Prevalence and incidence of selected sexually transmitted infections

Chlamydia trachomatis,
Neisseria gonorrhoeae,
syphilis and
Trichomonas vaginalis

Methods and results

used by WHO to generate 2005 estimates

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Executive summary

Sexually transmitted infections (STIs) are a major global cause of acute illness, infertility, long-term disability and death, with serious medical and psychological consequences to millions of men, women and infants. Over 30 bacterial, viral and parasitic pathogens have been identified to date that can be transmitted sexually.

This report presents the methods used to generate global and regional estimates for 2005 of the prevalence and incidence of four curable STIs, *Chlamydia trachomatis (C. trachomatis)*, *Neisseria gonorrhoeae (N. gonorrhoeae)*, syphilis and *Trichomonas vaginalis (T. vaginalis*), in adults between 15 and 49 years of age. The general approach used to generate the 2005 estimates is similar to the approach used in 1995 and 1999. However, a number of changes were made to the methods and to various parameters that mean that the 2005 estimates are not directly comparable to the earlier estimates.

Regional prevalence estimates were back calculated from incidence estimates based on case-reporting data or based on data extracted from the World Health Organization's STI database and data compiled for this project. The first approach was followed for *C. trachomatis*, *N. gonorrhoeae*, and syphilis in North America and for syphilis in the WHO Regional Office for Europe, where good case-reporting data are available. The second approach was used for the other infections and regions. In generating the 2005 estimates, the data from each study were explicitly adjusted to account for the sensitivity and specificity of the diagnostic tests used, the age group surveyed, and the geographic location. The regional and subregional estimates were then based on the median value of the adjusted prevalence estimates from all the studies in a particular region or subregion. For infections for which there were fewer than three data points regional estimates were based on the estimated prevalence of one of the other infections.

Two approaches were used to calculate incidence. The first approach was applied in regions with strong case-reporting surveillance systems and was only used to estimate the incidence of *C. trachomatis*, *N. gonorrhoeae*, syphilis in North America and syphilis in the WHO European Region. In the absence of good case-reporting data, the annual incidence (*I*) was estimated using the following equation:

$$I = P/D$$

Where *P* is the regional prevalence estimates and *D* is the duration of infection, or mean length of time an individual carries an infection within a population.

The duration of infection for each pathogen depends on a number of factors, including the average duration of infection in the absence of treatment for both symptomatic[a] and asymptomatic individuals, and treatment patterns for symptomatic individuals within a population. In addition, asymptomatic individuals may receive treatment as a result of screening programmes, or partner notification interventions, or inadvertent therapy while being treated for other health problems.

The methods used to estimate the mean duration of infection in 2005 were the same as those used in 1995 and 1999. However, a number of changes were made to the values assigned to several of the parameters used to estimate duration reflecting new natural history data and the use of newer, more sensitive and specific diagnostic tools, such as ligase chain reaction (LCR) and polymerase chain reaction (PCR).

Using the approaches described above, the total number of new cases of the four STIs in adults between the ages of 15 and 49 in 2005 was estimated to be 448 million.

- 101 million cases of *C. trachomatis*
- 88 million cases of *N. gonorrhoeae*
- 11 million cases of syphilis
- 248 million cases of *T. vaginalis*.

[a] For all infections, the term "symptomatic" refers to individuals who have symptoms and recognize these symptoms, such that recognition influences health-care seeking behaviour.

In addition, at any point in 2005 there were approximately 318 million prevalent cases of the four STIs in adults:

- 98 million with *C. trachomatis*
- 31 million with *N. gonorrhoeae*
- 36 million with syphilis
- 153 million with *T. vaginalis*.

1. Introduction

Sexually transmitted infections (STIs) are among the most common infections in adults. There are more than 30 bacterial, viral and parasitic pathogens that can be transmitted sexually. If untreated, a number of them can lead to serious complications and sequelae. Quantifying the incidence and burden of these infections is important for planning appropriate interventions and advocating for resources, as necessary.

- The main sources of information for generating national prevalence and incidence estimates are surveillance systems and epidemiological surveys. For infections with distinctive symptoms, the number of reported cases is a reasonable proxy for the total number of infections. Many STIs, however, are asymptomatic or have nonspecific symptoms, and this means that any report-based surveillance system will underestimate the true numbers of cases. In addition, the social stigma associated with STIs and economic hardship of having to pay for services may deter many people who are symptomatic from seeking care in the formal sector, so these cases are unlikely to be captured by a surveillance system.
- Epidemiological surveys on the prevalence of one or more STIs are the other main source of data for estimating prevalence and incidence. Surveys of prevalence generally provide information on one or more STIs in a specific population (e.g. women attending an antenatal clinic in a specific geographical location), but care must be taken when extrapolating data from these studies to the general population. Surveys of incidence are very complex and costly and only a small number have been done in very specific populations (Grosskurth et al. 2000).

This document presents the methods and results from a WHO-supported exercise to generate global and regional estimates of the prevalence and incidence of four curable STIs in adults in 2005, building on the approach used to generate estimates in 1995 and 1999 (see Box 1). A parallel exercise in collaboration with Imperial College in London was conducted to estimate the prevalence and incidence of HSV-2 and to look at different approaches for estimating the prevalence and incidence of viral infections (Looker et al., 2008; see also Annex 4).

Box 1. Previous global incidence estimates of STIs

In 1990, the WHO used a modified Delphi approach to generate global estimates of the number of new cases of STIs in adults aged between 15 and 49 years. The expert panel estimated that in 1990 there were over 78 million new cases of the three "classic" STIs (*Chlamydia trachomatis (C. trachomatis) Neisseria gonorrhoeae (N. gonorrhoeae)* and syphilis) and an additional 120 million new cases of *Trichomonas vaginalis (T. vaginalis)* (Gerbase et al., 1998).

In 1998, the WHO and the Rockefeller Foundation used a different approach that was based on an epidemiological survey to generate estimates for 1995. They estimated that in 1995 there were 163 million new cases of *C. trachomatis, N. gonorrhoeae* and syphilis and 170 million new cases of *T. vaginalis* (Gerbase et al., 1998).

The same approach was used to generate estimates for 1999, whereby there were global estimates of 167 million new cases of *C. trachomatis*, *N. gonorrhoeae* and syphilis and 173 million new cases of *T. vaginalis* (World Health Organization, 2001).

2. Methods for 2005 prevalence estimates

2.1 Collating prevalence data

Prevalence data for the 2005 estimates were drawn from the WHO STI database[b] and a literature review was conducted specifically for this exercise.

2.1.1 WHO STI database

The WHO STI database provides information on the prevalence of *C. trachomatis*, *N. gonorrhoeae*, syphilis and *T. vaginalis* from both published and unpublished reports[c] and includes incidence data (where available).

The database was developed by the WHO between 2003 and 2005 specifically for this project and initially focused on studies that collected data during the period 1997–2003. Data were also opportunistically included from studies conducted pre-1997. Data collection focused on countries outside of Western Europe and North America.

The database includes information on the age, sex, geographical location (urban, rural) of the sampled population, the type of population (e.g. antenatal attendees, the general community, sex workers, family planning clients or students), the dates and duration over which data were collected, the study design (sampling strategy and size) and the diagnostic methods used (type of sample and specific test).

2.1.2 Literature review

A series of Medline searches were conducted at the end of 2005 and again in December 2006 to identify any studies published in 2000 or later that were not in the WHO STI database.[d] In addition, any study brought to the team's attention was also reviewed if it met the specified criteria.

2.1.3 Study inclusion criteria

Each of the data points was reviewed against a set of inclusion criteria (Box 2).

Box 2. Entry criteria for the study

- Studies with sample sizes of at least 100.
- Studies with specimens collected between 2000 and 2005. For studies in which no date was specified, the study had to be published in 2000 or later.
- Studies with populations considered representative of the general population, such as Demographic and Health Survey (DHS) surveys, pregnant women and women attending family planning clinics.
- Studies with no apparent bias in the selection of study participants (e.g. patients seeking care because of an STI or genital symptoms were not included).
- Studies that used one of the diagnostic tests listed in Table 1.
- Studies that appear to have no deficiencies in the handling of specimens or performance of laboratory tests.

b For more information on the WHO STI database which covers the period 1997–2003 (please contact the STI Team in the Department of Reproductive Health Research, WHO, Geneva.

c Unpublished literature includes country reports, reports written following country visits for technical support and UNAIDS database of studies on HIV prevalence and/or incidence.

d The keywords used in the Medline search included (a) prevalence or incidence AND (b) *chlamydia*, syphilis, gonorrhoeae and trichomoniasis AND (c) the country name.

