

An estimate of the global prevalence and incidence of herpes simplex virus type 2 infection

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Objective To estimate the global prevalence and incidence of herpes simplex virus type 2 (HSV-2) infection in 2003.

Methods A systematic review was undertaken of published seroprevalence surveys describing the prevalence or incidence of HSV-2 by age and gender. For each of 12 regions, pooled prevalence values by age and gender were generated in a random-effect model. HSV-2 incidence was then estimated from these pooled values using a constant-incidence model. Values of the HSV-2 seroprevalence from the model fits were applied to the total population to estimate the numbers of people infected.

Findings The total number of people aged 15–49 years who were living with HSV-2 infection worldwide in 2003 is estimated to be 536 million, while the total number of people who were newly infected with HSV-2 in 2003 is estimated to be 23.6 million. While the estimates are limited by poor availability of data, general trends are evident. For example, more women than men were infected, and the number infected increased with age. Although prevalence varied substantially by region, predicted prevalence was mostly higher in developing regions than developed regions.

Conclusion The prevalence of HSV-2 is relatively easy to measure since infection is lifelong and has a specific serological test. The burden of disease is less easy to quantify. Despite the often sparse data on which these estimates are based, it is clear that HSV-2 infection is widespread. The dramatic differences in prevalence between regions are worthy of further exploration.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

Genital herpes may be caused by either herpes simplex virus type 1 (HSV-1) or type 2 (HSV-2) but, globally, the large majority of cases are caused by HSV-2; infection is common in both the industrialized and developing worlds, and HSV-2 uncommonly causes infection by non-sexual means.^{1–5} The ability of the virus to successfully avoid clearance by the immune system by entering a non-replicating state known as latency leads to lifelong infection, although whether latency always accompanies infection is unclear.⁴ Periodic reactivation from latency is possible and leads to viral shedding from the site of the initial infection.

The large majority of persons with genital herpes do not know they have the disease⁶ and infection and reactivation are typically “asymptomatic” although, with teaching, most persons with positive HSV-2 serology (46 of 53, in one study) recognize genital

lesions.⁵ Despite the typically asymptomatic nature of genital herpes, which facilitates its spread in the population, and means it is a useful marker of sexual behaviour,⁷ genital herpes is associated with considerable morbidity and even mortality. Genital lesions due to herpes are often very painful, and can lead to substantial psychological morbidity.⁴ The virus can also be passed from mother to child during birth. Neonatal infection can be very serious.⁸ Without treatment, 80% of infants with disseminated disease die, and those who do survive are often brain damaged.⁹ In one study in the United States of America (USA), four of nine infants born to women who acquired genital herpes shortly before labour developed neonatal infection, of whom one died.⁸

In addition, genital herpes is associated with an increased risk of HIV acquisition by two- to threefold, HIV transmission on a per-sexual act basis

by up to fivefold, and may account for 40–60% of new HIV infections in high HSV-2 prevalence populations.^{10–15} Indeed, the impact of suppressing HSV-2 shedding and associated disease on the rate of HIV acquisition is currently being tested in three proof-of-concept trials.¹⁶

Estimating the global burden of an infection is important for appreciating the scale of an epidemic, stimulating interest from governments and funding bodies, and the efficient distribution of resources to those most affected. The approach taken depends on the infection being measured. For example, estimates of the incidence of chancroid could be based on numbers of reported clinical cases, because chancroid has characteristic clinical features and is a disease for which asymptomatic infection is uncommon.¹⁷ For other infections where a high proportion of infected individuals are asymptomatic or have non-specific symptoms, esti-

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mates based on case report alone will vastly underestimate the total number of infections.¹⁷ Estimates for these infections are instead based on data from prevalence surveys which measure either the presence of the infectious organism (e.g. chlamydia, gonorrhoea) or the presence of antibodies to the infectious agent (e.g. HIV).

Previous work has been done to estimate the global burden of four curable sexually transmitted infections (chlamydia, gonorrhoea, syphilis and trichomoniasis) first for the year 1995^{18,19} and most recently for 1999,²⁰ while estimates of the total number of people infected with HIV are produced twice annually by the Joint United Nations Programme on HIV/AIDS (UNAIDS).²¹ These estimates commonly rely on data from surveys of antenatal clinic attendees, since the prevalence of infection among pregnant women is considered by many to be a good proxy for the prevalence in the general population in the absence of good population-based data.

