Educational Fund

IAS

EVIDENCIA DEL INICIO DEL ART EL MISMO DÍA

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Potenciales conlfictos de Interés

He participado en consultorías para MSD, Gilead y ViiV

Mi Institución recibe grants para la conducción de ensayos clínicos de MSD, Janssen, GSK.

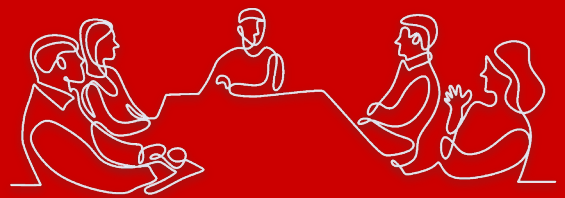
CONTENIDO

01 INTRODUCCIÓN

02 INICIO de ART el Mismo Día

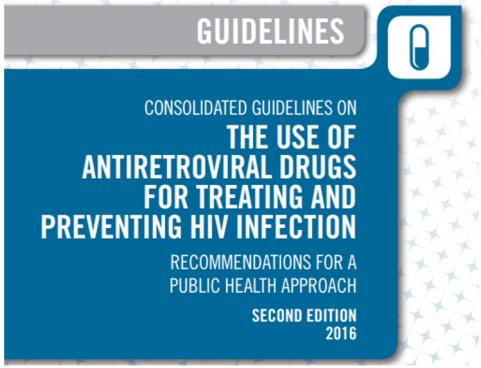
- Guías actuales
- Situaciones especiales
- Experiencia en LA
- Perspectivas

03 CONCLUSIÓN



INTRODUCCIÓN

En **2015** la OMS actualizó sus guías y recomendó el inicio de ART temprano a partir del momento de diagnóstico, sin importar los CD4

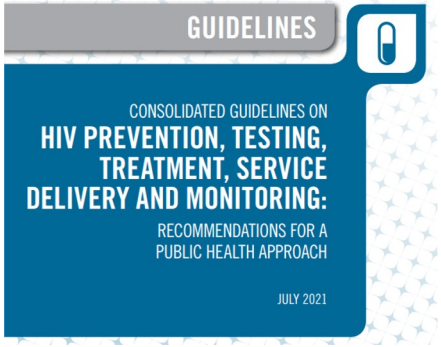


"The available data are currently inadequate to support a recommendation in these guidelines in favour of same-day or otherwise accelerated ART initiation"

INTRODUCCIÓN

En **2017** la OMS recomendó el inicio de ART dentro de los primeros 7 días después del diagnóstico de VIH o el **mismo día** si la persona se sentía lista

Inicio Rápido



Recommendation (2017)

Rapid ART initiation[a,b] should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment *(strong recommendation: high-certainty evidence for adults and adolescents; low-certainty evidence for children).*

ART initiation should be offered on the same day to people who are ready to start *(strong recommendation: high-certainty evidence for adults and adolescents; low-certainty evidence for children).*

[a] Rapid initiation is defined as within seven days from the day of HIV diagnosis; people with advanced HIV disease should be given priority for assessment and initiation.

Otra Evidencia en LA...

Crabtree-Ramírez BE et al. *Journal of the International AIDS Society* 2019, **22**:e25413
http://onlinelibrary.wiley.com/doi/10.1002/jia2.25413/full | https://doi.org/10.1002/jia2.25413

JIAS JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Temporal changes in ART initiation in adults with high CD4 counts in Latin America: a cohort study

Brenda E Crabtree-Ramírez[1,§], Yanink Caro-Vega[1], Pablo F Belaunzarán-Zamudio[1], Bryan E Shepherd[2], Peter F Rebeiro[2], Valdilea Veloso[3], Claudia P Cortes[4], Denis Padgett[5], Eduardo Gotuzzo[6], Juan Sierra-Madero[1], Catherine C McGowan[2] and Anna K Person[2] on behalf of the Caribbean, Central, South America Network for HIV Epidemiology (CCASAnet)

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- N=3171 (2003- 2017)
- 1650 tenían CD4 >500 despues del 2013.
- 24% nunca iniciaron (63% se perdieron)
- Disminución de 6.2 a 4.7 semanas >2015