The studies that met the entry criteria were compiled into a workbook format in Microsoft Excel with separate spreadsheets for each WHO region. The spreadsheets were circulated to the relevant regional STI advisors who were asked to provide any additional information and details of any studies they were aware of.

Table 1. Diagnostic tests that met the study's inclusion criteria

Infection	Sample	Test
Chlamydia trachomatis	Urine	NAAT ELISA or EIA
	Genital secretions	NAAT NAT Culture ELISA or EIA
Neisseria gonorrhoeae	Urine	NAAT
	Genital secretions	NAAT Culture NAT
Trichomonas vaginalis	Urine	NAAT
	Genital secretions	NAAT Culture MWM
Syphilis	Serum	Reaginic test and Treponemal antibody test

EIA, enzyme immunoassay; ELISA, enzyme-linked immunosorbent assay; MWM, wet mount of genital secretions; NAAT, nucleic acid amplification test; NAT, nucleic acid probe test.

Tables 2–5 summarize the prevalence studies that met the study entry criteria for each infection by region. They do not provide information for the WHO European Region or North America as prevalence data were not systematically collated from these regions (another approach was used to estimate prevalence and incidence).

Table 2. Quantity of data (meeting the study's entry criteria) available in each region for chlamydial infection in males and females

Sex	WHO region	Total number of data points	Countries with data available	Countries with three or more data points
Females	African Region	24	14	3
	Region of the Americas (excluding North America)	9	6	1
	South-East Asia Region	10	3	1
	Eastern Mediterranean Region	10	5	1
	Western Pacific Region	32	16	3
Males	African Region	14	7	2
	Region of the Americas (excluding North America)	4	3	0
	South-East Asia Region	6	2	1
	Eastern Mediterranean Region	1	1	0
	Western Pacific Region	9	5	1

Table 3. Quantity of data (meeting the study's entry criteria) available in each region for *Neisseria gonorrhoeae* infection in males and females

Sex	WHO region	Total number of data points	Countries with data available	Countries with three or more data points
Females	African Region	24	13	3
	Region of the Americas (excluding North America)	7	5	0
	South-East Asia Region	8	2	1
	Eastern Mediterranean Region	11	6	0
	Western Pacific Region	25	15	2
Males	African Region	10	6	2
	Region of the Americas (excluding North America)	3	3	0
	South-East Asia Region	4	2	1
	Eastern Mediterranean Region	1	1	0
	Western Pacific Region	5	4	0

Table 4. Quantity of data (meeting the study's entry criteria) available in each region for syphilis in males and females

Sex	WHO region	Total number of data points	Countries with data available	Countries with three or more data points
Females	African Region	32	17	3
	Region of the Americas (excluding North America)	9	6	0
	South-East Asia Region	9	3	1
	Eastern Mediterranean Region	10	6	0
	WHO Western Pacific Region	21	13	1
Males	African Region	8	5	1
	Region of the Americas (excluding North America)	3	2	0
	South-East Asia Region	7	3	1
	Eastern Mediterranean Region	2	2	0
	Western Pacific Region	2	1	0

Table 5. Quantity of data (meeting the study's entry criteria) available in each region for *Trichomonas vaginalis* infection in males and females

Sex	WHO region	Total number of data points	Countries with data available	Countries with three or more data points
Females	African Region	16	9	1
	Region of the Americas (excluding North America)	3	3	0
	South-East Asia Region	5	2	1
	Eastern Mediterranean Region	13	8	0
	Western Pacific Region	15	9	2
Males	African Region	3	2	0
	Region of the Americas (excluding North America)	0	0	0
	South-East Asia Region	1	1	1
	Eastern Mediterranean Region	0	0	0
	Western Pacific Region	0	0	0

2.2 Adjusting prevalence data

The studies that met the study entry criteria used a variety of laboratory tests and were from different populations. To improve the consistency of data across these studies the observed prevalence values were converted into true prevalence estimates by adjusting for the sensitivity and specificity of the specific diagnostic test used. The prevalence data from individual studies were also adjusted to take into account:

- the age of the study population (for chlamydial infection only)
- the geographic location of the study population.

This procedure was not explicitly performed for the 1995 or 1999 estimates.

The standardized prevalence estimate for each study (*SP*) was generated using the following equation:

$$SP = \text{True prevalence} \times \text{Age adjustor} \times \text{Geography adjustor}$$

More information on how each of the terms used to calculate *SP* can be found in sections 2.2.1–2.2.3.

2.2.1 Adjusting for laboratory test performance

The *true prevalence* for each study was estimated using the following equation

$$\text{True prevalence} = \frac{(\text{Observed prevalence} + \text{Specificity} - 1)}{(\text{Sensitivity} + \text{Specificity} - 1)}$$

When the equation was applied to the data and a negative number was generated for the estimated true prevalence, then the true prevalence was estimated to be 0. Annex 1 summarizes the values used for the sensitivity and specificity of each laboratory test.

2.2.2 Adjusting for age

Prevalence data for chlamydial infection in women were systematically adjusted for age, but no adjustments were made for the other three infections because the age differences in the incidence and prevalence of these infections are not as marked as with chlamydial infection. No adjustments were made for males for any of the four infections.

The decision to adjust the prevalence data for women for *C. trachomatis* was based on the observed variation in the prevalence of chlamydial infection among women of different ages. For example, in 2007 Franceschi et al. conducted an investigation across four continents that revealed greater prevalence in women aged 15–24 years than in those aged 25–44 years; chlamydia affected 4.5% vs 2.6% in these age groups respectively (the population prevalence was 3.0%). In contrast, they showed that *N. gonorrhoeae* had similar prevalence in both age groups.

For each study providing chlamydial infection prevalence data, information on the age of the participating women was examined. The studies were then classified into one of three groups:

- youths (15–24 years)
- adults (25–49 years)
- other (studies that covered both age groups or where no ages were specified).

Age adjustors were generated from the Franceschi data to create an estimate for women aged 15–49. For example, the data from a study in young women aged 15–24 years was multiplied by 0.67 to yield a figure applicable to all women aged 15–49 (Table 6).

Table 6. Age adjustors for estimates for women aged 15–49 years with chlamydial infection

Age range (years)	Adjustment factor
Youths (15–24)	0.67
Adults (25–49)	1.15
Other (or no) information	1.0

2.2.3 Adjusting for geography

In studies where information was available for both rural and urban areas, the prevalence in urban areas was generally higher than in rural areas. However, the number of studies from rural areas was small and independent prevalence estimates in rural areas could not be determined, so the ratio of the prevalence in rural to urban areas for all four infections in all regions of the world was estimated to be 0.9.[e]

The value of the geography adjustor was based on the ratio of the prevalence of the infection in rural areas to its prevalence in urban areas. It also took into account estimates of the proportion of the population living in urban areas, using the 2005 UN World Urbanization Prospects data (United Nations, 2005) for less developed[f] and more developed regions. This report estimated that 42.9% of people lived in urban areas in less developed regions and 74.1% in more developed regions. Therefore, the two figures were applied to different WHO regions, thus:

- 42.9% was used as the estimate of the percentage of the population living in urban areas for all countries in the South-East Asia, Western Pacific, Eastern Mediterranean regions and the Region of the Americas (excluding North America)
- 74.1% was used as the estimate of the percentage of the population living in urban areas for all countries in the European Region and North America. Table 7 shows the geography adjustors.

As an example, data from a study in a rural area in the WHO South-East Asia Region was multiplied by 1.048 to yield a national estimate.

Table 7. Geography adjustors

Type of population	Adjustor for all regions except WHO European Region and North America	Adjustor for WHO European Region and North America
National	1	1
Urban	0.943	0.974
Rural	1.048	1.082
Unknown	1	1

2.3 Generating regional prevalence estimates

Ideally, prevalence estimates for each country would have been generated, but unfortunately only limited data were available. For this reason, countries were grouped together. In 1995, countries were grouped according to the Global Burden of Disease Study and the same system was followed in 1999. In 2005, the WHO regional groupings were used.

Initially the countries in each of the WHO regions were to be grouped into subregions based upon the prevalence of the infection and certain epidemiologic considerations. However, because there were insufficient data, this was only possible for the WHO African and Western Pacific Regions. Countries in the WHO African and Western Pacific regions were divided into two groups following

[e] The value of this estimate was determined during an Expert Consultation sponsored by the WHO in November 2008.

[f] Less developed regions comprise all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Federated States of Micronesia and Polynesia.

consultations with the WHO Regional Advisors (see Annex 2). The WHO Region of the Americas was also divided into two subregions – North America (Canada and the United States) and the remaining countries – because a different approach was used to estimate prevalence and incidence in North America from the rest of the WHO Region of the Americas.

One of two different approaches was used to generate the prevalence estimates in each region:

- Approach 1 used the STI prevalence worksheets described in section 2.1.3
- Approach 2 involved back-calculations of the prevalence from estimates of the incidence.