The global burden of HSV-2 infection has never been systematically estimated. In common with other sexually transmitted infections, any estimate based on the number of reported cases of genital herpes will underestimate the prevalence of infection, since most people with HSV-2 are unaware they are infected.^{4,6} However, diagnostic tests can detect the presence of antibodies to HSV-2 with a high degree of precision, and since infection with HSV-2 is lifelong, diagnose prevalent HSV-2 infection. Several studies have been conducted to estimate the prevalence of antibodies to HSV-2 in particular settings, either using blood collected specifically to measure HSV-2 seroprevalence, or using residual blood collected for other purposes. The nature, size and selection of the samples vary widely from study to study. A small number of studies are large in size and examine prevalence in the population as a whole.^{6,22–27} More commonly, studies are relatively small in size and limited to a specific group.

A study in 2002 systematically reviewed the available prevalence data for HSV-2 by country,²⁸ but did not pool these data to produce prevalence estimates for entire regions, nor attempt to calculate numbers of individuals with

Table 1. Global estimates of the prevalence of the herpes simplex virus type 2 infection, in 2003

| Age in years | Global prevalence in millions (percentage per population) | | |
|--------------|---|---------------------|---------------------|
| | Females | Males | Both |
| 15–19 | 25.8 (9.0) | 14.6 (4.8) | 40.4 (6.9) |
| 20–24 | 39.4 (15.1) | 24.1 (8.8) | 63.5 (11.9) |
| 25–29 | 46.5 (19.0) | 30.5 (12.0) | 77.1 (15.4) |
| 30–34 | 51.5 (21.4) | 36.1 (14.6) | 87.6 (18.0) |
| 35–39 | 52.9 (23.8) | 38.8 (17.1) | 91.8 (20.3) |
| 40–44 | 50.8 (25.9) | 38.8 (19.4) | 89.6 (22.6) |
| 45–49 | 47.9 (27.7) | 37.8 (21.5) | 85.6 (24.6) |
| Total | 314.8 (19.4) | 220.7 (13.1) | 535.5 (16.2) |

prevalent HSV-2 infection. Furthermore, this study only looked at prevalence data and did not consider incident infections. Using tables of seroprevalence data compiled in this review²⁸ and in our update of this review,²⁹ and using recently published data, pooled values of the HSV-2 prevalence by age and gender for all areas of the world are calculated. Model fits are then performed to estimate the numbers of people with prevalent HSV-2 infection, and the numbers of new cases of HSV-2 infection, for the year 2003.

Methods

PubMed® (1966–present) and EMBASE (1980–present) were used to identify cross-sectional studies with HSV-2 seroprevalence data and prospective studies with HSV-2 seroincidence data published since the earlier seroprevalence review²⁸ and the systematic review of the interaction between HSV-1 and HSV-2 and seroprevalence update.²⁹

The MeSH terms used in the PubMed® search (8 September 2005) were “antibodies, viral/(analysis/blood/immunology)”, “incidence”, “prevalence”, “epidemiologic study characteristics”, “herpes simplex/(complications/epidemiology/immunology/pathology)” and “simplex virus/(immunology/pathology)”, while the key terms used in the EMBASE search (20 September 2005) were “seroepidemiology”, “incidence”, “prevalence”, “infection rate”, “herpes simplex virus”, “genital herpes” and “herpes labialis”. No restrictions were placed on the searches with respect to language.

The number of studies identified as being potentially relevant through

PubMed® and EMBASE was 248 and 318, respectively. Studies identified as being relevant in the previous systematic reviews were also searched for incidence data. The abstract of each identified study was checked and those studies obviously not relevant were discarded. The full text of each of the remaining studies was then checked and relevant studies retained.

The small number of studies presenting HSV-2 seroincidence data precluded use of these data in the calculation of the global estimates of incident HSV-2 infection. Instead, the HSV-2 prevalence data were used to estimate the numbers of both prevalent and incident infection. (Data on the prevalence and incidence of HSV-2 identified in this review are available from the contact author on request.)

Data were grouped into 12 geographic regions, based largely on groupings used by the WHO (for listing of countries in each region see Box 1, available at: <http://www.who.int/bulletin/volumes/86/10/07-046128/en/index.html>).^{18–20} These regions were: north America; Latin America and the Caribbean; north Africa and the Middle East; sub-Saharan Africa; western Europe; eastern Europe and central Asia; eastern Asia; Japan; the Pacific; south Asia; south-east Asia; and Australia and New Zealand. Only data from “general” populations were used in the analyses, i.e. we did not include studies with apparent biases towards high-risk populations.