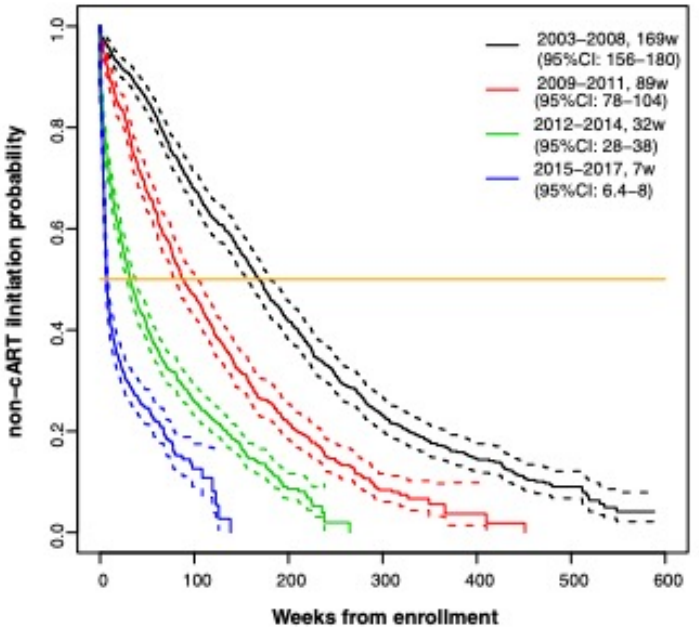


Figure 1. Kaplan-Meier analysis of the probability of cART initiation over different periods of time among all patients.

GUÍAS DE DHHS, 2019

Inicio **INMEDIATO** → Mismo día
Inicio **Temprano** → Dentro de las primeras 2 semanas

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality **(AI)** and to prevent the transmission of HIV to others **(AI)**.
• The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV **(AII)**.
• When initiating ART, it is important to educate patients regarding the benefits of ART and to deploy strategies to optimize care engagement and treatment adherence **(AIII)**.

- Aceptación del TAR
- Vinculación a los sistemas de salud
- Llegar a ser indetectable

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2019

¿Por qué podría ser bueno el mismo día/rápido?

- Mismo día del diagnóstico, el individuo está vinculado
  - La persona entiende la importancia de su infección
    - Se pueden evitar potenciales transmisiones
  - Hay circunstancias de beneficios clínicos claros: embarazo, infección aguda, enfermedad avanzada
- No hay una razón particular para retrasarlo (IO SNC)

GUÍAS EACS 12, 2023

¡Siempre que el paciente esté listo!
Sin presionarlo y tomando en cuenta sus preferencias

A menos que existan indicaciones médicas

Immediate (i.e. same day) start of ART should be considered, and especially in the following situations:

- In the setting of primary HIV infection, especially in case of clinical signs and symptoms of meningoencephalitis (within hours). In this situation, the clinician may start ART immediately after a positive screening HIV test and before obtaining confirmatory HIV test results such as a HIV-VL
- The wish to start ART immediately
- In a setting where loss-to-follow-up is more likely if ART is not started the same day

Embarazo

Guidelines 12. European AIDS Clinical Society, October 2023.

GUÍAS EACS 12, 2023

Stages of readiness to start ART	
Precontemplation: *"I don't need it, I feel good"* *"I don't want to think about it"*	Support: Show respect for the person's attitude. / Try to understand the person's health and therapy beliefs. / Establish trust. / Provide concise, individualised information. / Schedule next appointment
Contemplation: *"I am weighing things up and feel torn about what to do about it"*	Support: Allow ambivalence. / Support the person in weighing pros and cons. / Assess the person's information needs and support his/her information seeking. / Schedule the next appointment
Preparation: *"I want to start, I think the drugs will allow me to live a normal life"*	Support: Reinforce the person's decision. / Decide with the person which is the most convenient regimen. / Educate the person on adherence, resistance and side effects. / Discuss integration into daily life. / Assess self-efficacy Ask: How confident are you that you can take your medicines as we discussed (specify) once you have started? Consider skills training: • Medicines-taking training, possibly Medication Event Monitoring System, e.g. electronic pill boxes • Directly observed therapy with educational support • Use aids: mobile phone alarm, pillboxes • Involve supportive tools/persons where appropriate
Action: ***"I will start now"***	**'Final check': With a treatment plan established, is the person capable of taking ART and is ART available?**
Maintenance: *"I will continue" or "I have difficulties continuing in the long run"* Caveat: A person can relapse to an earlier stage, even from "maintenance" to "precontemplation"	Assess: Adherence every 3-6 months[iii] Evaluate adherence: For persons with good adherence: show respect for their success Assess: The person's own perception of ability to adhere to and continue treatment Ask: In the next 3-6 months, how confident are you that you can take your medicines? For a person without sufficient adherence: use mirroring techniques[iv] on problems, ask open questions to identify dysfunctional beliefs Assess: Stage of readiness and provide stage-based support Assess: Barriers and facilitators[v] Schedule next appointment and repeat support

START ART

Guidelines 12. European AIDS Clinical Society, October 2023.

