

# PEP y DoxyPEP, ¿Qué más podemos hacer para prevenir el VIH y las ITS?


Àngel Rivero

**Curso en Avances VIH y hepatitis virales  
Vigo 26 de Enero de 2024**

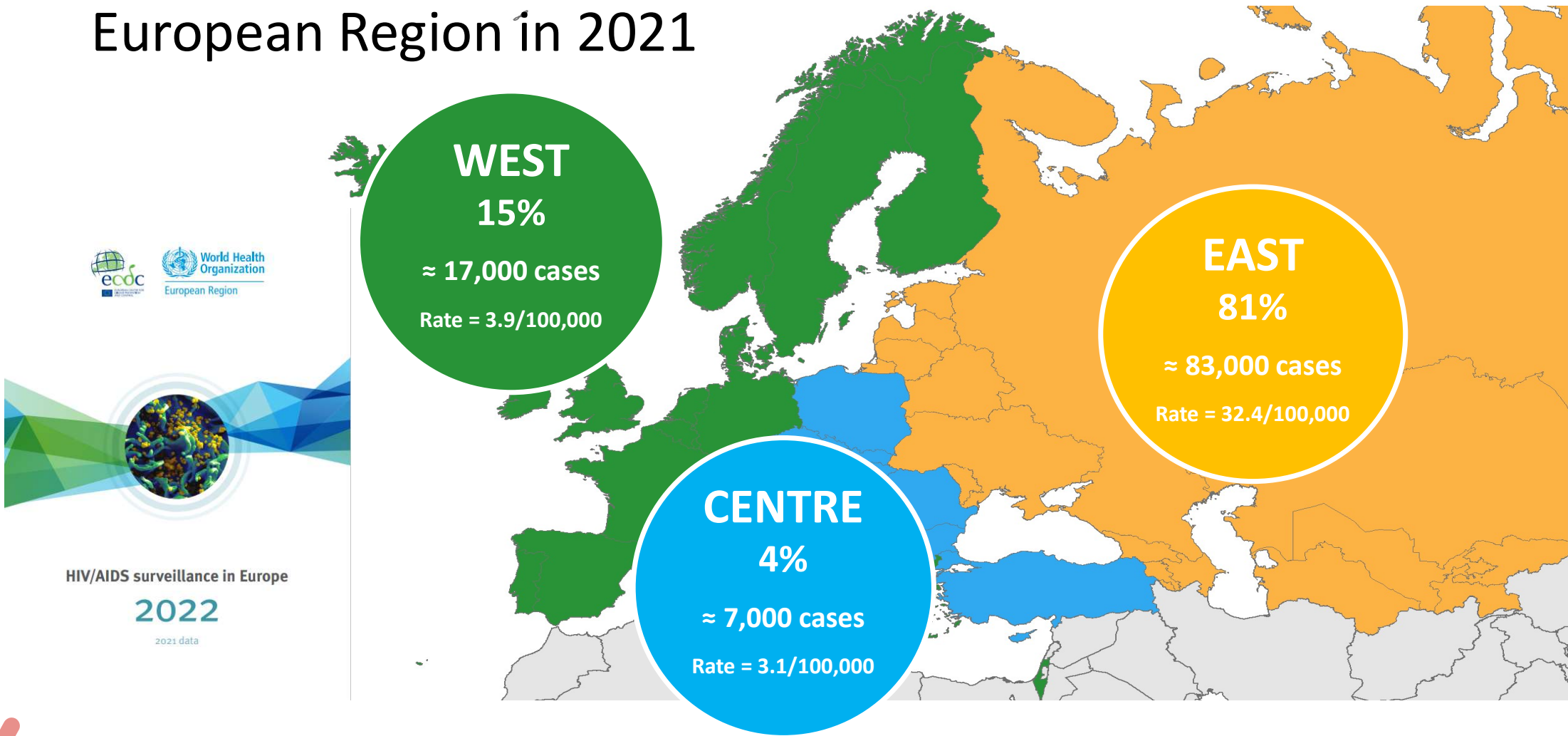




# Agenda

- Estrategias de prevención:
    - VIH
    - ITS
- 

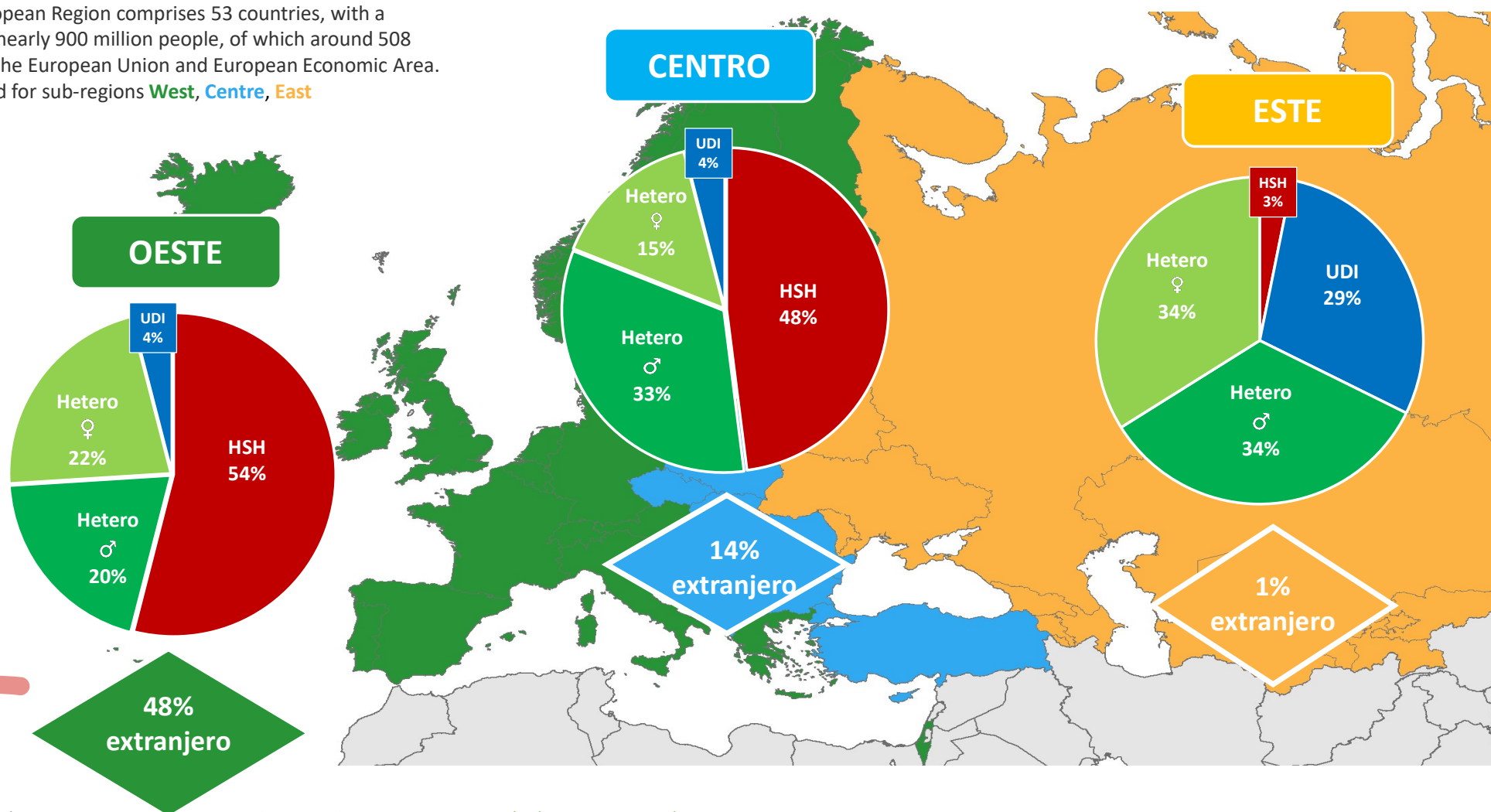
# ~107,000 persons were diagnosed with HIV in the WHO European Region in 2021



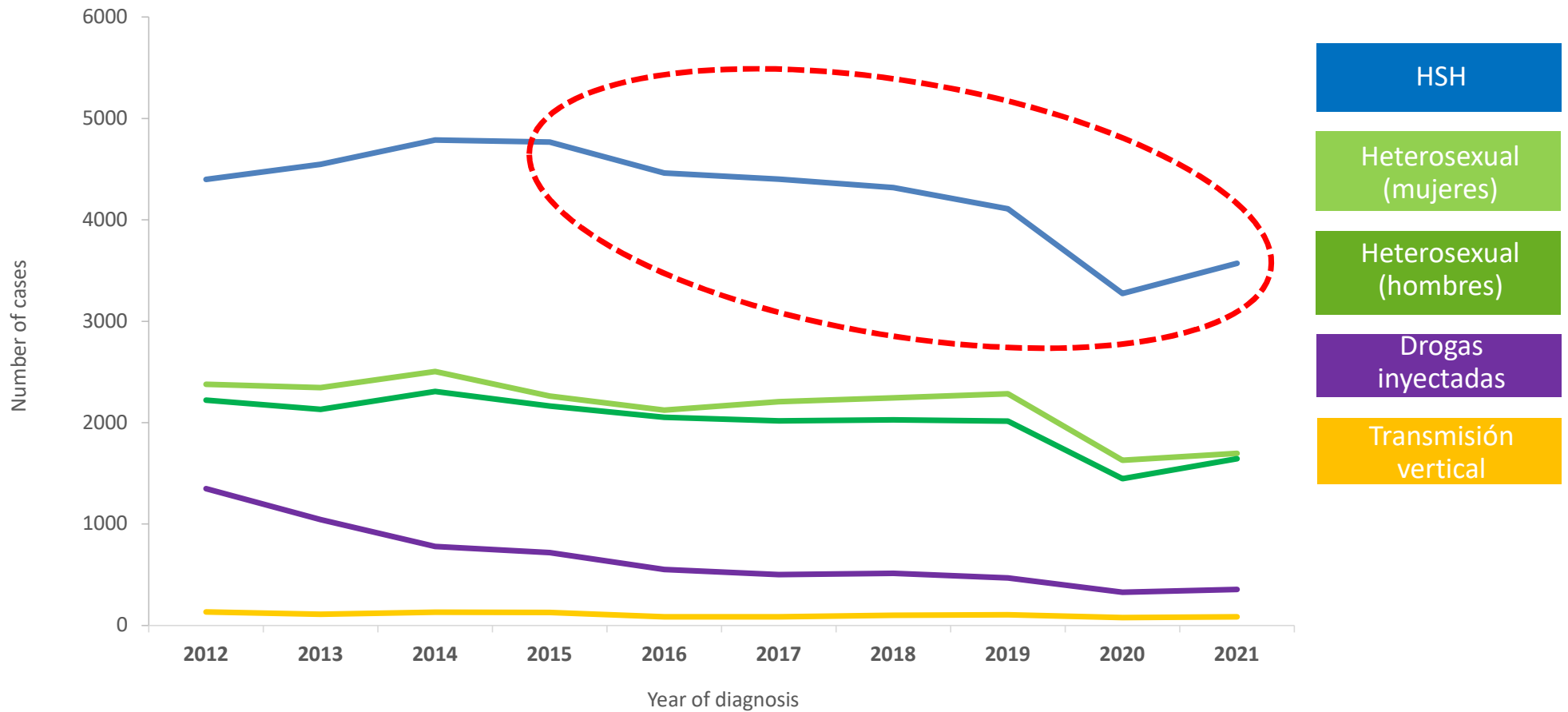
Source: ECDC/WHO (2022). HIV/AIDS Surveillance in Europe 2022 (2021 data): [www.ecdc.europa.eu/en/publications-data/hiv-aids-joint-report-surveillance-2021-data](http://www.ecdc.europa.eu/en/publications-data/hiv-aids-joint-report-surveillance-2021-data)