For each of the 12 regions, pooled prevalence values by age and gender were generated using a random-effect model. Pooled prevalence values by age

Table 2. Regional estimates of the prevalence of the herpes simplex virus type 2 infection among females, in 2003

| Region | Regional prevalence in millions, by age | | | | | | | Total |
|----------------------------------|---|-------------|-------------|-------------|-------------|-------------|-------------|--------------|
| | 15–19 years | 20–24 years | 25–29 years | 30–34 years | 35–39 years | 40–44 years | 45–49 years | |
| North America | 0.9 | 1.5 | 2.0 | 2.6 | 3.2 | 3.8 | 3.9 | 17.9 |
| Latin America and the Caribbean | 2.6 | 4.5 | 5.8 | 6.4 | 6.7 | 6.6 | 6.0 | 38.6 |
| North Africa and the Middle East | 1.0 | 1.5 | 1.6 | 1.5 | 1.4 | 1.3 | 1.1 | 9.6 |
| Sub-Saharan Africa | 9.0 | 13.1 | 13.6 | 12.5 | 11.2 | 10.0 | 8.8 | 78.2 |
| Western Europe | 0.7 | 1.3 | 1.8 | 2.2 | 2.6 | 2.6 | 2.5 | 13.7 |
| Eastern Europe and central Asia | 2.7 | 3.9 | 4.3 | 4.3 | 4.3 | 4.7 | 4.7 | 28.9 |
| Eastern Asia | 2.6 | 4.4 | 7.1 | 11.1 | 12.8 | 11.9 | 12.0 | 61.8 |
| Japan | 0.4 | 0.6 | 0.7 | 0.7 | 0.6 | 0.6 | 0.6 | 4.1 |
| Pacific | 0.03 | 0.04 | 0.05 | 0.06 | 0.06 | 0.06 | 0.05 | 0.3 |
| South Asia | 4.1 | 5.4 | 5.5 | 5.4 | 4.9 | 4.3 | 3.7 | 33.2 |
| South-east Asia | 1.7 | 3.1 | 4.0 | 4.6 | 4.9 | 4.8 | 4.4 | 27.6 |
| Australia and New Zealand | 0.03 | 0.06 | 0.09 | 0.1 | 0.2 | 0.2 | 0.2 | 0.9 |
| Total | 25.8 | 39.4 | 46.5 | 51.5 | 52.9 | 50.8 | 47.9 | 314.8 |

and gender were also calculated for four subregions within sub-Saharan Africa (eastern Africa, middle Africa, southern Africa and western Africa) since it is thought that HSV-2 prevalence varies widely between regions in sub-Saharan Africa. Non-availability of data precluded similar subregional analyses for other regions where heterogeneity in prevalence might be expected (e.g. north Africa and the Middle East, and Asia). Prevalence data from all study years were used since infection with HSV-2 is lifelong and changes in behaviour are slow to affect the overall prevalence, and also because few data were available for some regions.

A constant-incidence model was fitted to the pooled prevalence values to estimate HSV-2 incidence. The values of the HSV-2 seroprevalence from the model fits were applied to regional population data by five-year age bands and by gender for 2003 obtained from the United Nations Population Division³⁰ to obtain estimates for the numbers of people with prevalent HSV-2 infection in 2003. The numbers of people newly infected with HSV-2 in 2003 were estimated by applying incidence values from the model to the same population data. A detailed description of the methods, including a description of the mathematical model, is available from the contact author on request. Further results and figures showing the pooled prevalence values and model fits are also available from the corresponding author on request.

Findings

HSV-2 prevalence

The estimated total number of people aged 15–49 years who were living with HSV-2 worldwide in 2003 is 536 million (Table 1). More women than men were infected, with an estimated 315 million infected women compared to 221 million infected men. The number infected increased with age, most markedly in the younger ages, until it peaked in the age stratum 35–39 years of age, after which it declined slightly. The number infected per age stratum is a combination of the size of the population in the age stratum multiplied by the prevalence of infection and, as the pool of susceptibles is used up with increasing age, the rate of increase in prevalence slows. In the model, prevalence itself does not decline with age, but because there were fewer people in total at older ages than at younger ages, the actual number with prevalent infection slightly decreased.

The HSV-2 prevalence varied substantially by region, although some commonalities are evident (data not shown). The HSV-2 prevalence increased with age and was generally higher among women than among men. The higher prevalence among men than women in some regions (the Pacific, south-east Asia, south Asia for older ages and north Africa and the Middle East for younger ages) is likely due to there being few available seroprevalence studies for these regions rather than

being a real result, although in theory different distributions of risk behaviour in the two sexes by region could explain such differences. Generally, the prevalence was higher in developing regions than developed regions. Exceptions to this are north America, which had a relatively high HSV-2 prevalence, and south Asia, which had a relatively low HSV-2 prevalence, though the latter may be a consequence of inadequate representation of individual countries within south Asia, combined with low sample size.