The second approach allowed estimation of the prevalence of *C. trachomatis*, *N. gonorrhoeae* and syphilis in North America and syphilis in the WHO European Region. This was possible because there were relatively comprehensive national case-reporting systems for these areas for estimating incidence. Table 8 shows which approach was used for each infection by region. Approach 2 was used to estimate the prevalence of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and syphilis in North America and syphilis in the WHO European Region because there are relatively comprehensive national case-reporting systems for these areas.

Table 8. Use of Approach 1 or Approach 2 to estimate the prevalence of STIs in different regions

WHO region	Infection			
	Chlamydia trachomatis	Neisseria gonorrhoeae	Trichomonas vaginalis	Syphilis
WHO African Region	1	1	1	1
WHO Region of the Americas (excluding North America)	1	1	1	1
North America [Region of the Americas (North America only)	2	2	1	2
WHO South-East Asia Region	1	1	1	1
WHO European Region	1	1	1	2
WHO Eastern Mediterranean Region	1	1	1	1
WHO Western Pacific Region	1	1	1	1

2.3.1 Approach 1: Using STI survey data

The regional and subregional estimates were based on the median value of the standardized prevalence estimates from all the studies in a particular region or subregion. The median was chosen because the prevalence data varied considerably in some regions. Furthermore, the Joint United Nations Programme on HIV/AIDS (UNAIDS) Reference Group on Estimates, Modelling and Projections uses the median for generating estimates for HIV infection.

For each infection, the regional or subregional sex ratios were calculated from all of the studies that met the inclusion criteria. If the male-to-female sex ratio was more then one standard deviation outside the global male-to-female sex ration for that infection (Table 9), then the male prevalence estimate was adjusted so that the ratio was plus or minus one standard deviation. The female prevalence was chosen as the basis for this ratio because there were considerably more data points for females than males.

This approach is somewhat different from the one used to generate the 1995 and 1999 estimates, primarily because of improvements in the quantity and quality of data. In 1995 there was a shortage of data, and it was assumed that the prevalence of *N. gonorrhoeae* in females was 50% that of the prevalence of *C. trachomatis* in females and that the prevalence of *T. vaginalis* in females was twice that of *C. trachomatis*. The 2005 estimate was based on the global mean male-to-female ratio from all the studies that met the inclusion criteria and which provided data for males *and* females from similar population groups. There were not enough data to generate a ratio for *T. vaginalis*, so the same ratio as that used in 1995 and 1999 was used – that is, a male-to-female ratio of 0.1.

Table 9. Global male-to-female ratios used for generating estimates in 2005 and 1995/1999

Infection	2005		1995/1999
	Mean ratio	Standard deviation	Ratio
Chlamydia trachomatis	0.80	0.66	0.50
Neisseria gonorrhoeae	0.86	0.60	0.66
Syphilis	0.98	0.33	1.00

Estimating prevalence when there are three or fewer data points

There were considerably more data for females than males and for all of the infections there were at least three data points[g] for females in each region or subregion. This was not, however, the case for males. When there were fewer than three prevalence data points for males for a particular infection in a region or subregion, the global male-to-female sex ratio (Table 9) was used to generate the male estimate from the female estimate.

Adjusting for the contribution of high-risk populations

The 1995 and 1999 estimates were based on data from populations that were considered to be at low risk of infection, and no systematic adjustment was made for the contribution of populations considered to be at high risk.

In generating the 2005 estimates it was decided to introduce an adjustment factor to reflect the differences in rates of infection among populations of high and low risk. Thus the initial estimates based on low-risk populations were adjusted to reflect the differences in rates of infection among populations of high and low risk.

Given the lack of information both on the measured prevalence of the infections in various higher-risk populations and the size of those populations, a single adjustment factor was used for all four infections, and for both males and females, thus:

$$\text{Final regional prevalence} = \text{Regional estimate} \times \text{High-risk adjustor}$$

For the 2005 estimates, the high-risk adjustor was assumed to be 1.1. This 10% increase in prevalence was based on an approximation of the contribution of these key populations to the prevalence and incidence of STIs within the general population. It was reviewed and accepted during the Expert Consultation sponsored by WHO in November 2008.

2.3.2 Approach 2: Calculating prevalence from incidence

For the infections for which incidence was estimated directly, the prevalence (P) was generated from the estimated incidence (I) using the equation:

$$P = I \times D$$

where D is the average duration of infection. The duration estimate was based on the methods described in Annex 3.

g Relying on only one or two studies to generate estimates can produce unrealistic results.

3. Methods for 2005 incidence estimates

Two approaches were used to calculate incidence. The first approach, Approach A, was applied in regions with strong case-reporting surveillance systems. Unfortunately, case-reporting data were limited and it was only possible to use this approach to estimate the incidence of *C. trachomatis*, *N. gonorrhoeae* and syphilis in North America, and syphilis in the WHO European Region.

When good case-reporting data were not available, annual incidence was estimated from the regional and subregional prevalence estimates using Approach B. Table 10 lists which approach was used for which infection.

Table 10. Approach (A or B) used to estimate the incidence of infection

WHO region	Infection			
	Chlamydia trachomatis	Neisseria gonorrhoeae	Trichomonas vaginalis	Syphilis
African Region	B	B	B	B
Region of the Americas (excluding North America)	B	B	B	B
North America	A	A	B	A
South-East Asia Region	B	B	B	B
European Region	B	B	B	A
Eastern Mediterranean Region	B	B	B`	B
Western Pacific Region	B	B	B	B

3.1 Approach A: Estimating incidence from case reports

3.1.1 North America: estimating incidence of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and syphilis

C. trachomatis, *N. gonorrhoeae* and syphilis are notifiable diseases in North America. The level of reporting coverage of these infections, however, is variable. In 2004, Weinstock and colleagues from the Centers for Disease Control and Prevention (CDC, Atlanta, USA) published a paper on the prevalence and incidence of STIs among youths in the USA (Weinstock et al., 2004). The estimated levels of reporting and diagnosis by infection and sex among youths between the ages of 15 and 24 years were:

- 25% for chlamydial infections
- 50% for gonococcal infections
- 41% for early syphilis infections.[h]

These percentages were used to adjust the 2005 case reports for the USA (Centers for Disease Control and Prevention, 2005) and for Canada (Public Health Agency of Canada, 2006). The resulting estimates of prevalence and incidence for North America were then incorporated into the regional estimates for the WHO Region of the Americas. *T. vaginalis* is not a notifiable disease in North America. For this reason the incidence estimates for this infection in North America were based on the estimated prevalence of *T. vaginalis*.

3.1.2 WHO European Region: Estimating incidence of syphilis

Estimates of the incidence of syphilis in the WHO European Region were based on case reports in the database of the European Centralized Information System for Infectious Disease (CISID) (http://data.euro.who.int/cisid). This database contains information on the numbers of reported

[h] "Early syphilis" was defined as a primary, secondary or early latent infection acquired in the preceding year.

cases of syphilis for each year and country. Estimates for 2005 were based on the number of cases reported in 2005, where numbers were available. When no numbers were available, data from the most recent year (before 2005) were used. The case reports for each country were then adjusted to correct for both undiagnosed ("unidentified") and unreported cases (Table 11).

Table 11. Estimated percentage of syphilis cases diagnosed and reported in the WHO European Region

WHO European Region	Cases diagnosed (%)	Reporting coverage (%)	Cases diagnosed and reported (%)
Central	70.9	74.5	52.8
Eastern	70.9	75.5	53.5
Western	70.9	79.0	56.0

The reasons for undiagnosed and unreported cases of syphilis are different and should be considered differently:

- ***Undiagnosed cases:*** Not every person infected with the causative organism for syphilis (*Treponema pallidum*) will present for care. Some people do not develop symptoms, and others may not realize that their symptoms require medical treatment. It was assumed that 32% of new infections are undiagnosed during the primary or secondary stage[i] and that 10% of these cases are then identified during the latent period through screening and partner tracing.
- ***Reporting coverage:*** Not every case of infection presenting to the medical system will be reported. The European Surveillance of Sexually Transmitted Infections (ESSTI) conducted a survey in 2003 to assess surveillance systems in 24 countries (Lowndes and Fenton, 2004). They estimated the reporting coverage for all cases of syphilis (both early and late forms) for 19 countries. Regional estimates of the reporting coverage for Western, Central and Eastern Europe (Table 12) were generated using the midpoint coverage estimates for each country and weighted by the proportion of cases from that country in each of the three regions. This figure was then used for adjusting the WHO European Region case reports.

