

# NOVEDADES DEL TRATAMIENTO ARV EN EL ADOLESCENTE CON INFECCIÓN VIH. SIMPLIFICACIÓN.

Lola Falcón Neyra. Hospital Virgen del Rocío

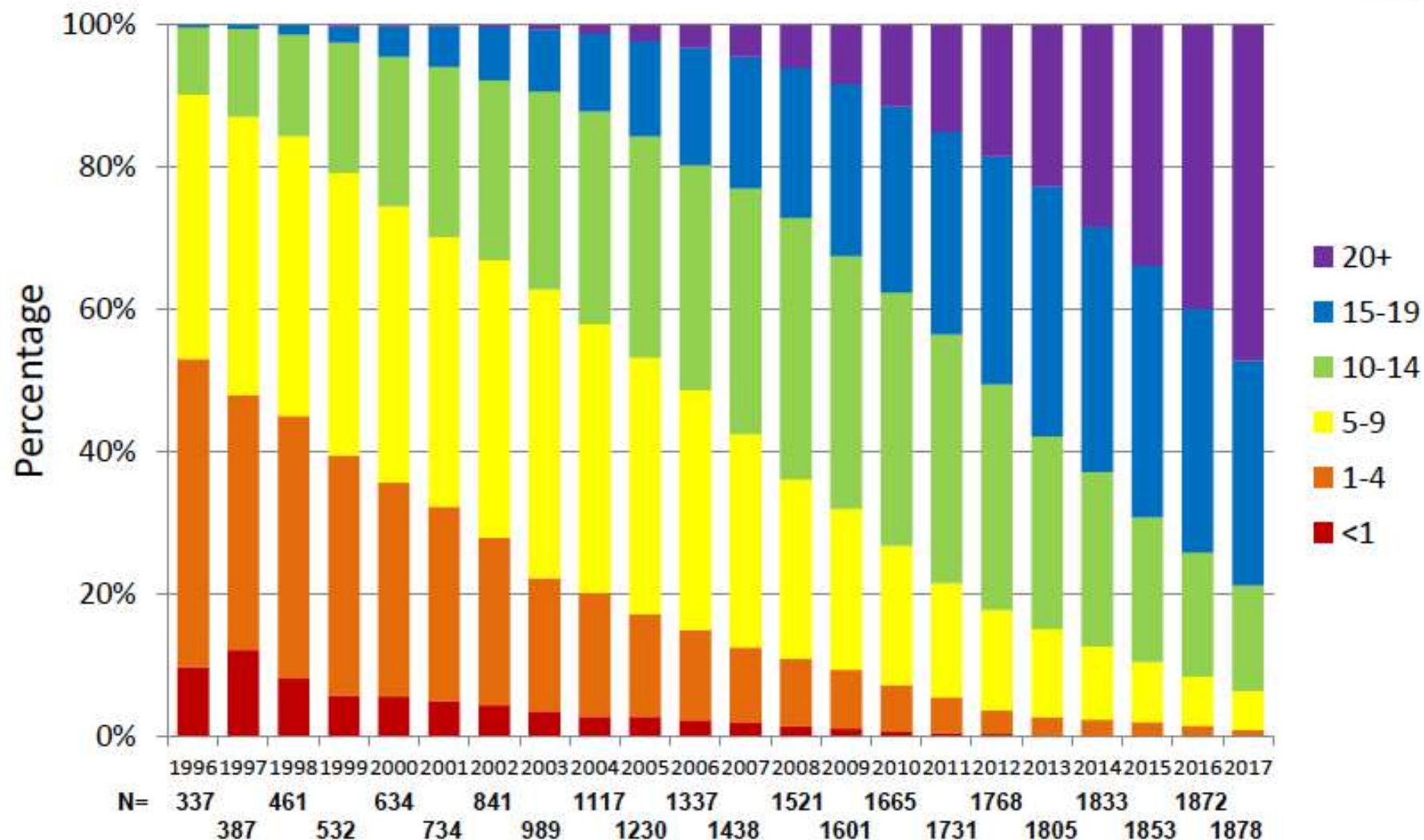


# NOVEDADES DEL TRATAMIENTO ARV EN EL ADOLESCENTE CON INFECCIÓN VIH. SIMPLIFICACIÓN.

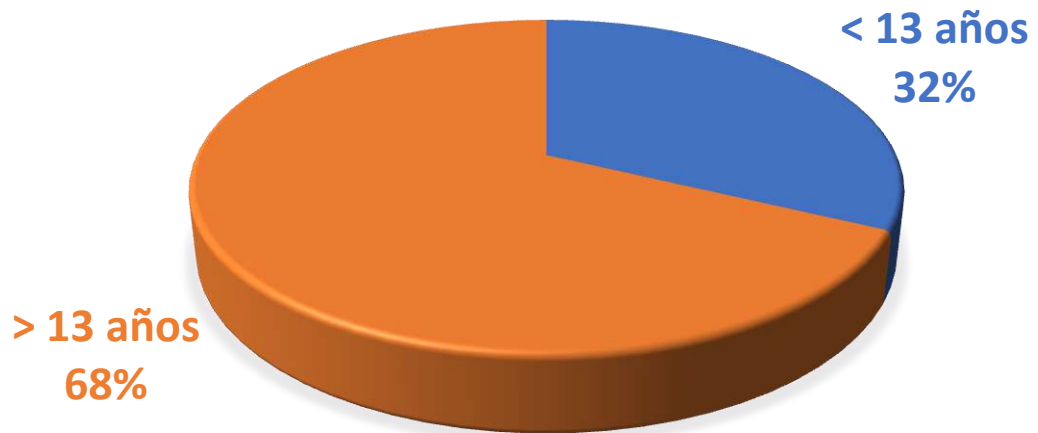
Lola Falcón Neyra. Hospital Virgen del Rocío



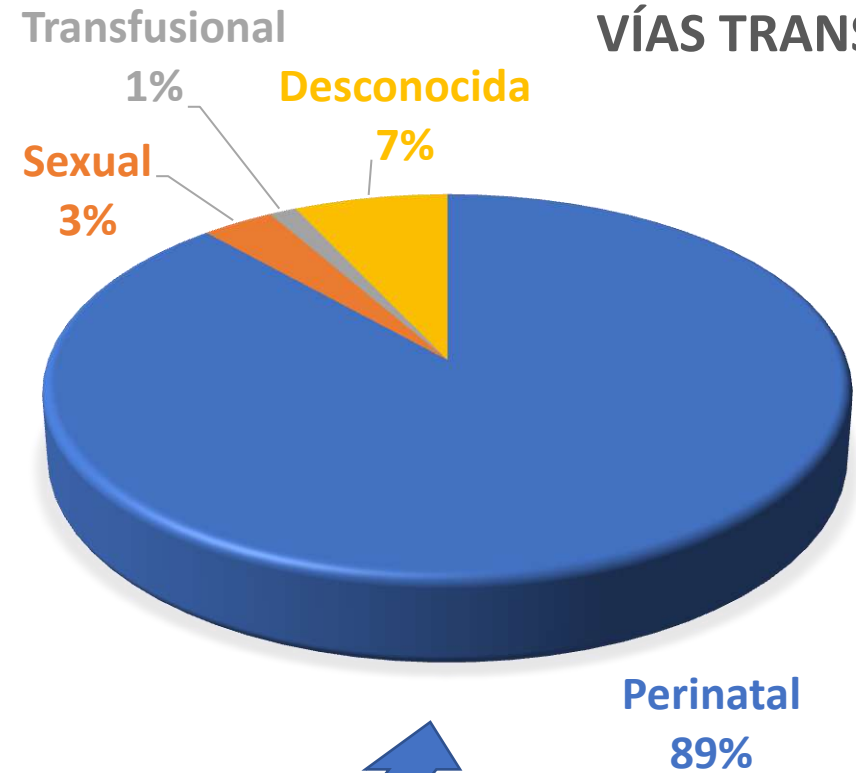
# Age of UK/Irish cohort of patients with HIV acquired in childhood, 1996-2017



