Global burden and trends of sexually transmitted infections from 1990 to 2019: an observational trend study

Yang Zheng, Qi Yu*, Yushi Lin*, Yuqing Zhou, Lei Lan, Shigui Yang, Jie Wu*

Summary

Background Sexually transmitted infections (STIs) are a major public health issue worldwide, but there is a paucity of literature on their burden and trends globally. We aimed to assess the global disease burden and trends of STIs from 1990 to 2019.

Methods In this observational trend study, we collected data on incident cases, age-standardised incidence rate, and disability-adjusted life-years (DALYs), and calculated age-standardised DALY rates, for five STIs (syphilis, chlamydia, gonorrhoea, trichomonas, and genital herpes) between 1990 and 2019, by sex, geographical region, and cause using data exclusively from the Global Burden of Disease study 2019. The estimated annual percentage changes in the age-standardised incidence rate and age-standardised DALY rate were calculated to quantify the changing trend.

Findings Globally, the age-standardised incidence rate of STIs showed a decreasing trend with an estimated annual percentage change of –0·04 (95% uncertainty interval [UI] –0·08 to 0·00) from 1990 to 2019, reaching 9535·71 per 100 000 person-years (8169·73 to 11 054·76) in 2019. The age-standardised DALY rate showed a decreasing trend with an estimated annual percentage change of –0·92 (–1·01 to –0·84) and reached 22·74 per 100 000 person-years (14·37 to 37·11) in 2019. The sub-Saharan African region had the highest age-standardised incidence rate (19 973·12 per 100 000 person-years, 17 382·69 to 23 001·57) and age-standardised DALY rate (389·32 per 100 000 person-years, 154·27 to 769·74). Adolescents had the highest incidence rate (18 377·82 per 100 000 person-years, 14 040·38 to 23 443·31) and showed stable total STI trends, except for an upward trend of syphilis between 2010 (347·65 per 100 000 person-years, 203·58 to 590·69) and 2019 (423·16 per 100 000 person-years, 235·70 to 659·01). Male individuals had a higher age-standardised incidence rate (10 471·63 per 100 000 person-years, 8892·20 to 12 176·10) than female individuals (8602·40 per 100 000 person-years, 7358·00 to 10001·18) , whereas female individuals had a higher age-standardised DALY rate (33·31 per 100 000 person-years, 21·05 to 55·25) than male individuals (12·11 per 100 000 person-years, 7·63 to 18·93).

Interpretation Although most countries showed a decrease in age-standardised rates of incidence and DALYs for STIs, the absolute incident cases and DALYs increased from 1990 to 2019. Therefore, STIs still represent a global public health challenge, especially in sub-Saharan Africa and Latin America, which warrants more attention and health prevention service.

Funding Mega-Project of National Science and Technology for the 13th Five-Year Plan of China and the National Natural Science Foundation of China.

Copyright © 2021 Elsevier Ltd. All rights reserved.

Lancet Infect Dis 2021

Published Online December 20, 2021 https://doi.org/10.1016/S1473-3099(21)00448-5

For the XX translation of the abstract see Online for appendix 1

*Contributed equally

State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Centre for Infectious Diseases, Collaborative Innovation Centre for Diagnosis and Treatment of Infectious Diseases (Y Zheng MD, Y Lin MS, Y Zhou MD, L Lan MS, Prof S Yang PhD, J Wu PhD), **and Department of General Practice** (Y Zheng), **The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China; Department of Cardiology and Endodontics, The Stomatology Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China** (Q Yu MS)

Correspondence to:
Dr Jie Wu, State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Centre for Infectious Diseases, Collaborative Innovation Centre for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang 310003, China
zjwujie@zju.edu.cn

Introduction

Sexually transmitted infections (STIs) constitute one of the most common acute infectious conditions and remain a major public health issue worldwide.[1] The global incidence of common STIs was estimated to be as high as 563·3 million in 2016, including 6·3 million cases of syphilis, 86·9 million cases of gonorrhoea, 127·2 million cases of chlamydia, 156·0 million cases of trichomonas, and 186·9 million cases of genital herpes.[1,2] Although most STIs are not life threatening, the large number of people infected with STIs worldwide imposes a substantial strain on the budgets of both households and national health systems and compromises the quality of life of individuals. Left untreated, some STIs can cause consequences that threaten reproductive and neonatal health.[3] Considering these factors, the WHO global health sector strategy on STIs sets out guiding principles and priority actions for ending the STI epidemic as a public health problem by 2030.[4]

STIs represent a tremendous health and economic burden for people worldwide. Historically, however, STIs have been largely ignored as a public health priority.[5] In the 1960s, major social changes led to greater sexual liberation, facilitated by the availability of the oral contraceptive pill. Many industrialised countries have reported increasing trends in STIs and have established screening and surveillance programmes in recognition of STIs as a major public health problem.[6] Since the emergence of HIV in the 1980s, STI control efforts have increasingly been defined in relation to HIV programme priorities.[7] Many national public health campaigns for behavioural interventions have been implemented,

Research in context

Evidence before this study

We used the key words "sexually transmitted infection", "STI", "sexually transmitted disease", "STD", "syphilis", "gonorrhea", "chlamydia", "trichomonas", "genital herpes", "global burden", "incidence", and "epidemiology" to search PubMed, Web of Science, and Google Scholar databases in English as well as the Wan-Fang database in Chinese up to Jan 31, 2021. Although multiple international analyses have revealed trends in the most common sexually transmitted infections (STIs), including syphilis, gonorrhoea, chlamydia, and herpes, in the past 20 years in the general population, these studies have been limited to countries and regions or targeted to specific populations or specific STIs. To date, there has been no international comparative analysis of STI burdens and its trends. This is the first comprehensive report on the disease burden of STIs and their trends from 1990 to 2019 at the global, regional, and country levels on the basis of results from the Global Burden of Disease (GBD) 2019 study.

Added value of this study

This study investigated the incidence and disability-adjusted life-years (DALYs) of STIs in the general population by sex, social development index, and cause for the 1990–2019 period at the national, regional, and global levels. This study provides valuable insights for evidence-based health-care planning and resource allocation for STI control and prevention and provides a better understanding of the global burden of STIs as an important complement to previous GBD studies.

Implications of all the available evidence

Our results show that most countries had a decrease in age-standardised rates of incidence and DALY for STIs, whereas the absolute incident cases and DALYs increased from 1990 to 2019. Therefore, STIs still represent a global public health challenge, especially in sub-Saharan Africa and Latin America, which warrants more policy-maker attention and STI health-prevention services.

which probably led to behavioural changes and substantial reductions in STIs in the early 1990s.[6]

Since the 1990s, many studies have aimed to estimate the international STI burden.[8,9] However, a consistent and comparative picture of the global burden of STIs is still absent. The original Global Burden of Disease (GBD) study was commissioned by the World Bank and described in the landmark World Development Report 1993, Investing in Health.[10] The GBD study is the most comprehensive effort to systematically measure the world's health problems since 1990. We therefore examined data from the GBD to calculate the incidence and disability-adjusted life-years (DALYs) of STIs in the general population by sex, social development index (SDI), and cause for the 1990–2019 period at national, regional, and global levels. Our results will provide valuable insights for evidence-based health-care planning and resource allocation for STI control and prevention and provide a better understanding of the global burden of STIs as an important complement to previous GBD studies.