The lowest prevalence was in western Europe, where prevalence reached a maximum of around 18% among women and 13% among men. The highest prevalence was in sub-Saharan Africa, where prevalence reached a maximum of 70% among women and around 55% among men. Subregional analysis for sub-Saharan Africa reveals that the prevalence was high in eastern, middle and southern Africa, and lower in western Africa (data not shown).

The patterns in the numbers infected within each region predictably mirror the trends in prevalence, with more women than men infected, and higher numbers of cases among those at older age (Table 2 and Table 3). Regions with very large populations (such as south Asia and eastern Asia) contribute more prevalent infections to the global totals compared to regions with smaller population size. As reflected in the global totals, the number infected by age reached a peak before declining slightly in some

Table 3. Regional estimates of the prevalence of the herpes simplex virus type 2 infection among males, in 2003

| Region | Regional prevalence in millions, by age | | | | | | | Total |
|----------------------------------|---|-------------|-------------|-------------|-------------|-------------|-------------|--------------|
| | 15–19 years | 20–24 years | 25–29 years | 30–34 years | 35–39 years | 40–44 years | 45–49 years | |
| North America | 0.6 | 1.0 | 1.4 | 1.7 | 2.2 | 2.5 | 2.6 | 11.9 |
| Latin America and the Caribbean | 0.9 | 1.6 | 2.1 | 2.4 | 2.7 | 2.8 | 2.7 | 15.1 |
| North Africa and the Middle East | 1.4 | 1.6 | 1.5 | 1.3 | 1.1 | 0.9 | 0.8 | 8.6 |
| Sub-Saharan Africa | 4.1 | 6.5 | 7.5 | 7.5 | 7.1 | 6.7 | 6.2 | 45.5 |
| Western Europe | 0.2 | 0.5 | 0.7 | 1.1 | 1.4 | 1.6 | 1.7 | 7.2 |
| Eastern Europe and central Asia | 0.6 | 1.1 | 1.5 | 1.8 | 2.1 | 2.6 | 2.8 | 12.3 |
| Eastern Asia | 2.0 | 3.4 | 5.4 | 8.4 | 9.8 | 9.3 | 9.5 | 47.8 |
| Japan | 0.02 | 0.05 | 0.08 | 0.1 | 0.1 | 0.1 | 0.2 | 0.7 |
| Pacific | 0.05 | 0.08 | 0.09 | 0.09 | 0.09 | 0.08 | 0.06 | 0.5 |
| South Asia | 1.8 | 3.1 | 4.0 | 4.8 | 5.2 | 5.4 | 5.2 | 29.4 |
| South-east Asia | 3.1 | 5.2 | 6.3 | 6.9 | 7.0 | 6.6 | 6.0 | 41.2 |
| Australia and New Zealand | 0.02 | 0.03 | 0.05 | 0.06 | 0.08 | 0.1 | 0.1 | 0.4 |
| Total | 14.6 | 24.1 | 30.5 | 36.1 | 38.8 | 38.8 | 37.8 | 220.7 |

regions as a consequence of the underlying population pyramid for these regions, especially for those regions with an expansive population structure (very high numbers of individuals in the younger ages and lower numbers of individuals in the older ages).

HSV-2 incidence

The estimated number of new HSV-2 infections among 15–49 year olds worldwide in 2003 is 23.6 million, of whom 12.8 million were women and 10.8 million were men (Table 4). The number of new infections was highest in the youngest age groups, and declined thereafter due to a decline in the number of susceptibles with increased prevalence. The rate of decline in the number of new infections was higher among women than among men because the high initial incidence for women (in terms of numbers) means that the pool of susceptibles is used up more quickly. The estimates for the percentage of the total population (infected and uninfected combined) newly infected with HSV-2 in 2003 (Table 4) are of a comparable magnitude to the estimates of HSV-2 incidence obtained in our review of incidence data.

Analysis by region reveals similar trends (Table 5 and Table 6). Those regions where prevalence reached saturation at relatively young age had comparatively higher numbers infected at younger ages and many fewer infections at older ages. These regions include north Africa and the Middle East, and, for females only, western Europe, east-

ern Europe and central Asia, Japan and south Asia. In some instances saturation in prevalence, or a lack of saturation, may be observed in the best fit when it is not statistically supported because of a lack of data. As well as saturation in prevalence, the underlying population structure may also cause there to be fewer new infections at older ages.