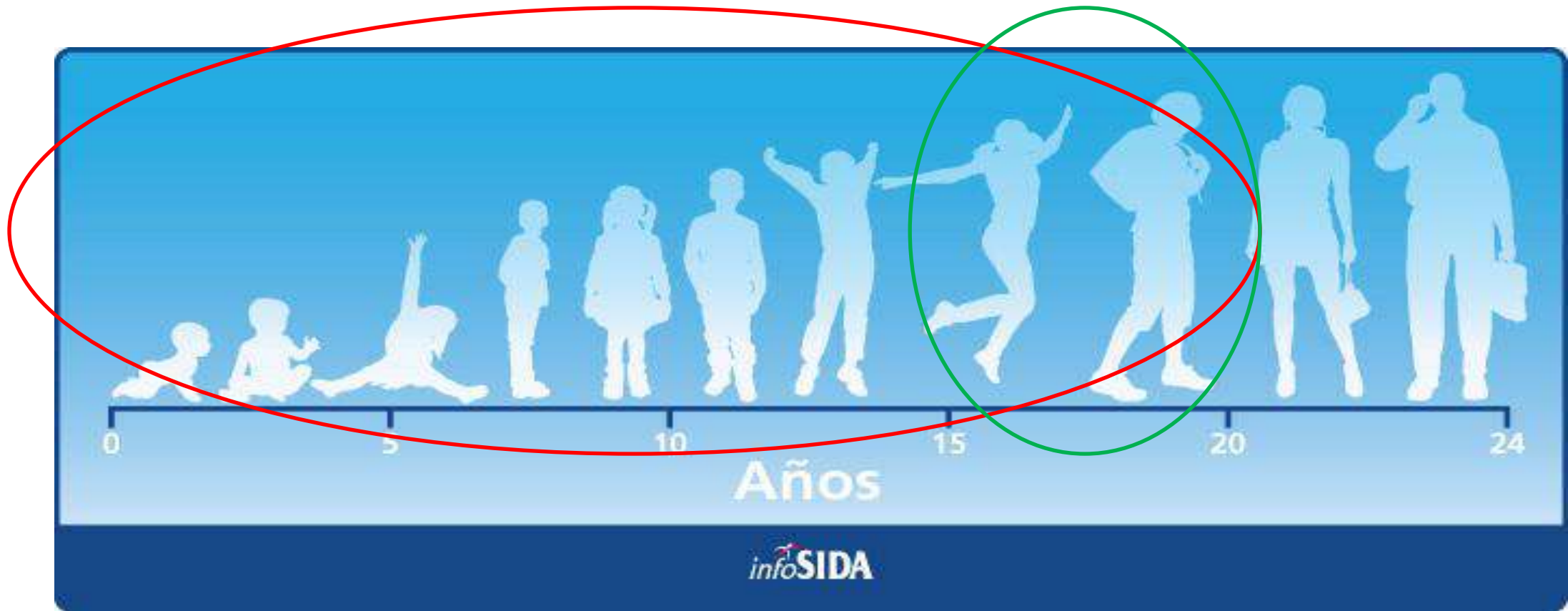
### GRUPOS DE EDAD



### VÍAS TRANSMISIÓN



# Adolescentes con infección VIH....





# Transmisión perinatal

Numerosos tratamientos ARVc

Acúmulo de resistencias

Acúmulo toxicidad de ARV

Estigma

Familias desestructuradas

Fracaso escolar



*Malignancy and all-cause mortality: Incidence in teenage young adults living with perinatally acquired HIV.*

Chhabra S et al. 22nd International AIDS Conference, Amsterdam, abstract THAB0104, 2018



- 290 adolescentes y jóvenes (10-24 años) entre 2004 – 2017
- **Mortalidad global 9.4 veces superior** que la población general (IRR 9.4, 95% CI 3.4-20.4,  $p < 0.0001$ )
- **Neoplasias 12 veces superior** a la población general (95% CI 5-25  $p < 0.0001$ )
- **Linfomas 44 veces superior** a la población general (95% CI 16- 97  $p < 0.0001$ )

# High Incidence of Psychosis In a Cohort of Adults With Perinately Acquired HIV Infection: a Case Series

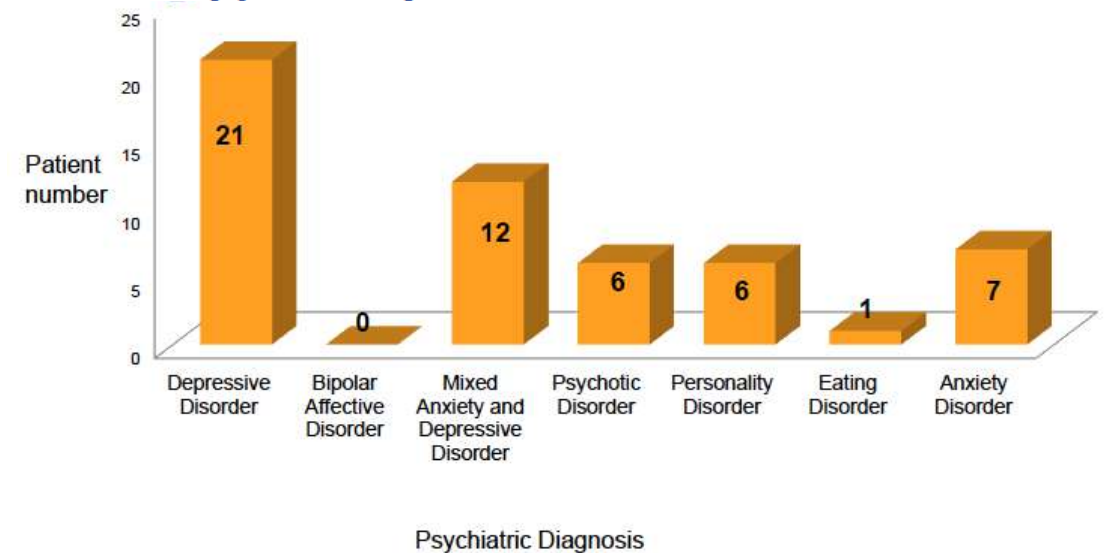
Imperial College Healthcare NHS Trust

T Pasvol. BHIVA 2018

- 161 jóvenes y adolescentes (14-26 años)
- 7.5% episodios psicóticos
- 33% historia familiar
- 25% dificultades severas del aprendizaje
- 33% adicción a drogas/alcohol



## Mental health diagnoses in HIV infected young people: a HIV in Young People Network audit



Dwyer E. 19th Annual Conference of the British HIV Association (Manchester 2013)



# Conductas de riesgo en pacientes con patologías crónicas

• Tabaco	1.32 (1.13, 1.54)
• Drogas ilegales	1.49 (1.15, 1.92)
• Inicio precoz de relaciones sexuales	1.33 (1.03, 1.72)
• Desórdenes alimentarios	1.44 (1.26, 1.74)
• Conductas antisociales	1.48 (1.26, 1.74)
• Intento de suicidio	2.24 (1.55, 3.24)



*JC Suris et al, 2007 J Beagent CHIVA 2010*

# Transmisión VIH comportamental

Transmisión sexual

Desconocimiento de su estado de infección

Estadios iniciales:

Intervención precoz para aumentar adherencia

Alta carga viral (resistencias)

Acúmulo resistencias (parejas mayores)





## HIV/AIDS

### HIV/AIDS

#### HIV Basics

#### HIV by Group

–

#### Gay and Bisexual Men

+

#### Gender

+

#### Race/Ethnicity

+

#### Age

–

#### Youth

[HIV/AIDS](#) > [HIV by Group](#) > [Age](#)

### HIV Among Youth



In 2016, youth aged 13 to 24<sup>a</sup> made up 21% of all new HIV diagnoses in the United States. Most (81%) of those new diagnoses occurred among young gay and bisexual men. Young black/African American<sup>b</sup> and Hispanic/Latino<sup>c</sup> gay and bisexual men were especially affected.

Having a very low level of virus in the blood and reduces the risk of transmitting HIV. The youth group to be linked to care in a timely manner.



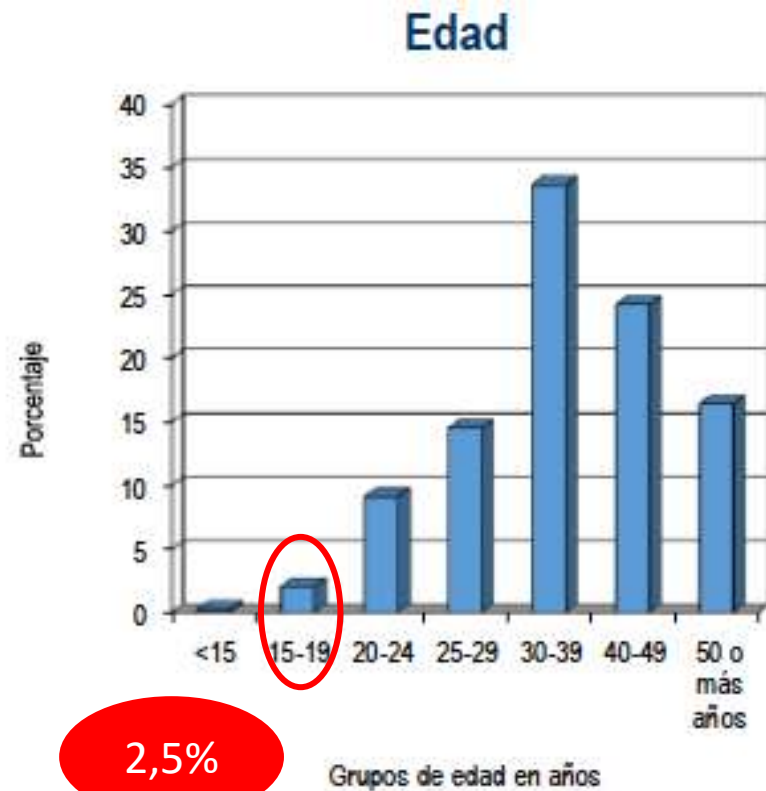
## Maternal, newborn, child and adolescent health

### HIV and youth

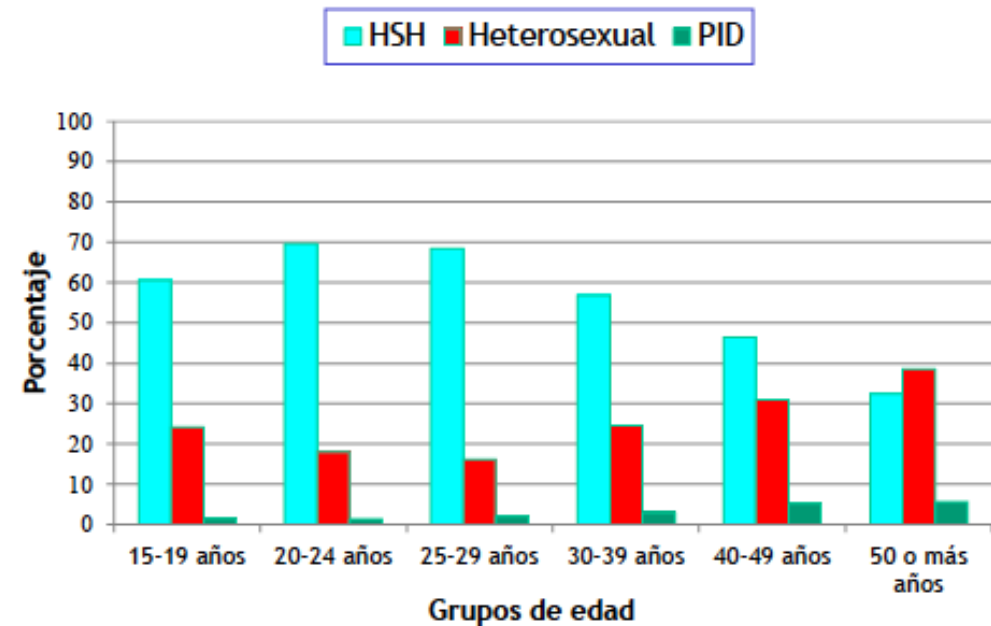
Currently, over 30% of all new HIV infections globally are estimated to occur among youth ages 15 to 25 years. Also, increasingly, children infected at birth grow into adolescents who have to deal with their HIV positive status. Combining the two, there are 5 million youth living with HIV.

# VIGILANCIA EPIDEMIOLÓGICA DEL VIH y SIDA EN ESPAÑA 2016

Nuevos diagnósticos de VIH.



Nuevos diagnósticos de VIH. Edad y modo de transmisión.  
España, año 2016. Datos no corregidos por retraso de notificación.

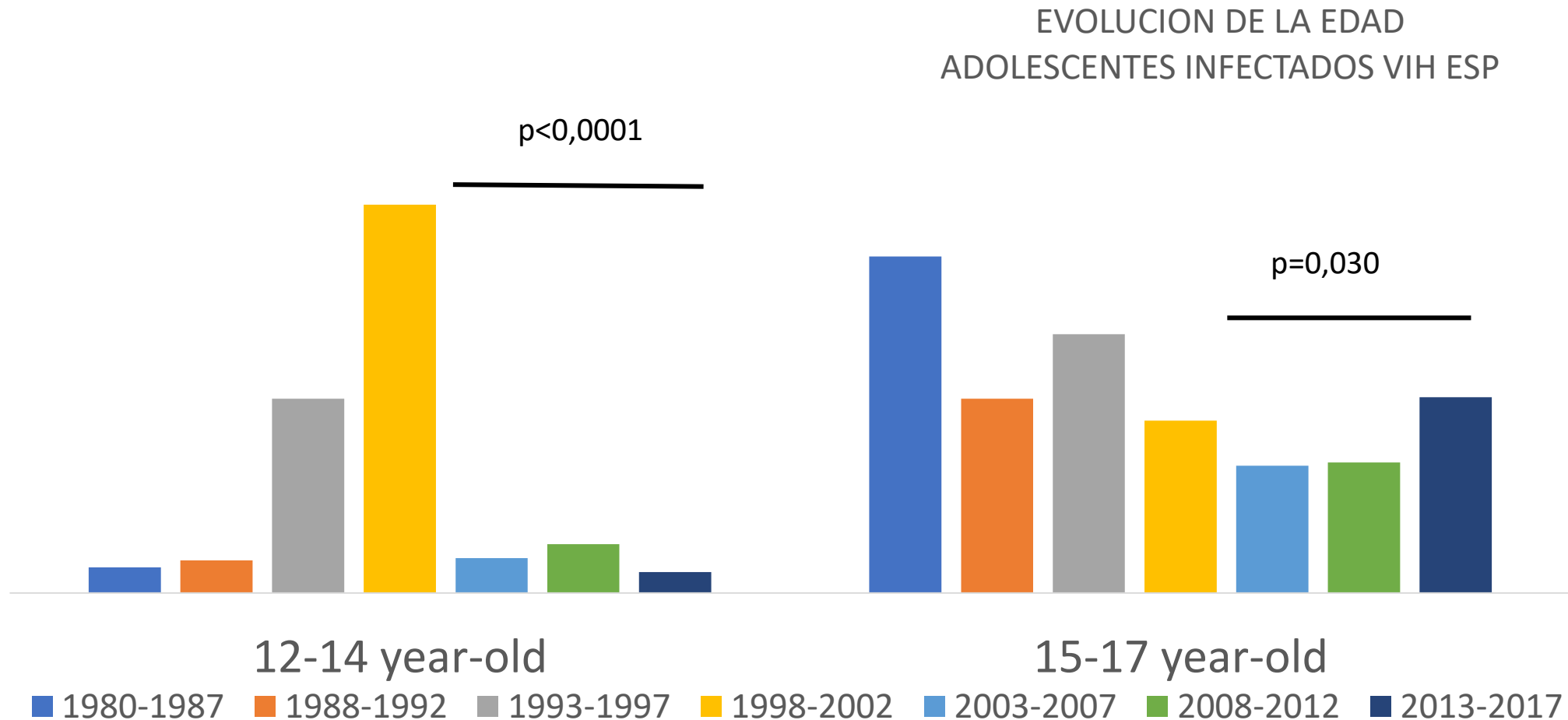


DIRECCIÓN GENERAL DE SALUD PÚBLICA, CALIDAD E INNOVACIÓN

SISTEMAS AUTONÓMICOS DE VIGILANCIA EPIDEMIOLÓGICA  
CENTRO NACIONAL DE EPIDEMIOLOGÍA

# NUEVOS DIAGNOSTICOS por VIH en ADOLESCENTES en España

Estudio descriptivo de los nuevos diagnósticos por VIH en adolescentes (**12-20 años**)



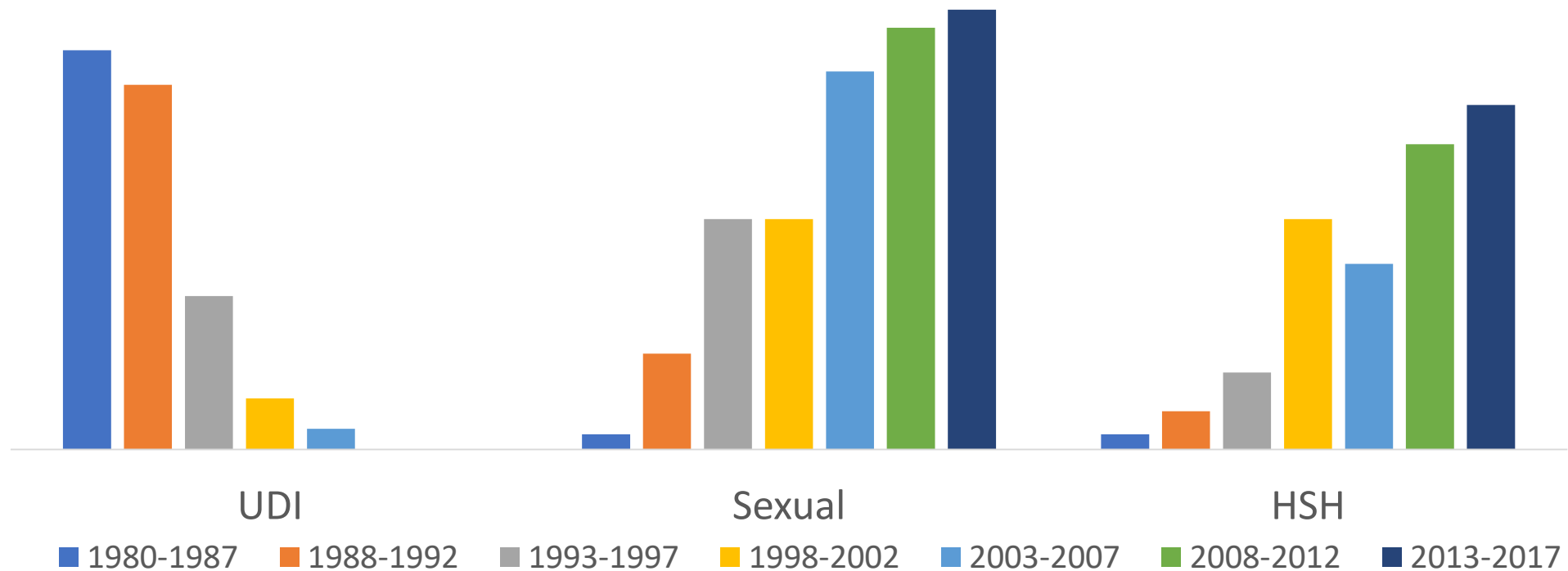
**Dra. Cristina Epalza.** Estudio colaborativo de **CoRISpe y CoRIS** (datos no publicados).



# NUEVOS DIAGNOSTICOS por VIH en ADOLESCENTES en España

Infección comportamental 92,2%. Sexual 72%.

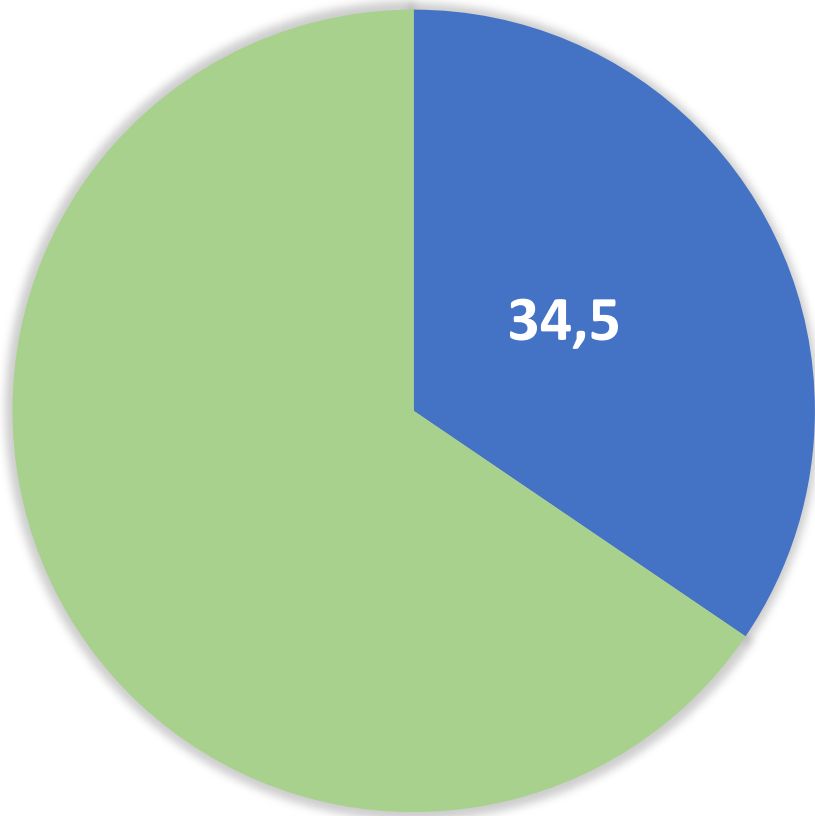
## EVOLUCION de la VIA de INFECCIÓN



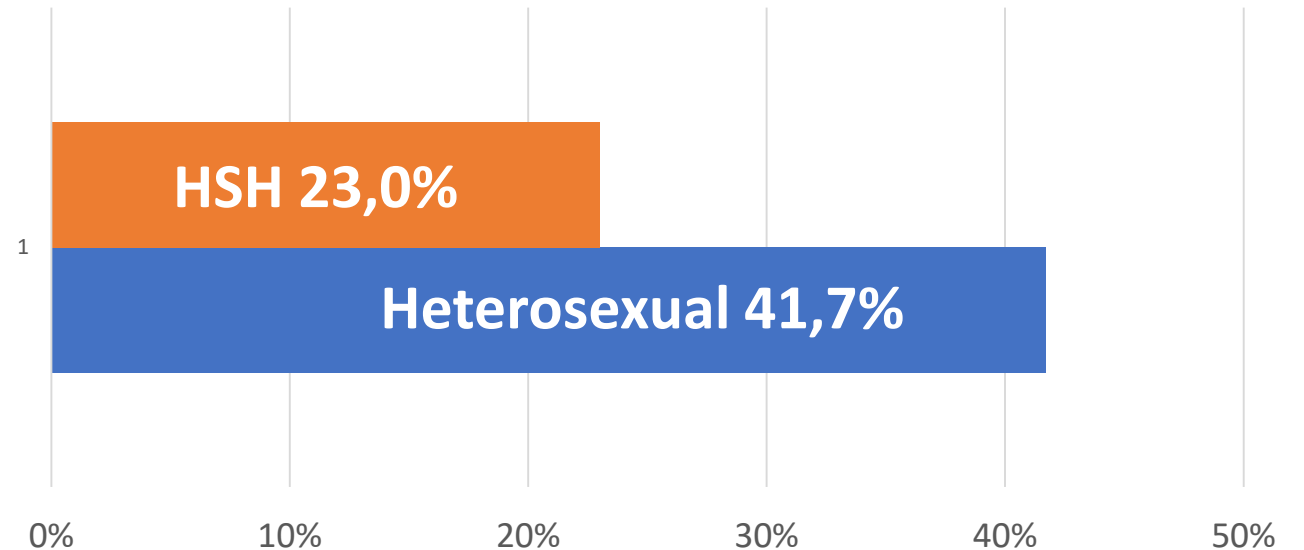
**Dra. Cristina Epalza.** Estudio colaborativo de **CoRISpe y CoRIS** (datos no publicados).

# NUEVOS DIAGNOSTICOS por VIH en ADOLESCENTES en España

Diagnóstico tardío=  $CD4 < 350/mm^3$  (si posible confirmado) o SIDA al diagnóstico



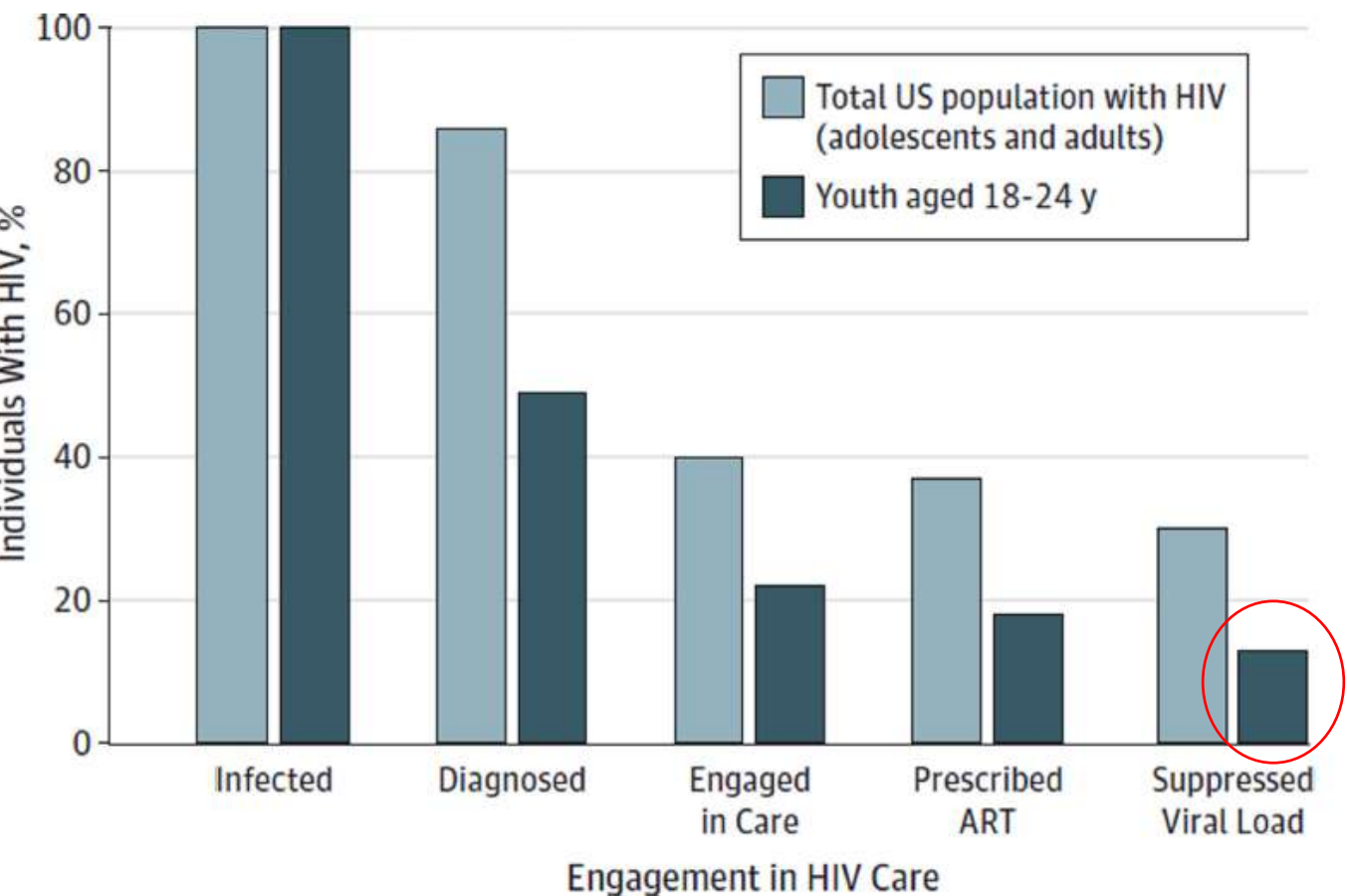
DIAGNÓSTICO TARDÍO SEGÚN VÍA INFECCIÓN



**Dra. Cristina Epalza.** Estudio colaborativo de **CoRISpe y CoRIS** (datos no publicados).

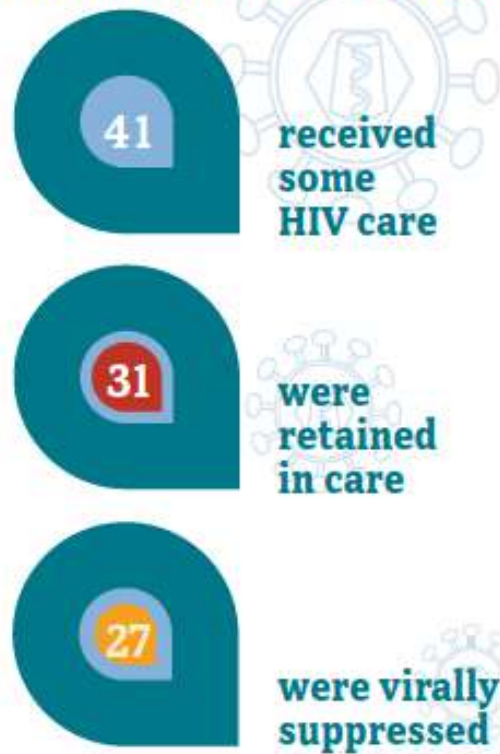
# Time to Improve the Global Human Immunodeficiency Virus/ AIDS Care Continuum for Adolescents:

