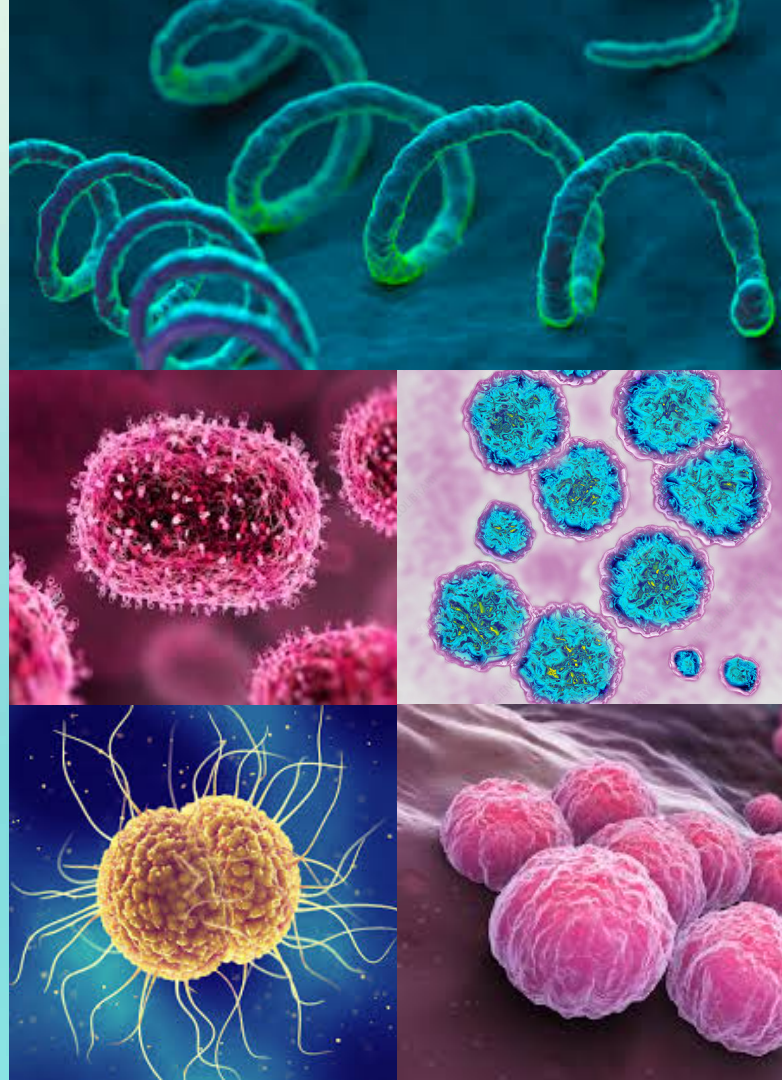
Sanquin

Epidemiology of syphilis and other sexually transmitted infections

Thijs van de Laar
Medical Molecular Microbiologist
Laboratory of Blood-borne Infections
Sanquin Research, the Netherlands

May 14th, 2025

For Life.



Transfusion transmitted syphilis (TTS)

- **Zero TTS in the US since 1965**
- **Should we still test for syphilis?**

  Movement to non-renumerated donors.

  Deferral of (sexually) high-risk donors.

  Relatively low syphilis incidence rate.

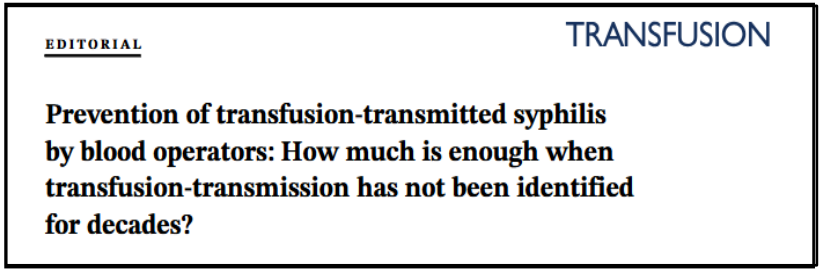
  Most TP-Ab positive donors are not infectious (<2%)

  Impact of refrigeration / storage time on bacterial survival.

  Use of antibiotics in hospitalized patients.

- **Screen blood and blood products for TP antibodies**

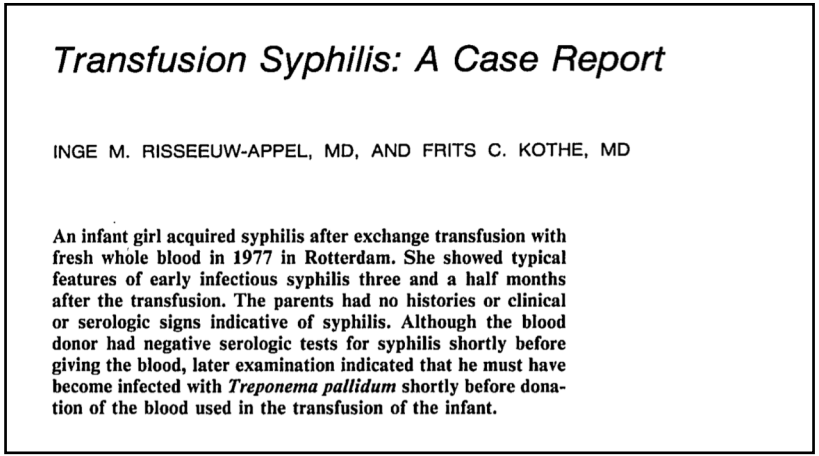
  WHO: **Yes / ** EU directive 2002/98/EC: **No**



EDITORIAL

TRANSFUSION

Prevention of transfusion-transmitted syphilis by blood operators: How much is enough when transfusion-transmission has not been identified for decades?



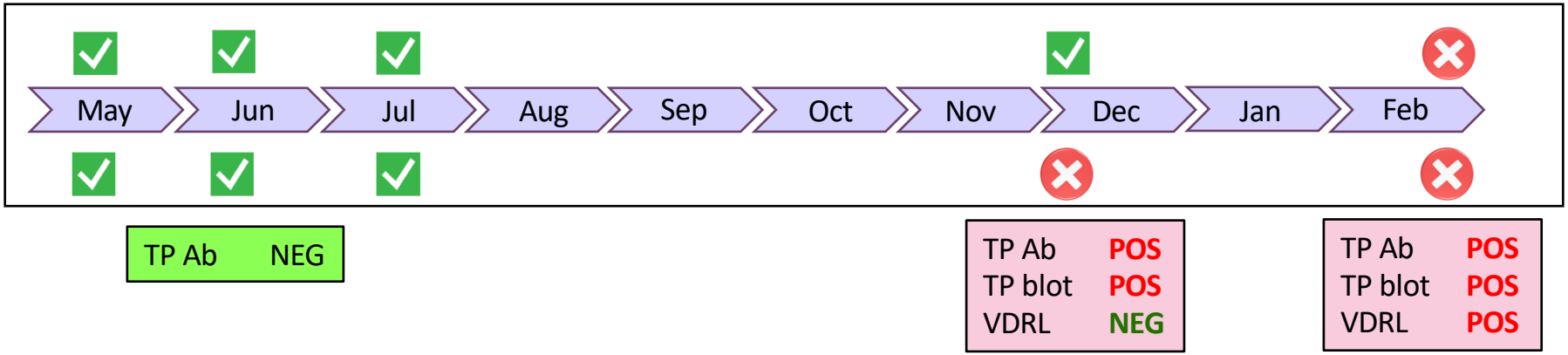
Transfusion Syphilis: A Case Report

INGE M. RISSEEUW-APPEL, MD, AND FRITS C. KOTHE, MD

An infant girl acquired syphilis after exchange transfusion with fresh whole blood in 1977 in Rotterdam. She showed typical features of early infectious syphilis three and a half months after the transfusion. The parents had no histories or clinical or serologic signs indicative of syphilis. Although the blood donor had negative serologic tests for syphilis shortly before giving the blood, later examination indicated that he must have become infected with *Treponema pallidum* shortly before donation of the blood used in the transfusion of the infant.

Drews et al (2021) Transfusion 61: 3055-3060
Risseeuw Appel et al STD (1983) 10: 200-201

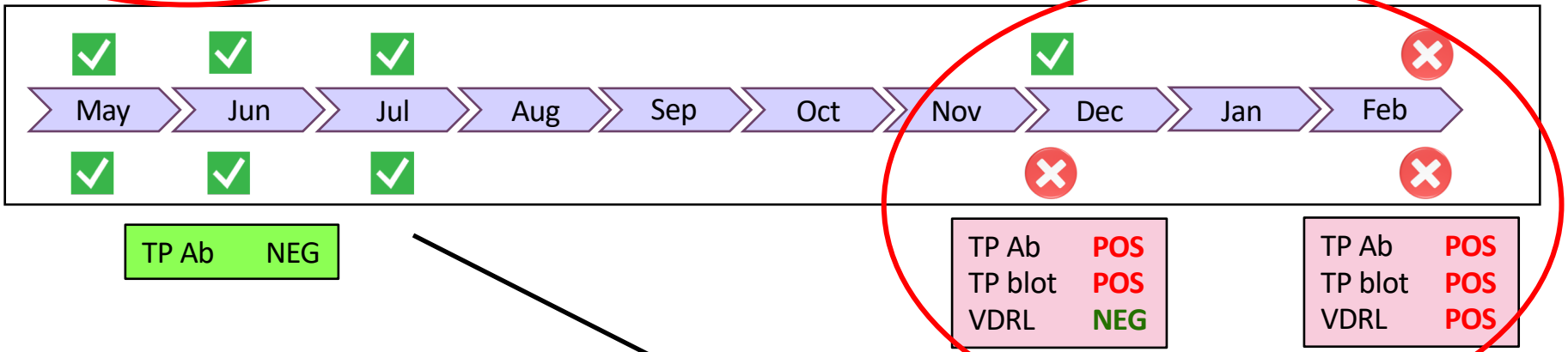
Platelet donor A: male, 44 years, 51 donations



Posttest counselling

Past: Homo- and heterosexual contacts
Present: Long-term heterosexual relationship
No sexual contacts past 12 months
Ulcus on penis december 2023
Exanthema hand palms january/february 2024