Table 12. Estimates of reporting coverage for syphilis in the WHO European Region (*unweighted figure is in parentheses*)

WHO European Region	Reporting coverage (%)
Central	74.5 *(72.7)*
Eastern	75.5 *(85.0)*
Western	79.0 *(74.1)*

3.2 Approach B: Estimating incidence from prevalence

The general approach used in 2005 to estimate incidence from prevalence was the same as that used in 1995 and 1999. This approach, while providing a useful approximation, does not account for changes in prevalence or population size over time, or for age-related variations in the incidence or duration of infections in the 15–49 year age group.

[i] The number of people with primary and secondary syphilis who are asymptomatic and do not seek medical care is poorly researched, although Singh *et al*. (1999) determined that up to 60% of people with primary or secondary syphilis are asymptomatic. Accordingly, it was estimated here that 60% of cases of primary syphilis and 40% of cases of secondary syphilis were asymptomatic, and that 85% of symptomatic primary or secondary cases were diagnosed and treated appropriately.

The annual incidence of infection was determined using the following equation in 1995 for all four infections, and in 1999 for three of the infections (not *T. vaginalis*).

$$I = [P/(1-P)] \times (1/D)$$

where I is annual incidence, P is prevalence and D is the average duration of infection. This provides an estimate of the incidence of infection among people who are *not* yet infected rather than the entire population.

In 1999, no prevalence estimates were made for *T. vaginalis*, and incident rates for males and females were based on the 1995 rates after adjustment for population growth.

In 2005, estimates for all four infections were derived using the following equation:

$$I = P/D$$

This provides an estimate of the annual incidence for the entire population. This equation was used to bring about more consistency with the WHO's incidence estimates for other infections and diseases.

The methods and values of parameters used to estimate the average duration for each of the four infections are detailed in Annex 3.

4. Results

4.1 Prevalence

Figure 1 shows the prevalence of each of the four infections in 2005 among adult females in different WHO regions.

Figure 1. Prevalence of STIs in adult females in 2005 in different WHO regions

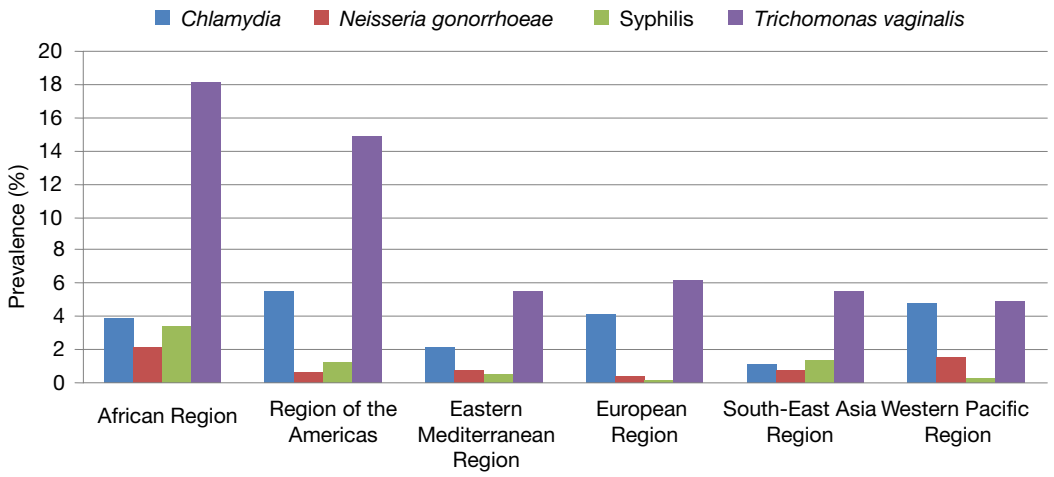
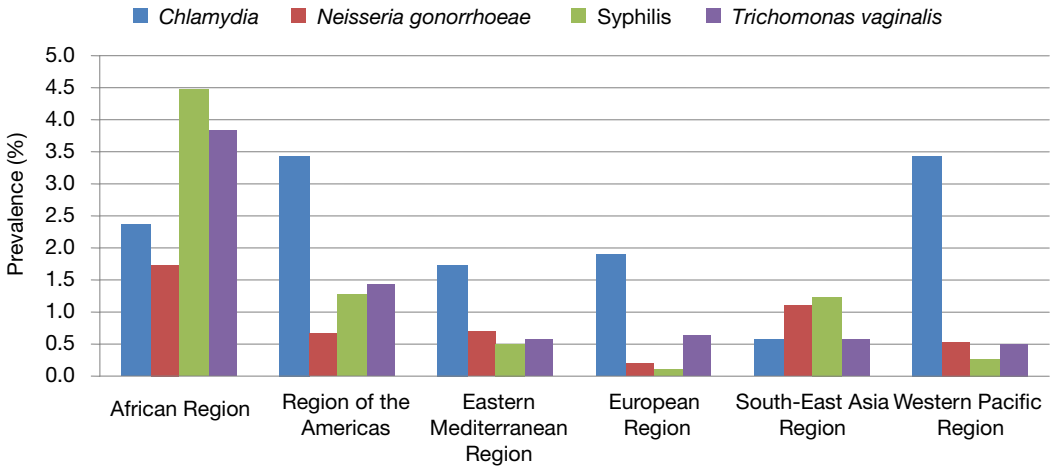


Figure 2 shows the prevalence of each of the four infections in 2005 among adult males in different WHO regions.

Figure 2. Prevalence of STIs in adult males in 2005 in different WHO regions



More detailed information for each of the infections can be found in Tables 13–16.

Table 13. Prevalence estimates for *Chlamydia trachomatis* for 2005

WHO region	Percentage (%)		Cases (millions)		
	Females	Males	Females	Males	Total
African Region	3.89	2.36	6.96	4.20	11.16
Region of the Americas	5.50	3.45	12.61	7.98	20.59
Eastern Mediterranean Region	2.15	1.72	2.89	2.46	5.35
European Region	4.16	1.89	9.41	4.32	13.73
South-East Asia Region	1.09	0.57	4.76	2.63	7.39
Western Pacific Region	4.81	3.43	22.65	17.04	39.69
Global total	3.53	2.22	59.28	38.63	97.91

Table 14. Prevalence estimates for *Neisseria gonorrhoeae* for 2005

WHO region	Percentage (%)		Cases (millions)		
	Females	Males	Females	Males	Total
African Region	2.10	1.72	3.76	3.06	6.82
Region of the Americas	0.57	0.68	1.30	1.56	2.86
Eastern Mediterranean Region	0.79	0.68	1.06	0.98	2.04
European Region	0.40	0.21	0.90	0.47	1.37
South-East Asia Region	0.75	1.10	3.28	5.09	8.37
Western Pacific Region	1.45	0.52	6.82	2.61	9.43
Global total	***1.02***	***0.79***	***17.12***	***13.77***	***30.89***

Table 15. Prevalence estimates for syphilis for 2005

WHO region	Percentage (%)		Cases (millions)		
	Females	Males	Females	Males	Total
African Region	3.45	4.47	6.16	7.95	14.11
Region of the Americas	1.22	1.27	2.80	2.95	5.75
Eastern Mediterranean Region	0.52	0.51	0.70	0.73	1.43
European Region	0.09	0.09	0.20	0.20	0.40
South-East Asia Region	1.37	1.25	5.99	5.78	11.77
Western Pacific Region	0.27	0.26	1.25	1.29	2.54
Global total	***1.02***	***1.09***	***17.1***	***18.9***	***36.00***

Table 16. Prevalence estimates for *Trichomonas vaginalis* for 2005

WHO region	Percentage (%)		Cases (millions)		
	Females	Males	Females	Males	Total
African Region	18.12	3.82	32.40	6.80	39.20
Region of the Americas	14.8	1.43	33.90	3.32	37.22
South-East Asia Region	5.58	0.56	24.33	2.58	26.91
Eastern Mediterranean Region	5.58	0.56	7.49	0.80	8.29
European Region	6.22	0.62	14.1	1.42	15.52
Western Pacific Region	4.95	0.49	23.3	2.46	25.76
Global total	***8.08***	***1.00***	***135.52***	***17.38***	***152.9***

These estimates indicate that at any point in 2005 there were approximately:

- 98 million adults infected with *C. trachomatis*
- 31 million adults infected with *N. gonorrhoeae*
- 36 million adults infected with syphilis
- 153 million adults infected with *T. vaginalis.*

The total prevalence estimate was therefore approximately 318 million.

Geographically, the vast majority of cases were in developing countries, reflecting distribution among the global population. For example, just over 40% of adults infected with *C. trachomatis* were in the WHO Western Pacific Region and 22% of adults with *N. gonorrhoeae* were in the WHO African Region.

The highest regional prevalence estimates (in percentage terms) for *N. gonorrhoeae*, syphilis and *T. vaginalis* for both females and males were in the WHO African Region.