A Generation at Stake Wood et al. JAMA Pediatr



6-13%

FOR EVERY 100 YOUNG PEOPLE LIVING WITH HIV IN 2014:



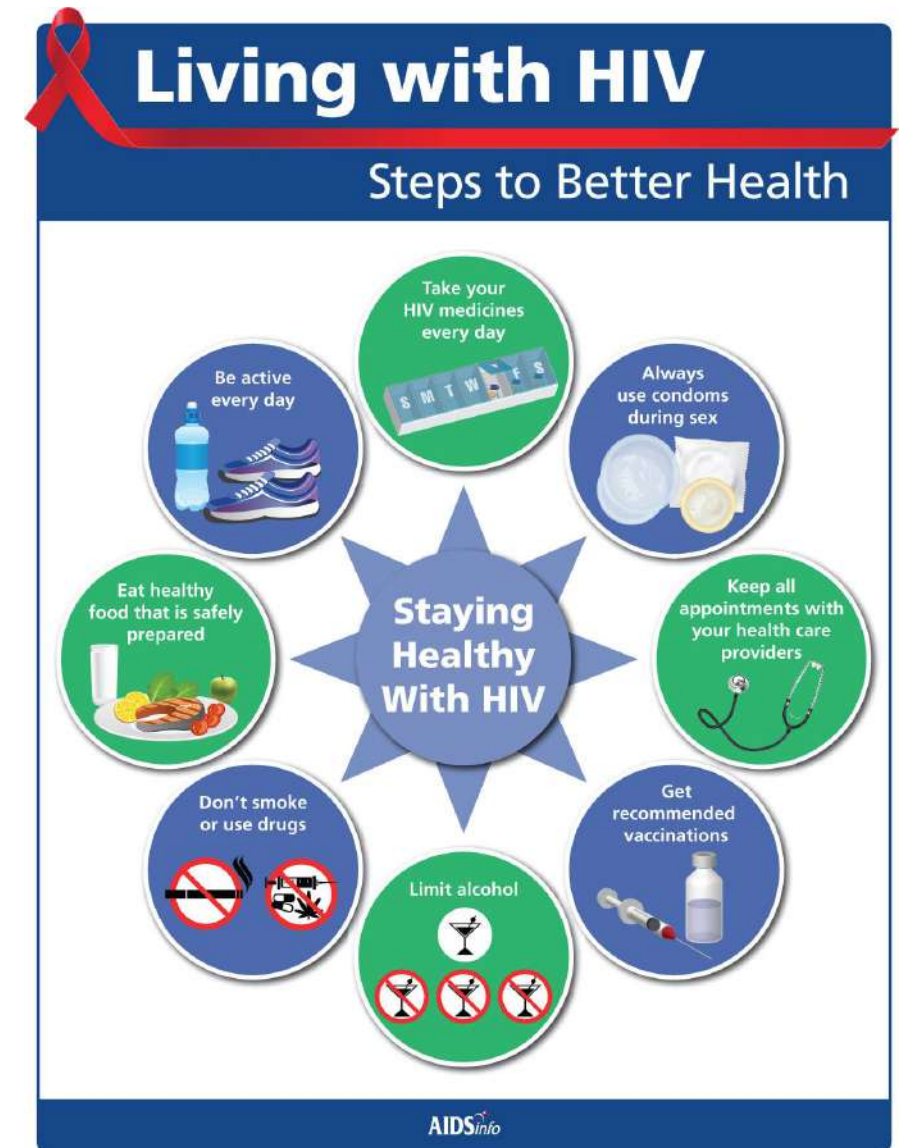
Independencia

Autonomía

Relaciones con iguales

Auto-imagen

Conductas de riesgo



# Tratamiento **ARVc** en **TODOS** los **jóvenes** con infección VIH: **ADHERENCIA**

1. Negación de diagnóstico
2. Desinformación
3. Desconfianza hacia sistema sanitario
4. Miedo y/o falta de confianza hacia el TAR
5. Baja autoestima
6. Estilo de vida desorganizado
7. Falta de soporte socio-familiar



1. Diferir inicio (reinicio) de ARVc hasta mejorar adherencia
2. Evitar tratamientos ARVc con baja barrera genética
3. Simplificar tratamientos ARVc