For more on the **GBD 2019 Input Sources Tool** http://ghdx.healthdata.org/gbd-2019

For more on the **Global Health Data Exchange query tool** see http://ghdx.healthdata.org/gbd-results-tool

Methods

Overview

In this observational trend study, we used data exclusively from GBD 2019. GBD 2019 provided the most up-to-date and comprehensive estimation of the global burden of 369 diseases and injuries on prevalence, incidence, mortality, and DALYs for different age groups, sexes, and 204 countries and territories from 1990 to 2019, with the methodological basis described in detail elsewhere.[11] For STIs, input data were acquired by systematic literature reviews, manual search of national ministry of health websites, antenatal clinic surveillance reports, data from the GBD collaborator network, and case notification, which can be found using the GBD 2019 Data Input Sources Tool. Of 204 countries, 161 provided data on syphilis, 64 on gonorrhoea, 94 on chlamydia, 56 on trichomonas, and 77 on herpes.[11]

Modelling was done using a Bayesian meta-regression tool, DisMod-MR. This tool is designed as a geographical cascade in which a first model is run on all the world's data, which produces an initial global fit and estimates coefficients for predictor variables and adjustments for alternative study characteristics. The global fit adjusted by the values of random effects for each of seven GBD super-regions, the coefficients on sex, and country predictors are passed down as data to a model for each super-region, together with the input data for that geography. The same steps are repeated going from super-region to 21 region fits and then to 204 fits by country.[11] Previous studies showed that DisMod-MR can produce robust and valid estimates compared with real surveillance data.[12]

Data sources

Data were collected from the Global Health Data Exchange query tool, including annual incident cases, age-standardised incidence rate, DALYs, and age-standardised DALY rate, with 95% uncertainty intervals (UIs), by sex, region and super-region, country, and STI cause from 1990 to 2019. Countries and territories were further categorised into five SDI quintiles. WHO has identified nine infections (excluding human papillomavirus and HIV) with a predominantly sexual mode of transmission in the International Classification of Diseases, 10th version. Of these nine STIs, the GBD only included five STIs, comprising syphilis, chlamydia, gonorrhoea, trichomonas, and genital herpes, because they contribute to the highest STI disease burden (95·4% of global STI DALYs).

Therefore, we restricted our analysis to these infections. We categorised age into four groups (adolescents, aged 10–24 years; young adults, aged 25–44 years; middle-aged adults, aged 45–64 years; and older people, aged 65 years or older).

Statistical analysis

The age-standardised incidence rate was directly extracted from the GBD database, and age-standardised DALY rate was calculated using the following formula:

$$\text{Age standardised DALY rate (per 100 000 population)} = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} w_i} \times 100\,000$$

where a_i is the DALY rate in the ith age group and w_i is the number of GBD standard populations in the same age group. Furthermore, estimated annual percentage changes in age-standardised rates were estimated to quantify the changing trends within a specific time interval. The natural logarithm of age-standardised rates is assumed to fit a linear regression model, $Y=\alpha+\beta X+\varepsilon$, in which Y is equal to the natural logarithm of age-standardised rates, α is a constant, β indicates the positive or negative changing trends, X refers to calendar year, and ε is error. Thus, estimated annual percentage changes $=100\times(e^{\beta}-1)$.

Finally, a hierarchy cluster analysis was done to categorise the countries into clusters in terms of their estimated annual percentage changes in age-standardised incidence rates (appendix 2 p 2). All statistical analyses were done in R (version 3.5.3).

This analysis adheres to the Guidelines for Accurate and Transparent Health Estimates Reporting (appendix 2 pp 3–4).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit the study for publication.

Results

Globally, in 2019, the age-standardised incidence rate of STIs was 9535·71 per 100 000 person-years (95% UI 8169·73–11 054·76) and the age-standardised DALY rate was 22·74 per 100 000 person-years (14·37–37·11). There were 769·85 million (558·68–1033·71) incident cases of STIs and 1·31 million (0·80–2·20) DALYs caused by STIs in 2019 (table 1).

The highest age-standardised incidence rates were observed in the regions of sub-Saharan Africa and Latin America and Caribbean, whereas the lowest age-standardised incidence rates were seen in North America, western Europe, and Australasia (figure 1A). Syphilis, herpes, and trichomonas shared a similar geographical pattern of age-standardised incidence rate as total STIs. However, chlamydia and gonorrhoea showed different geographical patterns from the total STIs. In addition to the sub-Saharan African region, the highest age-standardised incidence rate was also identified in central Asia, east Asia, and southeast Asia for chlamydia and in eastern Europe and central Asia for gonorrhoea (appendix 2 pp 5–9). Age-standardised DALY rates varied considerably across the world, with the highest DALY rates found in sub-Saharan Africa, southeast Asia, and Oceania and the lowest found in North America, western Europe, and Australasia (appendix 2 p 10).

The most pronounced increase in age-standardised incidence rate was detected in the region of central Latin America, whereas the most substantial decrease was detected in Southern sub-Saharan Africa and east Asian regions (figure 1B; table 2). According to the results of the cluster analysis (appendix 2 pp 11–12), 29 countries were categorised into the increase group, 118 countries were categorised into the stable group, 49 countries were categorised into the minor decrease group, and eight countries were categorised into the substantial decrease group. The changing trends of the age-standardised incidence rate for each country are presented (appendix 2 pp 13–14). Gonorrhoea and chlamydia had decreasing age-standardised incidence rates, syphilis and herpes had stable age-standardised incidence rates, whereas trichomonas had increasing age-standardised incidence rates between 1990 and 2019. The age-standardised DALY rate of total STIs decreased by an average of –0·92 (95% UI –1·01 to –0·84)per year globally (table 2). Syphilis, gonorrhoea, and chlamydia exhibited declining trends in age-standardised DALY rates, whereas for the other STIs they remained constant between 1990 and 2019 (appendix 2 pp 19–28).

See Online for appendix 2

Despite the decline in the age-standardised incidence rates and age-standardised DALY rates, the global incident cases and DALYs of total STIs increased between 1990 and 2019 (table 1). The incident cases of STIs increased from 486·77 million (95% UI 355·60–650·73) in 1990 to 769·85 million (558·68–1033·71) in 2019 (figure 1C; table 1). 176 countries had increased incident cases, whereas 28 countries had decreased incident cases from 1990 to 2019 (appendix 2 pp 29–63). The geographical pattern of incident cases for the five individual STIs was roughly similar to that of total STIs (appendix 2 pp 5–9). Accordingly, total STI DALYs also increased from 0·99 million (0·65–1·53) to 1·31 million (0·80–2·20) from 1990 to 2019 globally (table 1). 164 countries had increased DALYs and 40 countries had decreased DALYs (appendix 2 p 10).

For SDI quintiles, the age-standardised incidence rate of total STIs was decreasing except for high SDI; the number of incident cases for total STIs steadily grew from 1990 to 2019 (table 1; figure 2). Low-SDI countries had the highest age-standardised incidence rate of total STIs, followed by middle-SDI countries, and high-SDI countries had the lowest age-standardised incidence rate. Trichomonas was the STI with the highest

