Patrocinador Científico:

AGIDEI
ASOCIACIÓN GALLEGA PARA LA INVESTIGACIÓN Y DOCENCIA EN ENFERMEDADES INFECCIOSAS

Patrocinadores:

GILEAD

Late Presenters:

Un problema no resuelto

Juan Ambrosioni

VII Jornada de Excelencia en VIH

Vigo, 30 de Junio y

1 de Julio de 2023

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Contenido

- Epidemiología de la presentación tardía en Europa y España
- Oportunidades de mejora
- Manejo y pronóstico
- Conclusiones y mensajes finales

Contenido

- **Epidemiología de la presentación tardía en Europa y España**
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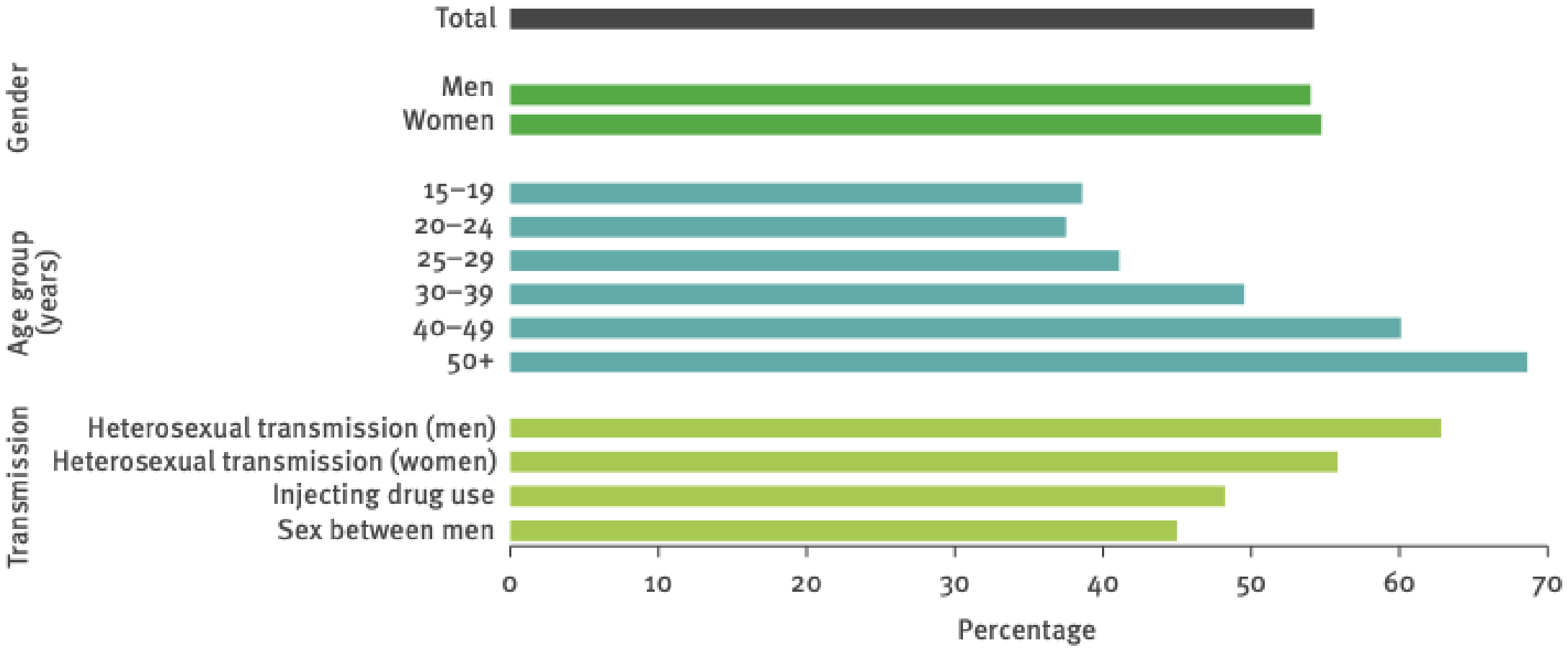
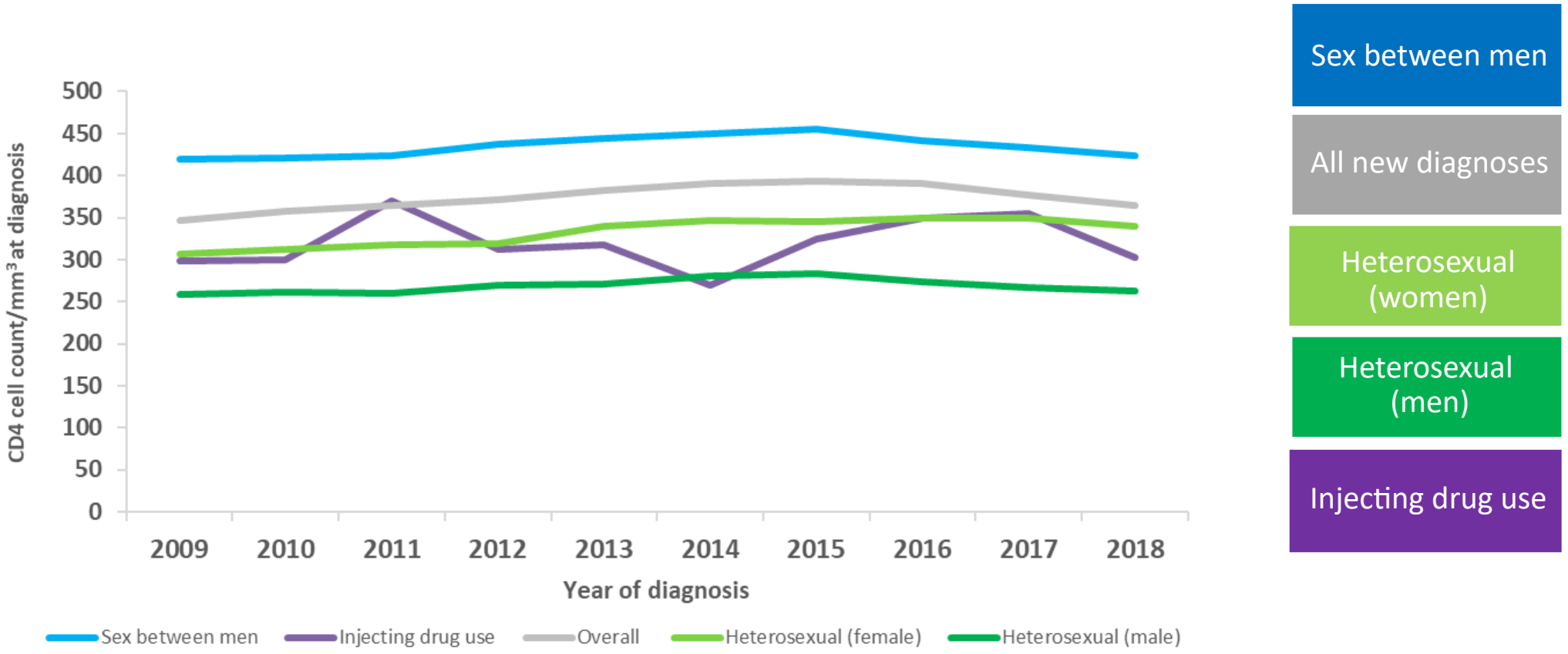
Fig. B. Proportion of people diagnosed late (CD4 cell count < 350 per mm³) by gender, age and transmission, WHO European Region, 2021 (n = 28 742)



Source: ECDC/WHO (November 2022). HIV/AIDS Surveillance in Europe 2021 data

Median CD4 cell count per mm^3 at HIV diagnosis, overall and by route of HIV transmission, EU/EEA, 2009-2018



Sex between men

All new diagnoses

Heterosexual (women)

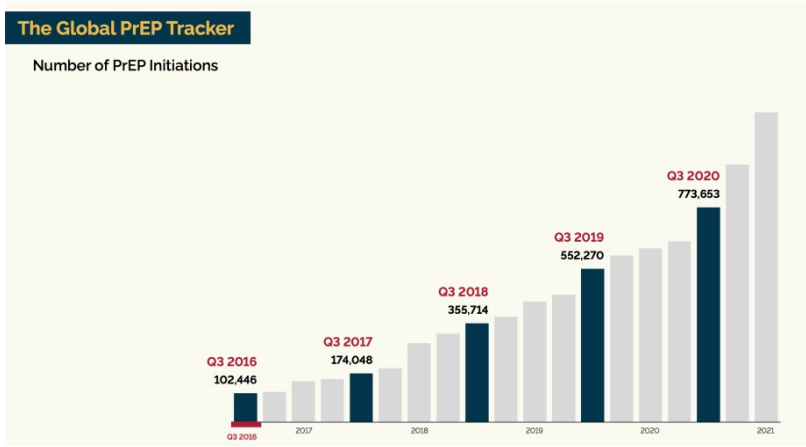
Heterosexual (men)

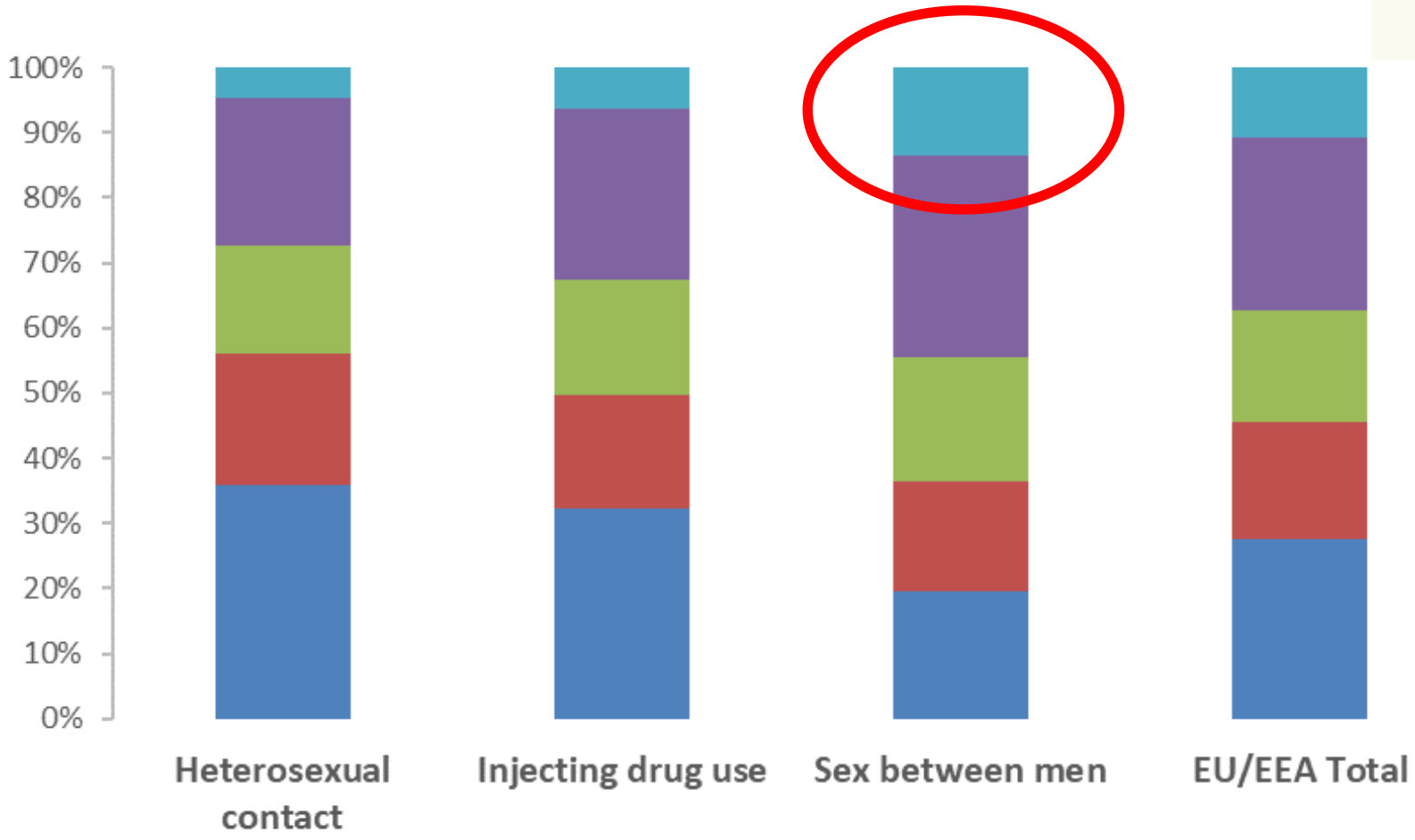
Injecting drug use

Note: Excludes countries with >60% incomplete data on CD4 cell count during any year over the period (Bulgaria, Croatia, Estonia, Germany, Hungary, Italy, Ireland, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Sweden). Acute infections are excluded from this analysis.