CONSIDERACIONES ESPECIALES

Timing of ART (2018 recommendations)

Immediate ART initiation is not recommended among adults, adolescents and children living with HIV who have cryptococcal meningitis because of the risk of increased mortality and should be deferred 4–6 weeks from the initiation of antifungal treatment.

Strong recommendation; low-certainty evidence for adults and very-low-certainty evidence for children and adolescents

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

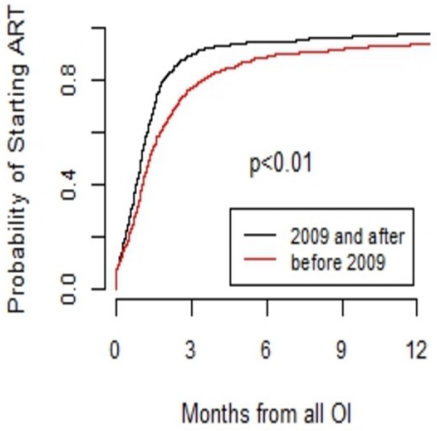
	Initiation of ART	Comments
General recommendation	As soon as possible within 2 weeks after starting treatment for the opportunistic infection	
TB meningitis	In persons with CD4 < 50 cells/μL, ART should be initiated within the first 2 weeks after initiation of TB treatment, if close monitoring and optimal TB treatment can be ensured ART initiation should be delayed for 4 weeks in all other cases	Corticosteroids are recommended as adjuvant treatment Where very close monitoring and optimal treatment are available, ART could be initiated early in selected cases
Cryptococcal meningitis	Defer initiation of ART for at least 4 weeks	Corticosteroids are not recommended as adjuvant treatment Where very close monitoring and optimal treatment are available, earlier ART start could be considered in selected cases

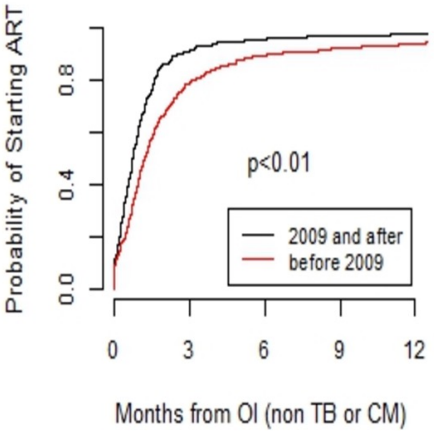
Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. 2019
Guidelines 12. European AIDS Clinical Society, October 2023. Diagnosis, preventing and managing cryptococcal disease among adulta, adolescents and children living with HIV. WHO, 2022

Otra Evidencia en LA..

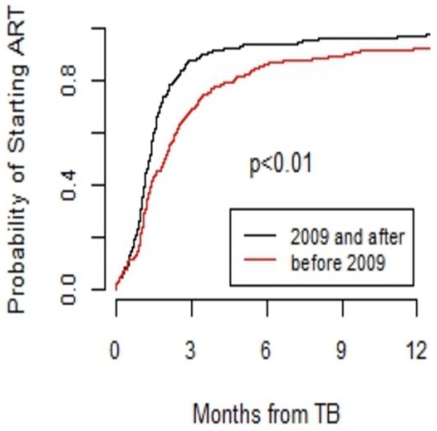
Time to HAART Initiation after Diagnosis and Treatment of Opportunistic Infections in Patients with AIDS in Latin America

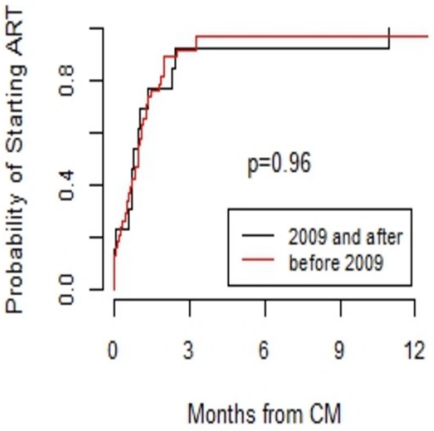
Brenda Crabtree-Ramírez, Yanink Caro-Vega, Bryan E. Shepherd, Beatriz Grinsztejn, Marcelo Wolff, Claudia P. Cortes, Denis Padgett, Gabriela Carriquiry, Valeria Fink, Karu Jayathilake, Anna K. Person, Catherine McGowan, Juan Sierra-Madero, Caribbean, Central and South America Network for HIV Epidemiology (CCASAnet), of the International Epidemiologic Databases to Evaluate AIDS (IeDEA) Program





- N=1457 (2001- 2012)
- Los factores asociados con el inicio ART dentro de las 4 semanas posteriores a la IO fueron CD4 bajos (p-<0,001), tener una IO no TB (p<0,001), el sitio de estudio (p<0,001) y los años más recientes (p<0,001).





