

**ACQUIRED SYPHILIS IN THE CONTEXT OF PRE-EXPOSURE PROPHYLAXIS: A SYSTEMATIC REVIEW OF THE SCIENTIFIC LITERATURE**

**Supplementary Table 1. Characterization of the selected articles**

<b>id</b>	<b>Study</b>	<b>Article title</b>	<b>Journal</b>	<b>Year of publication</b>	<b>Quality assessment*</b>
1	Solomon et al., 2014 <sup>2</sup>	Syphilis predicts HIV incidence among men and transgender women who have sex with men in a preexposure prophylaxis trial	Clin. Infect. Dis.	2014	Low risk of bias
2	Volk et al., 2015 <sup>2</sup>	No New HIV Infections with Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting	Clin. Infect. Dis.	2015	Satisfactory
3	Liu et al., 2016 <sup>3</sup>	Preexposure prophylaxis for HIV infection integrated with municipal and community-based sexual health services	JAMA Intern. Med.	2016	Good
4	Nguyen et al., 2018 <sup>4</sup>	Incidence of sexually transmitted infections before and after preexposure prophylaxis for HIV	AIDS	2018	Good
5	Spinelli et al., 2018 <sup>5</sup>	Provider adherence to pre-exposure prophylaxis monitoring guidelines in a large primary care network	Open Forum Infect. Dis.	2018	Good
6	Beymer et al., 2018 <sup>6</sup>	Does HIV pre-exposure prophylaxis use lead to a higher incidence of sexually transmitted infections? A case-crossover study of men who have sex with men in Los Angeles, California	Sex. Transm. Infect.	2018	Satisfactory
7	Hevey et al., 2018 <sup>7</sup>	Prep continuation, HIV and STI testing rates, and delivery of preventive care in a clinic-based cohort	AIDS Educ. Prev.	2018	Good
8	Phanuphak et al., 2018 <sup>8</sup>	Princess PrEP program: The first key population-led model to deliver pre-exposure prophylaxis to key populations by key populations in Thailand	Sex. Health	2018	Good
9	Traeger et al., 2019 <sup>9</sup>	Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection	JAMA	2019	Good
10	Hoth et al., 2019 <sup>10</sup>	Iowa TelePrEP: a public-health-partnered telehealth model for human immunodeficiency virus preexposure prophylaxis delivery in a rural state.	Sex Transm Dis	2019	Satisfactory
11	Montaño et al., 2019 <sup>11</sup>	Differences in sexually transmitted infection risk comparing preexposure prophylaxis users and propensity score matched historical controls in a clinic setting.	AIDS	2019	Good
12	Hightow-Weidman et al., 2019 <sup>12</sup>	Incidence and correlates of sexually transmitted infections among black men who have sex with men participating in the HIV Prevention Trials Network 073 Preexposure Prophylaxis Study	Clin. Infect. Dis.	2019	Good
13	McManus et al., 2020 <sup>13</sup>	Comparison of trends in rates of sexually transmitted infections before vs after initiation of HIV preexposure prophylaxis among men who have sex with men.	JAMA Netw Open	2020	Good
14	Schumacher et al., 2020 <sup>14</sup>	Sexually transmitted infection screening among gay, bisexual, and other men who have sex with men prescribed pre-exposure prophylaxis in Baltimore City, Maryland	Clin. Infect. Dis.	2020	Good
15	Van Praet et al., 2020 <sup>15</sup>	<i>Mycoplasma genitalium</i> ; acquisition and macrolide resistance after initiation of HIV pre-exposure prophylaxis in men who have sex with men.	Sex. Transm. Infect.	2020	Satisfactory
16	Freeborn, Portillo, Boyer and Santos, 2020 <sup>16</sup>	Misclassification of sexual health risks in a self-identified low risk cohort of men who have sex with men (MSM) enrolled in a community based PrEP program	AIDS Care Psychol. Socio-Med. Asp. AIDS HIV	2020	Good
17	Morgat et al., 2020 <sup>17</sup>	Number, type and cost of microbiological tests during HIV Pre-Exposure Prophylaxis: The experience of a French hospital	Med. Mal. Infect.	2020	Satisfactory
18	Peel et al., 2021 <sup>18</sup>	Clinical presentation of incident syphilis among men who have sex with men taking HIV Pre-Exposure Prophylaxis in Melbourne, Australia	Clin. Infect. Dis.	2021	Satisfactory
19	Van Dijck et al., 2021 <sup>19</sup>	Antibacterial mouthwash to prevent sexually transmitted infections in men who have sex with men taking HIV pre-exposure prophylaxis (PReGo): a randomized, placebo-controlled, crossover trial.	Lancet Infect. Dis.	2021	Low risk of bias
20	Iniesta et al., 2021 <sup>20</sup>	Implementation of pre-exposure prophylaxis program in Spain. Feasibility of four different delivery models.	PLoS One	2021	Good