The highest estimates for *C. trachomatis* for both females and males were from the WHO Region of the Americas, and the lowest prevalence estimates for both females and males were from the WHO South-East Asia Region.

The lowest prevalence estimates for *N. gonorrhoeae* and syphilis for both males and females were from the WHO European Region, and the WHO Western Pacific Region had the lowest estimates for both males and females for *T. vaginalis*.

The prevalence of infection was generally higher among females than males for *C. trachomatis*, *N. gonorrhoeae* and *T. vaginalis*. For syphilis the values for males and females were very similar.

4.2 Incidence

Figure 3 shows the annual incidence of the four infections per 1000 females in 2005 for each within each WHO region.

Figure 3. Incidence of STIs per 1000 adult females in 2005 in each region

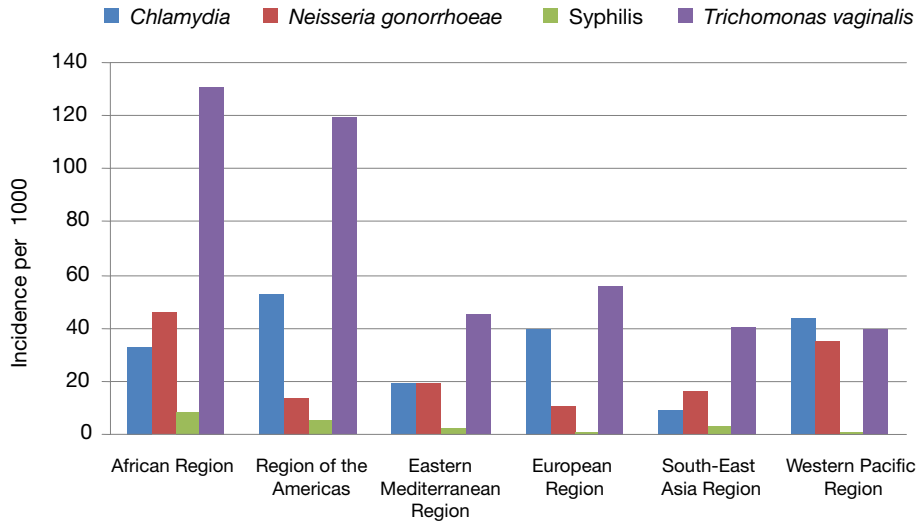
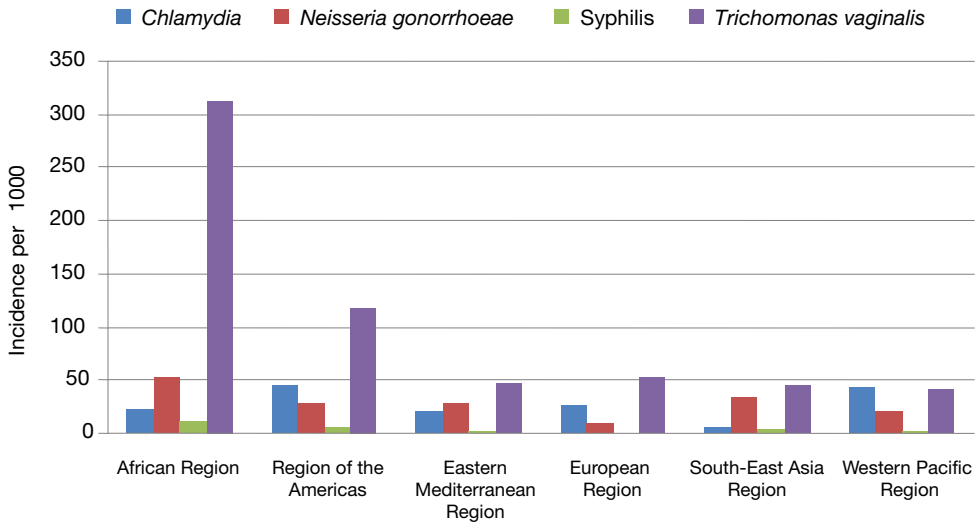


Figure 4 shows the annual incidence of the four infections per 1000 males in 2005 for each within each WHO region.

Figure 4. Incidence of STIs per 1000 adult males in 2005 in each region



It is estimated that in 2005 there were approximately:

- 101 million new cases of *C. trachomatis*
- 88 million new cases of *N. gonorrhoeae*
- 11 million new cases of syphilis
- 248 million new cases of *T. vaginalis*.

This gave a global total of 448 million new cases as shown in Table 17.

Table 17. Global incidence of STIs among men and women aged 15–49 years in 2005

WHO region	Incidence (millions of cases)				
	Chlamydia trachomatis	Neisseria gonorrhoeae	Syphilis	Trichomonas vaginalis	Total
African Region	10.0	17.5	3.4	78.8	109.70
Region of the Americas	22.4	9.5	2.4	54.9	89.20
South-East Asia Region	6.6	22.7	2.9	38.60	70.80
Eastern Mediterranean Region	5.7	6.5	0.6	12.60	25.40
European Region	15.2	4.6	0.3	24.50	44.60
Western Pacific Region	41.6	26.9	1.1	39.10	108.70
Global total	***101.5***	***87.7***	***10.6***	***248.5***	***448.30***

Tables 18–21 show the breakdown of the four infections by sex and WHO region.

Table 18. Incidence estimates for *Chlamydia trachomatis* in 2005

WHO region	Incidence per 1000		New cases (in millions)		
	Females	Males	Females	Males	Total
African Region	32.79	23.39	5.86	4.16	10.02
Region of the Americas	53.04	44.32	12.15	10.26	22.41
South-East Asia Region	9.20	5.63	4.01	2.60	6.61
Eastern Mediterranean Region	19.35	21.40	2.60	3.06	5.66
European Region	39.89	27.06	9.03	6.17	15.20
Western Pacific Region	43.31	42.70	20.38	21.22	41.60
Global total	***32.22***	***27.32***	***54.04***	***47.48***	***101.52***

Table 19. Incidence estimates for *Neisseria gonorrhoeae* in 2005

WHO region	Incidence per 1000		New cases (in millions)		
	Females	Males	Females	Males	Total
African Region	45.61	52.68	8.16	9.36	17.52
Region of the Americas	13.89	27.17	3.18	6.29	9.47
South-East Asia Region	16.32	33.61	7.11	15.55	22.66
Eastern Mediterranean Region	19.14	27.32	2.57	3.91	6.48
European Region	10.71	9.72	2.42	2.22	4.64
Western Pacific Region	35	20.94	16.47	10.41	26.88
Global total	***23.8***	***27.47***	***39.91***	***47.74***	***87.65***

Table 20. Incidence estimates for syphilis in 2005

WHO region	Incidence per 1000		New cases (in millions)		
	Females	Males	Females	Males	Total
African Region	8.34	10.82	1.49	1.92	3.41
Region of the Americas	5.06	5.33	1.16	1.23	2.39
South-East Asia Region	3.33	3.02	1.45	1.40	2.85
Eastern Mediterranean Region	2.14	2.09	0.29	0.30	0.59
European Region	0.68	0.68	0.15	0.15	0.30
Western Pacific Region	1.1	1.07	0.52	0.53	1.05
Global total	***3.02***	***3.19***	***5.06***	***5.54***	***10.60***

Table 21. Incidence estimates for *Trichomonas vaginalis* in 2005

WHO region	Incidence per 1000		New cases (in millions)		
	Females	Males	Females	Males	Total
African Region	130.74	311.83	23.38	55.43	78.81
Region of the Americas	119.55	118.83	27.40	27.51	54.91
South-East Asia Region	40.30	45.53	17.56	21.06	38.62
Eastern Mediterranean Region	44.76	46.23	6.01	6.62	12.63
European Region	55.60	52.01	12.59	11.87	24.46
Western Pacific Region	39.73	41.00	18.70	20.37	39.07
Global total	***62.98***	***82.21***	***105.63***	***142.85***	***248.48***

5. Discussion

This paper describes the methods and results used to generate global and regional estimates for the prevalence and incidence of *C. trachomatis*, *N. gonorrhoeae*, syphilis and *T. vaginalis* in 2005.

In 2005 it was estimated that there were 448 million new cases of these four infections in adults 15 to 49 years of age:

- 101 million new cases of *C. trachomatis*
- 88 million new cases of *N. gonorrhoeae*
- 11 million new cases of syphilis
- 248 million new cases of *T. vaginalis*.

At any point in 2005 it was also estimated that there were 318 million prevalent cases of the infections among adults, comprising:

- 98 million with *C. trachomatis*
- 31 million with *N. gonorrhoeae*
- 36 million with syphilis
- 153 million with *T. vaginalis*.