INICIO EL MISMO DÍA: ensayos clínicos

Estudio aleatorizado, controlado, no ciego del inicio en el **mismo día (347) vs inicio estándar del ART (356)** en Haití.

Table 3. Unadjusted and adjusted risk ratios of study outcomes.

	Unadjusted			Adjusted for All Baseline Co-variates		
	RR	95% CI	*p*-value	RR	95% CI	*p*-value
	Retained in care with viral load <50 copies/ml					
Standard ART Group	1.0			1.0		
Same-Day ART Group	1.21	(1.04, 1.38)	0.015	1.24	(1.06, 1.41)	0.008
	Retained in care with viral load <1,000 copies/ml					
Standard ART Group	1.0			1.0		
Same-Day ART Group	1.18	(1.04, 1.31)	0.012	1.20	(1.05, 1.33)	0.008
	Mortality during study period					
Standard ART Group	1.0			1.0		
Same-Day ART Group	0.51	(0.24, 1.08)	0.073	0.43	(0.19, 0.94)	0.033

ART, antiretroviral therapy; RR, risk ratio.

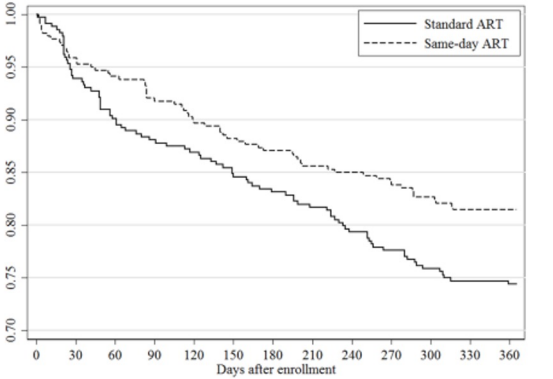


Fig 3. Retention in care by study group.

https://doi.org/10.1371/journal.pmed.1002357.g003

Disminuye mortalidad y mejora la retención del paciente

En un sistema de salud que no es sólido, puede beneficiarse de iniciar el ART el mismo día: Facilita los procesos burocráticos para el paciente, refuerza el optimismo.

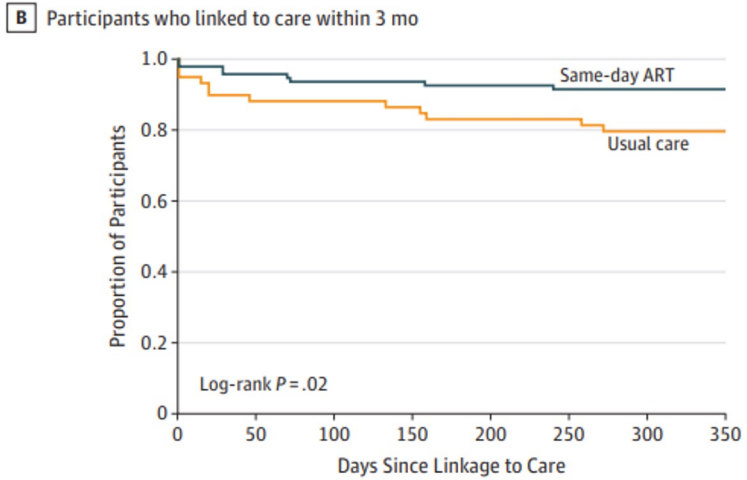
Koenig S, Dorvil N, Devieux J, Hedt B. Same-day HIV testing with initiation of antiretroviral therapy versus standard care for persons living with HIV:A randomized unblinded trial. PloS mED, 2017

INICIO EL MISMO DÍA: Ensayos clínicos

Estudio aleatorizado, abierto, con dos grupos , del inicio en el **mismo día (138) vs inicio estándar del ART (140)** en Lesotho.

Table 2. Primary and Secondary End Points of the Trial and Post Hoc Analyses

	No. (%) of Participants			
	Same-Day ART (n = 137)	Usual Care (n = 137)	Absolute Difference, % (95% CI)	*P* Value
Primary Outcomes				
Linkage to care at 90 d after enrollment	94 (68.6)	59 (43.1)	25.6 (13.8 to 36.3)	<.001
Viral load <100 copies/mL, 11-14 mo after enrollment[a]	69 (50.4)	47 (34.3)	16.0 (4.4 to 27.2)	.007



Iniciar el mismo día el ART, mejoró la retención a los 3 meses y supresión viral a los 12 meses

Labhardt N, Ringera I, Lejone T. Effect of Offering Same-day ART vs Usual Health Facility referrral during home-based HIV testing on Linkage to care and viral Suppression among adults with HIV in Lesotho. The CASCADE Randomized Clinical Trial. JAMA, 2018

INICIO EL MISMO DÍA: Ensayos clínicos

Estudio aleatorizado, abierto de pacientes con VIH y síntomas de TB, del inicio en el **mismo día (Tratamiento de TB o ART si TB negativo) vs inicio estándar del ART (Inicio de tratamiento para TB con retraso de 7 días el inicio del ART)** en Haiti

Table 2. Primary and secondary study outcomes by group.