Platelet donor A: male, 44 years, 51 donations



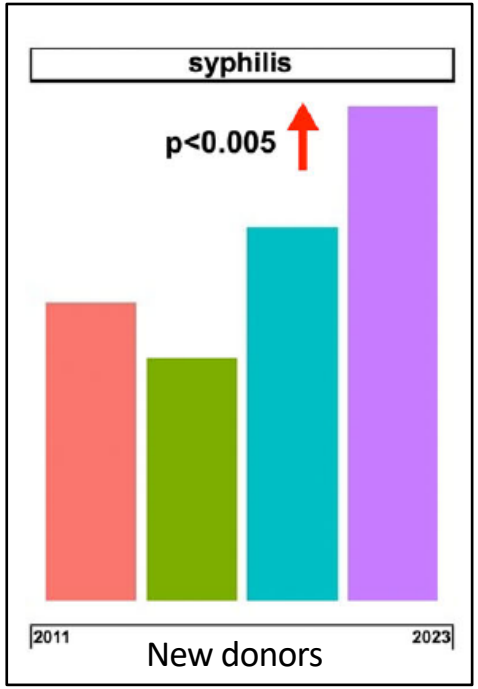
Posttest counselling

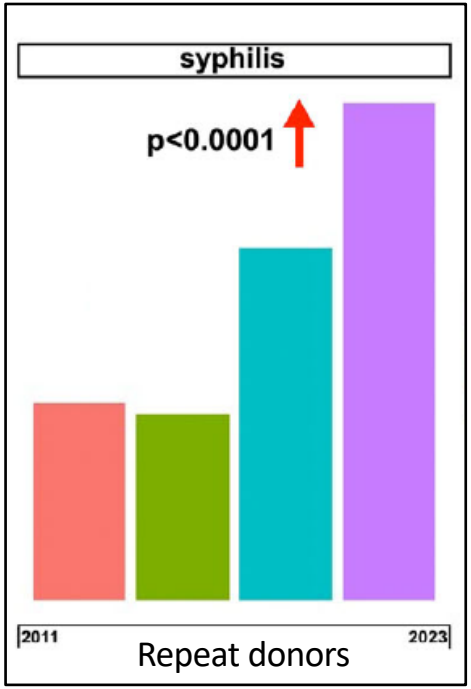
Past: Homo- and heterosexual contacts
Present: Long-term heterosexual relationship
No sexual contacts past 12 months
Ulcus on penis december 2023
Exanthema hand palms january/february 2024

Look back

Recipients: both anti-TP negative (no transmission)

Syphilis among Dutch donors





Quee et al (2024) Transfusion 64: 1732-1742

MSM Deferral

- Permanent
- Temporary (12 months)
- Temporary (4 months)
- No deferral (longterm monogamous)

Syphilis in donors (period 2011 – 2023)

Prevalence:	21.5 to 46.8 /100.000	**(+118%)**
Incidence:	1.7 to 4.6 /100.000	**(+171%)**

- **Proportion MSM-associated syphilis increases**

  New donors: 2 → 34%
  Repeat donors: 12 → 38%

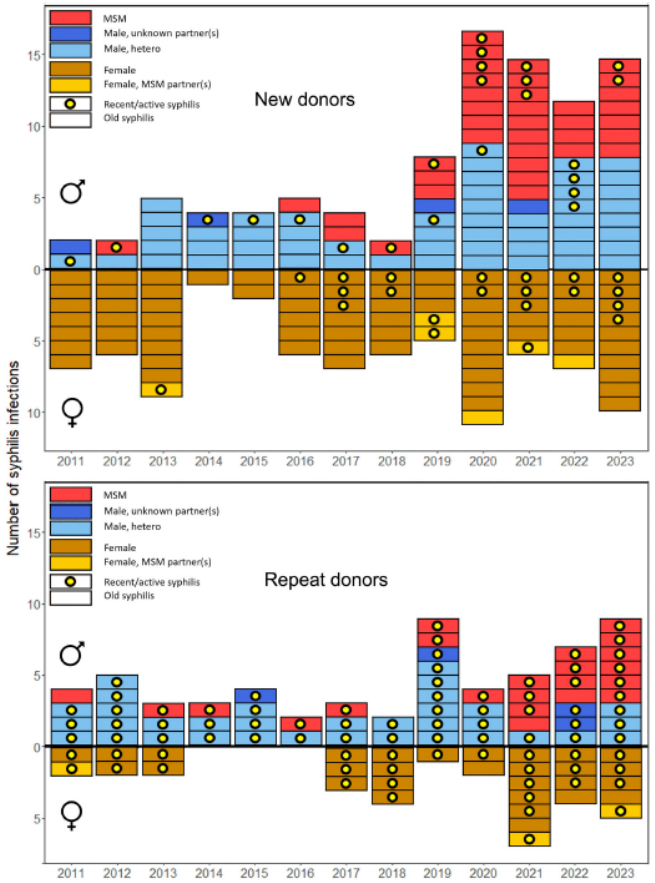
  From 3 month MSM deferral onwards:
  32% *MSM new donors has a recent/active syphilis*

- **Female donors with syphilis (2021-2023)**

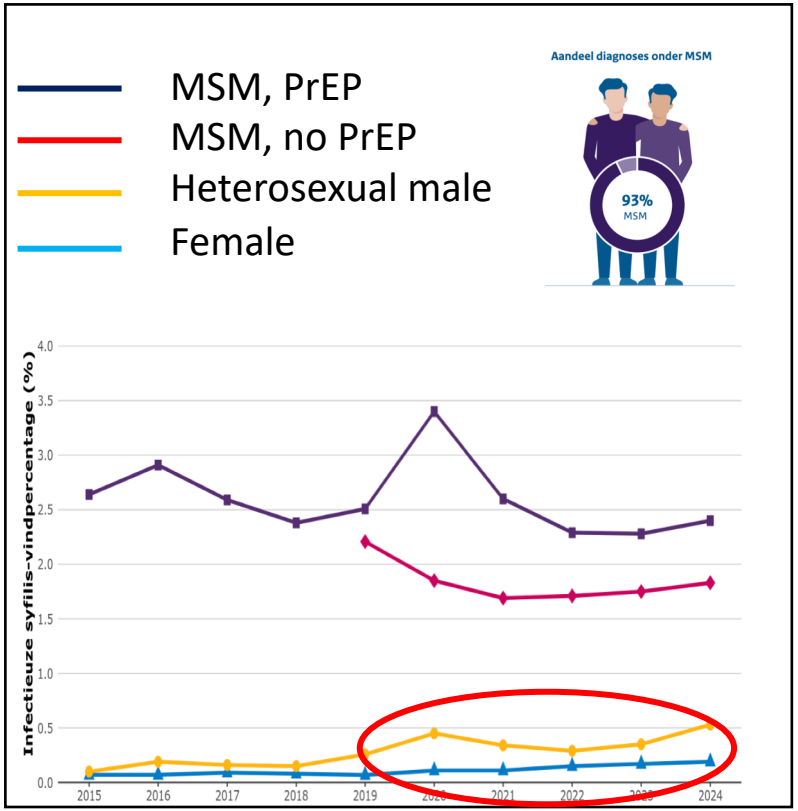
  43% female new donors has recent/active syphilis

  43% syphilis positive repeat donors is female.

  Small proportion women reports MSM partners



Quee et al (2024) Transfusion 64: 1732-1742



Syphilis in the general Dutch population

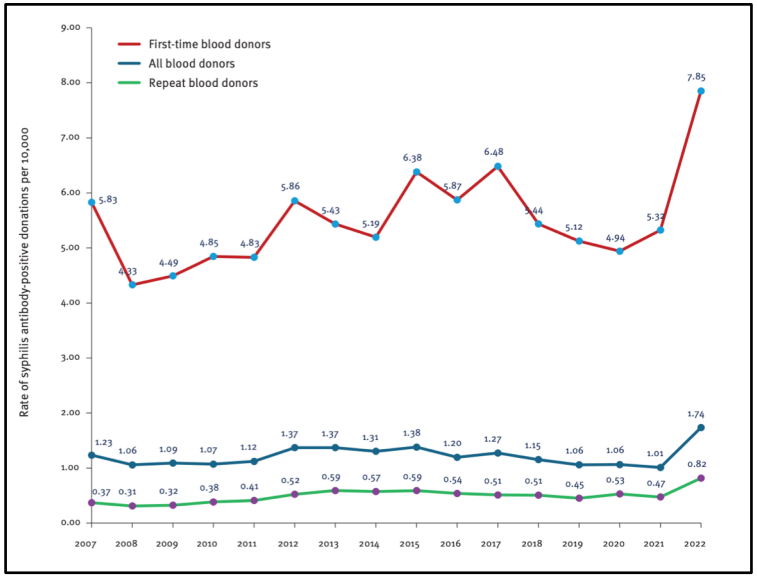
- 93% of infectious syphilis in MSM.
- **Antenatal screening:**

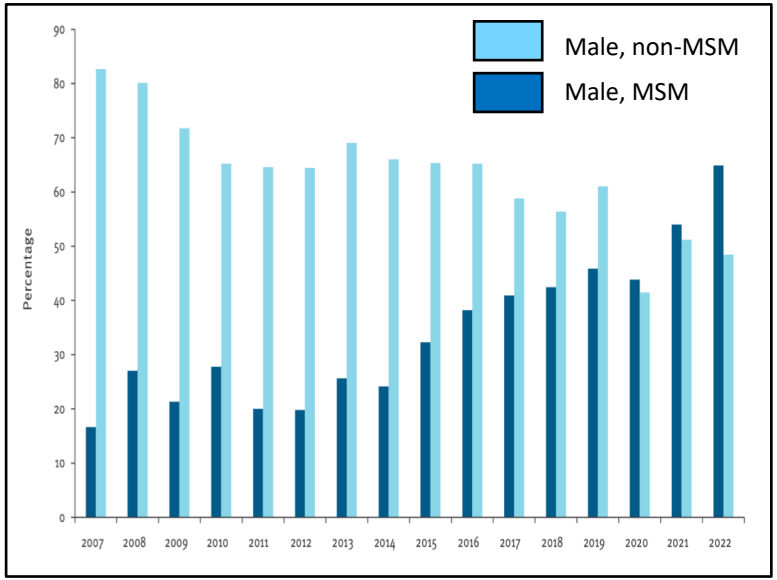
  2014: 135/176,070 (0.08%)
  2024: 14/168,329 (0.01%)

- Congenital syphilis (max 1 case a year)

No evident increase of syphilis in general population.
Rise of syphilis in donors might reflect the changes
In MSM policy, but ….