	1990				2019			
	Incidence		DALY		Incidence		DALY	
	Number	Age-standardised rate	Number	Age-standardised rate	Number	Age-standardised rate	Number	Age-standardised rate
Global	486 770 168 (355 604 077–650 728 006)	9323·71 (7994·18–10 804·75)	986 335 (647 481–1 529 032)	27·94 (18·69–42·72)	769 850 699 (55 867 694–1 033 713 444)	9535·71 (8169·73–11 054·76)	1 307 700 (800 832–2 196 658)	22·74 (14·37–37·11)
Gender								
Male	271 107 822 (195 907 263–365 646 646)	10 369·15 (8814·94–12 091·21)	288 970 (183 297,434 973)	16·15 (10·51–23·83)	426 071 454 (30 713 613–574 837 816)	10 471·63 (8892·20–12 176·10)	358 341 (219 070–574 559)	12·11 (7·63–18·93)
Female	215 662 346 (159 696 814–285 081 361)	8262·58 (7107·40–9594·72)	697 365 (464 184–1 094 060)	39·87 (26·93–61·88)	343 779 244 (25 154 081–458 875 628)	8602·40 (7358·00–10 001·18)	949 359 (581 761–1 622 099)	33·31 (21·05–55·25)
Age group, years								
10–24	108 215 522 (82 754 825–140 457 249)	18 076·58 (13 658·04–23 359·86)	183 638 (125 583–270 415)	30·32 (20·59–45·40)	131 983 286 (10 104 818–170 326 992)	18 377·82 (14 040·38–23 443·31)	188 350 (123 650–294 102)	26·05 (16·75–41·24)
25–44	294 335 773 (213 351 562–394 778 206)	16 872·65 (12 248·83–22 601·24)	532 061 (344 522–835 990)	33·60 (21·83–52·95)	460 671 640 (33 270 991–620 083 481)	17 385·71 (12 796·18–23 036·80)	703 976 (425 912–1 187 508)	28·43 (17·45–47·60)
45–64	77 264 701 (54 367 504–106 176 312)	3930·18 (2959·03–5209·93)	210 037 (135 094–331 166)	21·38 (14·52–32·37)	161 863 668 (11 363 865–222 764 414)	3983·50 (3039·36–5192·47)	324 175 (193 118–562 313)	14·93 (9·52–24·77)
>65	6 954 172 (5 130 186–9 316 239)	1127·38 (837·15–1496·12)	60 600 (42 281–91 460)	14·92 (10·69–21·4)	15 332 106 (11 280 193–20 538 557)	1154·52 (869·74–1506·69)	91 199 (58 152–152 735)	9·54 (6·66–14·70)
SDI region								
High SDI	53 073 581 (37 602 067–73 103 571)	5940·18 (5004·14–6988·20)	102 633 (58 087–182 785)	14·34 (8·98–23·61)	65 804 366 (46 436 468–90 950 340)	6117·57 (5136·38–7209·63)	116 831 (63 109–215 272)	12·53 (7·60–20·71)
Higher-middle SDI	112 059 779 (81 461 496–150 016 820)	9238·83 (7913·02–10 785·43)	165 428 (102 208–271 837)	37·54 (20·51–64·55)	148 390 756 (10 699 429–199 593 876)	9222·42 (7864·23–10 753·14)	199 865 (113 131–351 614)	31·71 (16·95–55·02)
Middle SDI	181 587 190 (131 849 893–242 915 461)	10 830·67 (9263·26–12 636·21)	282 100 (175 274–457 973)	87·75 (39·78–168·36)	264 895 992 (19 166 289–356 295 298)	10 085·26 (8646·52–11 806·73)	387 208 (220 625–676 480)	76·86 (33·34–148·74)
Lower-middle SDI	89 265 353 (65 294 115–119 104 275)	8906·49 (7649·99–10 325·71)	246 860 (167 841–364 989)	173·84 (73·45–344·79)	160 814 660 (11 726 885–215 359 905)	8883·31 (7608·08–10 298·21)	342 193 (218 696–540 942)	125·01 (53·77–244·69)
Low SDI	50 472 735 (36 922 943–67 349 145)	11 817·48 (10 145·19–13 761·86)	188 721 (109 076–291 564)	437·18 (174·28–874·70)	107 712 475 (78 456 661–144 316 335)	10 933·50 (9332·30–12 773·10)	260 686 (159 687–421 691)	264·04 (111·65,510·94)
Type of STI								
Syphilis	8 844 181 (4 659 297–14 687 958)	160·03 (120·66–208·10)	123 337 (82 038–163 900)	3·58 (2·22–4·83)	14 112 902 (7 547 124–23 387 744)	178·48 (134·94–232·34)	100 156 (72 719–132 281)	1·67 (1·18–2·20)
Gonorrhoea	67 732 225 (40 396 245–108 811 109)	1178·58 (912·29–1536·00)	154 842 (115 981–193 708)	4·34 (3·09–5·49)	87 951 953 (52 448 062–140 828 948)	1124·39 (872·97–1441·08)	162 925 (122 976–212 083)	2·78 (2·08–3·63)
Chlamydia	151 695 680 (88 289 761–237 249 126)	2867·67 (2150·60–3741·43)	121 117 (83 425–172 747)	3·31 (2·17–4·93)	232 534 841 (13 425 412–364 885 684)	2883·87 (2161·21–3762·80)	159 666 (105 008–237 270)	2·77 (1·75–4·28)
Trichomonas	205 446 488 (115 144 596–331 143 082)	4157·14 (3061·97–5439·34)	168 622 (56 206–393 493)	4·93 (1·68–11·25)	354 466 575 (20 064 095–567 037 408)	4327·29 (3176·53–5645·76)	287 193 (95 744–668 822)	5·15 (1·79–11·55)
Genital herpes	53 051 595 (37 722 348–72 435 538)	960·29 (822·81–1116·81)	142 425 (45 887–350 194)	4·47 (1·45–10·78)	80 784 427 (56 090 742–111 904 107)	1021·68 (869·15–1191·20)	252 863 (80 515–624 044)	4·60 (1·51–10·97)
Southeast Asia, east Asia, and Oceania								
Southeast Asia	49 962 312 (36 465 760–66 863 524)	11 326·64 (9713·89–13 174·51)	68 849 (38 482–116 892)	99·08 (41·09–206·54)	82 548 957 (59 771 451–111 126 495)	11 230·92 (9620·76–13 068·46)	102 176 (55 718–180 003)	106·90 (41·73–219·52)
Oceania	871 372 (629 562–1 178 491)	14 588·13 (12 549·89–16 873·11)	1476 (770–2755)	550·83 (198·54–1149·10)	1 862 949 (1 327 077–2 551 633)	14 285·59 (12 118·18–16 679·43)	3046 (1498–5915)	513·40 (186·81,1022·52)
East Asia	137 725 313 (97 786 188–186 968 104)	10 607·48 (8996·37–12 490·97)	176 066 (105 545–292 462)	46·85 (23·19–85·20)	178 904 298 (12 689 593–243 433 865)	10 476·70 (8849·86–12 376·60)	204 332 (110 559–366 203)	33·07 (16·43–60·22)

(Table 1 continues on next page)

www.thelancet.com/infection Published online December 20, 2021 https://doi.org/10.1016/S1473-3099(21)00448-5