Outcome	Standard group (n = 250)	Same-day treatment group (n = 250)	RD (95% CI)	p-Value
Primary outcome				
48-week HIV-1 RNA <200 copies/mL*	168 (67·2)	152 (60·8)	−0·06 (−0·15, 0·02)	0·14
Secondary outcomes				
48-week HIV-1 RNA <50 copies/mL*	159 (63·6)	137 (54·8)	−0·09 (−0·17, −0·002)	0·045
48-week HIV-1 RNA <1,000 copies/mL*	176 (70·4)	159 (63·6)	−0·07 (−0·15, 0·01)	0·11
Forty-eight-week outcomes**				
Attended 48-week study visit*	229 (91·6)	218 (87·2)	−0·04 (−0·10, 0·01)	0·11
Died	6 (2·4)	9 (3·6)	0·01 (−0·02, 0·05)	0·43
Lost to follow-up	10 (4·0)	14 (5·6)	0·02 (−0·02, 0·06)	0·40
Missed 48-week visit due to gap in care, with subsequent return to care	4 (1·6)	6 (2·4)	0·01 (−0·02, 0·04)	0·52
Transferred	1 (0·4)	3 (1·2)	0·01 (-0·01, 0·03)	0·62

*Nine participants in the standard treatment and 7 in the same-day group attended 48-week visit without HIV-1 RNA testing.

**These are mutually exclusive outcomes which include all 500 randomized participants.

CI, confidence interval; RD, risk difference.

En pacientes con VIH y síntomas de TB, el iniciar el ART el mismo día, no se asoció con una mejor retención o supresión viral.

Dorvil N, Rivera V, Riviere C, Berman R. Same-day testing with initiation of antiretroviral therapy or tuberculosis treatment versus standard care for persons presenting with tuberculosis symptoms at HIV diagnosis: Arandomized open-label trial from Haiti. PLoS Med, 2023.

INICIO EL MISMO DÍA: Estudios Cohorte

Estudio de los participantes con diagnóstico de VIH a partir de la recomendación de *same-day treatment* en la cohorte de IeDEA

Total: 29,017
Same-day: 18,584 (64%)
Not Same-day: 10 433 (36%)

Iniciar ART el mismo día fue menos probable en **estadios avanzados** de la enfermedad (aRR 0.83)
Sin diferencias en la supresión viral

