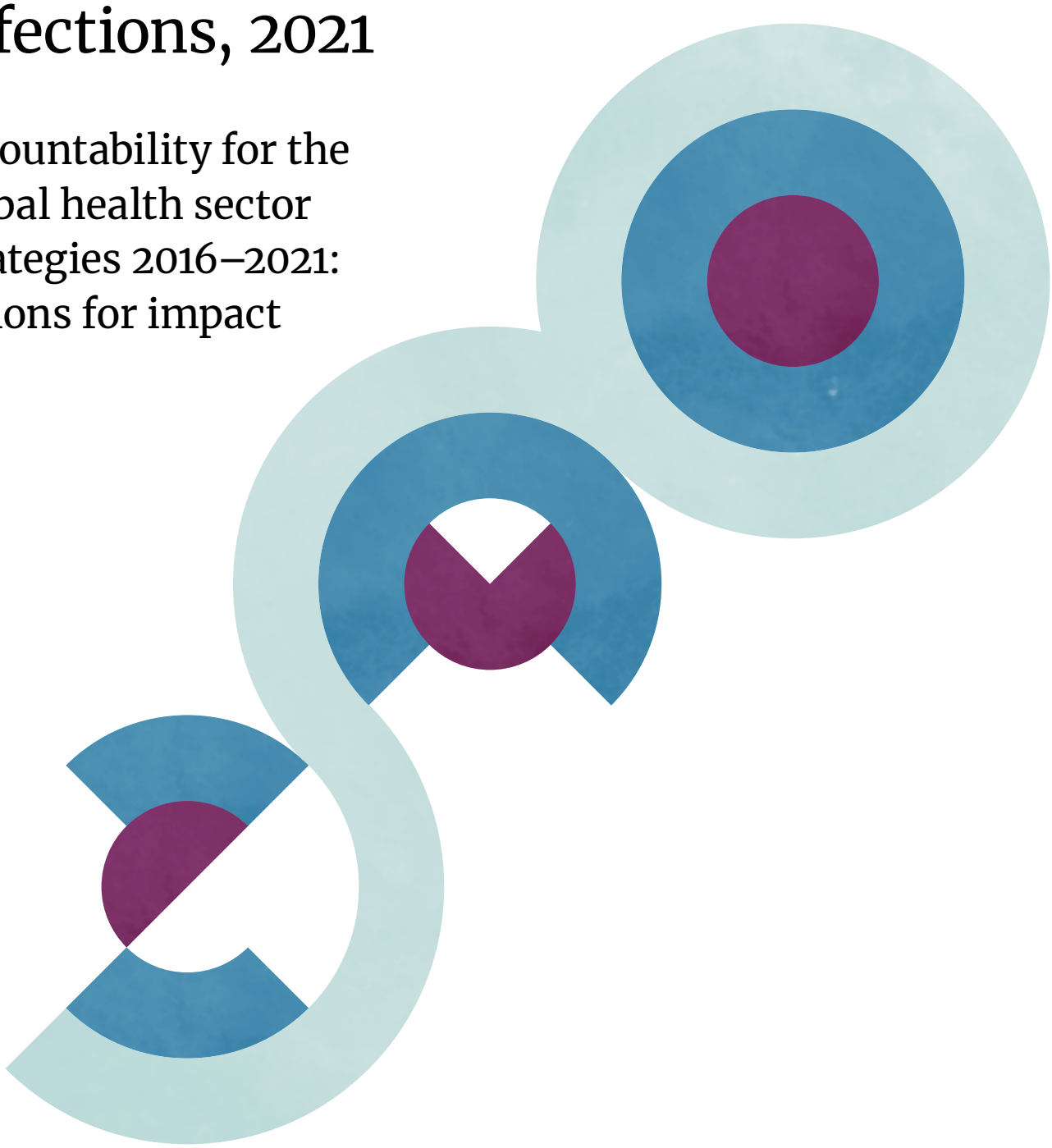
Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021

Accountability for the global health sector strategies 2016–2021: actions for impact



Web Annex 2: Data methods

World Health Organization

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A. HIV

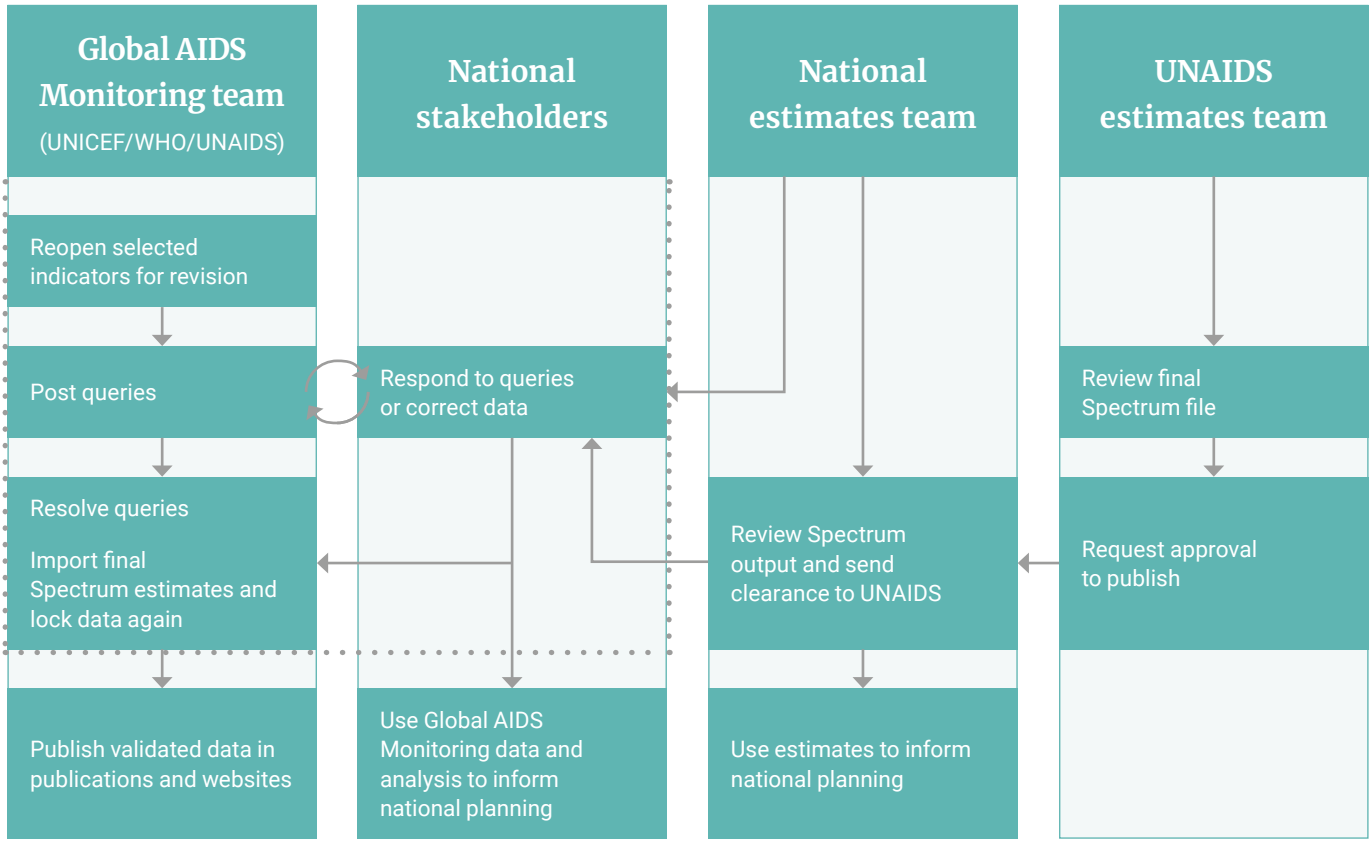
1. Global AIDS Monitoring

Data on HIV are collected from countries and validated by partners as part of Global AIDS Monitoring. Global AIDS Monitoring reporting has four parts:

- indicator data – including disaggregation;
- National Commitments and Policy Instrument (NCPI);
- narrative report (optional); and
- AIDS Medicines and Diagnostics Survey.

Compared with previous years, there was one new indicator. An indicator (10.3B, completion of TB preventive treatment) was introduced to report on the proportion of people receiving antiretroviral therapy who completed a course of TB preventive treatment.

The following diagram shows the process of validation of data submitted by countries, which involves UNAIDS, WHO, UNICEF and other partners working closely with national stakeholders.



The reported data should be validated and reconciled between all partners in the country. After countries submit Global AIDS Monitoring reports through the online reporting tool, UNAIDS, WHO, UNICEF and partners review the data submitted to do the following:

- support countries in reviewing any errors in entering data; and
- verify that the data submitted respond to the indicator definitions as outlined in the Global AIDS Monitoring guidelines.

At the same time, estimates developed with the Spectrum software are submitted and reviewed by the UNAIDS estimates team. Spectrum is a key tool for generating denominators used in Global AIDS Monitoring reporting, such as the number of people living with HIV in different groups. Countries have the option to import Spectrum data into the Global AIDS Monitoring online reporting tool for certain indicators.

Global AIDS Monitoring reporting involves multisectoral engagement. Countries are encouraged to engage a multisectoral group of stakeholders in the Global AIDS Monitoring reporting process, including community and civil society representatives.

Technical support is also available from UNAIDS, UNICEF and WHO country, regional and global offices. Reported data are available at www.aidsinfo.unaids.org.

2. Modelled estimates

Global, regional and country-specific modelled estimates are also provided annually by UNAIDS with technical partners, using the best available epidemiological and programmatic data to track the HIV epidemic.

Country teams use UNAIDS-supported software to develop estimates annually. The country teams primarily comprise monitoring and evaluation specialists, programme officers, epidemiologists, demographers and others from the national health ministry, national AIDS bodies and technical partners.

The software used to produce the estimates is Spectrum (developed by Avenir Health) with additional models that interact with Spectrum to estimate HIV incidence. The UNAIDS Reference Group on Estimates, Modelling and Projections provides technical guidance on developing the HIV component of the software, in which detailed description of the methods, adjustments over time and process can be found.

In 2021, 39 countries in sub-Saharan Africa created and used subnational estimates.

For countries where HIV transmission is high enough to sustain an epidemic in the general population, available epidemiological data typically consist of HIV prevalence results from pregnant women attending antenatal clinics and from nationally representative population-based surveys, together with surveillance data among key populations.

In the remaining countries, where HIV transmission occurs largely among key populations at higher risk of HIV and the epidemic can be described as low-level, the estimates are derived from either surveillance among key populations and the general, low-risk population or from HIV case reporting data, depending on which data are most reliable in a particular country.

