Herpes simplex virus: global infection prevalence and incidence estimates, 2016

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Objective To generate global and regional estimates for the prevalence and incidence of herpes simplex virus (HSV) type 1 and type 2 infection for 2016.

Methods To obtain data, we undertook a systematic review to identify studies up to August 2018. Adjustments were made to account for HSV test sensitivity and specificity. For each World Health Organization (WHO) region, we applied a constant incidence model to pooled prevalence by age and sex to estimate the prevalence and incidence of HSV types 1 and 2 infections. For HSV type 1, we apportioned infection by anatomical site using pooled estimates of the proportions that were oral and genital.

Findings In 2016, an estimated 491.5 million people (95% uncertainty interval, UI: 430.4 million–610.6 million) were living with HSV type 2 infection, equivalent to 13.2% of the world's population aged 15–49 years. An estimated 3752.0 million people (95% UI: 3555.5 million–3854.6 million) had HSV type 1 infection at any site, equivalent to a global prevalence of 66.6% in 0–49-year-olds. Differing patterns were observed by age, sex and geographical region, with HSV type 2 prevalence being highest among women and in the WHO African Region.

Conclusion An estimated half a billion people had genital infection with HSV type 2 or type 1, and several billion had oral HSV type 1 infection. Millions of people may also be at higher risk of acquiring human immunodeficiency virus (HIV), particularly women in the WHO African Region who have the highest HSV type 2 prevalence and exposure to HIV.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

Herpes simplex virus (HSV) infections are widespread among humans globally.[1,2] The infection is lifelong and characterized by periodic reactivations at the infection site. HSV type 1 is primarily transmitted by oral-to-oral contact and commonly causes orolabial herpes (cold sores).[3] Type 1 virus also causes rarer conditions, such as keratitis and other ocular sequalae, and encephalitis.[4] HSV type 1 genital infection from oral-to-genital contact is becoming increasingly common, although reactivations are less frequent than for HSV type 2.[5–10] HSV type 2 is almost entirely sexually transmitted, causing genital herpes.[11] Genital HSV infection may be unrecognized or result in painful genital ulcer disease in a proportion of those infected. Neonates can acquire HSV infection from genitally infected mothers during birth and from oral contact with caregivers postnatally.[12] Neonatal infection, although rare, has a high fatality and disability rate in surviving infants.[12] Evidence also suggests that HSV type 2 infection increases the risk of acquiring human immunodeficiency virus (HIV).[13] Symptomatic and asymptomatic viral shedding are common for both HSV type 1 and type 2.[14,15] Thus, infected individuals can be asymptomatic yet infectious, allowing these viruses to be transmitted unknowingly, a factor which contributes to the large global prevalence of HSV infection.

The World Health Organization (WHO) has produced global and regional estimates of HSV type 2 infection prevalence and incidence (derived from prevalence) among individuals 15–49 years or age twice before: for the years 2005 and 2012.[2,16] The first estimates of HSV type 1 infection at any site in those aged 0–49 years of age, and of genital HSV type 1 infection in those aged 15–49 years of age, were done for 2012.[1] The Global Burden of Disease (GBD) study has also produced estimates for HSV type 2 infection (again deriving incidence from estimated prevalence, similar to the WHO estimates), most recently for 2017.[17] However, these estimates are not directly comparable to the WHO estimates as they extend to age 99 years of age, are not adjusted for assay performance and use different regional groupings than the WHO estimates. Furthermore, the GBD study does not produce any estimates for HSV type 1 infection, an increasingly important cause of genital infection.

Estimates of HSV infection across geographical regions, age, sex, HSV type and infection site (oral versus genital) are needed for advocacy and resource planning. In 2016, the World Health Assembly adopted the Global Health Sector Strategy on Sexually Transmitted Infections, 2016–2021,[18] which aims to end sexually transmitted infections as a public health concern by 2030. The strategy sets out reduction targets, which in turn depend on reliable baseline estimates for each sexually transmitted infection. Quantifying HSV infection and disease is also necessary to guide the development of new products, such as vaccines.[19–21] Infection estimates can be used as a starting point for estimating the burden of HSV-related disease when direct incidence data are lacking, by applying the risks of particular outcomes to the number of people infected, as has been done for neonatal herpes.[22] In this systematic review we made global and regional estimates of HSV type 2 and genital HSV type 1 infection for the year 2016, incorporating newly available data, and estimates specifically for oral HSV type 1 infection.

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Methods

We used similar methods as for our previous estimates.[1,2,16] We conducted a systematic literature search followed by pooling of extracted data using meta-analysis. First, we searched the online databases MEDLINE® and Embase® to identify relevant studies with publication dates between August 2013 (to ensure overlap with the literature searches informing the 2012 estimates) and August 2018. We included studies of the prevalence and incidence of HSV type 1 and type 2 infection, as measured by the detection of type-specific immunoglobulin G antibodies, in any language. We applied broad inclusion and exclusion criteria to the studies to extract the data and then applied additional criteria to the extracted data for calculating the estimates. We excluded high-risk populations and based the calculations on prevalence data from general populations only. Incidence data were used solely for comparison and validation purposes. Further details of the search strategy, data extraction and synthesis, and definitions of general populations are in the data repository.[23]

We then pooled the newly extracted data with data from our previous estimates, using studies from year 2004 or later. Thus, there was a large overlap in the studies included between the current and previous set of estimates. We pooled prevalence values by sex where possible and 5-year age groups for each WHO region (African, Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific) and separately for HSV type 1 and type 2. The force of the infection was then calibrated to each set of pooled prevalence values over age, assuming a constant force of infection with age. Before pooling, we adjusted the prevalence values for the sensitivity and specificity of the tests used to detect HSV in different studies (data repository).[23] Smoothed prevalence and derived incidence (that is, from the calibrated force of infection) were applied to population data for 2016[24] to obtain the most up-to-date estimates of the number of people with prevalent (existing) and incident (newly-acquired over one year) HSV type 1 and 2 infection by WHO region. Estimates for oral HSV type 1 infection were done for individuals 0–49 years of age, and estimates for HSV type 2 and genital HSV type 1 infection were done for individuals 15–49 years of age. We also did a speculative analysis to estimate the number of older individuals infected by applying the prevalence in those 45–49 years of age to population numbers for those 50–99 years of age. Further details of the calculation of prevalence, incidence and uncertainty bounds are in the data repository.[23]

To estimate the proportion of individuals infected at different sites, we first pooled values from longitudinal studies of the proportions of adults with oral (pooled estimate: 36.4%) and genital (pooled estimate: 72.4%) symptoms among all adults with HSV type 1 seroconversion, which was accompanied by symptoms (either or both sites).[25–28] In other words, we estimated the proportions of new HSV type 1 infections that were oral versus genital for individuals where the site of infection could be determined on the basis of symptoms. Pooling was done using the *metan* command in Stata, version 16 (StataCorp, College Station, United States of America) and assuming a random effects model. We then applied these proportions to HSV type 1 incidence only in those 15–49 years of age to estimate the numbers with oral and genital HSV type 1 infection separately. This method was slightly different to the method of estimating genital HSV type 1 infection for 2012, in which values from two studies of symptomatic HSV type 1 seroconversions were used to generate two separate sets of estimates in adults.[1] HSV type 1 infection in those younger than 15 years was assumed to be all oral. In a separate sensitivity analysis, we limited those able to be infected with genital HSV type 1 to the proportion of individuals by age who engaged in oral sex in the last 12 months (data for females and males combined) according to the National Health and Nutrition Evaluation Survey 2015–2016, the largest, national population-based survey in the USA.[29] We calculated the total percentage of people with genital infection due to either HSV type 1 by summing the prevalence of each infection, and then adjusting for the percentage of people assumed to be genitally infected with both viral types.

Results

Literature search

We identified a total of 4262 publications in the updated literature search (Fig. 1). After removal of duplicates, we screened 3511 records on the basis of title and abstract, and excluded a further 3111 records, which did not meet the criteria for relevance. We obtained full texts for the remaining 400 records along with an additional 13 publications identified from reference lists.[8,30,31] Of these 413 publications, 182 contained relevant data and were subsequently included in the data extraction: 48 HSV type 1 prevalence studies, 136 HSV type 2 prevalence studies, 1 HSV type 1 incidence study and 20 HSV type 2 incidence studies (some studies contributed data in more than one category). However, not all of these studies met our criteria for inclusion in the estimates, while some studies identified in previous reviews were still sufficiently recent (after 2004).

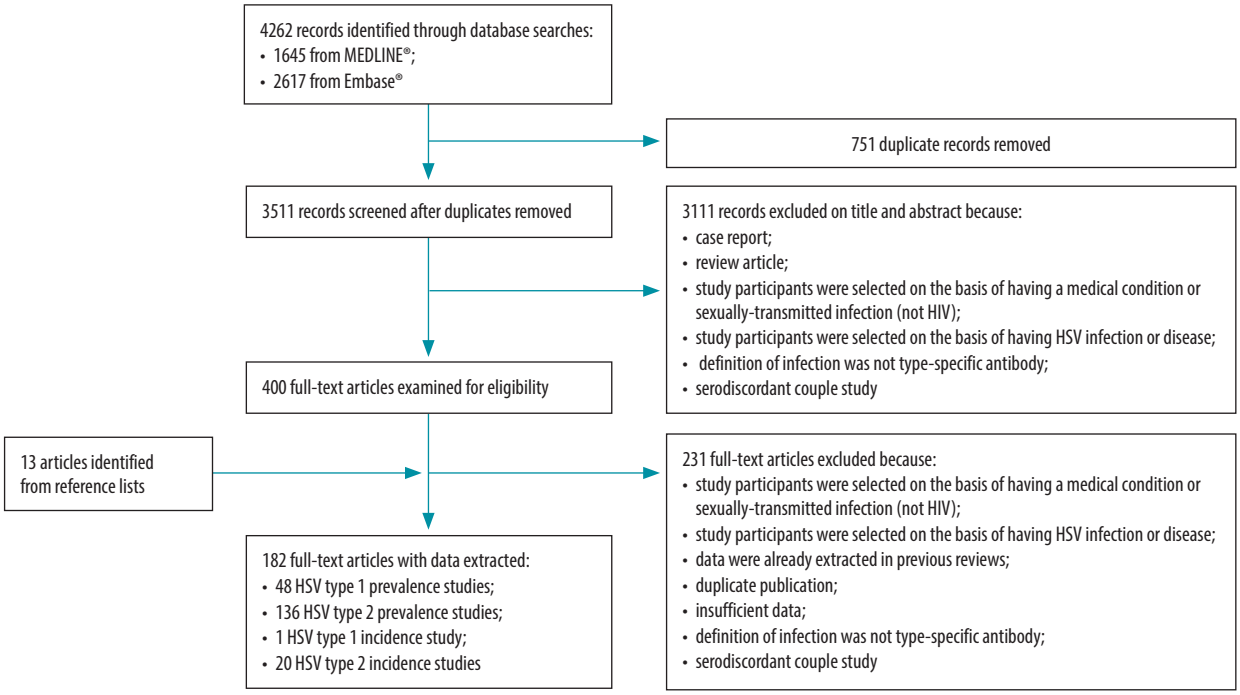
Pooling data from all the studies meeting our criteria we made the estimates using 474 HSV type 2 prevalence data points (262 from newly identified studies) and 223 HSV type 1 prevalence data points (128 from newly identified studies). The number of data points by age and sex, the countries contributing data and the inclusion criteria applied is available in the data repository.[23]

In comparison with the 2012 estimates, the number of available prevalence data points for 2016 improved for both HSV types 1 and 2. However, this increase did not generally follow from an increase in the number of countries represented, as the number of contributing countries mostly declined between the 2012 and 2016 estimates. The decline was particularly apparent for the WHO Region of the Americas, where HSV type 1 estimates for males were based solely on data from individuals in the USA. The prevalence and incidence data from studies newly extracted for this review[32–122] are shown in the data repository.[23]

Prevalence of infection

Our estimates for 2016 found that a total of 491.5 million (95% UI: 430.4 million–610.6 million) individuals 15–49 years of age worldwide were living with HSV type 2 infection (Table 1 and Fig. 2). More women (313.5 million) than men (178.0 million) were infected. The number of people infected was highest in the WHO African Region (102.9 million females and 59.3 million males), followed by the Western Pacific, South-East Asia and Americas Regions. The estimated prevalence of HSV type 2 in the global population

Fig. 1. **Flowchart on the selection of studies for estimating infection prevalence and incidence of herpes simplex virus, 2016**



HIV: human immunodeficiency virus; HSV: herpes simplex virus.

of 3735.6 million people 15–49 years of age was 13.2% (95% UI: 11.5–16.3) and was highest among the population of the African Region, followed by the Region of the Americas, and among women. The number infected increased with age, largely mirroring increases in the prevalence with age, although differences in population sizes also affected the observed numbers. The regional pooled prevalence values and model fits for HSV type 2 infection is available in the data repository.[23]

An estimated 3583.5 million (95% UI: 3322.2 million–3715.8 million) of the 5632.6 million global population 0–49 years of age were infected orally with HSV type 1, a prevalence of 63.6% (95% UI: 59.0–66.0; Table 2). The number of people with oral HSV-1 was largest in the WHO South-East Asia Region, followed by the Western Pacific Region. Genital HSV type 1 infection affected an estimated 192.0 million (95% UI: 123.0 million–294.0 million) individuals 15–49 years of age worldwide (Table 3), equivalent to a prevalence of 5.2% (95% UI: 3.3–8.0). The number of people with genital HSV type 1 was highest in the Region of the Americas, followed by the European Region. There was a general trend of increasing numbers of people infected with both oral and genital HSV type 1 infection by age, mirroring the increasing prevalence of both infections in our model.

