Estrategias innovadoras de alcanzar las metas de los 90’

Dra. Lucrecia Castillo

Reunión MCR, Marzo 2016

HIV Care and Treatment TWG

Presentation for CAR PEPFAR team for ROP planning

Contenido de la Presentación

A. Evolución de las guías de OMS para promover el control de la epidemia.

B. Estudios científicos apoyan las nuevas estrategias

C. Porqué PEPFAR se suma a esta iniciativa

Nueva directriz de la OMS sobre TARV

- Tratamiento para todos (sin importar el nivel de CD4) – todos, sin importar edad;
- Los PV más enfermos continúan siendo la prioridad (enfermedad sintomática y/o CD4<350)
- Nuevo rango de edad para adolescentes (10-19 años)
- Nuevo estándar: Opción B+
- PrEP como una elección de prevención adicional para todos aquellos en riesgo sustancial de infectarse (>3% incidencia)
- “Guía de entrega de Servicios”

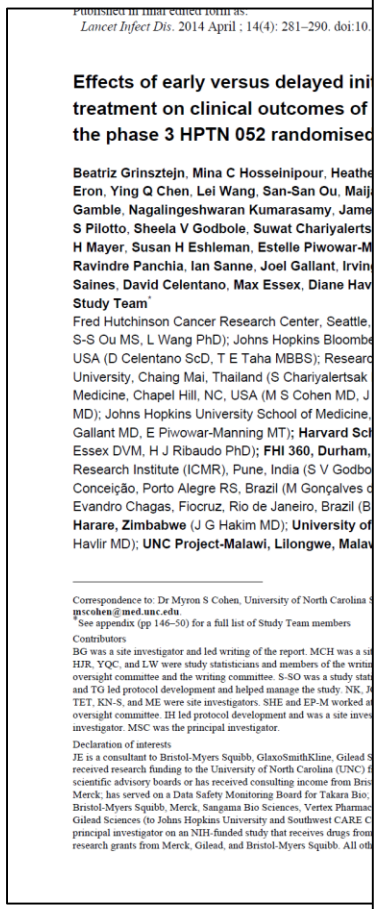
PEPFAR
U.S. President's Emergency Plan for AIDS Relief

Prueba y Tratamiento

- La OMS ha evolucionado sus guías de atención basados en la evidencia cada vez mas elocuente sobre como el inicio temprano del tratamiento muestra beneficios en el paciente y en la salud publica:
  - En 2010, OMS recomendó iniciar tratamiento con una cuenta de 350 CD4
  - En 2013, OMS recomendó iniciar TARV a los 500 CD4, basado en estudios observacionales y varias pruebas de eficacia del tratamiento para reducir la transmisión en parejas sero-discordantes, además de los beneficios individuales
  - En noviembre 2015, OMS lanza la recomendación de iniciar TARV sin tomar en cuenta el valor de CD4.

- Contexto: Tratamiento se ha hecho mas simple, mas tolerable y más asequible, y los sistemas de suministro de ARV se han simplificado para permitir ampliar esta estrategia.

Inicio más temprano de TAR, previene morbilidad y mortalidad relacionada al VIH



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Effects of early versus delayed ini
treatment on clinical outcomes of
the phase 3 HPTN 052 randomised

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*See appendix (pp 146–50) for a full list of Study Team members

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HJR, YQC, and LW were study statisticians and members of the writin
oversight committee and the writing committee. S-SO was a study stat
and TG led protocol development and helped manage the study. NK, J
TET, KN-S, and ME were site investigators. SHE and EP-M worked a
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Declaration of interests
JE is a consultant to Bristol-Myers Squibb, GlaxoSmithKline, Gilead S
received research funding to the University of North Carolina (UNC) E
scientific advisory boards or has received consulting income from Bris
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research grants from Merck, Gilead, and Bristol-Myers Squibb. All oth

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

ABSTRACT

BACKGROUND
In sub-Saharan Africa, the burden of human immunodeficiency virus (HIV)–associated tuberculosis is high. We conducted a trial with a 2-by-2 factorial design to assess the benefits of early antiretroviral therapy (ART), 6-month isoniazid preventive therapy (IPT), or both among HIV-infected adults with high CD4+ cell counts in Ivory Coast.