In countries with high-quality HIV surveillance data among the key populations, the data from repeated HIV prevalence studies that focus on key populations are used to derive national estimates and trends. Estimates of the size of key populations are increasingly derived empirically in each country; when studies are not available, they are derived based on regional values and consensus among experts.

3. Uncertainty bounds for estimates

The estimation software calculates uncertainty bounds around each estimate. These bounds define the range within which the true value lies (if it can be measured). Narrow bounds indicate that an estimate is precise, while wide bounds indicate greater uncertainty regarding the estimate. In countries using HIV surveillance data, the quantity and source of the available data partly determine the precision of the estimates: countries with more HIV surveillance data have smaller ranges than countries with less surveillance data or smaller sample sizes. Countries in which a national population-based survey has been conducted generally have smaller ranges around estimates than countries where such surveys have not been conducted.

4. Reporting against targets (90–90–90 and 95–95–95)

The availability of data for reporting on the HIV cascade and 90–90–90 and 95–95–95 targets as reported by UNAIDS/WHO in 2021 (for 2020 data used in this report) is shown below.

	Year	Asia and the Pacific	Caribbean	Eastern and southern Africa	Eastern Europe and central Asia	Latin America	Middle East and North Africa	Western and central Africa	Western and central Europe and North America	Global
Countries	2020	38	16	21	16	17	20	25	39	193
Countries in UNAIDS/ WHO global estimates	2020	28	10	20	16	17	20	25	36	172
Countries with publicly available data on estimates of people living with HIV	2020	21	9	20	12	17	16	25	15	133
Countries with publicly available data on knowledge of HIV status	2020	18	8	20	12	13	14	25	6	116
Countries with publicly available data on treatment	2020	26	10	20	15	17	20	25	16	150
Countries with publicly available data on people with suppressed viral load	2020	11	8	15	11	10	5	7	6	73

5. Key population and subpopulation data

The distribution of new HIV infections among subpopulations globally and by region was estimated based on data for 170 countries using four data sources. The underlying number of new infections for each country is estimated with Spectrum. New infections among men and women 15–49 years old are used.

For countries that model their HIV epidemic based on data from subpopulations, including key populations, the numbers of new infections were extracted from Spectrum 2021 files.

New HIV infections among countries without a direct data source were calculated from regional benchmarks. The benchmarks were set by the median proportion of new infections in the specific subpopulation in all available countries in the same region.

New infections among the sex partners of key populations were estimated using the number of sex partners and transmission probabilities from the literature.

UNAIDS, WHO, UNICEF and partners have developed more detailed guidance on the HIV Global Aids Monitoring, estimation and methods, such as measuring key population data and calculating progress against the 90–90–90 and 95–95–95 targets. This is available at https://www.unaids.org/en/global-aids-monitoring.

B. Viral hepatitis B and C

This section summarizes the methods and initial results of the global estimates and reporting of viral hepatitis B and C globally and by WHO region for 2020. These estimates have been generated for the 2021 report on HIV, viral hepatitis and sexually transmitted infections (STIs) to the World Health Assembly. WHO acknowledges the close collaboration with the countries providing the data, the WHO regional offices that validated all the data and partners, especially the CDA Foundation, which supported each stage of methods, country support and validation together with Imperial College, University of Bristol, the WHO Immunization, Vaccines and Biologicals Department, Institute for Health Metrics and Evaluation and the International Agency for Research on Cancer.

In 2021, WHO is reporting back to the World Health Assembly on the progress of the global health sector strategy on viral hepatitis at the global, regional and country levels.

1. Background to data collection

In May 2016, the World Health Assembly endorsed the global health sector strategy on viral hepatitis, which aims to eliminate viral hepatitis as a public health threat by 2030 (defined as 90% reduction in incidence and 65% reduction in mortality). To eliminate viral hepatitis as a public health threat, the global health sector strategy on viral hepatitis focuses on priority indicators, including disease burden, prevention coverage, harm reduction, blood safety, testing and treatment for hepatitis.

To monitor and evaluation the progress of hepatitis elimination, WHO needs to collect data to assess the hepatitis B virus and hepatitis C virus disease burden and service delivery in its 194 Member States and monitor the global, regional and country progress. Based on WHO's work plan, the CDA Foundation, Imperial College London and Bristol University have been working together with the WHO regional offices and country offices to collect and validate data and develop the global hepatitis estimates.

2. Methods and indicators

WHO developed a work plan and timetable to collect and validate the data. The work plan and timetable were discussed in the regular strategic information monthly meeting and reached a consensus. WHO also invited the CDA Foundation, Imperial College London and Bristol University to contribute to the data collection and participate in the validation process in collaboration with the six WHO regional offices and country offices when needed.

WHO used several steps to collect and validate the data. First, WHO developed a template tool called the global hepatitis reporting form for countries to report their data. The form included key indicators, defined and described each indicator, specified the years when the data were needed and suggested sources. In this form, the country and regional office were also requested to provide any comments or explanations they have on the data issues.

Second, WHO headquarters communicated with regional offices and asked for input from focal points and strategic information officers on hepatitis in each region on the accuracy of the indicator definitions, period of data collection and procedures for reporting. Eventually, 10 indicators were given priority to be reported for monitoring the progress towards elimination in 2020.

Third, WHO worked with partners to prefill the data from available sources so countries had the full information available. When multiple data resources were available, all were listed for countries to review.

Fourth, WHO headquarters shared the preliminary results with the regional offices and initiated the validation process, which the regional office was requested to coordinate in each region. Focus were given to the priority countries in the region, and meetings with these countries were scheduled when needed.

Fifth, WHO regional offices provided the collected data to WHO country offices to validate with each country. Countries were given the option to provide their own data or accept partner data for one or more of the 10 indicators. The country inputs were provided to the regional office and aggregated globally.

Sixth, WHO provided support to regions where help was needed most, mainly focused on priority countries and the African Region.

Finally, WHO and the CDA Foundation reviewed all the validated data and comments, compared the data with partner data (such as from the Institute for Health Metrics and Evaluation, Imperial College, University of Bristol and the International Agency for Research on Cancer) and WHO resources (such as the WHO Immunization, Vaccines and Biologicals Department, 2015 baseline data and the latest data released by WHO), communicated with the regions again to accommodate the comments and integrated the adjusted data.

3. Enhancements to 2019 global reporting

The global reporting mechanisms for the 2019 report were used with several enhancements.

- Partner data were provided to countries as background for their validation, and they could use them as a reference or to fill in gaps. WHO wants to particularly thank the CDA Foundation for its close collaboration in supporting the process.
- WHO regional and country offices provided support for all countries but especially priority countries since the national staffing of viral hepatitis programmes was limited because of COVID-19 constraints.
- A stepwise process was used to support country reporting and data validation.
- The reporting completeness increased fivefold to 130 countries reporting validated data. In addition, partner data were available to fill in the remaining gaps to improve the accuracy of the global and regional estimates.
- An extensive partner support and alignment process was used, specifically with the CDA Foundation, Imperial College, University of Bristol, WHO Immunization, Vaccines and Biologicals Department and Institute for Health Metrics and Evaluation.
- In addition, dedicated country consultations within regions were included: for example, the WHO Regional Office for South-East Asia conducted their own country consultation process.
- WHO regional offices validated and reviewed all data to ensure consistency and include the latest data available.
- Data entry options were provided, included a one-page form, web-based forms and the global reporting system.
- Uncertainty intervals were calculated for all the key estimates.

4. Stepwise global data reporting and inclusion

The following stepwise process was used for reporting.

- **Country data.** Country-validated data was given priority for developing the cascade of care and disease burden estimates.
- **Country data already validated with WHO regional offices.** Next, if the regional office completed an exercise with countries to validate hepatitis data before this process, these data were selected.
- **Partner data.** Countries were also given the option to use any of the available partner data if there were major gaps in national data.
- **Regional averages.** If none of the above was available, a regional average was applied to the country, with priority given to the regional average provided by the WHO regional office.
- **Gaps in reporting.** WHO requested that countries fill the data based on the sources available and asked countries to provide the data or clarification when the data were not available. If there were gaps, countries were asked to comment on the reasons.

5. Indicators and improvements in reporting completeness

To improve reporting completeness and report back on the progress of the global health sector strategy on viral hepatitis, the date for reporting was simplified to focus on the cascade of diagnosis and care and cure and the burden of infection, incidence, prevalence and mortality, specifically:

- Cascade of diagnosis and care and cure (testing and diagnosis) (C6):
  - Number of people diagnosed with hepatitis B virus infection at the end of 2019
  - Number of people diagnosed with hepatitis C virus infection at the end of 2019
- Cascade of diagnosis and care and cure (treatment) (C7):
  - Number of people receiving hepatitis B virus treatment at the end of 2019
  - Number of people completing hepatitis C virus treatment at the end of 2019
- Burden of disease (prevalence data for 1 January 2019 or earliest in 2019) (C1)
  - Prevalence of hepatitis B infection (hepatitis B surface antigen positive) (%), defined by (number of chronic hepatitis B virus infections/total population) × 100%
  - Prevalence of hepatitis B infection among children younger than five years (%), defined by (number of chronic hepatitis B virus infections among children younger than five years/total number of children younger than five years) × 100%
  - Prevalence of hepatitis C infection not achieving sustained viral response (hepatitis C virus RNA/hepatitis C virus core antigen positive) (%), defined by (number of chronic hepatitis C virus infections/total population) × 100%
- Burden of disease (incidence, data for 1 January–31 December 2019) (C9)
  - Hepatitis B incidence (per 100 000 population), defined by (number of new chronic hepatitis B virus infections (vertical and horizontal)/total population by year) × 100 000
  - Hepatitis C incidence (per 100 000 population), defined by (number of new hepatitis C virus infections/total population by year) × 100 000
  - New hepatitis C virus infections among people who inject drugs (per 100 000 population), defined by (number of new hepatitis C virus infections among people who inject drugs/total number of people who inject drugs) × 100 000

- Burden of disease (mortality, data for 1 January 2019 to 31 December 2019) (C10)
    - Liver-related mortality of hepatitis B (per 100 000 population), defined by (number of deaths caused by hepatitis B virus infection/total population) × 100 000
    - Mortality of hepatitis C (per 100 000 population), defined by (number of deaths caused by hepatitis C virus infection/total population) × 100 000

At the time this project was undertaken, 2020 country data were not available yet. Best efforts were made to collect and report hepatitis C and hepatitis B prevalence in all ages, which resulted in a higher total infection but lower prevalence rate than the numbers reported among adults (children have a lower prevalence of hepatitis C and hepatitis B).

The global reporting results were included in the following manner.