Source: ECDC/WHO (2019). HIV/AIDS Surveillance in Europe 2019– 2018 data

Acute infection or CD4 cell count per mm^3 at HIV diagnosis, overall and by transmission group, EU/EEA





Acute Infection

500+

350 to <500

200 to <350

<200

Source: ECDC/WHO (2019). HIV/AIDS Surveillance in Europe 2019– 2018 data

Primary HIV infection: definitions

-Primary HIV infection (PHI)

-Acute HIV infection (<1 month)

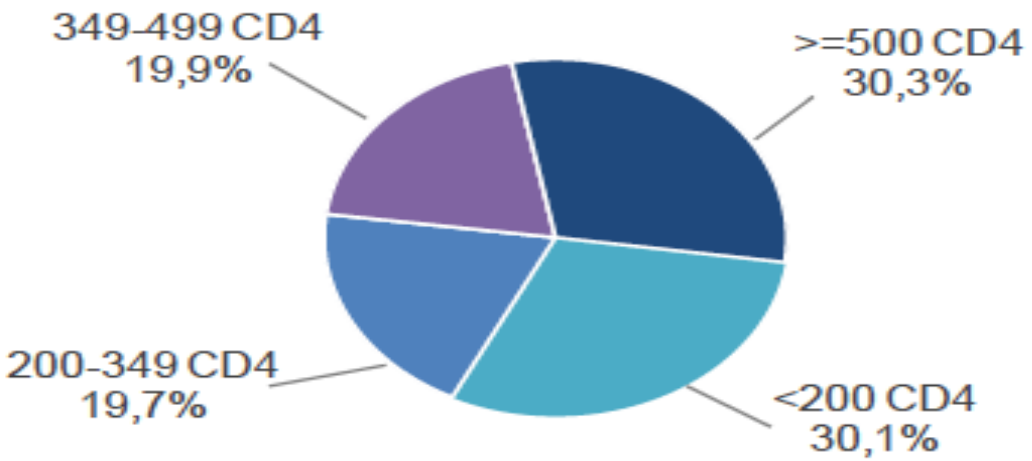
-Recent HIV infection (<6 months)

By definition, every new HIV infection in a PrEP user is a PHI (PrEP users are controlled every 3 months)

Although MSM are less affected, still 45% have late presentation in Europe

EACS guidelines 11.1, Oct 2022.

Figura 8
Nuevos diagnósticos de VIH. Diagnóstico tardío
España, año 2021. Datos no corregidos por retraso en la notificación.

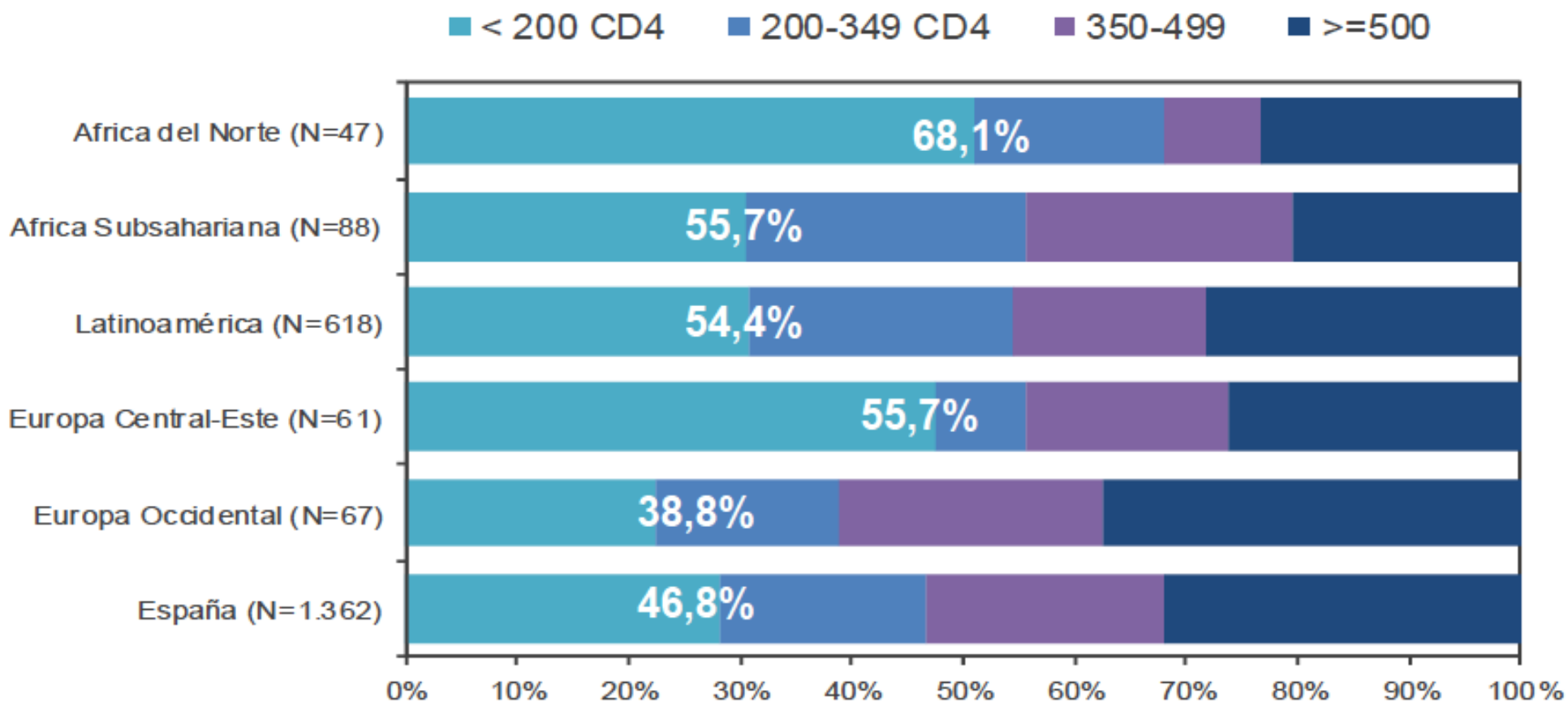


n= 2.382

N=2382

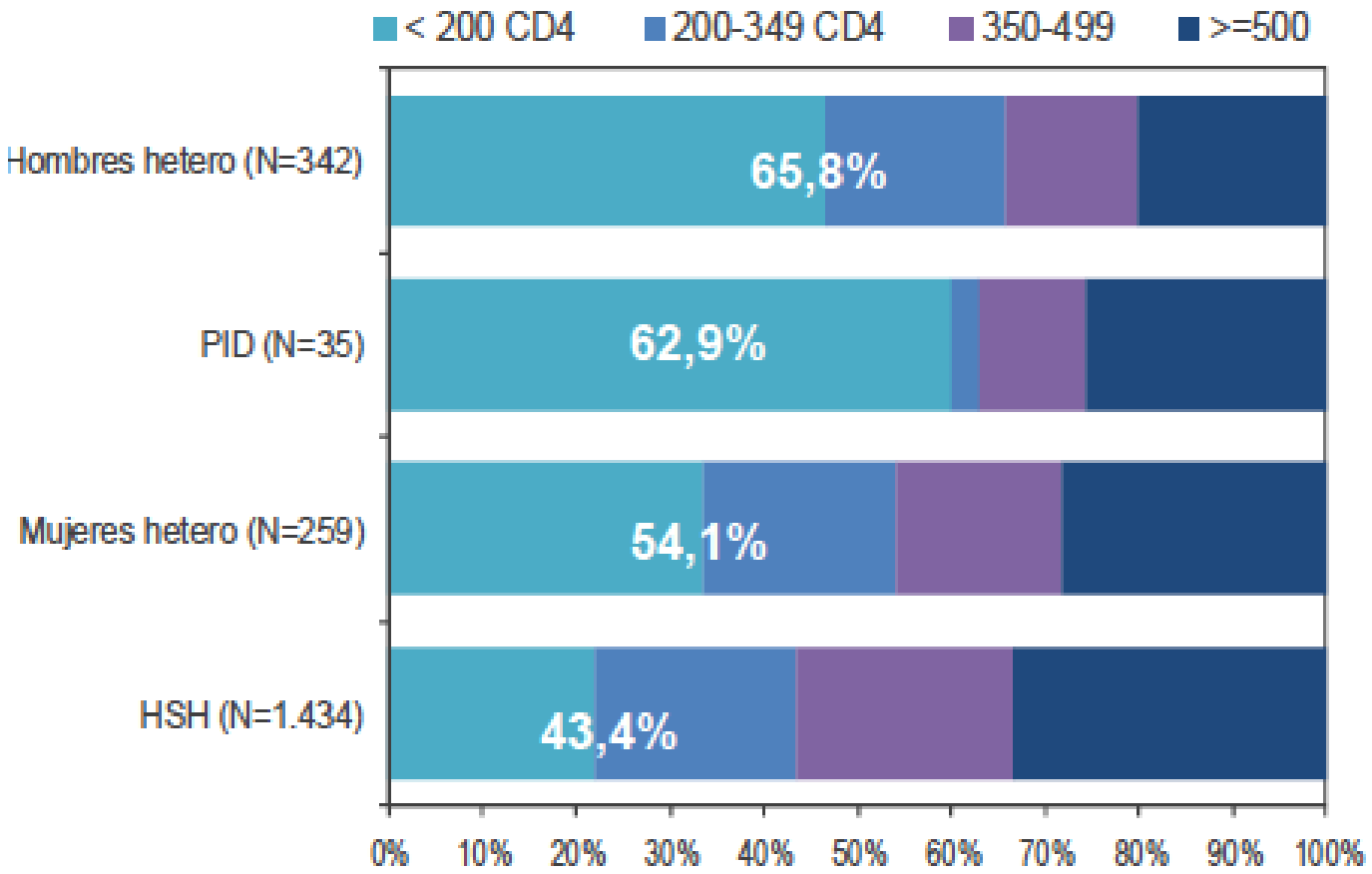
Unidad de vigilancia de VIH, ITS y hepatitis. Vigilancia Epidemiológica del VIH y sida en España 2021: Sistema de Información sobre Nuevos Diagnósticos de VIH y Registro Nacional de Casos de Sida. Centro Nacional de Epidemiología. Instituto de Salud Carlos III/ División de control de VIH, ITS, Hepatitis virales y tuberculosis. Ministerio de Sanidad. Madrid; noviembre 2022.

Nuevos diagnósticos de VIH. Diagnóstico tardío según zona geográfica de origen. España, año 2021. Datos no corregidos por retraso en la notificación.

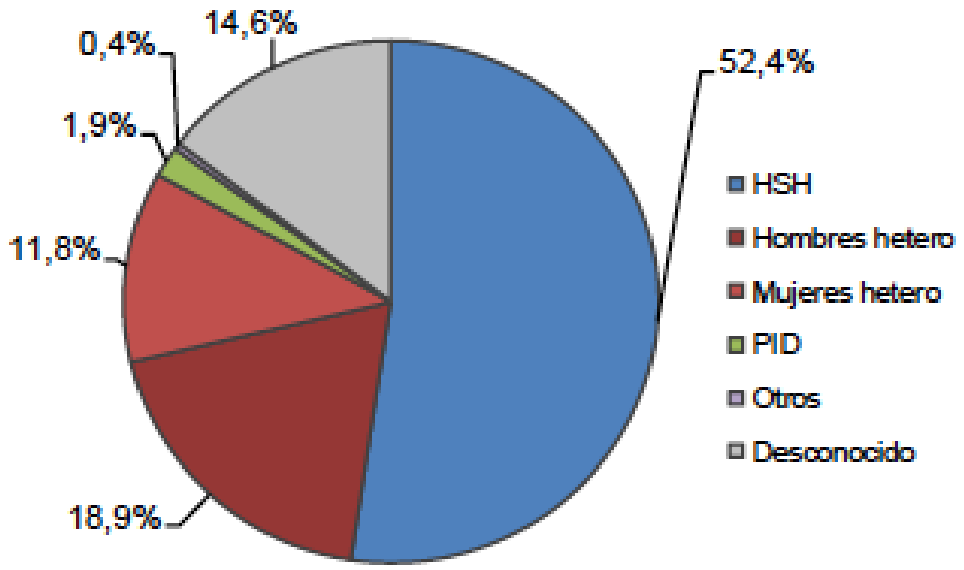


Unidad de vigilancia de VIH, ITS y hepatitis. Vigilancia Epidemiológica del VIH y sida en España 2021: Sistema de Información sobre Nuevos Diagnósticos de VIH y Registro Nacional de Casos de Sida. Centro Nacional de Epidemiología. Instituto de Salud Carlos III/ División de control de VIH, ITS, Hepatitis virales y tuberculosis. Ministerio de Sanidad. Madrid; noviembre 2022.

Diagnóstico tardío según modo de transmisión



Modo de transmisión en pacientes con diagnóstico tardío



n= 2.382

Unidad de vigilancia de VIH, ITS y hepatitis. Vigilancia Epidemiológica del VIH y sida en España 2021: Sistema de Información sobre Nuevos Diagnósticos de VIH y Registro Nacional de Casos de Sida. Centro Nacional de Epidemiología. Instituto de Salud Carlos III/ División de control de VIH, ITS, Hepatitis virales y tuberculosis. Ministerio de Sanidad. Madrid; noviembre 2022.