	1990				2019			
	Incidence		DALY		Incidence		DALY	
	Number	Age-standardised rate	Number	Age-standardised rate	Number	Age-standardised rate	Number	Age-standardised rate
(Continued from previous page)								
Sub-Saharan Africa								
Western	20 613 819 (14 925 098–27 697 981)	13 319·18 (11 355·57–15 603·23)	70 341 (42 083–105 431)	305·55 (124·53–614·28)	51 607 539 (37 223 337–69 740 033)	13 358·91 (11 298·50–15 721·57)	106 809 (61 174–185 516)	236·07 (96·71–462·23)
Southern	10 475 890 (7 763 165–13 789 542)	21 090·11 (18 370·38–24 194·60)	26 756 (16 287–43 797)	591·30 (240·31–1142·86)	16 722 273 (12 327 860–22 137 341)	19 973·12 (17 382·69–23 001·57)	31 119 (17 303–55 281)	361·62 (146·45,699·97)
Central	5 650 861 (4 190 599–7 518 006)	12 289·81 (10 723·69–14 164·84)	21 217 (9330–42 266)	676·76 (257·14–1322·85)	14 097 679 (10 433 614–18 756 549)	12 093·61 (10 531·43–13 910·25)	34 015 (17 546–63 702)	389·32 (154·27,769·74)
Eastern	26 026 243 (18 926 032–35 039 265)	17 597·87 (14 939·06–20 625·45)	98 323 (49 930–167 050)	699·93 (280·07–1388·07)	59 742 580 (42 843 960–81 206 350)	17 033·30 (14 330·44–20 087·35)	134 134 (76 704–222 757)	375·74 (161·83,726·19)
South Asia	67 171 973 (48 180 193–91 489 187)	6818·42 (5796·52–8055·92)	228 647 (156 410–329 398)	163·05 (66·57–324·83)	125 287 371 (89 897 477–170 476 074)	6652·49 (5662·30–7819·84)	306 971 (199 689–467 091)	93·51 (40·05–184·97)
Latin America and Caribbean								
Tropical	18 910 417 (13 769 274–25 320 622)	12 809·55 (10 978·92–14 976·17)	34 392 (20 475–59 381)	58·47 (44·93–79·20)	32 029 014 (23 139 204–43 229 856)	12 955·71 (11 074·32–15 125·80)	53 793 (29 565–98 156)	45·31 (31·36–65·25)
Caribbean	4 325 380 (3 143 653–5 834 281)	12 460·65 (10 649·93–14 467·67)	8788 (4919–15 344)	188·92 (78·51–375·84)	6 136 811 (4 433 897–8 307 650)	12 540·87 (10 720·36–14 571·42)	12 494 (7262–21 314)	240·97 (101·17,475·04)
Andean	3 163 525 (2 321 175–4 211 858)	9278·14 (7938·01–10 763·57)	6525 (3675–11 364)	199·92 (74·27–415·70)	6 028 737 (4 349 716–8 128 642)	9213·75 (7866·87–10 748·10)	11 255 (6020–20 345)	96·72 (41·73–190·20)
Central	18 546 425 (13 503 869–24 845 078)	12 590·93 (10 713·35–14 664·66)	30 788 (17 709–54 180)	31·03 (21·28–47·30)	33 539 477 (24 060 651–45 425 473)	12 756·44 (10 798·14–14 937·03)	53 454 (28 982–98 071)	23·40 (14·88–38·77)
North Africa and Middle East	28 844 960 (20 882 434–39 073 339)	9552·82 (8178·98–11 091·56)	37 121 (20 692–64 326)	54·87 (24·58–108·22)	58 679 256 (42 291 766–79 623 992)	8946·10 (7619·55–10 371·37)	75 868 (41 357–132 777)	50·16 (22·41–98·43)
Central Europe, eastern Europe, and central Asia								
Central Asia	8 196 692 (5 787 087–11 418 542)	12 383·96 (10 497·47–14 530·25)	12 839 (8012–20 576)	30·78 (21·29–44·94)	12 178 672 (86 351 12–16 849 338)	12 235·85 (10 365·83–14 354·40)	15 684 (8889–27 207)	27·02 (16·80–42·58)
Central Europe	11 629 240 (8 370 597–15 800 012)	9173·26 (7807·47–10 696·18)	14 003 (8114–24 181)	14·72 (9·28–23·57)	10 679 915 (7 665 676–14 503 295)	9126·48 (7756·82–10 664·06)	11 678 (6223–21 482)	11·12 (6·89–17·81)
Eastern Europe	23 434 721 (16 939 256–31 676 464)	9909·11 (8510·07–11 739·04)	40 249 (26 063–62 982)	17·06 (12·29–25·42)	21 459 578 (15 447 391–29 043 785)	9895·41 (8480·04–11 724·59)	32 070 (19 628–54 278)	13·43 (8·87–21·23)
High-income regions								
Western Europe	15 705 098 (10 833 157–22 100 655)	3768·35 (3139·71–4497·39)	30 885 (17 939–54 373)	9·01 (5·73–14·75)	17 190 109 (11 778 884–24 288 129)	3729·40 (3099·27–4444·56)	30 920 (16 253–58 704)	7·97 (4·75–13·66)
Southern Latin America	2 747 355 (1 998 411–3 721 908)	5654·43 (4850·87–6571·61)	7905 (4717–13 276)	26·88 (20·71–37·43)	3 990 237 (2 832 999–5 454 322)	5651·23 (4849·22–6583·30)	10 140 (5725–17 899)	17·05 (11·49–26·75)
North America	20 552 235 (14 003 831–29 205 467)	6692·36 (5494·37–8065·15)	46 176 (25 382–84 791)	14·97 (8·75–26·25)	24 479 585 (16 686 149–34 873 022)	6489·07 (5320·69–7797·60)	51 783 (27 330–97 755)	12·78 (7·00–23·09)
Asia Pacific	11 073 015 (7 881 208–15 228 636)	5780·52 (4877·69–6788·02)	22 304 (12 417–39 021)	17·03 (10·40–27·05)	11 164 335 (7 828 509–15 521 487)	5705·97 (4794·87–6714·58)	22 798 (12 408–40 844)	15·92 (9·71–25·12)
Australasia	1 143 323 (811 301–1 566 006)	5247·11 (4465·01–6157·35)	2688 (1484–4744)	12·64 (7·92–20·83)	1 521 326 (1 068 808–2 109 776)	5018·90 (4251·70–5907·28)	3163 (1642–5845)	10·15 (5·88–17·45)

Data are presented as point estimates with 95% uncertainty intervals. Age-standardised rates are per 100 000 person years. DALYs=disability-adjusted life years. STIs=sexually transmitted infections. SDI=social development index.

Table 1: **The number and age-standardised rate of incidence and DALYs of STIs in 1990 and 2019**

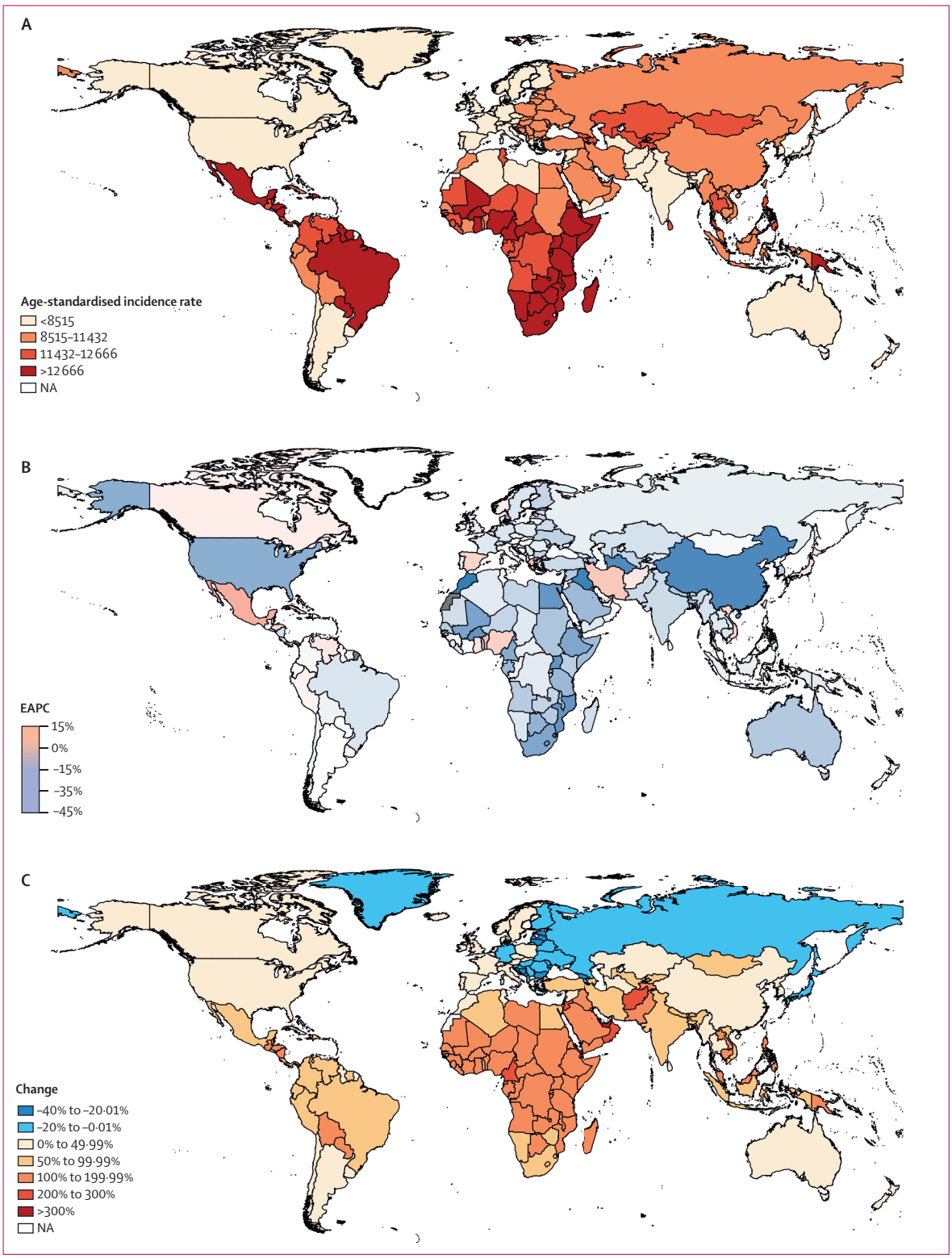

Figure 1: **Age-standardised incidence rate in 2019, EAPC in age-standardised incidence rates, and change of incident cases between 1990 and 2019 for total STIs**