# Via de transmission conocida por sub-regiones, 2021

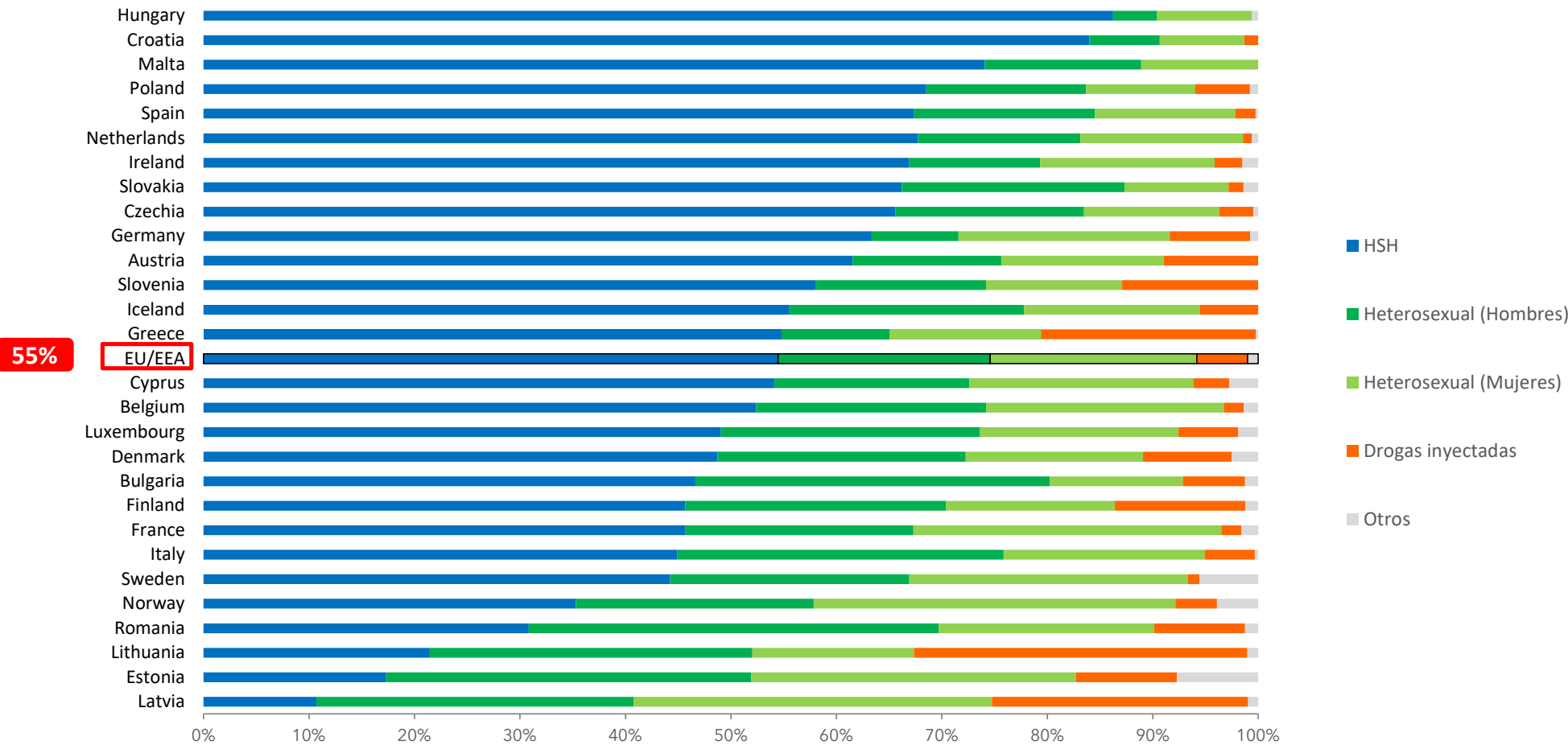
The WHO European Region comprises 53 countries, with a population of nearly 900 million people, of which around 508 million live in the European Union and European Economic Area. Data presented for sub-regions **West**, **Centre**, **East**



# Diagnósticos de VIH por vía de transmisión, 2012-2021, EU/EEA

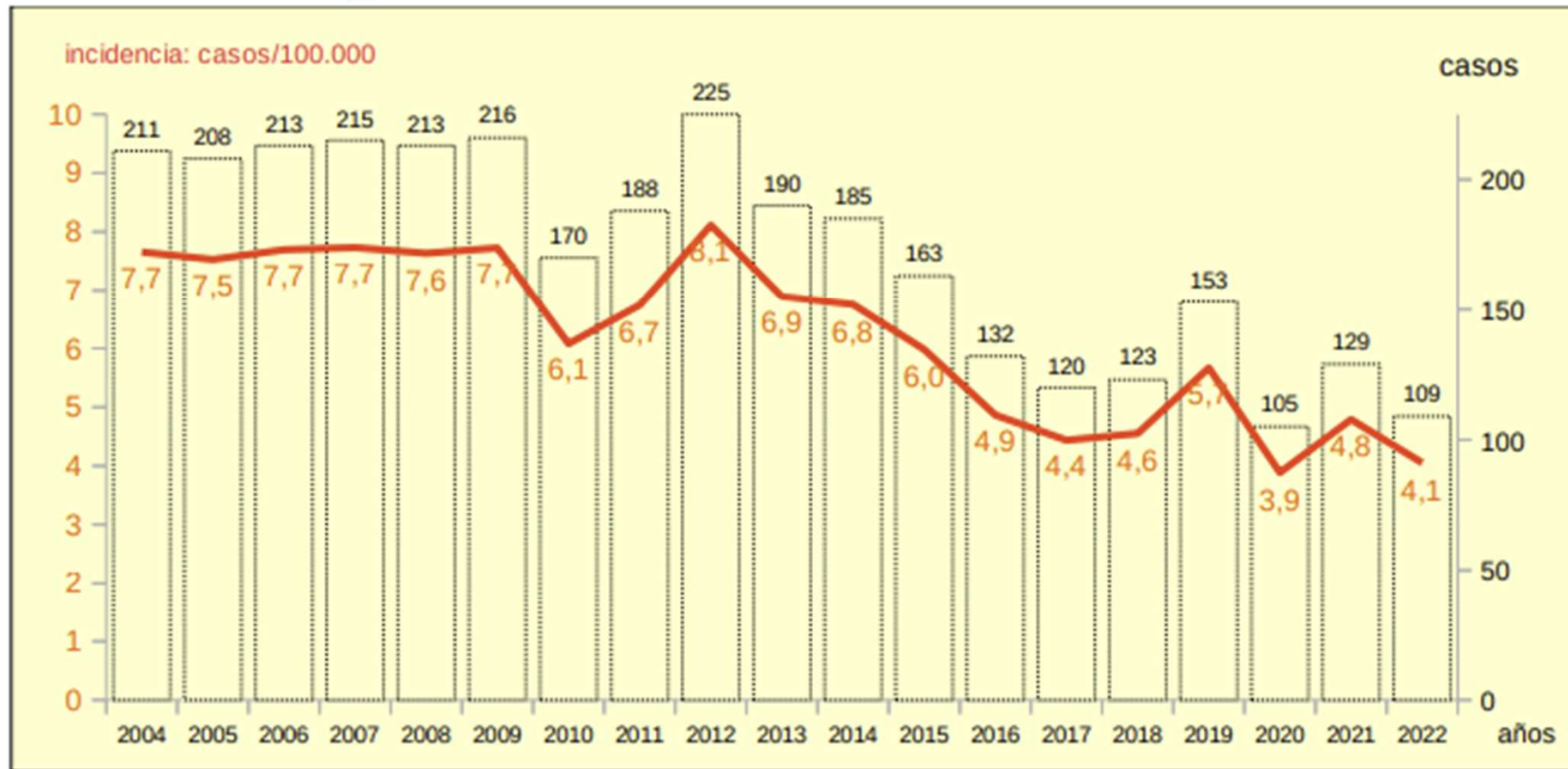


# Porcentaje de nuevas infecciones VIH por vía de transmisión conocida



Source: ECDC/WHO (2022). HIV/AIDS Surveillance in Europe 2022 (2021 data): [www.ecdc.europa.eu/en/publications-data/hiv-aids-joint-report-surveillance-2021-data](http://www.ecdc.europa.eu/en/publications-data/hiv-aids-joint-report-surveillance-2021-data)

# Epidemiología VIH en Galicia



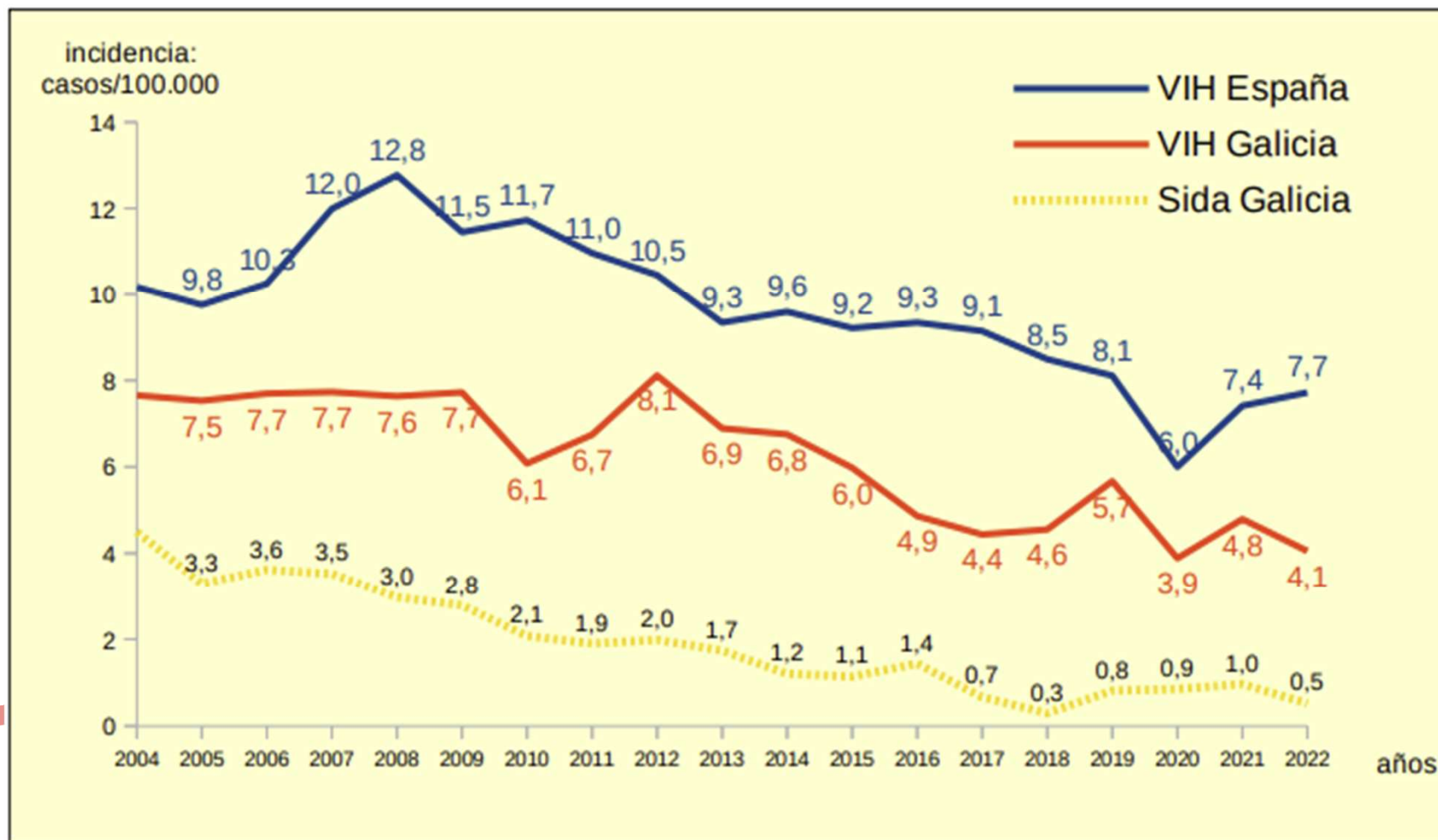
[DGSP: datos del 30 de junio de 2023]



SERVIZO  
GALEGO  
DE SAÚDE



# Tasa de incidencia VIH en Galicia

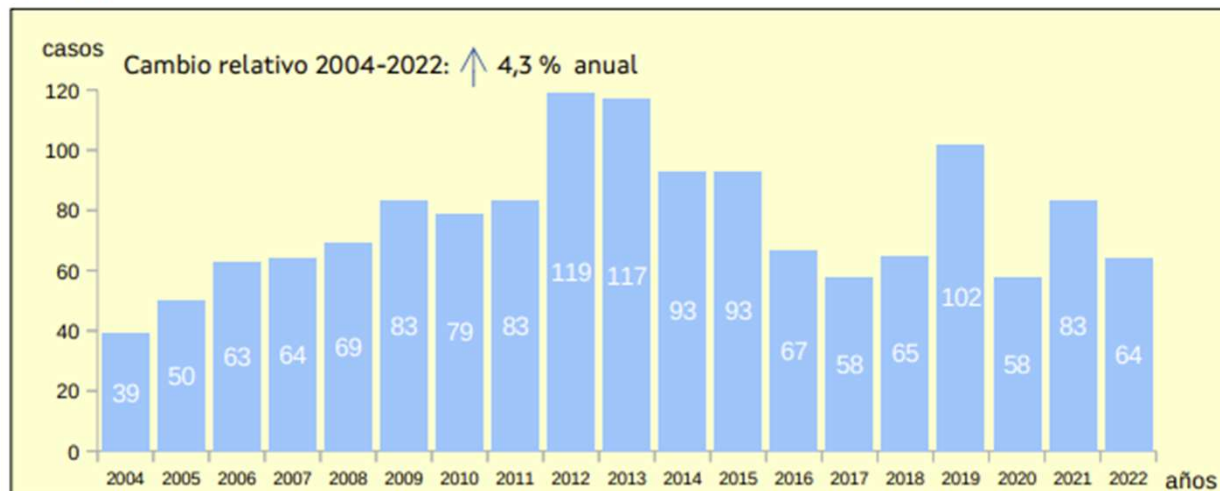


(DGSP, datos del 30 de junio de 2023)