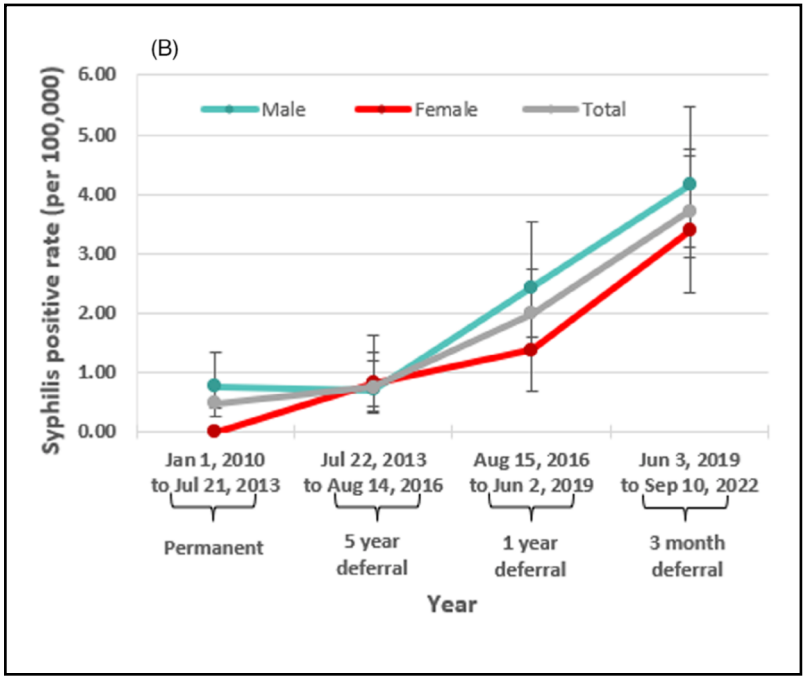
Syphilis in French donors





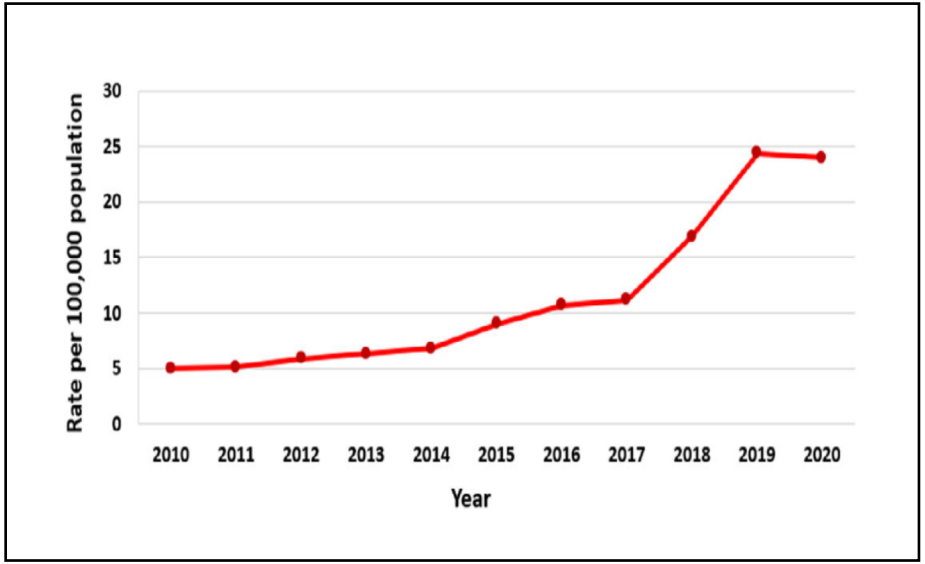
Laperche et al (2024) Eurosurveillance 29: 2400036

Syphilis among Canadian donors



O'Brien et al (2023) Transfusion 63: 1195-2023

Syphilis among general Canadian population

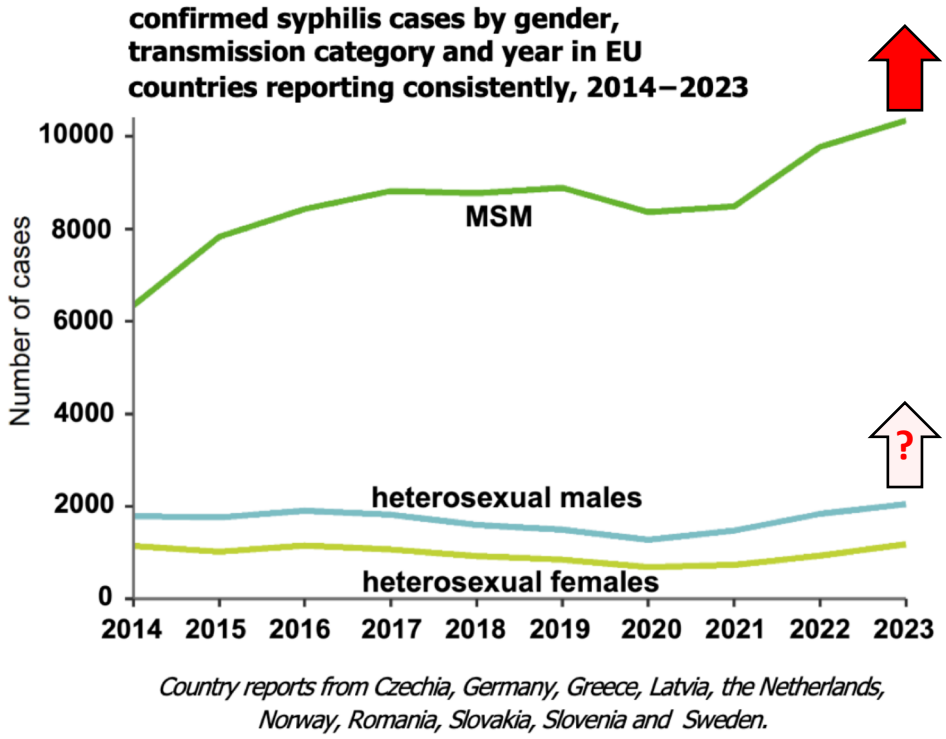


Two clearly separated large syphilis epidemics:

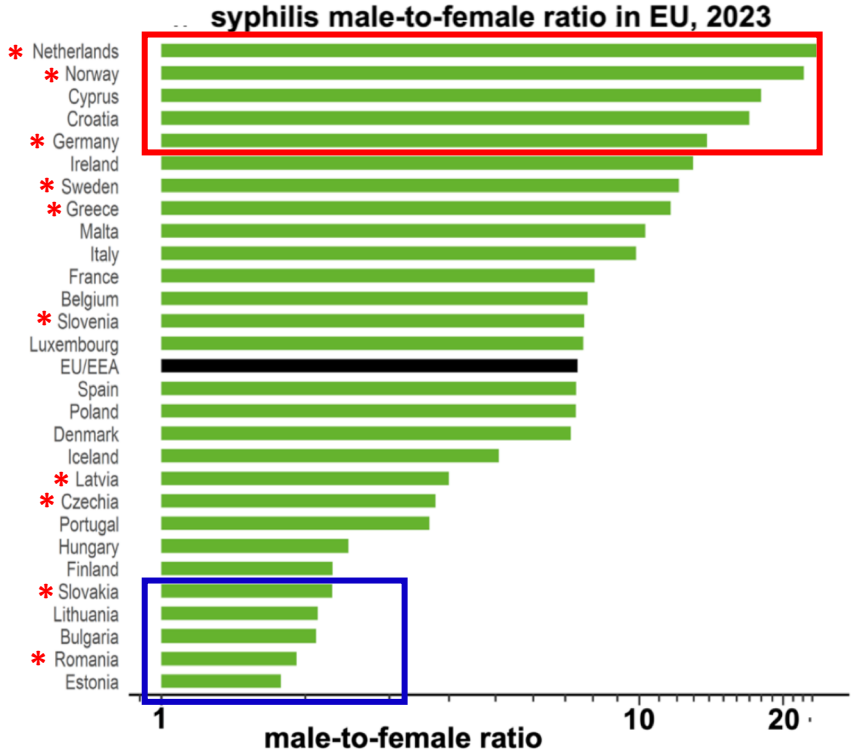
- MSM ↑ (40%)
- Heterosexual ↑↑ (60%)

Syphilis in Europe

ECDC report, Feb. 2025

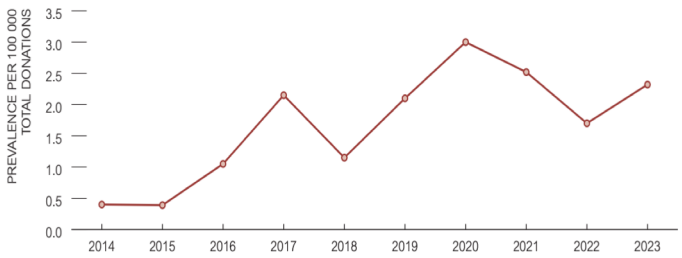


Country reports from Czechia, Germany, Greece, Latvia, the Netherlands, Norway, Romania, Slovakia, Slovenia and Sweden.