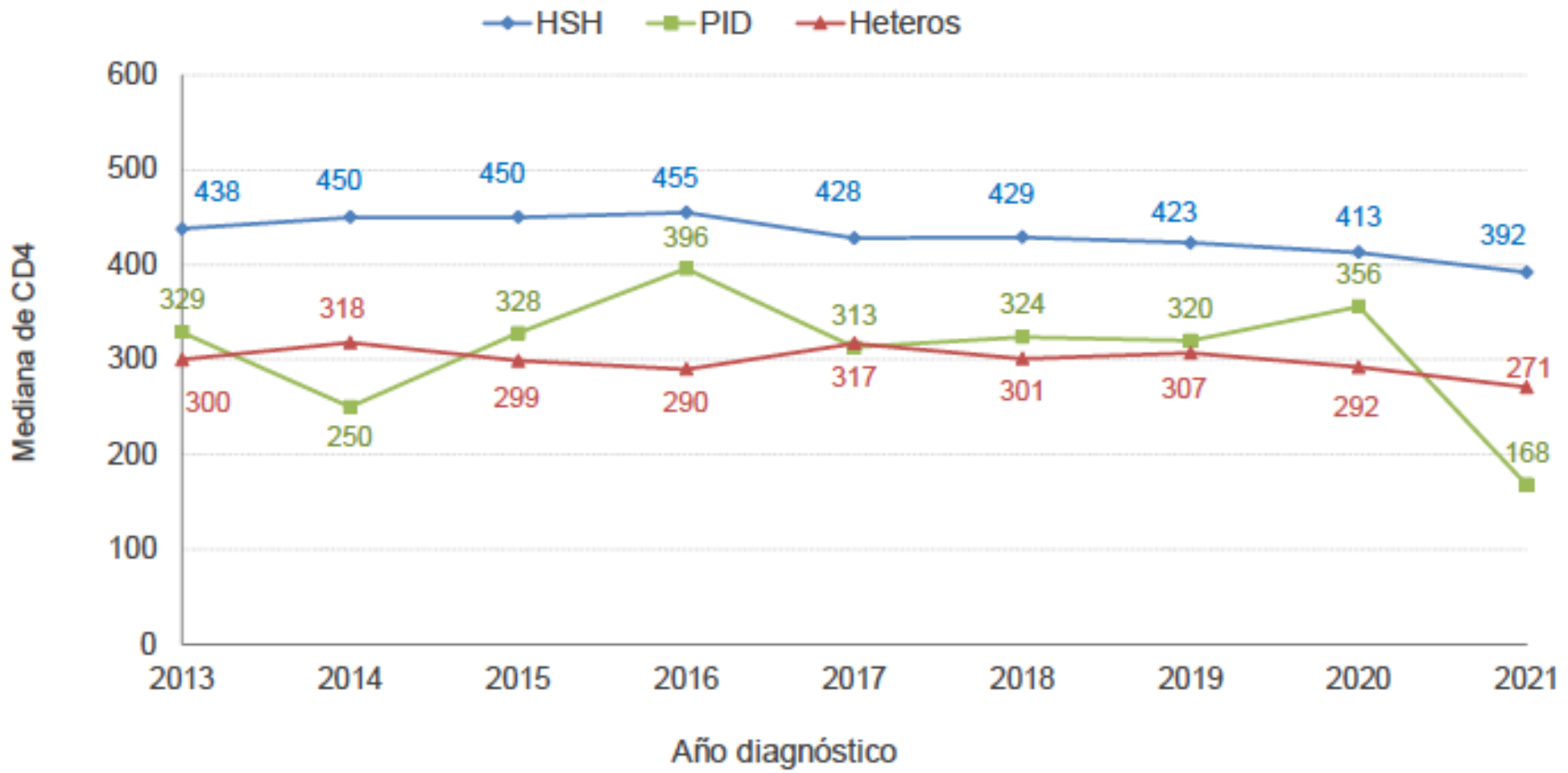
MSM population much more aware of risk…

Most of patients (>90%) in our PHI cohort are MSM

People on PrEP also controlled regularly every 3 months

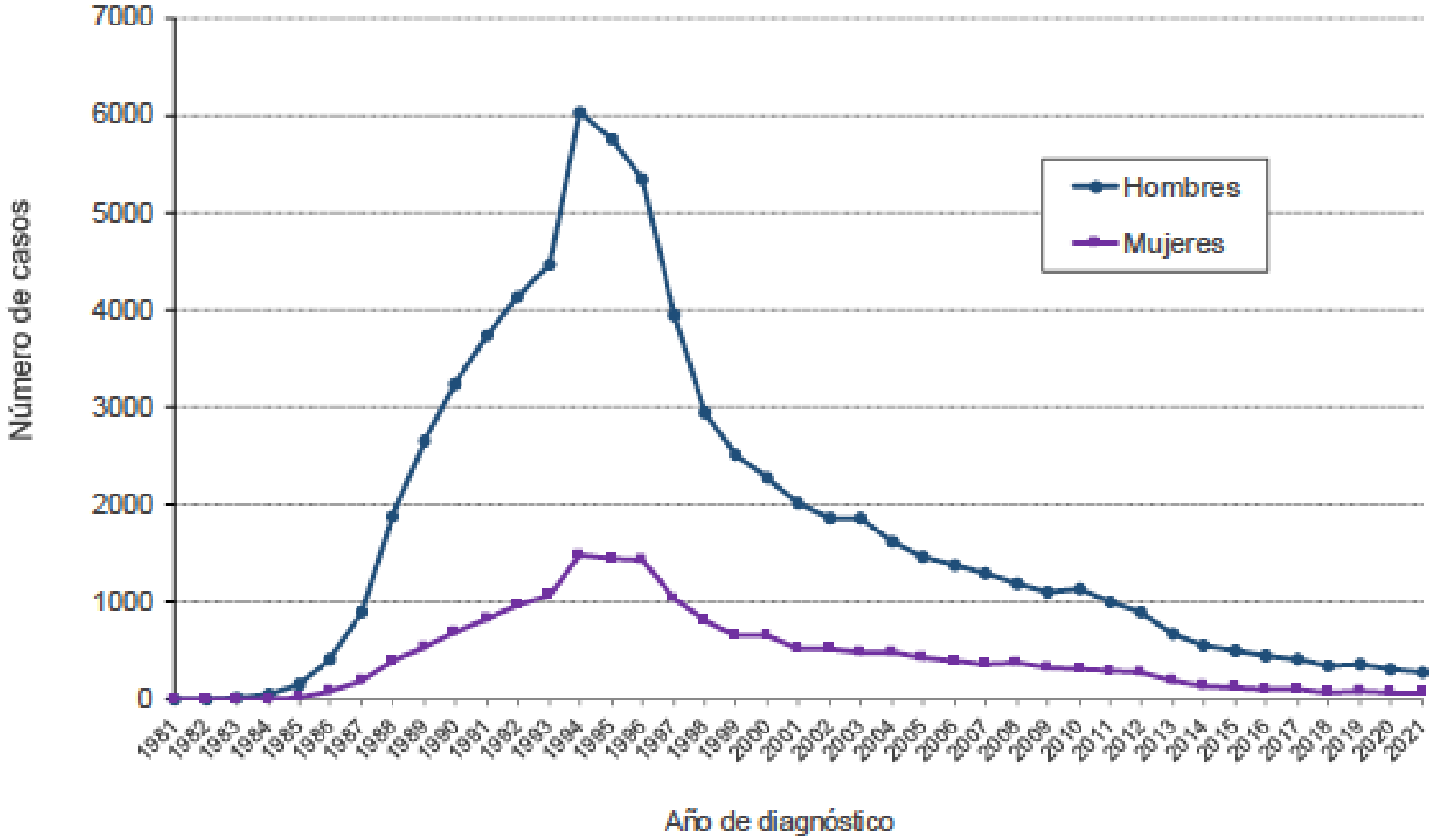
Consistent with European data (43.4%)

Mediana del recuento de CD4 al diagnóstico de VIH por modo de transmisión, 2013-2021. Datos no corregidos por retraso en la notificación.



Unidad de vigilancia de VIH, ITS y hepatitis. Vigilancia Epidemiológica del VIH y sida en España 2021: Sistema de Información sobre Nuevos Diagnósticos de VIH y Registro Nacional de Casos de Sida. Centro Nacional de Epidemiología. Instituto de Salud Carlos III/ División de control de VIH, ITS, Hepatitis virales y tuberculosis. Ministerio de Sanidad. Madrid; noviembre 2022.

Casos de sida en España* por sexo, 1981-2021.
Registro Nacional de Sida. Datos no corregidos por retraso en la notificación.

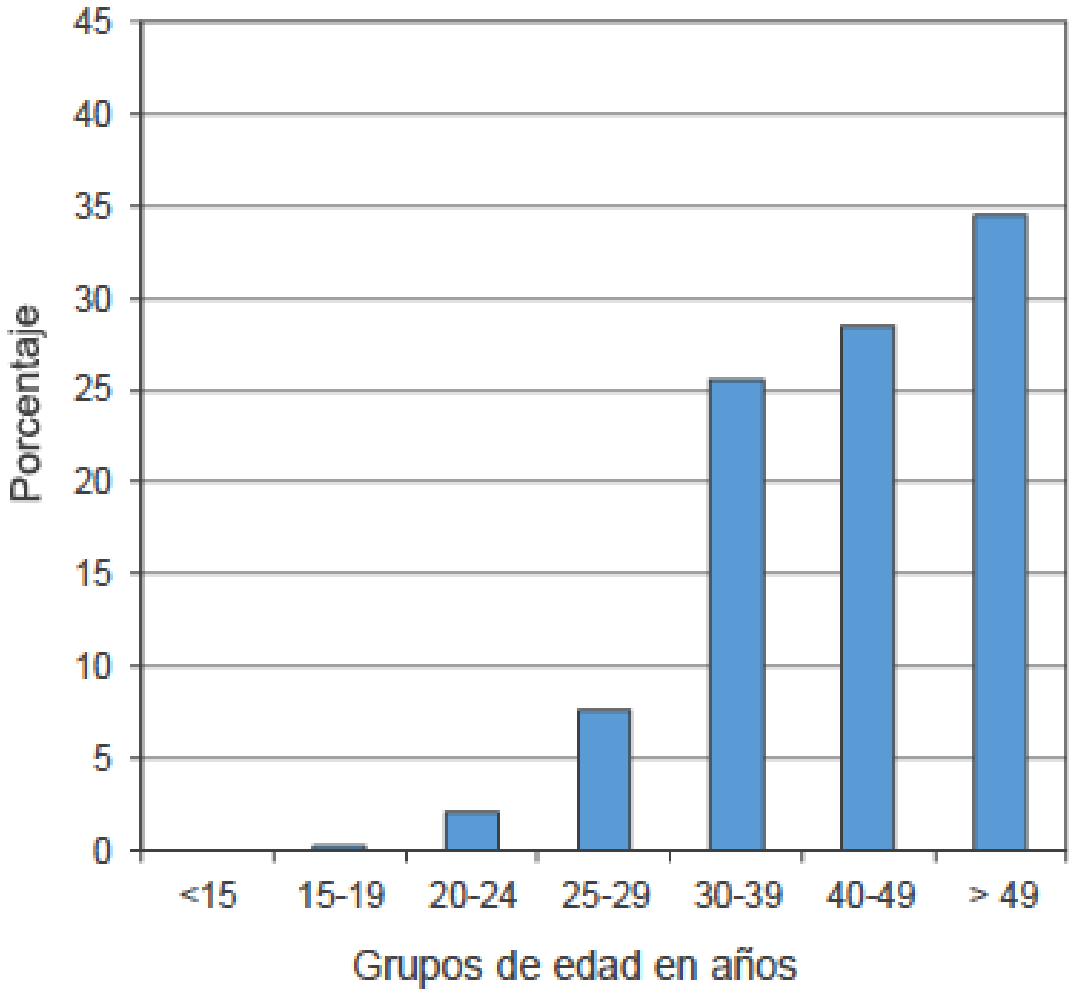


Unidad de vigilancia de VIH, ITS y hepatitis. Vigilancia Epidemiológica del VIH y sida en España 2021: Sistema de Información sobre Nuevos Diagnósticos de VIH y Registro Nacional de Casos de Sida. Centro Nacional de Epidemiología. Instituto de Salud Carlos III/ División de control de VIH, ITS, Hepatitis virales y tuberculosis. Ministerio de Sanidad. Madrid; noviembre 2022.

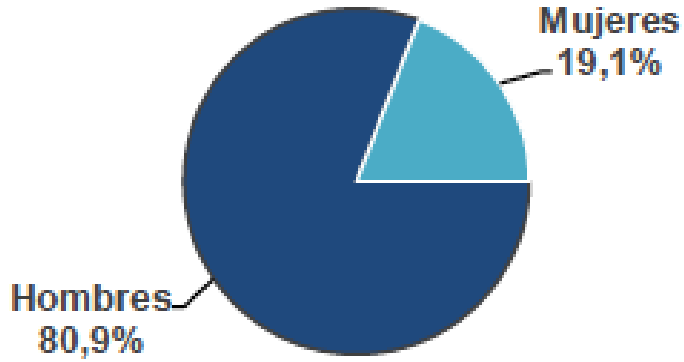
Casos de sida diagnosticados en España* en 2021. Distribución por edad y sexo.

Registro Nacional de Sida. Datos no corregidos por retraso en la notificación.

Edad



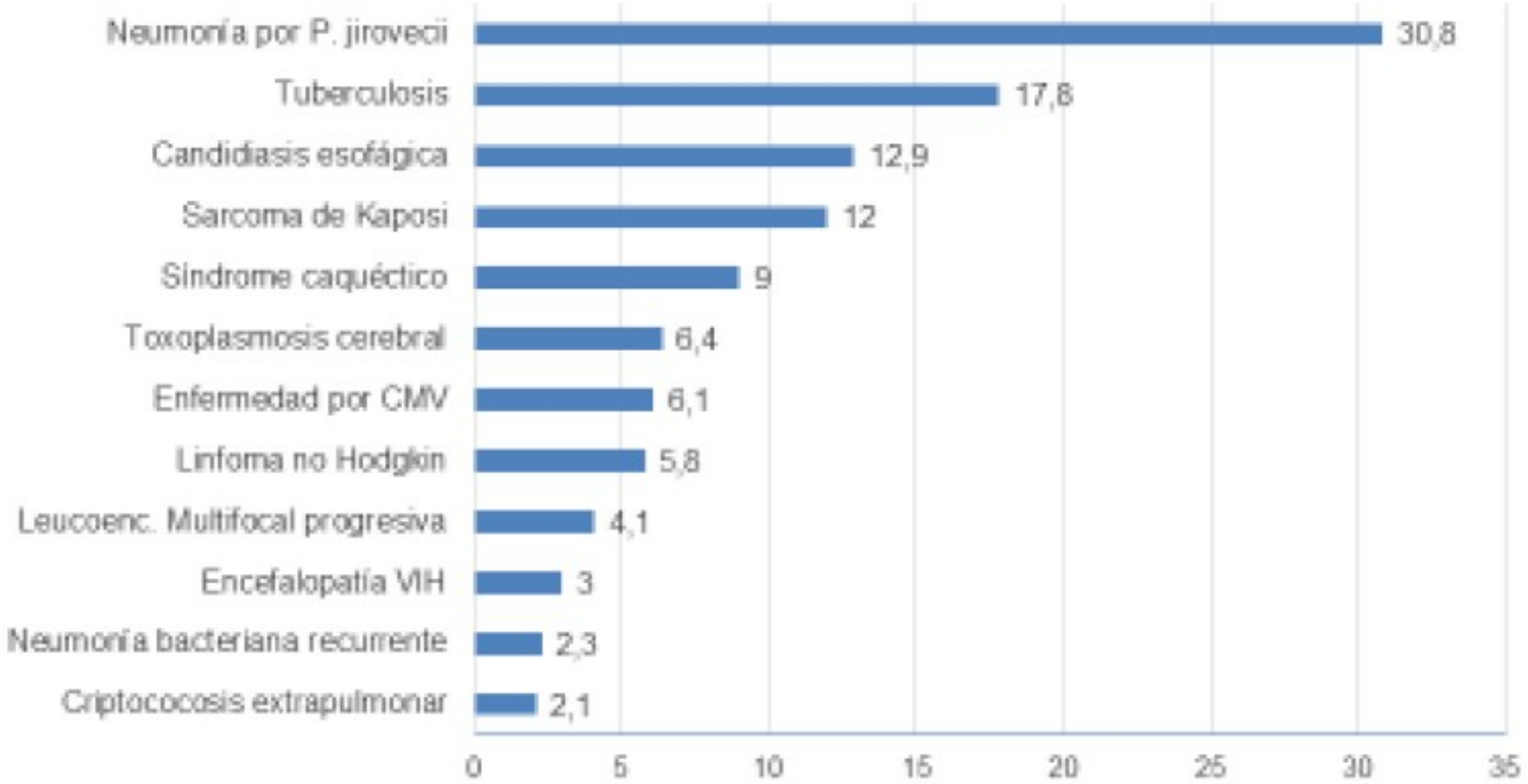
Sexo



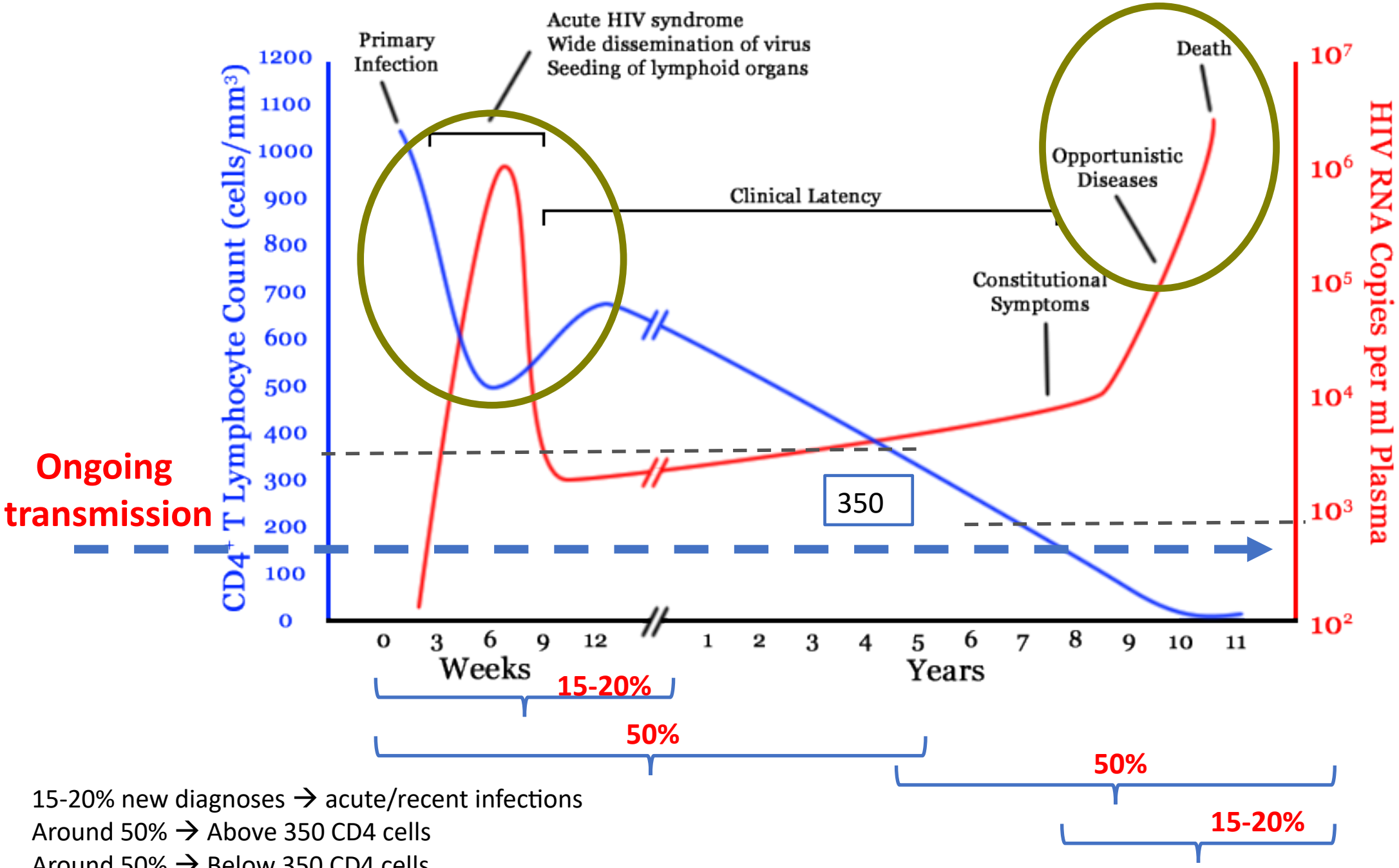
n =340*

* Por razones técnicas no se han podido incluir los casos de la Comunidad Valenciana a partir de 2014.

Enfermedades definitorias de sida más frecuentes en España*, 2012-2021
Registro Nacional de Sida. Datos no corregidos por retraso en la notificación.



Unidad de vigilancia de VIH, ITS y hepatitis. Vigilancia Epidemiológica del VIH y sida en España 2021: Sistema de Información sobre Nuevos Diagnósticos de VIH y Registro Nacional de Casos de Sida. Centro Nacional de Epidemiología. Instituto de Salud Carlos III/ División de control de VIH, ITS, Hepatitis virales y tuberculosis. Ministerio de Sanidad. Madrid; noviembre 2022.

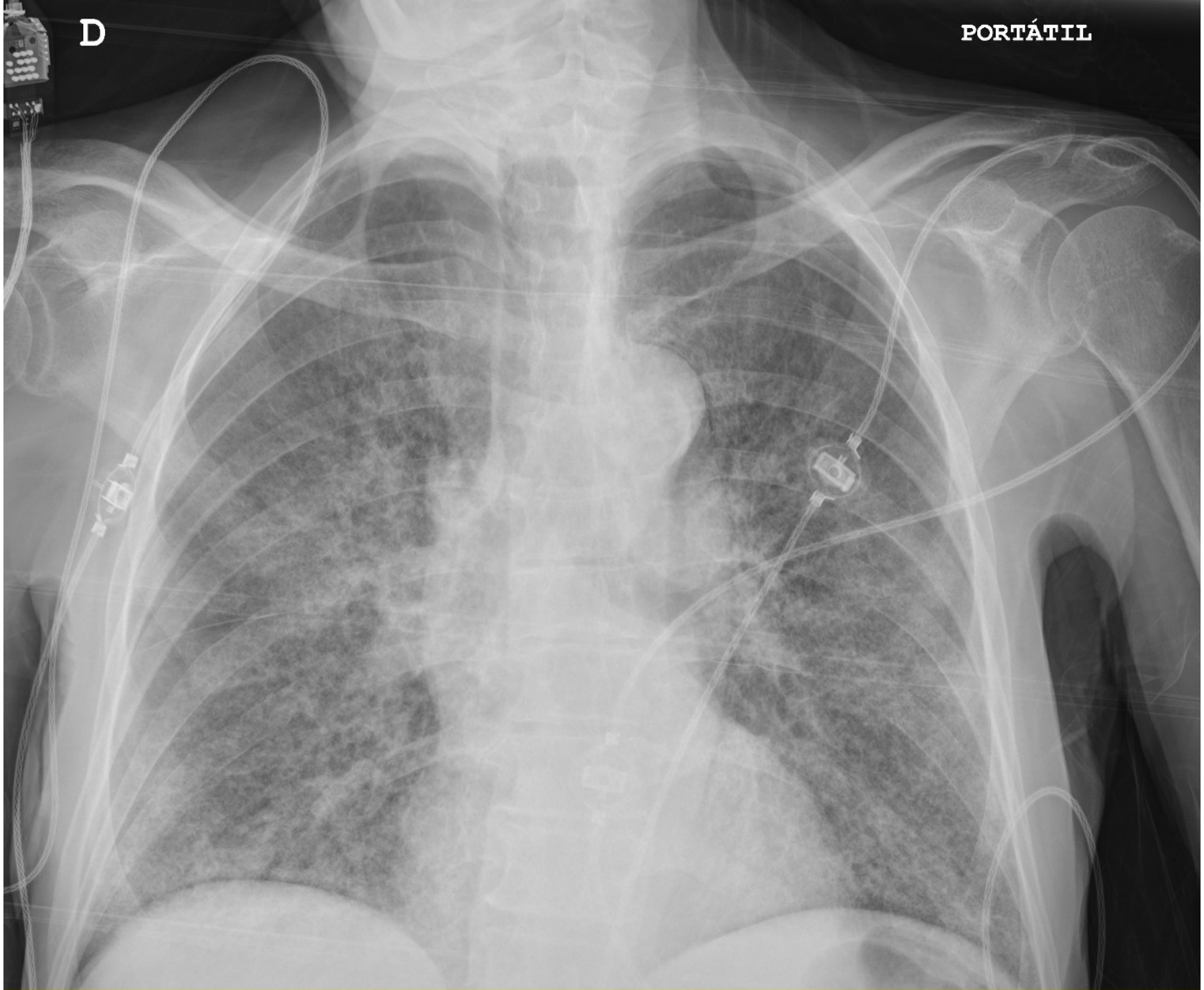


15-20% new diagnoses → acute/recent infections
Around 50% → Above 350 CD4 cells
Around 50% → Below 350 CD4 cells
15-20% → Advanced disease (<200)

ECDC/WHO (2021). HIV/AIDS Surveillance in Europe 2019– 2020 data
Romero A et al, Sex Transm Infect 2009.

El caso prototípico

- Hombre de 65 años, sin antecedentes patológicos de relevancia
- Heterosexual, casado, latinoamericano, en España hace 10 años, esposa fallecida en febrero 2023 por complicación post-quirúrgica de cadera
- HERPES ZÓSTER FACIAL complicado con neuritis post-herpética tratado en marzo de 2023
- Últimos meses, pérdida de peso progresiva atribuida a la situación personal
- Junio 2023, disnea progresiva hasta disnea de reposo con fiebre de bajo grado


D
PORTÁTIL

- LBA: abundantes quistes de *Pj*
- Serología VIH pos, CV=70000 copias/mL
- CD4= 4 mm^3 (2%)
- Ratio CD4/CD8=0.01
- Hospitalización directa en UCI, lenta mejoría con pase a planta general 3 semanas más tarde

- Nunca se había realizado una serología de VIH
- Jamás consideró que podía estar a riesgo
- Múltiples contactos con el sistema sanitario entre 2011 y 2021, por distintos motivos
- Nunca él mismo ni los médicos consideraron indicado un test de VIH
- Tampoco fue realizado cuando tuvo un zóster en marzo

¿Hubo oportunidades perdidas?

-¿AP?

-¿Urgencias?

Contenido

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- **Oportunidades de mejora**
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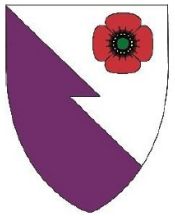
The Royal College of Emergency Medicine

Best Practice Guideline

UK

HIV Testing in the Emergency Department



Revised: December 2020

Summary of Recommendations

1. Human Immunodeficiency Virus (HIV) testing should be performed in the emergency department (ED) setting when it influences immediate clinical management and improves patient care. Any doctor working in an emergency department should be able to organise and consent a patient for an HIV test. *Strong recommendation.*

2. The HIV seroprevalence rate in the catchment population should be known before any HIV testing program is introduced into the emergency department. *Strong recommendation.*

3. Consider offering routine Emergency Department HIV testing where the local diagnosed HIV prevalence is 2/1000 or greater, providing that appropriate funding, and systems are in place to support this. Emergency Departments are not a suitable environment for ad hoc screening programs where local prevalence rates are uncertain or below 2/1000. *Strong recommendation.*

4. Safeguards are required before introducing routine Emergency Department HIV or blood borne virus testing. These safeguards include: a systems-wide approach; adequate resources for training and education of staff, testing and follow up; and, the development of robust protocols for the transfer of patient care with reactive or positive results to appropriate care and support services. *Strong recommendation.*

→ España > 4/1000

Table 1: Conditions that would be AIDS defining in an individual living with HIV

Table 2: Non-AIDS-defining conditions associated with an undiagnosed HIV seroprevalence >1 per 1000

Sexually transmitted infections
Malignant lymphoma
Anal cancer/dysplasia
Cervical dysplasia
Herpes zoster
Hepatitis B or C (acute or chronic)
Unexplained lymphadenopathy
Mononucleosis-like illness
Community-acquired pneumonia
Unexplained leukocytopenia/ thrombocytopenia lasting >4 weeks
Seborrheic dermatitis/exanthema
Peripheral neuropathy
Severe or atypical psoriasis
Mononeuritis
Unexplained weight loss
Unexplained oral candidiasis

HIV Testing in Emergency Departments

The evidence regarding how HIV testing in the Emergency Department affects length of stay and patient flow in the Emergency Department is contradictory. Evidence from the UK

DOCUMENTO DE CONSENSO

Recomendaciones dirigidas a los servicios de urgencias para el diagnóstico precoz de pacientes con sospecha de infección por VIH y su derivación para estudio y seguimiento

Juan González del Castillo[1], Guillermo Burillo-Putze[2], Alfonso Cabello[3], Adrián Curran[4], Eissa Jaloud Saavedra[5], Pierre Malchair[6], María José Marchena[7], Òscar Miró[8], Alberto Pizarro[9], Cesar Sotomayor[10], Francisco Javier Candel[11], Santiago Moreno[12]

Tabla 3. Propuesta de procesos de automatización para la realización de serologías para el VIH en los servicios de urgencias

NAC	– Inclusión de avisos automáticos de serología para el VIH ante un diagnóstico de NAC, o cuando en el historial del paciente exista un diagnóstico previo de NAC con o sin serología para el VIH realizada.
SM	– Inclusión de avisos automáticos de serología para el VIH ante la petición de la prueba de Paul-Bunnell, la solicitud de cualquier tipo de serología en urgencias (Epstein Barr, Citomegalovirus…) o ante el diagnóstico de SM. – Valorar añadir preconfigurados para perfiles específicos de pacientes con SM.
HZ	– Inclusión de avisos automáticos de serología para el VIH ante un diagnóstico de HZ, o cuando en el historial del paciente exista un diagnóstico previo de HZ con o sin serología para el VIH realizada.
ITS	– Inclusión de avisos automáticos de serología para el VIH tras la solicitud de un exudado uretral, si el motivo de consulta en el Sistema de Triaje Manchester es "Enfermedad de trasmisión sexual", ante el diagnóstico de ITS, o cuando en el historial del paciente exista un diagnóstico previo de ITS con o sin serología para el VIH realizada. – Valorar añadir preconfigurados para perfiles específicos de pacientes con ITS.
PPE	– Inclusión de avisos automáticos de serología para el VIH ante el diagnóstico de PPE. – Inclusión de avisos automáticos de serología para el VIH ante la prescripción electrónica de los antirretrovirales incluidos en la PPE. – Valorar añadir preconfigurados para perfiles específicos de pacientes con ITS.
Chemsex	– Inclusión de avisos automáticos de serología para el VIH ante el diagnóstico de o ante la petición de estudios toxicológicos específicos en orina. – Valorar añadir preconfigurados para perfiles específicos de pacientes con ITS.

VIH: virus de inmunodeficiencia humana; NAC: neumonía adquirida en la comunidad; SM: síndrome mononucleósico; HZ: herpes zoster; ITS: infección de transmisión sexual; PPE: profilaxis postexposición.

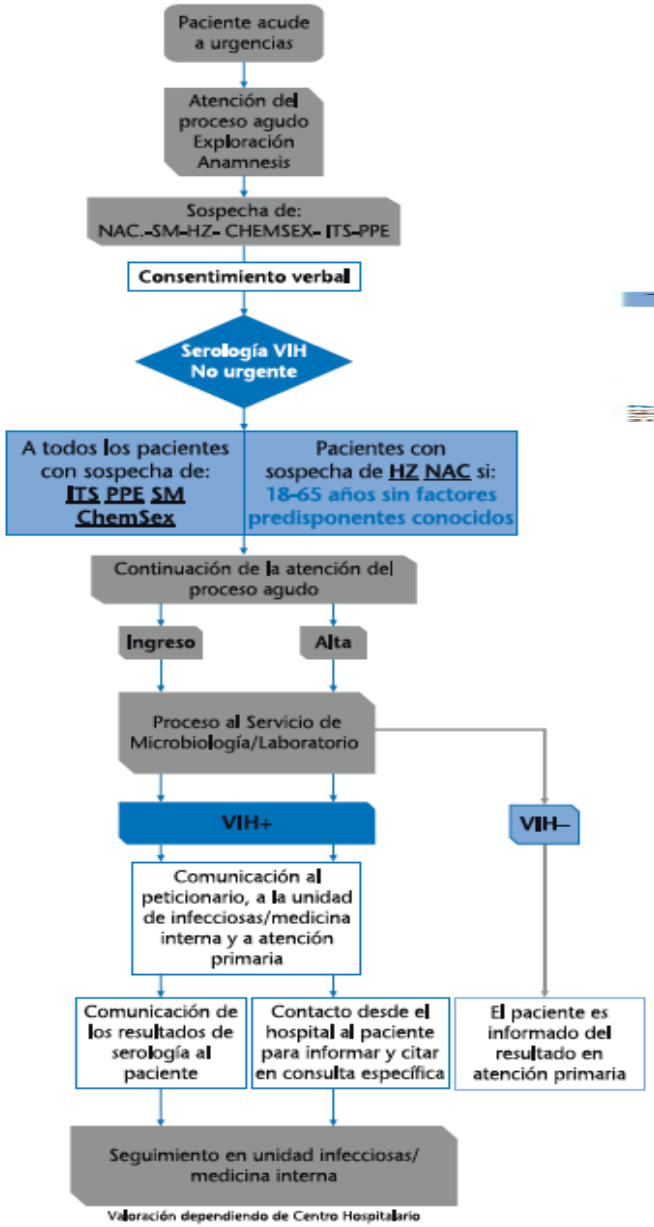


Figura 1. Algoritmo para el diagnóstico precoz del VIH en los servicios de urgencias en pacientes con sospecha de neumonía adquirida en la comunidad (NAC), síndrome mononucleósico (SM), herpes zoster (HZ), infección de transmisión sexual (ITS), profilaxis postexposición (PPE) o práctica del *chemsex*.

Aten Primaria. 2018;50(3):159–165

Atención Primaria

www.elsevier.es/ap

ORIGINAL

Diagnóstico precoz del VIH en atención primaria en España. Resultados de una prueba piloto de cribado dirigido basado en condiciones indicadoras, criterios conductuales y de origen

Cristina Agustí[a,b,c,*], María Martín-Rabadán[d], José Zarco[e], Cristina Aguado[f], Ricard Carrillo[g,h], Roger Codinachs[i], Jose Manuel Carmona[j] y Jordi Casabona[a,b,c,k]

Objectives: To estimate the prevalence of HIV infection in patients diagnosed with an indicator condition (IC) for HIV and/or risk behavior for their acquisition and/or coming from high prevalence countries. To determine the acceptability and feasibility of offering HIV testing based on IC and behavioral and origin criteria in Primary Care (PC).
Design: Cross-sectional study in a convenience sample.
Location: Six PC centers in Spain.
Participants: The inclusion criteria were: patients between 16 and 65 years old who presented at least one of the proposed ICs and/or at least one of the proposed behavioral and/or origin criteria. A total of 388 patients participated.
Intervention: HIV serology was offered to all patients who met the inclusion criteria.
Main measurements: Description of IC frequency, behavioral and origin criteria. Prevalence of HIV infection. Level of acceptability and feasibility of the HIV screening based on IC and behavioral and origin criteria.
Results: A total of 174 patients had an IC (44.84%). The most common behavioral criterion was: having unprotected sex at some time in life with people who did not know their HIV status (298; 76.8%). Four HIV+ patients (1.03%) were diagnosed. All had an IC and were men who had sex with men. The level of acceptability in PC was high.
Conclusions: Offering HIV testing to patients with IC and behavioral criteria is feasible and effective in PC.

-Realizable y efectivo, pero la prevalencia fue 1%...

-Sobrecarga de la AP

-En ciertos ámbitos, resistencia de la persona para la realización del test, y del propio professional para solicitarlo…

Contenido

- Epidemiología de la presentación tardía en Europa y España
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Tabla 2. Recomendaciones sobre TAR de inicio en pacientes con infección por el VIH-1

Recomendaciones
Se recomienda la administración de TAR a todos los pacientes con infección por el VIH-1[1]. **(A-I)**.
El TAR debe iniciarse tan pronto como sea posible tras el diagnóstico[2]. **(A-II)**

Nota:

1. Se consideran como excepción los pacientes que mantienen CVP indetectable de form mantenida sin TAR (controladores de élite). En este caso no existe información que permita valor el efecto beneficioso del TAR, por lo que no se puede establecer una recomendación al respect
2. La disposición y la motivación del paciente es un factor crítico a la hora de tomar la decisión c empezarlo. Es importante hacer una valoración individualizada del momento de inicio del TAR de los FAR que deben formar parte del régimen inicial, sopesando las ventajas e inconveniente de cada una de las opciones.

Recommendations take into account the level of evidence, the degree of progression of HIV disease and the presence of, or high risk for, developing various types of (co-morbid) conditions.

ART is recommended in all adult persons with HIV, irrespective of CD4 counts(i)

i ART is recommended irrespective of the CD4 count. In certain situations (i.e lower CD4 count or pregnancy), there is a greater urgency to start ART immediately

- In persons with OIs, ART initiation may have to be deferred, see page 123, for ART initiation in the presence of specific OIs. For ART initia- s with TB, see page 20

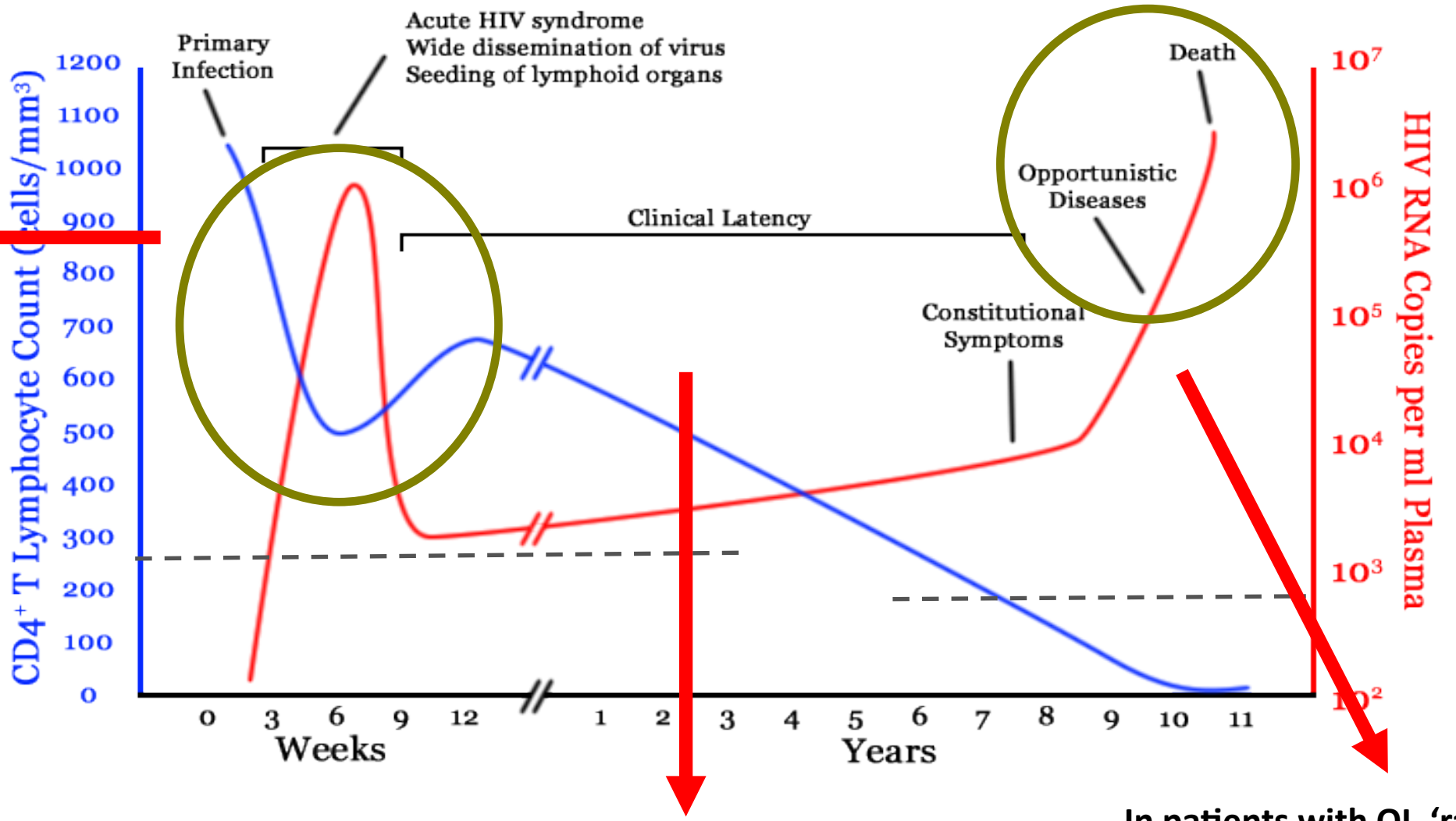
Box 1. Key Recommendations for When to Start Antiretroviral Therapy (ART)