# Simplificación



Menor número de FARs

Ciclos 5 días on/ 2 días off

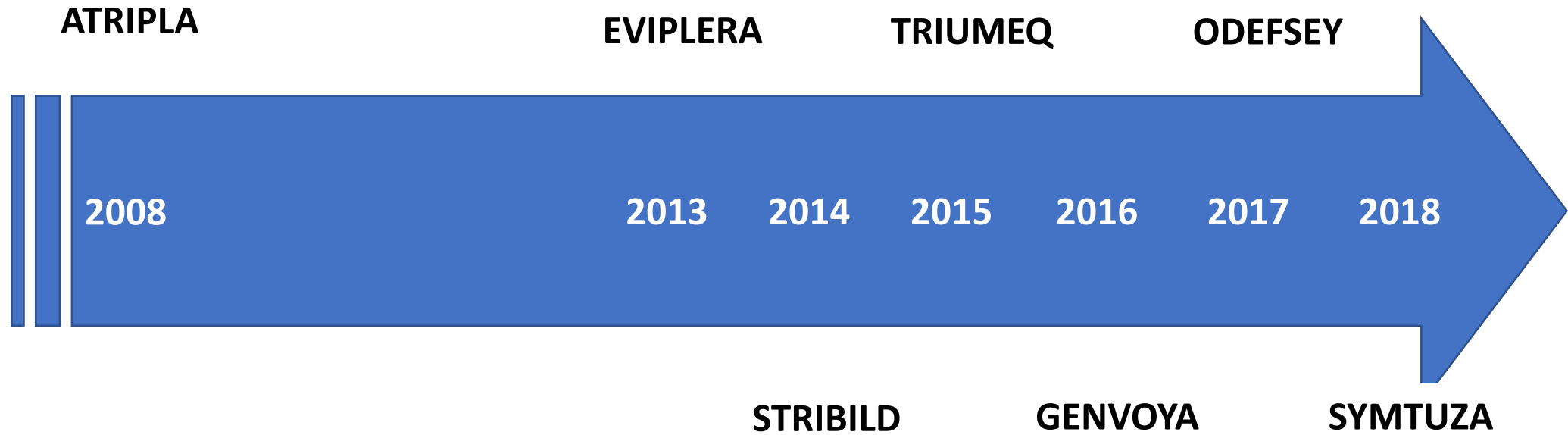
Long-Term  
Medication Adherence

Reduced Risk of  
Treatment Failure

Improved Quality  
of Life

## OBJETIVOS

# Tratamientos de comprimido único



OPEN

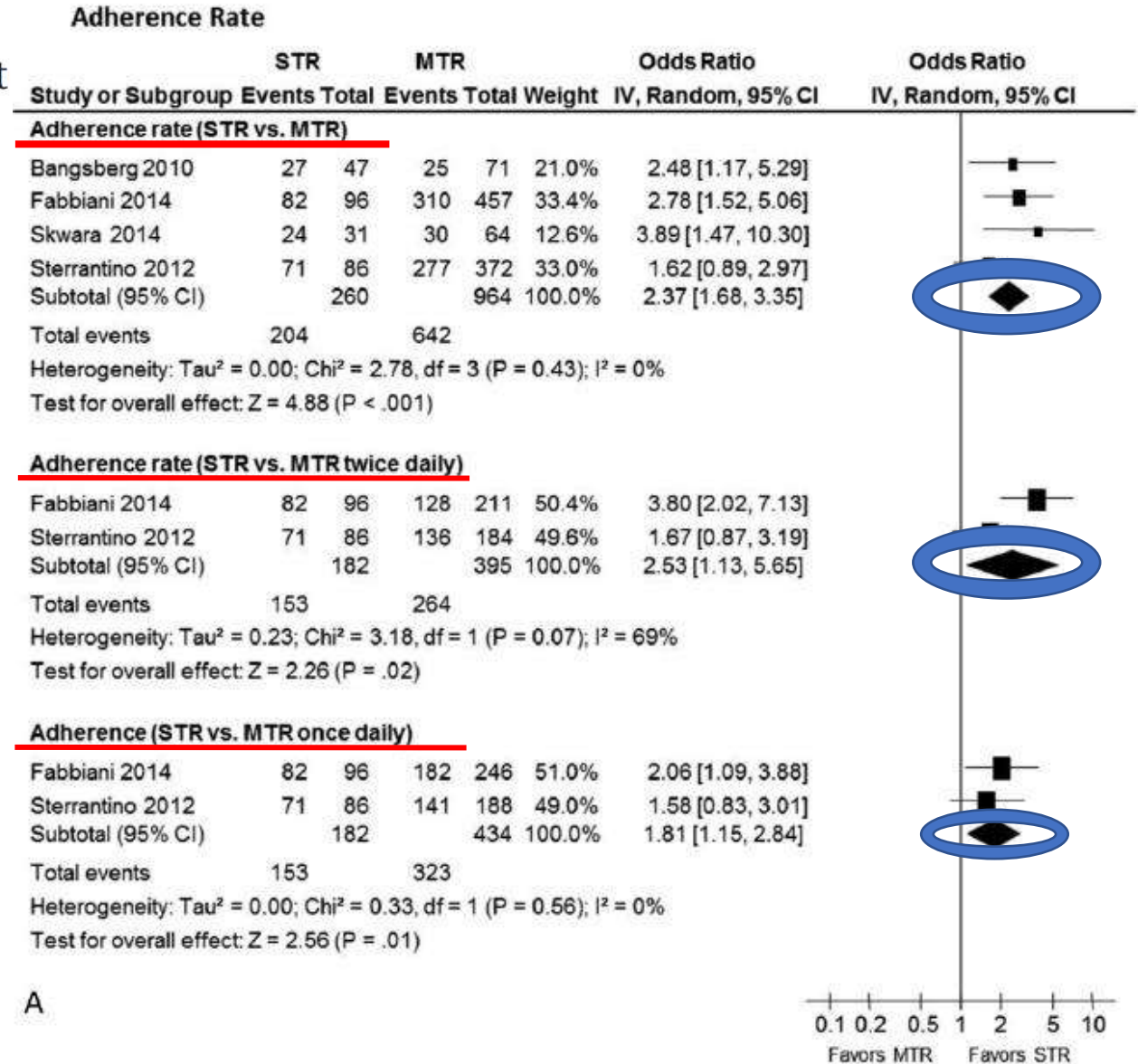
# Meta-Analysis of Studies Comparing Single and Multi-Tablet Fixed Dose Combination HIV Treatment Regimens

P.G. Clay, PharmD, S. Nag, PhD, C.M. Graham, PhD, and S. Narayanan, MS, MHS

Mayor adherencia

Mayor supresión viral

Menos efectos adversos analíticos



Raltegravir 1200 mg once daily versus raltegravir 400 mg twice daily, with tenofovir disoproxil fumarate and emtricitabine, for previously untreated HIV-1 infection: a randomised, double-blind, parallel-group, phase 3, non-inferiority trial

Cahn P. et al. Lancet HIV 2017

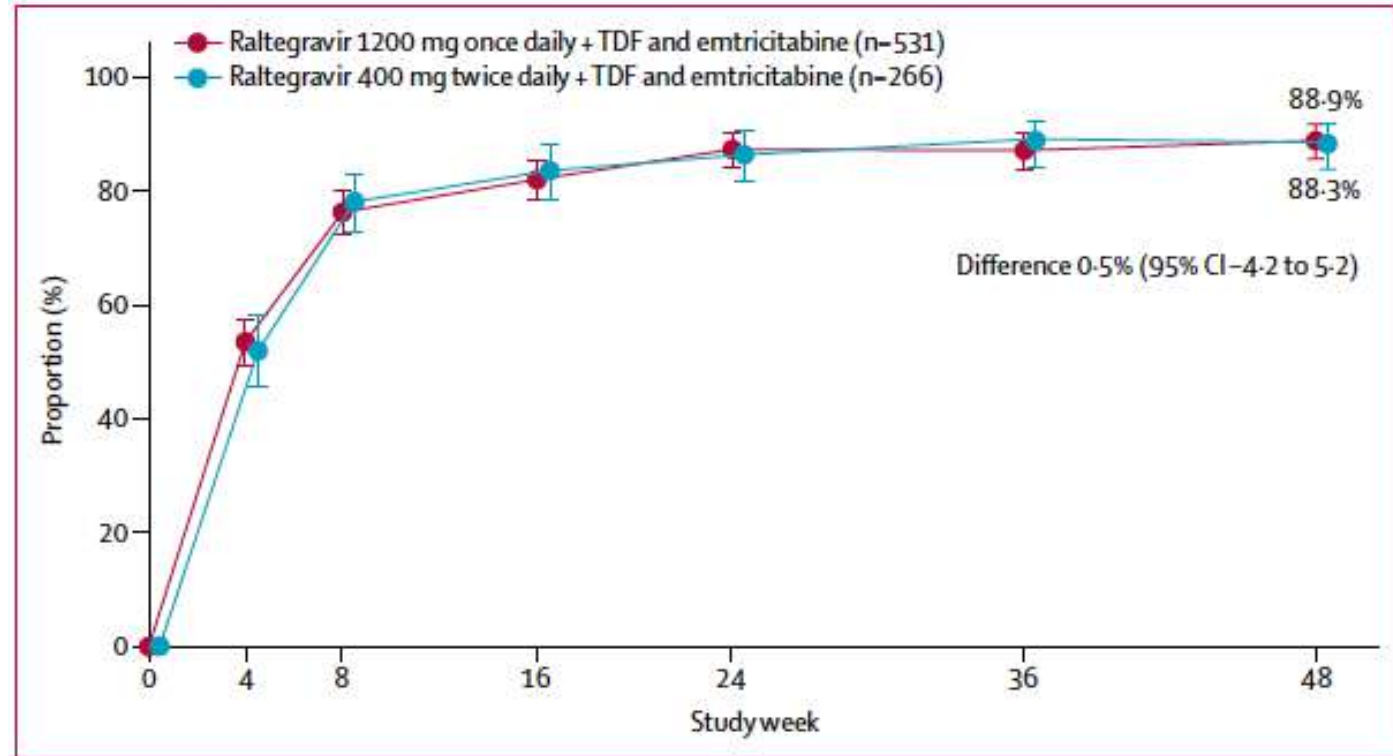


Figure 2: Proportion of participants with HIV-1 RNA less than 40 copies per mL

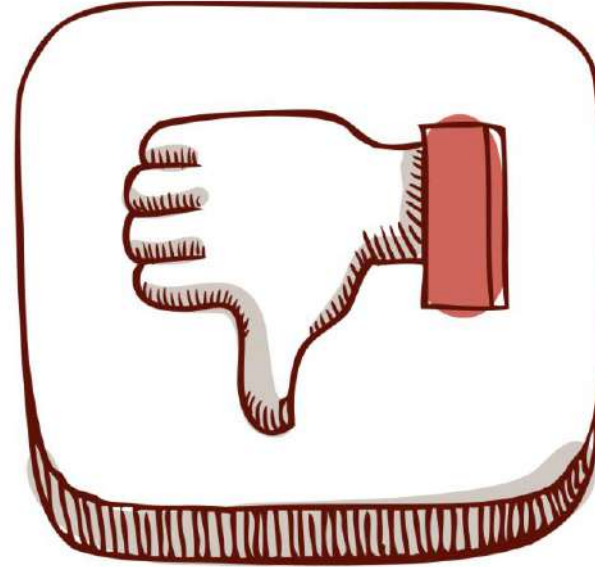
**Interpretation** A once daily raltegravir 1200 mg regimen was non-inferior compared with raltegravir 400 mg twice daily for initial treatment of HIV-1 infection. These results support the use of raltegravir 1200 mg once daily for first-line therapy.

# Disminuir número de FARs



Terapia dual

- **Lamivudina + PI/r**
- **Dolutegravir + Rilpivirina**



Monoterapia

- **Monoterapia con IP/r**
- **Monoterapia DTG**



# Terapia dual: lamivudina + PI/r

Dual treatment with lopinavir–ritonavir plus lamivudine versus triple treatment with lopinavir–ritonavir plus lamivudine or emtricitabine and a second nucleos(t)ide reverse transcriptase inhibitor for maintenance of HIV-1 viral suppression (OLE): a randomised, open-label, non-inferiority trial

Arribas JR et al. Lancet Infect Dis 2015;15: 785–92



Dual treatment with atazanavir–ritonavir plus lamivudine versus triple treatment with atazanavir–ritonavir plus two nucleos(t)ides in virologically stable patients with HIV-1 (SALT): 48 week results from a randomised, open-label, non-inferiority trial