(A) Age-standardised incidence rate per 100 000 person-years in 2019. (B) EAPC of age-standardised incidence rate between 1990 and 2019. (C) Change of incident cases from 1990 to 2019. EAPC=estimated annual percentage change. NA=not applicable. STIs=sexually transmitted infections.

age-standardised incidence rate and incident cases, followed by chlamydia, and syphilis had the lowest age-standardised incidence rate and incident cases of all SDIs.

For SDI quintiles, the age-standardised DALY rate decreased or remained stable for total STIs, whereas the DALYs increased from 1990 to 2019 (table 1; appendix 2 p 15). High-SDI countries had stable low age-standardised DALY rates. Low-SDI, lower-middle-SDI, middle-SDI, and higher-middle-SDI countries had much higher age-standardised DALY rates before 2010, but then saw rates decline to rates similar to high-SDI countries. Notably, for syphilis, the age-standardised DALY rate declined drastically, from 14·17 per 100 000 person-years (4·29–27·65) in 1990 to 5·20 per 100 000 person-years (2·37–8·84) in 2019, for low-SDI countries.

Age-specific STI incidence rates are presented (figure 3). Among the four age groups, adolescents had the highest incidence rate (table 1), followed by young adults, middle-aged adults, and older adults, both for total STIs and individual STIs, with the exception of trichomonas, for which young adults ranked first for incidence rate, surpassing adolescents. With regard to trends, the incidence rate of total STIs and each STI in all age groups were stable between 1990 and 2019, except for syphilis, for which an upward trend was noted in adolescents from 347·65 per 100 000 person-years (95% UI 203·58–590·69) in 2010 to 423·16 per 100 000 person-years (235·70–659·01) in 2019 (appendix 2 pp 19–28). Incident cases were greatest in young adults and lowest in older adults (appendix 2 p 16). Young adults and adolescents had similar DALY rates, which were higher than those of middle-aged adults and older adults (appendix 2 p 17). For trends, syphilis, gonorrhoea, and chlamydia had decreasing DALY rates, whereas the DALY rates of other STIs were stable for all age groups (with the exception of herpes in older adults).

The age-standardised incidence rate and incident cases were higher in male individuals, whereas the age-standardised DALY rate and DALYs were disproportionately higher in female individuals for total STIs (appendix 2 p 18; table 1). For specific STIs, the age-standardised DALY rate of syphilis in male individuals decreased up to 2010 and then stayed at a low rate similar to other STIs. Trichomonas caused the largest DALYs with the highest age-standardised DALY rate in female individuals.

Discussion

To our knowledge, this is the first comprehensive report on the disease burden of curable STIs and their trends from 1990 to 2019 at the global, regional, and country levels. Our results have highlighted several key points. Considerable variation (up to five times) in the burden and trends in total and particular STIs across the globe was found in our analysis. In general, sub-Saharan Africa and Latin America and the Caribbean were the so-called hotspot regions with the highest age-standardised incidence rate of total STIs in 2019. Most countries

	Incidence	DALY
Global	−0·04 (−0·08 to 0·00)	−0·92 (−1·01 to −0·84)
Gender		
Male	−0·04 (−0·08 to 0·00)	−1·28 (−1·39 to −1·17)
Female	−0·04 (−0·08 to 0·01)	−0·81 (−0·88 to −0·75)
Age group, years		
10–24	−0·05 (−0·05 to −0·05)	−0·73 (−0·81 to −0·65)
25–44	−0·06 (−0·06 to −0·05)	−0·78 (−0·85 to −0·7)
45–64	0·04 (0·03 to 0·05)	−1·49 (−1·59 to −1·39)
>65	0·06 (0·05 to 0·07)	−1·82 (−1·94 to −1·70)
SDI region		
High SDI	0·06 (0·01 to 0·12)	−0·34 (−1·46 to 0·80)
Higher-middle SDI	−0·20 (−0·24 to −0·15)	−0·66 (−1·34 to 0·02)
Middle SDI	−0·15 (−0·19 to −0·11)	−0·55 (−1·00 to −0·09)
Lower-middle SDI	−0·05 (−0·10 to −0·01)	−1·45 (−1·78 to −1·13)
Low SDI	−0·09 (−0·13 to −0·06)	−2·05 (−2·28 to −1·83)
Type of STI		
Syphilis	0·17 (−0·16 to 0·49)	−3·23 (−3·49 to −2·97)
Gonorrhoea	−0·13 (−0·25 to −0·01)	−1·75 (−1·97 to −1·53)
Chlamydia	−0·21 (−0·28 to −0·13)	−0·83 (−1·07 to −0·60)
Trichomonas	0·06 (0·00 to 0·13)	−0·02 (−0·20 to 0·17)
Genital herpes	0·09 (−0·04 to 0·22)	−0·01 (−0·20 to 0·19)
Southeast Asia, east Asia, and Oceania		
Southeast Asia	−0·03 (−0·07 to 0·00)	0·40 (−0·01 to 0·81)
Oceania	0·01 (−0·03 to 0·04)	−0·74 (−0·91 to −0·57)
East Asia	−0·40 (−0·44 to −0·36)	−0·75 (−1·38 to −0·10)
Sub-Saharan Africa		
Western	−0·01 (−0·05 to 0·02)	−0·83 (−1·09 to −0·57)
Southern	−0·26 (−0·29 to −0·23)	−1·85 (−2·05 to −1·65)
Central	−0·07 (−0·11 to −0·03)	−2·47 (−2·63 to −2·30)
Eastern	−0·22 (−0·25 to −0·19)	−2·54 (−2·72 to −2·35)
South Asia	−0·11 (−0·16 to −0·06)	−2·22 (−2·57 to −1·88)
Latin America and Caribbean		
Tropical	−0·06 (−0·10 to −0·03)	−0·71 (−1·30 to −0·11)
Caribbean	−0·01 (−0·04 to 0·03)	0·62 (0·32 to 0·91)
Andean	0·00 (−0·05 to 0·04)	−3·51 (−3·85 to −3·17)
Central	0·11 (0·08 to 0·15)	−0·92 (−1·72 to −0·10)
North Africa and Middle East	−0·20 (−0·25 to −0·16)	−1·17 (−1·69 to −0·65)
Central Europe, eastern Europe, and central Asia		
Central Asia	−0·10 (−0·13 to −0·06)	−0·64 (−1·39 to 0·12)
Central Europe	−0·04 (−0·09 to 0·00)	−1·04 (−2·18 to 0·12)
Eastern Europe	−0·06 (−0·10 to −0·02)	−1·91 (−2·86 to −0·95)
High-income regions		
Western Europe	−0·03 (−0·09 to 0·04)	−0·01 (−1·42 to 1·42)
Southern Latin America	−0·01 (−0·06 to 0·05)	−1·48 (−2·39 to −0·56)
North America	−0·24 (−0·29 to −0·19)	−0·74 (−1·83 to 0·37)
Asia Pacific	−0·02 (−0·08 to 0·03)	0·00 (−1·04 to 1·05)
Australasia	−0·15 (−0·21 to −0·09)	−0·62 (−1·87 to 0·64)

Data are presented as point estimates with 95% uncertainty intervals. DALYs=disability-adjusted life-years. STIs=sexually transmitted infections. SDI=social development index.