id	Study	Article title	Journal	Year of publication	Quality assessment*
21	Kiefer et al., 2021 <sup>21</sup>	Incident Cases of Sexually Transmitted Infections among Users of Pre-Exposure Prophylaxis for HIV Prevention in Honolulu, Hawaii	Hawaii J Health Soc Welf	2021	Low
22	Azarnoosh, Johansen and Martin-Iguacel 2021 <sup>22</sup>	Incidence of sexually transmitted infections after initiating HIV pre-exposure prophylaxis among MSM in Southern Denmark	Am J Mens Health	2021	Good
23	Laurent et al., 2021 <sup>23</sup>	HIV pre-exposure prophylaxis for men who have sex with men in west Africa: a multicountry demonstration study	Lancet HIV	2021	Good
24	Jongen et al., 2021 <sup>24</sup>	Choosing event-driven and daily HIV pre-exposure prophylaxis - data from two European PrEP demonstration projects among men who have sex with men	Journal of the International AIDS Society	2021	Good
25	Chemtob et al., 2021 <sup>25</sup>	"HIV Pre-Exposure Prophylaxis (PrEP) purchase patterns and STI occurrence among Israeli men: a cohort analysis"	PLoS One	2021	Satisfactory
26	Saxton et al., 2022 <sup>26</sup>	Adherence, sexual behavior and sexually transmitted infections in a New Zealand prospective PrEP Cohort: 12 months follow- up and ethnic disparities	AIDS and Behavior	2022	Good
27	Lemmet et al., 2022 <sup>27</sup>	High syphilis prevalence and incidence in people living with HIV and preexposure prophylaxis users: a retrospective review in the French Dat'AIDS cohort	PLoS One	2022	Good
28	Barbosa, Monteiro, Montenegro, Batista and Montarroyos, 2022 <sup>28</sup>	HIV Pre-Exposure Prophylaxis (PrEP) in a Brazilian clinical setting: adherence, adverse events, sexual behavior, and sexually transmitted infections	Arch Sex Behav	2022	Good
29	Zeggagh et al., 2022 <sup>29</sup>	Incidence and risk factors for recurrent sexually transmitted infections among MSM on HIV pre-exposure prophylaxis	AIDS	2022	Good
30	Tabatabavakili et al., 2022 <sup>30</sup>	Incidence of hepatitis C virus infections among users of human immunodeficiency virus pre-exposure prophylaxis	Clinical Gastroenterology and Hepatology	2022	Satisfactory
31	Traeger et al., 2022 <sup>31</sup>	Latent class analysis of sexual behaviors and attitudes to sexually transmitted infections among gay and bisexual men using PrEP	AIDS and Behavior	2022	Satisfactory
32	Schmidt et al., 2022 <sup>32</sup>	Low incidence of HIV infection and decreasing incidence of sexually transmitted infections among PrEP users in 2020 in Germany	Infection	2022	Good
33	Traeger et al., 2022 <sup>33</sup>	Real-world trends in incidence of bacterial sexually transmitted infections among gay and bisexual men using HIV pre-exposure prophylaxis (PrEP) in Australia following nationwide PrEP implementation: an analysis of sentinel surveillance data	Lancet Infect. Dis.	2022	Satisfactory
34	Candler et al., 2022 <sup>34</sup>	Retrospective audit of a convenience cohort of individuals on HIV pre-exposure prophylaxis in Alberta, Canada	JAMMI	2022	Good
35	Hechter et al., 2022 <sup>35</sup>	Sexually transmitted infections among men and transgender women using HIV pre-exposure prophylaxis in a large integrated health system-a cohort study	J. Acquired Immune Defic. Syndr.	2022	Satisfactory

\*Assessed using the NOS Scale for observational studies (good, satisfactory or low quality) or the Cochrane Scale for clinical trials (low risk of bias or high risk of bias).

**Supplementary Table 2. Characterization of the selected studies**

id	Study	Type of study	Place (country) of research	Study period	Target population with PrEP criteria	Type of PrEP	Follow-up interval (months)	Diagnostic test for syphilis
1	Solomon et al., 2014 <sup>1</sup>	Randomized clinical trial	Brazil, United States, Thailand, Ecuador, South Africa and Peru	July/2007 to December/2009	Male at birth, ≥18 years	Daily dose	1	RPR*, VDRL**, FTA-ABS***
2	Volk et al., 2015 <sup>2</sup>	Clinical cohort	United States	July/2012 to February/2015	Any PrEP user	Not informed	1 to 3 months	Not informed
3	Liu et al., 2016 <sup>3</sup>	Cohort	United States	October/2012 to January/2014	Male at birth, ≥18 years	Daily dose	1, 3, 6, 9, 12	RPR, VDRL, FTA-ABS
4	Nguyen et al., 2018 <sup>4</sup>	Retrospective cohort	Canada	2010 to 2015	Group 1 (PrEP users): MSM, ≥18 years; Group 2: MSM, who have been prescribed PEP	Daily dose and on demand	3	IgG enzyme-linked immunosorbent assay, RPR, TPPA****
5	Spinelli et al., 2018 <sup>5</sup>	Cohort	United States	January/2013 to July/2017	Any PrEP user	Not informed	Not informed	Not informed
6	Beymer et al., 2018 <sup>6</sup>	Crossover case	United States	October/2015 to May/2017	MSM	Not informed	Not informed	Not informed
7	Hevey et al., 2018 <sup>7</sup>	Retrospective cohort	United States	December/2010 to July/2016	Any PrEP user	Daily dose	Not informed	Not informed
8	Phanuphak et al., 2018 <sup>8</sup>	Cohort	Thailand	January/2016 to December/2017	MSM or transgender women who have sex with men	Daily dose	6	TPHA*****, RPR
9	Traeger et al., 2019 <sup>9</sup>	Cohort	Australia	July/2016 to April/2018	Any PrEP user	Daily dose	3	Serological test used to diagnose syphilis
10	Hoth et al., 2019 <sup>10</sup>	Retrospective cohort	United States	February/2017 to October/2018	Any PrEP user	Not informed	3	Not informed
11	Montaño et al., 2019 <sup>11</sup>	Retrospective cohort	United States	October/2011 to September/2017	MSM	Not informed	0, 1, 3, 6...	RPR, TPPA
12	Hightow-Weidman et al., 2019 <sup>12</sup>	Cohort	United States	August/2012 to September/2014	Male at birth, ≥18 years old, black	Daily dose	1, 2, 3, 6, 9, 12	RPR and confirmatory treponemal test
13	McManus et al., 2020 <sup>13</sup>	Retrospective cohort	Australia	March/2016 to April/2018	MSM	Daily dose	3	Not informed
14	Schumacher et al., 2020 <sup>14</sup>	Retrospective cohort	United States	September/2015 to March/2018	MSM, gays and bisexuals	Not informed	6	Not informed
15	Van Praet et al., 2020 <sup>15</sup>	Retrospective cohort	Belgium	June/2017 to March/2019	MSM	109 people used the daily dose	3	Highly sensitive molecular screening
16	Freeborn, Portillo, Boyer and Santos, 2020 <sup>16</sup>	Cohort	United States	November/2014 to May/2016	MSM, Gay, Bisexual, Transgender, ≥18 years old	Not informed	0,1, 3, 6, 9, 12	Not informed
17	Morgat et al., 2020 <sup>17</sup>	Retrospective cohort	France	March/2016 to December/2019	Any PrEP user	Not informed	Not informed	Chemiluminescence together with RPR/VDRL
18	Peel et al., 2021 <sup>18</sup>	Retrospective cohort	Australia	February/2016 to March/2019	MSM	Not informed	3	RPR, chemiluminescence immunoassay, TPPA
19	Van Dijck et al., 2021 <sup>19</sup>	Randomized clinical trial	Belgium	April/2019 to March/2020	Any PrEP user	Not informed	3	RPR, TPA
20	Iniesta et al., 2021 <sup>20</sup>	Cohort	Spain	December/2017 to October/2019	GBHSH, sex workers, aged 18 to 65	Daily dose	3	Not informed
21	Kiefer et al., 2021 <sup>21</sup>	Retrospective cohort	United States	April/2018 to May/2019	Any PrEP user	Daily dose	3	RPR, specific antibody test for <i>Treponema</i> .
22	Azarnoosh, Johansen and Martin-Iguacel 2021 <sup>22</sup>	Crossover case	Denmark	2017 to 2019	Any PrEP user	Daily dose	3	Not informed

id	Study	Type of study	Place (country) of research	Study period	Target population with PrEP criteria	Type of PrEP	Follow-up interval (months)	Diagnostic test for syphilis
23	Laurent et al., 2021 <sup>23</sup>	Prospective cohort	Africa	November/2017 to April/2020	MSM or transgender women who have sex with men, ≥18 years old	Daily dose and on demand	0,1, 3, 6	Not informed
24	Jongen et al., 2021 <sup>24</sup>	Retrospective cohort	Germany and Belgium	August/2015 to June/2016 (Amprep); October/2015 to December/2018 (Be-PrEP-ared)	MSM or transgender women who have sex with men, ≥18 years old	Daily dose and on demand	3	RPR, TPA <sup>1</sup> /TPPA
25	Chemtob et al., 2021 <sup>25</sup>	Retrospective cohort	Israel	September/2017 to June/2019	Any PrEP user	Daily dose	6	TPHA, VDRL, rapid plasma reagin test ('Syphilis Ab')
26	Saxton et al., 2022 <sup>26</sup>	Prospective cohort	New Zealand	February/2017 to February/2019	GBHSH	Daily dose	3	Not informed
27	Lemmet et al., 2022 <sup>27</sup>	Retrospective cohort	France	2016 to 2020	Group 1: PLHIV; Group 2: PrEP users	Not informed	3 for Prep and 12 for PLHIV	TPHA, FTA-ABS, Elisa, chemiluminescence, VDRL, RPR
28	Barbosa, Monteiro, Montenegro, Batista and Montarroyos, 2022 <sup>28</sup>	Prospective cohort	Brazil	March/2018 to February/2020	MSM, transgender women, sex workers and serodiscordant couples	Daily dose	0, 1, 3, 6	Rapid test, VDRL
29	Zeggagh et al., 2022 <sup>29</sup>	Prospective cohort	France and Canada	February/2012 to June/2016	MSM or transgender women who have sex with men, ≥18 years old	On demand	0, 1, 2, 4, 6, 8, ... until 2016 (test every six months)	Not informed
30	Tabatabavakili et al., 2022 <sup>30</sup>	Cohort	Canada	October/2012 to June/2019	Any PrEP user	Not informed	Not informed	Not informed
31	Traeger et al., 2022 <sup>31</sup>	Prospective cohort	Australia	March to June/2020	Any PrEP user	Daily dose	3	Not informed
32	Schmidt et al., 2022 <sup>32</sup>	Retrospective cohort	Germany	October/2019 to December/2019	Any PrEP user	Daily dose and on demand	Not informed	Not informed
33	Traeger et al., 2022 <sup>33</sup>	Retrospective cohort	Australia	January/2016 to December/2019	Cis or transgender people who are gay, bisexual, ≥16 years old	Daily dose	3	Not informed
34	Candler et al., 2022 <sup>34</sup>	Retrospective cohort	Canada	March/2016 to June/2019	MSM, transgender women, injecting drug users and serodiscordant couples	Daily dose	3	Elisa, RPR, TPPA
35	Hechter et al., 2022 <sup>35</sup>	Cohort	United States	June to December/2018	MSM or transgender women who have sex with men, ≥18 years old	Daily dose	Not informed	RPR

\* RPR - Rapid Plasm Reagin

\*\* VDRL - Venereal Disease Research Laboratory

\*\*\*FTA-ABS Fluorescent Treponemal Antibody-Absorption

\*\*\*\* TPPA - *Treponema pallidum* particle agglutination

\*\*\*\*\* TPHA - *Treponema pallidum* hemagglutination assay

<sup>1</sup> TPA - *Treponema pallidum* Antibodies

**Supplementary table 3. Characteristics of participants and diagnosis of acquired syphilis**

id	Study	n	Age (years)	Syphilis acquired before PrEP or at baseline			Syphilis acquired during follow-up		
				n	%	Cases per 100 person-years	n	%	Cases per 100 person-years
1	Solomon et al., 2014 <sup>1</sup>	2.499	Approximately half were between 18-24	333	13.30%	NI	279	NI	7.3
2	Volk et al., 2015 <sup>2</sup>	657	Average = 37 (Range = 20-68)	NI	NI	NI	NI	Month 6 = 3.3% (1.9-5.6%); Month 12 = 5.5% (3.3%-9.1%)	
3	Liu et al., 2016 <sup>3</sup>	557	37.5% were between 26-35	24	4.30%	NI	NI	NI	12 (95%CI 9.4-16)
4	Nguyen et al., 2018 <sup>4</sup>	304	Median PrEP Group Median = 36; Median PEP Group Median = 34	9	NI	8.26	16	NI	14.68
5	Spinelli et al., 2018 <sup>5</sup>	405	Median = 34	NI	NI	NI	NI	NI	2.4
6	Beymer et al., 2018 <sup>6</sup>	275	Approximately half were between 25-39 years old	11	NI	11.94	29	NI	17.65
7	Hevey et al., 2018 <sup>7</sup>	134	Median = 35 (Range = 19-71)	5	5%	NI	3	4% (69 tests)	NI
8	Phanuphak et al., 2018 <sup>8</sup>	1.697	Average = 28.8 (SD = 7.2)	103	6.30%	NI	NI	NI	7.2 (P=0007)
9	Traeger et al., 2019 <sup>9</sup>	2.981	Median = 34 (IQR = 28-42)	34	1.10%	NI	252	NI	8.0 (95%CI 7.1-9.0)
10	Hoth et al., 2019 <sup>10</sup>	127	Median = 31	NI	NI	NI	NI	NI	NI
11	Montaño et al., 2019 <sup>11</sup>	1.095	Mean PrEP Group = 30.6 (SD = 8.7); Mean Non-PrEP Group = 30.1 (8.6)	NI	NI	NI	NI	NI	PrEP group = 6.9 Non-PrEP group: 2.3
12	Hightow-Weidman et al., 2019 <sup>12</sup>	226	Median = 26 (IQR = 23-32)	NI	1.30%	NI	NI	Week 26 = 2.5%; Week 52 = 4.3%	NI
13	McManus et al., 2020 <sup>13</sup>	2.404	Average = 36 (SD = 10.4)	NI	1.10 % (95%CI 0.94-1.29%)	NI	NI	NI	1.12 (1.02-1.23)
14	Schumacher et al., 2020 <sup>14</sup>	290	Approximately half were aged 25-34	18	7.80%	NI	Month 6 = 14; Month 12 = 8	Month 6 = 9.9%; Month 12 = 8.7%	NI
15	Van Praet et al., 2020 <sup>15</sup>	131	Median = 40 (Range = 20-79)	NI	3.10%	NI	NI	NI	14.8 ( 9.7-21.9)
16	Freeborn, Portillo, Boyer and Santos, 2020 <sup>16</sup>	81	Average = 37 (Range = 22-71)	NI	1%	NI	Month 1 = 9 Month 4 = 1 Month 7 = 9 Month 10 = 3 Month 13 = 1	Month 1 = 1.11% Month 4 = 1% Month 7 = 15% Month 10 = Month 13 = 1%	NI
17	Morgat et al., 2020 <sup>17</sup>	135	Median = 36	NI	NI	NI	36	32,70%	NI
18	Peel et al., 2021 <sup>18</sup>	572	Not informed	18	NI	NI	61	NI	8.6 ( 95%CI 6.7-10.9)
19	Van Dijck et al., 2021 <sup>19</sup>	343	Median = 40 (IQR = 32-47.5)	141	41.10%	NI	Group LP = period I 2; period II 4 Group PL = period I 6; period II 4	LP group = period I (1.7%); period II (5.2%) PL group = period I (5.0%) period II (5.4%)	NI
20	Iniesta et al., 2021 <sup>20</sup>	321	Median = 36	NI	2.9% (95%CI 1.4-5.6)	NI	NI	NI	15.99 (CI95% 11.94-21.41)
21	Kiefer et al., 2021 <sup>21</sup>	78	Median = 33	1 (63)	2%	NI	Month 3 = 1/24; Month 6 = 0/19; Month 9 = 10/12; Month 12 = 0/16;	4%	