- Initiation of ART is recommended as soon as possible after diagnosis, ideally within 7 days, including on the same day as diagnosis or at the first clinic visit if the patient is ready and there is no suspicion for a concurrent opportunistic infection (evidence rating: AIII)

WHO → within 1 week

GeSIDA, EACS, IAS-USA, WHO

The clinical dimension of rapid and immediate ART



Clinical urgency for immediate therapy

Rapid and Immediate therapy as an elective strategy

In patients with OI, 'rapid' may be undestood as <14 días (unless Crypto menigitis)

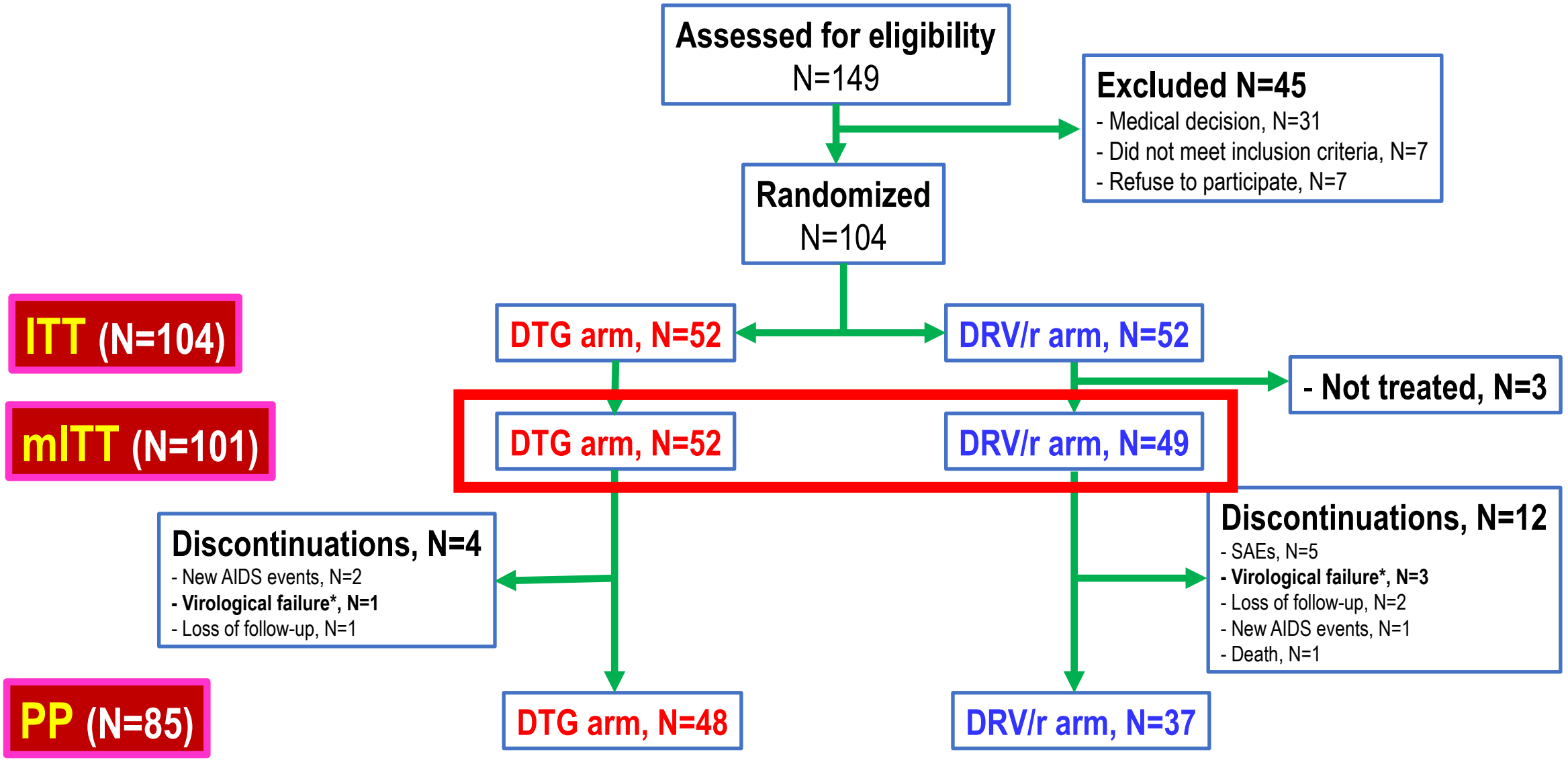
Modified from Pantaleo G et al. N Engl J Med 1993.

When to start ART in persons with Opportunistic Infections (OIs)

	Initiation of ART	Comments
General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection	
Tuberculosis	As soon as possible within two weeks of starting TB treatment, regardless of CD4 count	For details, see ART in TB/HIV Co-infection section, page 20
- TB meningitis	ART should be delayed for 4 weeks, but can be initiated within the first 2 weeks in persons with TB meningitis and CD4 < 50 (100) cells/μL	Corticosteroids are recommended as adjuvant treatment for TB meningitis
Cryptococcal meningitis	Defer initiation of ART for at least 4 weeks (WHO recommends a delay of 4-6 weeks and some specialists recommend a delay of 6-10 weeks in severe cryptococcal meningitis)	Corticosteroids are not recommended as adjuvant treatment

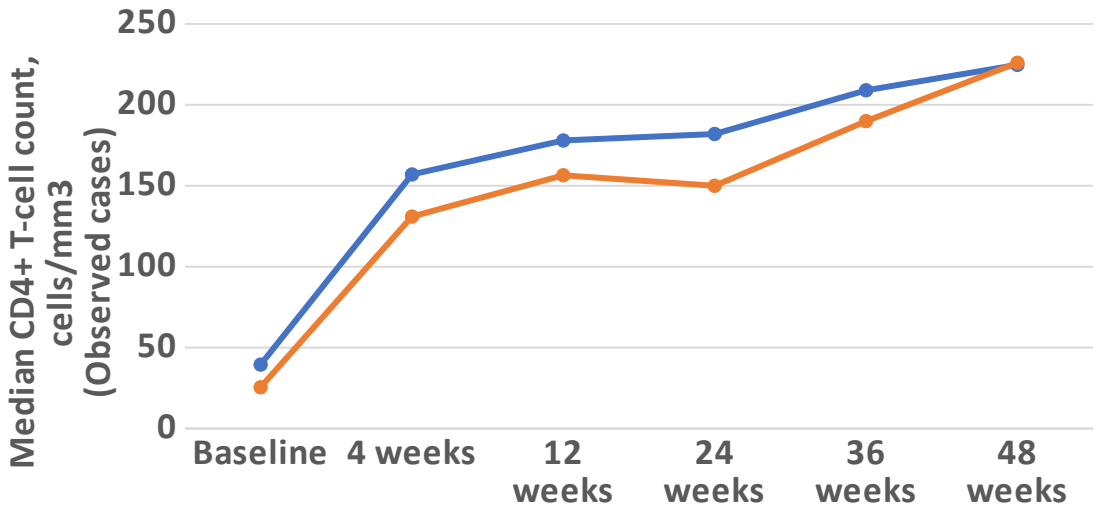
EACS Guidelines 11.1,October 2022

PI vs InSTI. RCT ADVANZ-4



ITT: Intention-to-treat; mITT: modified ITT; PP: Per protocol analysis; *Virological failure: Two consecutive plasma VL samples >200 copies/mL. The four samples could not be amplified for genotypic resistance studies.

Results (III): mITT (M=F) analysis



- **Median (IQR) increase in the CD4** count after 48 weeks by **mITT (M=F)** analysis was +172 (118; 255) and 157 (66; 277) cells/mm^3 in the **DTG** and **DRV/r** arms, respectively (p=0.430).
- **Plasma HIV-1 RNA VL suppression** (<50 copies/ml) was significatively faster in the **DTG** arm at 4 and 12 weeks. **At week 48**, the rate of suppressed patients by **mITT (M=F)** analysis was **77% vs. 63% (p=0.191**) for **DTG** and **DRV/r** arms, respectively.
- **Inflammation** (TNF-alpha, IL-6, hsCRP), **immune activation** (CD8+CD38+ T cells, CD8+CD38+DR+) and

- **Triple DTG-based ART was as effective as and had fewer discontinuations than triple DRV/r-based ART in very advanced ART-naive HIV-1-infected patients.**
- **Triple DTG-based ART was superior to the boosted-PI regimen in reducing the bacterial translocation.**

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Journal of Antimicrobial Chemotherapy

Mortality and immunovirological outcomes in patients with advanced HIV disease on their first antiretroviral treatment: differential impact of antiretroviral regimens

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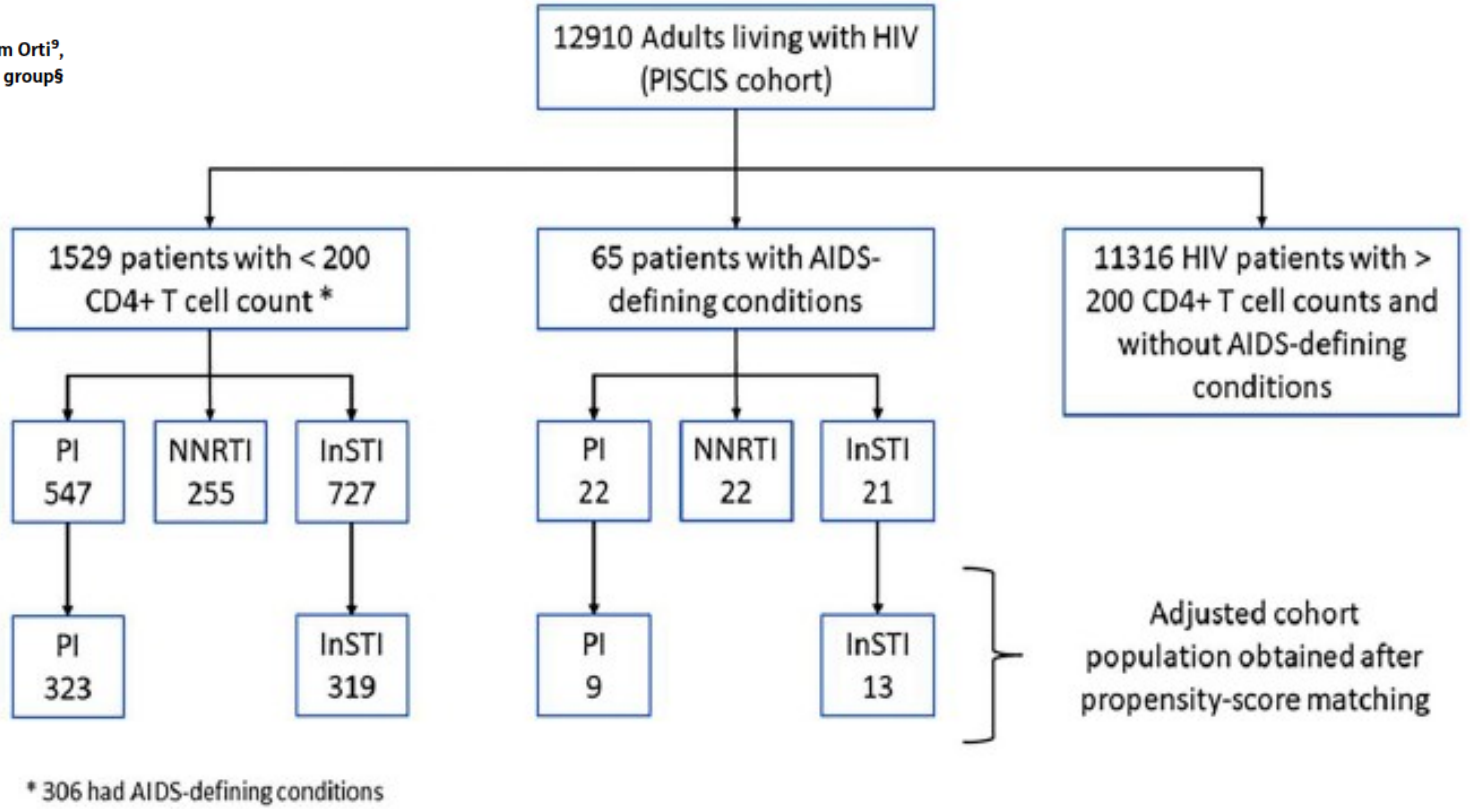
Objectives: To assess the clinical and immunovirological outcomes among naive patients with advanced HIV presentation starting an antiretroviral regimen in real-life settings.