Conclusion

The estimated number of people aged 15–49 years who were living with HSV-2 worldwide in 2003 is 536 million, or roughly 16% of the world's population in this age range. The prevalence is assumed to increase with age since infection is lifelong, and this is observed in the data. The prevalence was also higher among women than among men, which has been found previously.²⁸ The reasons for the higher prevalence among women

are unclear. One possible reason that occurs with sexually transmitted infections is the anatomical difference between women and men meaning that women may be more susceptible to infection.^{31–34} Alternatively, differences in the pattern of mixing between the genders may expose women to a higher prevalence of infection at younger ages.³⁵ For example, there may be a tendency for young women to form partnerships with older men who have higher HSV-2 prevalence than younger men.³⁶ However, modelling the prevalence of HSV-2 in the USA using reported sexual behaviours, Garnett et al. found that a sixfold higher transmission probability from men to women compared to that from women to men was needed to explain the observed sex differences.³⁷ Differences in the distribution of sexual risk behaviours between men and women may also be a contributing factor.³⁸

Table 4. Global estimates of the incidence of the herpes simplex virus type 2 infection, in 2003

| Age in years | Global incidence in millions (percentage per population) | | |
|--------------|--|-------------------|-------------------|
| | Females | Males | Both |
| 15–19 | 4.3 (1.5) | 2.7 (0.9) | 6.9 (1.2) |
| 20–24 | 2.7 (1.0) | 2.1 (0.8) | 4.8 (0.9) |
| 25–29 | 1.9 (0.8) | 1.7 (0.7) | 3.5 (0.7) |
| 30–34 | 1.4 (0.6) | 1.4 (0.6) | 2.9 (0.6) |
| 35–39 | 1.1 (0.5) | 1.2 (0.5) | 2.3 (0.5) |
| 40–44 | 0.8 (0.4) | 1.0 (0.5) | 1.8 (0.4) |
| 45–49 | 0.6 (0.3) | 0.8 (0.4) | 1.4 (0.4) |
| Total | 12.8 (0.8) | 10.8 (0.6) | 23.6 (0.7) |

Table 5. Regional estimates of the incidence of the herpes simplex virus type 2 infection among females, in 2003

| Region | Regional incidence in thousands, by age | | | | | | | Total |
|----------------------------------|---|-------------|-------------|-------------|-------------|-------------|-------------|-------|
| | 15–19 years | 20–24 years | 25–29 years | 30–34 years | 35–39 years | 40–44 years | 45–49 years | |
| North America | 157 | 123 | 97 | 82 | 72 | 62 | 48 | 641 |
| Latin America and the Caribbean | 475 | 375 | 287 | 215 | 162 | 119 | 82 | 1714 |
| North Africa and the Middle East | 170 | 101 | 55 | 30 | 17 | 10 | 5 | 388 |
| Sub-Saharan Africa | 1528 | 907 | 513 | 285 | 162 | 96 | 57 | 3547 |
| Western Europe | 120 | 83 | 60 | 45 | 32 | 21 | 12 | 373 |
| Eastern Europe and central Asia | 389 | 191 | 92 | 43 | 22 | 12 | 6 | 755 |
| Eastern Asia | 503 | 418 | 441 | 503 | 457 | 344 | 290 | 2957 |
| Japan | 25 | 2 | 0.2 | 0 | 0 | 0 | 0 | 28 |
| Pacific | 5 | 4 | 3 | 2 | 2 | 1 | 0.7 | 17 |
| South Asia | 574 | 242 | 101 | 44 | 19 | 8 | 3 | 991 |
| South-east Asia | 327 | 272 | 217 | 174 | 137 | 103 | 76 | 1305 |
| Australia and New Zealand | 6 | 6 | 6 | 6 | 6 | 6 | 5 | 41 |