When considering HSV type 1 infection at any site, we estimated 3752.0 million people (95% UI: 3555.5 million–3854.6 million) of the world's population 0–49 years of age were infected, a prevalence of 66.6% (95% UI: 63.1–68.4; data repository).[23] The regional pooled prevalence values and model fits are available in the data repository.[23] Note that the number of people with oral and genital HSV type 1 infections do not sum exactly to the number with HSV type 1 infection at any site, as we assumed a small proportion of people can be infected at both sites simultaneously. The estimates were highly sensitive to our assumption that anyone aged 15 years of age and older who does not have an existing infection can acquire genital HSV type 1. If only those individuals who engaged in oral sex in the last year are at risk of acquiring genital HSV type 1 infection, then we estimate 122.3 million (3.3%) of those 15–49 years of age had prevalent genital HSV type 1 infections in 2016 (data repository).[23]

Taken together, an estimated 596.0 million–655.7 million people, 16.0–17.6% of the world's population 15–49 years of age, had genital HSV type 1 or HSV type 2 or both, based on 122.3 million–192.0 million genital HSV type 1 infections.

Applying the prevalence in those aged 45–49 years of age to population numbers for those aged 50–99 years of age, we estimated that globally, a total of 1290.1 million and 344.5 million people aged 50–99 years were infected with HSV type 1 (any site) and HSV type 2, respectively, bringing the totals to 4850.1 million and 836.0 million, respectively (data repository).[23]

The global prevalence of HSV type 2 for 2016 (13.2%; 95% UI: 11.5–16.3) was estimated to be somewhat higher than that estimated for 2012 (11.3%; 95% UI: 7.4–18.4),[2] although the 95% UI overlapped. Applying equal population numbers by age, sex, WHO region and estimate year, the observed increase in global HSV type 2 prevalence between 2012 and 2016 remained but was somewhat diminished (13.7% versus 15.2%). This pattern was seen across all regions and especially for females, except for the Eastern Mediterranean Region, where a decrease was observed.

Incidence of infection

We estimated that 23.9 million (95% UI: 21.0 million–29.5 million) people 15–49 years of age became infected with HSV type 2 in 2016, an incidence of 0.6% (95% UI: 0.6–0.8; Table 4). Of

Table 1. **Global and regional estimates of the prevalence of herpes simplex virus type 2 infections by age and sex, 2016**

WHO region by sex	No. of infected people in millions (population prevalence, %) by age group							95% UI[a]
	15–19 years	20–24 years	25–29 years	30–34 years	35–39 years	40–44 years	45–49 years	Total	
Total	27.8 (4.8)	49.6 (8.5)	68.6 (11.4)	78.9 (14.3)	83.3 (16.8)	89.6 (18.8)	93.7 (20.8)	491.5 (13.2)	430.4–610.6 (11.5–16.3)
Female									
Africa	10.1 (21.7)	15.3 (35.9)	17.5 (46.5)	17.8 (54.2)	16.3 (60.0)	14.1 (64.2)	11.9 (67.3)	102.9 (43.9)	85.0–120.0 (36.3–51.2)
Americas	2.6 (7.8)	5.1 (14.4)	7.3 (20.5)	9.1 (26.1)	10.3 (31.4)	11.3 (36.3)	12.0 (40.8)	57.7 (24.0)	46.4–71.6 (19.3–29.7)
Eastern Mediterranean	0.7 (2.5)	1.3 (4.6)	1.9 (6.8)	2.3 (8.8)	2.3 (10.9)	2.2 (12.9)	2.2 (14.8)	12.8 (7.6)	5.7–29.4 (3.4–17.6)
Europe	0.7 (3.0)	1.5 (5.7)	2.5 (8.3)	3.4 (10.8)	4.0 (13.2)	4.8 (15.6)	5.4 (17.9)	22.2 (10.7)	10.4–45.2 (5.0–21.7)
South-East Asia	2.3 (3.0)	4.4 (5.6)	6.3 (8.2)	7.8 (10.7)	8.7 (13.1)	9.3 (15.5)	9.5 (17.8)	48.4 (9.6)	20.2–105.2 (4.0–20.9)
Western Pacific	2.0 (4.2)	4.7 (7.8)	8.7 (11.3)	10.0 (14.7)	10.9 (17.9)	14.9 (21.0)	18.3 (24.0)	69.5 (14.6)	43.8–106.3 (9.2–22.3)
Total	18.4 (6.6)	32.2 (11.4)	44.1 (15.0)	50.3 (18.5)	52.7 (21.6)	56.5 (24.1)	59.2 (26.4)	313.5 (17.1)	265.7–389.1 (14.5–21.3)
Male									
Africa	4.6 (9.8)	7.6 (17.8)	9.4 (25.1)	10.3 (31.8)	10.1 (37.9)	9.3 (43.4)	8.1 (48.5)	59.3 (25.4)	44.1–77.1 (18.9–33.0)
Americas	1.2 (3.6)	2.5 (6.7)	3.5 (9.7)	4.4 (12.6)	5.0 (15.5)	5.5 (18.2)	5.9 (20.8)	28.0 (11.6)	18.2–42.0 (7.5–17.3)
Eastern Mediterranean	0.2 (0.9)	0.5 (1.6)	0.7 (2.4)	0.9 (3.2)	0.9 (4.0)	0.9 (4.7)	0.9 (5.5)	5.1 (2.8)	1.1–23.9 (0.6–13.2)
Europe	0.3 (1.5)	0.8 (2.8)	1.3 (4.1)	1.7 (5.4)	2.0 (6.6)	2.4 (7.9)	2.7 (9.1)	11.1 (5.3)	5.1–23.1 (2.4–11.0)
South-East Asia	1.9 (2.2)	3.6 (4.2)	5.0 (6.2)	6.2 (8.1)	6.9 (10.0)	7.3 (11.8)	7.5 (13.7)	38.5 (7.2)	12.2–117.6 (2.3–22.1)
Western Pacific	1.1 (2.0)	2.5 (3.7)	4.5 (5.5)	5.1 (7.2)	5.6 (8.8)	7.8 (10.5)	9.4 (12.1)	36.0 (7.1)	15.8–79.7 (3.1–15.7)
Total	9.4 (3.1)	17.3 (5.8)	24.4 (7.9)	28.6 (10.2)	30.6 (12.2)	33.1 (13.8)	34.5 (15.2)	178.0 (9.3)	140.6–270.1 (7.4–14.2)

UI: uncertainty interval; WHO: World Health Organization.

[a] 95% UI of the total no. of infected people in millions (95% UI of percentage prevalence).

Notes: Numbers are the year 2016 estimated number of people living with herpes simplex virus type 2 infection. Prevalences are the percentage of infected people in the age- sex- and region-specific population. Numbers do not always sum exactly to the totals due to rounding. Regions are World Health Organization definitions.

these, 14.7 million (95% UI: 12.4 million–18.1 million) were women and 9.2 million (95% UI: 7.4 million–13.6 million) were men. The number was highest in the WHO African Region, and there was an overall trend of decreasing incidence with age, as prevalence increased. However, the pattern was less marked for those settings where prevalence increased steadily with age (data repository).[23]

An estimated 120.4 million (95% UI: 114.3 million–130.1 million) people 0–49 years of age acquired HSV type 1 infection at any site, an incidence of 2.1% (95% UI: 2.0–2.3; Table 5). The number was highest in the African Region, and decreased with age, most notably in regions where prevalence saturated at younger ages (data repository).[23] The available empirical incidence data suggested that the force of infection may vary with age (data repository),[23] but the data were too limited to draw further conclusions.

Discussion

Our estimates updated to 2016 found around 491 million people living with HSV type 2 infection, 3583.5 million with oral HSV type 1 infection and 122 million –192 million with genital HSV type 1 infection, in those up to 49 years of age. An estimated 596 million–656 million people were genitally infected with either HSV type 1 or 2, meaning that HSV has a substantial effect on the sexual and reproductive health of millions of people worldwide. HSV type 2 infection disproportionately affected women and the WHO African Region. It is concerning that around half of women aged 25–34 years of age in the African Region were infected with HSV type 2, as young women in this region are also at particularly high risk of acquiring HIV.[1,2,3]

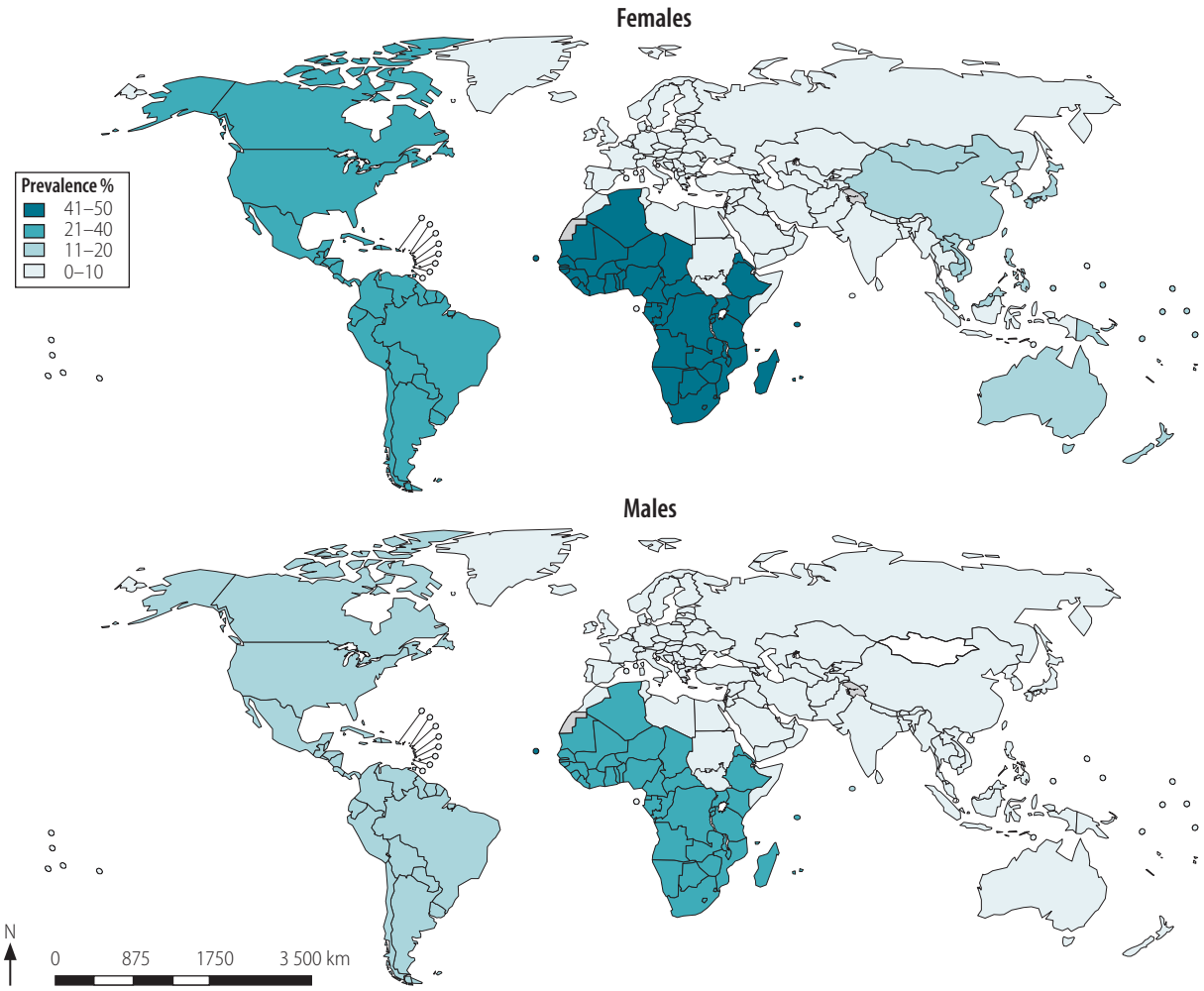
These estimates for 2016 were informed by extensive literature reviews, with 474 and 223 prevalence data points for HSV type 2 and type 1, respectively, contributing to the estimates. For this update, we also made separate estimates for the numbers of people with oral HSV type 1 infection. Our estimates provide a global picture of the overall numbers of HSV infections and can be built upon to better understand the global burden of HSV-associated disease.