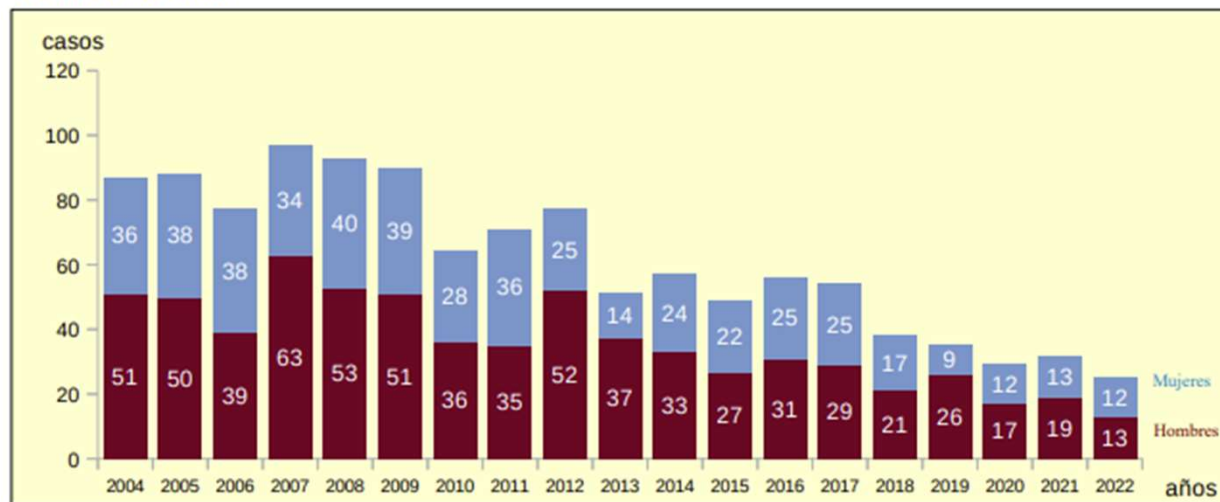


# Nuevos diagnósticos de VIH en Galicia

10 a. HSH

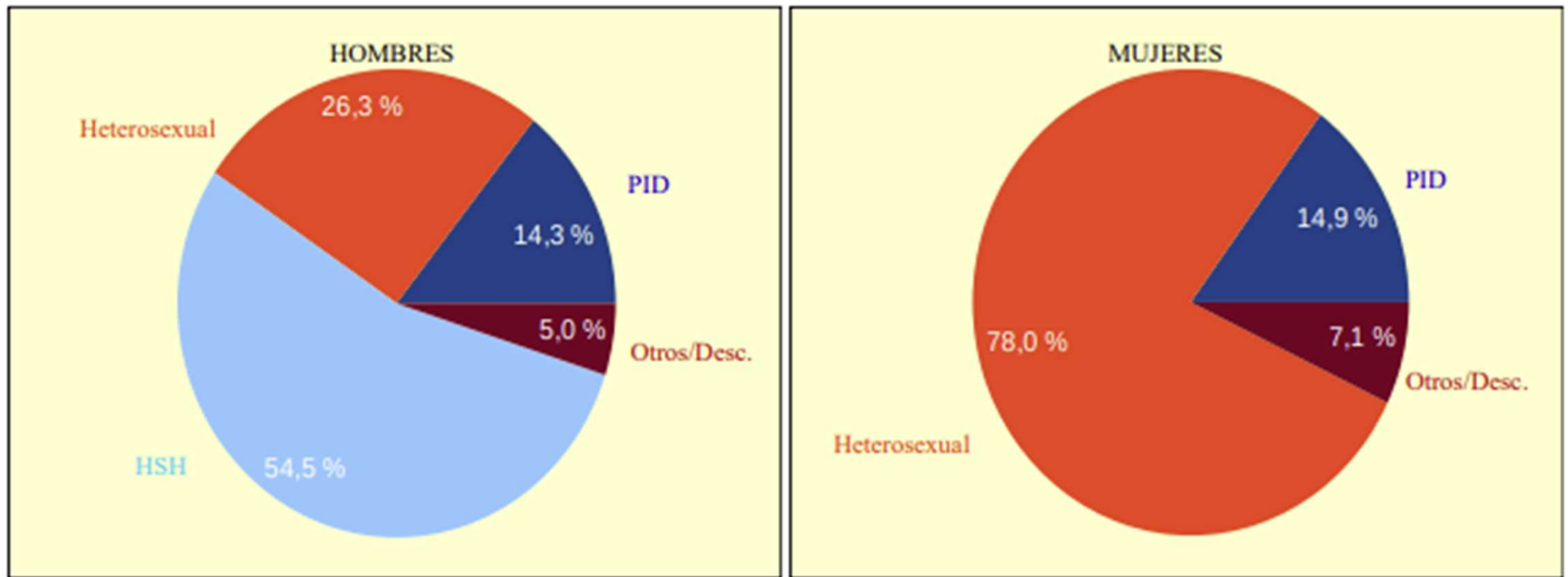


10 b. Heterosexual



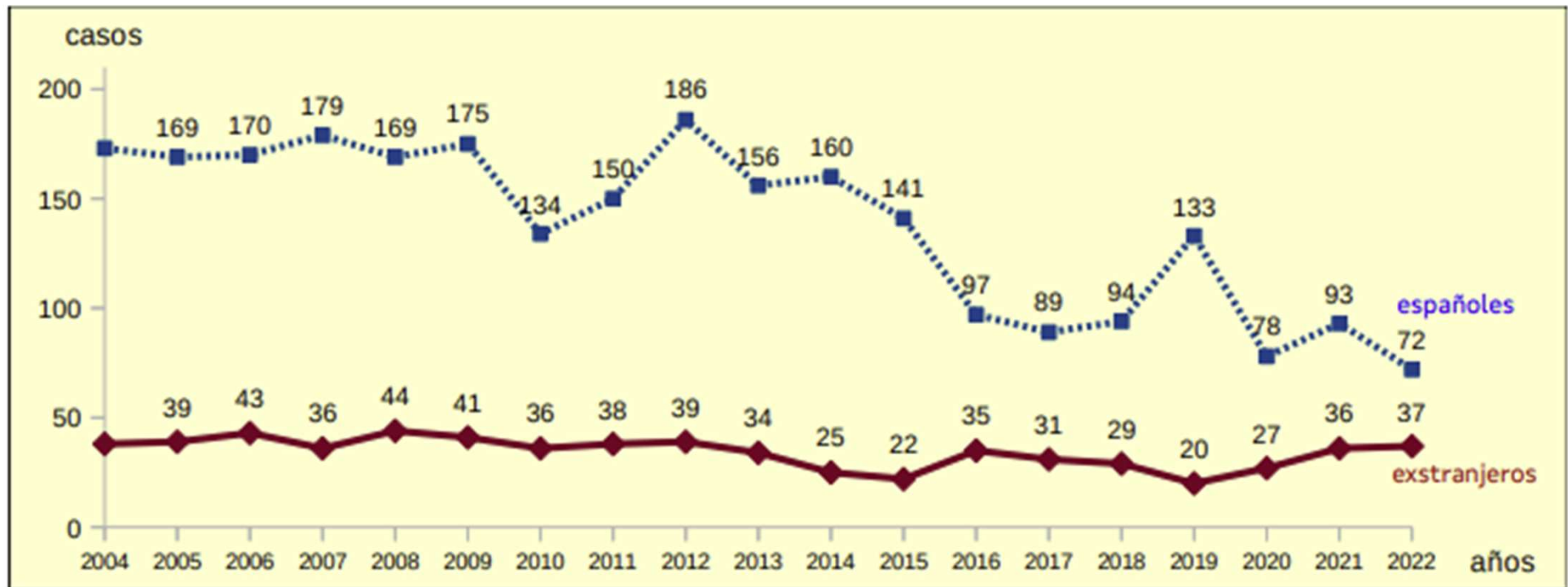
(IGCSP, datos del 30 de junio de 2023)

# Via de transmisión VIH en Galicia



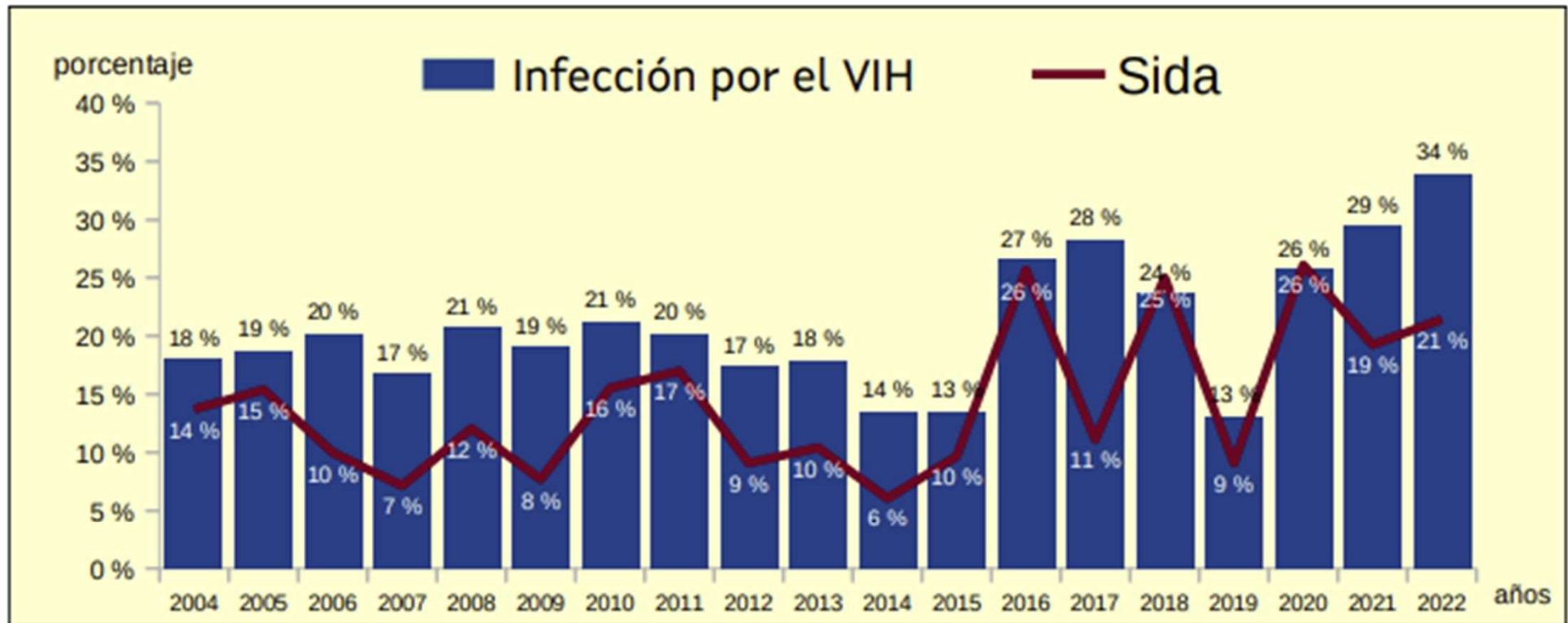
(DGSP: datos del 30 de junio de 2023)