The prevalence estimates by region were highly heterogeneous. Again, the reasons for this are unknown. The prevalence of HSV-2 was generally higher in developing regions than in developed regions. Factors that likely contribute to differences in prevalence by region for herpes are likely to be similar to those for HIV.³⁹ These may include regional differences in the frequency and pattern of sexual risk behaviour including rates of oral versus vaginal sex, differences in age at first sex,^{40,41} differences in the prevalence of sexually transmitted infection cofactors for HSV-2 transmission such as HIV¹⁰ and differences in the structure of sexual networks.^{38,42–44} It could be that HSV-2 prevalence is a product of

slowly spreading pandemics with regions experiencing different epidemic stages. However, well-conducted, population-based studies conducted sequentially are rare, and this question is very difficult to address. In perhaps the two best-conducted such surveys, carried out in the USA, there was a surprising 30% increase in prevalence between the late 1970s and early 1990s, which lends support to this hypothesis.⁶ In some parts of the world, immune suppression associated with HIV could have increased the transmission of HSV. Different rates of HSV-1 infection may also contribute to differences in the pattern of HSV-2 infection across regions as a consequence of cross-immunity.²⁹

Our estimates are only that – estimates. No matter how sophisticated the statistical methods used to produce them, estimates are only as good as the data from which they are calculated. Except for one study with a very high number of equivocal samples,⁴⁵ no study was excluded on the basis of quality due to the small number of available studies. For the same reason, no attempt was made to control for possible intraregional variation in prevalence by country, by geographical location (e.g. rural versus urban), across different “general” population groups or over time, beyond employing a random-effects model to pool prevalence data from different studies (which increases the width of the 95%

Table 6. Regional estimates of the incidence of the herpes simplex virus type 2 infection among males, in 2003

| Region | Regional incidence in thousands, by age | | | | | | | Total |
|----------------------------------|---|-------------|-------------|-------------|-------------|-------------|-------------|-------|
| | 15–19 years | 20–24 years | 25–29 years | 30–34 years | 35–39 years | 40–44 years | 45–49 years | |
| North America | 104 | 85 | 70 | 61 | 56 | 50 | 40 | 466 |
| Latin America and the Caribbean | 168 | 152 | 133 | 115 | 100 | 85 | 68 | 820 |
| North Africa and the Middle East | 149 | 36 | 8 | 2 | 0.4 | 0.1 | 0 | 195 |
| Sub-Saharan Africa | 775 | 585 | 422 | 300 | 216 | 160 | 119 | 2575 |
| Western Europe | 44 | 45 | 47 | 52 | 55 | 51 | 45 | 340 |
| Eastern Europe and central Asia | 113 | 104 | 94 | 83 | 77 | 79 | 74 | 624 |
| Eastern Asia | 396 | 327 | 344 | 393 | 360 | 280 | 241 | 2341 |
| Japan | 4 | 5 | 5 | 5 | 5 | 4 | 4 | 32 |
| Pacific | 9 | 6 | 3 | 2 | 1 | 0.7 | 0.4 | 23 |
| South Asia | 348 | 296 | 250 | 221 | 188 | 158 | 128 | 1589 |
| South-east Asia | 548 | 409 | 292 | 209 | 148 | 101 | 68 | 1776 |
| Australia and New Zealand | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 21 |

confidence intervals) and performing a subregional analysis for sub-Saharan Africa. Heterogeneity between studies may mean that individual data cannot be generalized to one country, let alone an entire region. This is particularly problematic for those regions with only one or a few available studies, and for those regions that are densely populated, as these regions contribute the most numbers to the global totals. There is little that can be done given the scarcity of the available data. Thus, while it is possible to produce a rough figure for the numbers of people with prevalent and incident HSV-2 infection, and highlight general patterns, the estimates should not be taken as being definitive.

The estimates are also dependent on the assumptions about the natural history of HSV-2 infections. For instance, a constant incidence of infection over age is assumed. Higher rates of partner change among those at younger age may lead to high incidence after sexual debut and decreasing incidence thereafter. However, high partner change rates do not necessarily equate to high transmission rates. There are several complicating factors affecting the probability of transmission per partnership, such as the number of sex acts per partnership (and the relationship between risk of transmission and act number), rates of condom use and the extent to which mixing is assortative.^{44,46}

The analysis was limited to estimating rates of HSV-2 infection. HSV-2

seroprevalence is a good proxy for the prevalence of genital HSV-2 infection because it is likely that the majority of HSV-2 infections are genital, and comparatively few infections are oral. This is suggested by the very low prevalence of HSV-2 among children.²⁸ Viral isolation studies also show that the frequency of oral HSV-2 reactivation is low,⁴⁷ suggesting that onward transmission is rare. The proportion of infections at each site cannot be directly measured because seroprevalence studies are unable to distinguish between oral and genital infections. In contrast, genital herpes due to HSV-1 is of significant public-health importance,⁴⁸⁻⁵³ but the inability of seroprevalence studies to distinguish between the two infection sites means it is much more difficult to generate estimates of the burden of genital HSV-1 infection.