METHODS
We included participants who had HIV type 1 infection and a CD4+ count of less than 800 cells per cubic millimeter and who met no criteria for starting ART according to World Health Organization (WHO) guidelines. Participants were randomly assigned to one of four treatment groups: deferred ART (ART initiation according to WHO criteria), deferred ART plus IPT, early ART (immediate ART initiation), or early ART plus IPT. The primary end point was a composite of diseases included in the case definition of the acquired immunodeficiency syndrome (AIDS), non-AIDS-defining cancer, non-AIDS-defining invasive bacterial disease, or death from any cause at 30 months. We used Cox proportional models to compare outcomes between the deferred-ART and early-ART strategies and between the IPT and no-IPT strategies.

RESULTS
A total of 2056 patients (41% with a baseline CD4+ count of ≥500 cells per cubic millimeter) were followed for 4757 patient-years. A total of 204 primary end-point events were observed (3.8 events per 100 person-years; 95% confidence interval [CI], 3.3 to 4.4), including 68 in patients with a baseline CD4+ count of at least 500 cells per cubic millimeter (3.2 events per 100 person-years; 95% CI, 2.4 to 4.0). Tuberculosis and invasive bacterial diseases accounted for 42% and 27% of primary end-point events, respectively. The risk of death or severe HIV-related illness was lower with early ART than with deferred ART (adjusted hazard ratio, 0.56; 95% CI, 0.41 to 0.76; adjusted hazard ratio among patients with a baseline CD4+ count of ≥500 cells per cubic millimeter, 0.56; 95% CI, 0.33 to 0.94) and lower with IPT than with no IPT (adjusted hazard ratio, 0.65; 95% CI, 0.48 to 0.88; adjusted hazard ratio among patients with a baseline CD4+ count of ≥500 cells per cubic millimeter, 0.61; 95% CI, 0.36 to 1.01). The 30-month probability of grade 3 or 4 adverse events did not differ significantly among the strategies.

CONCLUSIONS
In this African country, immediate ART and 6 months of IPT independently led to lower rates of severe illness than did deferred ART and no IPT, both overall and among patients with CD4+ counts of at least 500 cells per cubic millimeter. (Funded by the French National Agency for Research on AIDS and Viral Hepatitis; TEMPRANO ANRS 12136 ClinicalTrials.gov number, NCT00495651.)

The members of the writing group, who are listed in the Appendix, assume responsibility for the content and integrity of this article. Address reprint requests to Dr. Anglaret at INSERM Unité 897, Université de Bordeaux, 146 rue Léo Saignat, 33076 Bordeaux, France, or at xavier.anglaret@isped.u-bordeaux2.fr.

*A list of additional members of the TEMPRANO ANRS 12136 Study Group is provided in the Supplementary Appendix, available at NEJM.org.

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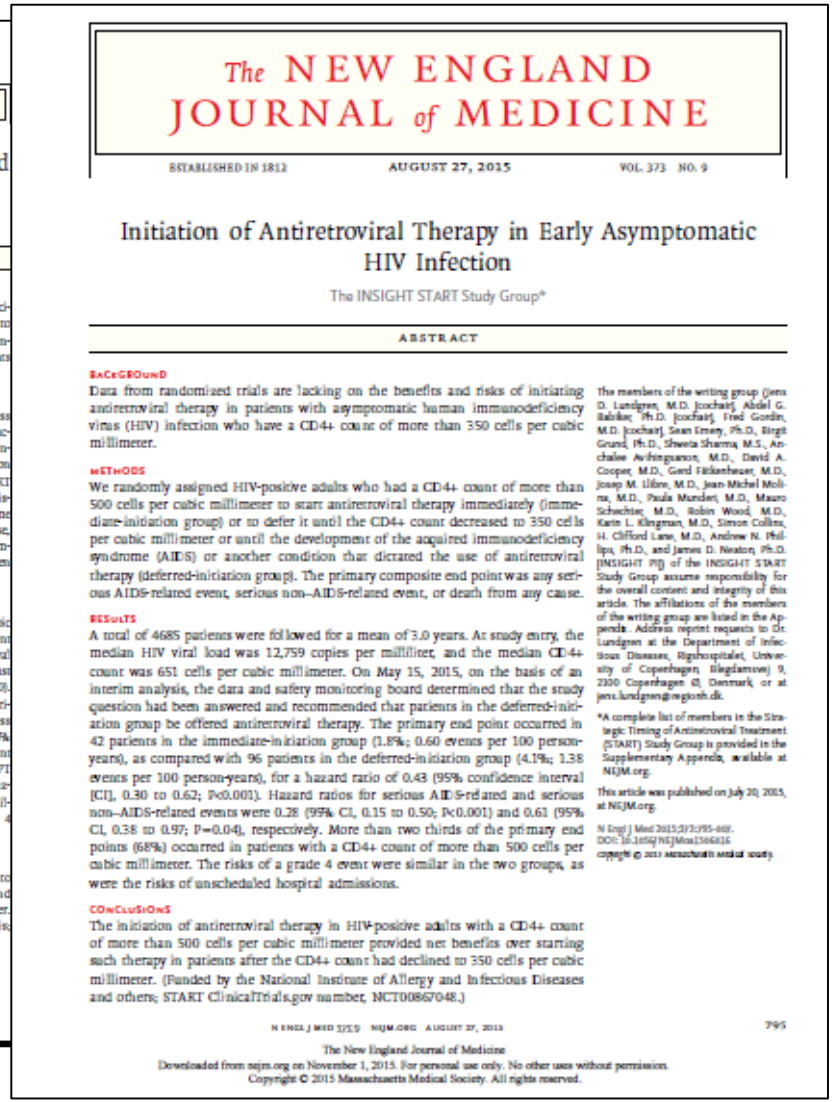