Australia (Infectious syphilis)

Figure 31 Prevalence of potentially infectious syphilis in all tested blood donations in Australia, by year of donation, 2014-2023



	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Prevalence in all donations	0.40	0.39	1.05	2.15	1.15	2.10	3.00	2.52	1.70	2.32

ARC Life Blood TTI Report 2024

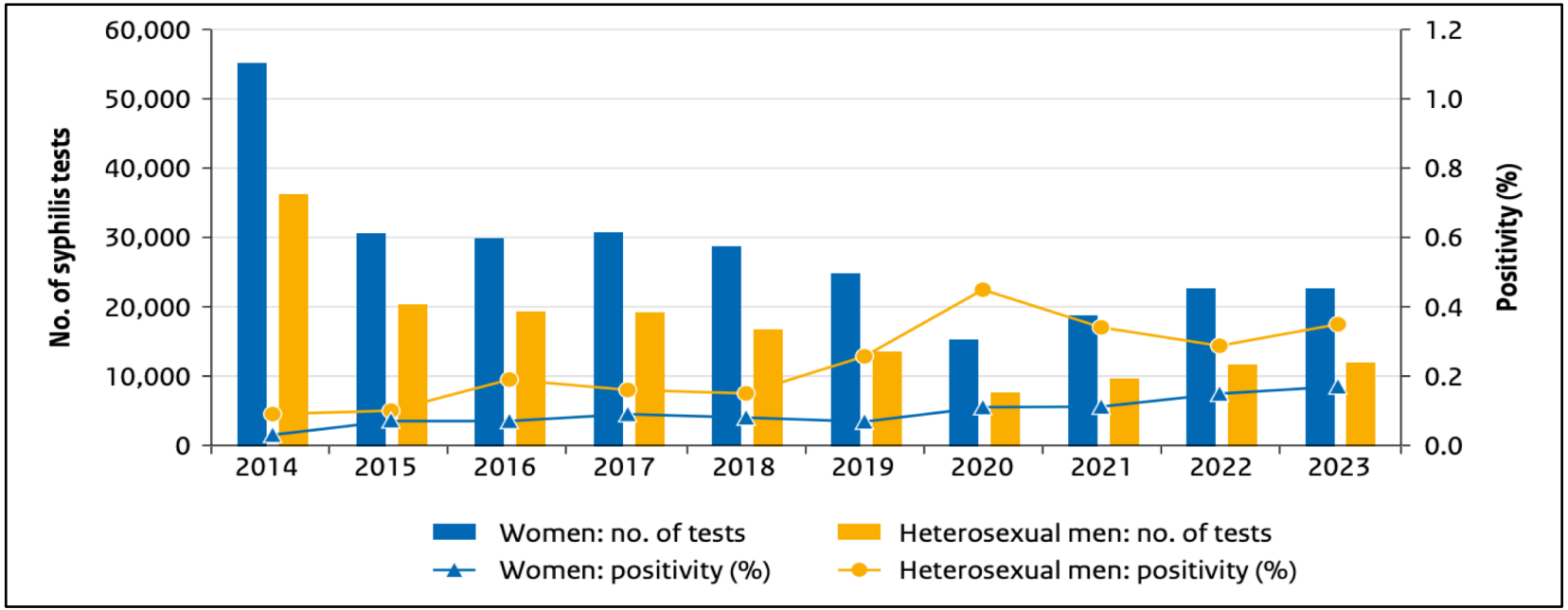
Classical risk groups general population:
- MSM
- Heterosexuals remote areas (aboriginals / Torres Strait)

Recent rise in syphilis
- MSM
- Other male and female heterosexuals

Comparison of prevalence of potentially infectious syphilis among blood donors and the general population

As noted above, prevalence of potentially infectious syphilis in first-time donors in 2023 and the ten-year study period 2014-2023 was 10.4 and 6.2 per 100 000 donations, respectively (Supplementary Table 3B and Table 1C). However, estimates on population prevalence for infectious syphilis are unknown and information is only available on infectious syphilis notifications.[1] It is therefore difficult to compare the prevalence of syphilis among Australian blood donors and the general population as notifications likely represent only a proportion of the total cases (those for which health care was sought, a test conducted and a diagnosis made, followed by a notification to health authorities).

Netherlands: syphilis in heterosexuals



Positivity rate depends on test-policy, triage and eventual number of tests performed.

Syphilis as surrogate marker for sexual risk behaviour and HIV

DONOR INFECTIOUS DISEASE TESTING

Monitoring syphilis serology in blood donors: Is there utility as a surrogate marker of early transfusion transmissible infection behavioral risk?

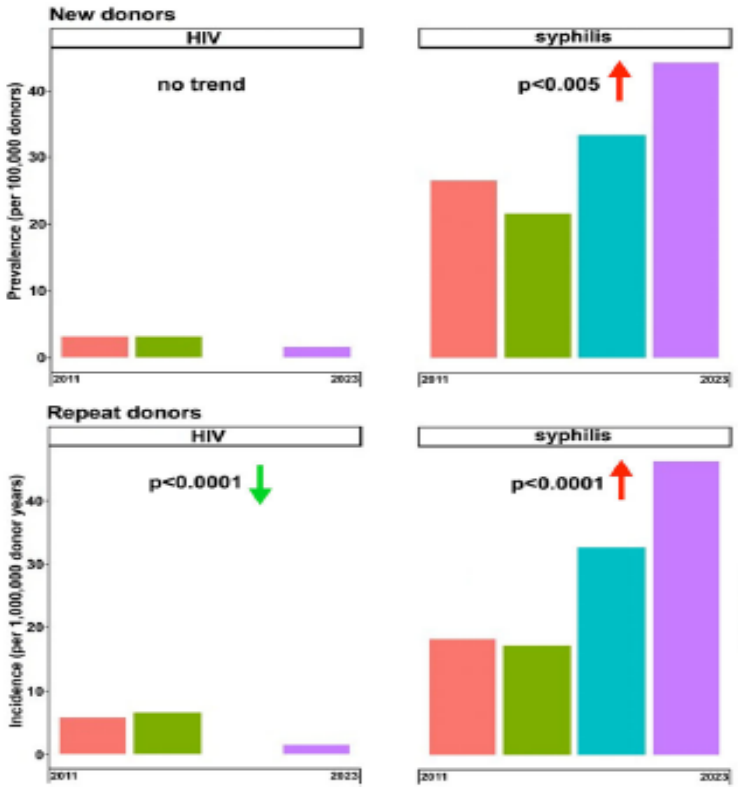
Sheila F. O'Brien[1,2] | Steven J. Drews[3,4] | Qi-Long Yi[1] | Lori Osmond[1] | Vanessa Tran[5,6] | Hong Yuan Zhou[7,8] | Mindy Goldman[1,9]

O'Brien et al (2023) Transfusion 63: 1195-2023

STI	Incidence 2024	% MSM 2024	Serological screening available	Blood-borne
Chlamydia	70.000	<25%	No	No
Gonorrhea	30.000	70-75%	No	No
Syphilis	1,500 - 2.000	90-95%	Yes	Yes
HIV	450-500	60% (80-90%)*	Yes	Yes
HCV	<50	100%	Yes	Yes

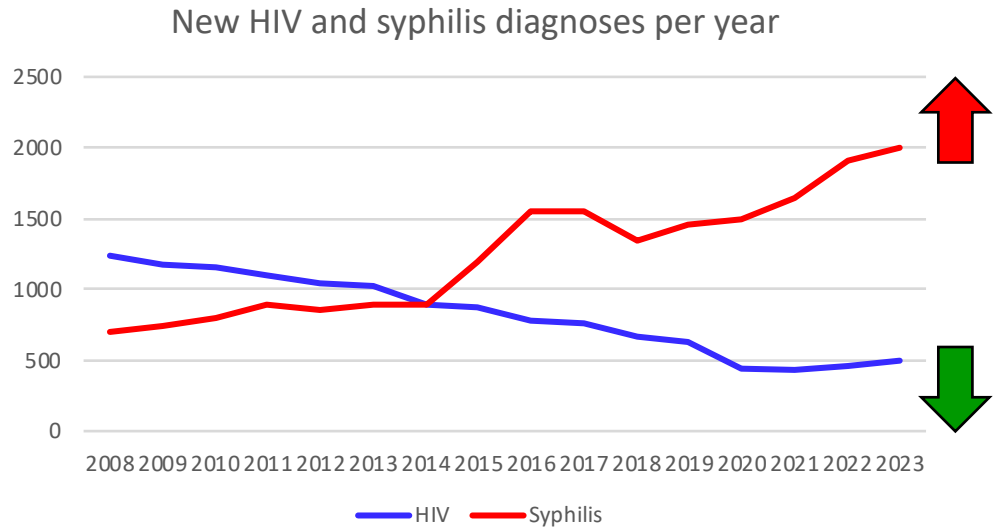
** Excluding new HIV diagnoses among migrants infected in country of origin*

Dutch donors



Quee et al (2024) Transfusion 64: 1732-1742

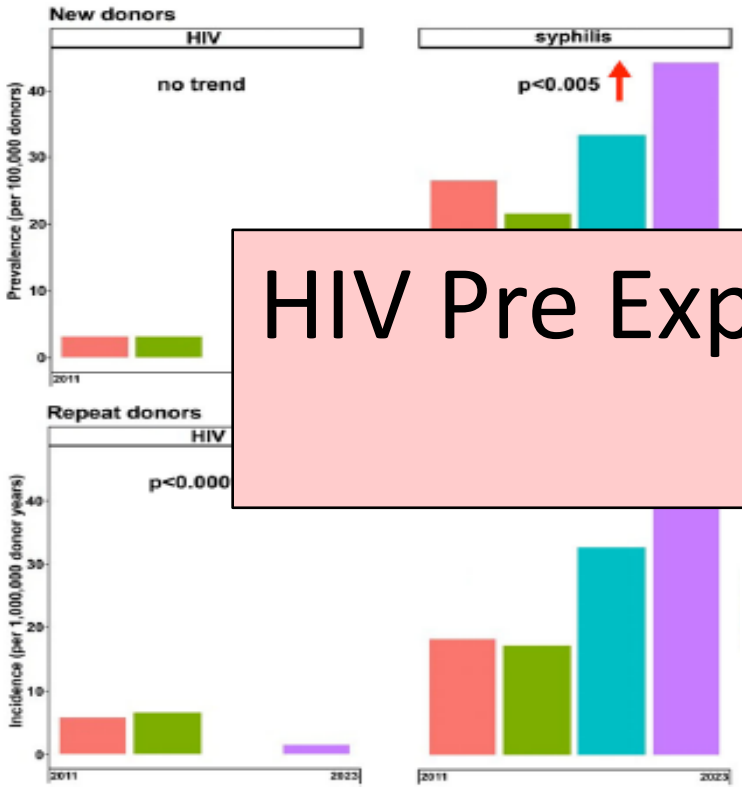
Dutch general population



SHM Report 2024
RIVM STI report 2025

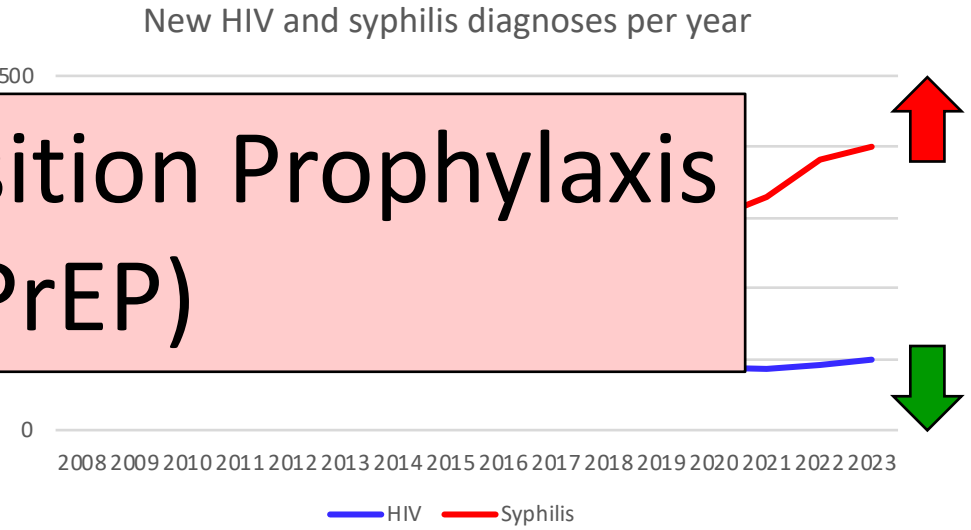
HIV Pre Exposition Prophylaxis (PrEP)