This is the first attempt to estimate the global burden of HSV-2 infection. Estimates of the number of people with incident and prevalent infection are useful to get a general impression of who is infected and in which areas of the world, to guide public-health policy to those groups most at need. Reducing the number of HSV-2 infections is important not only because HSV-2 is a cause of significant adult morbidity and infant mortality in itself, but also because the presence of a genital herpetic infection may increase an individual's chances of becoming infected with HIV.¹⁰ Moreover, areas with high HSV-2 prevalence com-

monly have a high prevalence of other sexually transmitted infections, such as chlamydia and gonorrhoea.²⁰ Therefore, increasing sexual health-care capacity and prevention measures to reduce HSV-2 incidence will likely lead to simultaneous reductions in the rates of these other infections.

Generating estimates of the burden of herpes infections is also useful to highlight areas where data are particularly lacking. The estimates for some regions are severely limited by the quantity and quality of available seroprevalence data, and it is these regions for which data are most needed. Even where the availability of seroprevalence data is good, continual investment in surveillance programmes is essential to monitor trends in infection rates and respond appropriately. ■

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Résumé

Estimation de la prévalence et de l'incidence mondiales de l'infection par l'herpesvirus de type 2

Objectif Estimer la prévalence et l'incidence mondiales en 2003 de l'infection par le virus de l'herpes simplex de type 2 (HSV-2).

Méthodes On a procédé à une revue systématique des enquêtes de séroprévalence publiées et indiquant la prévalence ou l'incidence du HSV-2 par âge et par sexe. Pour chacune des 12 régions étudiées, un modèle d'effet aléatoire a permis de générer des valeurs de la prévalence agrégées par âge et par sexe. On a ensuite estimé l'incidence de l'herpesvirus à partir de ces valeurs agrégées en utilisant un modèle à incidence constante. Les valeurs de la séroprévalence du HSV-2 fournies par ce modèle une fois ajusté ont été appliquées à la population totale pour estimer les nombres de personnes infectées.

Résultats Le nombre total de personnes de 15 à 49 ans vivant en 2003 dans le monde avec le HSV-2 a été estimé à 536 millions, tandis que le nombre total de personnes nouvellement infectées par ce virus en 2003 était évalué à 23,6 millions. Même si ces

estimations se heurtent au manque de disponibilité des données, des tendances générales sont clairement observables. Par exemple, les femmes sont plus nombreuses que les hommes à être infectées et le nombre de personnes infectées augmente avec l'âge. Malgré des variations substantielles de la prévalence d'une région à l'autre, la valeur prédite de ce paramètre est dans la plupart des cas plus élevée dans les régions en développement que dans les régions développées.

Conclusion La prévalence du virus HSV-2 est relativement facile à mesurer car il infecte les malades à vie et fait l'objet d'un test sérologique spécifique. La charge de morbidité est moins aisée à quantifier. Si les données sur lesquelles reposent ces estimations sont souvent claires, il est cependant clair que l'infection par le HSV-2 est très répandue. Les différences considérables du taux de prévalence entre les régions méritent une étude plus poussée.

Resumen

Estimación de la prevalencia e incidencia mundial de la infección por virus del herpes simple de tipo 2

Objetivo Estimar la prevalencia e incidencia mundial de la infección por virus del herpes simple de tipo 2 (VHS-2) en 2003.

Métodos Se llevó a cabo una revisión sistemática de estudios de seroprevalencia publicados en los que se describía la prevalencia o la incidencia de la infección por VHS-2 por edad y sexo. Para cada una de las 12 regiones consideradas, se generaron valores de prevalencia a partir de muestras combinadas por edad y sexo mediante un modelo de efectos aleatorios. La incidencia de VHS-2 se estimó a partir de esos valores combinados utilizando un modelo de incidencia constante. Los valores de la seroprevalencia de VHS-2 obtenidos mediante los ajustes del modelo se aplicaron a la población total para calcular el número de personas infectadas.

Resultados Se estima en 536 millones el número total de personas de 15-49 años afectadas por el VHS-2 en 2003, mientras que el número total de casos nuevos de infección por el

virus en 2003 ascendió a 23,6 millones. Si bien esas estimaciones se ven limitadas por la falta de datos, se observan con claridad algunas tendencias generales. Por ejemplo, hay más mujeres que hombres infectados, y el número de infectados aumenta con la edad. Aunque la prevalencia varía considerablemente según la región, la prevalencia prevista fue por lo general mayor en las regiones en desarrollo que en las desarrolladas.