# Origen personas diagnosticadas de VIH



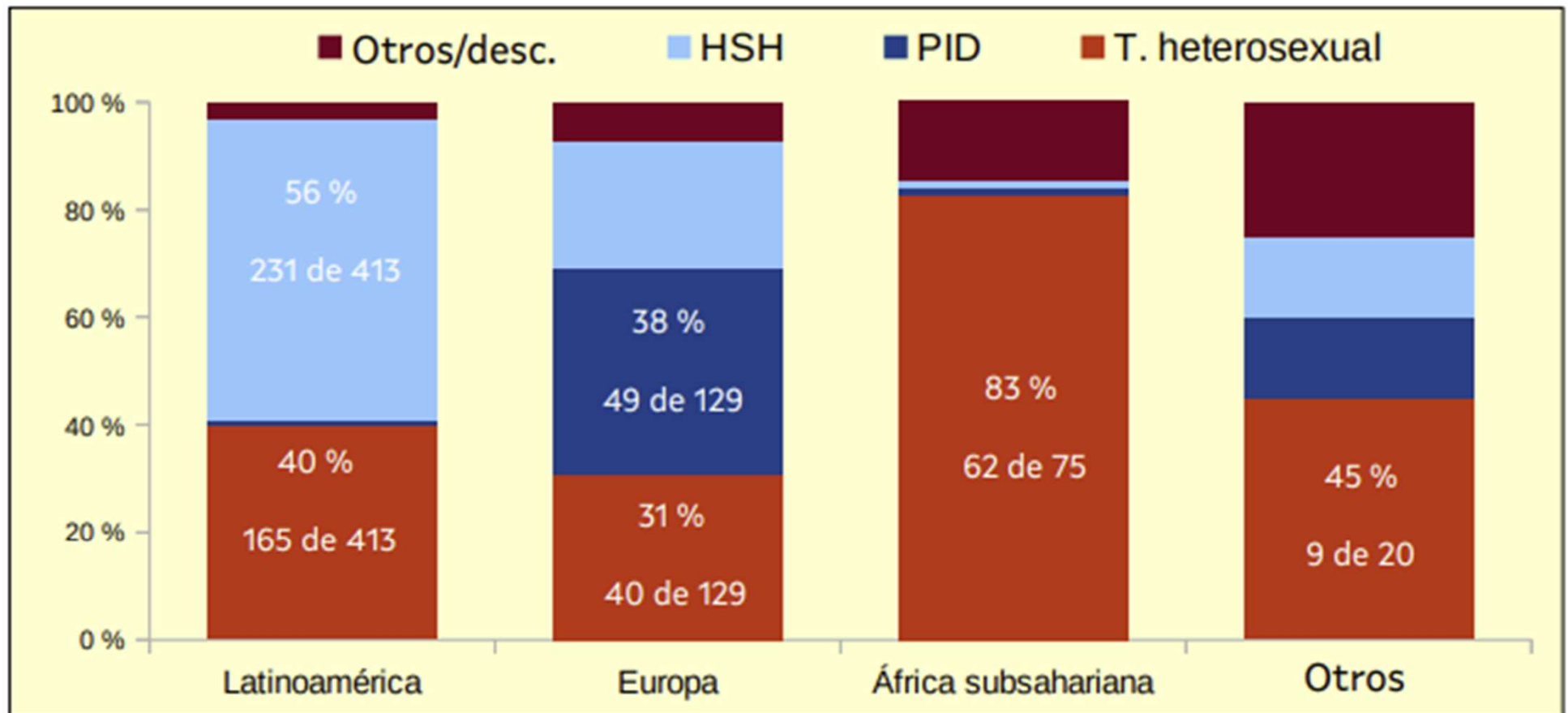
(DGSP: datos del 30 de junio de 2023)

# Diagnósticos tardíos en extranjeros



(DGSP: datos del 30 de junio de 2023)

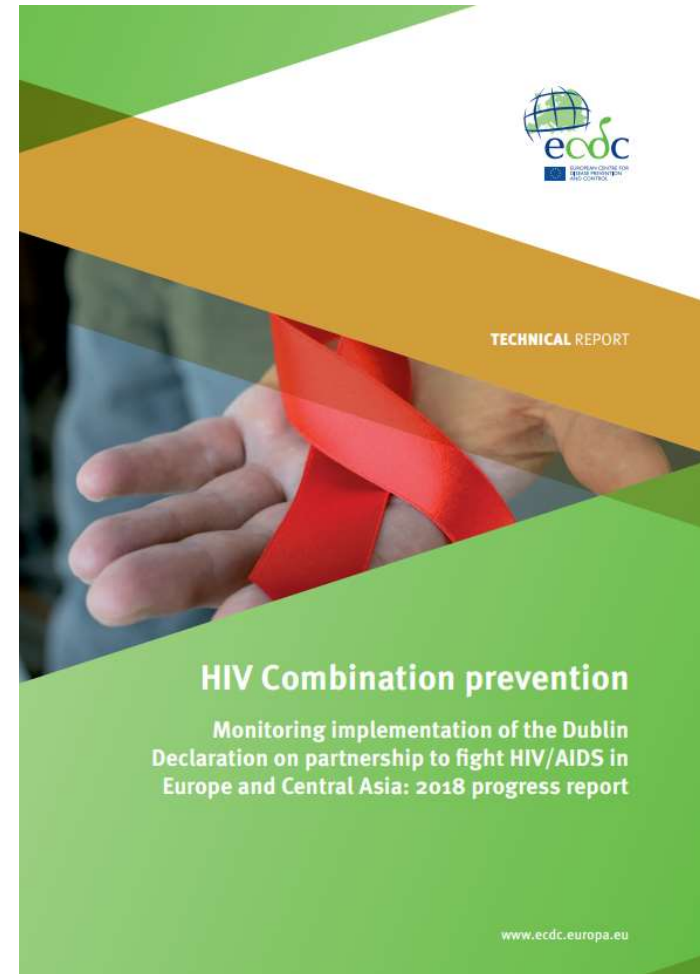
# Vía de transmisión según origen



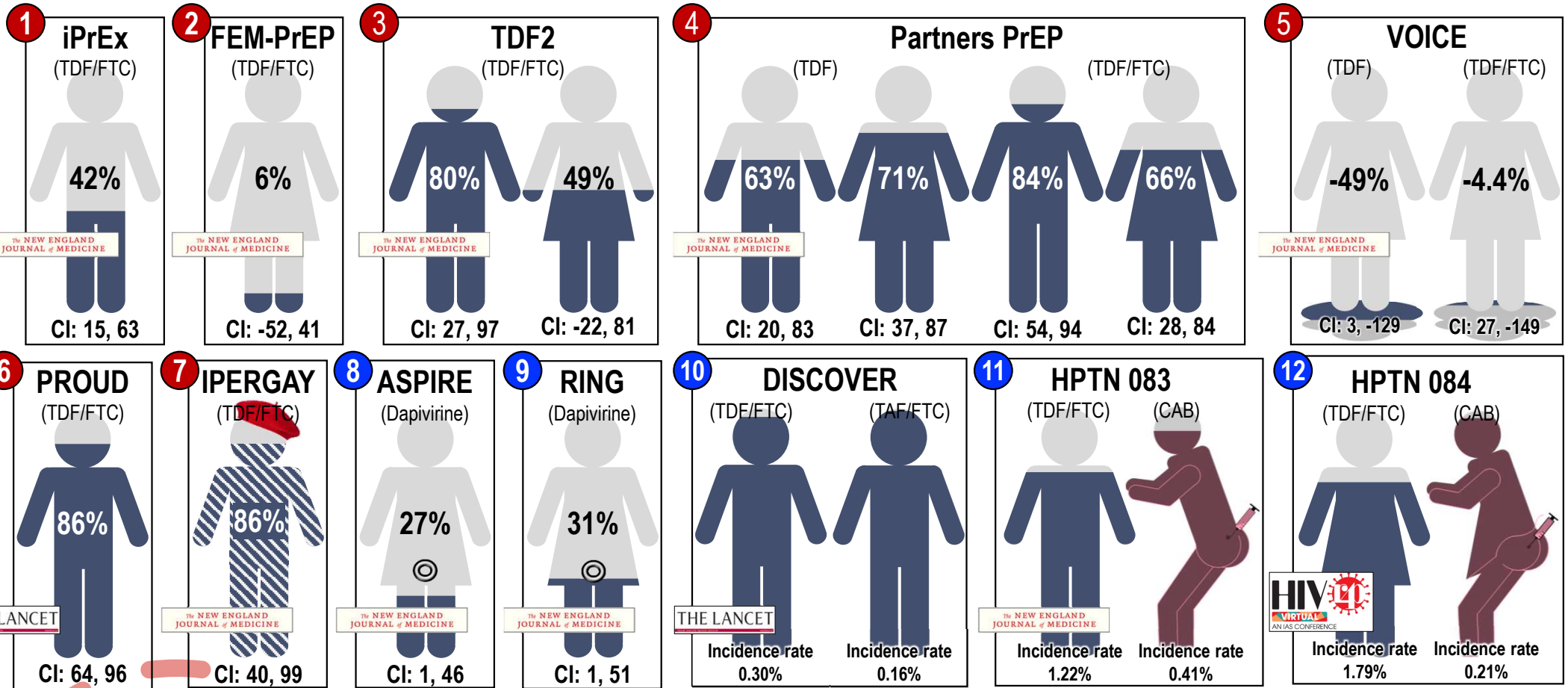
(DGSP: datos del 30 de junio de 2023)



# PrEP en el context de la prevención combinada



# Efectividad de la PrEP en Ensayos Clínicos Randomizados



1. Grant et al. NEJM. 2010.  
 2. Van Damme et al. NEJM. 2012.  
 3. Thigpen et al. NEJM. 2012.  
 4. Baeten et al. NEJM. 2012.

5. Murrain et al. NEJM. 2015.  
 6. McCormack et al. Lancet. 2016.  
 7. Molina et al. NEJM. 2015.  
 8. Baeten et al. NEJM. 2016.

9. Nel et al. NEJM. 2016.  
 10. Mayer et al. Lancet. 2020.  
 11. Landovitz et al. NEJM. 2021.  
 12. Delany-Moretlwe et al. HIV R4P. 2021.



# Vacunas VIH?





# Futuro de la PrEP

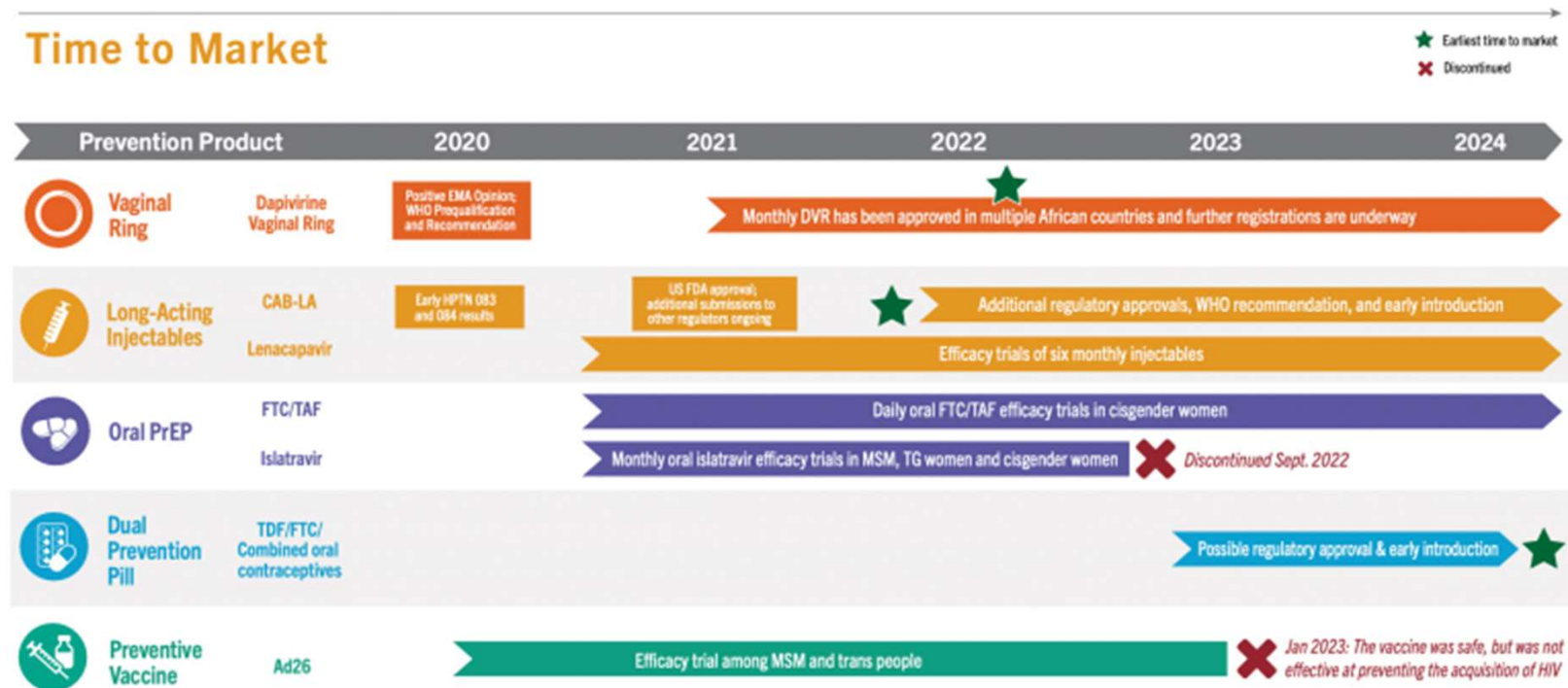
- Uso de inyectable semestrales
- Todavía en ensayos clínicos.