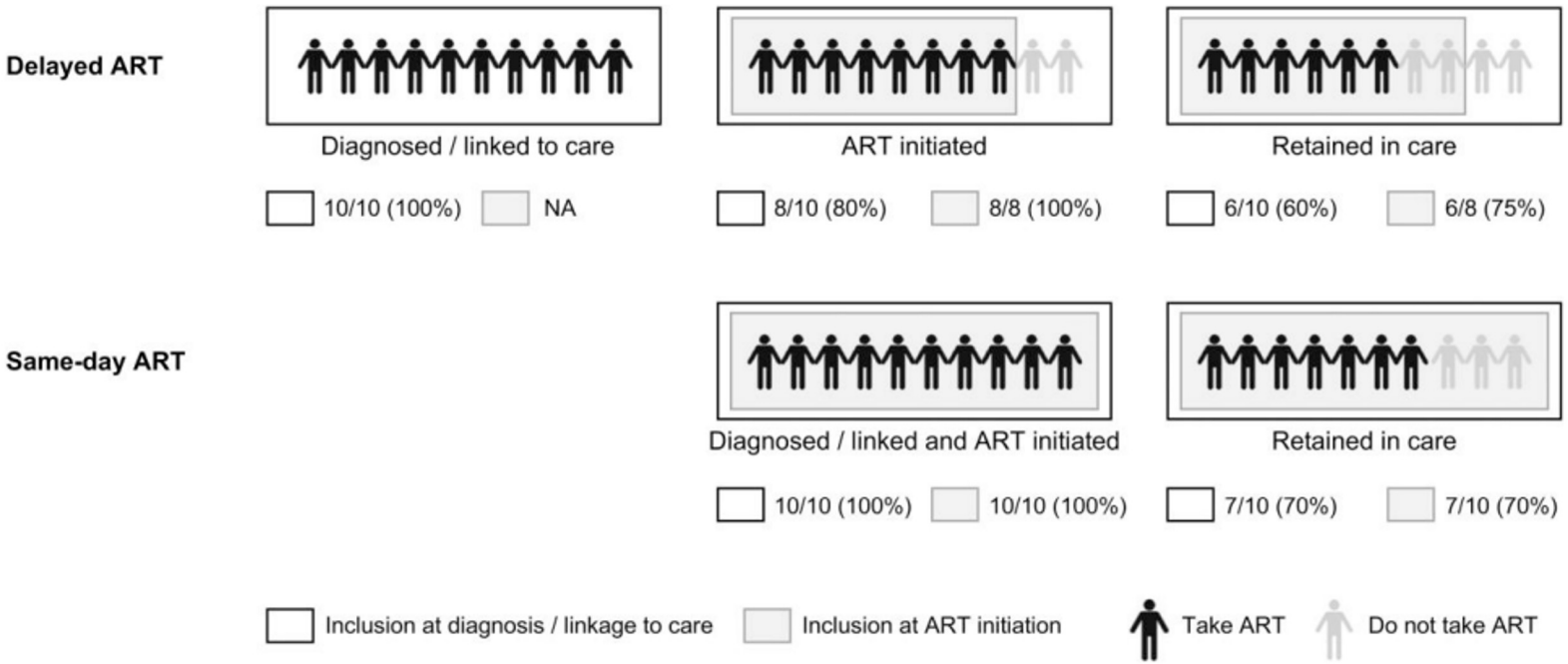
La pérdida de seguimiento a los 12 meses, fue 34% **menor** en el grupo de que no iniciaban el ART el mismo día.
(aRR 0.66, IC 95% 0.57-0.76)

Table 3. Factors Associated With Loss to Follow-Up Within 12 Months After Antiretroviral Therapy Initiation

Variables	N/n	LTFU Within 12 Months, n (%)	Median Time to LTFU, Days (IQR)	HR (95% CI)[a]	aHR (95% CI)[a,b]
Total	29 017	7293 (25.1)	29 (1–153)	…	…
Patient-level					
Same-day ART initiation					
Initiated ≥1 day after enrollment	10 433	2146 (20.6)	56 (1–183)	.71 (.59–.84)	.66 (.57–.76)
Initiated on same day as enrollment (ref)	18 584	5147 (27.7)	19 (1–136)	1	1

Ross J, Brazier E, Fatti G, Jaquet A, Tanon A. Same-day ART initiation as a predictor of loss to follow-up and viral suppression among people with HIV in Sub-Saharan Africa. CID, 2023.

¿POR QUÉ HAY DISCREPANCIAS?



Diferente **momento de reclutamiento** → Diferente **DENOMINADOR**→ Diferente **resultados**

Labhardt N, Brown J, Sass N, Ford N, Rosen S. Treatment Outcomes after Offering Same-day Initiation of HIV treatment-How to interpret discrepancies between different Studies. CID, 2023.

Resumen de la Evidencia

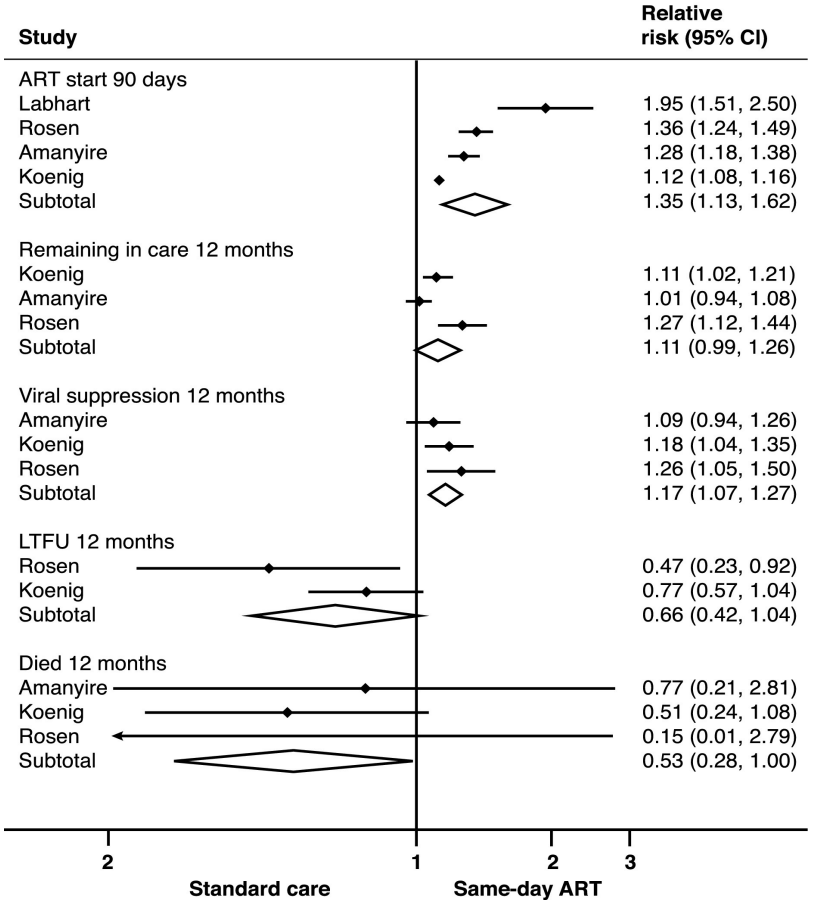
DOI: 10.1111/hiv.12708
HIV Medicine (2019), **20**(Suppl. 1), 3–11