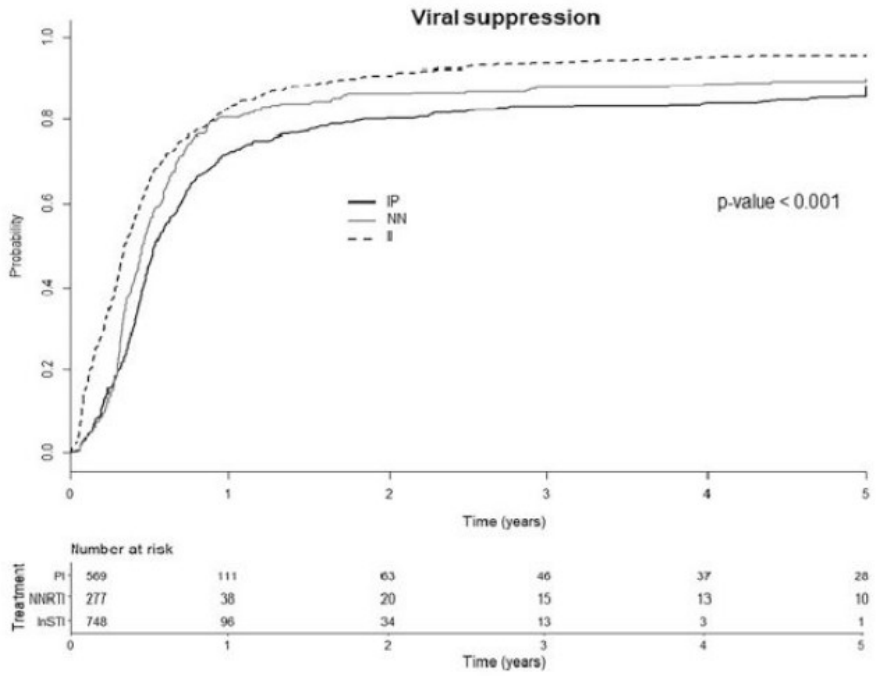
Methods: This was a multicentre, prospective cohort study. We included all treatment-naive adults with advanced HIV disease (CD4+ T cell count < 200 cells/mm^3 or presence of an AIDS-defining illness) who started therapy between 2010 and 2020. The main outcomes were mortality, virological effectiveness (percentage of patients with viral load of ≤50 copies/mL) and immune restoration (percentage of patients with CD4+ T cell count above 350 cells/mm^3). Competing risk analysis and Cox proportional models were performed. A propensity score-matching procedure was applied to assess the impact of the antiretroviral regimen.

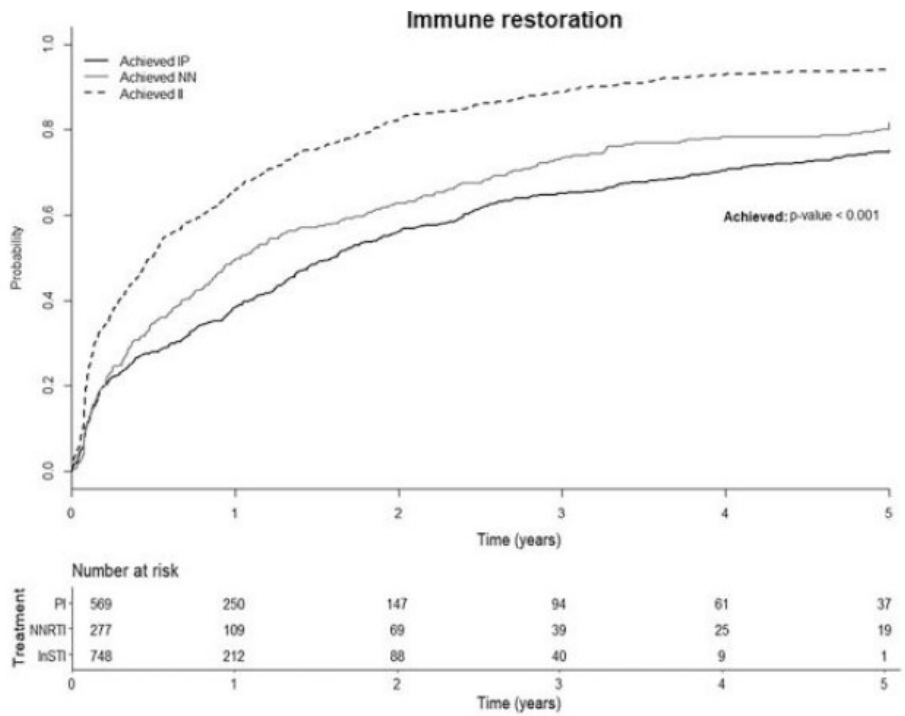
Results: We included 1594 patients with advanced HIV disease [median CD4+T cell count of 81 cells/mm^3 and 371 (23.3%) with AIDS-defining illness] and with a median follow-up of 4.44 years. The most common ART used was an integrase strand transfer inhibitor (InSTI) regimen (46.9%), followed by PI (35.7%) and NNRTI (17.4%), with adjusted mortality rates at 3 years of 3.1% (95% CI 1.8%–4.3%), 4.7% (95% CI 2.2%–7.1%) and 7.6% (95% CI 5.4%–9.7%) (P = 0.001), respectively. Factors associated with increased mortality included older age and history of injection drug use, whilst treatment with an InSTI regimen was a protective factor [HR 0.5 (95% CI 0.3–0.9)]. A sensitivity analysis with propensity score procedure confirms these results. Patients who started an InSTI achieved viral suppression and CD4+ T cell count above 350 cells/mm^3 significantly earlier.

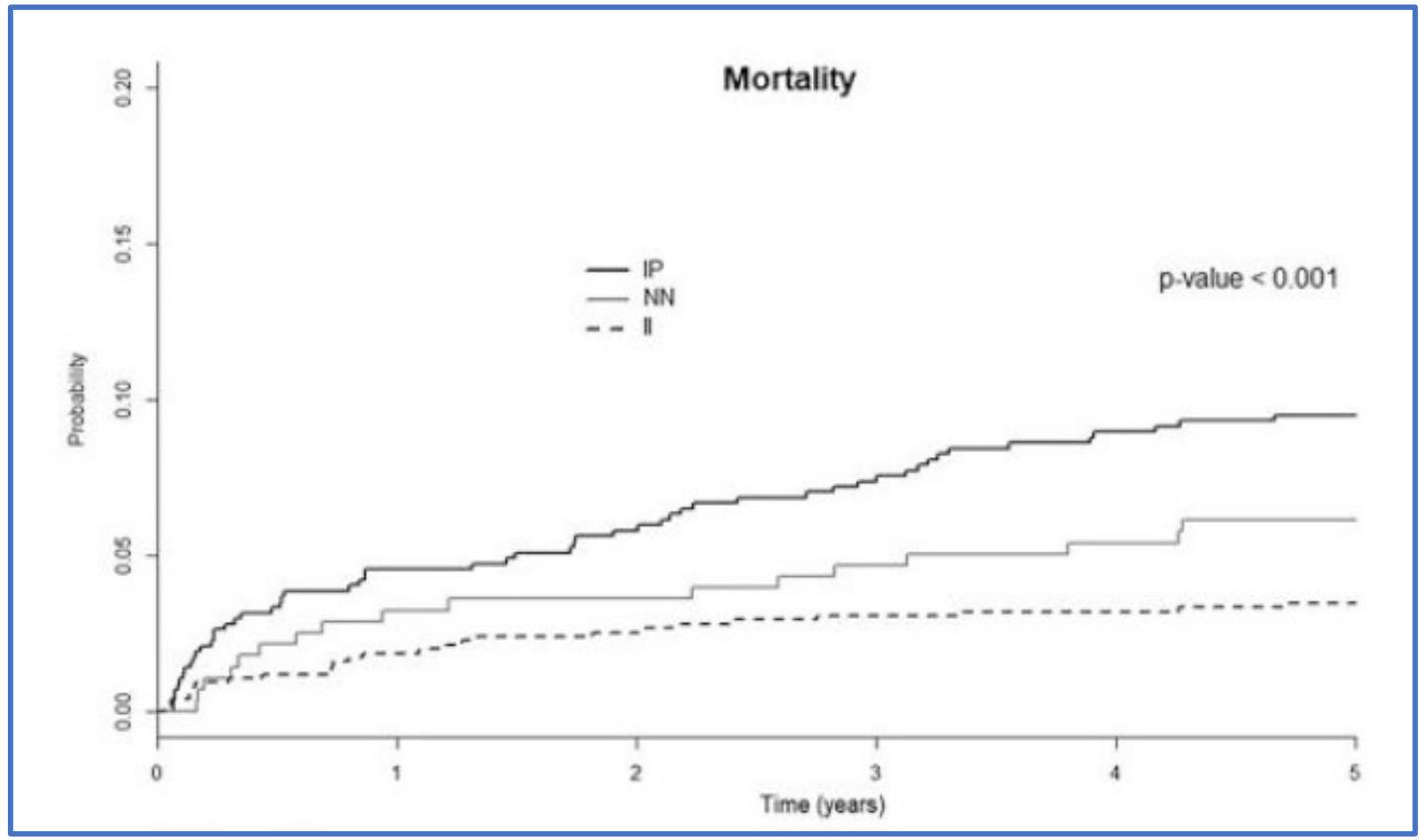
Conclusions: In this large real-life prospective cohort study, a significant lower mortality, earlier viral suppression and earlier immune reconstitution were observed among patients with advanced HIV disease treated with InSTIs.



Burgos J et al. *J Antimicrob Chemother* 2023







Burgos J et al. *J Antimicrob Chemother* 2023

Documento de consenso de GeSIDA/ División de Control de VIH, ITS, Hepatitis virales y Tuberculosis del Ministerio de Sanidad respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana

(Actualización enero 2023)

Panel de expertos de GeSIDA y de la División de Control de VIH, ITS, Hepatitis virales y Tuberculosis del Ministerio de Sanidad

GeSIDA GRUPO DE ESTUDIO DEL SIDA-SEIMC

GOBIERNO DE ESPAÑA MINISTERIO DE SANIDAD

Tabla 3. Combinaciones de TAR de inicio recomendadas†

3er Fármaco	Pauta†	Comentarios
Preferentes. *Pautas aplicables a la mayoría de los pacientes, que en ensayos clínicos aleatorizados han mostrado una eficacia no inferior o superior a otras pautas también consideradas actualmente como preferentes y presentan ventajas adicionales por número de comprimidos, barrera de resistencia, tolerancia, toxicidad o un bajo riesgo de interacciones farmacológicas*		
INI	BIC/FTC/TAF	
	DTG/ABC/3TC	- ABC está contraindicado en pacientes con HLA-B*5701 positivo - No utilizar en pacientes con hepatitis B crónica
	DTG+FTC/TAF*	
	DTG/3TC	- No recomendado en pacientes concifra basal de CD4+ <200 células/µL. - No utilizar en pacientes con hepatitis B crónica - No recomendada tras fracaso de PrEP sin disponer del resultado de estudio de resistencias.

Regimen	Main requirements
Recommended regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
TAF/FTC or TDF/XTC + RAL qd or bid	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure

Box 2. Recommended Initial Antiretroviral Therapy (ART) Regimens

Recommended for Most People With HIV

- The following are recommended (in alphabetical order) for most people with HIV:
  - BIC/TAF/FTC (evidence rating: AIa)
  - Dolutegravir plus TXF/XTC (evidence rating: AIa)
  - DTG/3TC (only if HIV RNA <500 000 copies/mL and HBV coinfection not present). This regimen should not be used for rapid initiation when genotype, HIV RNA, and HBV serology results are not yet available (evidence rating: AIa)

GeSIDA, EACS, IAS-USA

Outcomes of Late Presentation

Epigenetic ageing accelerates before antiretroviral therapy and decelerates after viral suppression in people with HIV in Switzerland: a longitudinal study over 17 years

Lancet Healthy Longev 2023; 4: e211–18

Isabella C Schoepf, Andrés Esteban-Cantos*, Christian W Thorball*, Berta Rodés, Peter Reiss, Javier Rodríguez-Centeno, Carlotta Riebensahm, Dominique L Braun, Catia Marzolini, Marco Seneghini, Enos Bernasconi, Matthias Cavassini, Hélène Buvelot, Maria Christine Thurnheer, Roger D Kouyos, Jacques Fellay, Huldrych F Günthard, José R Arribas*, Bruno Ledergerber*, Philip E Tarr*, and the Swiss HIV Cohort Study*

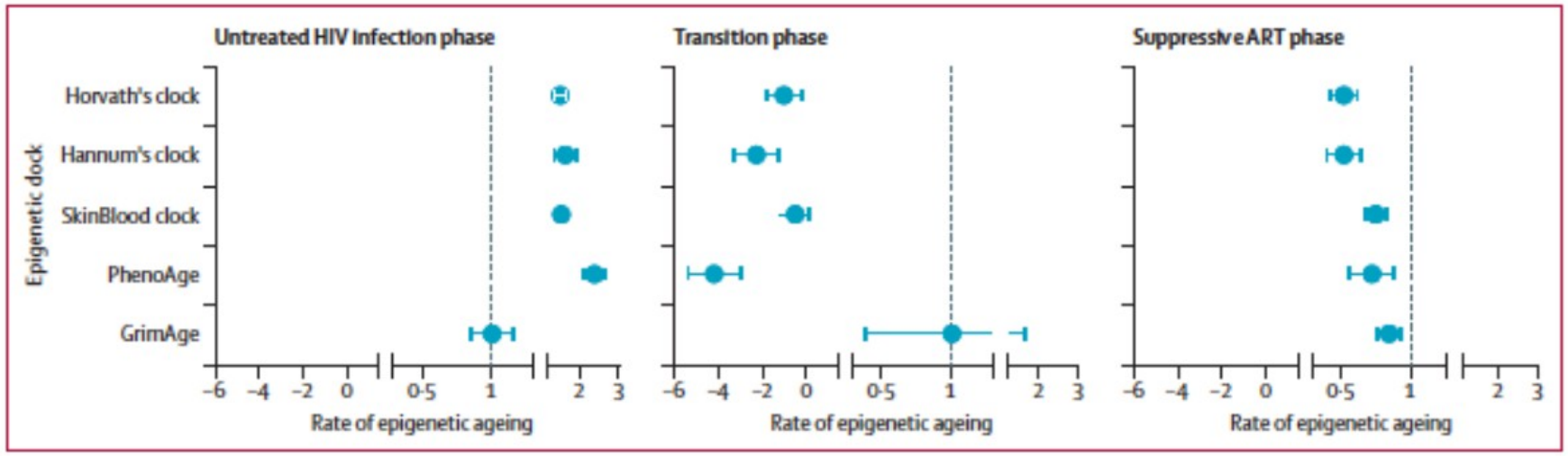


Figure 4: **Rates of epigenetic ageing for different epigenetic clocks**
Data are mean, error bars indicate 95% CI. Rate of epigenetic ageing (R) was calculated as reported by Sehl and colleagues.[18] The vertical dashed line (R=1) indicates that 1 year of epigenetic age increases per 1 year chronologically, with R greater than 1 suggesting faster or accelerated ageing, and R less than 1 suggesting slower or decelerated ageing (see appendix p 5 with x-axis adjusted to the respective scale).