- For the 130 countries that provided validated data, these were included directly in the global and regional totals.
- For 70 countries for which reporting was not present, partner data were included from the CDA Foundation, Imperial College, University of Bristol, Institute for Health Metrics and Evaluation and WHO Immunization, Vaccines and Biologicals Department to provide more than 200 country data points. Note that the results refer to six countries in addition to the 194 WHO Member States.
- For the above 70 countries, data from WHO regional offices, validated before this project, took priority when estimating regional and global figures.
- For hepatitis B virus prevalence among children younger than five years, global and regional data from the WHO Immunization, Vaccines and Biologicals Department were used since this has been reported towards Sustainable Development Goal progress. Where there were country differences, these were reviewed and will be used to inform and improve future estimates.
- For hepatitis B and C mortality, the Institute for Health Metrics and Evaluation figures and other partner data were similar globally, but differences were apparent between hepatitis B and C as in the previous 2017 WHO report. These will be used as the basis of a subsequent partner meeting to improve estimates.
- Private sector data: drug procurement information was compared with reported treatment data for large countries, such as China and India, to validate whether private sector data was included.
- Uncertainty intervals were calculated and provided for the point estimates, considering three methods, with the widest range chosen for each region and indicator. First, 95% uncertainty intervals were calculated for all the service and disease burden estimates. For most indicators, traditional 95% uncertainty intervals (considering the number of observations, mean and standard deviation with a *z* value of 1.96) produced ranges that were narrower than would be expected given the level of uncertainty in provided data. The second method used the minimum and maximum of all country-level estimates (including all partner data when multiple partners provided data for a common indicator; country-provided data; region-provided data). Under this method, the minimum datapoint for each country was aggregated to the regional level, with the process repeated for the maximum data point. This method recognized that the true uncertainty may be higher (thus the 95% uncertainty interval). The third calculation considered the variance in previous regional estimates for data that had been reported for an earlier time point or a variance of up to ±20% for indicators for which ranges had not previously been reported. The low bound from these three estimates and the high bound from these three estimates (for each indicator and each region) were captured at the regional level to ensure that the captured uncertainty was sufficient.

This resulted in the following global and regional reporting (including subregions in the WHO African Region) on testing and diagnosis (Table A1.1) and on treatment and cure (Table A1.2).

Table A1.1 Number of people with hepatitis B and C infection diagnosed by WHO region, 2019

	Testing and diagnosis	
WHO region	**Number of people with hepatitis B virus infection diagnosed to end 2019**	**Number of people with hepatitis C virus infection diagnosed to end 2019**
African Region	1 800 000 [1 400 000–2 500 000]	500 000 [400 000–630 000]
WHO subregion – eastern and southern Africa	1 300 000 [1 100 000–2 000 000]	190 000 [150 000–250 000]
WHO subregion – western and central Africa	440 000 [350 000–550 000]	310 000 [250 000–420 000]
Region of the Americas	990 000 [790 000–1 200 000]	1 500 000 [1 200 000–1 900 000]
South-East Asia Region	1 200 000 [430 000–1 900 000]	730 000 [260 000–910 000]
European Region	2 500 000 [2 000 000–3 200 000]	3 300 000 [2 700 000–4 200 000]
Eastern Mediterranean Region	2 500 000 [900 000–3 100 000]	5 600 000 [4 500 000–7 000 000]
Western Pacific Region	21 400 000 [17 100 000–26 700 000]	3 500 000 [2 800 000–4 400 000]
Global	30 400 000 [24 300 000–38 000 000]	15 200 000 [12 200 000–1 9000 000]

Table A1.2. Global and WHO regional reporting on treatment and cure

	Testing and diagnosis		
WHO region	**Number of people receiving hepatitis B virus treatment to end 2019**	**Cumulative number of people initiating hepatitis C virus treatment, 2015–2019**	**Number of people initiating hepatitis C virus treatment to end 2019**
African Region	110 000 [51 000–130 000]	51 000 [17 000–64 000]	23 000 [7 700–29 000]
WHO subregion – eastern and southern Africa	35 000 [20 000–43 000]	Not calculated	18 000 [2 800–22 000]
WHO subregion – western and central Africa	70 000 [32 000–88 000]	Not calculated	5 500 [4 400–6 900]
Region of the Americas	150 000 [120 000–190 000]	1 300 000 [1 000 000–1 600 000]	220 000 [170 000–270 000]
South-East Asia Region	140 000 [110 000–170 000]	500 000 [130 000–630 000]	100 000 [25 000–120 000]
European Region	210 000 [170 000–260 000]	1 200 000 [740 000–1 500 000]	250 000 [160 000–320 000]
Eastern Mediterranean Region	440 000 [130 000–550 000]	4 900 000 [3 900 000–6 200 000]	2 100 000 [1 700 000–2 600 000]
Western Pacific Region	5 600 000 [4 500 000–7 000 000]	1 500 000 [1 200 000–1 800 000]	300 000 [240 000–370 000]
Global	6 600 000 [5 300 000–8 300 000]	9 400 000 [7 500 000–11 700 000]	3 000 000 [2 400 000–3 700 000]

6. Disease burden results and supporting modelling

The following global and regional results for the disease burden were included. For the prevalence of hepatitis B infection among children younger than five years, data were aligned with those of the WHO Immunization, Vaccines and Biologicals Department, which reports on the progress of the Sustainable Development Goals, and country differences were tabulated to improve future reporting. Where there were gaps in country and regional reporting, partner modelling based on country data and country consultations was included. The methods were presented to the countries and are described below.

Table A1.3 shows the prevalence of hepatitis B and C infection globally and by region.

Table A1.3. Prevalence of hepatitis B and C globally and by WHO region, 2019

	Prevalence of hepatitis B surface antigen		Prevalence of hepatitis C virus
WHO region	**Prevalence of hepatitis B infection among the general population**	**Prevalence of hepatitis B infection among children younger than five years**	**Prevalence of hepatitis C infection among the general population at the start of 2019**
African Region	7.5% [5.7–10.5%]	2.5% [1.7–4.0%]	0.8% [0.6–1.4%]
WHO subregion – eastern and southern Africa	6.5% [4.9–9.1%]	1.8% [1.1–2.8%]	1.2% [0.5–1.8%]
WHO subregion – western and central Africa	8.3% [6.3–11.6%]	3.1% [2.1–4.9%]	0.6% [0.4–1.1%]
Region of the Americas	0.5% [0.3–1.2%]	0.1% [<0.1–0.2%]	0.5% [0.4–0.5%]
South-East Asia Region	3.0% [2.3–6.0%]	0.4% [0.3–1.0%]	0.5% [0.4–0.9%]
European Region	1.5% [1.1–2.4%]	0.3% [0.1–0.5%]	1.3% [1.1–1.5%]
Eastern Mediterranean Region	2.5% [2.0–3.3%]	0.8% [0.5–1.1%]	1.6% [1.4–1.8%]
Western Pacific Region	5.9% [4.9–7.3%]	0.3% [0.2–0.5%]	0.5% [0.4–0.7%]
Global	3.8% [3.0–5.5%]	0.9% [0.7–1.6%]	0.8% [0.6%–1.0%]

Table A1.4. Hepatitis B and C incidence globally and by WHO region, 2019

WHO region	Hepatitis B incidence	Hepatitis C incidence
African Region	990 000 [660 000–1 600 000]	210 000 [150 000–370 000]
WHO subregion – eastern and southern Africa	170 000 [110 000–260 000]	54 000 [39 000–95 000]
WHO subregion – western and central Africa	820 000 [550 000–1 300 000]	160 000 [110 000–280 000]
Region of the Americas	10 000 [5100–26 000]	67 000 [63 000–73 000]
South-East Asia Region	260 000 [180 000–590 000]	230 000 [200 000–430 000]
European Region	19 000 [9400–38 000]	300 000 [240 000–320 000]
Eastern Mediterranean Region	100 000 [79 000–140 000]	470 000 [240 000–520 000]
Western Pacific Region	140 000 [96 000–210 000]	230 000 [220 000–260 000]
Global	1 500 000 [1 100 000–2 600 000]	1 500 000 [1 300 000–1 800 000]

Table A1.5 provides mortality globally and by region. Partner alignment meetings occurred with the CDA Foundation, International Agency for Research on Cancer and Institute for Health Metrics and Evaluation. Differences between hepatitis B and C were noted, despite similar global figures. These differences will be further compared in a partner collaboration meeting in June 2021 to further align future country data and assumptions.

Table A1.5. Global hepatitis B and C mortality by WHO region, 2019

WHO region	Number of deaths caused by hepatitis B virus infection	Number of deaths caused by hepatitis C virus infection
African Region	80 000 [47 000–110 000]	45 000 [23 000–72 000]
WHO subregion – eastern and southern Africa	36 000 [17 000–41 000]	10 000 [10 000–30 000]
WHO subregion – western and central Africa	45 000 [30 000–72 000]	35 000 [13 000–41 000]
Region of the Americas	15 000 [8500–23 000]	31 000 [19 000–84 000]
South-East Asia Region	180 000 [140 000–300 000]	38 000 [37 000–130 000]
European Region	43 000 [34 000–51 000]	64 000 [39 000–72 000]
Eastern Mediterranean Region	33 000 [26 000–60 000]	31 000 [31 000–74 000]
Western Pacific Region	470 000 [200 000–490 000]	77 000 [77 000–140 000]
Global	820 000 [450 000–950 000]	290 000 [230 000–580 000]

Where partner data was used for country estimates, WHO worked closely with the CDA Foundation to apply the latest methods based on country data points and, where feasible, country consultation.

Estimating hepatitis C virus disease burden – CDA Foundation modelling method

The Bright Model is a Microsoft Excel–based (version 365) Markov model for hepatitis C virus disease progression. Models were parameterized for 110 countries using national demographic data (population, all-cause mortality, births and sex ratio at birth), hepatitis C virus epidemiological data (anti–hepatitis C virus prevalence, viraemic rate and age and sex distribution) and annual hepatitis C virus intervention coverage data (screening, diagnosis, antiviral treatment and sustained viral response) *(1)*. Relevant inputs were identified through the literature (including peer-reviewed studies, grey literature and government reports) and were scored for quality and generalizability. A Delphi process was used to gain country expert consensus and validate inputs for a subset of countries in which country experts were available and able to collaborate. Experts were identified through hepatitis C virus–related scientific contributions, WHO focal points, health ministries or referrals and recommendations from leading researchers. Two or more meetings were held to get consensus around input variables and outputs and validate the outputs against available empirical data.

A literature review was conducted to estimate the national prevalence of hepatitis C virus (anti–hepatitis C virus and hepatitis C virus RNA) and a single point estimate[1] was chosen through a combination of data quality scoring (all countries) and expert validation (where available). When anti–hepatitis C virus was reported, the proportion of cases that are hepatitis C virus-RNA positive was identified from the literature or local sources to convert anti–hepatitis C virus prevalence to hepatitis C virus RNA prevalence. The original published data was entered in the model, in the year of report, and then aged and progressed through annually, following the natural history of disease. Each year, incident cases were added to the prevalent population, while cured cases and deaths (background and liver-related) were removed from the prevalent population. For countries without a prevalence estimate, a regional average was used.