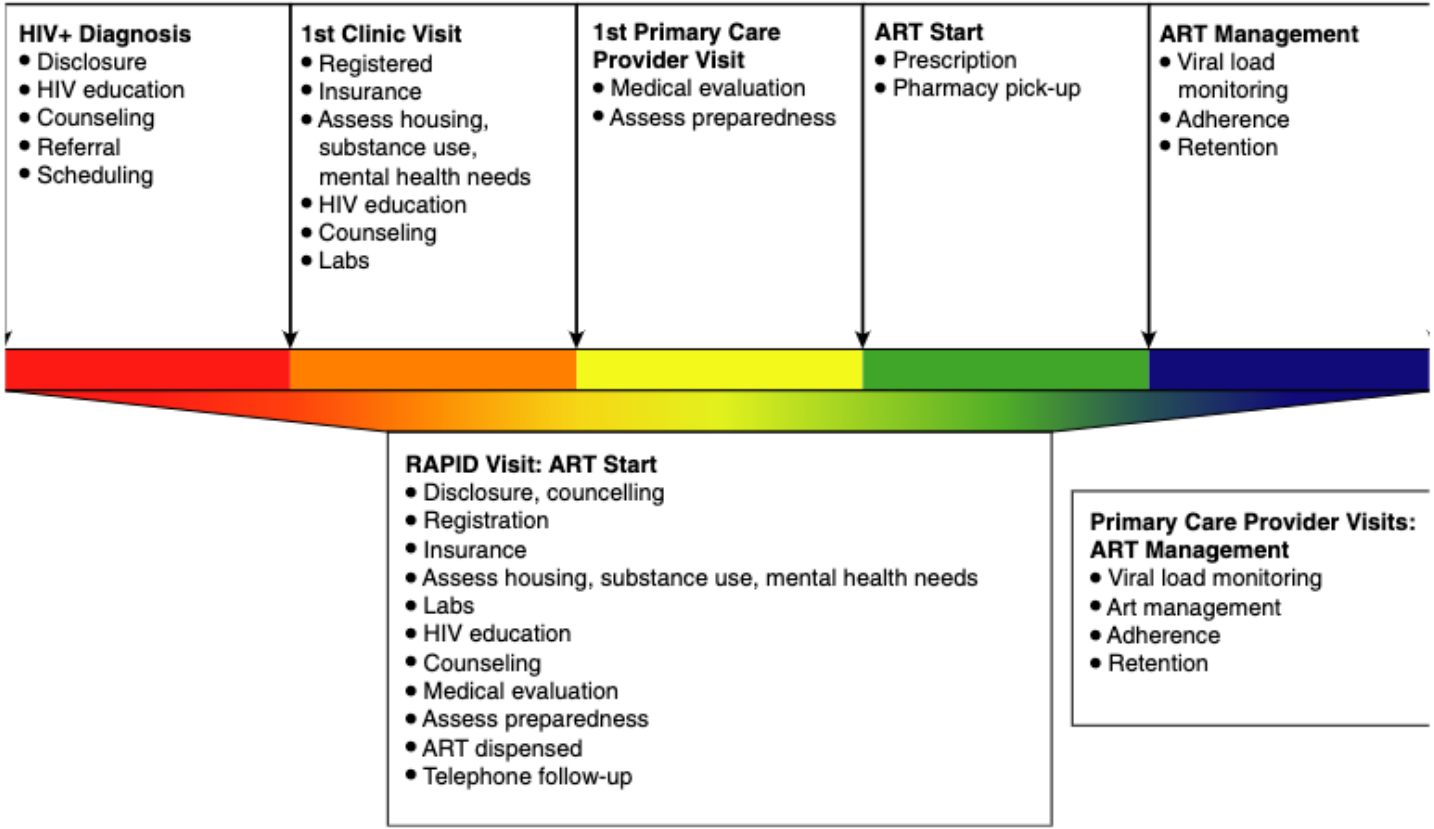
REVIEWS IN ANTIRETROVIRAL RESEARCH

Rapid initiation of antiretroviral therapy at HIV diagnosis: definition, process, knowledge gaps