Dutch donors



Quee et al (2024) Transfusion 64: 1732-1742

Dutch general population



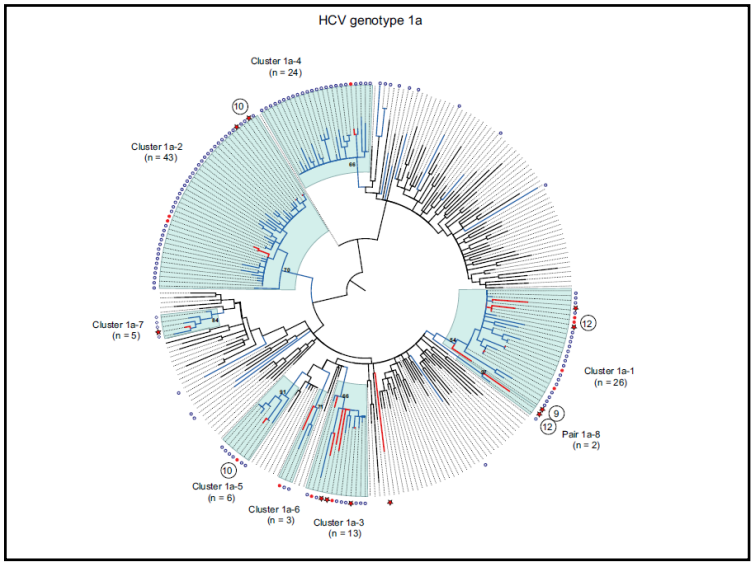
SHM Report 2024
RIVM STI report 2025

PrEP and its effect on sexually transmitted infections other than HIV: Hepatitis C

Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

High incidence of HCV in HIV-negative men who have sex with men using pre-exposure prophylaxis



Hoornenborg et al (2020) J Hepatology 72: 855-864

Before PrEP:

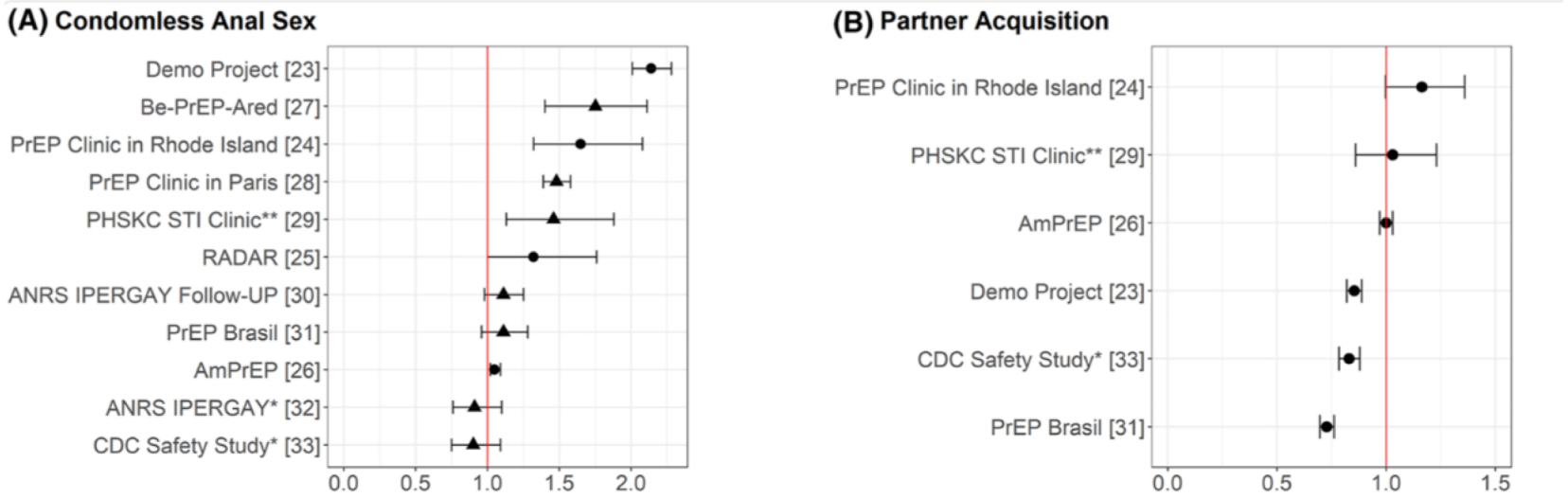
- Sexually transmitted HCV confined to HIV+ MSM.
- Multiple circulating MSM-specific HCV strains.

After PrEP:

- Increasing HCV incidence in HIV- MSM.
- HCV MSM strains enter HIV- MSM population.
- Overlap sexual networks HIV+ / HIV-

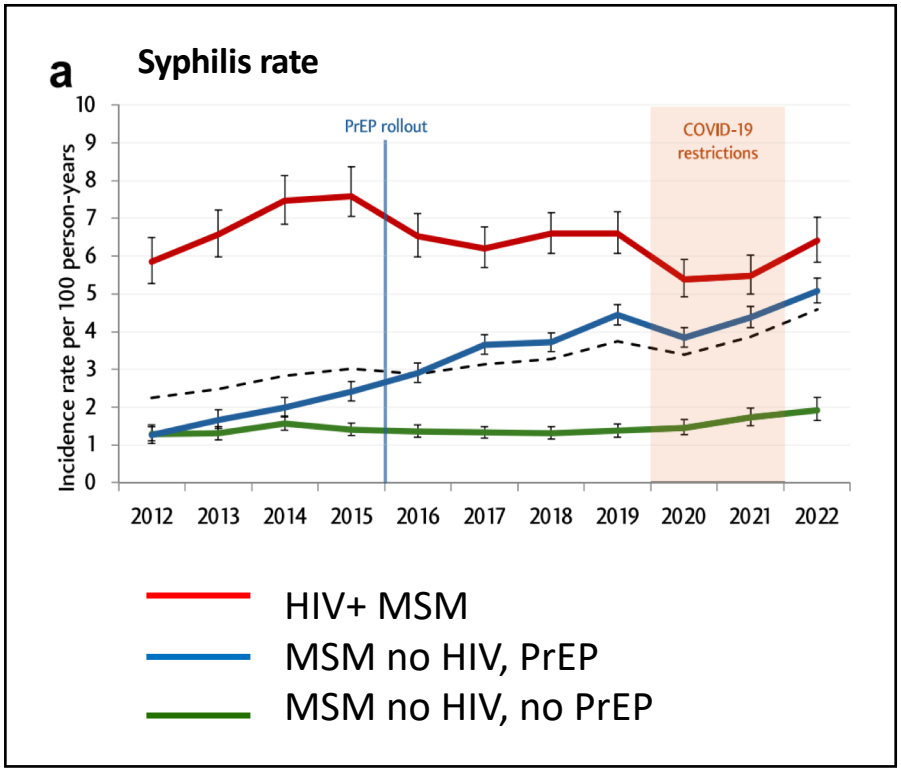
HCV became a surrogate marker for (part of the) prevented HIV-infections due to PrEP.

Sexual Risk Behavior and PrEP



Kumar et al (2020) AIDS behaviour 25: 1810-1820

PrEP and its effect on sexually transmitted infections other than HIV: Syphilis



- MSM population level study from Australia
- HIV+ MSM: highest rate of syphilis (constant).
- MSM on PrEP: increasng rate of syphilis.
- MSM no PrEP: lowest rate of syphilis (constant).

MSM on PrEP start to ‘ behave as’ HIV+ MSM with increasingly overlapping sexual networks

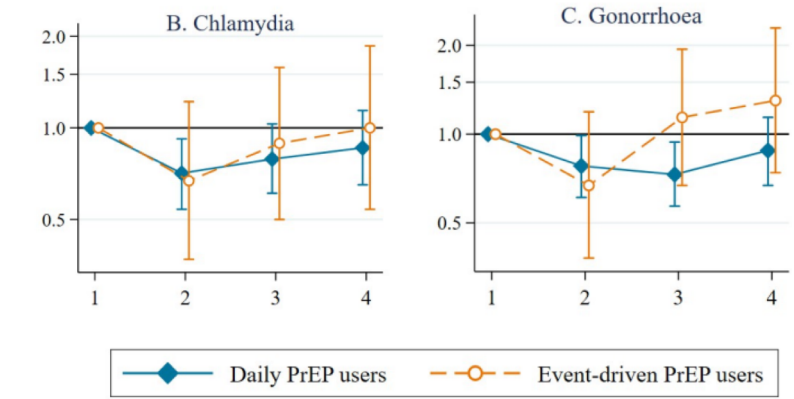
Contrast: chlamydia and gonorrhea do not show (such a) profound increase in MSM on PrEP

Traeger et al (2024) Lancet RHWP 51: 101175; Traeger et al (2022) Lancet ID 22: 1231-1241

Impact of PrEP on different STI

STI	Incidence 2024	% MSM 2024	Impact
Chlamydia	70.000	<25%	No
Gonorrhea	30.000	70-75%	No
Syphilis	2.000	90-95%	Yes
HIV	450-500	60% (80-90%)*	Yes
HCV	<50	100%	Yes

STI incidence rate



MSM on Daily PrEP

- Sex with casual partners: 52 per year
- STI Rate: 97/100 PY

Saturation with more 'common' STIs?