Conclusión La prevalencia del VHS-2 es relativamente fácil de medir pues se trata de una infección de por vida y existe una prueba serológica específica para ello, pero la carga de morbilidad es menos fácil de cuantificar. Pese a los datos a menudo escasos en que se basan esas estimaciones, se deduce claramente que la infección por VHS-2 está muy extendida. La gran variación de la prevalencia observada entre las regiones merece ser objeto de nuevos estudios.

ملخص

تقدير معدل الانتشار ومعدل الوقوع على الصعيد العالمي للعدوى بالنمط 2 من فيروس الهربس البسيط

الذين أصيبوا بعدوى جديدة بالنمط الثاني لفيروس الهربس البسيط عام 2003 بـ 23.6 مليوناً. ورغم أن قلة توافر المعطيات تحدُّ من إمكانية عمل تقديرات دقيقة، إلا أن الاتجاه العام لها واضح، ومن ذلك على سبيل المثال أن النساء يصبن بالعدوى أكثر من الرجال، وأن أعداد المصابين بالعدوى تزداد بتقدم العمر. وعلى الرغم من أن معدل الانتشار يختلف باختلاف المناطق والأقاليم، فإن المعدل المتوقع للانتشار كان أعلى في الأقاليم النامية، في معظم الأحوال، منه في الأقاليم المتقدمة.

الاستنتاج: إن من السهل بشكل عام قياس معدل انتشار العدوى بالنمط 2 من فيروس الهربس البسيط لأن العدوى تدوم طيلة الحياة، وهي ذات اختبار مصلي نوعي؛ إلا أن الحساب الكمي لعبء المرض يعد أكثر صعوبة. ورغم شح المعطيات التي تبنَّى عليها هذه التقديرات في معظم الأحوال، إلا أنه من الواضح أن العدوى بالنمط 2 لفيروس الهربس البسيط هي عدوى واسعة الانتشار، وأن الفروق الكبيرة في معدلات الانتشار بين المناطق والأقاليم تستحق المزيد من الاستقصاء.

الهدف: تقدير معدل الانتشار ومعدل الوقوع على الصعيد العالمي للعدوى بالنمط 2 من فيروس الهربس البسيط عام 2003.

الطريقة: أجري الباحثون استعراضاً منهجياً للمسوحات المنشورة حول معدلات الانتشار المصلي، والتي تصف الحدوث أو الوقوع للعدوى بالنمط 2 من فيروس الهربس البسيط وفقاً للعمر والجنس. وشملت الدراسة 12 منطقة، جمع الباحثون فيها قيم معدلات الانتشار باستخدام نموذج التأثير العشوائي وفقاً للعمر والجنس، ثم حصلوا على تقديرات لمعدل وقوع العدوى بالنمط 2 لفيروس الهربس البسيط من هذه القيم المجمعة باستخدام نموذج الوقوع الثابت. وقد طُبِّقَت قيم معدلات الانتشار المصلي للعدوى بالنمط 2 لفيروس الهربس البسيط المتوافقة مع النموذج على مجمل المجموعات السكانية من أجل تقدير معدل المصابين بالعدوى.

الموجودات: يقدر العدد الإجمالي للأشخاص الذين تتراوح أعمارهم بين 15 و49 عاماً والذين يتعايشون مع العدوى بالنمط 2 لفيروس الهربس البسيط في عام 2003 في جميع أنحاء العام بـ 536 مليوناً، فيما يقدر عدد الأشخاص

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Box 1. Listing of countries in each of 12 regions**Australia and New Zealand**

Australia, New Zealand

Eastern Asia

Brunei Darussalam, China, Democratic People's Republic of Korea, Mongolia, Republic of Korea, Singapore

Europe and central Asia

Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Hungary, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Montenegro, Poland, Romania, Russian Federation, Serbia, Slovakia, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, Uzbekistan

Japan

Japan

Latin America and the Caribbean

Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela (Bolivarian Republic of)

North Africa and Middle East

Algeria, Bahrain, Cyprus, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Israel, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Malta, Morocco, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates, Yemen

North America

Canada, United States of America

Pacific

Cook Islands, Fiji, Kiribati, Marshall Islands, Micronesia (Federated States of), Nauru, Niue, Palau, Papua New Guinea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu

South Asia

Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka

South-east Asia

Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, Philippines, Thailand, Timor-Leste, Viet Nam

Sub-Saharan Africa

Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, Sudan, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, Zimbabwe

Western Europe

Andorra, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom