

Risk Factors and Incidence of Sexually Transmitted Infections in the Swiss HIV Cohort Study

Daive Bosetti,^{1,2,a} Catrina Mugglin,^{1,a} Alexandra Calmy,³ Matthias Cavassini,⁴ Marcel Stöckle,⁵ Dominique Braun,⁶ Julia Notter,⁷ David Haerry,⁸ Benjamin Hampel,^{9,10} Helen Kovari,¹¹ Enos Bernasconi,¹² Gilles Wandeler,² and Andri Rauch,² the Swiss HIV Cohort Study

¹Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, ²Department of Infectious Diseases, University Hospital of Geneva, University of Geneva, Geneva, Switzerland, ³HIV/AIDS Unit, Department of Infectious Diseases, Geneva, Switzerland, ⁴University Hospital of Lausanne, University of Lausanne, Lausanne, Switzerland, ⁵Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, University of Basel, Basel, Switzerland, ⁶Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Zurich, University of Zurich, Zurich, Switzerland, ⁷Division of Infectious Diseases and Hospital Epidemiology, St. Gallen, Switzerland, ⁸Positive Council Switzerland, Switzerland, ⁹Department of Public and Global Health, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland, ¹⁰Checkpoint Zurich, Zurich, Switzerland, ¹¹Zentrum für Infektionskrankheiten, Klinik im Park, Zurich, Switzerland, and ¹²Ente Ospedaliero Cantonale, Lugano, University of Geneva, and University of Southern Switzerland, Lugano, Switzerland

Background. Sexually transmitted infections (STIs) are common among people with human immunodeficiency virus (PWH), but there are limited data about risk factors and incidence of STIs in large, representative cohort studies.

Methods. We assessed incidence and risk factors of STIs reported by treating physicians within the Swiss HIV Cohort Study (SHCS). Sexually transmitted infections and demographic, clinical, and behavioral characteristics were prospectively collected at 6-month follow-up visits between October 2017 and November 2019. We used multilevel Poisson regression to assess incidence rate ratios of different STIs.

Results. Among 10 140 study participants, a total of 1634 STIs in 1029 SHCS participants were reported over 17 766 person-years of follow up (PYFUP). The overall incidence of any reported STI was 91.9 per 1000 PYFU (95% confidence interval [CI], 85.8–98.5). Among the 1634 STI episodes, there were 573 (35.1%) incident cases of syphilis, 497 gonorrhea (30.4%), and 418 chlamydia (25.6%). Men who have sex with men (MSM) younger than 50 years represented 21% of the study population, but accounted for 61% of reported STIs. Male sex (adjusted incidence rate ratio [aIRR], 2.03; 95% CI, 1.36–3.02), MSM (aIRR, 3.62; 95% CI, 2.88–4.55), age group 18–34 years (aIRR, 1.78; 95% CI, 1.51–2.10), history of sexual relationships with occasional partners (aIRR, 6.87; 95% CI, 5.40–8.73), and reporting injecting drug use (aIRR, 2.48; 95% CI, 1.91–3.23) were associated with a higher risk of incident STIs.

Conclusions. Sexually transmitted infections were frequent among PWH and varied considerably between age and risk groups. Screening programs and recommendations for STI testing need to be adapted according to risk factors and demographic characteristics.

Keywords. HIV; MSM; STI; incidence.

Sexually transmitted infections (STIs) are frequent among people with human immunodeficiency virus (PWH) [1–4]. Several reports described increasing trends in STIs incidence among PWH [3, 5]. For example, in the Swiss HIV Cohort Study (SHCS), syphilis incidence increased from 30.1 to 59.2 per 1000 patient-years between 2006 and 2017 [5, 6].

Improved screening methods, intensified testing campaigns, accessibility to point-of-care testing, but also increased

transmission rates in at-risk populations contribute to the rise in diagnosed STIs [7]. Among PWH, increases in condomless sex and a greater number of sexual partners, as well as increased testing frequencies are associated with higher rates of STIs diagnoses [5, 6, 8–10]. There is an interplay between human immunodeficiency virus (HIV) and STIs: HIV-associated ulcerative lesions can increase the acquisition of STIs and on the other hand STIs promote local inflammation in the genital tract facilitating HIV shedding and increasing HIV-risk transmission [11].

The ability to obtain reliable incidence estimates of STIs is challenging: the majority of infections are asymptomatic, coinfections are frequent, and testing options are limited due to high costs and laboratory burden in many settings [12, 13]. Until recently, most studies investigating STIs epidemiology among PWH were limited to certain HIV transmission risk groups such as men who have sex with men (MSM), and there have been limited data about prevalence and long-term incidence of STIs in large, representative cohort studies. The aim of this nationwide representative cohort study was to assess the prevalence, incidence, and the related risk factors of the most common STIs among PWH.

Received 01 July 2022; editorial decision 27 October 2022; accepted 15 November 2022; published online 16 November 2022

^aD. B. and C. M. contributed equally to this work.

Correspondence: Catrina Mugglin, MSc, MD, PhD, Inselspital, Bern University Hospital, Freiburgstrasse, CH-3010 Bern, Switzerland (catrina.mugglin@insel.ch).

Open Forum Infectious Diseases®

© The Author(s) 2022. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact journals.permissions@oup.com <https://doi.org/10.1093/ofid/ofac592>

METHODS

Study Design and Study Population

The Swiss HIV cohort study ([SHCS] www.shcs.ch) is a nationwide longitudinal observational study of PWH in Switzerland. Participants are seen every 3 to 6 months, and data are collected during the follow-up visits and entered into a secure electronic database. Five Swiss University Hospitals, 2 Cantonal Hospitals, 15 affiliated hospitals, and 36 private physicians gather the data for the SHCS (listed in <http://www.shcs.ch/180-health-care-providers>). For this analysis, we included all patients under observation in the SHCS during the study period from April 2017 to November 2019. We did not consider the severe acute respiratory syndrome coronavirus 2 period, given its impact on testing frequencies, treatment uptake, and sexual behavior, which could have altered STI prevalence and incidence estimates.

Patient Consent Statement

The SHCS was approved by the local ethical committees of the participating centers, and written informed consent was obtained from all participants.