To estimate the population diagnosed with hepatitis C virus (hepatitis C virus RNA positive), the following were reviewed (in order of priority): national notification or registry data, peer-reviewed literature and expert opinion. When annual registry data were available, they were adjusted for mortality, treatment and sustained viral response. The number of individuals treated annually was estimated with (in order of priority) national databases, audit sales data, government reports, estimates from major treatment centres and drug suppliers. When diagnosis or treatment data were not available, the regional averages were used to extrapolate.

The impact of hepatitis C virus treatment as prevention was calculated in the model for horizontally and vertically acquired incident infections in future years. Horizontally acquired infections were calculated as a function of prevalence in future years, considering fibrosis restrictions for treatment. In countries without treatment or reimbursement restrictions by fibrosis stage (F0 on the METAVIR scale), future horizontal incident cases were assumed to change at the same rate as the prevalence. However, in countries with restrictions (F1 or greater on the METAVIR scale), future horizontal incident cases were assumed to change at the same rate as the modelled F0 prevalence. Vertically acquired infections were calculated considering the fertility rates among women of childbearing age *(2)*, the mother-to-child transmission rate of hepatitis C virus *(3)* and the modelled age-specific chronic prevalence of hepatitis C virus. The subsequent disease progression of infants with hepatitis C virus infection was also tracked in the model.

The number of deaths caused by hepatitis C virus infection (liver-related deaths among hepatitis C virus-RNA-positive people) was calculated in the model annually by age and disease stage. The annual age-specific background mortality was calculated in the model to inform the change in prevalent infections but is not reported in this exercise.

Estimating the hepatitis B virus disease burden – CDA Foundation modelling method

PRoGReSs is a compartmental, deterministic, dynamic Markov disease progression model for hepatitis B virus infection. It models the population with hepatitis B virus infection in a country or region from infection (vertically or horizontally acquired) to progression of liver disease to eventual death. The population susceptible to hepatitis B virus infection excludes anyone with a history of at least three doses of hepatitis B virus vaccine or a history of previous exposure to hepatitis B virus.

The country-specific inputs of the model are divided into two major groups: demographic and epidemiological. The demographic inputs include population, background mortality, births, and male-to-female sex ratios at birth. Epidemiological inputs include the prevalence of hepatitis B e-antigen among hepatitis B surface antigen–positive women of childbearing age, and intervention coverage (diagnosis and antiviral treatment of people with hepatitis B virus infection in the general population, peripartum antiviral treatment of mothers and vaccination of infants (timely birth dose and ≥3 doses), catch-up vaccination and liver transplantation). The age and sex distribution of the prevalence of hepatitis B surface antigen in a given year is used to calibrate the model.

A literature review was conducted to estimate the country-level prevalence of hepatitis B surface antigen. The titles and abstracts were reviewed for relevance, and only studies that

[1] If similarly conducted, nationally representative studies were available at multiple points in time, all studies were included in the analysis (such as Egypt and Pakistan).

included hepatitis B surface antigen prevalence were included. The analysis also included grey literature, health ministry reports, conference presentations, local journals and personal communications with local experts. Studies conducted solely in non-representative populations were excluded, such as blood donors, people who inject drugs, people with haemophilia and specific ethnic groups.

To estimate the population diagnosed with hepatitis B surface antigen, the following were reviewed (in order of priority): national notification or registry data, peer-reviewed literature and expert opinion. The number of individuals treated annually was estimated using (in order of priority) national databases, audit sales data, government reports, estimates from major treatment centres and drug suppliers.

Country-level estimates from WHO and UNICEF were used as a baseline for estimating the proportion of infants receiving the first dose of vaccination within the first 24 hours of life and those receiving a complete schedule of vaccination. Estimates of the proportion of infants born to hepatitis B surface antigen–positive mothers who received both timely birth dose and hepatitis B immunoglobulin were based on country interviews, national immunization guidelines and WHO reports. Estimates of the antiviral treatment among mothers with high viral loads, as a method to prevent perinatal transmission, were based mostly on expert opinion.

Other epidemiological inputs are constant across all country or regional models: progression rates of liver disease (specified by stage, serological status, sex and age group); mother-to-child transmission rates of hepatitis B virus (specified by the serological status of mother and the vaccination status of infant); proportions of hepatitis B e-antigen-negative and hepatitis B e-antigen-positive cases with a high viral load; and the risk of developing a chronic hepatitis B virus infection. Razavi-Shearer et al. *(4)* describe the values and sources of inputs and assumptions of the model.

The primary outputs of the model are the annual prevalence of hepatitis B surface antigen by stage of liver disease, serological status (low viral load, high viral load and receiving treatment), sex and age, and annual hepatitis B virus–related deaths by stage of liver disease, sex and age.

7. References

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C. Four curable STIs: chlamydia, gonorrhoea, trichomoniasis and syphilis

This section summarizes the methods and initial results of the prevalence and incidence of four of the most common curable STIs: chlamydia (*Chlamydia trachomatis* infection), gonorrhoea (*Neisseria gonorrhoeae* infection), trichomoniasis (*Trichomonas vaginalis* infection) and syphilis (*Treponema pallidum* infection) among women and men 15–49 years old by WHO region in 2020. These estimates were generated for the 2021 HIV, hepatitis and STI report to the World Health Assembly.

1. Methods

The methods used to generate the estimates for the four curable STIs are based on the methods used to generate the 2012 and 2016 WHO estimates *(1,2)*. As in 2012 and 2016, syphilis estimates were generated using a different approach from the other three STIs, reflecting the availability of prevalence data for syphilis.

1.1. Chlamydia, gonorrhoea and trichomoniasis

Estimates were generated using the same 10 estimation regions as in 2012 and 2016. The 10 regions were based on those used by the Global Burden of Disease project in 2010 and on epidemiology, geography and data availability. Table A1.6 shows the relationship between the estimation regions and WHO regions.

Table A1.6. Allocation of each of the 10 estimation regions to the six WHO regions

WHO region	Population 15–49 years (thousands)	African Region	Region of the Americas	Eastern Mediterranean Region	European Region	South-East Asia Region	Western Pacific Region
Central, eastern and western sub-Saharan Africa	480 451	98.4%	0.0%	1.6%	0.0%	0.0%	0.0%
Southern sub-Saharan Africa	43 824	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Latin America and the Caribbean	344 426	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%
North America	169 564	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%
North Africa and the Middle East	328 510	6.8%	0.0%	79.7%	13.5%	0.0%	0.1%
Australasia and high-income Asia and the Pacific	92 583	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%
Western, central and eastern Europe and central Asia	384 429	0.0%	0.0%	0.0%	99.5%	0.0%	0.4%
Oceania	6 277	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%
South Asia	974 093	0.0%	0.0%	11.7%	0.0%	88.3%	0.0%
East Asia and South-East Asia	1 103 392	0.1%	0.0%	0.0%	0.0%	21.2%	78.7%

The only differences between the methods and parameter values used to generate the 2020 estimates and the 2012 and 2016 estimates, except for an updated data set, were:

- an increase in the uncertainty range around the prevalence ratios used when there were insufficient data to generate an estimate from ±33% to ±50%; and
- an increase in the uncertainty range around the duration estimates from ±33% to ±50%.

Estimating prevalence – all regions except for North America

Prevalence data for chlamydia, gonorrhoea and trichomoniasis were drawn from the data collected for the 2016 WHO estimates, PubMed literature searches (last search conducted in January 2021) and requests to the WHO regional STI advisers and other leading experts in the field. Duplicate data points were removed, and if data were published in more than one article, the article with the most information was included in the database.

Study inclusion criteria were:

- a sample size of at least 100;
- specimens collected from 2013 through 2020 (for studies in which no specimen collection date was specified, the study had to be published in 2014 or later);
- the study used an internationally recognized diagnostic test with adequate performance characteristics on urine, urethral or cervicovaginal specimens; and
- the population could be considered representative of the general population: study populations included pregnant women, women at delivery, women attending family planning clinics, military recruits or individuals selected for participation in a Demographic and Health Survey.

Studies conducted among the following groups were excluded because of reasons that are known to bias estimates of general population STI prevalence: people seeking care for an STI or genital symptoms, women with abnormal Papanicolaou smears, blood donors, remote or indigenous populations, gay men and other men who have sex with men and commercial sex workers.

All of the studies identified in the first screen were entered into a spreadsheet and reviewed again. The studies that were not deemed to be representative of the general population were then excluded.

Data from studies that met the inclusion criteria were standardized to approximate the prevalence in the general population of a country by applying adjustment factors for the laboratory diagnostic test used, study location (rural versus urban) and the age of the study population *(2)*. When the standardized prevalence for a study was zero or negative, the standardized prevalence was assumed to be 0.1.

For the STIs with three or more data points among women in a specific estimation region, Bayesian meta-analytic approach was used to produce pooled prevalence estimates. The same thing was done for men. The beta-binomial approach for pooling overdispersed binomial data was used since it provides a robust estimate for the average proportion based on data from heterogeneous studies and provides estimates of uncertainty that take into account the heterogeneity observed between studies. Uncertainty ranges were generated using the same approach as in 2012 and 2016 *(1,2)*.

When there were insufficient data to generate an estimate for a particular STI in a region (less than three data points) or when the results of the meta-analysis did not look plausible, ratios were used.

Females – STI prevalence ratios

The 2016 STI prevalence ratios were used; these were based on those studies that met the 2016 study eligibility criteria and had data for chlamydia and either gonorrhoea or trichomoniasis.

	Gonorrhoea to chlamydia	Trichomoniasis to chlamydia
Upper-middle and high-income countries	0.15 ±50%	0.42 ±50%
Low- and lower-middle-income countries	0.44 ±50%	2.11 ±50%

Males

In any estimation region with less than three data points, the global male-to-female prevalence ratios were used: chlamydia −0.8 (±50%), gonorrhoea −0.86 (±50%) and trichomoniasis −0.1 (±50%).

All regional estimates, except for North America, for women and men were increased by 10% to reflect the contribution of populations at higher risk of infection missing from or undersampled in the studies included.

Appendix 1 provides more information on how the estimates were generated for each estimation region.

Estimating incidence – all regions except for North America

There were no changes to the 2012 and 2016 WHO methods for estimating the incidence of gonorrhoea, chlamydia or trichomoniasis. Regional incidence estimates were estimated from prevalence estimates for all estimation regions apart from North America (see subsection 1.3).