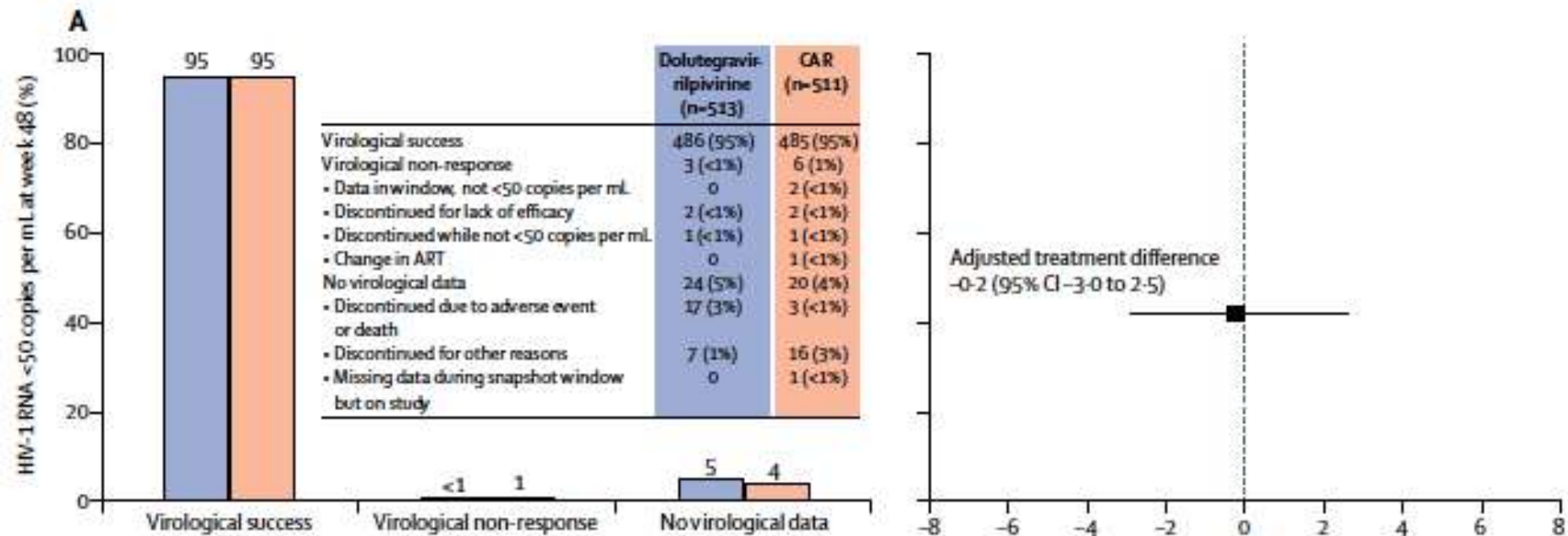
Pérez-Molina JA et al. Lancet Infect Dis 2015;15: 775–84



Dual Therapy With Darunavir and Ritonavir Plus Lamivudine vs Triple Therapy With Darunavir and Ritonavir Plus Tenofovir Disoproxil Fumarate and Emtricitabine or Abacavir and Lamivudine for Maintenance of Human Immunodeficiency Virus Type 1 Viral Suppression: Randomized, Open-Label, Noninferiority DUAL-GESIDA 8014-RIS-EST45 Trial



# Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies



**Interpretation** Dolutegravir-rilpivirine was non-inferior to CAR over 48 weeks in participants with HIV suppression and showed a safety profile consistent with its components. Results support the use of this two-drug regimen to maintain HIV suppression.

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## > HIV

- > Treatment Guidelines
- > EPIICAL
- > ODYSSEY (PENTA 20)
- > SMILE (PENTA 17)
- > GEPPPO
- > EPPICC
- > BREATHER LTFU (PENTA 16 LTFU)
- > Support in LMIC
- > PANNA Study
- > REALITY
- > Past Projects

## SMILE (PENTA 17)

**Strategy for Maintenance of HIV suppression with integrase inhibitor + darunavir/ritonavir in children (PENTA 17).**

SMILE is a multicentre randomised study evaluating safety and antiviral effect of a once daily integrase inhibitor administered with Darunavir/Ritonavir compared to standard of care among HIV-1 infected, virologically suppressed paediatric participants.

PENTA is sponsor of this study, with 300 children due to be enrolled from about 30 sites from 10 countries.

**Febrero 2018:** nuevas inclusiones de pacientes

**Diciembre 2016:** nueva propuesta con "INSTI + DRV / r"

**DTG**



**Suspensión de inclusión de pacientes**

**Octubre 2016:** se notifica EVG no se comercializa como agente único

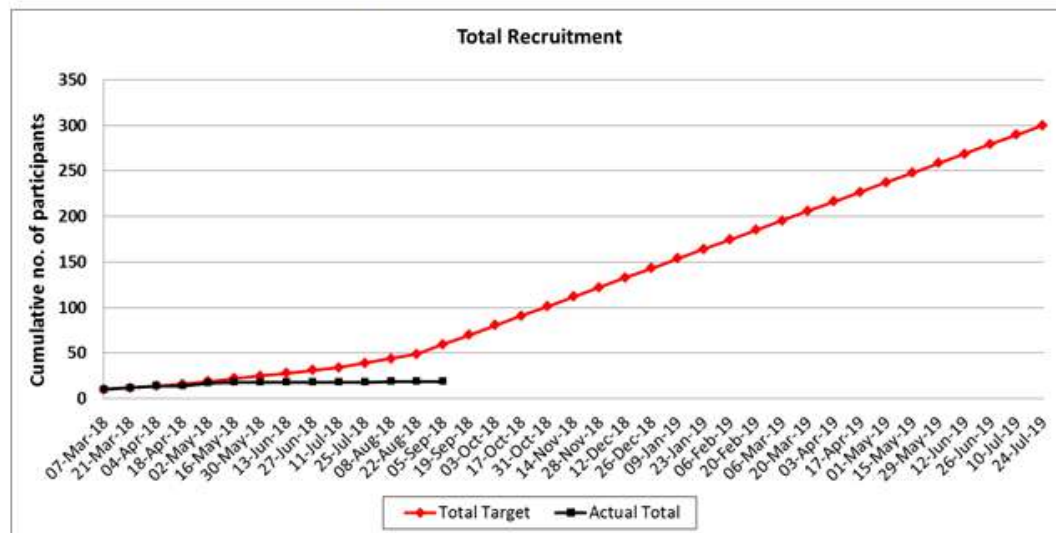
**Junio 2016:** primer paciente randomizado

**Diciembre 2015:** primera aprobación





## Accrual graph to 03-September-2018



(Fortnight end of)