# PrEP En desarrollo

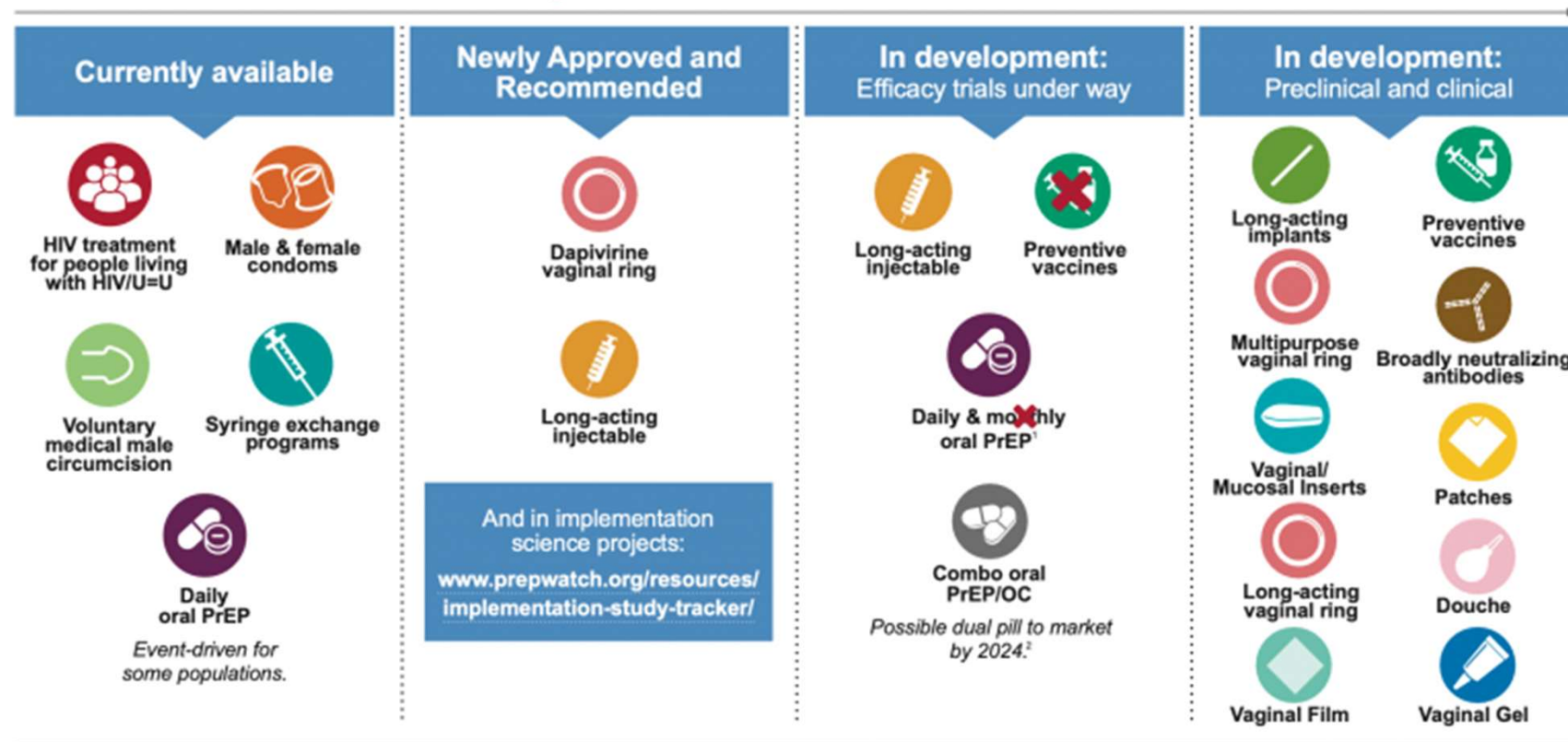
## Years Ahead in HIV Prevention Research

### Time to Market



# Pipeline actual de PrEP

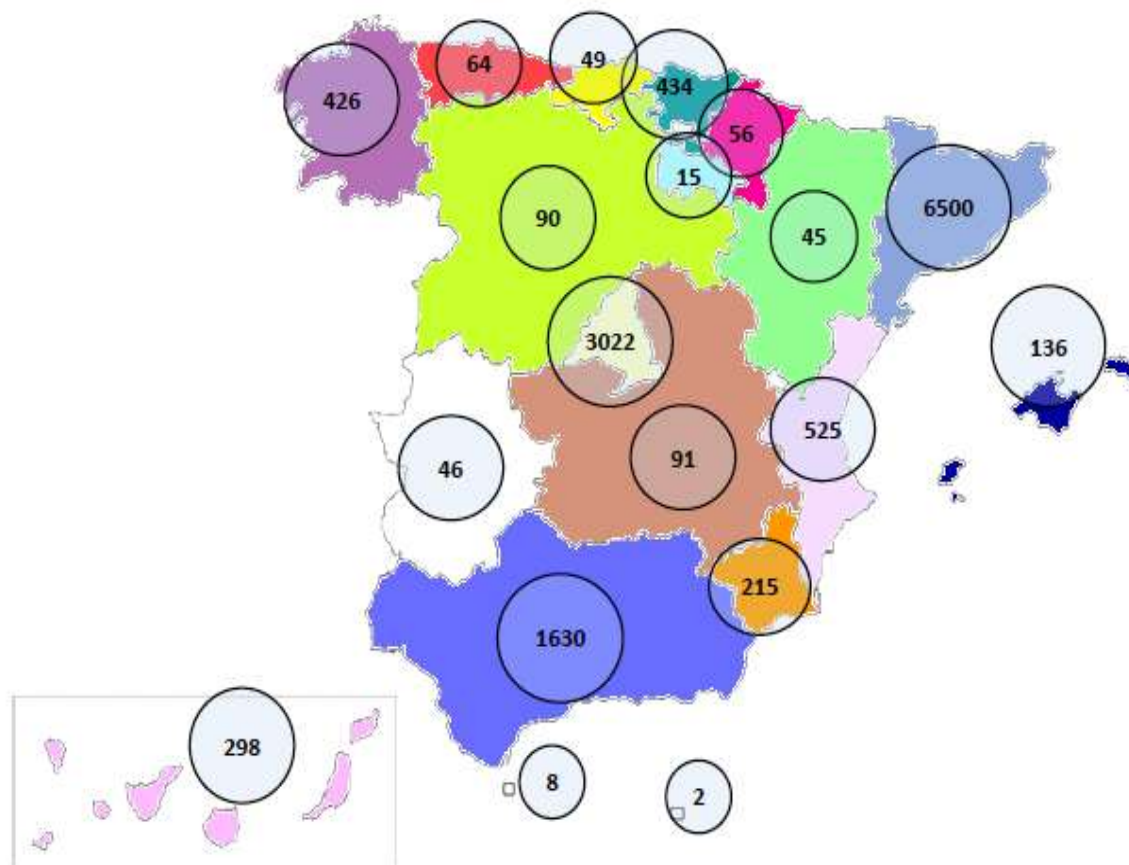
## The HIV Prevention Pipeline



<sup>1</sup>In Oct 2019, US FDA approved F/TAF for adults and adolescents who have no HIV risk from receptive vaginal sex; still in development for cisgender women.

<sup>2</sup>Efficacy trials not required; bioequivalency of the two approved products when dosed together may be all that is required.

## PrEP en España



Total: 13.652  
(Mayo 2022)

LO QUE HAY DETRÁS DEL "NEGATIVO-TOMO PREP"

## La pastilla azul que dispara las ITS en la comunidad gay: "Todos mis amigos han tenido clamidia"

Es la alternativa al preservativo para evitar el sida, pero está provocando serios efectos colaterales

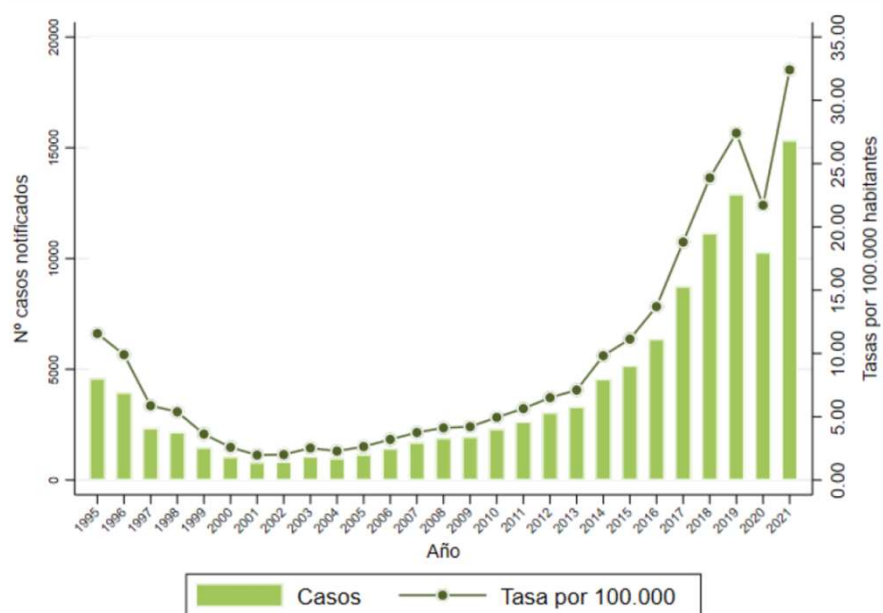


Un usuario de la PrEP (PreExposure Prophylaxis) muestra la...



# ITS antes de la PrEP

**Figura 1. Incidencia de infección gonocócica**  
Número de casos y tasas por 100.000 hab. España, 1995-2021



Fuente: Enfermedades de Declaración Obligatoria (EDO). Red Nacional de Vigilancia Epidemiológica

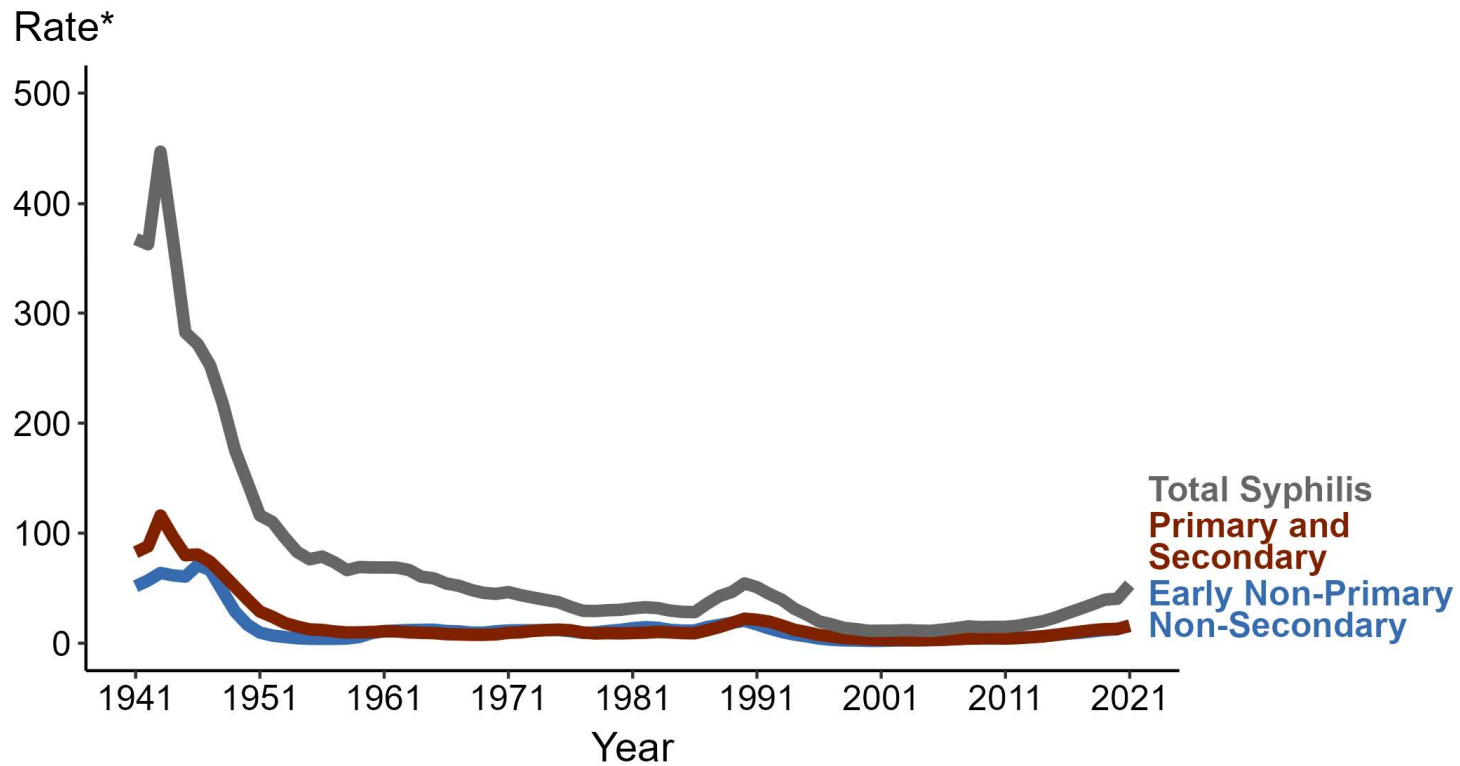
**Figura 8. Incidencia de sífilis.**  
Número de casos y tasas por 100.000 hab. España, 1995-2021