Incidence was calculated using the equation: incidence = prevalence/average duration of infection, and the average duration of infection in each region was assumed to depend on the average duration of infection in the absence of treatment for symptomatic and asymptomatic individuals and the probability that symptomatic and asymptomatic individuals are treated appropriately. The same parameter values were used as in 2012 and 2016 *(2)*.

Estimating prevalence and incidence in North America

Estimates for North America (United States of America and Canada) were based on the national chlamydia, gonorrhoea and trichomoniasis estimates for 2018 produced by the United States Centers for Disease Control and Prevention *(3,4)*. Age- and sex-specific data consisting of 10 000 simulations were obtained from the model of the United States Centers for Disease Control and Prevention for each STI and merged against population data for 2020. The mean of the simulations was used as the best estimate for both incidence and prevalence in this region and the 2.5th and 97.5th percentiles of the frequency distribution were used as the uncertainty interval. In generating

the 2020 estimates, it was assumed that the prevalence and incidence rates did not change from 2018 to 2020 in the United States of America, the prevalence and incidence rate of each infection in Canada was the same as in the United States of America, the United States Centers for Disease Control and Prevention estimates for chlamydia and gonorrhoea for people 24–39 years old could be extrapolated to people 40–49 years old and that the estimates for trichomoniasis for people 40–59 years old by the United States Centers for Disease Control and Prevention could be applied to people 40–49 years old. The geography, age and higher risk adjustments used for other regions were not applied to North America.

1.2. Syphilis

The methods used to generate the 2020 estimates were based on the methods used to generate the 2016 WHO syphilis estimates *(1,5,6)*. Briefly, national syphilis prevalence trend estimates in adults were generated using Spectrum-STI and the Spectrum-STI syphilis database. National estimates were then summed to generate WHO regional and global estimates.

The key differences in methods and parameter values between the current 2020 estimates and preceding 2016 estimates, apart from updated prevalence and population data sets, were changes to the following parameters:

- diagnostic test adjusters: added a category for prevalence data points that used a rapid plasma reagin titre cut-off; and
- an increase in the uncertainty range around the duration estimates (and consequently on incidence) from ±33% to ±50%.

Syphilis prevalence data: Spectrum-STI database

The Spectrum-STI database was compiled by Avenir Health to generate the 2016 WHO maternal and congenital syphilis estimates *(1,5)*. The database contains syphilis prevalence data for women and men representative of the general adult population. Eligible studies included community studies, household surveys and data from pregnant women from 1970 to 2016. For a subset of countries, data from blood donor screening are also included.[2]

The Spectrum-STI syphilis database was partly updated in March 2021. This update incorporated:

- antenatal surveys and surveillance and routine programmatic screening reported by countries through Global AIDS Monitoring for 2017, 2018 and 2019;
- country-vetted prevalence data sets compiled during Spectrum-STI country or regional national estimation exercises conducted between 2018 and 2020: Bangladesh, Yunnan province of China, El Salvador, Fiji, Honduras, Indonesia, Federal States of Micronesia, Nicaragua, Papua New Guinea, Paraguay, Peru and Samoa *(7–13)*;
- updated and final results from the PHIA surveys in Kenya, Uganda, United Republic of Tanzania, Zambia and Zimbabwe;
- reports and studies identified by Avenir Health through collaborations with national HIV and STI programmes; and
- PubMed searches for a subset of countries.

Standardizing prevalence data

Prevalence data were standardized to reflect active syphilis, defined as positive on both a non-treponemal (rapid plasma reagin or Venereal Disease Research Laboratory test) and a treponemal test (such as TPHA or TPPA) *(14)*, as in previous WHO estimations *(1,2)*. In the interim 2020 estimates the same test type correctors are used as in 2016 but with one added refinement for those studies with a rapid plasma reagin titre cut-off (Table A1.7). No other adjustments were made to the data (no adjustments for age or location sampled).

Table A1.7. Syphilis diagnostic test adjustment factors used on syphilis prevalence data points

Diagnostic test	Correction factor	Source or justification
Treponemal and non-treponemal positive	1.0	Gold standard
Treponemal and non-treponemal positive, with rapid plasma reagin ≥1:8 titre	2.5	Avenir Health analysis of comparative prevalence with and without RPRP threshold in Bangladesh and Peru data *(7,10)*
Treponemal positive without non-treponemal confirmation	0.53	Ham et al. *(14)*
Non-treponemal positive without treponemal confirmation	0.53	Ham et al. *(14)*
Rapid test	0.70	Korenromp et al. (Avenir Health and advisers) *(15)*
Unknown	0.75	Ham et al. *(14)*, slightly adjusted upward to account for increasing use of dual (treponemal plus non-treponemal) algorithms since the Ham et al. analysis

[2] For studies in blood donors that provided information stratified by first or repeat donor, the data were entered for first-time donors only, since repeat donors should already have been screened for blood-transmittable infections.

Weighting data

Each prevalence data point was assigned a weight that reflected its national coverage and representativeness. The weights were based on the weights used to generate the 2016 estimates but with some modifications to ensure consistency over all data points within a country. When studies are weighted, no systematic difference is assumed between the data types included *(16)*: between pregnant women tested in antenatal care, other (pregnant or non-pregnant) women in the general population and men in the general population.

Estimating syphilis prevalence

The approach used to estimate the adult syphilis prevalence in a country reflected the number of antenatal care, general population or blood donor data points in the Spectrum-STI database. As in 2016, if a country had:

- one or more prevalence data point from 2011 or later and three or more data points in total, then Spectrum-STI[3] was used to generate trend estimates;
- one or more prevalence data point from 2011 or later and two data points in total, then the weighted average was used; and
- only one data point or no data from 2011 or later, then the prevalence was estimated using the appropriate WHO regional average.

There were sufficient data to generate trend estimates using Spectrum-STI or a weighted average for 183 of the 205 countries and territories in the analysis. For 22 countries, 1.4% of the world's population 15–49 years old, there were insufficient data and the appropriate WHO regional average was used. For three countries (Indonesia, Papua New Guinea and the United States of America, 7.8 % of the world's people 15–49 years old) in the final Spectrum-STI estimates were replaced with recently generated national estimates.[4]

In generating the national prevalence trend estimates, data from women and men were pooled assuming that the male-to-female prevalence ratio was 1:1, as in the 2016 syphilis estimation round, and the resulting pooled prevalence (rate) was assumed to hold for both women and men.

As in 2016, the national trend estimates, which were based on prevalence data from low-risk populations, were converted into estimates by adding a fixed 10% to the estimates for each year to reflect the contribution of key populations that typically have higher prevalence and are missing or under-sampled in general population surveys.

Corresponding annual numbers of prevalent cases were calculated using World Population Prospects 2019 population estimates for men or women15–49 years old[5] *(18)*.

Incidence estimation

Incidence was estimated using the same approach as in 2016. In each country, incidence was calculated by dividing the prevalence estimate by the average duration of syphilis infection, except for the United States of America, where published incidence estimates were used *(17)*. The estimates of the average duration of infection were those used in the 2012 and 2016 global and regional estimations. Countries were allocated into 1 of 3 groups based on access to treatment. The average duration of syphilis duration of infection in regions with low, medium or high treatment access were 4.13, 2.42 and 1.28 years, respectively *(1,2)*.

Uncertainty bounds

For countries where the estimates were generated in Spectrum were used, Spectrum calculated the 95% confidence interval on the prevalence values. For all other countries, the 95% confidence interval was taken to be –55% (0.45-fold) to +100% (2-fold) the point estimate. These bounds were based on the proportional bounds on Spectrum estimates for 2016 and 2020. To calculate regional-level uncertainty in the trend estimates, it was assumed that uncertainties in prevalence trends were independent across countries within a region. Global-level uncertainty was calculated assuming independence across the six regional prevalence estimates.

The vast majority of data included in the trend estimates are from women. The male regional prevalence confidence intervals incorporate an additional ±33% around the average, to account for uncertainty in the male-to-female prevalence ratio *(1,2)*. This uncertainty was applied at the regional level, assuming that male-to-female ratios are generally similar within each region.

For incidence estimates, the 95% confidence interval includes an additional ±50% to reflect uncertainty in the average duration of infection *(1,2)*. This uncertainty was applied at the regional level, since it was assumed that infection duration (which varies with syphilis treatment coverage) is generally similar within each region.

[3] Spectrum-STI fitted the country data using second-order segmented (smoothed splines) polynomial regression *(16)*. Both the number and positions of the knots were estimated (up to a maximum of two knots) using the Akaike information criterion *(16)*. Country prevalence was assumed to be time-constant following the year with the most recent national data point.

[4] The United States of America has published new national estimates *(17)*. Indonesia and Papua New Guinea held national STI estimation workshops in 2020, where the Syphilis Interventions towards Elimination (SITE) model *(6)* was calibrated using national prevalence, behavioural and intervention coverage data *(8,9)* to estimate transmission and incidence across high-risk and lower-risk adult populations in a country and programme intervention impact. The national SITE prevalence estimate for the subgroups of low-risk plus medium-risk women combined was used for both countries.

[5] World Population Prospects *(18)* estimates do not include countries with populations of less than 90 000 people. For these (Cayman Islands, Dominica, Montserrat, Saint Kitts and Nevis, Turks and Caicos Islands, Andorra, Monaco, San Marino, Cook Islands, Marshall Islands, Nauru, Niue, Palau and Tuvalu) and for the Netherlands Antilles and Kosovo (in accordance with United Nations Security Council resolution 1244/1999), the population estimates from the 2016 global syphilis estimates were used. These 18 countries had a total population 15–49 years old of 681 556 women and 693 115 men.

2. Results – data availability

2.1. Chlamydia, gonorrhoea and trichomoniasis

Table A1.8 summarizes the number of data points that met the study entry criteria. There were more data points for chlamydia than for the other two STIs and more data for women than for men for each of the three infections. Excluding North America, for women there were three or more data points for all estimation regions for all three STIs, apart from Australasia and high-income Asia and the Pacific. For men, the only STI and region with more than three data points was chlamydia in western, central and eastern Europe.

2.2. Syphilis

The global Spectrum-STI database as of 22 March 2021 contains more than 1862 eligible data points from 170 countries. The vast majority of data points and samples tested were from routine antenatal care programme screening, followed by antenatal care sentinel sample surveys, general population or community surveys and blood donor screening. More than 90% of data points and samples were from 2000 onwards. Among the WHO regions, the African Region had the most data points, whereas the Western Pacific Region contributed most samples tested.