Elshout et al (2024) Plos Med 21: 1004328

Impact of PrEP on different STI

STI	Incidence 2024	% MSM 2024	Impact
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STI incidence rate



MSM on

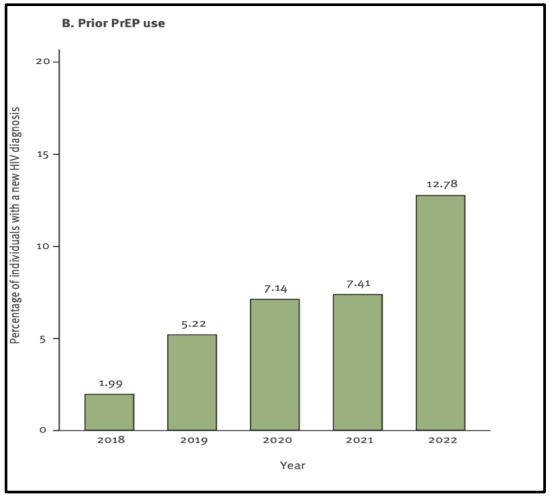
- partners: 52 per year
- 97/100 PY

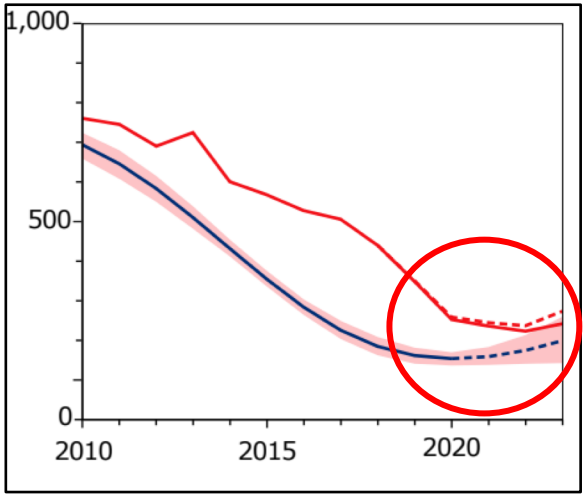
ation with more 'common' STIs?

These are not our donors

Elshout et al (2024) Plos Med 21: 1004328

HIV PrEP use and HIV incidence in the Netherlands : recent developments







M184V/I

K65R

17%

Prior PrEP use among MSM With new HIV diagnosis rises to 12% in 2023

After years declining number of new HIV-infections in MSM stagnates or even might go up.

High rate of HIV resistance Mutations among MSM with new HIV diagnosis and prior PrEP use

Jongen et al (2024) Eurosurveillance 29 2400083

Nieuws

Nieuwe cijfers: aantal nieuwe hiv-besmettingen in Amsterdam bijna nul

In Amsterdam wordt bijna niemand meer besmet met hiv. Dat blijkt uit maandag gepubliceerde cijfers van het Aidsfonds-Soa Aids Nederland. Volgens het fonds is dat omdat preventiemiddel PrEP steeds beter beschikbaar is.

Het Parool 25 september 2023, 03:00



FALSE SENSE OF SECURITY

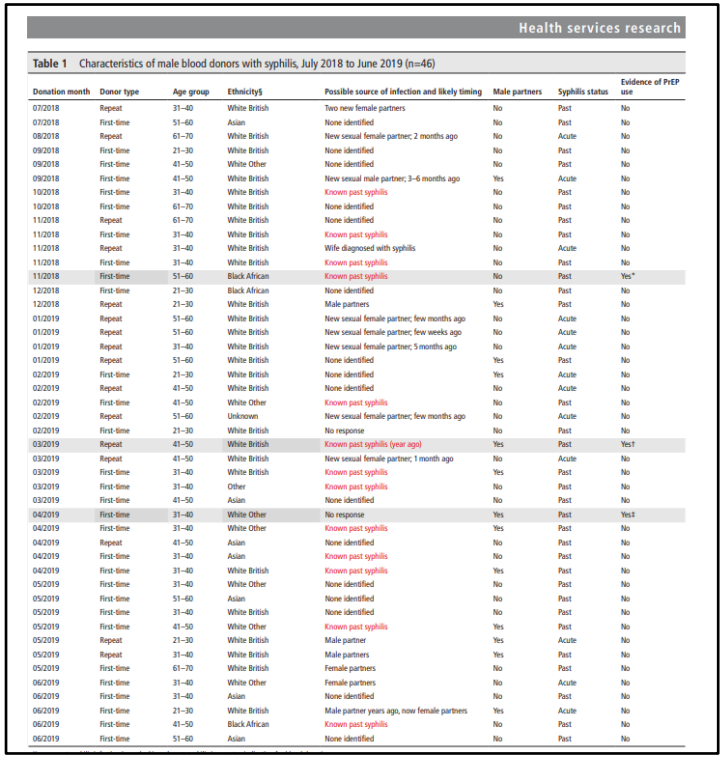
National newspaper:
Only 9 new HIV-infections in Amsterdam in 2022 due to the succes of PrEP

Reality:
Only in ‘my’ hospital in Amsterdam we had over 50 new HIV diagnoses in 2022.

Don’t celebrate victory too early, we have not won the battle yet.

Syphilis might still represent a population at risk for HIV with declining PrEP compliance.

Donors, syphilis and HIV PrEP



Health services research

Table 1 Characteristics of male blood donors with syphilis, July 2018 to June 2019 (n=46)

Donation month	Donor type	Age group	Ethnicity§	Possible source of infection and likely timing	Male partners	Syphilis status	Evidence of PrEP use
07/2018	Repeat	31–40	White British	Two new female partners	No	Past	No
07/2018	First-time	51–60	Asian	None identified	No	Past	No
08/2018	Repeat	61–70	White British	New sexual female partner; 2 months ago	No	Acute	No
09/2018	First-time	21–30	White British	None identified	No	Past	No
09/2018	First-time	41–50	White Other	None identified	No	Past	No
09/2018	First-time	41–50	White British	New sexual male partner; 3–6 months ago	Yes	Acute	No
10/2018	First-time	31–40	White British	Known past syphilis	No	Past	No
10/2018	First-time	61–70	White British	None identified	No	Past	No
11/2018	Repeat	61–70	White British	None identified	No	Past	No
11/2018	First-time	31–40	White British	Known past syphilis	No	Past	No
11/2018	Repeat	31–40	White British	Wife diagnosed with syphilis	No	Acute	No
11/2018	First-time	31–40	White British	Known past syphilis	No	Past	No
11/2018	First-time	51–60	Black African	Known past syphilis	No	Past	Yes*
12/2018	First-time	21–30	Black African	None identified	No	Past	No
12/2018	Repeat	21–30	White British	Male partners	Yes	Past	No
01/2019	Repeat	51–60	White British	New sexual female partner; few months ago	No	Acute	No
01/2019	Repeat	51–60	White British	New sexual female partner; few weeks ago	No	Acute	No
01/2019	Repeat	31–40	White British	New sexual female partner; 5 months ago	No	Acute	No
01/2019	Repeat	51–60	White British	None identified	Yes	Past	No
02/2019	First-time	21–30	White British	None identified	Yes	Acute	No
02/2019	Repeat	41–50	White British	None identified	No	Acute	No
02/2019	First-time	41–50	White Other	Known past syphilis	No	Past	No
02/2019	Repeat	51–60	Unknown	New sexual female partner; few months ago	No	Acute	No
02/2019	First-time	21–30	White British	No response	No	Past	No
03/2019	Repeat	41–50	White British	Known past syphilis (year ago)	Yes	Past	Yes†
03/2019	Repeat	41–50	White British	New sexual female partner; 1 month ago	No	Acute	No
03/2019	First-time	31–40	White British	Known past syphilis	Yes	Past	No
03/2019	First-time	31–40	Other	Known past syphilis	No	Past	No
03/2019	First-time	41–50	Asian	None identified	No	Past	No
04/2019	First-time	31–40	White Other	No response	Yes	Past	Yes‡
04/2019	First-time	31–40	White Other	Known past syphilis	Yes	Past	No
04/2019	Repeat	41–50	Asian	None identified	No	Past	No
04/2019	First-time	31–40	Asian	Known past syphilis	No	Past	No
04/2019	First-time	31–40	White British	Known past syphilis	Yes	Past	No
05/2019	First-time	31–40	White Other	None identified	No	Past	No
05/2019	First-time	51–60	Asian	None identified	No	Past	No
05/2019	First-time	31–40	White British	None identified	No	Past	No
05/2019	First-time	41–50	White Other	Known past syphilis	Yes	Past	No
05/2019	Repeat	21–30	White British	Male partner	Yes	Acute	No
05/2019	Repeat	31–40	White British	Male partners	Yes	Past	No
05/2019	First-time	61–70	White British	Female partners	No	Past	No
06/2019	First-time	31–40	White Other	Female partners	No	Acute	No
06/2019	First-time	31–40	Asian	None identified	No	Past	No
06/2019	First-time	21–30	White British	Male partner years ago, now female partners	Yes	Acute	No
06/2019	First-time	41–50	Black African	Known past syphilis	No	Past	No
06/2019	First-time	51–60	Asian	None identified	No	Past	No

Harvala et al (2022) STI 98: 132-135

UK (2018-2019)

6.5% male donors with syphilis had PrEP in their blood

Netherlands (2018-2019)

0.02% male donors from large cities had PrEP in their blood

2.5% male donors with syphilis had PrEP in their blood

High rates of PrEP use among syphilis positive males donors suggests syphilis is still a good surrogate marker for sexual risk behaviour even if its epidemiology diverges from the epidemiology of HIV.

The ongoing fight against bacterial STI

ORIGINAL ARTICLE

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

A PrEP Cohort

Analyses	Doxycycline	Standard Care	Relative Risk (95% CI)	P Value
	no. of quarterly visits with event /total no. of visits (%)			
Primary analysis				<0.001
Any STI	61/570 (10.7)	82/257 (31.9)	0.34 (0.24–0.46)	
Secondary analysis				
Any gonorrhea	52/570 (9.1)	52/257 (20.2)	0.45 (0.32–0.65)	
Urethral	5/570 (0.9)	12/257 (4.7)	0.19 (0.06–0.55)	
Pharyngeal	38/570 (6.7)	34/257 (13.2)	0.50 (0.32–0.78)	
Rectal	25/570 (4.4)	29/257 (11.3)	0.40 (0.23–0.69)	
Any chlamydia	8/570 (1.4)	31/257 (12.1)	0.12 (0.05–0.25)	
Urethral	1/570 (0.2)	6/257 (2.3)	0.07 (0.01–0.59)	
Pharyngeal	2/570 (0.4)	4/257 (1.6)	0.22 (0.04–1.14)	
Rectal	7/570 (1.2)	23/257 (8.9)	0.14 (0.06–0.32)	
Any early syphilis	2/570 (0.4)	7/257 (2.7)	0.13 (0.03–0.59)	

Luetkemeyer et al (2023) NEJM 388: 1296 - 1306

Rationale:

- Rise bacterial STI after PrEP roll out.
- Bacterial STI facilitate HIV acquisition.