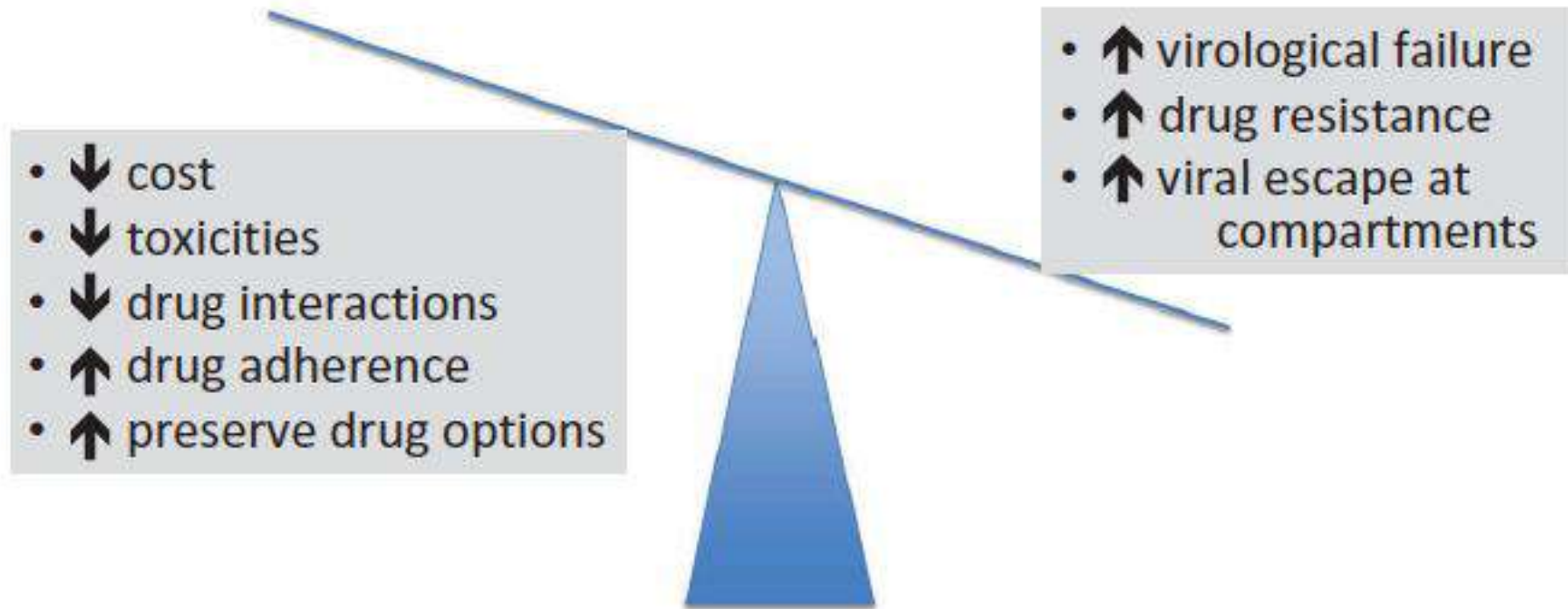


## Accrual summary by site to 03-September-2018

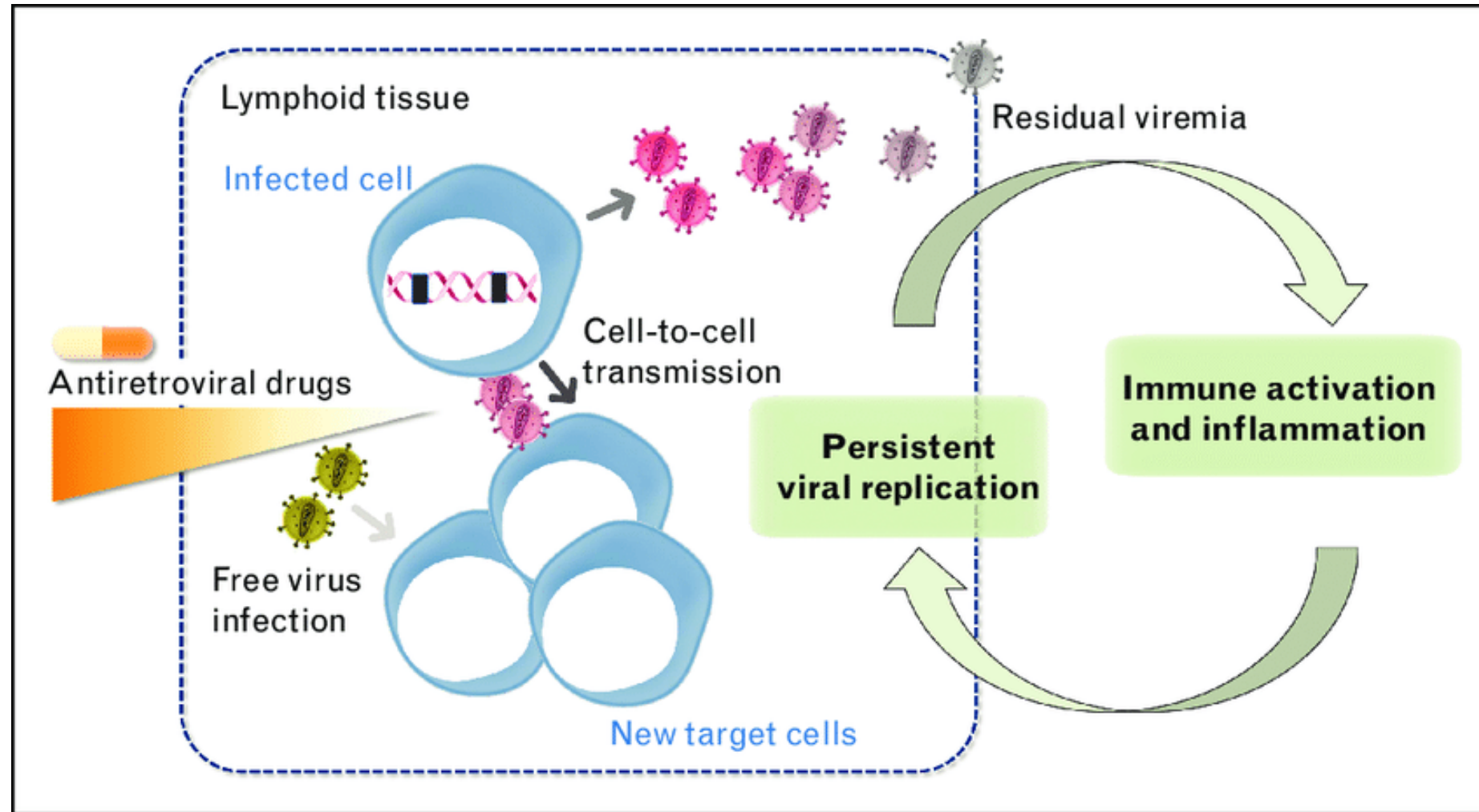
CTU	Country	Centre	Date of First Randomisation	Numbers Screened	Numbers Randomised
INSERM	CH	Kinderspital Zurich	08-Mar-18	2	2
	ES	Hospital Universitario 12 de Octubre	10-Jun-16	4	3
	ES	Hospital La Paz	20-Sep-16	2	1
	ES	Hospital Sant Joan De Deu	19-Jul-16	2	2
	ES	Hospital Gregorio Maranon	02-Aug-16	2	1
	ES	Hospital Universitario de Getafe	26-Jul-16	1	1
	ES	Hospital Clinico San Carlos	23-Sep-16	2	2
	FR	Centre Hospitalier de Cayenne (Guyana)		1	
	FR	CHU Hotel-Dieu	07-May-18	1	1
	PT	Centro Materno Infantil do Norte	12-Mar-18	4	3
	PT	Hospital Dona Estefania	24-Apr-18	1	1
	PT	Hospital Sao Joao		1	
MRC	GB	Birmingham Heartlands Hospital	02-May-18	1	1
	GB	St Thomas Hospital (London)	31-Jul-18	1	1
<b>Total</b>				<b>25</b>	<b>19</b>
Number of women enrolled: 13					
Number of pregnancies on DTG: 0					



# Pros y cons de terapia dual



# Reservorio → viremia residual



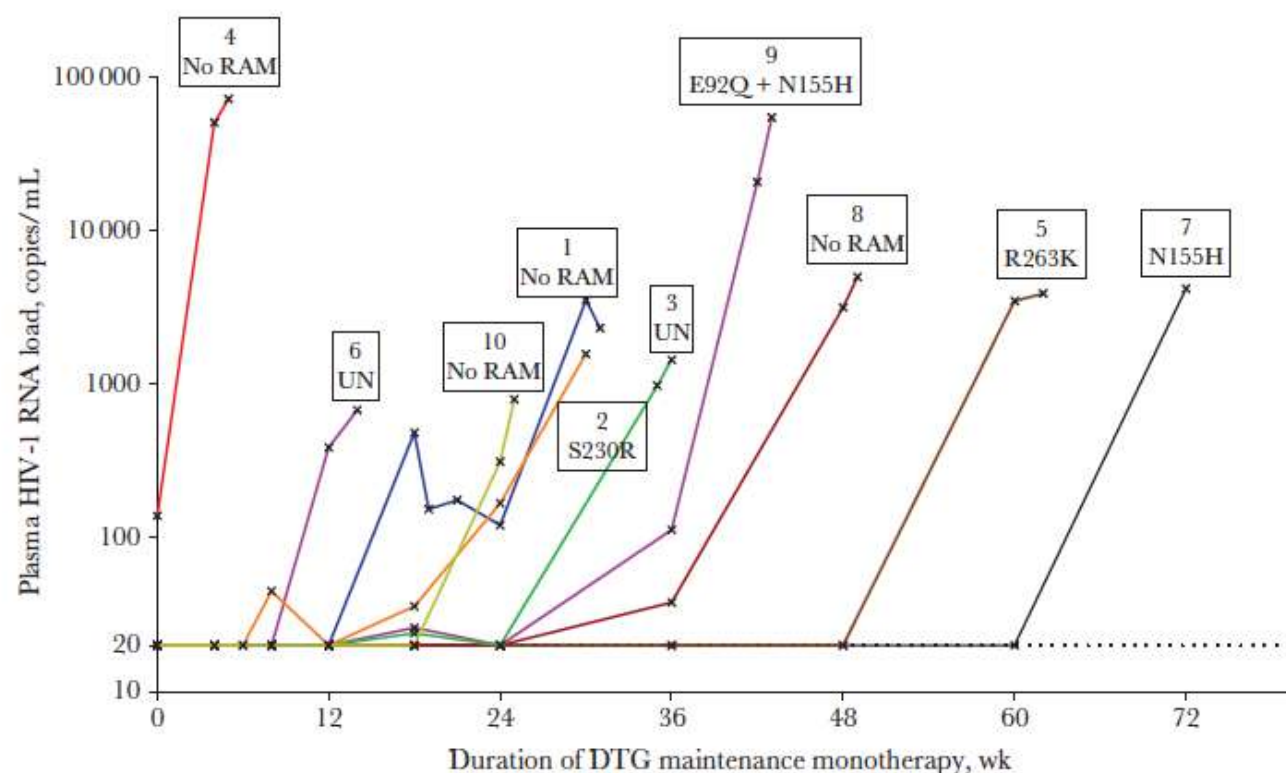
# Efficacy of protease inhibitor monotherapy vs. triple therapy: meta-analysis of data from 2303 patients in 13 randomized trials

- ✓ **Mayor riesgo de episodios de carga viral detectable**
- ✓ Resupresión de carga viral tras introducción de análogos
- ✓ No aumento de desarrollo de resistencias
- ✓ No mayor número de episodios de CV detectable en LCR
- ✓ No aumento de replicación en reservorio



JID 2018:218 (1 September) • Wijting et al

# HIV-1 Resistance Dynamics in Patients With Virologic Failure to Dolutegravir Maintenance Monotherapy



**Conclusions.** The genetic barrier to resistance is too low to justify dolutegravir maintenance monotherapy because single INSTI-RAMs are sufficient to cause VF. The large variation in time to VF suggests that stochastic reactivation of a preexisting provirus containing a single INSTI-RAM is the mechanism for failure. Changes in the 3'-PPT point to a new dolutegravir resistance mechanism in vivo.



# Weekends-off efavirenz-based antiretroviral therapy in HIV-infected children, adolescents and young adults (BREATHER): Extended follow-up results of a randomised, open-label, non-inferiority trial

## Conclusions

Sustainable non-inferiority of virological suppression in young people was shown for SCT versus CT over median 3.6 years. Standard-dose efavirenz-based SCT is a viable option for virologically suppressed HIV-1 infected young people on first-line ART with 3-monthly VL monitoring.

# Conclusiones