Outcomes and Definitions

We collected information about STI occurrence in the SHCS at 6-month intervals from October 2017 to November 2019. We analyzed information on all reported STIs including the 6 months before the first cohort visit from October 2017 onwards. Follow up ended at the last recorded cohort visit. At each cohort visit, the treating physician or the study nurse recorded all STIs diagnoses or treatment episodes since the last cohort visit. An STI during the study period was reported if a least one of the following had occurred since the last cohort visit: (1) a positive STI test result with or without symptoms or (2) a presumptive STI diagnosis (syndromic approach with no or negative diagnostic tests). All STIs diagnosed within or outside the cohort center were considered. Syphilis is screened for routinely at annual intervals among MSM and every 2 years for other transmission risk groups using serological testing. Screening for other STIs is not implemented routinely. Gonorrhea and chlamydia infections were diagnosed according to local clinical standard of care, in most cases by a positive urethral, anal, or pharyngeal polymerase chain reaction (PCR) test, or by direct urine PCR. In asymptomatic persons, samples from various anatomical sites were pooled.

Information on date of diagnosis, type of infection (gonorrhea, chlamydia, syphilis, others), symptoms, and infection site was collected. All reported episodes were considered independently whether diagnosed at the SHCS centers or in other testing sites. We collected data on infection with *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Treponema pallidum*, and others. Other infections were recorded as free text in the database (eg, *Mycoplasma genitalium*, herpes viruses type 1–2). Reporting of concurrent diagnosis of different STIs on the

same date were considered as separate infections. Having an un-suppressed viral load was defined as having 2 consecutive measurements of >50 copies/mL. Information on depression and alcohol use was collected at each follow-up visit. Alcohol Use Disorders Identification Test-Concise (AUDIT-C) was used to assess alcohol use and depression was defined by the treating physicians according to local standard-of-care definitions.

The primary outcome was the incidence of each specific STI during the study period. Secondary outcomes were risk factors for STIs, type of infections, and their distribution across HIV-transmission risk groups.

Statistical Analyses

We used descriptive statistics to describe demographic and clinical characteristics at baseline. We measured the frequencies of the different STIs at the end of follow up and calculated period prevalence of STIs over the whole observation period. We compared demographic and clinical characteristics between patients with a prevalent STI and participants with no STI during the study period. We calculated crude STI incidence rates as events per 1000 patient-years of follow up. We used multilevel Poisson regression to assess incidence rate ratios (IRR) of different STIs, and we calculated uni- and multivariable incidence ratios for different participants' characteristics. Risk factors analysis was restricted to participants who reported to be sexually active during the study period. All statistical analyses were performed using STATA, version 16.

RESULTS

Participant Characteristics

Of 10 140 SHCS participants with at least 1 follow-up visit after October 2017, 7667 (76%) reported to be sexually active during the follow-up period. The median age of all study participants was 51.0 years (interquartile range [IQR], 42.0–57.0), and 76.9% were of white ethnicity. The majority of participants were male (72.8%) and 46.7% were MSM. The percentage of people having condomless sex with an occasional partner was higher in the MSM group compared to the non-MSM group (41.1% vs 6.9%). The overall median CD4 cell count at first visit during study period was 670 cells/ μ L (IQR, 504.0–862.2) (Table 1).

Proportion of Individuals With at Least One Episode of Sexually Transmitted Infections

Overall, at least 1 STI episode was reported among 1029 (10.1%) participants. The most common STI was syphilis with 507 (5.0%) of participants ever experiencing at least 1 episode during the follow-up period, followed by gonorrhea ($n = 392$, 3.9%) and chlamydia ($n = 361$, 3.6%) (Supplementary Table 2). The majority of patients with at least 1 STI episode were male, MSM, and of white ethnicity. Patients with at least 1 STI during follow up were younger compared to those without, and they had a shorter median time on antiretroviral therapy.

Table 1. Characteristics of Study Participants

Characteristics	HIV Transmission Risk Group MSM (n = 4733)	HIV Transmission Risk Group Non-MSM (n = 5407)	Total N = 10 140
Age (years), median (IQR)	51.0 (41.0–57.0)	51.0 (43.0–57.0)	51.0 (42.0–57.0)
Age Group			
18–34	514 (10.9%)	444 (8.2%)	958 (9.4%)
35–49	1642 (34.7%)	1924 (35.6%)	3566 (35.2%)
50–64	2056 (43.4%)	2534 (46.9%)	4590 (45.3%)
> 64	521 (11.0%)	505 (9.3%)	1026 (10.1%)
Gender			
Male	4733 (100%)	2647 (49.0%)	7380 (72.8%)
Female	0 (0%)	2760 (51.0%)	2760 (27.2%)
Number of participants with at least 1 episode of STI	909 (19.2%)	120 (2.2%)	1029 (10.1%)
Median follow-up time (years), median (IQR)	1.9 (1.5–2.0)	1.9 (1.5–2.0)	1.9 (1.5–2.0)
Time on antiretroviral therapy (years), median (IQR)	11.1 (6.6–19.9)	14.8 (8.9–21.7)	12.9 (7.6–21.0)
Ever had an unsuppressed HIV VL during study period ^a	642 (13.6%)	859 (15.9%)	1501 (14.8%)
CD4 cell count at first visit during study period (cells/μL), median (IQR)	684.9 (533.1–865.2)	650.5 (474.0–860.0)	670.0 (504.0–862.2)
HIV Risk Group			
Heterosexual contact	0 (0.0%)	3829 (70.8%)	3829 (37.8%)
MSM	4733 (100.0%)	0 (0.0%)	4733 (46.7%)
People who report injecting drugs use	0 (0.0%)	702 (13.0%)	702 (6.9%)
Other/unknown	0 (0.0%)	876 (16.2%)	876 (8.6%)
Ethnicity, n (%)			
White, n (%)	4228 (89.3%)	3572 (66.0%)	7800 (76.9%)
Black, n (%)	76 (1.6%)	1404 (26.0%)	1480 (14.6%)
Hispanic-American, n (%)	246 (5.2%)	150 (2.8%)	396 (3.9%)
Asian, n (%)	170 (3.6%)	258 (4.8%)	428 (4.2%)
Other/unknown n (%)	13 (0.3%)	23 (0.4%)	36 (0.4%)
History of HCV Infection ^b			
Yes	352 (7.4%)	1279 (23.7%)	1631 (16.1%)
No	4304 (90.9%)	4018 (74.3%)	8322 (82.1%)
Missing	77 (1.7%)	110 (2.0%)	187 (1.8%)
History of HBV Infection ^c
Yes	216 (4.6%)	263 (4.9%)	479 (4.7%)
No	4142 (87.5%)	4861 (89.9%)	9003 (88.8%)
Missing	375 (7.9%)	283 (5.2%)	658 (6.5%)
People having condomless sex with stable partner	2133 (45.1%)	2417 (44.7%)	4550 (44.9%)
Ever reported sexual relationship with occasional partner(s)	2964 (62.6%)	931 (17.2%)	3895 (38.4%)
People having condomless sex with occasional partner(s)	1946 (41.1%)	372 (6.9%)	2318 (22.9%)
People who reported drug use during study period
None	3653 (77.2%)	4945 (91.5%)	8598 (84.8%)
Noninjecting	119 (2.5%)	157 (2.9%)	276 (2.7%)
Injecting	961 (20.3%)	305 (5.6%)	1266 (12.5%)
Alcohol Consumption
Never/monthly or less	1366 (28.9%)	2566 (47.5%)	3932 (38.8%)
2–3 times per month/week	2492 (52.6%)	2074 (38.4%)	4566 (45.0%)
> 3 days per week	875 (18.5%)	767 (14.1%)	1642 (16.2%)
History of depression	1212 (25.6%)	1399 (25.9%)	2611 (25.7%)

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; MSM, men who have sex with men; STI, sexually transmitted infection; VL, viral load.

^aTwo consecutive measurements > 50 copies/mL.

^bEver HCV-Ab positive.

^cEver HbsAg positive.

Overall, 354 of 1029 (34.4%) participants had more than 1 STI episode. Among patients with STIs, 20.8% had 2 episodes ($n = 214$), 7.4% had 3 episodes ($n = 76$), 3.7% had 4 episodes ($n = 38$), and 2.5% had 5 episodes or more ($n = 26$). [Figure 1](#) shows the number of infections grouped by age group and

transmission group: although MSM account for less than half (46.7%) of the study population, they experienced the majority (88.3%) of STIs during the follow-up period. Participants aged 18–34 had more episodes of STIs compared to the older age groups. Sixty-one percent of all persons experiencing at least

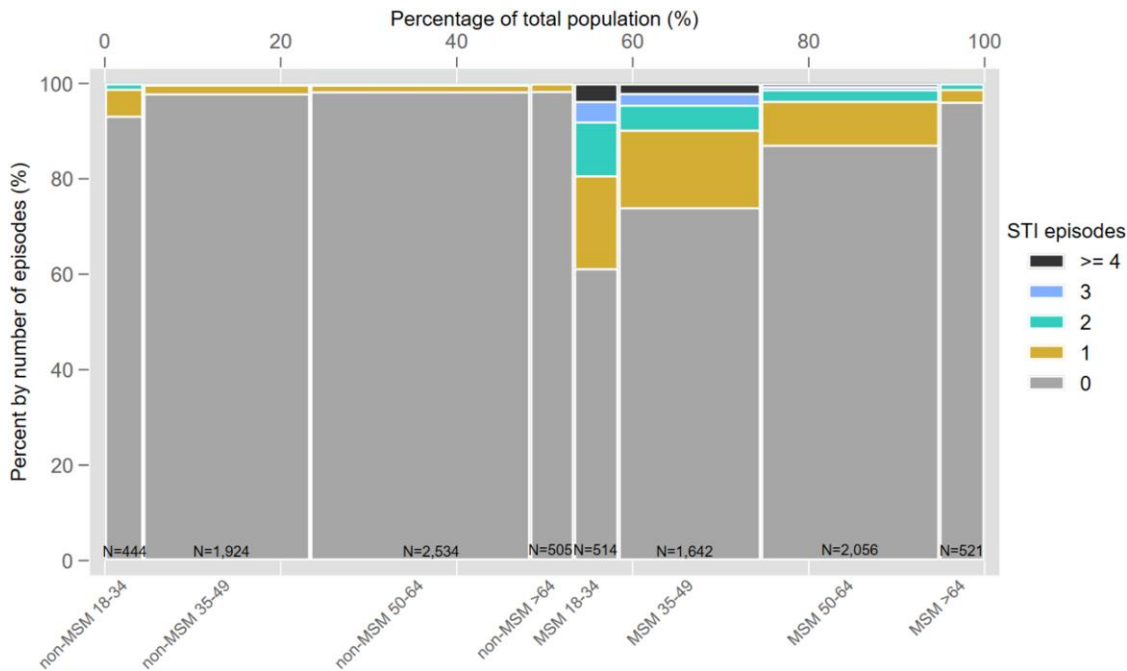


Figure 1. Distribution of sexually transmitted infection (STI) diagnoses by number of infections per participant during follow up and by transmission group (men who have sex with men [MSM] and non-MSM) and age group (years).

1 STI were MSM younger than 50 years. Thirty-eight percent of MSM with an STI had several episodes compared to only 18% among the other HIV-transmission risk groups.

Incident Sexually Transmitted Infections

Among 10 140 study participants, a total of 1634 STIs in 1029 participants were reported over 17 766 person-years of follow up (PYFUP). The overall incidence of any reported STI was 91.9 per 1000 PYFU (95% confidence interval [CI], 85.8–98.5). Among the 1634 STI episodes, there were 573 (35.1%) incident cases of syphilis, 497 gonorrhea (30.4%), and 418 chlamydia (25.6%) (Table 2). Reinfections with the same STI accounted for 120 episodes. The highest incidence rate was for syphilis 32.2 per 1000 PYFU (95% CI, 29.5–35.2) (Table 3). The following groups had the highest incidence rates: age group 18–34 years (260.8 cases per 1000 PYFU; 95% CI, 227.3–299.2), MSM (178.4 cases per 1000 PYFU; 95% CI, 166.3–191.5), MSM who ever reported a sexual relationship with occasional partner(s) (267.8 cases per 1000 PYFU; 95% CI, 250.0–286.8), and reporting of injecting drug use (304.6 cases per 1000 PYFU; 95% CI, 241.9–383.6) (Table 3, Supplementary Figure 1).

Overall, only half of STI episodes (824, 50.5%) were symptomatic. Although 54.3% of all reported gonorrhea cases were symptomatic, the proportion of symptomatic cases was slightly lower for syphilis (46.2%) and chlamydia (45.1%). In more than half of all STI cases, the site of infection was known (54.3%). If site of infection was known and specified, genital infections (21.4%) were the most common, followed by anal (12.5%), oral (2.4%), and

disseminated infections (1.6%) (Table 2). In 14.4% of all cases, the site was known but not specified.

Incidence Rates Ratios and Risk Factors for Sexually Transmitted Infections

A total of 7674 patients reporting to be sexually active during the follow-up period with a total of 1601 episodes of STIs included in the risk factor analysis. In multivariable Poisson regression, being male (adjusted IRR [aIRR], 2.03; 95% CI, 1.36–3.02), MSM (aIRR, 3.62; 95% CI, 2.88–4.55), age group 18–34 years (aIRR, 1.78; 95% CI, 1.51–2.10), ever reported sexual relationship with occasional partner(s) (aIRR, 6.87; 95% CI, 5.40–8.73), and reporting injecting drug use (aIRR, 2.48; 95% CI, 1.91–3.23) were associated with a higher risk of incident STIs. Factors associated with a lower incidence of STIs were age 50–64 years (aIRR, 0.59; 95% CI, .51–.68) and age older than 64 years (aIRR, 0.30; 95% CI, .20–.44) (Figure 2, Supplementary Table 1). Risk factors were similar for the different STIs (Figure 2).

DISCUSSION

In this nationwide representative cohort study among PWH, we found a high STIs incidence rate of 91.9 per 1000 PYFU. Almost half (41.1%) of incident cases were asymptomatic. Incidence of any STI was highest among younger participants, MSM, people who ever reported sexual relationship with occasional partner(s), and people who reported drug use (injecting and noninjecting). The MSM younger than 50 years represented 21% of the study population, but they accounted for 61% of

Table 2. Incident Cases of STIs and Patients' Characteristics

Characteristics	Total No.	%	Gonorrhea No.	%	Syphilis No.	%	Chlamydia No.	%	Others ^a No.	%	P Value ^b
Age at time of infection (years), median (IQR)	42.0 (34–50)	100	497	30.4	573	35.1	418	25.6	146	8.9	
Age group											
18–34	417	25.5	160	32.2	111	19.4	109	26.1	37	25.3	...
35–49	755	46.2	232	46.7	265	46.2	200	47.8	58	39.7	...
50–64	428	26.2	104	20.9	172	3.0	104	24.9	48	32.9	...
>64	34	2.1	1	0.2	24	4.4	5	1.2	3	2.1	...
Gender											
Male	1600	97.9	495	99.6	567	99.0	406	97.1	132	90.4	<.001
Female	34	2.1	2	0.4	6	1.0	12	2.9	14	9.6	<.001
Median follow-up time (years), median (IQR)	1.9 (1.6–2.0)	...	1.9 (1.6–2.0)	...	1.9 (1.5–2.1)	...	1.9 (1.6–2.0)	...	1.9 (1.5–2.1)33
Time on ART (years), median (IQR)	7.8 (4.2–11.7)	...	6.9 (4.1–10.5)	...	8.3 (4.2–12.9)	...	8.0 (4.2–11.5)	...	8.4 (4.3–14.9)006
Ever had an unsuppressed HIV VL during study period ^c	306	18.7	85	17.1	116	20.2	73	17.5	32	21.9	.37
CD4 cell count at first visit during study period (cells/ μ L) median (IQR)	701 (549–871)	...	742.5 (602–900)	...	659.5 (515–842)	...	702.0 (542–865)	...	667.0 (566–846)	...	<.001
HIV Risk Group											
Heterosexual contact	92	5.6	12	2.4	33	5.8	30	7.2	17	11.6	...
MSM	1498	91.7	475	95.6	526	91.8	380	90.9	117	80.2	...
People who inject drugs	10	0.6	2	0.4	2	0.3	1	0.2	5	3.4	...
Other/unknown	34	2.1	8	1.6	12	2.1	7	1.7	7	4.8	...
Ethnicity											
White	13 855	84.8	413	83.1	489	85.3	356	85.2	127	87.0	.004
Black	52	3.2	8	1.6	15	2.6	20	4.8	9	6.2	...
Hispanic-American	137	8.4	60	12.1	41	7.2	29	6.9	7	4.8	...
Asian	58	3.5	15	3.0	27	4.7	13	3.1	3	2.0	...
Other/unknown	2	0.1	1	0.2	1	0.2	0	0	0	0	...
History of HCV Infection ^d	182	11.1	48	9.7	76	13.3	30	7.2	28	19.2	<.001
History of HBV Infection ^e	41	2.5	5	1.0	20	3.5	10	2.4	6	4.1	.18
People having condomless sex with stable partner	907	55.5	290	58.4	285	49.7	249	59.6	83	55.5	.007
Ever reported sexual relationship with occasional partner(s)	1514	92.7	479	96.4	528	92.1	387	92.6	129	92.7	<.001
People having condomless sex with occasional partner(s)	1311	80.2	429	86.3	437	76.3	341	81.6	104	80.2	<.001
People who reported drug use during study period059
None	870	53.2	238	47.9	318	55.5	225	53.8	89	61.0	...
Noninjecting	150	9.2	52	10.5	53	9.2	32	7.7	13	8.9	...
Injecting	614	37.6	207	41.6	202	35.3	161	38.5	44	30.1	...
Alcohol Consumption
Never/monthly or less	425	26.0	123	24.7	145	25.3	112	26.8	45	30.8	...
2–3 times per month/week	980	60.0	304	61.2	342	59.7	246	58.9	88	60.3	...
>3 day per week	229	14.0	70	14.1	86	15.0	60	14.3	13	8.9	...
People who ever had depression	424	25.9	138	27.8	146	25.5	101	24.2	39	26.7	...

Table 2. Continued

Characteristics	Total		Gonorrhea		Syphilis		Chlamydia		Others ^a		P Value ^b
	No.	%	No.	%	No.	%	No.	%	No.	%	
Symptoms	<.001111
Yes	824	50.5	270	54.3	265	46.2	193	45.1	96	66.0	...
No	672	41.1	182	36.6	268	46.8	185	44.3	37	25.2	...
Unknown	138	8.4	45	9.1	40	7.0	40	9.6	13	8.8	...
Site of infection	<.001
Anal infection	205	12.5	60	12.1	9	1.6	107	25.6	29	19.9	...
Genital infection	349	21.4	164	33.0	50	8.7	83	19.9	52	35.6	...
Oral infection	39	2.4	19	3.8	15	2.6	3	.7	2	1.4	...
Two sites (anal, genital or oral)	33	2.0	14	2.8	1	0.2	13	3.1	5	3.4	...
Disseminated infection	26	1.6	1	0.2	16	2.8	2	0.5	7	4.8	...
Site known, but not specified	236	14.4	3	0.6	227	39.6	2	0.5	4	2.7	...
Site unknown	746	45.7	236	47.5	255	44.5	208	49.7	47	32.2	...

Abbreviations: ART, antiretroviral therapy; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; MSM, men who have sex with men; STI, sexually transmitted infection; VL, viral load.

^aHerpes simplex virus-1/2, *Mycoplasma genitalis*.

^bP value from Pearson χ^2 test for binary and categorical variables or Wilcoxon rank-sum test for continuous variables, comparing the distribution of the demographic and clinical characteristics between the different STIs.

^c2 consecutive measurements > 50 copies/mL.

^dEver HCV-antibody positive.

^eEver hepatitis B surface antigen positive.

participants with at least 1 episode of any STI. Sexually active PWH with occasional sex partner(s) had a more than 6-fold increased STIs incidence in multivariable analysis.

In Switzerland, the annual STI incidence in the general population is estimated to be 0.06/1000 person-years for syphilis, 0.4/1000 person-years for gonorrhea, and 1.3/1000 person-years for chlamydia [7]. In our study among PWH, we found incidences that were 530-, 70-, and 18-fold higher for syphilis, gonorrhea, and chlamydia, respectively. The STI with the highest incidence in this study was syphilis, whereas chlamydia incidence is highest in the general population. Of note, in the SHCS, syphilis is screened for routinely every 1–2 years irrespective of symptoms, which might contribute to the high syphilis incidence in this study compared with other STIs. In a recent survey among asymptomatic MSM with at least 3 sexual partners attending voluntary counseling and testing (VCT) sites in Switzerland, the incidence for syphilis was 42/1000 PYFU, the incidence for gonorrhoea was 147/1000 PYFU, and the incidence for was chlamydia 90/1000 PYFU [13]. Of note, in this VCT sites study, only 3.6% of the participants had a diagnosed HIV infection at the time of enrollment. Incidence rates were highest among MSM with occasional partners. Of note, MSM without occasional partners had a lower STI incidence compared to non-MSM with occasional partners.

It is interesting to note that, in our study, only half (50.5%) of the STI episodes were symptomatic. This underscores the need to implement STI testing that is not limited to symptomatic infections. In other screening studies, 25% to 95% of STIs are asymptomatic, especially in extra genital regions [14–17]. The site of infections was not known in 45.7% of all STIs. This might be explained by the screening approach with pooled swabs from genital and extra genital regions and the high proportion of asymptomatic cases.

Most of the pre-exposure prophylaxis (PrEP) studies published in recent years showed 3 to 5 times higher incidence and prevalence of the common STIs compared to our study [18–21]. For example, in the ANRS IPERGAY study, the incidence of a first bacterial STI was 750/1000 PYFU, compared to 178/1000 PYFU among MSM in our study, reflecting differences in demographic characteristics and risk behavior between PWH and PrEP users [22]. A similar cohort study in PWH in the United States reported a lower incidence (38 per 1000 PYFU) in comparison to the SHCS [23]. The lower proportion of MSM in this population (39% compared to 46% in our study) might partly explain this difference.

After comparing the risk factors for the different STIs among sexually active study participants, we did not find any distinct patterns. This is in line with previous studies, which also reported risk factors to be similar for each specific STI [23]. In our study, people who ever had a depression had a lower risk to experience any STIs. This is in contrast with other studies that found a positive correlation, possibly due to increased reported use of alcohol and drugs [24, 25]. The risk factors

Table 3. Incidence Rates of Different STIs per 1000 PYFU (95% Confidence Interval) (N = 10 140)

Subgroup	Any STI	Gonorrhoea	Syphilis	Chlamydia	Others ^a
Overall incidence rate per 1000 PYFU	91.9 (85.8–98.5)	27.9 (25.1–31.1)	32.2 (29.5–35.2)	23.5 (21.1–26.2)	8.2 (6.8–9.8)
Age Groups					
18–34	260.8 (227.3–299.2)	100.0 (83.0–120.6)	69.4 (57.0–84.5)	68.1 (55.4–83.9)	23.1 (16.2–32.9)
35–49	121.3 (109.5–134.2)	37.2 (31.8–43.6)	42.5 (37.3–48.5)	32.1 (27.4–37.6)	9.3 (7.0–12.3)
50–64	52.7 (46.5–59.7)	12.8 (10.3–15.8)	12.8 (10.3–15.8)	21.1 (18.0–24.8)	5.9 (4.3–7.9)
>64	18.6 (12.6–27.4)	0.55 (0.08–3.8)	2.7 (1.1–6.5)	13.7 (9.1–20.5)	5.9 (4.3–7.9)
Sex					
Male	123.1 (114.8–132.0)	38.0 (34.1–42.3)	43.6 (39.9–47.7)	31.2 (28.0–34.9)	10.2 (8.4–12.3)
Female	8.8 (6.4–12.2)	1.2 (0.5–2.7)	1.8 (0.9–3.8)	2.8 (1.7–4.8)	2.8 (1.7–4.8)
HIV Transmission Group					
MSM	178.4 (166.3–191.5)	56.5 (50.8–63.1)	62.6 (57.2–68.5)	45.2 (40.4–50.6)	13.9 (11.4–16.99)
Non-MSM ^b	14.5 (12.0–17.4)	2.3 (1.5–3.6)	5.0 (3.7–6.7)	4.0 (2.9–5.6)	3.1 (2.1–4.5)
People sexually active during study period					
Ever reported sexual relationship with occasional partner(s) during study period	217.2 (202.9–232.6)	68.7 (61.8–76.4)	55.5 (49.7–62.0)	75.8 (69.3–82.8)	17.2 (14.2–20.9)
MSM with occasional partner(s)	267.8 (250.0–286.8)	85.9 (77.2–95.7)	68.2 (60.9–76.3)	93.6 (85.5–102.4)	20.2 (16.4–24.8)
Non-MSM with occasional partner(s)	49.6 (38.7–63.4)	11.8 (7.4–18.8)	13.6 (8.7–21.4)	16.7 (11.4–24.6)	7.4 (4.0–13.7)
Never had occasional partner(s) during study period					
MSM	20.6 (15.5–27.6)	4.9 (3.0–8.3)	7.9 (5.4–11.9)	4.9 (3.0–8.3)	2.7 (1.3–5.3)
Non-MSM	7.3 (5.5–9.6)	0.4 (0.1–1.2)	2.6 (1.6–4.2)	2.1 (1.3–3.4)	2.2 (1.4–3.5)
People who reported drug use during study period					
None	57.9 (52.9–63.3)	15.8 (13.6–18.3)	14.9 (12.9–17.3)	21.1 (18.8–23.8)	5.9 (4.7–7.3)
Noninjecting	272.9 (244.7–304.4)	92.0 (78.2–108.1)	71.5 (60.2–85.0)	89.7 (77.5–103.9)	19.5 (14.1–27.1)
Injecting	304.6 (241.9–383.6)	105.6 (74.0–150.6)	64.9 (44.1–95.7)	107.6 (82.1–141.0)	26.4 (14.3–48.6)

Abbreviations: HIV, human immunodeficiency virus; PYFU, person-years of follow up; MSM, men who have sex with men; STI, sexually transmitted infection.

^aHerpes simplex virus-1/2, *Mycoplasma genitalis*.