Table 2: **Estimated annual percentage change of age-standardised rates from 1990 to 2019**

showed a decrease in age-standardised incidence and DALY rates, whereas the incident cases and DALYs increased from 1990 to 2019. Adolescents have a higher STI burden than other age groups, and an upward trend of the age-standardised incidence rate was revealed among the young population in developed countries after 2010. Male individuals had higher age-standardised incidence rates and incident cases, but female individuals were more affected by STIs, as indicated by their higher age-standardised DALY rates and DALYs.

We identified that sub-Saharan Africa and Latin America and the Caribbean had the highest age-standardised incidence rates of total STIs, whereas North America, western Europe, and Australasia had the lowest. The geographical pattern of STIs in our study aligns with previous WHO findings in 1999,[8] in which sub-Saharan Africa, south and southeast Asia, and Latin America had the highest age-standardised incident rate. WHO re-estimated the age-standardised incidence rate of syphilis, gonorrhoea, chlamydia, and trichomonas, indicating that sub-Saharan African and Latin American countries were still the most affected regions in 2016.[1] The reasons for the high disease burden in sub-Saharan African and Latin American countries are probably attributed to long-term poverty, poor access to health care, a lower awareness regarding sexual health, inadequate screening, and a lower proportion of treatment, which together make low-income countries more susceptible to STIs than high-income countries.[13] Thus, in the subsequent campaign of eliminating STIs, more attention and health resources were warranted in low-income countries.

Although most countries exhibited a decreasing trend in the age-standardised incident rate, the number of incidence cases increased between 1990 and 2019. Many reasons might explain the increase, one of which was growth in the sexually active population.[14] The most rapid population growth was found in sub-Saharan African countries, whereas negative growth was found in Japan and some European countries, which is largely consistent with changes in incidence STI cases in these regions.[14] In addition, the scaling up of STI testing in many countries might also have contributed to an increase in identified cases globally, as evidenced by expanded screening of asymptomatic individuals and routine testing of at-risk populations.[15]

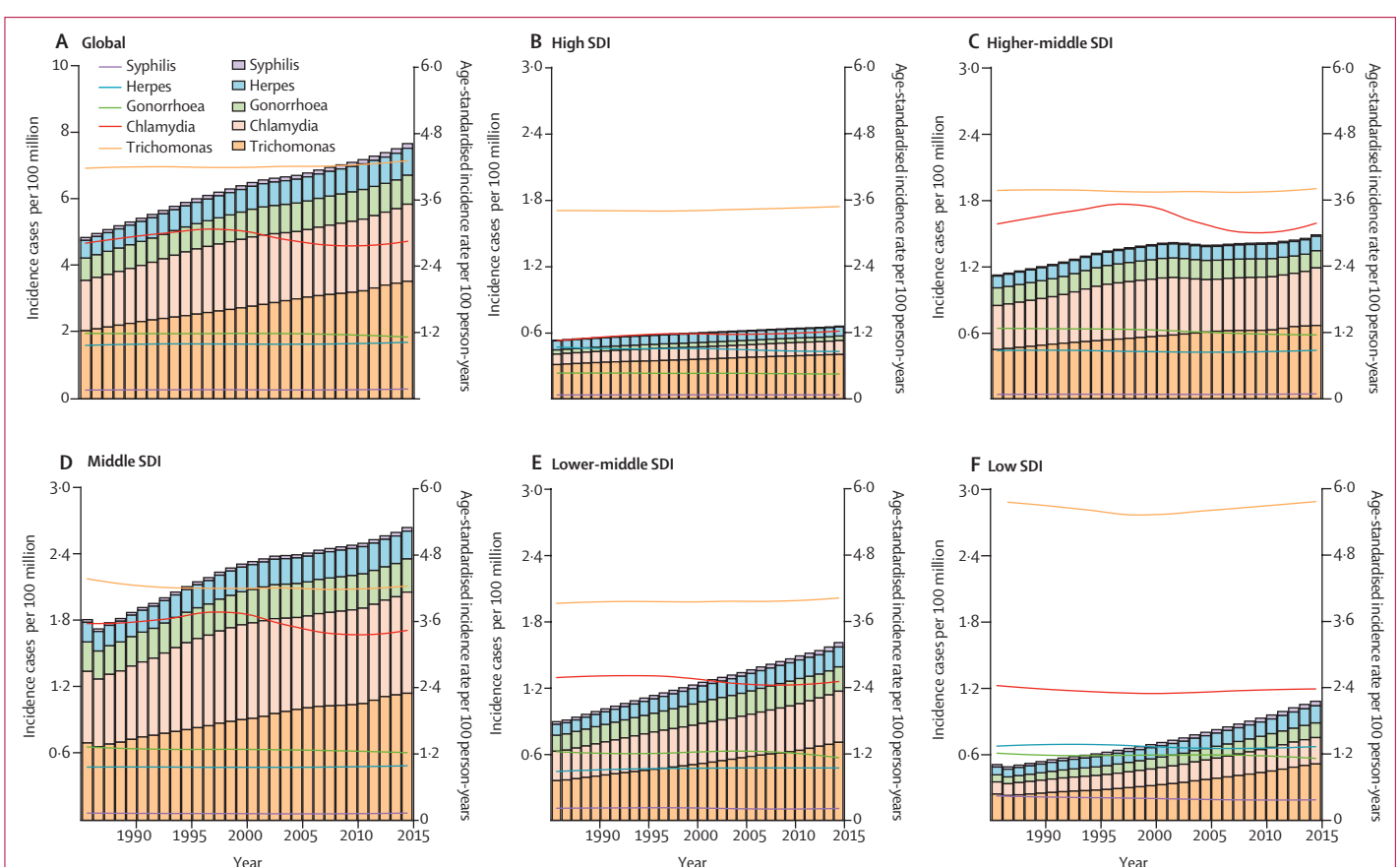

Figure 2: **Age-standardised incidence rate and incident cases of STIs among SDI quintiles between 1990 and 2019**
Age-standardised incidence rate and incident cases of STIs globally (A), in high-SDI countries (B), higher-middle-SDI countries (C), middle-SDI countries (D), lower-middle-SDI countries (E), and low-SDI countries (F). STI=sexually transmitted infection. SDI=social development index.

Of note, a sharp decrease in the age-standardised incidence rate was particularly observed in China and Morocco, possibly because of strong government commitment and leadership.[16] In China, it is mandatory to report new cases of HIV and AIDS, syphilis, and gonorrhoea to the surveillance system at community, provincial, and national levels. Accurate surveillance data are crucial for developing a prevention-and-control programme and providing valuable measures to assess the impact of those programmes.[16] In Morocco, similar practices were implemented, including political engagement at all levels and all phases of STI control, integration of activities into basic health care, and robust epidemiological surveillance.[17] The experience in China and Morocco could inform STI control strategies in developing countries, with a greater focus on government commitment and close collaboration between different sectors.