Fuente: Enfermedades de Declaración Obligatoria (EDO). Red Nacional de Vigilancia Epidemiológica



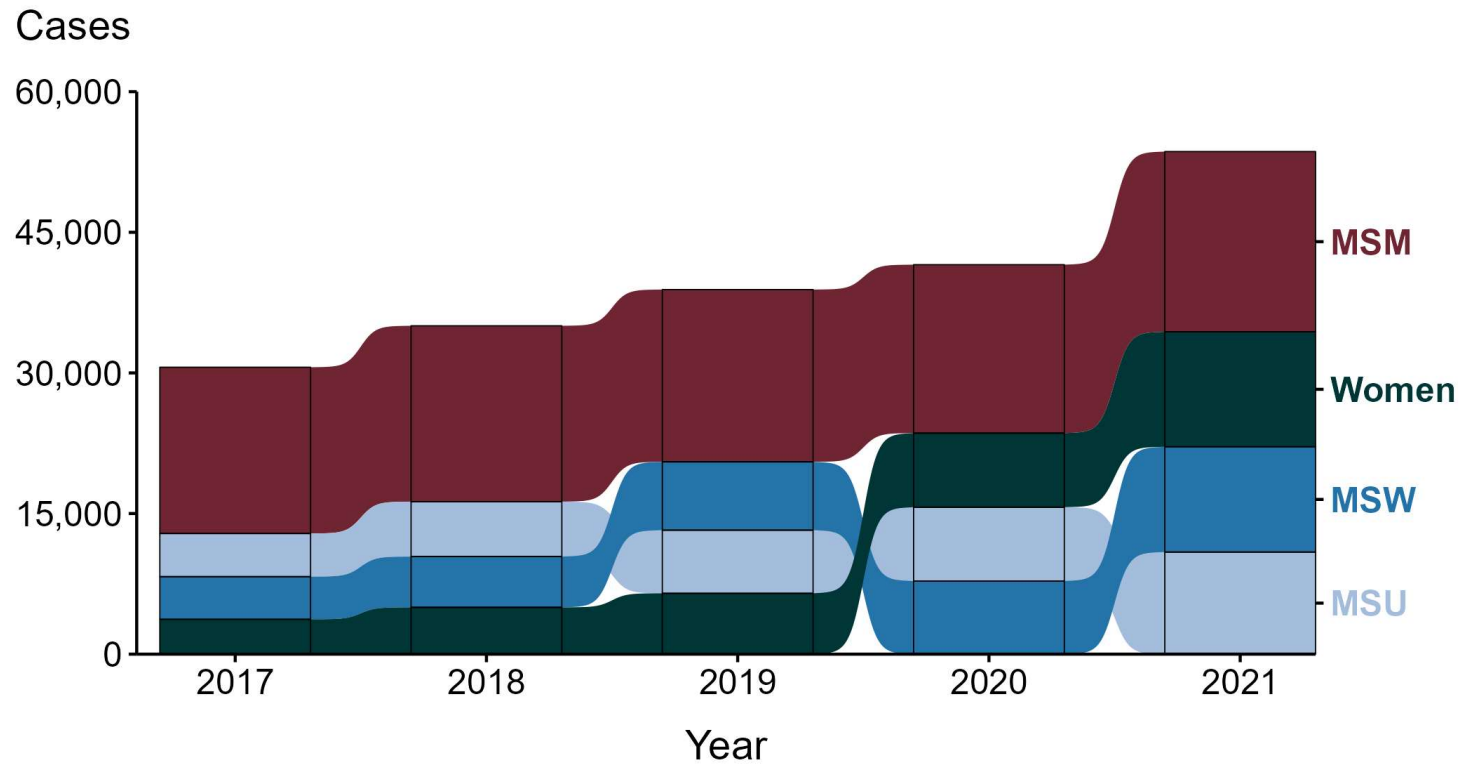
# Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2021



\* Per 100,000



# Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners, United States, 2017–2021

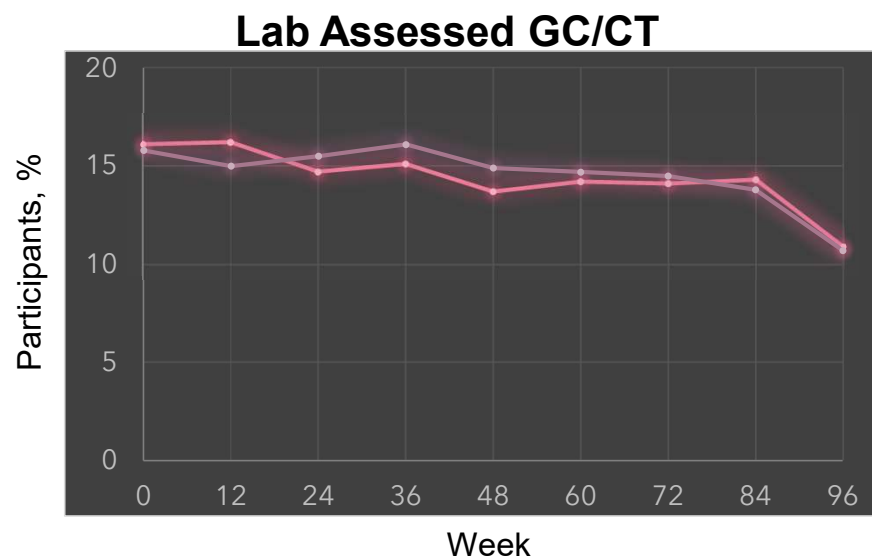


**ACRONYMS:** MSM = Gay, bisexual, and other men who have sex with men; MSU = Men with unknown sex of sex partners; MSW = Men who have sex with women only

**NOTE:** Over the five year period, 0.2% of cases were missing sex and were not included.



## DISCOVER ITS Hasta semana 96

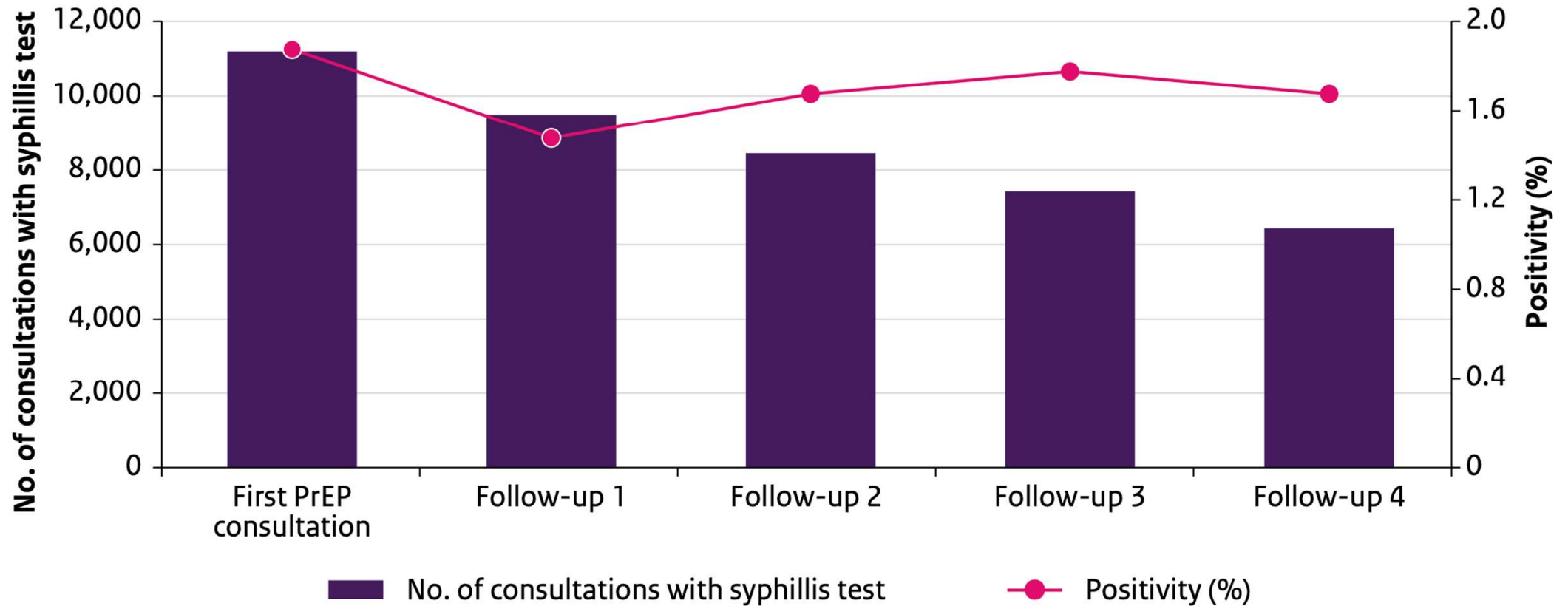


## Lab Assessed GC/CT Incidence

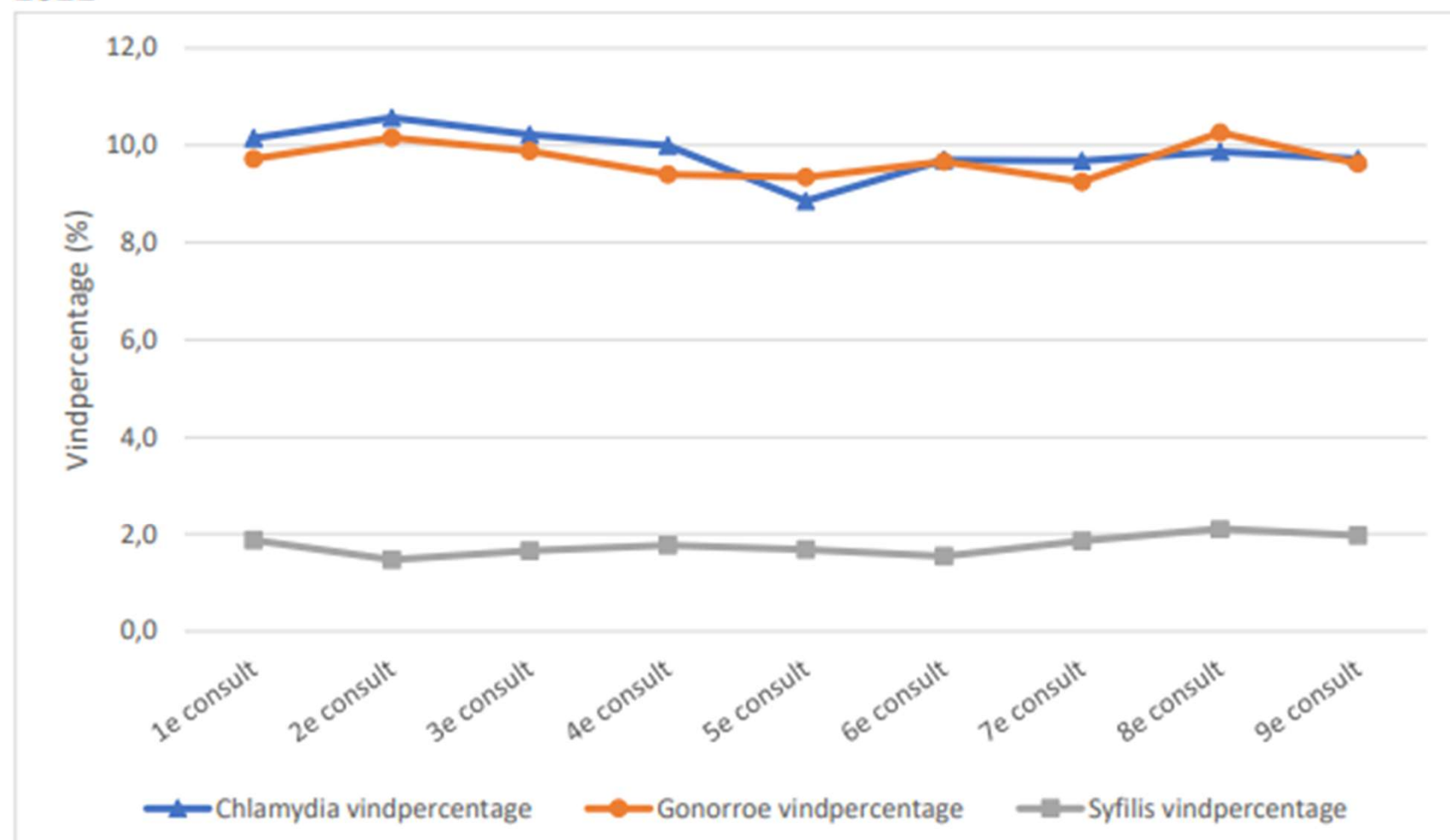
	n (Rate: n/100 py)	
	F/TAF	F/TDF
Gonorrhea (any site)	1053 (47.1)	1059 (45.3)
Rectal	651 (21.6)	662 (20.5)
Chlamydia (any site)	1049 (41.9)	1071 (41.6)
Rectal	810 (27.5)	835 (28.2)
Syphilis	365 (10.3)	370 (9.5)

- Incidence of gonorrhea, chlamydia, or syphilis while on study (based on AE reporting)
  - F/TAF = 145.1/100 py
  - F/TDF = 138.8/100 py

**Figure 5.6** Number of PrEP consultations with syphilis test and infectious syphilis positivity by PrEP consultation number among MSM participating in the national PrEP pilot at the Sexual Health Centres, July 2019 - December 2022



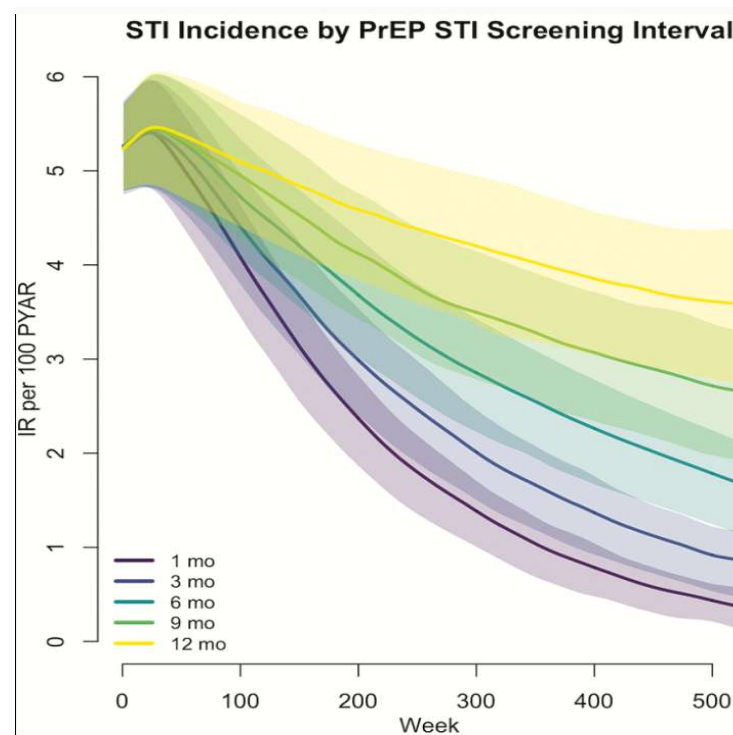
Figuur 4. Soa-vindpercentages onder PrEP-pilotdeelnemers bij het eerste PrEP consult en de driemaandelijke controles, augustus 2019 – december 2022



# Los Screening de ITS reducen la incidencia.

Incidence of Gonorrhea and Chlamydia Following Human Immunodeficiency Virus Preexposure Prophylaxis Among Men Who Have Sex With Men: A Modeling Study

Samuel M. Jenness,<sup>1</sup> Kevin M. Weiss,<sup>1</sup> Steven M. Goodreau,<sup>2</sup> Thomas Gift,<sup>3</sup> Harrell Chesson,<sup>3</sup> Karen W. Hoover,<sup>4</sup> Dawn K. Smith,<sup>4</sup> Albert Y. Liu,<sup>5</sup> Patrick S. Sullivan,<sup>1</sup> and Eli S. Rosenberg<sup>1</sup>



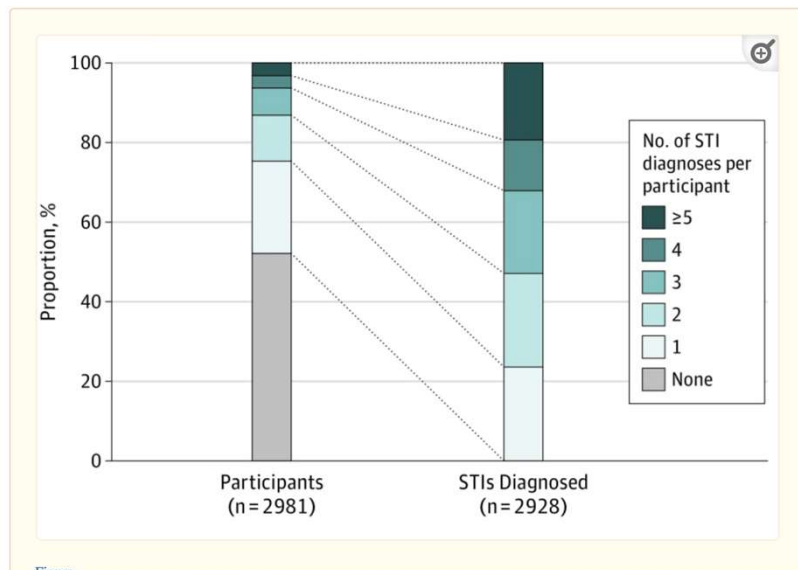
CID 2017

## Association of HIV Preexposure Prophylaxis With Incidence of Sexually Transmitted Infections Among Individuals at High Risk of HIV Infection

Michael W. Traeger, MSc,<sup>1</sup> Vincent J. Cornelisse, MBBS, PhD,<sup>2,3,4,5</sup> Jason Asselin, BSc,<sup>1</sup> Brian Price, MBA,<sup>2</sup>

Incidence of Sexually Transmitted Infections During Follow-up Among Included Participants (N = 2981)

	No. of Infections	Person-Years of Follow-up (n = 3185.0) <sup>a</sup>	Incidence Rate per 100 Person-Years (95% CI)
All STIs	2928		91.9 (88.7-95.3)



## Conclusion

Hay muchas ITS

Muchas se producen en usuarios de PrEP  
Pero no parece que la PrEP tenga un efecto mayor.



HIV Prevention and Transmission

# Doxycycline for Bacterial STI Prevention: A Different Type of PrEP

#8 in TheBodyPro's Top 10 HIV Clinical Developments of 2019

Nov 26, 2019

David Alain Wohl, M.D.



# ¿Qué es DoxyPEP?

Doxycycline para prevenir  
ITS=DoxyPEP

Antibiótico de amplio espectro

Usado para prevención de malaria  
y enfermedad de Lyme

Primer estudio publicado en 2015

Published in final edited form as:

*Sex Transm Dis.* 2015 February ; 42(2): 98–103. doi:10.1097/OLQ.0000000000000216.

## **Doxycycline Prophylaxis to Reduce Incident Syphilis among HIV-Infected Men who have Sex with Men who Continue to Engage in High Risk Sex: A Randomized, Controlled Pilot Study**

Robert K. Bolan, MD<sup>\*</sup>, Matthew R. Beymer, MPH<sup>†,‡</sup>, Robert E. Weiss, PhD<sup>†,‡</sup>, Risa P. Flynn<sup>\*</sup>, Arleen A. Leibowitz, PhD<sup>\*\*</sup>, and Jeffrey D. Klausner, MD, MPH<sup>‡</sup>

<sup>\*</sup>Los Angeles LGBT Center (The Center)

**N=30, doxy 100 mg once daily**

# Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

*Jean-Michel Molina, Isabelle Charreau, Christian Chidiac, Gilles Pialoux, Eric Cua, Constance Delaugerre, Catherine Capitant, Daniela Rojas-Castro, Julien Fonsart, Béatrice Bercot, Cécile Bébéar, Laurent Cotte, Olivier Robineau, François Raffi, Pierre Charbonneau, Alexandre Aslan, Julie Chas, Laurence Niedbalski, Bruno Spire, Luis Sagaon-Teyssier, Diane Carette, Soizic Le Mestre, Veronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group\**

- Lancet, 2018
- Open-label randomizado, en usuarios de PrEP (HSH i mujeres trans)
- Doxiciclina 200 mg <24 horas after sex versus no intervention, n=116 in each group
- Test ITS cada 2 meses
- 10 meses de seguimiento, media 8.7 meses/persona (7.8-9.7)
- Objetivo primario: suceso de primera ITS

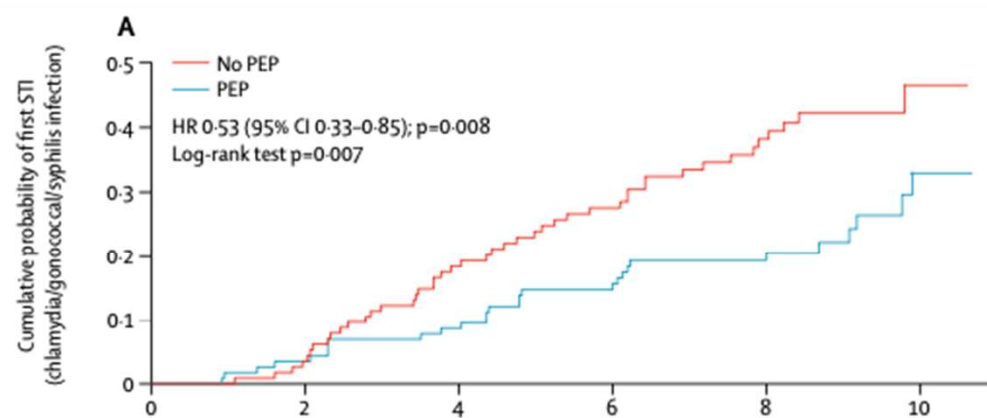
# Resultados

- **Doxy PEP**

- 28/116 al menos una infección
- Probabilidad 22% (15-32)
- Hazard ratio **0.53** (0.33-0.85,  $p=0.008$ )
- Clamidia: HR 0.30 (0.13-0.70)
- Sífilis: HR 0.27 (0.07-0.98)
- Gonorrea: HR 0.83 (0.47-1.47)

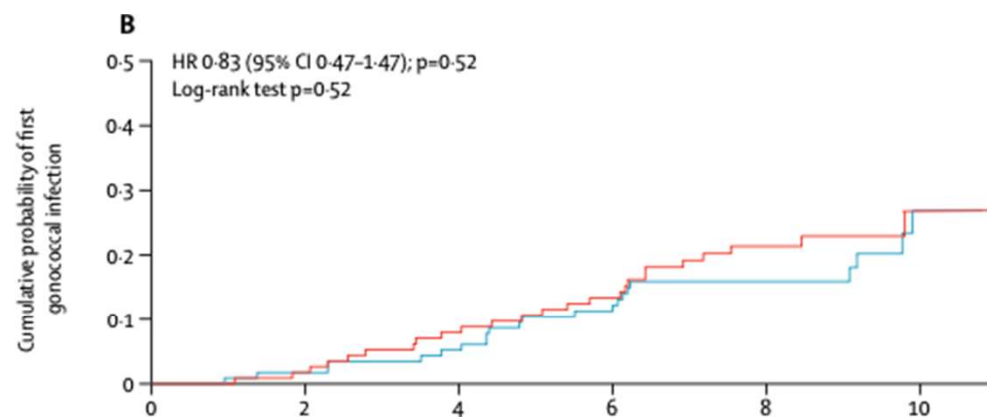
- **No intervención**

- 45/116 al menos 1 ITS
- Probabilidad 42% (33-53)  
 $p=0.007$



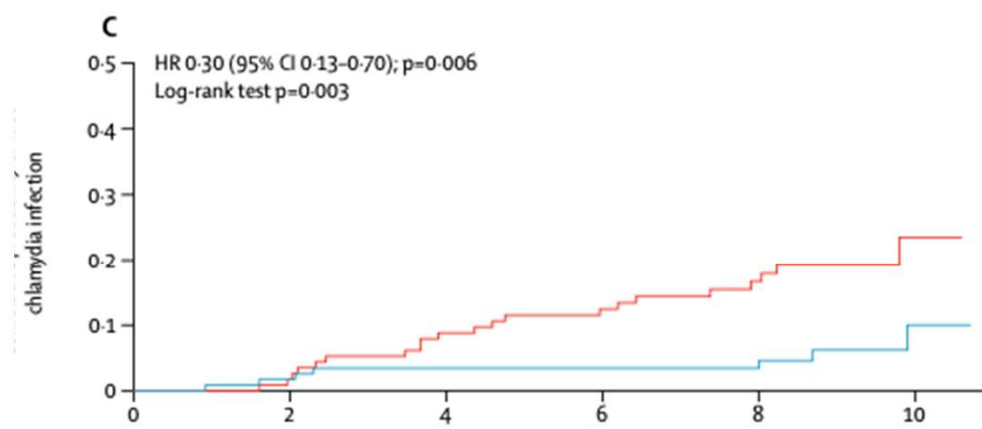
Number at risk

No PEP	116	110	91	76	50	6
PEP	116	112	105	93	69	18



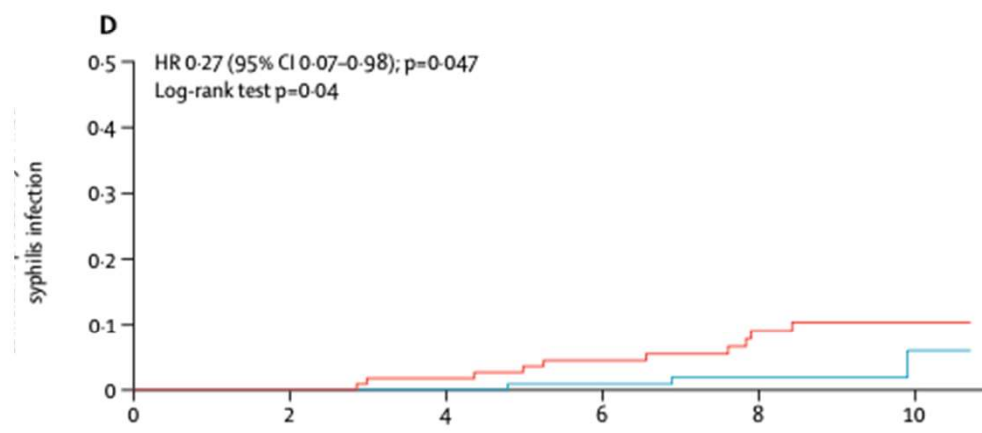
Number at risk

No PEP	116	112	103	92	64	9
PEP	116	114	109	97	71	19



Number at risk

No PEP	116	112	102	93	68	9
PEP	116	114	111	105	84	22



Number at risk

No PEP	116	114	110	102	74	7
PEP	116	116	115	107	83	21

# Resultados de resistencias

- Solo PCR, no se testaron cepas de ITS.
- No se testaron otras cepas.