^bAny other HIV transmission risk group

associated with experiencing any STI are in line with previous studies [23, 26–28]. In general, most of the risk factors identified in this study are also associated with high-risk sexual behavior and thus also a proxy for other factors associated with STI transmission. Furthermore, the decrease in condom use in the SHCS following the popularization of U = U might have contributed to STI transmissions [8]. The high STI incidence among MSM might be partly explained through the recommendation of more frequent testing, compared to non-MSM participants [29] because syphilis is screened routinely at annual intervals in MSM, and every 2 years in other transmission risk groups. However, a recent study in the SHCS described a more than 10-fold higher primary syphilis incidence in MSM compared to other participants who were all tested at least once during the study period (2004–2014) [5]. Our results showed a similar difference in syphilis incidence between MSM and other persons, suggesting that an overestimation of the incidence in the MSM group is unlikely to play a major role in our study.

Only 9% of STIs occurred with a detectable viremia at the time of STI diagnosis compared to 14.8% among everyone under active follow up. Thus, in our setting, STI incidence was not associated with disengagement to care or nonadherence to clinical care. In contrast, in a cohort of PWH in the United States, 41.8% of patients with incident STI had detectable viremia [23].

Strengths and Weaknesses of the Study

This study is among the largest investigations on STIs incidence among PWH in a nationwide population including all major HIV-transmission and age groups and diverse ethnicities [30]. The prospective assessment of incident STIs and associated risk factors provided estimates in a representative population. Some limitations should be noted. Overall, we assume that our estimates for gonorrhoea and chlamydia infections especially in the extra genital regions are an underestimation of the true incidence and prevalence because only syphilis is tested for routinely using serological assays irrespective of symptoms. There might be a bias towards symptom-based testing for gonorrhoea and chlamydia leading to an underestimation of the true incidence. Furthermore, there might be an underestimation of the overall cases if patients did not report all STIs diagnosed in external settings, including VCT sites, or missed to report specific symptoms. Of note, among people attending a VCT site, 3.8% were already known to be HIV positive [13]. However, in this context, it is important to optimize screening strategies according to clinical and behavioral characteristics. This should optimize diagnosis rates and treatment of STIs, and thereby reduce morbidity and onward STI transmissions. Optimized screening strategies should also reduce the number of false-positive tests, and thereby prevent overtreatment and the associated emergence of drug resistance.

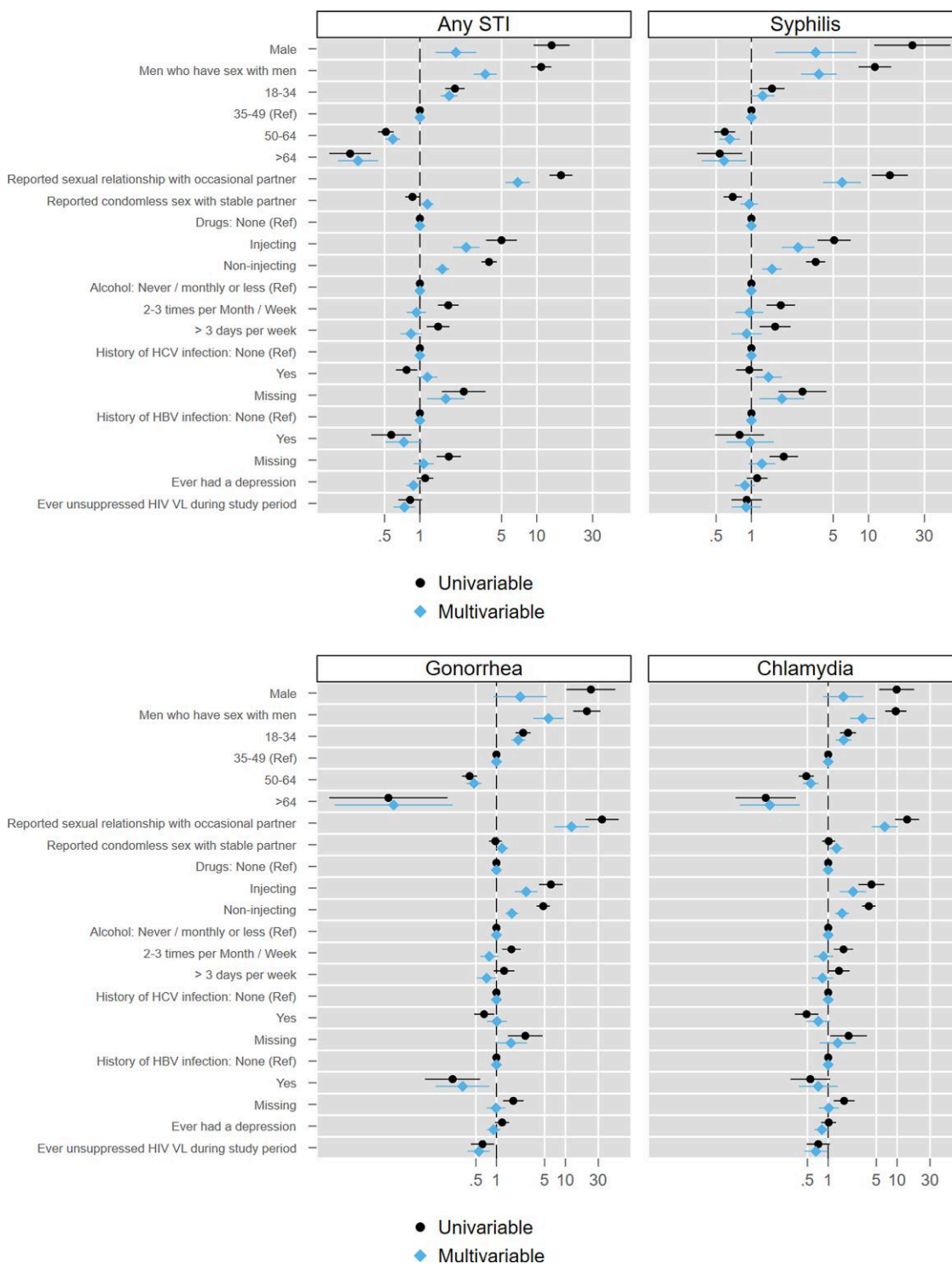


Figure 2. Incidence rate ratios among sexually active participants in the Swiss HIV Cohort Study (SHCS) ($N = 7674$). All sexually transmitted infections (STIs) combined: syphilis, gonorrhea, and chlamydia. HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; VL, viral load.