Adolescents were found to have disproportionately high incidence rates and DALY rates in total STIs, which might be due to both behavioural and physiological factors. Behaviourally, adolescents are more likely to engage in risky sexual behaviours, such as multiple partners and unprotected sex, and usually have poorer access to sexual health services than adults.[18] Physiologically, reproductive organs are relatively immature, making adolescents more susceptible to STI infection.[19] Thus, the higher incidence rate in adolescents might be caused by high exposure risk and more efficacy of transmission, and the high DALY rate in adolescents could be the result of poor access to treatment. Unlike other STIs, trichomonas showed higher rates of infection in people aged 25–50 years than in adolescents, which is consistent with previous studies.[20] However, the reason is still unknown.[20] Our findings call for an urgent need to accelerate efforts to reduce STIs burden in adolescents. Previous successfully implemented programmes could inform further interventions in adolescents. For example, the National Chlamydia Screening Programme reduced onward transmission and consequences of untreated infections in England.[21] In addition, studies have suggested that the combination of different sources, including parents, schools, and social media, contributed to communicating prevention messages to specific, targeted young audiences to promote safe-sex practices and access to treatment.[22]

Notably, we revealed an increasing incidence rate of syphilis after 2010 in adolescents. This upward trend is

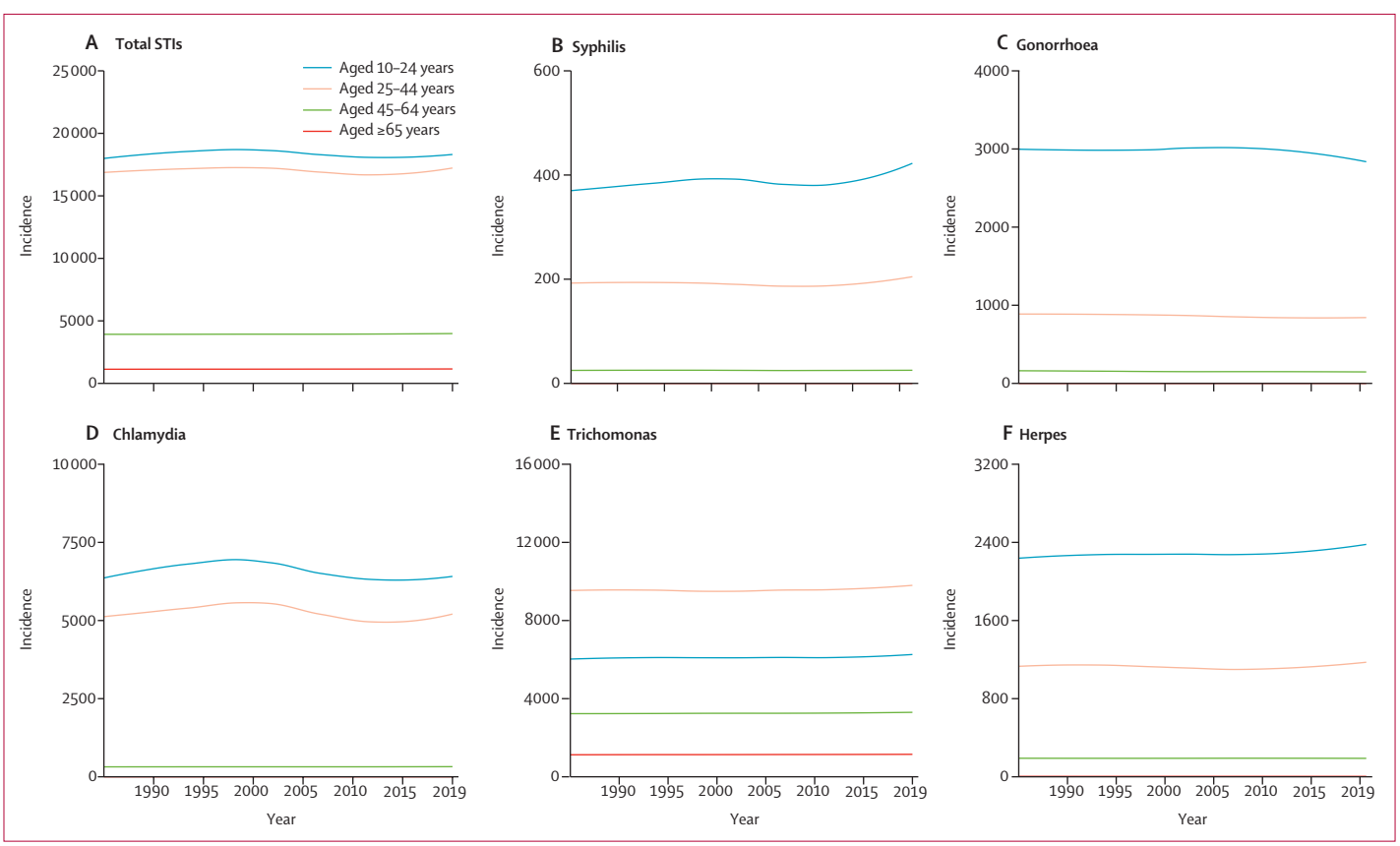

Figure 3: **Incidence rate of STIs among different age groups between 1990 and 2019**
Incidence rate per 100 000 person-years of STIs among different age groups for total STIs (A), syphilis (B), gonorrhoea (C), chlamydia (D), trichomonas (E), and genital herpes (F). Lines represent the incidence rate of each age group (blue, adolescent; orange, young adult; green, middle-aged adult; and red, older people). STI=sexually transmitted infection

probably related to an increase in risky sexual practices in high-risk populations, typically young men who have sex with men (MSM) in high-income countries.[23] As reported in the USA, syphilis incidence has seen the most marked increase since 1993. Until 2016, more than 58% of cases of syphilis were among young MSM.[18] Similarly in western Europe, there was an increasing incidence rate and number of incident cases of syphilis in MSM, yet a decreasing or stable incidence rate was noticed in female individuals and heterosexual male individuals in 2018.[24] The probable causes for the increase in syphilis among MSM might include condom fatigue, complacency about HIV, optimism about HIV treatments, and the adoption of seroadaptive strategies.[25] Despite the success of new HIV-prevention measures in MSM (eg, pre-exposure prophylaxis and HIV treatment as prevention), traditional evidence-based risk-reduction interventions still need to be strengthened in high-risk populations.

Male individuals generally had a higher age-standardised incidence rate but a lower age-standardised DALY rate than female individuals for total STIs, which aligned with previous studies,[26] possibly because of differences in sexual behaviours and anatomy. Behaviourally, male individuals tend to have an earlier sexual debut, a higher rate of partner changes, more sexual partners, and more control and dominance over condom use than women.[27] However, female individuals were more severely affected by STIs because of anatomical physiological characteristics. Infections in female individuals are likely to be asymptomatic or have symptoms that are confused with normal vaginal discharge, which can result in late diagnosis or no diagnosis. If left untreated, some STIs can lead to serious long-term complications, including pelvic inflammatory diseases, infertility, and gynaecological tumours in female individuals.[3]

A notable exception to this trend is syphilis, for which male individuals had a substantially higher age-standardised DALY rate than female individuals. Although men were more likely to contract STIs, syphilis diagnosis and treatment were more satisfactory in women because guidelines from many countries specifically target screening of the female population, as exemplified by pregnancy antenatal testing.[28] In addition, highly effective therapy for syphilis has become readily accessible, ensuring a good prognosis of early diagnosed syphilis.[29] By contrast, there is no explicit recommendation for syphilis diagnosis or therapy for men. We also revealed a decreasing trend of syphilis age-standardised DALY rates in both sexes. This finding agreed with the declining syphilis age-standardised DALY rate in the low-SDI and middle-SDI countries, which was attributed to advances in testing methods in these countries over the past 20 years.[30] Many new testing methods that provided rapid results, high sensitivity, and specificity were available, which greatly improved testing uptake and effectively eliminated 98% of congenital syphilis through early treatment.[29]

Several limitations of our study should be acknowledged. First, raw data are not available for all countries, especially developing countries, where estimates rely on Bayesian regression methods, which can lead to an underestimation of disease burden in these countries. Second, our analysis was restricted to only five common STIs. Other STIs are not included because of the small proportion of global burden or are already well reported (eg, HIV infection). Third, the 95% UIs are frequently wide, reflecting the low precision of the estimates and potentially limiting our ability to detect smaller differences among countries. Fourth, the GBD database only collected information on binary sexes but excluded individuals of other sexes disaggregated by sexual orientation. Fifth, the testing and diagnosis of STIs and their definition might not be consistent across the countries, which might affect the comparability of estimates. However, Bayesian modelling methods were used to reconcile data collected from different sources, correct for inconsistencies, and fill in gaps when data were incomplete, ultimately producing estimates of STIs.