These are only four infections, however, among over 30 infections that can be transmitted sexually. Other important ones include HIV, HSV-2 and human papillomavirus (HPV). In 2002, there were an estimated 23.6 million new cases of HSV-2 infection (Looker et al., 2008) (see Annex 4). There are no comparable incidence figures for HPV, but Bosch et al. (2008) estimate a point prevalence of 10.4% for HPV among women and many studies in men report prevalences greater than 20% (Dunne et al, [2006]).

The methods used to generate the 2005 estimates are similar to those used in 1995 and 1999. However, a number of improvements were made as described below:

- Systematic adjustments were made to the prevalence of infection in each study to take into account the performance of the laboratory test used, the location (urban or rural) of the study, and for *C. trachomatis* the age of the study population.
- Regional low-risk population estimates were generated using the median of all the studies that met the entry criteria.
- Global sex ratios for each infection were generated from those studies that provided data for both males and females, and these were used to generate regional prevalence estimates when there were insufficient data.
- Regional low-risk population prevalence estimates were adjusted to take into account the contribution of populations who were at higher risk of infection.[j]
- The 2005 incidence estimates are estimates of the incidence in the *entire* population rather than in the *susceptible* population. This makes the 2005 estimates consistent with the methods used by WHO to estimate the incidence of other infections.
- Regional incidence estimates were generated from data obtained in regions with case-reporting systems of reasonable quality.
- The 2005 estimates for *T. vaginalis* were based on prevalence data unlike the earlier estimates. In 1995 there were insufficient data and the prevalence of *T. vaginalis* was estimated from the prevalence of *C. trachomatis* and in 1999 no prevalence estimates were made for *T. vaginalis*.

For the 2005 estimates a number of changes were also made to the values of a number of the parameters used to determine the duration of the infections. These changes were made following

[j] The approach used to account for the contribution of high-risk populations was based on a global assumption, which is clearly not ideal. However to be more specific, better information would be required on the size and prevalence of the different STIs in the various higher-risk populations.

an expert consultation about the increasing usage of newer, more sensitive and specific diagnostic tools, such as LCR and PCR, and about new natural history data.

In view of the changes made to the methods and duration parameters, and the use of more sensitive tests in deriving the 2005 prevalence and incidence estimates, these figures *are not* comparable with the earlier estimates of 1995 and 1999, and should not be used to suggest trends over time. In particular, the combined total global figure for the four infections in previous years cannot be compared with the 2005 figure, because of the different methods used for assessing *T. vaginalis*. This infection alone accounted for 70% of the increase in the number of new STIs between 1999 and 2005.[k]

There is a great deal of uncertainty around the global and regional STI estimates. If these uncertainties are to be reduced a concerted effort is needed to obtain relevant data, particularly:

- ***Prevalence studies.*** There is a shortage of good quality surveillance studies. Specifically, there is a need for data from low risk urban and rural populations, disaggregated by age and sex; and for strengthened routine STI surveillance for incidence monitoring. This is especially pronounced for males and for trichomoniasis.
- ***Estimates of the duration of infection.*** Regional incidence estimates were based on the regional prevalence figures and the average duration of infection in each region. This average duration depended upon the pathogen, the health care seeking behaviour of the population, and access to health care. Information on all three of these factors is very limited, leading to imprecise estimates of the duration of infection.

These data have an important role in improving our understanding of the burden of these infections. They are also crucial in helping improve the design and implementation of STI interventions and in lobbying for further resources and political support.

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[k] Demographic growth also played a role between 1999 and 2005 as the total number of adults aged 15–49 years increased by 12.3% from 3040 million to 3415 million (United Nations, 2005).

Annex 1: Sensitivity and specificity of laboratory tests

Estimates of the performance characteristics of each laboratory test were based on published systematic reviews, when reviews existed. When multiple reviews existed for a specific procedure/test, then the most recent review was used in the analysis, such as the paper by Paz-Bailey et al. (2005).

There was no attempt to define a gold standard for each test, or to define a gold standard for a test applied to a specific type of sample (analyte). The estimates of sensitivity and specificity given by the investigators in the systematic reviews were used.

Some of the laboratory tests, such as syphilis serology, were not covered by the systematic reviews, and therefore these estimates were based on individual studies together with the advice from participants at two separate meetings (one on determining and revising the parameters used in the estimation process held in July 2007, and a WHO-sponsored Expert Consultation held in November 2008). It was sometimes difficult to find pooled estimates of sensitivity or specificity in reviews, or even an individual value from a single study. Authors used creative ways of presenting data on individual tests and analytes, and they sometimes pooled data such as combining data from different sexes or analytes. As a result, interpolations had to be made. In such cases, footnotes have been provided to explain how judgements were made.

No attempt was made in this report to make sensitivity or specificity estimates for individual nucleic acid amplification tests (NAATs). Minor differences have been reported between the tests but there have been few direct comparisons and results obtained this way were difficult to summarize.

The resulting figures were shared with the Expert Group for their review and figures were adjusted based on their advice. Tables A1.1–A1.4 list the estimates for the sensitivity and specificity of all the tests for the four STIs, as used in our estimations.

Table A1.1. Sensitivity and specificity of the diagnostic tests for *Chlamydia trachomatis* (key sources in parentheses)

Sex	Analyte	Test	Sensitivity %	Specificity %
Female	Genital fluid	NAAT	88.6 (Watson et al. 2002)	99.6 (Cook et al. 2005)
		Culture	63.4 (Paz-Bailey et al. 2005)	100 (unreferenced)
		ELISA	65 (Watson et al. 2002)	100 (Orroth et al. 2003)
		NAT	79.3 (Wylie et al. 1998)	100 (Wylie et al. 1998)
	Urine	NAAT	87.0 (Paz-Bailey et al. 2005)	99.8 (Paz-Bailey et al. 2005)
Male	Genital fluid	NAAT	87.5 (Cook et al. 2005)	99.2 (Cook et al. 2005)
	Urine	NAAT	87.8 (Paz-Bailey et al. 2005)	99.3 (Cook et al. 2005)

ELISA, enzyme-linked immunosorbent assay; NAAT, nucleic acid amplification test; NAT, nucleic acid (probe) test.

Table A1.2. Sensitivity and specificity of the diagnostic tests for *Neisseria gonorrhoeae* (key sources in parentheses)

Sex	Analyte	Test	Sensitivity %	Specificity %
Female	Genital fluid	NAAT	93.3 (Wylie et al. 1998)[a]	99.2 (Wylie et al. 1998)[b]
		Culture	75.7 (Paz-Bailey et al. 2005)	100 (unreferenced)[c]
		NAT	92.1 (Koumans et al. 1998)	99.7 (Koumans et al. 1998)
	Urine	NAAT	91.6 (Paz-Bailey et al. 2005)	100 (Paz-Bailey et al. 2005)
Male	Genital fluid	NAAT	96.1 (Cook et al. 2005)	99 (Cook et al. 2005)
		Culture	87.6 (Paz-Bailey et al. 2005)	100 (unreferenced)
	Urine	NAAT	80.9 (Paz-Bailey et al. 2005)	99.9 (Paz-Bailey et al. 2005)

NAAT, nucleic acid amplification test; NAT, nucleic acid (probe) test.
[a] *Modification. This is the mean of the midpoint estimated range of sensitivity for each of three NAATs.*
[b] *Modification. This is the mean of the midpoint estimated range of sensitivity for each of three NAATs.*
[c] *In some cases, particularly with culture, it was not possible to find an authoritative reference that indicated the specificity of culture.*

Table A1.3. Sensitivity and specificity of the diagnostic tests for *Trichomonas vaginalis* (key sources in parentheses)

Sex	Analyte	Test	Sensitivity %	Specificity %
Female	Genital fluid	NAAT	95 (Patel et al. 2000)	98 (Patel et al. 2000)
		Culture	68.8 (Paz-Bailey et al. 2005)[d]	100 (Hobbs et al. 1999)
		MWM	52 (Wendel et al. 2002)	100 (unreferenced)
	Urine	NAAT	66.9 (Kaydos-Daniels et al. 2003)	98.3 (Kaydos-Daniels et al. 2003)
Male	Genital fluid	NAAT	81.6 (Hobbs et al. 1999)	97.7 (Hobbs et al. 1999)
		MWM	44 (Watson-Jones et al. 2000)[e]	100 (unreferenced)
		Culture	74.5 (Hobbs et al. 1999)	100 (unreferenced; see Hobbs et al. 1999)
	Urine	NAAT	96.0 (Schwebke et al. 2004)	97.7 (Hobbs et al. 1999)[f]