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Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

ABSTRACT

BACKGROUND
Data from randomized trials are lacking on the benefits and risks of initiating antiretroviral therapy in patients with asymptomatic human immunodeficiency virus (HIV) infection who have a CD4+ count of more than 350 cells per cubic millimeter.

METHODS
We randomly assigned HIV-positive adults who had a CD4+ count of more than 500 cells per cubic millimeter to start antiretroviral therapy immediately (immediate-initiation group) or to defer it until the CD4+ count decreased to 350 cells per cubic millimeter or until the development of the acquired immunodeficiency syndrome (AIDS) or another condition that dictated the use of antiretroviral therapy (deferred-initiation group). The primary composite end point was any serious AIDS-related event, serious non–AIDS-related event, or death from any cause.

RESULTS
A total of 4685 patients were followed for a mean of 3.0 years. At study entry, the median HIV viral load was 12,759 copies per milliliter, and the median CD4+ count was 651 cells per cubic millimeter. On May 15, 2015, on the basis of an interim analysis, the data and safety monitoring board determined that the study question had been answered and recommended that patients in the deferred-initiation group be offered antiretroviral therapy. The primary end point occurred in 42 patients in the immediate-initiation group (1.8%; 0.60 events per 100 person-years), as compared with 96 patients in the deferred-initiation group (4.1%; 1.38 events per 100 person-years), for a hazard ratio of 0.43 (95% confidence interval [CI], 0.30 to 0.62; P<0.001). Hazard ratios for serious AIDS-related and serious non–AIDS-related events were 0.28 (95% CI, 0.15 to 0.50; P<0.001) and 0.61 (95% CI, 0.38 to 0.97; P=0.04), respectively. More than two thirds of the primary end points (68%) occurred in patients with a CD4+ count of more than 500 cells per cubic millimeter. The risks of a grade 4 event were similar in the two groups, as were the risks of unscheduled hospital admissions.

CONCLUSIONS
The initiation of antiretroviral therapy in HIV-positive adults with a CD4+ count of more than 500 cells per cubic millimeter provided net benefits over starting such therapy in patients after the CD4+ count had declined to 350 cells per cubic millimeter. (Funded by the National Institute of Allergy and Infectious Diseases and others; START ClinicalTrials.gov number, NCT00867048.)

The members of the writing group (Jens D. Lundgren, M.D. [cochair], Abdel G. Babiker, Ph.D. [cochair], Fred Gordin, M.D. [cochair], Sean Emery, Ph.D., Birgit Grund, Ph.D., Shweta Sharma, M.S., Anchalee Avihingsanon, M.D., David A. Cooper, M.D., Gerd Fätkenheuer, M.D., Josep M. Llibre, M.D., Jean-Michel Molina, M.D., Paula Munderi, M.D., Mauro Schechter, M.D., Robin Wood, M.D., Karin L. Klingman, M.D., Simon Collins, H. Clifford Lane, M.D., Andrew N. Phillips, Ph.D., and James D. Neaton, Ph.D. [INSIGHT PI]) of the INSIGHT START Study Group assume responsibility for the overall content and integrity of this article. The affiliations of the members of the writing group are listed in the Appendix. Address reprint requests to Dr. Lundgren at the Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark, or at jens.lundgren@regionh.dk.

*A complete list of members in the Strategic Timing of Antiretroviral Treatment (START) Study Group is provided in the Supplementary Appendix, available at NEJM.org.