The estimates have some limitations, however. First, our pooled esti-

mates rely on the accuracy of the data, which inform them and assume that the contributing studies are representative of their respective regions. Despite an increased number of studies contributing data compared with previous estimates, the number of contributing countries was lower in 2016. To help mitigate these issues, we used broad literature search terms and did not restrict the search by language. We adjusted the reported prevalence for assay sensitivity and specificity, since lack of adjustment tends to inflate HSV prevalence, and we generated estimate bounds to reflect the uncertainty in prevalence reported by publications. We also assumed a constant force of infection by age. However, we applied the force of infection only to those who were susceptible, allowing the number of infected people to decrease with age, and the fitting process also allowed the prevalence to saturate below 100% where suggested by the data. Nonetheless, future modelling analyses would be useful to explore how the limited available empirical incidence data could further inform estimates of infection. In the meantime, our estimates provide a snapshot of prevalence and the limitations of incidence estimates have less impact, as incidence only needs to be projected ahead by a single year.

Second, our estimates for genital HSV type 1 infection are particularly uncertain, as reflected in the wide uncertainty intervals. HSV type 1 prevalence data are lacking among children for all regions and across all ages for the WHO African and South-East Asia Regions. Accurate fitting to prevalence is important for predicting the potential for ac-

Fig. 2. **Map of regional estimates of the number and prevalence of herpes simplex virus type 2 infections in females and males, 2016**



	African Region	Region of the Americas	Eastern Mediterranean Region	European Region	South-East Asia Region	Western Pacific Region
Female						
Prevalence	43.9%	24.0%	7.6%	10.7%	9.6%	14.6%
Number	102.9 million	57.7 million	12.8 million	22.2 million	48.4 million	65.5 million
Male						
Prevalence	25.4%	11.6%	2.8%	5.3%	7.2%	7.1%
Number	59.3 million	28.0 million	5.1 million	11.1 million	38.5 million	36.0 million

Notes: Numbers are the year 2016 estimates of the number of people living aged 15–49 years of age with herpes simplex virus type 2 infection. Prevalences are the percentage of infected people in the age- sex- and region-specific population. Regions are World Health Organization definitions. Global estimates are presented in Table 1.

Table 2. **Global and regional estimates of the prevalence of oral herpes simplex virus type 1 infection by age and sex, 2016**

WHO region by sex	No. of infected people in millions (population prevalence, %) by age group											95% UI[a]
	0–4 years	5–9 years	10–14 years	15–19 years	20–24 years	25–29 years	30–34 years	35–39 years	40–44 years	45–49 years	Total	
Total	181.0 (27.4)	371.4 (58.5)	404.3 (67.1)	404.0 (69.7)	407.7 (70.0)	423.3 (70.5)	389.2 (70.5)	348.0 (70.4)	335.9 (70.6)	318.6 (70.7)	3583.5 (63.6)	3322.2–3715.8 (59.0–66.0)
Female												
Africa	37.9 (64.9)	62.9 (93.7)	57.4 (96.9)	49.8 (97.2)	43.0 (97.3)	37.4 (97.3)	32.3 (97.3)	26.7 (97.3)	21.5 (97.3)	17.3 (97.3)	386.2 (87.8)	354.8–400.9 (80.6–91.1)
Americas	2.1 (7.6)	6.9 (21.1)	11.2 (32.5)	14.3 (39.3)	15.7 (42.3)	16.4 (44.9)	16.7 (47.1)	16.3 (48.9)	15.8 (50.5)	15.4 (51.9)	130.8 (37.8)	121.8–140.6 (35.2–40.6)
Eastern Mediterranean	6.4 (20.9)	16.7 (49.6)	20.6 (66.8)	21.8 (74.3)	21.9 (76.6)	22.2 (78.0)	20.6 (78.8)	17.4 (79.3)	14.0 (79.6)	11.8 (79.7)	173.5 (63.3)	112.0–220.9 (40.9–80.7)
Europe	3.6 (17.2)	10.4 (42.1)	13.9 (58.1)	15.9 (65.6)	18.5 (68.0)	21.8 (69.6)	22.5 (70.6)	22.2 (71.3)	22.2 (71.7)	22.0 (72.0)	173.1 (60.6)	126.6–210.8 (44.4–73.9)
South-East Asia	23.5 (37.5)	51.4 (61.9)	57.5 (66.7)	57.3 (67.5)	55.2 (67.6)	53.3 (67.6)	50.7 (67.6)	45.9 (67.6)	41.0 (67.6)	36.6 (67.6)	472.5 (62.3)	449.4–485.5 (59.3–64.0)
Western Pacific	15.3 (35.0)	35.6 (67.2)	40.9 (78.1)	43.4 (80.9)	51.3 (81.4)	64.6 (81.5)	56.8 (81.6)	50.7 (81.6)	58.9 (81.6)	62.9 (81.6)	480.4 (74.8)	332.7–517.9 (51.8–80.6)
Total	88.9 (27.9)	184.0 (60.0)	201.5 (69.3)	202.4 (72.2)	205.6 (72.8)	215.8 (73.6)	199.7 (73.5)	179.1 (73.4)	173.4 (73.8)	165.9 (74.1)	1816.5 (66.1)	1641.5–1899.6 (59.8–69.2)
Male												
Africa	39.0 (64.9)	64.4 (93.7)	58.5 (96.9)	50.5 (97.2)	43.3 (97.3)	37.3 (97.3)	32.0 (97.3)	26.4 (97.3)	21.1 (97.3)	16.5 (97.3)	389.0 (87.6)	356.9–404.1 (80.4–91.0)
Americas	1.7 (6.1)	5.9 (17.2)	9.7 (27.0)	12.4 (33.0)	13.7 (35.7)	14.3 (38.2)	14.3 (40.3)	13.9 (42.2)	13.4 (43.9)	13.0 (45.4)	112.3 (31.9)	103.8–120.4 (29.5–34.2)
Eastern Mediterranean	6.8 (20.9)	17.6 (49.6)	21.8 (66.8)	23.2 (74.3)	23.3 (76.6)	23.8 (78.0)	22.1 (78.8)	19.0 (79.3)	15.8 (79.6)	13.2 (79.7)	186.6 (63.5)	120.6–237.3 (41.1–80.8)
Europe	1.8 (7.9)	5.7 (22.0)	8.4 (33.9)	10.4 (40.9)	12.5 (44.0)	15.0 (46.6)	15.8 (48.9)	15.7 (50.8)	16.0 (52.4)	15.9 (53.7)	117.1 (40.1)	102.2–134.7 (35.0–46.1)
South-East Asia	25.6 (37.5)	56.2 (61.9)	63.1 (66.7)	62.6 (67.5)	59.7 (67.6)	56.5 (67.6)	53.0 (67.6)	47.5 (67.6)	42.5 (67.6)	37.7 (67.6)	504.3 (62.2)	479.3–518.4 (59.1–63.9)
Western Pacific	17.1 (34.8)	37.7 (62.2)	41.3 (69.6)	42.6 (71.2)	49.5 (71.4)	60.5 (71.5)	52.3 (71.5)	46.4 (71.5)	53.8 (71.5)	56.5 (71.5)	457.6 (66.0)	301.0–488.0 (43.4–70.4)
Total	92.1 (27.0)	187.4 (57.1)	202.8 (65.0)	201.6 (67.3)	202.1 (67.4)	207.4 (67.5)	189.5 (67.5)	168.9 (67.4)	162.5 (67.5)	152.7 (67.4)	1767.0 (61.2)	1594.7–1837.6 (55.2–63.7)

UI: uncertainty interval; WHO: World Health Organization.

[a] 95% UI of the total no. of infected people in millions (95% UI of percentage prevalence).

Notes: Numbers are the year 2016 estimated number of people living with oral herpes simplex virus type 1 infection. Prevalences are the percentage of infected people in the age- sex- and region-specific population. Numbers do not always sum exactly to the totals due to rounding. Regions are World Health Organization definitions.

Table 3. **Global and regional estimates of the prevalence of genital herpes simplex virus type 1 infection by age and sex, 2016**

WHO region by sex	No. of infected people in millions (population prevalence, %) by age								95% UI[a]
	15–19 years	20–24 years	25–29 years	30–34 years	35–39 years	40–44 years	45–49 years	Total	
Total	5.8 (1.0)	17.9 (3.1)	27.5 (4.6)	32.6 (5.9)	34.7 (7.0)	36.3 (7.6)	37.2 (8.2)	192.0 (5.2)	123.0–294.0 (3.3–8.0)
Female									
Africa	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	0.2 (0.1)	< 0.1[c]–3.8 (0.0–1.8)
Americas	1.0 (3.4)	3.3 (9.4)	5.2 (14.5)	6.6 (18.9)	7.4 (22.6)	8.0 (25.7)	8.4 (28.4)	39.8 (16.2)	25.7–48.1 (10.5–19.6)
Eastern Mediterranean	0.8 (3.3)	2.1 (7.8)	2.9 (10.5)	3.1 (12.1)	2.9 (13.1)	2.4 (13.7)	2.1 (14.0)	16.2 (10.5)	1.9–27.7 (1.2–17.8)
Europe	0.6 (3.4)	2.1 (8.2)	3.5 (11.4)	4.2 (13.4)	4.5 (14.7)	4.8 (15.5)	4.9 (16.1)	24.7 (11.2)	8.2–36.4 (3.7–16.5)
South-East Asia	0.1 (0.2)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	0.2 (0.4)	1.8 (0.4)	0.1–8.3 (0.0–1.7)
Western Pacific	0.4 (1.0)	1.1 (1.9)	1.7 (2.2)	1.6 (2.3)	1.5 (2.3)	1.7 (2.4)	1.8 (2.4)	9.8 (2.0)	0.1–66.9 (0.0–13.5)
Total	3.0 (1.1)	9.0 (3.2)	13.6 (4.6)	15.8 (5.8)	16.6 (6.8)	17.1 (7.3)	17.4 (7.8)	92.5 (5.1)	54.6–154.6 (3.0–8.5)
Male									
Africa	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	0.2 (0.1)	< 0.1[c]–3.7 (0.0–1.7)
Americas	0.9 (3.0)	3.1 (8.5)	4.9 (13.4)	6.2 (17.7)	7.0 (21.5)	7.5 (24.8)	7.9 (27.7)	37.4 (15.4)	23.8–45.4 (9.8–18.7)
Eastern Mediterranean	0.8 (3.3)	2.2 (7.8)	3.1 (10.5)	3.4 (12.1)	3.1 (13.1)	2.7 (13.7)	2.3 (14.0)	17.7 (10.5)	2.1–30.2 (1.2–18.0)
Europe	0.7 (3.5)	2.6 (9.7)	4.7 (14.9)	6.1 (19.4)	7.1 (23.1)	8.0 (26.3)	8.5 (29.0)	37.7 (16.9)	24.3–45.7 (10.9–20.5)
South-East Asia	0.2 (0.2)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	1.9 (0.4)	0.2–8.8 (0.0–1.7)
Western Pacific	0.2 (0.5)	0.6 (0.9)	0.8 (1.0)	0.7 (1.0)	0.7 (1.0)	0.8 (1.0)	0.8 (1.0)	4.7 (0.9)	< 0.1[c]–59.7 (0.0–11.4)
Total	2.8 (0.9)	8.9 (3.0)	13.9 (4.5)	16.8 (6.0)	18.1 (7.2)	19.2 (8.0)	19.8 (8.7)	99.4 (5.3)	64.2–167.6 (3.4–8.9)

UI: uncertainty interval; WHO: World Health Organization.

[a] 95% UI of the total no. of infected people in millions (95% UI of percentage prevalence).

[b] Numbers are < 50 000 ≥ 10 000.

[c] Numbers are < 10 000.

Notes: Numbers are the year 2016 estimated number of people living with genital herpes simplex virus type 1 infection. Prevalences are the percentage of infected people in the age- sex- and region-specific population. Numbers do not always sum exactly to the totals due to rounding. Regions are World Health Organization definitions.

quiring genital infection when a person commences sexual activity. Our model fits suggested that in some regions, few HSV type 1 infections are acquired in adulthood, resulting in low estimates of genital HSV type 1 infection. However, since there were limited data to inform the model fits, the numbers could be higher than estimated. Conversely, we applied a relatively high value to the proportion of incident HSV type 1 infections that are genital during adulthood. Although we pooled this value across contributing studies, the incidence of genital HSV type 1 was based on data from only four longitudinal studies, all from the USA and in sexually active populations that may not be representative of other regions. In addition, the value was calculated by assuming that oral and genital HSV type 1 infections are equally likely to be symptomatic. The proportion of infections that were genital may vary across regions due to variations in the practice of oral sex, the main route of transmission of HSV type 1 genital herpes, as well as variations in the background prevalence of HSV type 1 infection.[5] Thus, there is also potential for overestimation of the contribution of genital infections to all HSV type 1 infections. Our sensitivity analysis showed how genital HSV type 1 infection estimates might change if fewer people were able to acquire infection.