MWM, manual wet mount; NAAT, nucleic acid amplification test.
[d] *Modification. The mean of cited sensitivity for two culture media.*
[e] *Modification. Watson-Jones cited a sensitivity of 66% compared to culture. Culture is, however, an imperfect gold standard as it lacks sensitivity (estimated at 66.9% as cited in the A1.3 table. 66.9% multiplied by 66% gives 44%.*
[f] *Modification/ extrapolation. Copied from the specificity cited in Hobbs* et al. *(1999) for NAAT and applied to genital secretions.*

Table A1.4. Sensitivity and specificity of the diagnostic tests for syphilis (key sources in parentheses)

Sex	Analyte	Test	Sensitivity %	Specificity %
Female and male	Serum	SNTTP	83 (Peeling, modification)[g]	100 (unreferenced)

SNTTP, serology non-treponemal and Treponema pallidum (combined positive reaginic and treponemal test required to be considered positive).
[g] *Modification. This is the midpoint of the range of sensitivity of reaginic tests (78–86%). For a study to be entered into the database we required both a reaginic test and a treponemal test to be positive. As the likelihood of a false-positive pair of tests is quite small, e.g. 1 per 10000, we assumed the specificity of the pair of tests was 100%.*

Annex 2: Categorization of countries in the WHO African and Western Pacific Regions

Table A2.1. Allocation of countries into subregions of the WHO African Region

Subregion 1	Subregion 2
Algeria	Angola
Benin	Botswana
Burkina Faso	Burundi
Cameroon	Central African Republic
Cape Verde	Congo
Chad	Democratic Republic of the Congo
Comoros	Eritrea
Côte d'Ivoire	Guinea-Bissau
Equatorial Guinea	Lesotho
Ethiopia	Liberia
Gabon	Madagascar
Gambia	Malawi
Ghana	Mozambique
Guinea	Namibia
Kenya	Rwanda
Mali	Sierra Leone
Mauritania	South Africa
Mauritius	Swaziland
Niger	Zambia
Nigeria	Zimbabwe
Kenya	
Mali	
Mauritania	
Mauritius	
Niger	
Nigeria	

Table A2.2. Allocation of countries into subregions of the WHO Western Pacific Region

Subregion 1	Subregion 2
Australia	Cook Islands
Brunei Darussalam	Federated States of Micronesia
Cambodia	Fiji
China	Marshall Islands
Japan	Mongolia
Lao People's Democratic Republic	Mongolia
Malaysia	Nauru
New Zealand	Papua New Guinea
Niue	Samoa
Philippines	Solomon Islands
Republic of Korea	Tonga
Singapore	Tuvalu
Viet Nam	

Annex 3: Estimating duration of infection

A3.1 Methods

The duration of an infection, or the mean length of time that a person carries an infection within a population, depends on a number of factors. These include the average duration of infection in the absence of treatment for both people who are symptomatic[l] and asymptomatic, and treatment patterns for those who are symptomatic within a population. People who are asymptomatic may receive treatment because of screening programmes, or partner notification, or inadvertent correct therapy while being treated for another health problem. The methods used to estimate the mean duration of each infection were the same in 2005 as in 1995 and 1999 (Gerbase et al., 1998; Rowley and Berkley, 1998), although some changes were made to the numerical values assigned to certain parameters

C. trachomatis, *N. gonorrhoeae* and *T. vaginalis*

For these three STIs, the duration of infection (D) for a person of sex (k) in treatment area (r) was estimated using the following equation:

$$D(k,r) = S(k,r) \times [V^S(k,r) \times T^S(k,r) + (1 - V^S(k,r)) \times U^S(k,r)] + (1 - S(k,r)) \times [V^A(k,r) \times T^A(k,r) + (1 - V^A(k,r)) \times U^A(k,r)]$$

where:

$S(k,r)$ is the probability that an infected person is symptomatic (S).

$V^S(k,r)$ and $V^A(k,r)$ are the probabilities that infected people who are *symptomatic* (S) and *asymptomatic* (A) are treated, respectively.

$T^S(k,r)$ and $U^S(k,r)$ are the average durations of infections for symptomatic (S) people who are treated (T) and not treated (U), respectively.

$T^A(k,r)$ and $U^A(k,r)$ are the average durations of infections for asymptomatic (A) people who are treated and not treated, respectively.

Syphilis

A similar approach was followed for syphilis, after adjusting for the different stages of infection (primary, secondary, and latent).

Adjusting for Access to Treatment

Treatment patterns vary widely between countries and within countries, and this situation depends on access to health care as well as cultural and economic factors. To adjust for these factors, the same approach was applied in 2005 as for 1995 and 1999. The WHO regions were divided into one of three treatment categories, based on the probability of someone with an infection being treated. These three categories are shown in Table A3.1. Category A denotes the WHO regions in which the probability of being adequately treated is highest and as a consequence the duration of infection is the shortest. (Tables A3.4, A3.7 and A3.8)

Table A3.1 Categorization of regions according to probability of treatment

Category	WHO region
Area A	WHO European Region, North America (Canada and USA)
Area B	WHO Eastern Mediterranean Region, WHO Region of the Americas (excluding North America) WHO Western Pacific Region
Area C	WHO African Region, WHO South-East Asia Region

[l] For all infections, we have used the term symptomatic to refer to people who have symptoms and who recognize these symptoms; such recognition influences healthcare-seeking behaviour.

A3.2 Parameter values

In 1995, the values assigned to the parameters used to generate estimates of duration were based on a review of the available data and discussions with leading experts in the field. The same values were used to generate the 1999 estimates. However, it was decided to review the duration parameters for the 2005 estimates and new estimates were produced based on a review of the literature. These were discussed at the July 2007 parameter estimation meeting and the Expert Consultation in November 2008.

Parameters used for C. trachomatis, N. gonorrhoeae *and* T. vaginalis

The values assigned to the various parameters for *C. trachomatis*, *N. gonorrhoeae* and *T. vaginalis* are recorded in Tables A3.2–A3.4. The values assigned to the syphilis parameters are recorded in Tables A3.5–A3.7. Also shown (in parentheses) are the values used in 1995 and 1999 where they differed.

Table A3.2. Probability of males and females developing symptoms for three STIs (alternative values from 1995/1999 in parentheses)

Infection	Males	Females
Chlamydia trachomatis	0.54 *(0.80)*	0.17 *(0.25)*
Neisseria gonorrhoeae	0.64 *(0.95)*	0.34 *(0.50)*
Trichomonas vaginalis	0.067 *(0.10)*	0.34 *(0.50)*

Table A3.3 Average duration of infections with three STIs (alternative values from 1995/1999 in parentheses)

Infection	Asymptomatic and not treated		Symptomatic and treated	
	Male	Female	Male	Female
Chlamydia trachomatis	15 months	15 months	4 weeks	8 weeks *(4 weeks)*
Neisseria gonorrhoeae	5 months *(6 months)*	6 months	2 weeks *(3 weeks)*	4 weeks *(3 weeks)*
Trichomonas vaginalis	1.5 months	18 months	1 month *(2 weeks)*	3 months *(26 weeks)*

Table A3.4. Probability that an asymptomatic person is adequately treated for one of the three STIs within each WHO region (alternative values from 1995/1999 in parentheses)†

Regional category	Probability in males	Probability in females
Area A	0.80 *(0.9)*	0.75 *(0.85)*
Area B	0.65	0.50 *(0.55)*
Area C	0.35	0.225 *(0.25)*

†*The probability that an asymptomatic person is treated was assumed to be 10% of the probability that a symptomatic person is treated. This is the same method as used to generate the 1995/1999 estimates.*

Table A3.5. Probability that a person with syphilis develops symptoms, according to stage of infection (alternative values from 1995/1999 in parentheses)

Stage of infection	Probability
Primary	0.40 *(0.90)*
Secondary	0.60

Table A3.6 Average duration of infection a person with syphilis depending on stage at which they are treated (alternative values from 1995/1999 in parentheses)

Stage of infection	Probability
Primary	1 month
Secondary	3 months
Latent	3 years
Tertiary	15 years *(10 years)*

Table A3.7 Probability that a person is adequately treated for syphilis according to WHO region

WHO region	Symptomatic primary and secondary stages	Latent stages
Area A	0.85	0.95
Area B	0.60	0.85
Area C	0.35	0.75

Parameters used for syphilis

The probability of adequate treatment was assumed to be the same for men and women. It was also assumed that people with primary and secondary syphilis who did not develop symptoms were not treated. The figures in Table A3.7 are the same as from 1995 and 1999.

A3.3 Results

The average duration of all four infections in each of the three WHO regional categories is presented in Table A3.8, together with the estimates used in 1995 and 1999 (where they differed).

In most cases, the incidence estimates were based on regional prevalence estimates adjusted for duration.

Note that any increase in the average duration of infection results in a decrease in its incidence. In other words, an increase in the average duration of chlamydial infection in adult males from 0.63 to 0.80 reduces its incidence in adult males by 21.2%.