CONCLUSIONS

In conclusion, STIs were frequent among PWH and varied considerably between age and risk groups. Interventions to reduce STI transmission among PWH need to be tailored to

demographic and behavioral characteristics. This implies that screening programs and recommendations need to be adapted to risk factors and to the STIs incidence among diverse populations. The high STIs incidence among young MSM observed

in this and other studies underscores the need for regular screening, access to STIs tests free of cost, and treatment efforts in this population. Furthermore, almost half of all STIs were asymptomatic, which underscores the need to implement routine screening irrespective of clinical presentation, particularly among PWH with the highest STIs incidence.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

Financial support. This study was funded within the framework of the Swiss HIV Cohort Study (SHCS), supported by the Swiss National Science Foundation (Grant Numbers 201369 and 179567), by SHCS Project Number 823, and by the SHCS Research Foundation. The data are gathered by the Five Swiss University Hospitals, 2 Cantonal Hospitals, 15 affiliated hospitals, and 36 private physicians (listed in <http://www.shcs.ch/180-health-care-providers>).

Potential conflicts of interest. C. M. reports support to her institution for travel grants from ViiV Healthcare. All remuneration went to her home institution and not to C. M. personally, and all remuneration was provided outside the submitted work. A. C. received research grants from MSD and unrestricted Education Grants paid to the institution by ViiV Healthcare, Gilead, and MSD. M. C.'s institution gave expert opinion to Gilead, MSD, and ViiV; fees were paid to M. C.'s institution. M. S. has been member of advisory boards to Gilead, MSD, and ViiV and has received travel grants from Gilead, MSD, and ViiV. D. Br. has been a consultant to Gilead, ViiV, and MSD and received honoraria for lectures from Abbvie, Gilead, ViiV, and MSD. J. N. reports support to her institution for travel grants from Gilead Sciences, all remuneration was provided outside the submitted work. D. H. has been a consultant for Gilead and ViiV Healthcare. Positive Council has received unconditional grants from Abbvie, Gilead, MSD, and ViiV Healthcare. SAFE-ID has received educational grants from Abbvie, Gilead, MSD, Pfizer, Roche, and ViiV Healthcare. E. B.'s institution received payments for E. B.'s participation to advisory boards of Gilead Sciences, ViiV Healthcare, Merck Sharp and Dohme, Pfizer, Eli Lilly, and travel grants from Gilead Sciences, ViiV Healthcare, Pfizer, and Abbvie. G. W. reports grants from Gilead Sciences, and grants from ViiV, outside the submitted work. All remuneration went to his home institution. A. R. reports support to his institution for advisory boards and/or travel grants from MSD, Gilead Sciences, Pfizer, and Abbvie and an investigator-initiated trial (IIT) grant from Gilead Sciences. All remuneration went to his home institution and not to A. R. personally, and all remuneration was provided outside the submitted work. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Members of the Swiss HIV Cohort Study

Abela I., Aebi-Popp K., Anagnostopoulos A., Battagay M., Bernasconi E., Braun D. L., Bucher H. C., Calmy A., Cavassini M., Ciuffi A., Dollenmaier G., Egger M., Elzi L., Fehr J., Fellay J., Furrer H., Fux C. A., Günthard H. F. (President of the SHCS), Hachfeld A., Haerry D. (deputy of "Positive Council"), Hasse B., Hirsch H. H., Hoffmann M., Hösli I., Huber M., Kahlert C. R. (Chairman of the Mother & Child Substudy), Kaiser L., Keiser O., Klimkait T., Kouyos R. D., Kovari H., Kusejko K. (Head of Data Centre), Martinetti G., Martinez de Tejada B., Marzolini C., Metzner K. J., Müller N., Nemeth J., Nicca D., Paioni P.,

Pantaleo G., Perreau M., Rauch A. (Chairman of the Scientific Board), Schmid P., Speck R., Stöckle M. (Chairman of the Clinical and Laboratory Committee), Tarr P., Trkola A., Wandeler G., Yerly S.

References

1. Flagg EW, Weinstock HS, Frazier EL, Valverde EE, Heffelfinger JD, Skarbinski J. Bacterial sexually transmitted infections among HIV-infected patients in the United States: estimates from the medical monitoring project. *Sex Transm Dis* **2015**; 42:171–9. doi: [10.1097/OLQ.0000000000000260](https://doi.org/10.1097/OLQ.0000000000000260).
2. Sprenger K, Evison JM, Zwahlen M, et al. Sexually transmitted infections in HIV-infected people in Switzerland: cross-sectional study. *PeerJ* **2014**; 2:e537. doi: [10.7717/peerj.537](https://doi.org/10.7717/peerj.537).
3. Secco AA, Akselrod H, Czeresnia J, et al. Sexually transmitted infections in persons living with HIV infection and estimated HIV transmission risk: trends over time from the DC cohort. *Sex Transm Infect* **2020**; 96:89–95. doi: [10.1136/sextrans-2019-054216](https://doi.org/10.1136/sextrans-2019-054216).
4. Kalichman SC, Pellowski J, Turner C. Prevalence of sexually transmitted co-infections in people living with HIV/AIDS: systematic review with implications for using HIV treatments for prevention. *Sex Transm Infect* **2011**; 87: 183–90. doi: [10.1136/sti.2010.047514](https://doi.org/10.1136/sti.2010.047514).
5. Shilaih M, Marzel A, Braun DL, et al. Factors associated with syphilis incidence in the HIV-infected in the era of highly active antiretrovirals. *Medicine (Baltimore)* **2017**; 96:e5849. doi: [10.1097/MD.00000000000005849](https://doi.org/10.1097/MD.00000000000005849).
6. Balakrishna S, Salazar-Vizcaya L, Schmidt AJ, et al. Assessing the drivers of syphilis among men who have sex with men in Switzerland reveals a key impact of screening frequency: a modelling study. *PLoS Comput Biol* **2021**; 17:e1009529. doi: [10.1371/journal.pcbi.1009529](https://doi.org/10.1371/journal.pcbi.1009529).
7. [Bundesamt für Gesundheit (BAG). *HIV, Syphilis, Gonorrhoe Und Chlamydie in Der Schweiz Im Jahr 2019: Eine Epidemiologische Übersicht*], BAG-Bulletin 48/2020 (Deutsch). 2020. Available at: <https://www.bag.admin.ch/bag/de/home/zahlen-und-statistiken/zahlen-zu-infektionskrankheiten/hiv-sti-statistiken-analysen-trends.html>. Accessed 22 November 2022.
8. Kouyos RD, Hasse B, Calmy A, et al. Increases in condomless sex in the Swiss HIV cohort study. *Open Forum Infect Dis* **2015**; 2:ofv077. doi: [10.1093/ofid/ofv077](https://doi.org/10.1093/ofid/ofv077).
9. 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. doi: [10.1080/14787210.2018.1446828](https://doi.org/10.1080/14787210.2018.1446828).
10. Braun DL, Marzel A, Steffens D, et al. High rates of subsequent asymptomatic sexually transmitted infections and risky sexual behavior in patients initially presenting with primary human immunodeficiency virus-1 infection. *Clin Infect Dis* **2018**; 66:735–42. doi: [10.1093/cid/cix873](https://doi.org/10.1093/cid/cix873).
11. Cohen MS, Council OD, Chen JS. Sexually transmitted infections and HIV in the era of antiretroviral treatment and prevention: the biologic basis for epidemiologic synergy. *J Int AIDS Soc* **2019**; 22:e25355. doi: [10.1002/jia2.25355](https://doi.org/10.1002/jia2.25355).
12. Thng CCM. A review of sexually transmitted infections in Australia – considerations in 2018. *Acad Forensic Pathol* **2018**; 8:938–46. doi: [10.1177/1925362118821492](https://doi.org/10.1177/1925362118821492).
13. Schmidt AJ, Rasi M, Esson C, et al. The Swiss STAR trial - an evaluation of target groups for sexually transmitted infection screening in the sub-sample of men. *Swiss Med Wkly* **2020**; 150:w20392. doi: [10.4414/smw.2020.20392](https://doi.org/10.4414/smw.2020.20392).
14. Spinner CD, Boesecke C, Jordan C, et al. Prevalence of asymptomatic sexually transmitted infections in HIV-positive men who have sex with men in Germany: results of a multicentre cross-sectional study. *Infection* **2018**; 46: 341–7. doi: [10.1007/s15010-018-1124-6](https://doi.org/10.1007/s15010-018-1124-6).
15. Templeton DJ, Jin F, McNally LP, et al. Prevalence, incidence and risk factors for pharyngeal gonorrhoea in a community-based HIV-negative cohort of homosexual men in Sydney, Australia. *Sex Transm Infect* **2010**; 86:90–6. doi: [10.1136/sti.2009.036814](https://doi.org/10.1136/sti.2009.036814).
16. Morris SR, Klausner JD, Buchbinder SP, et al. Prevalence and incidence of pharyngeal gonorrhoea in a longitudinal sample of men who have sex with men: the EXPLORE study. *Clin Infect Dis* **2006**; 43:1284–9. doi: [10.1086/508460](https://doi.org/10.1086/508460).
17. Turner AN, Reese PC, Ervin M, Davis JA, Fields KS, Bazan JA. HIV, rectal chlamydia, and rectal gonorrhoea in men who have sex with men attending a sexually transmitted disease clinic in a midwestern US city. *Sex Transm Dis* **2013**; 40: 433–8. doi: [10.1097/OLQ.0b013e31828fd163](https://doi.org/10.1097/OLQ.0b013e31828fd163).
18. Traeger MW, Cornelisse VJ, Asselin J, et al. Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. *JAMA* **2019**; 321:1380–90. doi: [10.1001/jama.2019.2947](https://doi.org/10.1001/jama.2019.2947).
19. Hoornenborg E, Coyer L, Achterbergh RCA, et al. Sexual behaviour and incidence of HIV and sexually transmitted infections among men who have sex with men using daily and event-driven pre-exposure prophylaxis in AMPREP: 2 year results