Third, our infection estimates do not translate into direct estimates of symptoms or disease. Of the more than half a billion people estimated to be genitally infected with either HSV type 1 or type 2 for example, many infections will be asymptomatic (or at least, not recognized as genital herpes), particularly those due to genital HSV type 1. Even in the absence of symptoms, infected people can transmit HSV to sex partners or neonates and may have a higher risk of acquiring HIV, as documented for HSV type 2.[13]

Fourth, time trends between estimates from different years should be interpreted cautiously. The estimated global prevalence of HSV type 2 for 2016 was somewhat higher than for 2012, although not significantly so. In addition, we used population data for a single year to make our estimates, but there was a large overlap in the available data between estimate years. At the same time, there were changes in the countries and types of populations contributing data between 2012 and 2016. Furthermore,

Table 4. **Global and regional estimates of the incidence of herpes simplex virus type 2 infection by age and sex, 2016**

WHO region by sex	No. of infected people in millions (population incidence, %) by age							95% UI[a]
	15–19 years	20–24 years	25–29 years	30–34 years	35–39 years	40–44 years	45–49 years	Total	
Total	5.2 (0.9)	4.4 (0.8)	3.9 (0.6)	3.2 (0.6)	2.7 (0.5)	2.4 (0.5)	2.1 (0.5)	23.9 (0.6)	21.0–29.5 (0.6–0.8)
Female									
Africa	1.8 (3.4)	1.1 (2.5)	0.7 (1.9)	0.5 (1.4)	0.3 (1.0)	0.2 (0.7)	0.1 (0.5)	4.6 (2.0)	4.1–4.9 (1.7–2.1)
Americas	0.5 (1.4)	0.5 (1.3)	0.4 (1.2)	0.4 (1.1)	0.3 (1.0)	0.3 (0.9)	0.3 (0.9)	2.7 (1.1)	2.2–3.3 (0.9–1.4)
Eastern Mediterranean	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.7 (0.4)	0.3–1.5 (0.2–0.9)
Europe	0.1 (0.5)	0.1 (0.5)	0.2 (0.5)	0.2 (0.5)	0.2 (0.5)	0.1 (0.5)	0.1 (0.5)	1.0 (0.5)	0.5–2.0 (0.2–1.0)
South-East Asia	0.5 (0.5)	0.4 (0.5)	0.4 (0.5)	0.4 (0.5)	0.3 (0.5)	0.3 (0.5)	0.2 (0.5)	2.5 (0.5)	1.1–5.2 (0.2–1.0)
Western Pacific	0.4 (0.7)	0.5 (0.7)	0.5 (0.7)	0.5 (0.7)	0.4 (0.6)	0.4 (0.6)	0.5 (0.6)	3.1 (0.7)	2.0–4.6 (0.4–1.0)
Total	3.4 (1.2)	2.7 (1.0)	2.4 (0.8)	1.9 (0.7)	1.6 (0.6)	1.4 (0.6)	1.3 (0.6)	14.7 (0.8)	12.4–18.1 (0.7–1.0)
Male									
Africa	0.9 (1.7)	0.7 (1.6)	0.5 (1.4)	0.4 (1.3)	0.3 (1.2)	0.2 (1.1)	0.2 (1.0)	3.3 (1.4)	2.5–4.1 (1.1–1.7)
Americas	0.2 (0.6)	0.2 (0.6)	0.2 (0.6)	0.2 (0.6)	0.2 (0.6)	0.2 (0.5)	0.2 (0.5)	1.4 (0.6)	0.9–2.1 (0.4–0.9)
Eastern Mediterranean	<0.1[b] (0.2)	<0.1[b] (0.2)	<0.1[b] (0.2)	<0.1[b] (0.2)	<0.1[b] (0.2)	<0.1[b] (0.2)	<0.1[b] (0.1)	0.3 (0.2)	0.1–1.3 (0.0–0.7)
Europe	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.3)	0.1 (0.2)	0.1 (0.2)	0.5 (0.3)	0.2–1.1 (0.1–0.5)
South-East Asia	0.4 (0.4)	0.4 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	0.2 (0.4)	2.0 (0.4)	0.7–5.9 (0.1–1.1)
Western Pacific	0.2 (0.4)	0.2 (0.4)	0.3 (0.3)	0.2 (0.3)	0.2 (0.3)	0.2 (0.3)	0.3 (0.3)	1.7 (0.3)	0.8–3.6 (0.2–0.7)
Total	1.8 (0.6)	1.6 (0.5)	1.5 (0.5)	1.3 (0.5)	1.1 (0.4)	1.0 (0.4)	0.9 (0.4)	9.2 (0.5)	7.4–13.6 (0.4–0.7)

UI: uncertainty interval; WHO: World Health Organization.

[a] 95% UI of the total no. of infected people in millions (95% UI of percentage incidence).

[b] Numbers are < 50 000 ≥ 10 000.

Notes: Numbers are the estimated number of people newly infected with herpes simplex virus type 2 during 2016. Incidences are the percentage of infected people in the age- sex- and region-specific population. Numbers do not always sum exactly to the totals due to rounding. Regions are World Health Organization definitions.

both overall prevalence and numbers of people infected are a function of the underlying demography of a region, and there has been a global shift towards an ageing population. This shift will increase the overall prevalence of infection even in the absence of a change in the force of infection, since HSV infection is lifelong, as shown by our analysis of age-standardized prevalence. Time trends can be investigated in future research through analyses of study-level data.

Lastly, by restricting the analysis to those younger than 50 years of age, we have underestimated the total burden of infection. Older age groups not only have highest prevalence of infection, but likely also contribute an important burden of disease in terms of continuing recurrences.[124] We used this cut-off because individuals 15–49 years of age is the most important age group in terms of risk of sexual transmission and sexual and reproductive health outcomes, and because data on HSV prevalence in older people are limited. Using this age range also allows us to align our data with other sexually transmitted infection estimates produced by WHO, which are done for individuals 15–49 years of age[125] To explore the potential for underestimation, we extended the age range and found that globally for 2016, 4850.1 million and 836.0 million people aged up to 99 years may have HSV type 1 and type 2 infection, respectively. Our HSV type 2 estimate is similar to the 956 million (95% UI: 847 million–1087 million) estimated by the 2017 GBD study, which included older ages.[17] The GBD study uses a Bayesian model with HSV type 2 prevalence data identified by a basic search string supplemented by data from our more comprehensive searches.[2,16] GBD HSV type 2 infection estimates were not adjusted for test underperformance, which tends to overestimate prevalence.[2] Differences in regional groupings will also influence global totals.

Although not all infections lead to symptoms, our estimate of more than half a billion people with genital HSV infection translates into a large burden of disease worldwide. Current methods of prevention against HSV infection, such as the use of condoms, or antiviral drugs by the infecting partner, are inadequate.[19] These estimates for 2016 can inform the development and subsequent targeting of interventions to maximize the impact on morbidity and mortality,

Table 5. **Global and regional estimates of the incidence of herpes simplex virus type 1 infection (at any site) by age and sex, 2016**

WHO region by sex	No. of infected people in millions (population incidence, %) by age											95% UI[a]
	0–4 years	5–9 years	10–14 years	15–19 years	20–24 years	25–29 years	30–34 years	35–39 years	40–44 years	45–49 years	Total	
Total	81.4 (12.3)	19.1 (3.0)	7.0 (1.2)	3.8 (0.7)	2.7 (0.5)	2.1 (0.3)	1.5 (0.3)	1.2 (0.2)	0.9 (0.2)	0.7 (0.2)	120.4 (2.1)	114.3–130.1 (2.0–2.3)
Female												
Africa	16.7 (21.4)	1.6 (2.4)	0.2 (0.3)	< 0.1[b] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	18.5 (4.2)	16.1–22.0 (3.6–5.0)
Americas	1.0 (3.0)	0.9 (2.5)	0.8 (2.1)	0.7 (1.8)	0.6 (1.6)	0.5 (1.3)	0.4 (1.1)	0.3 (1.0)	0.3 (0.8)	0.2 (0.7)	5.6 (1.6)	5.4–5.8 (1.5–1.7)
Eastern Mediterranean	3.1 (7.8)	1.7 (4.7)	0.9 (2.8)	0.5 (1.7)	0.3 (1.0)	0.2 (0.6)	0.1 (0.4)	< 0.1[b] (0.2)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	6.8 (2.5)	5.3–8.0 (1.9–2.9)
Europe	1.7 (6.5)	1.1 (4.2)	0.7 (2.7)	0.4 (1.7)	0.3 (1.1)	0.2 (0.7)	0.2 (0.5)	0.1 (0.3)	0.1 (0.2)	< 0.1[b] (0.1)	4.8 (1.7)	4.4–5.0 (1.5–1.8)
South-East Asia	10.5 (12.7)	2.2 (2.5)	0.4 (0.5)	0.1 (0.1)	< 0.1[b] (0.0)	< 0.1[b] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	13.2 (1.7)	12.6–14.2 (1.7–1.9)
Western Pacific	7.0 (12.3)	2.3 (4.2)	0.7 (1.4)	0.3 (0.5)	0.1 (0.2)	< 0.1[b] (0.1)	< 0.1[b] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	10.5 (1.6)	9.8–13.1 (1.5–2.0)
Total	40.0 (12.6)	9.8 (3.2)	3.7 (1.3)	2.0 (0.7)	1.3 (0.5)	0.9 (0.3)	0.7 (0.2)	0.5 (0.2)	0.3 (0.1)	0.3 (0.1)	59.4 (2.2)	56.3–63.9 (2.0–2.3)
Male												
Africa	17.2 (21.4)	1.7 (2.4)	0.2 (0.3)	< 0.1[b] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	19.0 (4.3)	16.5–22.6 (3.7–5.1)
Americas	0.9 (2.4)	0.8 (2.1)	0.7 (1.9)	0.6 (1.6)	0.6 (1.4)	0.5 (1.3)	0.4 (1.1)	0.3 (1.0)	0.3 (0.9)	0.2 (0.8)	5.2 (1.5)	4.9–5.5 (1.4–1.6)
Eastern Mediterranean	3.3 (7.8)	1.8 (4.7)	0.9 (2.8)	0.5 (1.7)	0.3 (1.0)	0.2 (0.6)	0.1 (0.4)	0.1 (0.2)	< 0.1[b] (0.1)	< 0.1[b] (0.1)	7.2 (2.4)	5.7–8.4 (1.9–2.9)
Europe	0.9 (3.1)	0.7 (2.6)	0.6 (2.2)	0.5 (1.9)	0.5 (1.6)	0.4 (1.4)	0.4 (1.1)	0.3 (1.0)	0.3 (0.8)	0.2 (0.7)	4.7 (1.6)	4.3–5.1 (1.5–1.7)
South-East Asia	11.4 (12.7)	2.4 (2.5)	0.5 (0.5)	0.1 (0.1)	< 0.1[b] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	14.4 (1.8)	13.8–15.5 (1.7–1.9)
Western Pacific	7.7 (12.0)	2.0 (3.2)	0.5 (0.9)	0.1 (0.2)	< 0.1[b] (0.1)	< 0.1[b] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	< 0.1[c] (0.0)	10.5 (1.5)	9.4–15.5 (1.3–2.2)
Total	41.3 (12.1)	9.3 (2.8)	3.4 (1.1)	1.9 (0.6)	1.4 (0.5)	1.1 (0.4)	0.9 (0.3)	0.7 (0.3)	0.5 (0.2)	0.4 (0.2)	61.0 (2.1)	57.6–66.8 (2.0–2.3)

UI: uncertainty interval; WHO: World Health Organization.

[a] 95% UI of the total no. of infected people in millions (95% UI of percentage incidence).

[b] Numbers are < 50 000 ≥ 10 000.

[c] Numbers are < 10 000.

Notes: Numbers are the estimated number of people newly infected with herpes simplex virus type 1 during 2016. Incidences are the percentage of infected people in the age- sex- and region-specific population. Incidence values of < 0.05% are rounded to 0.0%. Numbers do not always sum exactly to the totals due to rounding. Regions are World Health Organization definitions.

especially in low- and middle-income countries. ■

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ملخص

فيروس الهربس البسيط: تقديرات انتشار العدوى والإصابة العالمية، 2016

الغرض وضع تقديرات للانتشار والإصابة العالمية والإقليمية بعدوى فيروس الهربس البسيط (HSV)، النوعين الأول والثاني في عام 2016.

الطريقة للحصول على بيانات، قمنا بإجراء مراجعة لتحديد الدراسات حتى أغسطس/آب 2018. كما تم إجراء تعديلات لتناسب حساسية ومدى خصوصية اختبار فيروس HSV. لكل منطقة من مناطق منظمة الصحة العالمية (WHO)، قمنا بتطبيق نموذج حدوث ثابت على حالات الانتشار المصنفة حسب العمر والجنس، وذلك لتقدير انتشار وحدوث العدوى بفيروس HSV من النوعين الأول والثاني. بالنسبة للنوع الأول من فيروس HSV، قمنا بتقسيم العدوى إلى نسب حسب الموقع التشريحي، باستخدام تقديرات مجمعة للنسب التي كانت عن طريق الفم أو الأعضاء التناسلية.

النتائج في علم 2016، كان ما يقدر بـ 491.5 مليون شخص (فاصل عدم الثقة 95%: 430.4 مليون إلى 610.6 مليون) يعيشون وهم مصابون بعدوي فيروس HSV من النوع الثاني، أي ما يعادل 13.2% من سكان العالم الذين تتراوح أعمارهم بين 15 و49 عاماً. وما يقدر بـ 3752 مليون شخص (فاصل عدم ثقة 95%: 3555.5 مليون إلى 610.6 مليون) كان لديهم عدوي فيروس HSV من النوع الأول في أي موقع، أي ما يعادل انتشار عالمي بنسبة 66.6% من الأشخاص الذين تتراوح أعمارهم من سن الولادة إلى 49 عاماً. وتمت ملاحظة أنماط متباينة حسب العمر والجنس والمنطقة الجغرافية، مع وجود أعلى انتشار لفيروس HSV من النوع الثاني بين النساء، وفي المنطقة الأفريقية التابعة لمنظمة الصحة العالمية (WHO).