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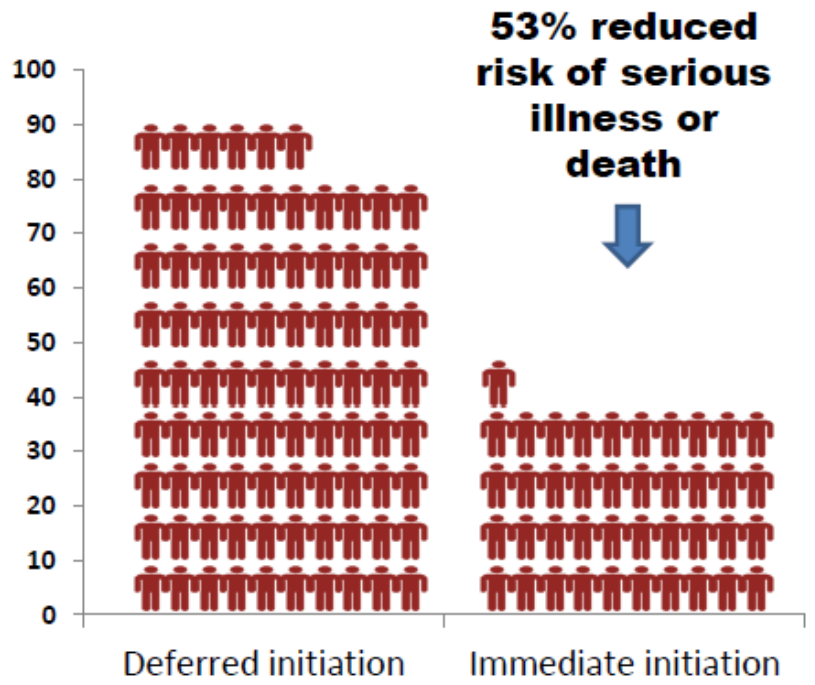
Inicio inmediato de TARV mejora el resultado en pacientes

Now we have **strong evidence** that early initiation significantly improves patient outcomes

START trial

Instances of AIDS, serious non-AIDS events or death



*Slide borrowed from CHAI presentation

Estudios en diversas poblaciones encontraron que, el inicio temprano esta asociado con mejores resultados.

Number of participants and location

HPTN052

- Total: 1761
  - Africa 54%

TEMPRANO

- Total: 2056
  - Africa 100%

START

- Total: 4651
  - Africa 21%

HPTN052: Grinsztejn, *Lancet Infect Dis* 2014; 14:281-90
Temprano: Temprano study group, *NEJM* 2015; 373:808-22
START: INSIGHT START study group, *NEJM* 2015; 373:795-807

Angalret ANRS Sept 2015

Implementación de P/T o Acceso Universal a ARVs

- Varios países han iniciado ya esta nueva estrategia para ciertas poblaciones: Opción B+, TB/HIV, hepatitis/HIV, Trabajadoras del sexo, HSH
  - Uganda – tratando a todos los niños menores de 15 años VIH positivos desde 2014.
  - Thailandia – empezó un estudio en 2012 tratando a HSH y población transgénero
  - Vietnam -- empezó un programa de T/T para usuarios de drogas desde 2014

- Varios países han empezado programas piloto de P/T en población general o a pequeña escala: Zambia, Kenya
- Múltiples estudios en poblaciones clave están siendo llevados por los CDC
- Brasil implementó P/T en población general desde 2013

PORQUÉ PEPFAR ESTA POYANDO LA INICIATIVA DE PRUEBA/TRATAMIENTO?

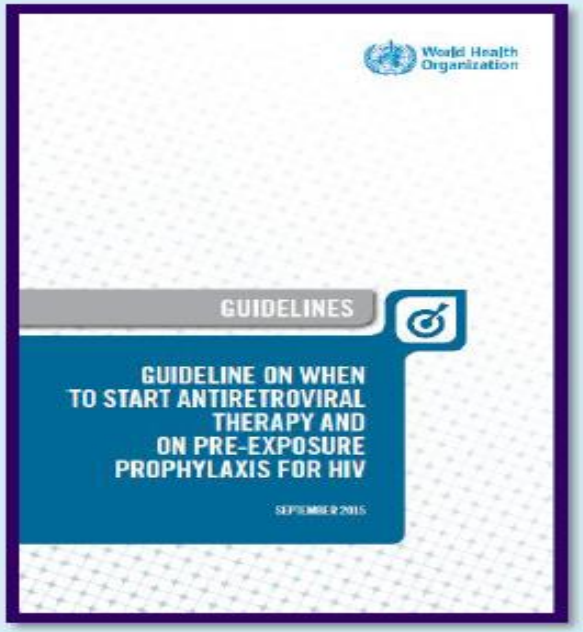
Acción Acelerada

1. Hacer las cosas correctas (eficiencia en las asignaciones)
2. En los lugares correctos (Maximización de Equidad, Eficiencia Técnica)
3. De la manera correcta (Eficiencia Técnica, Sostenibilidad)
4. Ahora mismo (fondos invertidos Genera ahorros)