Doxy-PEP: Take doxycyclin (200 mg) wthin 24 hours (max 72 hours) after condomless sex to abort a possible infection with a bacterial STI.

- 88% decrease Chlamydia ⬇
- 87% decrease Syphilis ⬇
- High adherence and acceptability
- Safe, no severe side-effects

Potential risks of broad implementation of doxy PEP

POPULATION LEVEL

- **Promotion of antimicrobial resistance**
  - Bacterial STI (*N. gonorrhoeae, LGV*)
  - Other bacterial infections
  - Gut Microbiome
- **Short and long-term adverse affects**
  - Gastrointestinal side effects
  - Photosensitivity
  - Contra-indicated (liver disease/pregnancy)

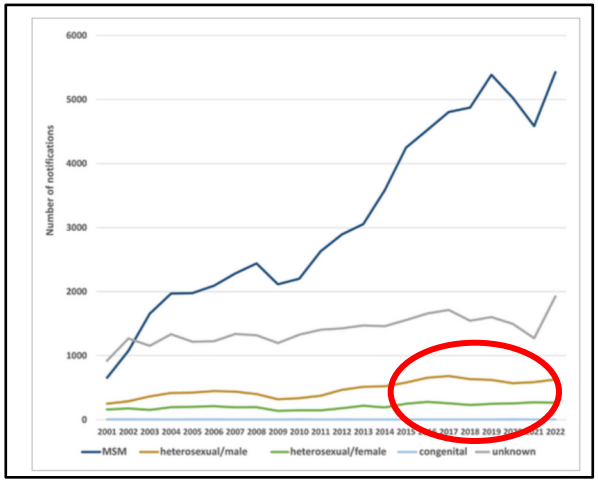
BLOOD BANK

- **Impact on TP seroconversion**
  - Absence (doxy-PEP success)
  - Prolonged (doxy-PEP failure)

syphilis potentially looses its value as a surrogate marker for sexual risk behaviour

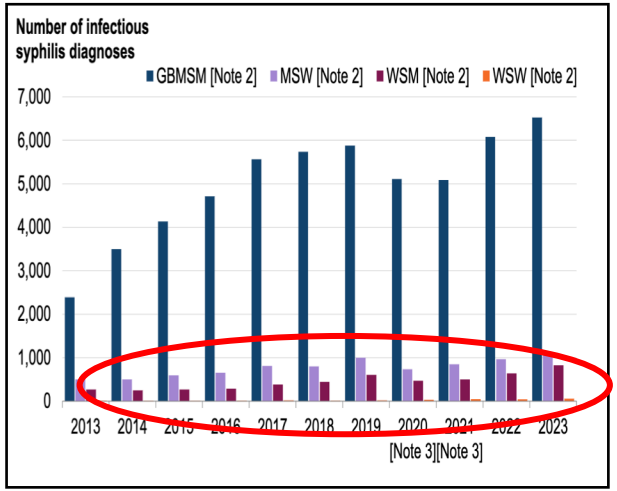
Syphilis among heterosexuals in Europe

Germany



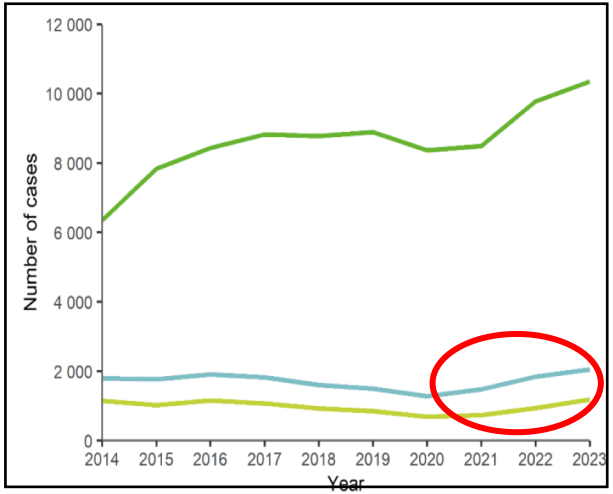
Werner et al (2024) JDDG 22: 466-478

UK



UKHSA

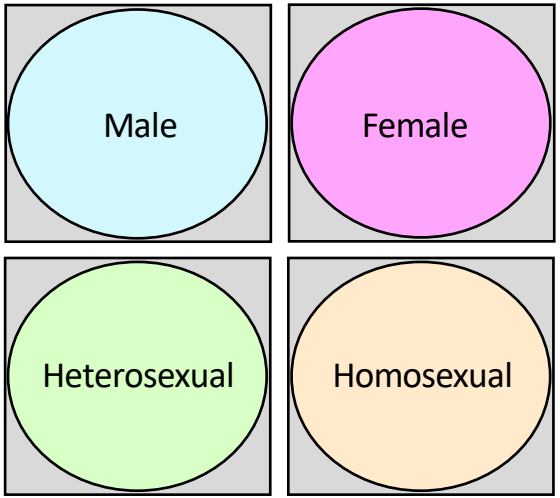
Europe

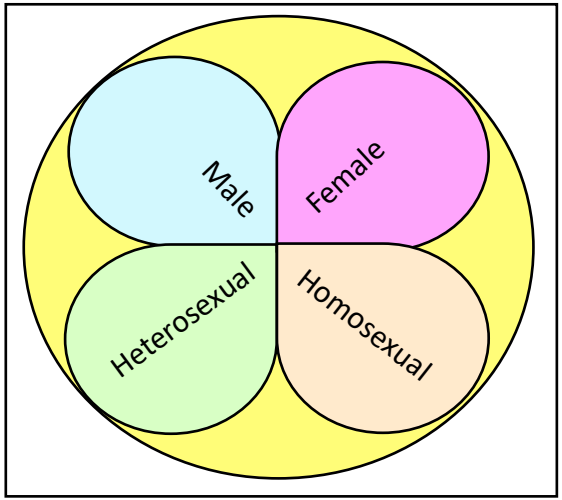


ECDC Syphilis Report 2023

Sexual Fluidity in Identity and Behavior Among Cisgender Youth: Findings from the Longitudinal Growing Up with Media Study

Sabra L. Katz-Wise, PhD[1,2,3], Nicholas S. Perry, PhD[4], Kimberly M. Nelson, PhD, MPH[5,6], Allegra R. Gordon, ScD[1,2,5], Michele L. Ybarra, MPH, PhD[7]