الاستنتاج تم تقدير أن قرابة نصف مليار شخص كانوا مصابين بعدوى فيروس HSV من النوع الثاني أو الأول في المنطقة التناسلية، مع إصابة عدة مليارات من الأشخاص بعدوى فيروس HSV من النوع الأول عن طريق الفم. قد يكون الملايين من الأشخاص أيضاً أكثر عرضة لخطر الإصابة بفيروس نقص المناعة البشرية (HIV)، وخاصة النساء في المنطقة الأفريقية التابعة لمنظمة الصحة العالمية (WHO)، والذين لديهم أعلى معدل لانتشار فيروس HSV من النوع الثاني، والتعرض للإصابة بفيروس HIV.

摘要

单纯疱疹病毒：2016 年全球感染患病率和发病率估计

目标 旨在估计 2016 年全球和区域范围内感染单纯疱疹病毒 (HSV) 1 型和 2 型的患病率和发病率。

方法 为了收集数据，我们选取截至 2018 年 8 月的研究进行系统性回顾。对单纯疱疹病毒 (HSV) 检测的敏感性和特异性进行了适当调整。对于世界卫生组织 (WHO) 的每个地区，我们利用恒定发病率模型，按年龄和性别混合患病率，以估计感染单纯疱疹病毒 1 型和 2 型的患病率和发病率。对于单纯疱疹病毒 1 型，我们使用口腔和生殖器比例的混合估计数，按解剖部位来分配感染。

结果 2016 年，估计有 4.915 亿人（95% 不确定区间，UI：4.304 亿 -6.106 亿）人感染单纯疱疹病毒 2 型，占世界 15-49 岁人口的 13.2%。估计有 37.52 亿人（95% UI：35.555 亿 -38.546 亿）在世界各地感染单纯疱疹病毒 1 型，相当于全球 66.6% 的 0-49 岁人群中的患病率。按年龄、性别和地理区域观察到不同的模式，其中单纯疱疹病毒 2 型患病率在妇女和世卫组织非洲地区最高。

结论 据估计，5 亿人患有单纯疱疹病毒 2 型或 1 型生殖器感染，另外有几十亿人患有单纯疱疹病毒 1 型口腔感染。数百万人还可能有更高风险感染人类免疫缺陷病毒 (HIV)，尤其是世卫组织非洲地区的妇女，她们的单纯疱疹病毒 2 型患病率和接触人类免疫缺陷病毒 (HIV) 的可能性最高。

Résumé

Virus Herpes simplex: estimation de la prévalence et de l'incidence des infections dans le monde, 2016

Objectif Estimer la prévalence et l'incidence, au niveau régional et mondial, des infections au virus Herpes simplex (HSV) de type 1 et de type 2 en 2016.

Méthodes Pour nous procurer les données nécessaires, nous avons entrepris une revue systématique afin d'identifier des études publiées en août 2018 au plus tard. Des ajustements ont été effectués pour tenir compte de la sensibilité et de la spécificité du dépistage HSV. Pour chaque région définie par l'Organisation mondiale de la Santé (OMS), nous avons appliqué un modèle d'incidence constante par groupe de prévalence en fonction de l'âge et du sexe. Notre but était d'estimer la prévalence et l'incidence des infections à HSV de type 1 et 2. Pour le HSV de type 1, nous avons réparti les infections selon le site anatomique, en utilisant des estimations groupées de la proportion d'atteintes orales et génitales.

Résultats En 2016, environ 491,5 millions de personnes (intervalle d'incertitude de 95%: 430,4 millions–610,6 millions) vivaient avec une infection à HSV de type 2, l'équivalent de 13,2 % de la population mondiale entre 15 et 49 ans. Nous estimons que 3752,0 millions de personnes (intervalle d'incertitude de 95%: 3555,5 millions–3854,6 millions) souffraient d'une infection à HSV de type 1 à un site quelconque, ce qui représente une prévalence globale de 66,6% chez les 0–49 ans. Différentes tendances ont été constatées en fonction de l'âge, du sexe et de la zone géographique, le plus fort taux de prévalence de HSV de type 2 étant observé chez les femmes de la région Afrique de l'OMS.

Conclusion Près d'un demi-milliard de personnes présentaient une infection génitale à HSV de type 2 ou type 1, et plusieurs milliards avaient une infection orale à HSV de type 1. Des millions de personnes pourraient également être plus susceptibles de contracter le virus de l'immunodéficience humaine (VIH), en particulier les femmes de la région Afrique de l'OMS qui possèdent la plus grande prévalence de HSV de type 2 et sont davantage exposées au VIH.

Резюме

Вирус простого герпеса: оценка распространенности и заболеваемости в мировом масштабе, 2016

Цель Оценка глобальных и региональных показателей распространенности и заболеваемости вирусом простого герпеса (HSV) 1-го и 2-го типов по состоянию на 2016 год.

Методы Для получения данных был проведен систематический обзор и выявлены соответствующие исследования вплоть до августа 2018 года. Данные были скорректированы с учетом чувствительности и специфики тестов на HSV. Для каждого из регионов по классификации Всемирной организации здравоохранения (ВОЗ) авторы применили модель постоянной заболеваемости в отношении общей распространенности по полу и возрасту для оценки распространенности и заболеваемости HSV 1-го и 2-го типов. Для HSV 1-го типа авторы разделили инфицированных по анатомическому участку с использованием обобщенных оценок пропорций орального и генитального герпеса.

Результаты По состоянию на 2016 год оценочное количество инфицированных HSV 2-го типа составило 491,5 млн (95%-й интервал неопределенности, ИН: 430,4–610,6 млн), что составляет 13,2% от мировой популяции лиц в возрасте 15–49 лет. Примерно 3752,0 миллиона человек (95%-й ИН: 3555,5–3854,6 млн) были инфицированы HSV 1-го типа в каком-либо из участков организма, что эквивалентно коэффициенту глобальной распространенности, равному 66,6% среди населения в возрасте от 0 до 49 лет. Наблюдались различия в распределении заболеваемости по возрастам, полу и географическим регионам, при этом HSV 2-го типа преобладал среди женщин и в Африканском регионе ВОЗ.

Выводы Примерно полмиллиарда людей имеет генитальную инфекцию HSV 2-го или 1-го типа, а оральную инфекцию HSV 1-го типа имеет несколько миллиардов человек. Миллионы людей также могут быть подвержены более высокому риску заражения вирусом иммунодефицита человека (ВИЧ), в частности женщины из Африканского региона ВОЗ, среди которых наблюдается самый высокий уровень распространенности HSV 2-го типа и которые сильнее всего подвергаются риску ВИЧ-инфекции.

Resumen

Virus del herpes simple: estimaciones de prevalencia e incidencia de la infección a nivel mundial, 2016

Objetivo Calcular las estimaciones mundiales y regionales de la prevalencia y la incidencia de la infección por el virus del herpes simple (VHS) tipo 1 y tipo 2 para 2016.

Métodos Se realizó una revisión sistemática para identificar los estudios hasta agosto de 2018 con el fin de obtener datos. Se hicieron ajustes para tener en cuenta la sensibilidad y la especificidad de la prueba de VHS. Se aplicó un modelo de incidencia constante para cada región de la Organización Mundial de la Salud (OMS) con el fin de agrupar la prevalencia por edad y sexo para estimar la prevalencia y la incidencia de las infecciones por VHS de los tipos 1 y 2. Para el VHS tipo 1, se repartió la infección por sitio anatómico utilizando estimaciones agrupadas de los porcentajes que eran orales y genitales.

Resultados En 2016, se estima que 491,5 millones de personas (95 % de intervalo de incertidumbre, UI: 430,4 millones a 610,6 millones) vivían con la infección por el VHS tipo 2, equivalente al 13,2 % de la población mundial de 15 a 49 años. Se estima que 3752,0 millones de personas (95 % UI: 3555,5 millones a 3854,6 millones) tenían la infección por VHS tipo 1 sin importar el lugar, lo que equivale a una prevalencia mundial del 66,6 % en las personas de 0 a 49 años. Se observaron patrones diferentes según la edad, el sexo y la región geográfica, siendo la mayor prevalencia del VHS tipo 2 entre las mujeres y en la región de África de la OMS.

Conclusión Se estima que 500 millones de personas tienen una infección genital con VHS tipo 2 o tipo 1, y varios miles de millones tienen una infección oral de VHS tipo 1. Millones de personas también pueden correr un mayor riesgo de contraer el virus de la inmunodeficiencia humana (VIH), en particular las mujeres de la Región de África de la OMS que tienen la mayor prevalencia del VHS tipo 2 y la mayor exposición al VIH.

