 2 (HHV-2) and human immunodeficiency virus (HIV) among pregnant women in Rio de Janeiro, Brazil. *AIDS Care -*

Psychological and Socio-Medical Aspects of AIDS/HIV 2018;30(3):378-82. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1080/09540121.2017.1378798
89. Paz-Bailey G, Isern Fernandez V, Morales Miranda S, et al. Unsafe sexual behaviors among HIV-positive men and women in Honduras: the role of discrimination, condom access, and gender. *Sex Transm Dis* 2012a;39(1):35-41.
90. Paz-Bailey G, Shah N, Creswell J, et al. Risk behaviors and STI prevalence among people with HIV in El Salvador. *Open AIDS J* 2012b;6:205-12.
91. Santos FC, De Oliveira SA, Setubal S, et al. Seroepidemiological study of herpes simplex virus type 2 in patients with the acquired immunodeficiency syndrome in the City of Niteroi, Rio de Janeiro, Brazil. *Memorias do Instituto Oswaldo Cruz* 2006;101(3):315-19.
92. Bahena-Roman M, Sanchez-Aleman MA, Contreras-Ochoa CO, et al. Prevalence of active infection by herpes simplex virus type 2 in patients with high-risk human papillomavirus infection: A cross-sectional study. *J Med Virol* 2020 doi: 10.1002/jmv.25668 [published Online First: 2020/01/12]
93. Calderon G, Pinto M, Pizarro R, et al. Viral infections associated in breast cancer patients in a Latin American cancer institute. *Annals of Surgical Oncology* 2018;25(2 Supplement 1):148-49. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1245/s10434-018-6534-2
94. Castle PE, Escoffery C, Schachter J, et al. Chlamydia trachomatis, herpes simplex virus 2, and human T-cell lymphotrophic virus type 1 are not associated with grade of cervical neoplasia in Jamaican colposcopy patients. *Sex Transm Dis* 2003;30(7):575-80.
95. DeBritton RC, Hildesheim A, De Lao SL, et al. Human papillomaviruses and other influences on survival from cervical cancer in Panama. *Obstet Gynecol* 1993;81(1):19-24.
96. Stone KM, Zaidi A, Rosero-Bixby L, et al. Sexual behavior, sexually transmitted diseases, and risk of cervical cancer. *Epidemiology* 1995;6(4):409-14.
97. Gomes Naveca F, Sabidó M, Amaral Pires de Almeida T, et al. Etiology of genital ulcer disease in a sexually transmitted infection reference center in Manaus, Brazilian Amazon. *PLoS One* 2013;8(5):e63953-e53.
98. Noda AA, Blanco O, Correa C, et al. Etiology of Genital Ulcer Disease in Male Patients Attending a Sexually Transmitted Diseases Clinic: First Assessment in Cuba. *Sex Transm Dis* 2016;43(8):494-7.
99. Valdespino-Gomez JL, Garcia-Garcia ML, del Rio-Chiriboga C, et al. Sexually transmitted diseases and the HIV/AIDS epidemic. *Salud publica de Mexico* 1995;37(6):549-55.
100. Balachandran N, Frame B, Chernesky M, et al. Identification and typing of herpes simplex viruses with monoclonal antibodies. *Journal of clinical microbiology* 1982;16(1):205-08.
101. Belli L, Irigoyen MH, Casco RH, et al. Pautas para el manejo de la infección herpética genital en la experiencia de un centro de atención de ETS en Buenos Aires (Argentina). *Med Cutan Ibero Lat Am* 1990;18(1):44-8.
102. do Nascimento MC, Sumita LM, de Souza VA, et al. Detection and direct typing of herpes simplex virus in perianal ulcers of patients with AIDS by PCR. *Journal of clinical microbiology* 1998;36(3):848-49.
103. Hun L, Fuentes LG. Diagnóstico del laboratorio de virus herpes simplex en Costa Rica. *Rev Costarric Cienc Med* 1987;8(3):143-8.
104. Orozco-Topete R, Sierra-Madero J, Cano-Dominguez C, et al. Safety and efficacy of Virend for topical treatment of genital and anal herpes simplex lesions in patients with AIDS. *Antiviral Research* 1997;35(2):91-103. doi: http://0-dx.doi.org.elibrary.qatar-weill.cornell.edu/10.1016/S0166-3542%2897%2900015-6
105. Prabhakar P, Allam MG, Prabhu PS, et al. Genital herpes in Jamaica. A clinical and pathological study (1982-1984). *West Indian Med J* 1987;36(3):154-8.
106. Schultz R, Suarez M, Saavedra T. Follow-up of pregnant women at high risk of transmitting herpes simplex virus. *Bulletin of the Pan American Health Organization* 1994;28(2):163-8. [published Online First: 1994/06/01]
107. Suárez M, Labbé V, Saavedra T, et al. Tipos víricos del herpes simple asociados a infecciones genitales primarias y recurrentes en Chile. *Bol Oficina Sanit Panam* 1988;105(1):13-9.

108. Suarez M, Briones H, Dubinovsky S, et al. Genital herpes infection in Chilean female university students. *Boletin de la Oficina Sanitaria Panamericana Pan American Sanitary Bureau* 1989;106(5):389-95.