Table A1.8. Number of studies that met the study entry criteria by estimation region: cells coloured green have seven or more data points and red fewer than three data points

	Chlamydia		Gonorrhoea		Trichomoniasis		Total population
WHO region	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**15–49 years old (thousands)**
Central, eastern and western sub-Saharan Africa	16	1	18	1	28	1	480 451
Southern sub-Saharan Africa	9	3	9	3	10	3	43 824
Latin America and the Caribbean	25	1	13	1	15	1	344 426
North America							169 564
North Africa and the Middle East	8	0	3	0	8	1	328 510
Australasia and high-income Asia and the Pacific	3	0	0	0	1	1	92 583
Western, central and eastern Europe and central Asia	14	9	5	3	7	2	384 429
Oceania	6	1	6	1	5	0	6 277
South Asia	6	0	3	0	4	0	974 093
East Asia and South East Asia	9	5	6	2	6	1	1 103 392
Total	96	20	63	11	84	10	3 927 550

3. Results – prevalence and incidence in 2020

Table A1.9 presents the global and regional prevalence and incidence estimates for 2020 for the four STIs. The global prevalence among people 15–49 years old was estimated to be:

- chlamydia: 4.0% (95% uncertainty interval (UI): 3.5–4.7%) for women and 2.5% (95% UI: 1.8–3.4%) for men;
- gonorrhoea: 0.8% (95% UI: 0.6–1.1%) for women and 0.7% (95% UI: 0.3–1.1%) for men;
- trichomoniasis: 4.9% (95% UI: 3.9–6.2%) for women and 0.5% (95% UI: 0.3–0.8%) for men; and
- syphilis: 0.58% (95% UI: 0.53–0.63%) for women and 0.56% (95% UI: 0.39–0.74%) for men.

These prevalence estimates correspond to 128.5 million new cases of chlamydia (95% UI: 90.0–173.8 million), 82.4 million new cases of gonorrhoea (95%UI: 47.7–130.4 million), 156.3 million new cases of trichomoniasis (95% UI: 96.4–235.8 million) and 7.1 million new cases of syphilis (95%UI: 3.8–10.3 million) among people 15–49 years old.

Fig. A1.1 and A1.2 show the estimated prevalence and incidence rates for 2020 by WHO region.

Table A1.9. Prevalence (%) and incidence estimates for 2020 by WHO region and 95% uncertainty intervals

	Females				Males			
WHO region	**Chlamydia**	**Gonorrhoea**	**Tricho-moniasis**	**Syphilis**	**Chlamydia**	**Gonorrhoea**	**Tricho-moniasis**	**Syphilis**
				Prevalence (%)				
African Region	5.5 [4.3–7.0]	1.6 [1.1–2.2]	12.0 [8.7–16.3]	1.7 [1.5–1.9]	4.0 [2.1–6.4]	1.2 [0.6–2.0]	1.3 [0.6–2.1]	1.7 [1.2–2.2]
Region of the Americas	6.8 [5.4–8.6]	0.6 [0.3–0.9]	7.1 [4.2–11.8]	1.1 [1.0–1.3]	3.7 [2.1–5.7]	0.5 [0.2–0.9]	0.8 [0.4–1.4]	1.1 [0.8–1.5]
South-East Asia Region	1.9 [1.3–2.9]	0.8 [0.4–1.5]	2.7 [1.4–5.3]	0.13 [0.03–0.24]	1.2 [0.7–2.2]	0.7 [0.2–1.4]	0.3 [0.1–0.6]	0.13 [0.02–0.24]
European Region	3.4 [2.5–4.6]	0.3 [0.1–0.5]	1.7 [1.0–2.7]	0.11 [0.09–0.13]	2.0 [1.3–2.9]	0.2 [0.1–0.5]	0.2 [0.1–0.3]	0.11 [0.08–0.15]
Eastern Mediterranean Region	4.4 [2.4–7.6]	0.5 [0.2–0.9]	4.7 [2.8–7.8]	0.65 [0.42–0.87]	3.5 [1.4–7.0]	0.4 [0.1–0.9]	0.5 [0.2–0.9]	0.61 [0.36–0.85]
Western Pacific Region	4.3 [3.5–5.2]	0.9 [0.5–1.3]	3.7 [2.2–5.9]	0.32 [0.25–0.39]	2.3 [1.7–3.2]	0.7 [0.3–1.3]	0.4 [0.2–0.7]	0.32 [0.21- 0.43]
Global total	**4.0 [3.5–4.7]**	**0.8 [0.6–1.1]**	**4.9 [3.9–6.2]**	**0.58 [0.53–0.63]**	**2.5 [1.8–3.4]**	**0.7 [0.3–1.1]**	**0.5 [0.3–0.8]**	**0.56 [0.39–0.74]**

	Females				Males			
WHO region	**Chlamydia**	**Gonorrhoea**	**Tricho-moniasis**	**Syphilis**	**Chlamydia**	**Gonorrhoea**	**Tricho-moniasis**	**Syphilis**
				Incidence (per 1000 population)				
African Region	46 [23–74]	34 [16–59]	87 [41–146]	4.1 [2.0–6.3]	40 [16–77]	37 [14–74]	103 [39–203]	4.1 [1.4–6.6]
Region of the Americas	68 [39–104]	17 [9–28]	63 [32–115]	4.6 [2.3–7.0]	48 [23–86]	21 [9–43]	63 [26–131]	5.0 [1.9–7.8]
South-East Asia Region	16 [7–28]	17 [6–37]	20 [7–44]	0.33 [0.01–0.65]	12 [5–25]	21 [6–51]	22 [6–55]	0.32 [<0.01–0.64]
European Region	31 [17–49]	7 [3–13]	14 [7–25]	0.56 [0.25–0.86]	27 [14–43]	11 [3–23]	14 [5–30]	0.56 [0.18–0.91]
Eastern Mediterranean Region	39 [16–78]	12 [4–25]	37 [17–70]	1.7 [0.28–3.2]	42 [13–99]	16 [4–38]	38 [13–82]	1.6 [0.10–3.1]
Western Pacific Region	38 [22–57]	20 [10–35]	29 [14–53]	1.2 [0.48–1.9]	29 [15–46]	27 [10–55]	30 [11–64]	1.2 [0.34–1.9]
Global total	**36 [23–51]**	**19 [11–29]**	**38 [23–57]**	**1.8 [0.8–2.9]**	**29 [17–45]**	**23 [10–43]**	**41 [19–74]**	**1.8 [0.4–3.0]**
				Incident cases (thousands)				
African Region	12 400 [6 300–20 100]	9 300 [4 400–16 000]	23 400 [11 200–39 400]	1 100 [540–1 700 000]	10 900 [4 300–20 800]	9 900 [3 800–19 900]	27 800 [10 500–54 900]	1 100 [370–1 800]
Region of the Americas	17 400 [10 000–26 700]	4 300 [2 400–7 300]	16 200 [8 100–29 500]	1 200 [580–1 800]	12 400 [5 800–22 200]	5 500 [2 400–11 000]	16 200 [6 700–33 700]	1 300 [500–2 000]
South-East Asia Region	8 300 [3 900–14 800]	9 200 [3 200–19 500]	10 500 [3 900–23 200]	180 [7–340]	6 900 [2 800–14 200]	11 900 [3 200–28 900]	12 600 [3 600–31 000]	180 [0–360]
European Region	6 600 [3 600–10 500]	1 500 [600–2 800]	3 000 [1 400–5 300]	120 [52–180]	5 700 [3 000–9 300]	2 300 [720–4 900]	3 100 [1 100–6 500]	120 [38–200]
Eastern Mediterranean Region	7 200 [3 000–14 300]	2 200 [800–4 500]	6 700 [3 100–12 800]	320 [52–580]	8 500 [2 700–19 700]	3 200 [890–7 600]	7 600 [2 700–16 400]	320 [20–610]
Western Pacific Region	17 800 [10 100–26 800]	9 400 [4 700–16 200]	13 800 [6 500–24 700]	540 [220–860]	14 300 [7 700–23 000]	13 700 [5 000–27 800]	15 300 [5 400–32 100]	580 [170–960]
Global total	**69 900 [44 200–97 800]**	**35 900 [20 700–55 500]**	**73 700 [44 200–109 300]**	**3 500 [1 500–5 500]**	**58 600 [33 800–90 400]**	**46 400 [20 000–86 300]**	**82 600 [37 200–148 300]**	**3 600 [890–6 000]**

The gonorrhoea estimates for women for the two estimation regions that account for most of the women 15–49 years old in the WHO South-East Asia Region and Western Pacific Region (South Asia and East Asia & South East Asia) were generated using the ratio approach rather than based on the available data. In both estimation regions, the available prevalence data were from populations considered to have a very low risk of infection, and the meta-estimate was viewed as underestimating the overall prevalence.