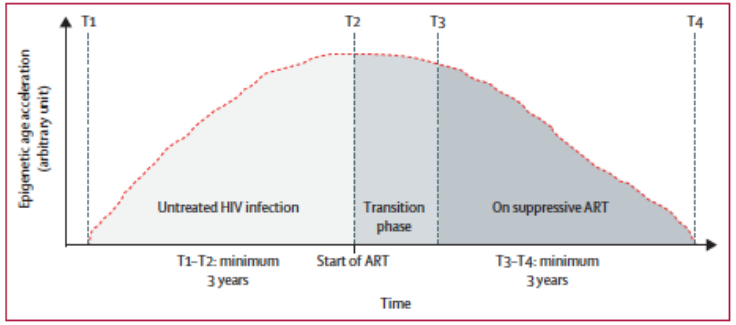


Figure 1: **Study hypothesis and timepoints T1–T4 for measurement of DNA methylation**
Median date was Aug 19, 1997, at T1 (IQR Dec 6, 1994, to May 1, 1999), March 21, 2006, at T2 (March 16, 2004, to Feb 12, 2008), June 1, 2007, at T3 (March 17, 2006, to Jan 26, 2010), and April 11, 2017, at T4 (Feb 14, 2017, to June 27, 2017). In each participant, we measured epigenetic age acceleration in the first available sample before ART start (T1) and in the last available sample before ART start (T2), in the first available sample after attaining viral suppression (T3), and in the last available sample during suppressive ART (T4). The light grey shaded area indicates the transition phase from ART start until viral suppression was attained (T2 to T3). The dark grey area indicates the suppressive ART phase (T3 to T4). ART=antiretroviral therapy.

	T1–T2	T2–T3	T3–T4
CD4 cell count, cells per μL	517·5 (367·0 to 678·5)	294·0 (224·0 to 362·5)	428·5 (320·5 to 554·0)
CD4 annual change, cells per μL	−27·0 (−51·6 to −13·1)	76·6 (26·7 to 145·7)	26·6 (9·8 to 38·0)
CD8 cell count, cells per μL	762·0 (590·5 to 951·0)	941·5 (675·0 to 1232·5)	775·5 (597·0 to 1008·5)
CD8 annual change, cells per μL	21·5 (−14·6 to 53·1)	−73 (−244·4 to 25·2)	−7·4 (−29·8 to 10·1)
CD4:CD8 ratio	0·7 (0·4 to 1·0)	0·3 (0·2 to 0·4)	0·5 (0·4 to 0·8)
CD4:CD8 ratio annual change, cells per μL	−0·04 (−0·09 to −0·03)	0·15 (0·06 to 0·23)	0·05 (0·02 to 0·06)
HIV RNA, log copies per mL	4·92 (4·57 to 5·31)	4·86 (4·34 to 5·24)	1·65 (1·53 to 1·78)

Data are median (IQR).

Table 1: **Immunovirological and HIV-related status in each phase**

Cuanto mayor el tiempo transcurrido sin TAR, mayor el desaceleramiento necesario en el envejecimiento celular para volver al nivel basal

Outcomes of Late Presentation

Life expectancy after 2015 of adults with HIV on long-term antiretroviral therapy in Europe and North America: a collaborative analysis of cohort studies

Lancet HIV 2023

Adam Trickey, Caroline A Sabin, Greer Burkholder, Heidi Crane, Antonella d'Arminio Monforte, Matthias Egger, M John Gill, Sophie Grabar, Jodie L Guest, Inma Jarrin, Fiona C Lampe, Niels Obel, Juliana M Reyes, Christoph Stephan, Timothy R Sterling, Ramon Teira, Giota Touloumi, Jan-Christian Wasmuth, Ferdinand Wit, Linda Wittkop, Robert Zangerle, Michael J Silverberg, Amy Justice, Jonathan A C Sterne

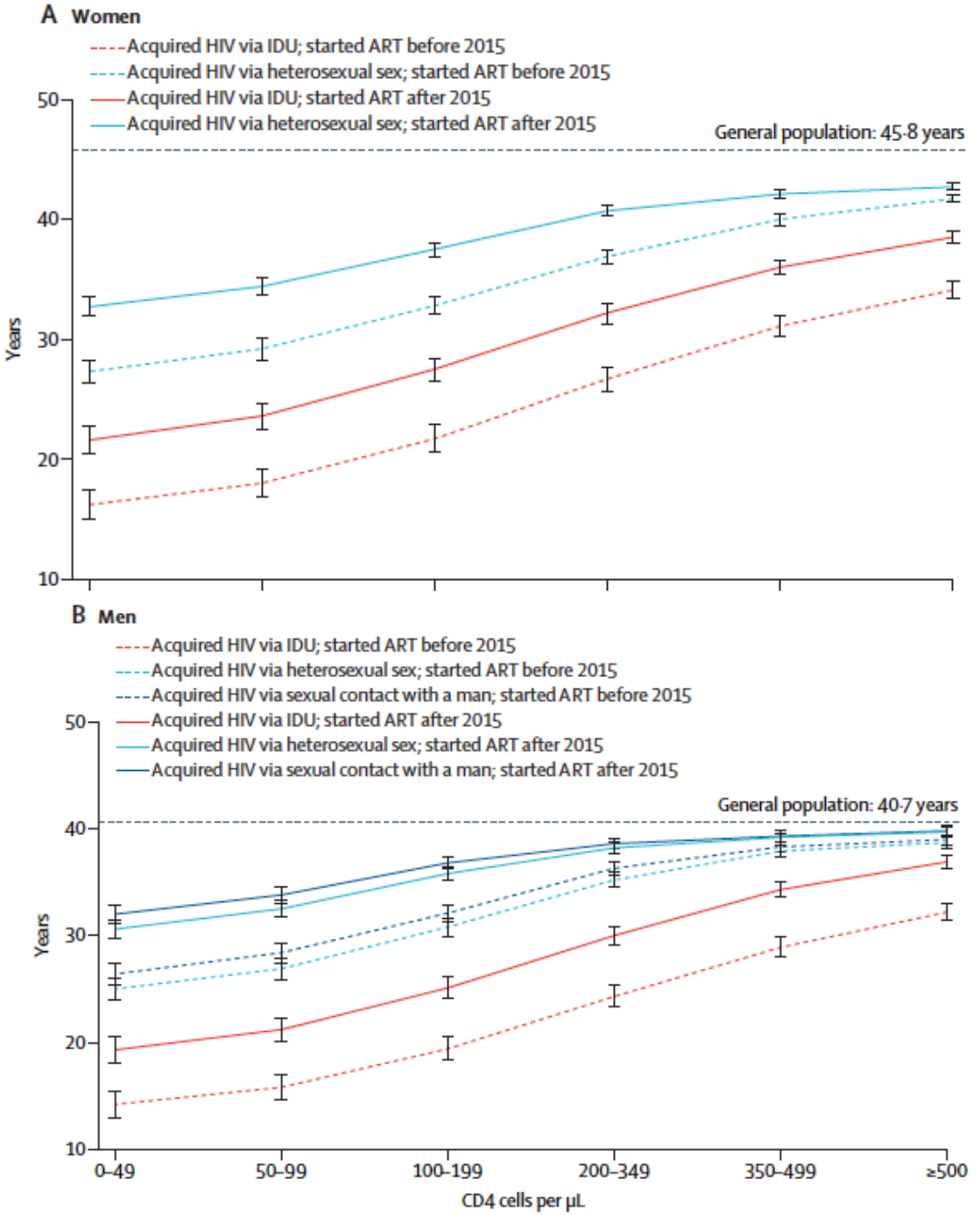
Summary

Background The life expectancy of people with HIV taking antiretroviral therapy (ART) has increased substantially over the past 25 years. Most previous studies of life expectancy were based on data from the first few years after starting ART, when mortality is highest. However, many people with HIV have been successfully treated with ART for many years, and up-to-date prognosis data are needed. We aimed to estimate life expectancy in adults with HIV on ART for at least 1 year in Europe and North America from 2015 onwards.

Methods We used data for people with HIV taking ART from the Antiretroviral Therapy Cohort Collaboration and the UK Collaborative HIV Cohort Study. Included participants started ART between 1996 and 2014 and had been on ART for at least 1 year by 2015, or started ART between 2015 and 2019 and survived for at least 1 year; all participants were aged at least 16 years at ART initiation. We used Poisson models to estimate the associations between mortality and demographic and clinical characteristics, including CD4 cell count at the start of follow-up. We also estimated the remaining years of life left for people with HIV aged 40 years who were taking ART, and stratified these estimates by variables associated with mortality. These estimates were compared with estimates for years of life remaining in a corresponding multi-country general population.

Findings Among 206 891 people with HIV included, 5780 deaths were recorded since 2015. We estimated that women with HIV at age 40 years had 35·8 years (95% CI 35·2–36·4) of life left if they started ART before 2015, and 39·0 years (38·5–39·5) left if they started ART after 2015. For men with HIV, the corresponding estimates were 34·5 years (33·8–35·2) and 37·0 (36·5–37·6). Women with CD4 counts of fewer than 49 cells per µL at the start of follow-up had an estimated 19·4 years (18·2–20·5) of life left at age 40 years if they started ART before 2015 and 24·9 years (23·9–25·9) left if they started ART after 2015. The corresponding estimates for men were 18·2 years (17·1–19·4) and 23·7 years (22·7–24·8). Women with CD4 counts of at least 500 cells per µL at the start of follow-up had an estimated 40·2 years (39·7–40·6) of life left at age 40 years if they started ART before 2015 and 42·0 years (41·7–42·3) left if they started ART after 2015. The corresponding estimates for men were 38·0 years (37·5–38·5) and 39·2 years (38·7–39·7).

Interpretation For people with HIV on ART and with high CD4 cell counts who survived to 2015 or started ART after 2015, life expectancy was only a few years lower than that in the general population, irrespective of when ART was started. However, for people with low CD4 counts at the start of follow-up, life-expectancy estimates were substantially lower, emphasising the continuing importance of early diagnosis and sustained treatment of HIV.



Contenido

- Epidemiología de la presentación tardía en Europa y España
- Oportunidades de mejora
- Manejo y pronóstico
- **Conclusiones y mensajes finales**

Conclusiones y mensajes finales

- Aunque los casos de SIDA continúan disminuyendo, la presentación tardía (<350 CD4) sigue siendo un problema relevante a nivel nacional y europeo
- Las consecuencias son clínicas a nivel individual, empeorando significativamente el pronóstico y disminuyendo la esperanza de vida, y epidemiológicas, en términos de transmisión
- Existen intervenciones que buscan disminuir su prevalencia, sobre todo actuando en los servicios de emergencias y en la AP
- El TAR debe ser iniciado inmediatamente, con las pautas recomendadas para cualquier persona con VIH, aunque las recomendaciones varían entre las guías clínicas en casos con menos de 200 CD4
- En personas con IO debe empezarse siempre dentro de los 14 días del diagnóstico, lo antes posible, salvo que se trate de una criptococosis meníngea
- **Es, lamentablemente, UN PROBLEMA NO RESUELTO más frecuente en personas heterosexuales, aunque más del 40% de los HSH son también**

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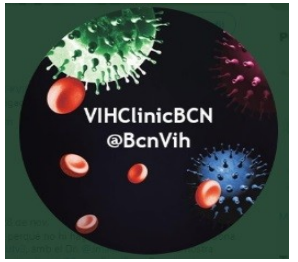

Muchas gracias por su atención