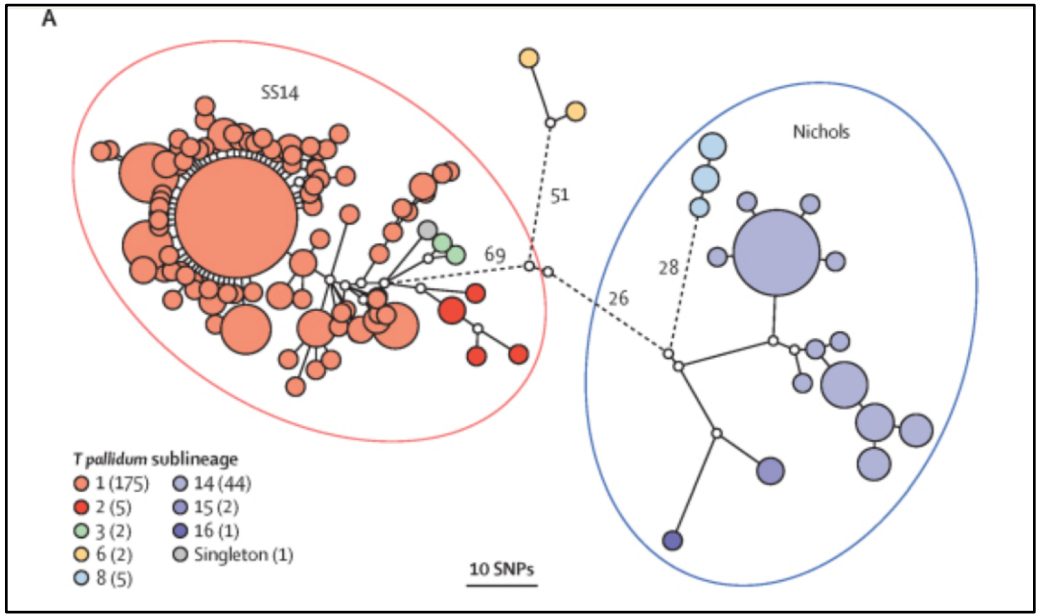


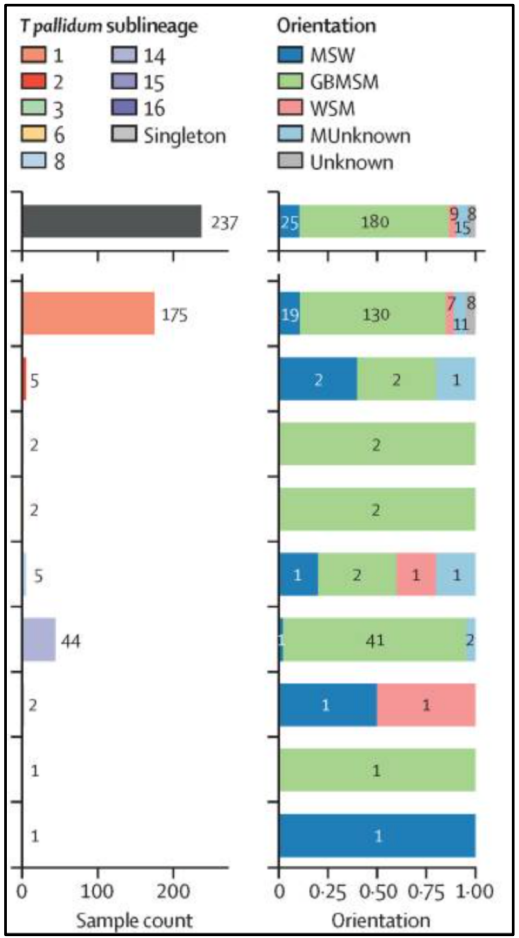


I DON'T SUPPORT THIS SLIDE

Katz-Wise et al (2024) J Pediatrics 257: 113355

Molecular Epidemioloy of syphilis in the UK



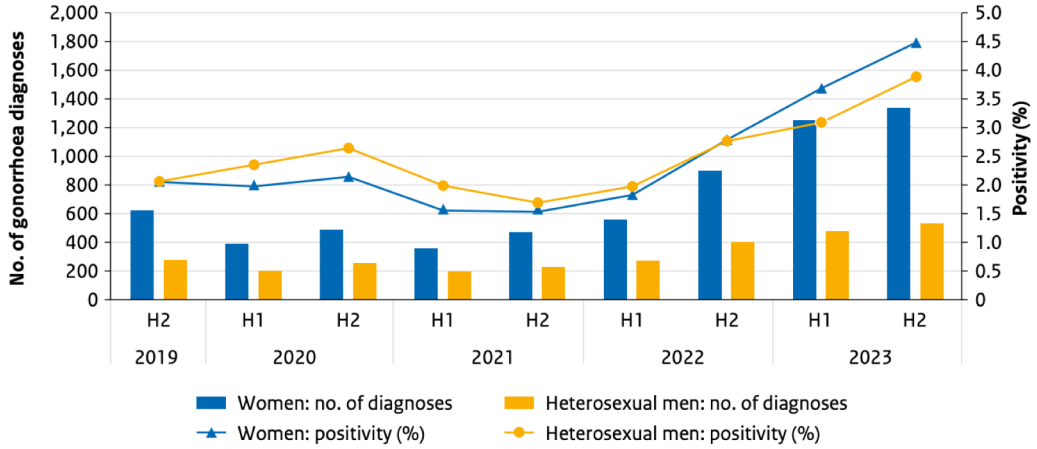


Partial bridging sexual networks of MSM and non-MSM

Beale et al (2023) Lancet Microbe 4: e770-e780

Trend of *N. gonorrhoeae* in the Netherlands

Figure 4.3a Half-yearly number of gonorrhoea diagnoses and gonorrhoea positivity in women and heterosexual men, mid 2019 to 2023



Footnote: H1=January-June, H2=July-December.

- **Increase highest in high-educated white Dutch young women (age<25)**

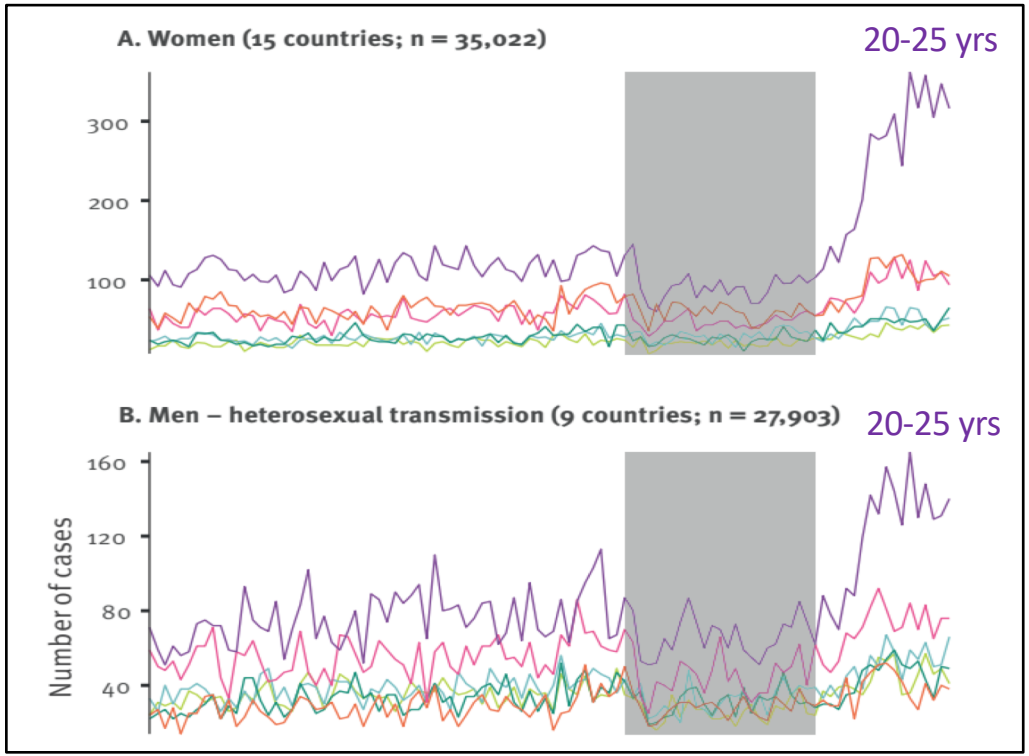
Fits sexual fluidity theory

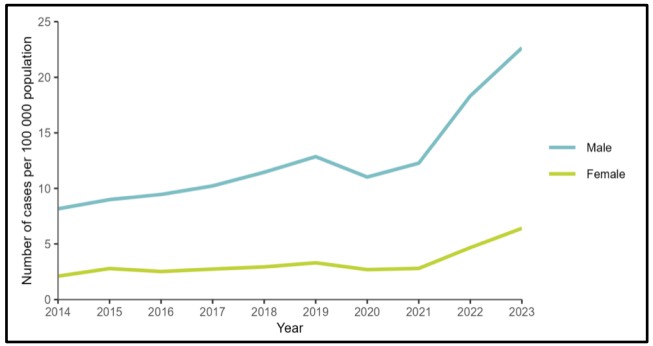
BUT it could also fit

(sexual) freedom after COVID-19

RIVM STI Report 2024

Trend of *N. gonorrhoeae* in Europe

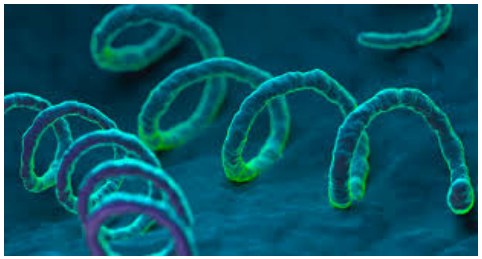




Significant rise in gonorrea in 20-25 year old heterosexual males and females in Europe after COVID

Nerlander et al (2024) Eurosurveillance 29: 2400113

Take home messages



- Not every (bacterial) STI behaves the same.
- STI epidemiologies can strongly differ, also between Western countries.
- General upsurge of syphilis among MSM catalysed by implementation of PrEP.
- Possible mild country-specific rise of syphilis among heterosexuals: needs clarification
- Syphilis epidemiology might currently NOT be in line with HIV epidemiology, but remains a good surrogate marker for sexual risk behaviour (among mostly MSM).

Nevertheless: Sanquin abandoned syphilis screening for plasma donors in 2024.

Sanquin

Thank you for listening

Sanquin Research: Laboratory of blood-borne infections

Hans Zaaijer
Mariet Feltkamp
Boris Hogema
Michel Molier
Ed Slot
Ryanne Lieshout-Krikke

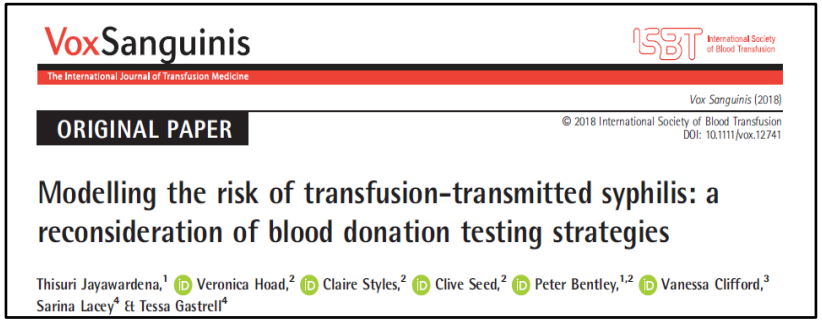
National Screening centre Sanquin
Nico Vreeswijk
Marco Koppelman
All technicians

Sanquin Diagnostics: Virology and MAT services
Maarten Koot
Marijke Molenaar-de Backer
All technicians

For Life.



Transfusion transmitted syphilis (TTS)



VoxSanguinis

The International Journal of Transfusion Medicine

ISBT International Society of Blood Transfusion

ORIGINAL PAPER

Vox Sanguinis (2018)

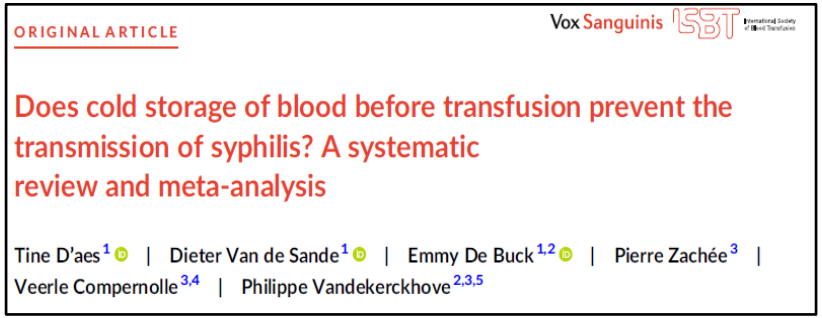
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DOI: 10.1111/vox.12741

Modelling the risk of transfusion-transmitted syphilis: a reconsideration of blood donation testing strategies

Thisuri Jayawardena,[1] Veronica Hoad,[2] Claire Styles,[2] Clive Seed,[2] Peter Bentley,[1,2] Vanessa Clifford,[3] Sarina Lacey[4] & Tessa Gastrell[4]

Jawardena et al (2018) Vox Sang 114: 107-116



ORIGINAL ARTICLE

Vox Sanguinis ISBT International Society of Blood Transfusion

Does cold storage of blood before transfusion prevent the transmission of syphilis? A systematic review and meta-analysis

Tine D'aes[1] | Dieter Van de Sande[1] | Emmy De Buck[1,2] | Pierre Zachée[3] | Veerle Compernolle[3,4] | Philippe Vandekerckhove[2,3,5]

D'aes et al (2024) Vox Sang 119: 219-231

Universal testing not cost-effective to keep TTS risk within tolerable limits (>500 milion dollar/DALY)

Cold Storage (>72 hrs) significantly decreases but does not fully eliminate TTS risk (even after 72 hrs).

Stakeholders do not support elimination of universal TP screening due to changing epidemiology

Lack of human studies

Unrealistically high titers used in experiments