References

1. Looker KJ, Magaret AS, May MT, Turner KME, Vickerman P, Gottlieb SL, et al. Global and regional estimates of prevalent and incident herpes simplex virus type 1 infections in 2012. PLoS One. 2015 10 28;10(10):e0140765. doi: http://dx.doi.org/10.1371/journal.pone.0140765 PMID: 26510007
2. Looker KJ, Magaret AS, Turner KME, Vickerman P, Gottlieb SL, Newman LM. Global estimates of prevalent and incident herpes simplex virus type 2 infections in 2012. PLoS One. 2015 01 21;10(1):e114989. doi: http://dx.doi.org/10.1371/journal.pone.0114989 PMID: 25608026
3. Higgins CR, Schofield JK, Tatnall FM, Leigh IM. Natural history, management and complications of herpes labialis. J Med Virol. 1993;41(S1) Suppl 1:22–6. doi: http://dx.doi.org/10.1002/jmv.1890410506 PMID: 8245888
4. Whitley R, Baines J. Clinical management of herpes simplex virus infections: past, present, and future. F1000 Res. 2018 10 31;7:1726. doi: http://dx.doi.org/10.12688/f1000research.16157.1 PMID: 30443341
5. 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 03 11;17(1):57. doi: http://dx.doi.org/10.1186/s12916-019-1285-x PMID: 30853029
6. Tuokko H, Bloigu R, Hukkanen V. Herpes simplex virus type 1 genital herpes in young women: current trend in Northern Finland. Sex Transm Infect. 2014 Mar;90(2):160. doi: http://dx.doi.org/10.1136/sextrans-2013-051453 PMID: 24431184
7. Brijwal M, Rawre J, Dhawan B, Khanna N, Choudhary A, Dar L. Herpes simplex virus type 1 genital ulcer disease at a tertiary care hospital in north India. Clin Infect Dis. 2019 May 2;68(10):1783–4. doi: http://dx.doi.org/10.1093/cid/ciy943 PMID: 30388201
8. Khadr L, Harfouche M, Omori R, Schwarzer G, Chemaitelly H, Abu-Raddad LJ. The epidemiology of herpes simplex virus type 1 in Asia: systematic review, meta-analyses, and meta-regressions. Clin Infect Dis. 2019 02 15;68(5):757–72. doi: http://dx.doi.org/10.1093/cid/ciy562 PMID: 30020453
9. Benedetti J, Corey L, Ashley R. Recurrence rates in genital herpes after symptomatic first-episode infection. Ann Intern Med. 1994 Dec 1;121(11):847–54. doi: http://dx.doi.org/10.7326/0003-4819-121-11-199412010-00004 PMID: 7978697
10. Corey L, Adams HG, Brown ZA, Holmes KK. Genital herpes simplex virus infections: clinical manifestations, course, and complications. Ann Intern Med. 1983 Jun;98(6):958–72. doi: http://dx.doi.org/10.7326/0003-4819-98-6-958 PMID: 6344712
11. Gupta R, Warren T, Wald A. Genital herpes. Lancet. 2007 Dec 22;370(9605):2127–37. doi: http://dx.doi.org/10.1016/S0140-6736(07)61908-4 PMID: 18156035
12. Pinninti SG, Kimberlin DW. Maternal and neonatal herpes simplex virus infections. Am J Perinatol. 2013 Feb;30(2):113–20. doi: http://dx.doi.org/10.1055/s-0032-1332802 PMID: 23303485
13. Looker KJ, Elmes JAR, Gottlieb SL, Schiffer JT, Vickerman P, Turner KME, et al. Effect of HSV-2 infection on subsequent HIV acquisition: an updated systematic review and meta-analysis. Lancet Infect Dis. 2017 12;17(12):1303–16. doi: http://dx.doi.org/10.1016/S1473-3099(17)30405-X PMID: 28843576
14. Ramchandani M, Kong M, Tronstein E, Selke S, Mikhaylova A, Magaret A, et al. Herpes simplex virus type 1 shedding in tears and nasal and oral mucosa of healthy adults. Sex Transm Dis. 2016 12;43(12):756–60. doi: http://dx.doi.org/10.1097/OLQ.0000000000000522 PMID: 27835628
15. Mark KE, Wald A, Magaret AS, Selke S, Olin L, Huang M-L, et al. Rapidly cleared episodes of herpes simplex virus reactivation in immunocompetent adults. J Infect Dis. 2008 Oct 15;198(8):1141–9. doi: http://dx.doi.org/10.1086/591913 PMID: 18783315
16. Looker KJ, Garnett GP, Schmid GP. An estimate of the global prevalence and incidence of herpes simplex virus type 2 infection. Bull World Health Organ. 2008 Oct;86(10):805–12. doi: http://dx.doi.org/10.2471/BLT.07.046128 PMID: 18949218
17. Collaborators Global Burden of Disease; Global Burden of Disease 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018 11 10;392(10159):1789–858. doi: http://dx.doi.org/10.1016/S0140-6736(18)32279-7 PMID: 30496104
18. Global health sector strategy on sexually transmitted infections 2016–2021. Towards ending sexually transmitted infections. WHO/RHR/16.09. Geneva: World Health Organization; 2016. Available from: https://www.who.int/reproductivehealth/publications/rtis/ghss-stis/en/ [cited 2019 Dec 11].
19. Gottlieb SL, Low N, Newman LM, Bolan G, Kamb M, Broutet N. Toward global prevention of sexually transmitted infections (STIs): the need for STI vaccines. Vaccine. 2014 Mar 20;32(14):1527–35. doi: http://dx.doi.org/10.1016/j.vaccine.2013.07.087 PMID: 24581979
20. Gottlieb SL, Deal CD, Giersing B, Rees H, Bolan G, Johnston C, et al. The global roadmap for advancing development of vaccines against sexually transmitted infections: update and next steps. Vaccine. 2016 06 3;34(26):2939–47. doi: http://dx.doi.org/10.1016/j.vaccine.2016.03.111 PMID: 27105564
21. Gottlieb SL, Giersing BK, Hickling J, Jones R, Deal C, Kaslow DC; HSV Vaccine Expert Consultation Group. Meeting report: Initial World Health Organization consultation on herpes simplex virus (HSV) vaccine preferred product characteristics, March 2017. Vaccine. 2019 Nov 28;37(50):7408–18. doi: http://dx.doi.org/10.1016/j.vaccine.2017.10.084 PMID: 29224963
22. Looker KJ, Magaret AS, May MT, Turner KME, Vickerman P, Newman LM, et al. First estimates of the global and regional incidence of neonatal herpes infection. Lancet Glob Health. 2017 03;5(3):e300–9. doi: http://dx.doi.org/10.1016/S2214-109X(16)30362-X PMID: 28153513
23. James C, Harfouche M, Welton NJ, Turner KME, Abu-Raddad LJ, Gottlieb SL et al. Supplementary webappendix: data from 2016 HSV infection estimates (02-2020). [data repository]. Bristol: University of Bristol; 2019. doi: http://dx.doi.org/10.5523/bris.w4tr95py62gh2v32ep33dahtxdoi: http://dx.doi.org/10.5523/bris.w4tr95py62gh2v32ep33dahtx
24. World population prospects 2017 [internet]. New York: United Nations; 2017. Available from: https://population.un.org/wpp/Download/Standard/Population/ [cited 2019 Mar 19].
25. Bernstein DI, Bellamy AR, Hook EW 3rd, Levin MJ, Wald A, Ewell MG, 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 Feb;56(3):344–51. doi: http://dx.doi.org/10.1093/cid/cis891 PMID: 23087395
26. Brown ZA, Selke S, Zeh J, Kopelman J, Maslow A, Ashley RL, et al. The acquisition of herpes simplex virus during pregnancy. N Engl J Med. 1997 Aug 21;337(8):509–16. doi: http://dx.doi.org/10.1056/NEJM199708213370801 PMID: 9262493
27. Langenberg AG, Corey L, Ashley RL, Leong WP, Straus SE; Chiron HSV Vaccine Study Group. A prospective study of new infections with herpes simplex virus type 1 and type 2. N Engl J Med. 1999 Nov 4;341(19):1432–8. doi: http://dx.doi.org/10.1056/NEJM199911043411904 PMID: 10547406
28. Mertz GJ, Ashley R, Burke RL, Benedetti J, Critchlow C, Jones CC, et al. Double-blind, placebo-controlled trial of a herpes simplex virus type 2 glycoprotein vaccine in persons at high risk for genital herpes infection. J Infect Dis. 1990 Apr;161(4):653–60. doi: http://dx.doi.org/10.1093/infdis/161.4.653 PMID: 2181031
29. National Health and Nutrition Examination Surveys. 1976 to 2016 [internet]. Atlanta: Centers for Disease Control and Prevention; 2016. Available from: https://wwwn.cdc.gov/nchs/nhanes/Default.aspx [cited 2019 Dec 10].
30. Chaabane S, Harfouche M, Chemaitelly H, Schwarzer G, Abu-Raddad LJ. Herpes simplex virus type 1 epidemiology in the Middle East and North Africa: systematic review, meta-analyses, and meta-regressions. Sci Rep. 2019 02 4;9(1):1136. doi: http://dx.doi.org/10.1038/s41598-018-37833-8 PMID: 30718696
31. Sukik L, Alyafei M, Harfouche M, Abu-Raddad LJ. Herpes simplex virus type 1 epidemiology in Latin America and the Caribbean: systematic review and meta-analytics. PLoS One. 2019 04 22;14(4):e0215487. doi: http://dx.doi.org/10.1371/journal.pone.0215487 PMID: 31009486
32. Abbai NS, Wand H, Ramjee G. Socio-demographic and behavioural characteristics associated with HSV-2 sero-prevalence in high risk women in KwaZulu-Natal. BMC Res Notes. 2015 05 5;8(1):185. doi: http://dx.doi.org/10.1186/s13104-015-1093-0 PMID: 25940115
33. Abdool Karim Q, Kharsany AB, Leask K, Ntombela F, Humphries H, Frohlich JA, et al. Prevalence of HIV, HSV-2 and pregnancy among high school students in rural KwaZulu-Natal, South Africa: a bio-behavioural cross-sectional survey. Sex Transm Infect. 2014 Dec;90(8):620–6. doi: http://dx.doi.org/10.1136/sextrans-2014-051548 PMID: 24873967
34. Abdool Karim SS, Abdool Karim Q, Kharsany AB, Baxter C, Grobler AC, Werner L, et al.; CAPRISA 004 Trial Group. Tenofovir gel for the prevention of herpes simplex virus type 2 infection. N Engl J Med. 2015 Aug 6;373(6):530–9. doi: http://dx.doi.org/10.1056/NEJMoa1410649 PMID: 26244306

35. Akinyi B, Odhiambo C, Otieno F, Inzaule S, Oswago S, Kerubo E, et al. Prevalence, incidence and correlates of HSV-2 infection in an HIV incidence adolescent and adult cohort study in western Kenya. PLoS One. 2017 06 6;12(6):e0178907. doi: http://dx.doi.org/10.1371/journal.pone.0178907 PMID: 28586396
36. Anjulo AA, Abebe T, Hailemichael F, Mihret A. Seroprevalence and risk factors of herpes simplex virus type 2 among pregnant women attending antenatal care at health facilities in Wolaita zone, Ethiopia. Virol J. 2016 03 15;13(1):43. doi: http://dx.doi.org/10.1186/s12985-016-0501-y PMID: 26979484
37. Behling J, Chan AK, Zeh C, Nekesa C, Heinzerling L. Evaluating HIV prevention programs: herpes simplex virus type 2 antibodies as biomarker for sexual risk behavior in young adults in resource-poor countries. PLoS One. 2015 05 26;10(5):e0128370. doi: http://dx.doi.org/10.1371/journal.pone.0128370 PMID: 26010772
38. Bradley J, Floyd S, Piwowar-Manning E, Laeyendecker O, Young A, Bell-Mandla N, et al.; HPTN 071 (PopART) Study Team. Sexually transmitted bedfellows: exquisite association between HIV and herpes simplex virus type 2 in 21 communities in Southern Africa in the HIV prevention trials network 071 (PopART) Study. J Infect Dis. 2018 07 2;218(3):443–52. doi: http://dx.doi.org/10.1093/infdis/jiy178 PMID: 29659909
39. Chattopadhyay K, Williamson AL, Hazra A, Dandara C. The combined risks of reduced or increased function variants in cell death pathway genes differentially influence cervical cancer risk and herpes simplex virus type 2 infection among black Africans and the Mixed Ancestry population of South Africa. BMC Cancer. 2015 10 12;15(1):680. doi: http://dx.doi.org/10.1186/s12885-015-1678-y PMID: 26458812
40. Celum C, Morrow RA, Donnell D, Hong T, Hendrix CW, Thomas KK, et al.; Partners PrEP Study Team. Daily oral tenofovir and emtricitabine-tenofovir preexposure prophylaxis reduces herpes simplex virus type 2 acquisition among heterosexual HIV-1-uninfected men and women: a subgroup analysis of a randomized trial. Ann Intern Med. 2014 07 1;161(1):11–9. doi: http://dx.doi.org/10.7326/M13-2471 PMID: 24979446
41. Daniels B, Wand H, Ramjee G; MDP Team. Prevalence of herpes simplex virus 2 (HSV-2) infection and associated risk factors in a cohort of HIV negative women in Durban, South Africa. BMC Res Notes. 2016 12 12;9(1):510. doi: http://dx.doi.org/10.1186/s13104-016-2319-5 PMID: 27955706
42. Fearon E, Wiggins RD, Pettifor AE, MacPhail C, Kahn K, Selin A, et al. Associations between friendship characteristics and HIV and HSV-2 status amongst young South African women in HPTN-068. J Int AIDS Soc. 2017 12;20(4):):e25029. doi: http://dx.doi.org/10.1002/jia2.25029 PMID: 29285883
43. Glynn JR, Kayuni N, Gondwe L, Price AJ, Crampin AC. Earlier menarche is associated with a higher prevalence of Herpes simplex type-2 (HSV-2) in young women in rural Malawi. eLife. 2014 01 28;3:e01604. doi: http://dx.doi.org/10.7554/eLife.01604 PMID: 24473074
44. Gumbe A, McLellan-Lemal E, Gust DA, Pals SL, Gray KM, Ndivo R, et al.; KICoS Study Team. Correlates of prevalent HIV infection among adults and adolescents in the Kisumu incidence cohort study, Kisumu, Kenya. Int J STD AIDS. 2015 Nov;26(13):929–40. doi: http://dx.doi.org/10.1177/0956462414563625 PMID: 25505039
45. Hallfors DD, Cho H, Mbai II, Millimo BW, Atieno C, Okumu D, et al. Disclosure of HSV-2 serological test results in the context of an adolescent HIV prevention trial in Kenya. Sex Transm Infect. 2015 Sep;91(6):395–400. doi: http://dx.doi.org/10.1136/sextrans-2015-052025 PMID: 26139208
46. Hazel A, Foxman B, Low BS. Herpes simplex virus type 2 among mobile pastoralists in northwestern Namibia. Ann Hum Biol. 2015;42(6):543–51. doi: http://dx.doi.org/10.3109/03014460.2014.970575 PMID: 25387244
47. Kalu EI, Ojide CK, Chuku A, Chukwuonye II, Agwu FE, Nwadike VU, et al. Obstetric outcomes of human herpes virus-2 infection among pregnant women in Benin, Nigeria. Niger J Clin Pract. 2015 Jul-Aug;18(4):453–61. doi: http://dx.doi.org/10.4103/1119-3077.154210 PMID: 25966714
48. Kalu EI, Ojide CK, Fowotade A, Nwadike VU. Sexual behavioral correlates with HSV-2 seroprevalence among pregnant women in Nigeria. J Infect Dev Ctries. 2014 08 13;8(8):1006–12. doi: http://dx.doi.org/10.3855/jidc.4336 PMID: 25116666
49. Luseno WK, Hallfors DD, Cho H, Iritani BJ, Adze J, Rusakaniko S, et al. Use of HIV and HSV-2 biomarkers in sub-saharan adolescent prevention research: a comparison of two approaches. J Prim Prev. 2014 Jun;35(3):181–91. doi: http://dx.doi.org/10.1007/s10935-014-0343-6 PMID: 24682861
50. Nakku-Joloba E, Kambugu F, Wasubire J, Kimeze J, Salata R, Albert JM, et al. Sero-prevalence of herpes simplex type 2 virus (HSV-2) and HIV infection in Kampala, Uganda. Afr Health Sci. 2015 Dec;14(4):782–9. doi: http://dx.doi.org/10.4314/ahs.v14i4.2 PMID: 25834483
51. Nakubulwa S, Kaye DK, Bwanga F, Tumwesigye NM, Nakku-Joloba E, Mirembe FM. Incidence and risk factors for herpes simplex virus type 2 seroconversion among pregnant women in Uganda: a prospective study. J Infect Dev Ctries. 2016 10 31;10(10):1108–15. doi: http://dx.doi.org/10.3855/jidc.6874 PMID: 27801374
52. Norris AH, Decker MR, Weisband YL, Hindin MJ. Reciprocal physical intimate partner violence is associated with prevalent STI/HIV among male Tanzanian migrant workers: a cross-sectional study. Sex Transm Infect. 2017 Jun;93(4):253–8. doi: http://dx.doi.org/10.1136/sextrans-2016-052873 PMID: 28052976
53. Okoye JO, Ngokere AA, Erinle CA. Screening for cervical abnormalities associated with EBV, HPV and HSV-2 infections in South-West Nigeria: a tale between sex and non-sex workers. J Oncol Sci. 2018;4(2):85–95. doi: http://dx.doi.org/10.1016/j.jons.2018.07.001
54. Otieno FO, Ndivo R, Oswago S, Pals S, Chen R, Thomas T, et al. Correlates of prevalent sexually transmitted infections among participants screened for an HIV incidence cohort study in Kisumu, Kenya. Int J STD AIDS. 2015 Mar;26(4):225–37. doi: http://dx.doi.org/10.1177/0956462414532447 PMID: 24810218
55. Pascoe SJ, Langhaug LF, Mavhu W, Hargreaves J, Jaffar S, Hayes R, et al. Poverty, food insufficiency and HIV infection and sexual behaviour among young rural Zimbabwean women. PLoS One. 2015 01 27;10(1):e0115290. doi: http://dx.doi.org/10.1371/journal.pone.0115290 PMID: 25625868
56. Perti T, Nyati M, Gray G, De Bruyn G, Selke S, Magaret A, et al. Frequent genital HSV-2 shedding among women during labor in Soweto, South Africa. Infect Dis Obstet Gynecol. 2014;2014:258291. doi: http://dx.doi.org/10.1155/2014/258291 PMID: 24963269
57. Pettifor A, MacPhail C, Hughes JP, Selin A, Wang J, Gómez-Olivé FX, et al. The effect of a conditional cash transfer on HIV incidence in young women in rural South Africa (HPTN 068): a phase 3, randomised controlled trial. [Erratum appears in Lancet Glob Health. 2017 Feb;5(2):e146; PMID: 28104183]. Lancet Glob Health. 2016;4(12):e978–88. doi: http://dx.doi.org/10.1016/S2214-109X(16)30253-4 PMID: 27815148
58. Pettifor A, MacPhail C, Selin A, Gómez-Olivé FX, Rosenberg M, Wagner RG, et al.; HPTN 068 protocol team. HPTN 068: a randomized control trial of a conditional cash transfer to reduce hiv infection in young women in South Africa – study design and baseline results. AIDS Behav. 2016 09;20(9):1863–82. doi: http://dx.doi.org/10.1007/s10461-015-1270-0 PMID: 26891839
59. Rosenberg M, Pettifor A, Van Rie A, Thirumurthy H, Emch M, Miller WC, et al. The relationship between alcohol outlets, HIV risk behavior, and HSV-2 infection among south African young women: a cross-sectional study. PLoS One. 2015 05 8;10(5):e0125510. doi: http://dx.doi.org/10.1371/journal.pone.0125510 PMID: 25954812
60. Sudfeld CR, Hewett PC, Abuelezam NN, Chalasani S, Soler-Hampejsek E, Kelly CA, et al. Herpes simplex virus type 2 cross-sectional seroprevalence and the estimated rate of neonatal infections among a cohort of rural Malawian female adolescents. Sex Transm Infect. 2013 Nov;89(7):561–7. doi: http://dx.doi.org/10.1136/sextrans-2012-050869 PMID: 23794069
61. Winston SE, Chirchir AK, Muthoni LN, Ayuku D, Koech J, Nyandiko W, et al. Prevalence of sexually transmitted infections including HIV in street-connected adolescents in western Kenya. Sex Transm Infect. 2015 Aug;91(5):353–9. doi: http://dx.doi.org/10.1136/sextrans-2014-051797 PMID: 25714102
62. Torrone EA, Morrison CS, Chen PL, Kwok C, Francis SC, Hayes RJ, et al.; sexually transmitted infectionMA Working Group. Prevalence of sexually transmitted infections and bacterial vaginosis among women in sub-Saharan Africa: an individual participant data meta-analysis of 18 HIV prevention studies. PLoS Med. 2018 02 27;15(2):e1002511. doi: http://dx.doi.org/10.1371/journal.pmed.1002511 PMID: 29485986
63. Arama VI, Vladareanu R, Mihailescu RA, Popescu CN, Tiliscan CV, Rafila AA, et al. Genital herpes: an underestimated infection in Romania. GINECO.eu J. 2013 Feb;9(31):32–4.
64. Balaeva T, Grjibovski AM, Sidorenkov O, Samodova O, Firsova N, Sannikov A, et al. Seroprevalence and correlates of herpes simplex virus type 2 infection among young adults in Arkhangelsk, Northwest Russia: a population-based cross-sectional study. BMC Infect Dis. 2016 10 28;16(1):616. doi: http://dx.doi.org/10.1186/s12879-016-1954-8 PMID: 27793121
65. Bochner AF, Madhivanan P, Niranjankumar B, Ravi K, Arun A, Krupp K, et al. The epidemiology of herpes simplex virus type 2 infection among pregnant women in rural Mysore Taluk, India. J Sex Transm Dis. 2013;2013:750415. doi: http://dx.doi.org/10.1155/2013/750415 PMID: 26316964