Most countries had a decrease in age-standardised rates of incidence and DALY for STIs, whereas the absolute incident cases and DALYs increased from 1990 to 2019. Therefore, STIs still represent a global public health challenge, especially in sub-Saharan Africa and Latin America, where more attention and health prevention services are warranted. Our study also suggested an upward trend of age-standardised incidence rates among young populations, especially for syphilis, after 2010. Thus, there remains an urgent need to accelerate efforts to reduce STIs burden in this population.

Contributors

JW, YaZ, and SY designed the study. YaZ, QY, YL, and JW accessed and verified the data. YaZ and JW analysed the data and interpreted the results. YaZ and JW wrote the manuscript. All authors revised the manuscript from the preliminary draft to submission. JW supervised the whole study and is responsible for the decision to submit the manuscript for publication.

Declaration of interests

We declare no competing interests.

Data sharing

All data are open-access and are available from the Global Health Data Exchange query tool (http://ghdx.healthdata.org/gbd-results-tool).

Acknowledgments

This study was funded by Mega-Project of National Science and Technology for the 13th Five-Year Plan of China (2018ZX10721102-003-006 and 2018ZX10715013-003-003) and the National Natural Science Foundation of China (71904170). We are also grateful for the GBD Study 2019, which provided the original data for this study.

References

1 Rowley J, Vander Hoorn S, Korenromp E, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. *Bull World Health Organ* 2019; **97:** 548–62P.

2 Looker KJ, Johnston C, Welton NJ, et al. The global and regional burden of genital ulcer disease due to herpes simplex virus: a natural history modelling study. *BMJ Glob Health* 2020; **5:** e001875.

3 WHO. Report on global sexually transmitted infection surveillance 2018. https://www.who.int/reproductivehealth/publications/stis-surveillance-2018/en/ (accessed Jan 31, 2021).

4 WHO. Global health sector strategy on sexually transmitted infections 2016–2021. https://www.who.int/reproductivehealth/publications/rtis/ghss-stis/en/ (accessed Jan 31, 2021).

5 Low N, Broutet N, Adu-Sarkodie Y, Barton P, Hossain M, Hawkes S. Global control of sexually transmitted infections. *Lancet* 2006; **368:** 2001–16.

6 Fenton KA, Lowndes CM. Recent trends in the epidemiology of sexually transmitted infections in the European Union. *Sex Transm Infect* 2004; **80:** 255–63.

7 Steen R, Wi TE, Kamali A, Ndowa FJ. Control of sexually transmitted infections and prevention of HIV transmission: mending a fractured paradigm. *Bull World Health Organ* 2009; **87:** 858–65.

8 WHO. Global prevalence and incidence of selected curable sexually transmitted infections: overview and estimates. https://www.who.int/reproductivehealth/publications/rtis/HIV_AIDS_2001_2/en/ (accessed Jan 31, 2021).

9 Gerbase A, Rowley J, Heymann D, Berkley S, Piot P. Global prevalence and incidence estimates of selected curable STDs. *Sex Transm Infect* 1998; **74** (suppl 1)**:** S12–16.

10 The World Bank. World Development Report 1993: investing in health, volume 1. https://elibrary.worldbank.org/doi/abs/10.1596/0-1952-0890-0 (accessed May 10, 2021).

11 Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396:** 1204–22.

12 Peterson HM, Flaxman AD. Meta-regression with DisMod-MR: how robust is the model? *Lancet* 2013; **381:** S110.

13 Aral SO, Fenton KA, Holmes KK. Sexually transmitted diseases in the USA: temporal trends. *Sex Transm Infect* 2007; **83:** 257–66.

14 The World Bank. Population ages 15–64, total. https://data.worldbank.org/indicator/SP.POP.1564.TO (accessed May 10, 2021).

15 Taylor MM, Frasure-Williams J, Burnett P, Park IU. Interventions to improve sexually transmitted disease screening in clinic-based settings. *Sex Transm Dis* 2016; **43** (2 suppl 1)**:** S28–41.

16 Wang L, Wang Y, Jin S, et al. Emergence and control of infectious diseases in China. *Lancet* 2008; **372:** 1598–605.

17 Hammou J, El Ajaroumi H, Hasbi H, Nakhlaoui A, Hmadna A, El Maaroufi A. In Morocco, the elimination of trachoma as a public health problem becomes a reality. *Lancet Glob Health* 2017; **5:** e250–51.

18 Shannon CL, Klausner JD. The growing epidemic of sexually transmitted infections in adolescents: a neglected population. *Curr Opin Pediatr* 2018; **30:** 137.

19 US Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2016. Division of STD Prevention. https://www.cdc.gov/nchhstp/newsroom/2017/2016-STD-Surveillance-Report.html (accessed March 10, 2021).

20 Stemmer SM, Mordechai E, Adelson ME, Gygax SE, Hilbert DW. *Trichomonas vaginalis* is most frequently detected in women at the age of peri-/premenopause: an unusual pattern for a sexually transmitted pathogen. *Am J Obstet Gynecol* 2018; **218:** 328e1–e13.

21 Public Health England. National Chlamydia Screening Programme (NCSP). 2003. https://www.gov.uk/government/collections/national-chlamydia-screening-programme-ncsp (accessed May 10, 2021).

22 Friedman AL, Kachur RE, Noar SM, McFarlane M. Health communication and social marketing campaigns for sexually transmitted disease prevention and control: what is the evidence of their effectiveness? *Sex Transm Dis* 2016; **43** (2 suppl 1)**:** S83–101.

23 Refugio ON, Klausner JD. Syphilis incidence in men who have sex with men with human immunodeficiency virus comorbidity and the importance of integrating sexually transmitted infection prevention into HIV care. *Expert Rev Anti Infect Ther* 2018; **16:** 321–31.

24 European Centre for Disease Prevention and Control. Syphilis–annual epidemiological report for 2018. https://www.ecdc.europa.eu/en/publications-data/syphilis-annual-epidemiological-report-2018 (accessed March 10, 2021).

25 Hess KL, Crepaz N, Rose C, Purcell D, Paz-Bailey G. Trends in sexual behavior among men who have sex with men (MSM) in high-income countries, 1990–2013: a systematic review. *AIDS Behav* 2017; **21:** 2811–34.

26 Sieving RE, O'Brien JRG, Saftner MA, Argo TA. Sexually transmitted diseases among US adolescents and young adults: patterns, clinical considerations, and prevention. *Nurs Clin North Am* 2019; **54:** 207–25.

27 Wong T, Singh A, Mann J, Hansen L, McMahon S. Gender differences in bacterial STIs in Canada. *BMC Womens Health* 2004; **4:** 1–8.

28 Cantor AG, Pappas M, Daeges M, Nelson HD. Screening for syphilis: updated evidence report and systematic review for the US preventive services task force. *JAMA* 2016; **315:** 2328–37.

29 Gupte S, Daly C, Agarwal V, Gaikwad SB, George B. Introduction of rapid tests for large-scale syphilis screening among female, male, and transgender sex workers in Mumbai, India. *Sex Transm Dis* 2011; **38:** 499–502.

30 Rietmeijer CA. Improving care for sexually transmitted infections. *J Int AIDS Soc* 2019; **22** (suppl 6): e25349.