MA Boyd,[1,2] M Boffito,[3,4] A Castagna[5] and V Estrada[6]

[1]*Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, SA, Australia,* [2]*Kirby Institute, University of New South Wales, Sydney, NSW, Australia,* [3]*Chelsea and Westminster Hospital, London, UK,* [4]*Imperial College London, London, UK,* [5]*Clinic of Infectious Diseases, San Raffaele Scientific Institute, Vita-Salute University, Milan, Italy and* [6]*Hospital Clinico San Carlos, Universidad Complutense, Madrid, Spain*



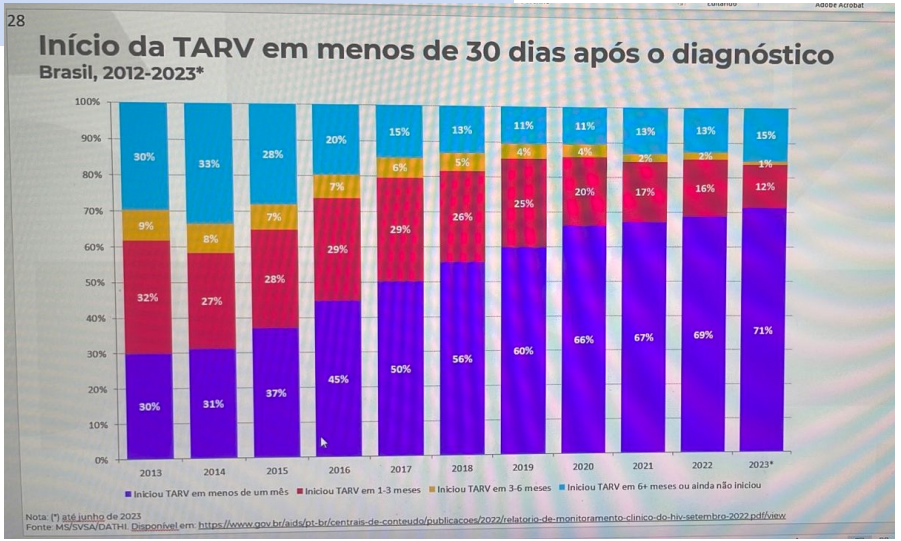

HIV+ Diagnosis
• Disclosure
• HIV education
• Counseling
• Referral
• Scheduling
1st Clinic Visit
• Registered
• Insurance
• Assess housing, substance use, mental health needs
• HIV education
• Counseling
• Labs
1st Primary Care Provider Visit
• Medical evaluation
• Assess preparedness
ART Start
• Prescription
• Pharmacy pick-up
ART Management
• Viral load monitoring
• Adherence
• Retention
RAPID Visit: ART Start
• Disclosure, councelling
• Registration
• Insurance
• Assess housing, substance use, mental health needs
• Labs
• HIV education
• Counseling
• Medical evaluation
• Assess preparedness
• ART dispensed
• Telephone follow-up
Primary Care Provider Visits: ART Management
• Viral load monitoring
• Art management
• Adherence
• Retention

¿Cuál es la frecuencia en LA?

Data sometida al CROI 2024, bajo embargo
Cohorte de CCASANet

- Haití, la gran mayoría desde 2017 inician el mismo día (<7 días)
- Resto de los sitios, menos de la mitad

De acuerdo a registros públicos en Brasil 30% inician en > 30 días.



PERSPECTIVAS...

¿Cuáles son las razones individuales o del sistema de salud?

¿Qué consecuencias tiene para nuestra región?

¿PreP será una oportunidad de acortar?

¿Los inyectables/larga duración ayudarán a acortar el tiempo?

CONCLUSIONES

- A pesar de la evidencia y recomendación del inicio rápido/temprano, representa todo un reto
- Hay evidencia en ensayos clínicos de inicio el mismo día con beneficios sólo a corto plazo y no hay diferencias demostradas con el inicio rápido
- Faltan modelos para distintos sitios de atención, así cómo entender los retos para lograrlo
- Adecuar las recomendación a circunstaincias específicos del individuo para que esté listo, es crucial

AGRADECIMIENTOS

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