66. Bolu A, Oznur T, Tok D, Balikci A, Sener K, Celik C, et al. Seropositivity of neurotropic infectious agents in first-episode schizophrenia patients and the relationship with positive and negative symptoms. Psychiatr Danub. 2016 Jun;28(2):132–8. PMID: 27287787
67. Breyer BN, Huang WY, Rabkin CS, Alderete JF, Pakpahan R, Beason TS, et al. Sexually transmitted infections, benign prostatic hyperplasia and lower urinary tract symptom-related outcomes: results from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. BJU Int. 2016 Jan;117(1):145–54. doi: http://dx.doi.org/10.1111/bju.13050 PMID: 25601300
68. Cheslack-Postava K, Brown AS, Chudal R, Suominen A, Huttunen J, Surcel HM, et al. Maternal exposure to sexually transmitted infections and schizophrenia among offspring. Schizophr Res. 2015 Aug;166(1-3):255–60. doi: http://dx.doi.org/10.1016/j.schres.2015.05.012 PMID: 26022653
69. Conde-Glez C, Lazcano-Ponce E, Rojas R, DeAntonio R, Romano-Mazzotti L, Cervantes Y, et al. Seroprevalences of varicella-zoster virus, herpes simplex virus and cytomegalovirus in a cross-sectional study in Mexico. Vaccine. 2013 Oct 17;31(44):5067–74. doi: http://dx.doi.org/10.1016/j.vaccine.2013.08.077 PMID: 24021305
70. Dargham SR, Nasrallah GK, Al-Absi ES, Mohammed LI, Al-Disi RS, Nofal MY, et al. Herpes simplex virus type 2 seroprevalence among different national populations of Middle East and North African men. Sex Transm Dis. 2018 07;45(7):482–7. doi: http://dx.doi.org/10.1097/OLQ.0000000000000791 PMID: 29465656
71. de Witte LD, van Mierlo HC, Litjens M, Klein HC, Bahn S, Osterhaus AD; GROUP Investigators. The association between antibodies to neurotropic pathogens and schizophrenia: a case–control study. NPJ Schizophr. 2015 11 4;1(1):15041. doi: http://dx.doi.org/10.1038/npjschz.2015.41 PMID: 27336045
72. Delaney S, Gardella C, Saracino M, Magaret A, Wald A. Seroprevalence of herpes simplex virus type 1 and 2 among pregnant women, 1989 type 2010. JAMA. 2014 Aug 20;312(7):746–8. doi: http://dx.doi.org/10.1001/jama.2014.4359 PMID: 25138337
73. Domercant JW, Jean Louis F, Hulland E, Griswold M, Andre-Alboth J, Ye T, 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 08 18;17(1):577. doi: http://dx.doi.org/10.1186/s12879-017-2674-4 PMID: 28821230
74. Dowd JB, Bosch JA, Steptoe A, Jayabalasingham B, Lin J, Yolken R, et al. Persistent herpesvirus infections and telomere attrition over 3 years in the Whitehall II cohort. J Infect Dis. 2017 09 1;216(5):565–72. doi: http://dx.doi.org/10.1093/infdis/jix255 PMID: 28931225
75. Finger-Jardim F, Avila EC, da Hora VP, Santos PCD, Gonçalves CV, Mor G, et al. Herpes simplex virus type 2 IgG antibodies in sera of umbilical cord as a proxy for placental infection in asymptomatic pregnant women. Am J Reprod Immunol. 2018 04;79(4):e12824. doi: http://dx.doi.org/10.1111/aji.12824 PMID: 29427299
76. Fruchter E, Goldberg S, Fenchel D, Grotto I, Ginat K, Weiser M. The impact of herpes simplex virus type 1 on cognitive impairments in young, healthy individuals: a historical prospective study. Schizophr Res. 2015 Oct;168(1 type 2):292–6. doi: http://dx.doi.org/10.1016/j.schres.2015.08.036 PMID: 26362735
77. Gilbert PB, Excler JL, Tomaras GD, Carpp LN, Haynes BF, Liao HX, et al. Antibody to HSV gD peptide induced by vaccination does not protect against HSV-2 infection in HSV-2 seronegative women. PLoS One. 2017 05 11;12(5):e0176428. doi: http://dx.doi.org/10.1371/journal.pone.0176428 PMID: 28493891
78. Gorfinkel IS, Aoki F, McNeil S, Dionne M, Shafran SD, Zickler P, et al. Seroprevalence of HSV-1 and HSV-2 antibodies in Canadian women screened for enrolment in a herpes simplex virus vaccine trial. Int J STD AIDS. 2013 May;24(5):345–9. doi: http://dx.doi.org/10.1177/0956462412472822 PMID: 23970700
79. Hamdani N, Daban-Huard C, Godin O, Laouamri H, Jamain S, Attiba D, et al. Effects of cumulative Herpesviridae and Toxoplasma gondii infections on cognitive function in healthy, bipolar, and schizophrenia subjects. J Clin Psychiatry. 2017 01;78(1):e18–27. doi: http://dx.doi.org/10.4088/JCP.15m10133 PMID: 27929612
80. Hartog L, van Rooijen MS, Ujčič-Voortman J, Prins M, van Valkengoed IGM. Ethnic differences in infectious burden and the association with metabolic risk factors for cardiovascular disease: a cross-sectional analysis. BMC Public Health. 2018 02 22;18(1):276. doi: http://dx.doi.org/10.1186/s12889-018-5162-x PMID: 29471811
81. Hochberg CH, Schneider JA, Dandona R, Lakshmi V, Kumar GA, Sudha T, et al. Population and dyadic-based seroincidence of herpes simplex virus-2 and syphilis in southern India. Sex Transm Infect. 2015 Aug;91(5):375–82. doi: http://dx.doi.org/10.1136/sextrans-2014-051708 PMID: 25605970
82. Hsu PC, Yolken RH, Postolache TT, Beckie TM, Munro CL, Groer MW. Association of depressed mood with herpes simplex virus-2 immunoglobulin-g levels in pregnancy. Psychosom Med. 2016 10;78(8):966–72. doi: http://dx.doi.org/10.1097/PSY.0000000000000374 PMID: 27490851
83. Jahanbakhsh F, Bagheri Amiri F, Sedaghat A, Fahimfar N, Mostafavi E. Prevalence of HAV Ab, HEV (IgG), HSV2 IgG, and syphilis among sheltered homeless adults in Tehran, 2012. Int J Health Policy Manag. 2018 03 1;7(3):225–30. PMID: 29524951
84. Jansen MA, van den Heuvel D, van der Zwet KV, Jaddoe VW, Hofman A, Escher JC, et al. Herpesvirus infections and transglutaminase type 2 antibody positivity in childhood: the generation R study. J Pediatr Gastroenterol Nutr. 2016 10;63(4):423–30. doi: http://dx.doi.org/10.1097/MPG.0000000000001163 PMID: 26881413
85. Jonker I, Klein HC, Duivis HE, Yolken RH, Rosmalen JG, Schoevers RA. Association between exposure to HSV1 and cognitive functioning in a general population of adolescents. The TRAILS study. PLoS One. 2014 07 1;9(7):e101549. doi: http://dx.doi.org/10.1371/journal.pone.0101549 PMID: 24983885
86. Jonker I, Rosmalen JGM, Schoevers RA. Childhood life events, immune activation and the development of mood and anxiety disorders: the TRAILS study. Transl Psychiatry. 2017 05 2;7(5):e1112. doi: http://dx.doi.org/10.1038/tp.2017.62 PMID: 28463238
87. Jonker I, Schoevers R, Klein H, Rosmalen J. The association between herpes virus infections and functional somatic symptoms in a general population of adolescents: the TRAILS study. PLoS One. 2017 10 18;12(10):e0185608. doi: http://dx.doi.org/10.1371/journal.pone.0185608 PMID: 29045430
88. Karachaliou M, Chatzi L, Roumeliotaki T, Kampouri M, Kyriklaki A, Koutra K, et al. Common infections with polyomaviruses and herpesviruses and neuropsychological development at 4 years of age, the Rhea birth cohort in Crete, Greece. J Child Psychol Psychiatry. 2016 11;57(11):1268–76. doi: http://dx.doi.org/10.1111/jcpp.12582 PMID: 27334233
89. Karachaliou M, de Sanjose S, Waterboer T, Roumeliotaki T, Vassilaki M, Sarri K, et al. Is early life exposure to polyomaviruses and herpesviruses associated with obesity indices and metabolic traits in childhood? Int J Obes. 2018 09;42(9):1590–601. doi: http://dx.doi.org/10.1038/s41366-018-0017-1 PMID: 29445241
90. Karachaliou M, et al. The natural history of human polyomaviruses and herpesviruses in early life – the rhea birth cohort in Greece.[Erratum appears in Am J Epidemiol. 2016 Jun 15;183(12):1174; PMID: 27226247]. Am J Epidemiol. 2016;183(7):671–9. doi: http://dx.doi.org/10.1093/aje/kwv281 PMID: 26968942
91. Kelly JD, Cohen J, Grimes B, Philip SS, Weiser SD, Riley ED. High rates of herpes simplex virus type 2 infection in homeless women: informing public health strategies. J Womens Health (Larchmt). 2016 08;25(8):840–5. doi: http://dx.doi.org/10.1089/jwh.2015.5579 PMID: 27243474
92. Korr G, Thamm M, Czogiel I, Poethko-Mueller C, Bremer V, Jansen K. Decreasing seroprevalence of herpes simplex virus type 1 and type 2 in Germany leaves many people susceptible to genital infection: time to raise awareness and enhance control. BMC Infect Dis. 2017 07 6;17(1):471. doi: http://dx.doi.org/10.1186/s12879-017-2527-1 PMID: 28683784
93. Li R, Liao MZ, Huang PX, Yang XG, Zhu XY, Su SL, et al. [Factors related to syphilis and other infections among female drug users in Shandong women's compulsory drug rehabilitation center in 2015]. Zhonghua Yu Fang Yi Xue Za Zhi. 2016 Sep 6;50(9):820–4. Chinese. PMID: 27655604
94. Marchi S, Trombetta CM, Gasparini R, Temperton N, Montomoli E. Epidemiology of herpes simplex virus type 1 and 2 in Italy: a seroprevalence study from 2000 to 2014. J Prev Med Hyg. 2017 Mar;58(1):E27–33. PMID: 28515628
95. Masel J, Deiss RG, Wang X, Sanchez JL, Ganesan A, Macalino GE, et al. Seroprevalence and seroincidence of herpes simplex virus (2006–2010), syphilis (2006–2010), and vaccine-preventable human papillomavirus subtypes (200 –2010) among US military personnel. Sex Transm Dis. 2015 May;42(5):253–8. doi: http://dx.doi.org/10.1097/OLQ.0000000000000277 PMID: 25868137
96. Memish ZA, Almasri M, Chentoufi AA, Al-Tawfiq JA, Al-Shangiti AM, Al-Kabbani KM, et al. Seroprevalence of herpes simplex virus type 1 and type 2 and coinfection with HIV and syphilis: the first national seroprevalence survey in Saudi Arabia. Sex Transm Dis. 2015 Sep;42(9):526–32. doi: http://dx.doi.org/10.1097/OLQ.0000000000000336 PMID: 26267880
97. Moore KR, Smith JS, Cole SR, Schoenbach VJ, Schlusser K, Gaydos CA, et al. Herpes simplex virus type 2 seroprevalence and ultrasound-diagnosed uterine fibroids in a large population of young African-American women. Am J Epidemiol. 2016 06 1;183(11):961–8. doi: http://dx.doi.org/10.1093/aje/kwv313 PMID: 27188945