Fig. A1.1. Prevalence (%) estimates for 2020 by WHO region

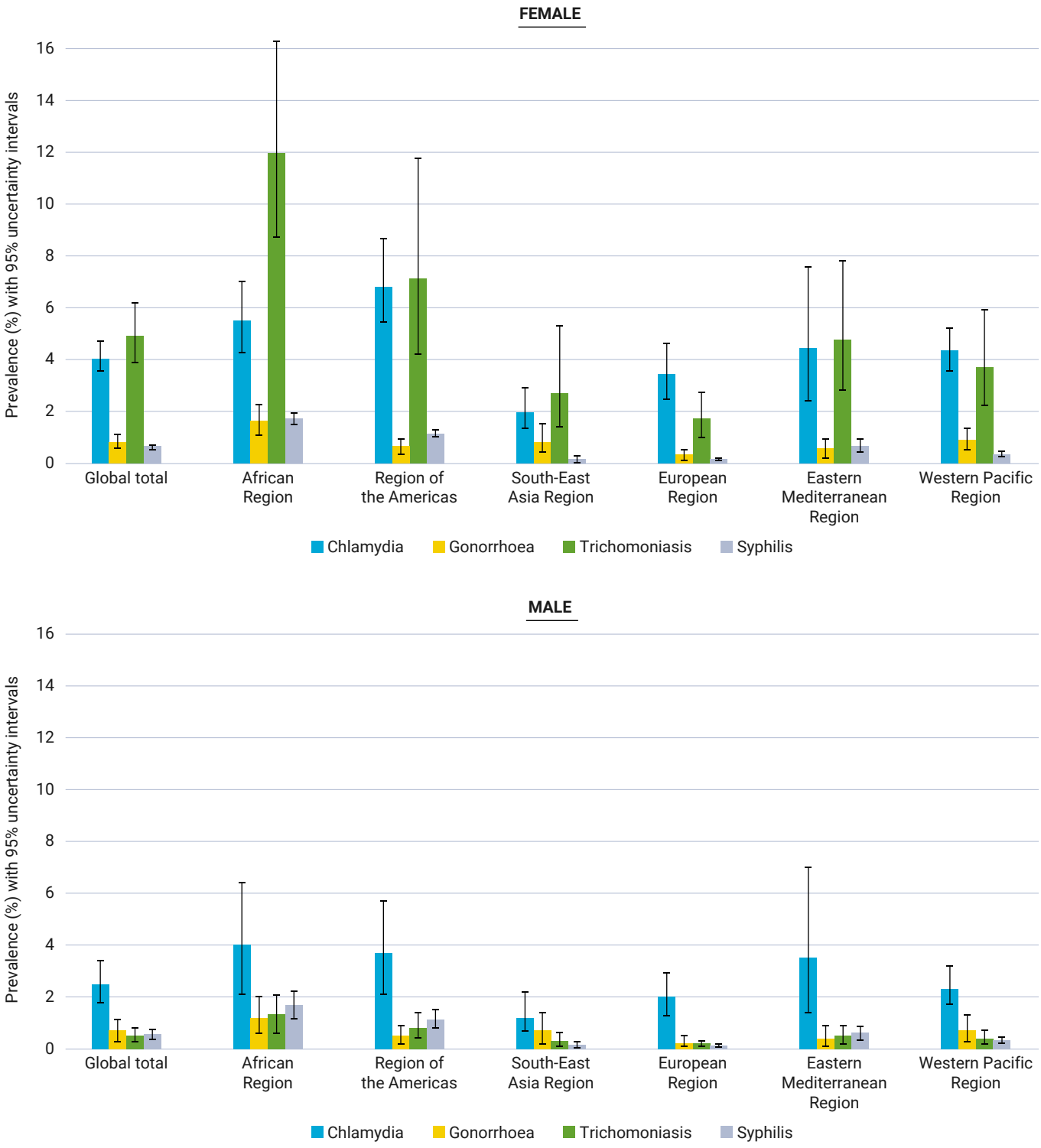
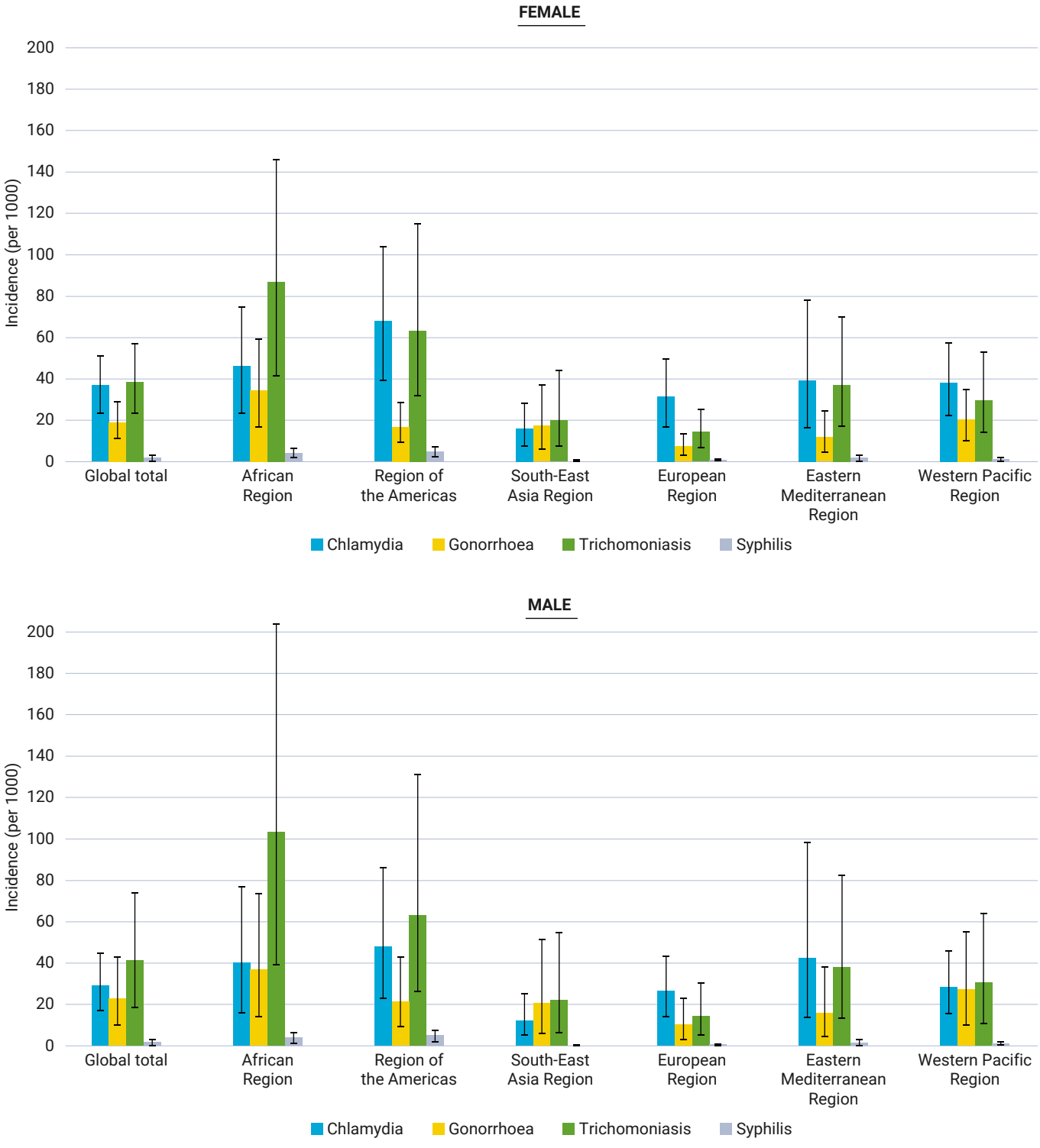


Fig. A1.2. Incidence (per 1000 population) estimates for 2020 by WHO region



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Appendix 1. Data availability and methods used to generate 2020 prevalence estimates by estimation region: chlamydia, gonorrhoea and trichomoniasis

1. Central, eastern and western sub-Saharan Africa

Table AA1.1 provides a summary of the number of studies that met the latest screen. The number in brackets is the number of countries that provided data out of the possible 41 countries in the region. Table AA1.2 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three infections in females and males.

Table AA1.1. Number of studies (countries) included in the estimation

	Females	Males
Chlamydia	16 (10)	1 (1)
Gonorrhoea	18 (10)	1 (1)
Trichomoniasis	28 (13)	1 (1)

Table AA1.2. Approaches used to generate the estimates for central, eastern and western sub-Saharan Africa in 2020

	Females	Males
Chlamydia	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Gonorrhoea	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Based on data	Global male-to-female ratio applied to the 2020 female estimate

2. Southern sub-Saharan Africa

Table AA1.3 provides a summary of the number of studies that met the secondary screen. The number in brackets is the number of countries that provided data out of the possible six countries in the region. Table AA1.3 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three STIs for women. For men, there were sufficient data in 2020 to generate estimates for all three STIs, unlike in 2016 estimates, when the gender ratios were used.

Table AA1.3. Number of studies (countries) included in the analysis

	Females	Males
Chlamydia	9 (2)	3 (1)
Gonorrhoea	9 (2)	3 (1)
Trichomoniasis	10 (3)	3 (1)

Table AA1.4. Approaches used to generate the estimates for southern sub-Saharan Africa in 2020. The text in blue highlights that the approach used in 2020 differs from the one used in 2016.

	Females	Males
Chlamydia	Based on data	Based on data
Gonorrhoea	Based on data	Based on data
Trichomoniasis	Based on data	Based on data

3. Latin America and the Caribbean

Table AA1.5 provides a summary of the number of studies that met the latest screen. The number in brackets is the number of countries that provided data of the possible 42 countries in the region. Table AA1.6 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three STIs for females and males.

Table AA1.5. Number of studies (countries) included in the estimation

	Females	Males
Chlamydia	25 (8)	1 (1)
Gonorrhoea	13 (5)	1 (1)
Trichomoniasis	15 (4)	1 (1)

Table AA1.6. Approaches used to generate the Latin America and the Caribbean estimates in 2020

	Females	Males
Chlamydia	Based on data	Male-to-female ratio used in the 2016 estimates for Latin America and the Caribbean applied to the 2020 female estimate
Gonorrhoea	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Based on data	Global male-to-female ratio applied to the 2020 female estimate

4. North America

Not applicable – estimates based on national estimates for the United States of America.

5. North Africa and the Middle East

Table AA1.7 provides a summary of the number of studies that met the secondary screen. The number in brackets is the number of countries that provided data of the possible 20 countries in the region. Table AA1.8 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three STIs for females and males.

Table AA1.7. Number of studies (countries) included in the analysis

	Females	Males
Chlamydia	8 (3)	0 (0)
Gonorrhoea	3 (2)	0 (0)
Trichomoniasis	8 (3)	1 (1)

Table AA1.8. Approaches used to generate the estimates for North Africa and the Middle East in 2020

	Females	Males
Chlamydia	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Gonorrhoea	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Based on data	Global male-to-female ratio applied to the 2020 female estimate

6. Australasia and high-income Asia and the Pacific

Table AA1.9 provides a summary of the number of studies that met the secondary screen. The number in brackets is the number of countries that provided data out of the possible 6 countries in the region. Table AA1.10 summarizes the approaches used to generate the estimates for this region in 2020. The approaches used in 2020 are different from those used in 2016. In 2020 the only infection with 3 or more data points was chlamydia in women. In 2016 there were sufficient data to generate estimates based on data for gonorrhoea in women and chlamydia in men.

Table AA1.9. Number of studies (countries) included in the analysis

	Females	Males
Chlamydia	3 (3)	0 (0)
Gonorrhoea	0 (0)	0 (0)
Trichomoniasis	1 (1)	1 (1)

Table AA1.10. Approaches used to generate the estimates for Australasia and high-income Asia and the Pacific in 2020. The text in blue highlights that the approach used in 2020 differs from the one used in 2016.

	Females	Males
Chlamydia	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Gonorrhoea	Gonorrhoea-to-chlamydia ratio for upper-middle and high-income countries used	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Trichomoniasis-to-chlamydia ratio for upper-middle and high-income countries used	Global male-to-female ratio applied to the 2020 female estimate

7. Western, central and eastern Europe and central Asia

Table AA1.11 provides a summary of the number of studies that met the secondary screen. The number in brackets is the number of countries that provided data of the possible 53 countries in the region. Table AA1.12 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for chlamydia and trichomoniasis for females and males. For gonorrhoea for both females and males, the 2020 estimates were based on data and the 2016 estimates used the global ratio.

To generate the 2020 prevalence of gonorrhoea for men, the global male-to-female ratio was used rather than the three identified data points since, after standardizing the data to account for the diagnostic test, all three studies produced an adjusted prevalence of less than or equal to zero and consequently the pooled estimate was determined to be invalid. The same was true for interpreting the prevalence data for trichomoniasis for women and, as a result, the 2020 estimate was generated using the ratio approach.