Table A3.8 Average duration of infection with four STIs by sex and treatment area (values for 1995/1999 in parenthesis)

Infection	WHO region	Duration of infection (years)	
		Males	Females
Chlamydia trachomatis	Area A	0.70 *(0.38)*	1.04 *(0.93)*
	Area B	0.80 *(0.63)*	1.11 *(1.04)*
	Area C	1.01 *(0.91)*	1.19 *(1.16)*
Neisseria gonorrhoeae	Area A	0.21 *(0.10)*	0.37 *(0.29)*
	Area B	0.25 *(0.23)*	0.41 *(0.37)*
	Area C	0.33 *(0.35)*	0.46 *(0.44)*
Trichomonas vaginalis	Area A	0.12 *(0.11)*	1.12 *(1.03)*
	Area B	0.12 *(0.11)*	1.25 *(1.20)*
	Area C	0.12 *(0.12)*	1.39 *(1.36)*
Syphilis	Area A	1.28 *(0.48)*	1.28 *(0.48)*
	Area B	2.42 *(1.28)*	2.42 *(1.28)*
	Area C	4.13 *(2.63)*	4.13 *(2.63)*

A3.4 Discussion

The 2005 estimates of duration are, in general, longer than those from 1995 and 1999. This change is most marked for *C. trachomatis* and *N. gonorrhoeae* in males, where the use of noninvasive screening tests has highlighted the proportion of males who are *asymptomatic* and thus remain infected and untreated.

There has also been a change in the definition of the word "symptomatic" in relation to primary syphilis, which has led to an increase in the number of people being classified as "asymptomatic". When the 1994 and 1999 estimates were made symptomatic was interpreted as "the presence of either signs or symptoms" but since 2005 – in line with other infections – it was interpreted as "symptoms recognized by the individual, that lead to health-care-seeking behaviour".

Annex 4: Estimating prevalence and incidence of HSV type 2

In 1995 and 1999, only the four curable STIs (*C. trachomatis*, *N. gonorrhoeae*, syphilis and *T. vaginalis*) were included in the global estimates. In 2002, it was suggested at a meeting in Italy hosted by the WHO (World Health Organization, 2002) that HSV-2 should also be included.

As a result, WHO staff worked with colleagues at Imperial College, London, to model the prevalence and incidence of HSV-2. The results were published in the *Bulletin of the World Health Organization* by Looker et al. (2008) and the abstract of that paper is reproduced in Box 3.

The original intention was that the HSV-2 estimates would cover the same period as the estimates for the other four infections. The two projects, however, started at different times and ended up generating estimates for different years; 2003 for HSV-2 and 2005 for the other four infections.

Box 3 Abstract from published paper on HSV-2 incidence and prevalence (Looker et al. 2008)

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 estimates by age and gender were generated in a random-effect model. HSV-2 incidence was then estimated from these pooled estimates 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 world-wide 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.

Conclusions: 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.

Annex 5: Bibliography

Bosch FX et al. Epidemiology and natural history of human papillomavirus infections and type-specific implications in cervical neoplasia. *Vaccine, 2008*, 26S:K1–16.

Centers for Disease Control and Prevention., 2005 *STD Surveillance Report* (http://www.cdc.gov/std/stats05/toc2005.htm, accessed 20 October 2010).

Cook RL et al. Systematic review: Noninvasive testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Annals of Internal Medicine, 2005*, 142:914–925.

Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV infection among men: A systematic review of the literature. *J Infect Dis* 2006;194:1044-57

Franceschi S. et al. Cervical infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in women from ten areas in four continents: a cross-sectional study. *Sexually Transmitted Diseases, 2007*, 34:563–569.

Gerbase AC et al.Global prevalence and incidence estimates of selected curable STDs. *Sexually Transmitted Infections* 1998, 74(Suppl. 1):S12–S16.

Grosskurth H et al. Operational performance of an STD control program in Mwanza Region, Tanzania. *Sexually Transmitted Infections*, 2000, 76:426–436.

Hobbs MM et al. *Trichomonas vaginalis* as a cause of urethritis in Malawian men. *Sexually Transmitted Diseases* 1999, 26:381–387.

Kaydos-Daniels SC et al. Validation of a urine-based PCR-enzyme-linked immunosorbent assay for use in clinical research settings to detect *Trichomonas vaginalis* in men. *Journal of Clinical Microbiology, 2003*, 41:318–323.

Korenromp EL et al. What proportion of episodes of gonorrhoea and *Chlamydia* become symptomatic? *International Journal of STDs and AIDS*, 2002, 13:91–101.

Koumans EH et al. Laboratory testing for *Neisseria gonorrhoeae* by recently introduced non-culture tests: a performance review with clinical and public health considerations. *Clinical Infectious Diseases,* 1998, 27:1171–1180.

Looker KJ et al. An estimate of the global prevalence and incidence of herpes simplex virus type 2 infections. *Bulletin of the WHO*, 2008, 86:805–812.

Lowndes CM, Fenton KA for the European Surveillance of STIs Network. Surveillance systems for STIs in the European Union: facing a changing epidemiology. *Sexually Transmitted Infections*, 2004, 80: 264–271.

Orroth KK et al. Comparison of STD prevalences in the Rakai, Masaka and Mwanza trial populations: The role of selection bias and diagnostic errors. *Sexually Transmitted Infections*, 2003, 79:98–105.

Patel SR et al. Systematic review of diagnostic tests for vaginal trichomoniasis. *Infectious Diseases in Ob/Gyn*, 2000, 8:248–257.

Paz-Bailey G et al. Changes in the etiology of sexually transmitted diseases in Botswana between 1993 and 2002: Implications for the clinical management of genital ulcer disease. *Clinical Infectious Diseases*, 2005, 41(9):1304–1312. Epub 2005 Oct 4.

Peeling RW, Htun Y. Diagnostic tests for preventing and managing maternal and congenital syphilis: an overview. *Bulletin of the WHO*, 2004, 82:439–446.

Public Health Agency of Canada. Brief Report on Sexually Transmitted Infections in Canada: 2006. ISBN: 978-1-100-12156-7 ((http://www.phac-aspc.gc.ca/publicat/2008/sti-its/index-eng.php).

Rowley JT, Berkley SFB. Sexually transmitted diseases. IIn: Health dimensions of sex and reproduction. Murray CJL, Lopez AD eds., Boston MA, Harvard School of Public Health, 1998.

Schwebke JR, Lawing LF. Improved detection by DNA amplification of *Trichomonas vaginalis* in males. *Journal of Clinical Microbiology*, 2002, 40:3681–3683.

Singh AE, Romanowski B. Syphilis: Review with emphasis on clinical, epidemiological, and some biologic features. *Clinical Microbiology Reviews* 1999, 12:187–209.

UNAIDS. *2008 Report on the Global AIDS Epidemic: UNAIDS 08/27*. Geneva, Joint United Nations Programme on HIV/AIDS, 2008.

United Nations. *World Urbanization Prospects: The 2005 Revision*. Department of Economic and Social Affairs, Population Division (http://www.un.org/esa/population/publications/WUP2005/2005wup.htm, accessed 20 October 2010).

Watson EJ et al. The accuracy and efficacy of screening tests for *Chlamydia trachomatis*: a systematic review. *Journal of Medical Microbiology*, 2002, 51:1021–1031.

Watson-Jones D et al. High prevalence of trichomoniasis in rural men in Mwanza, Tanzania: results from a population-based study. *Sexually Transmitted Infections*, 2000, 76:355–362.

Weinstock H, Berman S, Cates W. Sexually transmitted diseases among American youth: incidence and prevalence estimates for, 2000. *Perspectives in Sexual and Reproductive Health*, 2004, 36(1):6–10.

Wendel KA et al. *Trichomonas vaginalis* polymerase chain reaction compared with standard diagnostic and therapeutic protocols for detection and treatment of vaginal trichomoniasis. *Clinical Infectious Diseases, 200*2, 35:576–580.

World Health Organization. *Global prevalence and incidence of selected curable sexually transmitted infections. Overview and estimates*. Geneva, World Health Organization, 2001. WHO/CDS/CSR/EDC/2001.10.

World Health Organization. *Estimation of the incidence and prevalence of sexually transmitted infections: Report of a WHO consultation*. Treviso, Italy, 27 February–1 March 2002. Geneva, World Health Organization, 2002. WHO/COS/CSR/NCS/2002.6. WHO/HIV 2002.14.

Wylie JL et al. Comparative evaluation of *Chlamydia*zyme, PACE 2 and AMP-CT assays for detection of *Chlamydia trachomatis* in endocervical specimens. *Journal of Clinical Microbiology,* 1998, 36:3488–3491.

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