98. Moreira-Soto A, Cabral R, Pedroso C, Eschbach-Bludau M, Rockstroh A, Vargas LA, et al. Exhaustive TORCH pathogen diagnostics corroborate zika virus etiology of congenital malformations in Northeastern Brazil. MSphere. 2018 08 8;3(4):e00278–18. doi: http://dx.doi.org/10.1128/mSphere.00278-18 PMID: 30089647
99. Moretti E, Figura N, Campagna MS, Iacoponi F, Gonnelli S, Collodel G. Infectious burden and semen parameters. Urology. 2017 Feb;100:90–6. doi: http://dx.doi.org/10.1016/j.urology.2016.10.032 PMID: 27793655
100. Murdock KW, Fagundes CP, Peek MK, Vohra V, Stowe RP. The effect of self-reported health on latent herpesvirus reactivation and inflammation in an ethnically diverse sample. Psychoneuroendocrinology. 2016 10;72:113–8. doi: http://dx.doi.org/10.1016/j.psyneuen.2016.06.014 PMID: 27398881
101. Nag S, Sarkar S, Chattopadhyay D, Bhattacharya S, Biswas R, SenGupta M. Seroprevalence of herpes simplex virus infection in HIV coinfected individuals in eastern India with risk factor analysis. Adv Virol. 2015;2015:537939. doi: http://dx.doi.org/10.1155/2015/537939 PMID: 26557849
102. Nasrallah GK, Dargham SR, Mohammed LI, Abu-Raddad LJ. Estimating seroprevalence of herpes simplex virus type 1 among different Middle East and North African male populations residing in Qatar. J Med Virol. 2018 01;90(1):184–90. doi: http://dx.doi.org/10.1002/jmv.24916 PMID: 28817197
103. Nimgaonkar VL, Yolken RH, Wang T, Chang CC, McClain L, McDade E, et al. Temporal cognitive decline associated with exposure to infectious agents in a population-based, aging cohort. Alzheimer Dis Assoc Disord. 2016 Jul-Sep;30(3):216–22. doi: http://dx.doi.org/10.1097/WAD.0000000000000133 PMID: 26710257
104. Nowotny KM, Frankeberger J, Rodriguez VE, Valdez A, Cepeda A. Behavioral, psychological, gender, and health service correlates to herpes simplex virus type 2 infection among young adult Mexican-American women living in a disadvantaged community. Behav Med. 2019 Jan-Mar;45(1):52–61. doi: http://dx.doi.org/10.1080/08964289.2018.1447906 PMID: 29558260
105. Olsson J, Kok E, Adolfsson R, Lövheim H, Elgh F. Herpes virus seroepidemiology in the adult Swedish population. Immun Ageing. 2017 05 10;14(1):10. doi: http://dx.doi.org/10.1186/s12979-017-0093-4 PMID: 28491117
106. Patel EU, Frank MA, Hsieh YH, Rothman RE, Baker AE, Kraus CK, et al. Prevalence and factors associated with herpes simplex virus type 2 infection in patients attending a Baltimore City emergency department. PLoS One. 2014 07 18;9(7):e102422. doi: http://dx.doi.org/10.1371/journal.pone.0102422 PMID: 25036862
107. Patel EU, Laeyendecker O, Hsieh YH, Rothman RE, Kelen GD, Quinn TC. Parallel declines in HIV and hepatitis C virus prevalence, but not in herpes simplex virus type 2 infection: a 10-year, serial cross-sectional study in an inner-city emergency department. J Clin Virol. 2016 07;80:93–7. doi: http://dx.doi.org/10.1016/j.jcv.2016.05.003 PMID: 27232485
108. Puhakka L, Sarvikivi E, Lappalainen M, Surcel HM, Saxen H. Decrease in seroprevalence for herpesviruses among pregnant women in Finland: cross-sectional study of three time points 1992, 2002 and 2012. Infect Dis (Lond). 2016;48(5):406–10. doi: http://dx.doi.org/10.3109/23744235.2015.1123290 PMID: 26654892
109. Remis RS, Liu J, Loutfy M, Tharao W, Rebbapragada A, Perusini SJ, et al. The epidemiology of sexually transmitted co-infections in HIV-positive and HIV-negative African-Caribbean women in Toronto. BMC Infect Dis. 2013 11 17;13(1):550. doi: http://dx.doi.org/10.1186/1471-2334-13-550 PMID: 24238493
110. Rubicz R, Yolken R, Drigalenko E, Carless MA, Dyer TD, Kent J Jr, et al. Genome-wide genetic investigation of serological measures of common infections. Eur J Hum Genet. 2015 Nov;23(11):1544–8. doi: http://dx.doi.org/10.1038/ejhg.2015.24 PMID: 25758998
111. Sanchez-Aleman MA, Del Villar-Tapia YG, Gutierrez JP, Garcia-Cisneros S, Olamendi-Portugal ML, Herrera-Ortiz A, et al. Heterogeneity of herpes simplex virus type 2 seroprevalence from a national probability survey in Mexico, 2012. Sex Transm Dis. 2018 02;45(2):111–7. doi: http://dx.doi.org/10.1097/OLQ.0000000000000702 PMID: 28876288
112. Schulte JM, Bellamy AR, Hook EW 3rd, Bernstein DI, Levin MJ, Leone PA, et al. HSV-1 and HSV-2 seroprevalence in the United States among asymptomatic women unaware of any herpes simplex virus infection (Herpevac Trial for Women). South Med J. 2014 Feb;107(2):79–84. doi: http://dx.doi.org/10.1097/SMJ.0000000000000062 PMID: 24926671
113. Shannon B, Gajer P, Yi TJ, Ma B, Humphrys MS, Thomas-Pavanel J, et al. Distinct effects of the cervicovaginal microbiota and herpes simplex type 2 infection on female genital tract immunology. J Infect Dis. 2017 05 1;215(9):1366–75. doi: http://dx.doi.org/10.1093/infdis/jix088 PMID: 28201724
114. Shen JH, Huang KY, Chao-Yu C, Chen CJ, Lin TY, Huang YC. Seroprevalence of herpes simplex virus type 1 and 2 in Taiwan and risk factor analysis, 2007. PLoS One. 2015 08 7;10(8):e0134178. doi: http://dx.doi.org/10.1371/journal.pone.0134178 PMID: 26252011
115. Simanek AM, Cheng C, Yolken R, Uddin M, Galea S, Aiello AE. Herpesviruses, inflammatory markers and incident depression in a longitudinal study of Detroit residents. Psychoneuroendocrinology. 2014 Dec;50:139–48. doi: http://dx.doi.org/10.1016/j.psyneuen.2014.08.002 PMID: 25218654
116. Slawinski BL, Talge N, Ingersoll B, Smith A, Glazier A, Kerver J, et al. Maternal cytomegalovirus sero-positivity and autism symptoms in children. Am J Reprod Immunol. 2018 05;79(5):e12840. doi: http://dx.doi.org/10.1111/aji.12840 PMID: 29520885
117. Wang GC, Han C, Detrick B, Casolaro V, Levine DM, Fried LP, et al. Herpesvirus infections and risk of frailty and mortality in older women: women's health and aging studies. J Am Geriatr Soc. 2016 05;64(5):998–1005. doi: http://dx.doi.org/10.1111/jgs.14090 PMID: 27131018
118. Werler MM, Parker SE, Hedman K, Gissler M, Ritvanen A, Surcel HM. Maternal antibodies to herpes virus antigens and risk of gastroschisis in offspring. Am J Epidemiol. 2016 12 15;184(12):902–12. doi: http://dx.doi.org/10.1093/aje/kww114 PMID: 27856447
119. Woestenberg PJ, Tjhie JH, de Melker HE, van der Klis FR, van Bergen JE, van der Sande MA, et al. Herpes simplex virus type 1 and type 2 in the Netherlands: seroprevalence, risk factors and changes during a 12-year period. BMC Infect Dis. 2016 08 2;16(1):364. doi: http://dx.doi.org/10.1186/s12879-016-1707-8 PMID: 27484304
120. Zhang T, Yang Y, Yu F, Zhao Y, Lin F, Minhas V, et al. Kaposi's sarcoma associated herpesvirus infection among female sex workers and general population women in Shanghai, China: a cross-sectional study. BMC Infect Dis. 2014 02 5;14(1):58. doi: http://dx.doi.org/10.1186/1471-2334-14-58 PMID: 24498947
121. Dickson N, Righarts A, van Roode T, Paul C, Taylor J, Cunningham AL. HSV-2 incidence by sex over four age periods to age 38 in a birth cohort. Sex Transm Infect. 2014 May;90(3):243–5. doi: http://dx.doi.org/10.1136/sextrans-2013-051235 PMID: 24337730
122. Stoner MCD, Pettifor A, Edwards JK, Aiello AE, Halpern CT, Julien A, et al. The effect of school attendance and school dropout on incident HIV and HSV-2 among young women in rural South Africa enrolled in HPTN 068. AIDS. 2017 Sep 24;31(15):2127–34. doi: http://dx.doi.org/10.1097/QAD.0000000000001584 PMID: 28692544
123. Prevention gap report. Geneva: Joint United Nations Programme on HIV and AIDS; 2018. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf [cited 2018 Jun 12].
124. Phipps W, Saracino M, Magaret A, Selke S, Remington M, Huang ML, et al. Persistent genital herpes simplex virus-2 shedding years following the first clinical episode. J Infect Dis. 2011 Jan 15;203(2):180–7. doi: http://dx.doi.org/10.1093/infdis/jiq035 PMID: 21288817
125. Rowley J, Vander Hoorn S, Korenromp E, Low N, Unemo M, Abu-Raddad LJ, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull World Health Organ. 2019 Aug 1;97(8):548–562P. doi: http://dx.doi.org/10.2471/BLT.18.228486 PMID: 31384073