ORIGINAL ARTICLE

## Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Anne F. Luetkemeyer, M.D., Deborah Donnell, Ph.D.,  
Julia C. Dombrowski, M.D., M.P.H., Stephanie Cohen, M.D., M.P.H.,  
Cole Grabow, M.P.H., Clare E. Brown, Ph.D., Cheryl Malinski, B.S.,  
Rodney Perkins, R.N., M.P.H., Melody Nasser, B.A., Carolina Lopez, B.A.,  
Eric Vittinghoff, Ph.D., Susan P. Buchbinder, M.D., Hyman Scott, M.D., M.P.H.,  
Edwin D. Charlebois, Ph.D., M.P.H., Diane V. Havlir, M.D., Olusegun O. Soge, Ph.D.,  
and Connie Celum, M.D., M.P.H., for the DoxyPEP Study Team\*

- 2022
- Open-label, randomizado, en usuarios de PrEP y PLWHIV (HSH y mujeres trans)
- Doxycycline 200 mg < 24 (max 72) hours after sex versus no intervention, N=501
- ITS testadas cada 3 meses
- Media en el estudio: 8.9 meses
- Objetivo primario: Incidencia de al menos una ITS bacteriana por trimestre



# Resultados

- **Doxy PEP**
  - 10-11% una ITS/trimestre
  - RR **0.34** (0.24-0.49,  $p < 0.001$ )
  - Clamidia: RR 0.26 (0.12-0.57)
  - Sifilis: RR 0.23 (0.04-1.29)
  - Gonorrea: RR 0.45 (0.32-0.65)
- **No intervencion**
  - 30-32% una ITS por trimestre

# Resultados de resistencias

- Resistencia a la tetraciclina probada en un cultivo si la PCR para gonorrea fue positiva
- Muestras de nasofaringe analizadas para detectar resistencia de S. aureus a la doxiciclina
- N. gonorrea
- Basal: 4/15 (27%) aislamientos resistentes a la tetraciclina
- Seguimiento: 5/13 (38%) en el grupo doxyPEP versus 2/16 (12%) en el grupo estándar.

## S. aureus

- Basal: el 45% fue positivo, el 12% tenía una cepa resistente a doxy
- Seguimiento: el 28 % (doxyPEP) frente al 47 % fue positivo, el 16 % frente al 8 % tenía una cepa resistente a doxy.
- En general: el porcentaje de personas con una cepa de S. aureus resistente fue similar, 5 % frente a 4 %

# DoxyVAC, No publicado

- N=502 HSH en PrEP con al menos de 1ITS/año
- DoxyPEP vs no DoxyPEP i versus vacuna Meningococcal B
- Cerca de 85 no DoxyPEP y no vacuna
- Objetivo: Primera ITS
- HR para CT o sífilis: **0.16** (0.08-0.30)
- HR para GO: **0.49** (0.32-0.76)
- No news on resistance

# Efectos secundarios y tolerancia

- Pocos efectos adversos
- Adherencia auto-reportada, ALTA
- Uso medio 3-4 dosis al mes. Un 25% de los usuarios utilizaron 10 dosis o más.

# Uso informal de DoxyPEP por HSH

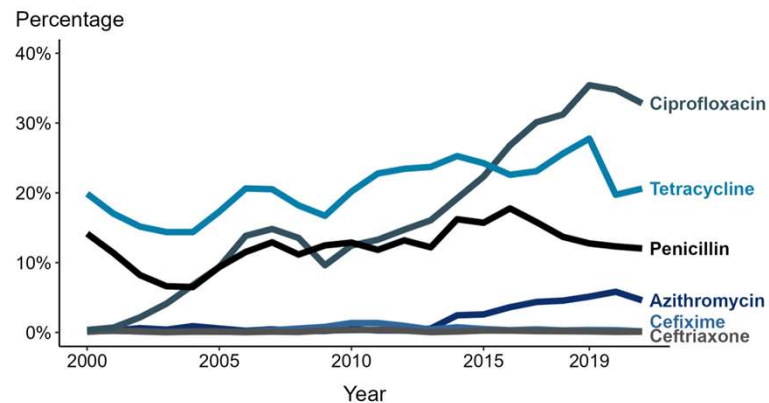
- Cohorte de estudio Amsterdam (2022):
  - N=593, edad 46 (IQR 36-53)
    - 37% han oído sobre DoxyPEP
    - 2,5% (n=15) la han usado
    - Intención de uso(7-point scale): 3 (IQR 2-4)
    - Mayor intención de uso en usuarios de PrEP i con parejas sexuales ocasionales.
- Den los centros de Salud sexual de Holanda (2018):
  - N=231, edad 41 (IQR 29-53)
    - 2,2% (n=7) la han usado

## Important to note:

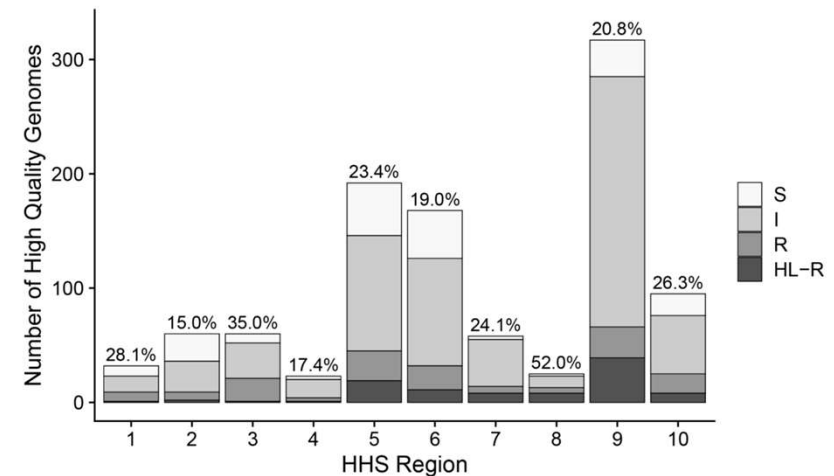
Efficacy of doxyPEP depends on background resistance of *N. gonorrhoea* isolates for tetracycline

In the Netherlands: resistance  $\pm 50\%$  (GGD Amsterdam) compared to around 20% in the US; variation per US region is 17-52%

***Neisseria gonorrhoeae* — Prevalence of Tetracycline, Penicillin, or Ciprofloxacin Resistance\* or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2021**



\* Resistance: Ciprofloxacin: MIC  $\geq 1.0$   $\mu\text{g}/\text{mL}$ ; Penicillin: MIC  $\geq 2.0$   $\mu\text{g}/\text{mL}$  or Beta-lactamase positive; Tetracycline: MIC  $\geq 2.0$   $\mu\text{g}/\text{mL}$   
 † Elevated MICs: Azithromycin: MIC  $\geq 1.0$   $\mu\text{g}/\text{mL}$ , 29 (2000–2004);  $\geq 2.0$   $\mu\text{g}/\text{mL}$  (2005–2020); Ceftriaxone: MIC  $\geq 0.125$   $\mu\text{g}/\text{mL}$ ; Cefixime: MIC  $\geq 0.25$   $\mu\text{g}/\text{mL}$   
 NOTE: Cefixime susceptibility was not tested in 2007 and 2008.



**Supplementary Figure 1. Tetracycline susceptibility across geographic regions.** Bars are shaded based on the number of isolates classified as susceptible (S, MIC  $\leq 0.25$   $\mu\text{g}/\text{mL}$ ), intermediate (I,  $0.25 < \text{MIC} < 2$   $\mu\text{g}/\text{mL}$ ), resistant (R,  $2 \leq \text{MIC} \leq 8$   $\mu\text{g}/\text{mL}$ ), or high-level resistant (HL-R, MIC  $> 8$   $\mu\text{g}/\text{mL}$ ). Bars are labeled with the percentage of isolates resistant to tetracycline



# Current international position statements and guidelines

CDC (2023)

UK (2022)

San Francisco (2022)

New York (2023)

Australia (2023)





# Current international position statements and guidelines

CDC (2023)

UK (2022)

## So **Considerations**

N  
A  
Based on the clinical trials, systematic reviews, and studies of populations who would likely benefit most from an intervention to reduce bacterial STIs, the following considerations are recommended: doxycycline 200mg taken once orally within 72 hours of oral, vaginal or anal sex should be considered for gay, bisexual, and other MSM, and for TGW, with a history of at least one bacterial STI (i.e., gonorrhea, chlamydia or syphilis) in the last 12 months and who are at ongoing risk for acquisition of bacterial STIs.



# Current international position statements and guidelines

CDC (2023)  
UK (2022)

## BASHH updated position statement on doxycycline as prophylaxis for sexually transmitted infections

Manik Kohli <sup>1,2</sup> Nicholas Medland,<sup>3,4</sup> Helen Fifer <sup>5</sup>  
John Saunders <sup>1,5</sup>

to advise patients about STI prophylaxis. Importantly, it remains the case that doxycycline taken as PEP or pre-exposure prophylaxis (PrEP) for STIs is not endorsed by BASHH or UKHSA.

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Kohli M, *et al.* *Sex Transm Infect* May 2022 Vol 98 No 3



# Current international position statements and guidelines

CDC (2023)

UK (2022)

San Francisco (2022)

New York (2023)



**POPULATION HEALTH DIVISION**  
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH



## Recommendations

1. **Recommend doxy-PEP** to cis men and trans women who: 1) have had a bacterial STI in the past year and 2) report condomless anal or oral sexual contact with  $\geq 1$  cis male or trans female partner in the past year. These were the eligibility criteria used for the DoxyPEP study. Patients with a history of syphilis should be prioritized for doxy-PEP.

# Current international position statements and guidelines

CDC (2023)

UK (2022)

San Francisco (2022)

New York (2023)

## New York guidelines

### Biomedical Prevention of STIs

- Clinicians should offer doxy-PEP to cisgender men and transgender women who are taking HIV PrEP or receiving HIV care and 1) engage in condomless sex with partner(s) assigned male sex at birth and 2) have had a bacterial STI diagnosed within the past year and are at ongoing risk of STI exposure. (A1)



# Current international position statements and guidelines

CDC (2023)

UK (2022)

San Francisco (2022)

New York (2023)

Australia (2023)

## Recommendations for community and clinicians

1. Doxy-PEP should be considered primarily for the prevention of syphilis in GBMSM who are at risk of this STI, although for some individuals the reduction in chlamydia, and the lesser reduction of gonorrhoea might be important. Some stakeholders held the view that Doxy-PEP should be considered *only* for the prevention of syphilis in GBMSM, for the reasons listed above.



# Advantages versus risks

## Advantages

People already use it, better prescribe it with care  
Less STI burden for person  
Less STI transmission (likely)  
Less use of other antibiotic medication????  
Empowerment/sexual pleasure/preferred by user

## Risks

- Long-term outcomes unknown
- Resistant strains are selected and transmitted
- Effects of antibiotic pressure on microbiome unknown
- Syphilis serology less well interpretable
- Specific for Dutch situation: Doxycycline is used to treat community acquired pneumonia

Environmental effects?

No placebo-controlled trials have been done; information on optimal dosing, eg 100 mg versus 200 mg, is lacking