Table AA1.11. Number of studies (countries) included in the analysis

	Females	Males
Chlamydia	14 (8)	9 (7)
Gonorrhoea	5 (5)	3 (3)
Trichomoniasis	7 (6)	2 (2)

Table AA1.12. Approaches used to generate the estimates for Europe and central Asia in 2020. The text in blue highlights that the approach used in 2020 differs from the one used in 2016.

	Females	Males
Chlamydia	Based on data	Based on data
Gonorrhoea	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Based on 2016 trichomoniasis-to-chlamydia ratio for upper-middle and high-income countries	Global male-to-female ratio applied to the 2020 female estimate

8. Oceania

Table AA1.13 provides a summary of the number of studies that met the secondary screen. The number in brackets is the number of countries that provided data of the possible 14 countries in the region. Table AA1.14 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three STIs for females and males, except for trichomoniasis among females. In 2020, there was sufficient data to generate an estimate, whereas in 2016 a ratio was used.

Table AA1.13. Number of studies (countries) included in the analysis

	Females	Males
Chlamydia	6 (3)	1 (1)
Gonorrhoea	6 (3)	1 (1)
Trichomoniasis	5 (2)	0 (0)

Table AA1.14. Approaches used to generate the estimates for Oceania in 2020. The text in blue highlights that the approach used in 2020 differs from the one used in 2016.

	Females	Males
Chlamydia	Based on data	Global male-to female ratio applied to the 2020 female estimate
Gonorrhoea	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Based on data	Global male-to-female ratio applied to the 2020 female estimate

9. South Asia

Table AA1.15 provides a summary of the number of studies that met the secondary screen. The number in brackets is the number of countries that provided data of the five countries in the region. Table AA1.16 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three STIs, except for chlamydia and gonorrhoea in males; in 2016 there were sufficient data to generate an estimate, whereas in 2020 ratios were used.

To generate the 2020 estimates for the prevalence of gonorrhoea and trichomoniasis for females, the decision was made to use ratios rather than the identified data. For gonorrhoea, three data points were identified: a study of antenatal care women in rural Nepal (0 positive of 591), a study of women younger than 25 years attending an antenatal care clinic in Msyore (2 positive of 213); and a study of asymptomatic women in a community-based HPV study in Karnataka (0 positive of 811). The prevalence estimate, after standardizing, was 0.15%. Given the study populations, the studies were deemed to underestimate the prevalence, and the ratio was used instead, which resulted in a prevalence of 0.5%. For trichomoniasis, four studies were identified for women, and the adjusted prevalence from these studies was 7.3%, which was considered to be too high relative to the prevalence data for chlamydia and gonorrhoea, and the ratio was used, which resulted in a prevalence of 2.4%.

Table AA1.15. Number of studies (countries) included in the analysis

	Females	Males
Chlamydia	6 (3)	0 (0)
Gonorrhoea	3 (2)	0 (0)
Trichomoniasis	4 (1)	0 (0)

Table AA1.16. Approaches used to generate the South Asia estimates in 2020. The text in blue highlights that the approach used in 2020 differs from the one used in 2016.

	Females	Males
Chlamydia	Based on data	Global male-to-female ratio applied to the 2020 female estimate
Gonorrhoea	Gonorrhoea-to-chlamydia ratio for low- and low-middle-income countries	Global male-to-female ratio applied to the 2020 female estimate
Trichomoniasis	Trichomoniasis-to-chlamydia ratio for low- and lower-middle income countries	Global male-to-female ratio applied to the 2020 female estimate

10 East Asia and South-East Asia

Table AA1.17 provides a summary of the number of studies that met the latest screen. The number in brackets is the number of countries that provided data of the possible 15 countries in the region. Table AA1.18 summarizes the approaches used to generate the estimates for this region in 2020. These are the same approaches used in 2016 for all three STIs for females and males, except for chlamydia in males; in 2020, there was sufficient data to generate an estimate, whereas in 2016 a ratio was used.

To generate the 2020 estimate of the prevalence of gonorrhoea among females, the decision was made to use a ratio rather than the identified data. Six data prevalence data points were identified and the gonorrhoea prevalence (after adjustments) was 0.2%, whereas the ratio gave a prevalence of 1.1%. Four of the six data points were from China and, after reviewing the study populations and their age range with the WHO Regional Office for the Western Pacific, the consensus was that the available data underestimated the prevalence, and the ratio approach should be used.

Table AA1.17. Number of studies (countries) included in the estimation

	Females	Males
Chlamydia	9 (3)	5 (1)
Gonorrhoea	6 (3)	2 (1)
Trichomoniasis	6 (4)	1 (1)

Table AA1.18. Approaches used to generate the estimates for East Asia and South-East Asia estimates in 2020. The text in blue highlights that the approach used in 2020 differs from the one used in 2016.

	Females	Males
Chlamydia	Based on data	Based on data
Gonorrhoea	Gonorrhoea-to-chlamydia ratio used; the ratio reflects the relative contribution of east Asia (middle upper and high-income ratio) and South-East Asia (low- and lower-middle income countries' ratio)	Global male-to-female ratio applied to the 2020 female estimates for East Asia and South-East Asia
Trichomoniasis	Based on data	Global male-to-female ratio applied to the 2020 female estimate

Appendix 2. Trends over time: comparison of 2012, 2016 and 2020 estimates for chlamydia, gonorrhoea and trichomoniasis

Table AA2.1 shows the 2020 prevalence estimates and the 2016 and 2012 WHO estimates *(1,2)*. These results should not be interpreted as showing a trend in prevalence – they are estimates for a specific year based on the available data for the previous eight years. In addition, the 95% uncertainty intervals overlap for all of the regions and STIs for both women and men, reflecting the considerable uncertainty in the point estimates (data not shown).

Table AA2.1. Comparison of 2020, 2016 and 2012 WHO estimates by WHO region

	Chlamydia			Gonorrhoea			Trichomoniasis		
WHO region	**2012**	**2016**	**2020**	**2012**	**2016**	**2020**	**2012**	**2016**	**2020**
	Prevalence (%) – women 15–49 years								
African Region	3.7%	5.0%	5.5%	1.7%	1.9%	1.6%	11.5%	11.7%	12.0%
Region of the Americas	7.6%	7.0%	6.8%	0.8%	0.9%	0.6%	7.7%	7.7%	7.1%
South-East Asia Region	1.8%	1.5%	1.9%	0.4%	0.7%	0.8%	1.8%	2.5%	2.7%
European Region	2.2%	3.2%	3.4%	0.3%	0.3%	0.3%	1.0%	1.6%	1.7%
Eastern Mediterranean Region	3.5%	3.8%	4.4%	0.5%	0.7%	0.5%	5.9%	4.7%	4.7%
Western Pacific Region	6.2%	4.3%	4.3%	1.2%	0.9%	0.9%	5.5%	5.6%	3.7%
Global	**4.2%**	**3.8%**	**4.0%**	**0.8%**	**0.9%**	**0.8%**	**5.0%**	**5.3%**	**4.9%**

	Chlamydia			Gonorrhoea			Trichomoniasis		
WHO region	**2012**	**2016**	**2020**	**2012**	**2016**	**2020**	**2012**	**2016**	**2020**
	Prevalence (%) – men 15–49 years								
African Region	2.5%	4.0%	4.0%	0.5%	1.6%	1.2%	1.2%	1.2%	1.3%
Region of the Americas	1.8%	3.7%	3.7%	0.7%	0.8%	0.5%	1.3%	1.3%	0.8%
South-East Asia Region	1.3%	1.2%	1.2%	0.5%	0.6%	0.7%	0.2%	0.2%	0.3%
European Region	1.5%	2.2%	2.0%	0.3%	0.3%	0.2%	0.1%	0.2%	0.2%
Eastern Mediterranean Region	2.7%	3.0%	3.5%	0.4%	0.6%	0.4%	0.6%	0.5%	0.5%
Western Pacific Region	5.2%	3.4%	2.3%	1.0%	0.7%	0.7%	0.6%	0.6%	0.4%
Global	**2.7%**	**2.7%**	**2.5%**	**0.6%**	**0.7%**	**0.7%**	**0.6%**	**0.6%**	**0.5%**

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Appendix 3. Trends over time: Comparison of 2012, 2016 and 2020 prevalence estimates for syphilis

Table AA3.1 shows both the 2020 estimates and the revised estimates for 2012 and 2016. The global prevalence of syphilis in women and men decreased between 2012 and 2016 but then increased between 2016 and 2020.

At the regional level, the prevalence of syphilis increased in five of the six WHO regions between 2016 and 2020. The exception was the South-East Asia Region, where the prevalence fell between 2016 and 2020. However, none of the differences were statistically significant (defined as non-overlapping confidence intervals) (see Table AA3.1).

The trends over time in incidence are similar to those for prevalence. The uncertainty intervals for the incidence estimates, however, are greater than those for prevalence, reflecting uncertainty around the average duration of infection,

The new estimates for 2012 and 2016 differ slightly from the published estimates for 2012 and 2016, mainly reflecting the new prevalence data added into the Spectrum-STI database.

Table AA3.1. Interim global and regional syphilis prevalence estimates for women and men 15–49 years old

	2012		2016		2020	
WHO region	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**
African Region	1.8% [1.6–2.1%]	1.8% [1.3–2.4%]	1.7% [1.5–1.9%]	1.6% [1.1–2.2%]	1.7% [1.5–1.9%]	1.7% [1.2–2.2%]
Region of the Americas	0.7% [0.6–0.9%]	0.7% [0.5–1.0%]	0.8% [0.7–0.9%]	0.8% [0.6–1.1%]	1.1% [1.0–1.3%]	1.1% [0.8–1.5%]
South-East Asia Region	0.4% [0.1–0.8%]	0.4% [0.1–0.8%]	0.2% [<0.1–0.4%]	0.2% [<0.1–0.4%]	0.13 [0.03–0.24]	0.13 [0.02–0.24]
European Region	0.1% [0.1–0.2%]	0.1% [0.1–0.2%]	0.1% [0.1–0.1%]	0.1% [0.1–0.1%]	0.11 [0.09–0.13]	0.11 [0.08–0.15]
Eastern Mediterranean Region	0.4% [0.2–0.6%]	0.4% [0.2–0.6%]	0.6% [0.5–0.7%]	0.5% [0.4–0.7%]	0.65 [0.42–0.87]	0.61 [0.36–0.85]
Western Pacific Region	0.3% [0.2–0.4%]	0.3% [0.1–0.4%]	0.3% [0.2–0.3%]	0.3% [0.2–0.4%]	0.32 [0.25–0.39]	0.32 [0.21- 0.43]
Global	**0.6% [0.5–0.7%]**	**0.5% [0.4–0.7%]**	**0.5% [0.4–0.6%]**	**0.5% [0.3–0.7%]**	**0.58 [0.53–0.63]**	**0.56 [0.39–0.74]**

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