- from a demonstration study. *Lancet HIV* **2019**; 6:e447–55. doi: [10.1016/S2352-3018\(19\)30136-5](https://doi.org/10.1016/S2352-3018(19)30136-5).
20. Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *Lancet HIV* **2017**; 4:e402–10. doi: [10.1016/S2352-3018\(17\)30089-9](https://doi.org/10.1016/S2352-3018(17)30089-9).
 21. Hovaguimian F, Martin E, Reinacher M, et al. Participation, retention and uptake in a multicentre pre-exposure prophylaxis cohort using online, smartphone-compatible data collection. *HIV Med* **2022**; 23:146–58. doi: [10.1111/hiv.13175](https://doi.org/10.1111/hiv.13175).
 22. Zeggagh J, Bauer R, Delaugerre C, et al. Incidence and risk factors for recurrent sexually transmitted infections among men who have sex with men on HIV pre-exposure prophylaxis. *AIDS* **2022**; 9:1129–34. doi: [10.1097/QAD.0000000000003187](https://doi.org/10.1097/QAD.0000000000003187).
 23. Lucar J, Hart R, Rayeed N, et al. Sexually transmitted infections among HIV-infected individuals in the District of Columbia and estimated HIV transmission risk: data from the DC cohort. *Open Forum Infect Dis* **2018**; 5:1–9. doi: [10.1093/ofid/ofy017](https://doi.org/10.1093/ofid/ofy017).
 24. Stahlman S, Javanbakht M, Cochran S, Hamilton A, Shoptaw S, Gorbach P. Self-reported STIs and sexual risk behaviors in the U. S. Military: how gender influences risk. *Sex Transm Dis* **2014**; 41:359–64. doi: [10.1097/OLQ.0000000000000133](https://doi.org/10.1097/OLQ.0000000000000133).
 25. Hampel B, Kusejko K, Kouyos RD, et al. Chemsex drugs on the rise: a longitudinal analysis of the Swiss HIV cohort study from 2007 to 2017. *HIV Med* **2020**; 21:228–39. doi: [10.1111/hiv.12821](https://doi.org/10.1111/hiv.12821).
 26. Nishijima T, Teruya K, Shibata S, et al. Incidence and risk factors for incident syphilis among HIV-1-infected men who have sex with men in a large urban HIV clinic in Tokyo, 2008–2015. *PLoS One* **2016**; 11:e0168642. doi: [10.1371/journal.pone.0168642](https://doi.org/10.1371/journal.pone.0168642).
 27. Thurnheer MC, Weber R, Toutous-Trellu L, et al. Occurrence, risk factors, diagnosis and treatment of syphilis in the prospective observational Swiss HIV cohort study. *AIDS* **2010**; 24:1907–16. doi: [10.1097/QAD.0b013e32833bfe21](https://doi.org/10.1097/QAD.0b013e32833bfe21).
 28. Dickson N, Ludlam A, Saxton P, Hughes A. Self-reported STIs and sexual health checks in a cross-sectional study of gay and bisexual men in New Zealand. *Sex Transm Infect* **2015**; 91:49–54. doi: [10.1136/sextrans-2013-051476](https://doi.org/10.1136/sextrans-2013-051476).
 29. Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines 2021. *MMWR Recomm Rep* **2021**; 70:1–187. doi: [10.15585/mmwr.rr7004a1](https://doi.org/10.15585/mmwr.rr7004a1).
 30. Scherrer AU, Traytel A, Braun DL, et al. Cohort profile update: the Swiss HIV cohort study (SHCS). *Int J Epidemiol* **2022**; 51:33–4j. doi: [10.1093/ije/dyab141](https://doi.org/10.1093/ije/dyab141).