id	Study	n	Age (years)	Syphilis acquired before PrEP or at baseline			Syphilis acquired during follow-up		
				n	%	Cases per 100 person-years	n	%	Cases per 100 person-years
22	Azarnoosh, Johansen and Martin-Iguacel 2021 <sup>22</sup>	46	Median = 39 (IQR = 35-48)	1	NI	4.3	5	NI	21.7
23	Laurent et al., 2021 <sup>23</sup>	598	Average = 24.6 (SD = 21.9-27.9)	1	0.20%	NI	Month 1 = 1 Month 6 = 3	Month 1 = 0.2% Month 6 = 1%	NI
24	Jongen et al., 2021 <sup>24</sup>	571	Median = 39	20	3.6% (95%CI 2.2-5%)	NI	116	NI	11.4 (CI95% 9.5- 3.7)
25	Chemtob et al., 2021 <sup>25</sup>	757	Median = 35	33	4.40%	NI	NI	6,8% (CI95% 4,5%-9,0%)	NI
26	Saxton et al., 2022 <sup>26</sup>	150	Approximately half were over 30	NI	NI	NI	NI	8.70%	NI
27	Lemmet et al., 2022 <sup>27</sup>	10.265	Median HIV Group Median = 41 (IQR = 33-51); Median PrEP group Median = 37 (IQR = 30-47)	HIV group = 1708 PrEP group = 434	HIV group = 19.9%; PrEP group = 25.8%	NI	HIV group = 861; PrEP group = 152	HIV group = 19.9%; PrEP group = 12.2%	NI
28	Barbosa, Monteiro, Montenegro, Batista and Montarroyos, 2022 <sup>28</sup>	219	Median = 30	36	17.60%	NI	Month 4 = 25 Month 7 = 28 Month 10 = 36	Month 4 = 14.0%; Month 7 = 15.6% Month 10 = 21.4%	NI
29	Zeggagh et al., 2022 <sup>29</sup>	429	Median = 35	18	4.20%	NI	NI	NI	13.0
30	Tabatabavakili et al., 2022 <sup>30</sup>	109	Median = 35 (Range = 23-68)	NI	NI	NI	NI	NI	5.2 (CI95% 1.4-13)
31	Traeger et al., 2022 <sup>31</sup>	1.225	Median = 42.1 (SD = 11.1)	NI	NI	NI	76	8.40%	NI
32	Schmidt et al., 2022 <sup>32</sup>	4.620	Median = 38 (IQR = 32-45)	234	3.63% (95%CI = 2.93-4.44%)	NI	NI	NI	10.08 (CI95% 9.18-11.03)
33	Traeger et al., 2022 <sup>33</sup>	22.730	Median = 34 (IQR = 28-43)	NI	NI	NI	1488	NI	9.4 (CI95%9.0-9.8)
34	Candler et al., 2022 <sup>34</sup>	511	Median = 34 (IQR = 28-43)	50	10.1% (95%CI = 7.6- 13.1%)	NI	5	NI	1.94 (CI95%0.73-5-12)
35	Hechter et al., 2022 <sup>35</sup>	5.042	Median = 34 (IQR = 28-43)	NI	NI	NI	NI	NI	7.8 (CI95%7.1-8.4)

SD - Standard deviation  
IQR - Interquartile Range  
NI - Not informed

**Supplementary table 4. Subgroup analysis of syphilis acquired before PrEP**

Styles of meta	n° of studies	Pooled rate (%)	CI 95%	I <sup>2</sup> (%)	p-value
- All studies with available data	14	6.0	3.0 - 9.0	99.0	<0.01
- Stratifying by regions of the Sustainable Development Goals					
-- Studies that occurred in Europe and Northern America	8	8.0	4.0 - 12.0	99.0	<0.01
-- Studies that occurred in Australia	2	2.0	<1.0 - 4.0	90.0	<0.01
-- Studies that occurred in South-Eastern Asian, Africa and Central and Southern Asia	4	5.0	1.0 - 14.0	97.0	<0.01
- Stratifying by population of study					
-- Any PrEP users	7	8.0	3.0 - 15.0	99.0	<0.01
-- MSM or transgender women who have sex with men	7	4.0	2.0 - 6.0	92.0	<0.01

CI - Confidence Interval

**Supplementary table 5. Subgroup analysis of syphilis acquired at baseline and during PrEP follow-up**

Styles of meta	N° of studies	Pooled Incidence ( per 100 person- years)	CI 95%	I <sup>2</sup> (%)	p-value
- All studies with available data	8	8.89	6.45 - 13.32	92.0	<0.01
- Stratifying by regions of the Sustainable Development Goals					
-- Studies that occurred in Europe and Northern America	5	11.79	5.18 - 18.39	94	<0.01
-- Studies that occurred in Australia	3	8.77	7.74 - 9.80	69	0.04
- Stratifying by population of study					
-- Any PrEP users	4	7.24	2.70 - 11.78	96	<0.01
-- MSM or transgender women who have sex with men	4	12.06	8.40 - 15.71	69	0.02

CI - Confidence Interval

## References

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