El tratamiento es clave para logar 90-90-90

Cosas correctas

- ARVT
- Circuncisión masculina
- PTMI-Opción B+
- Condones
- **TEST/ TRATAMIENTO**
- **PrEP**
- PPE

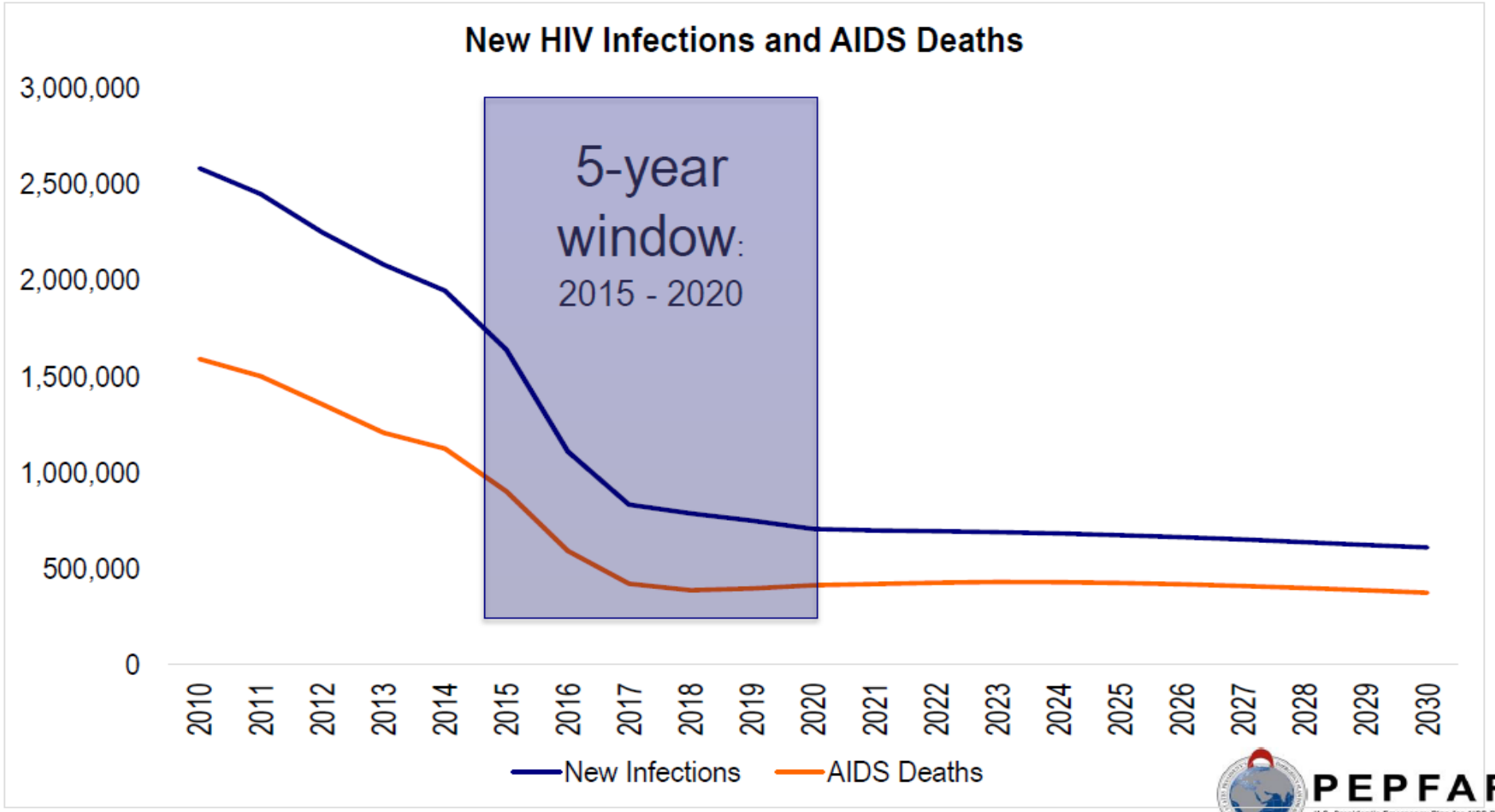


PEPFAR apoya la iniciativa de ONUSIDA “fast-track” Accion Acelerada para contener el VIH

- Metas de tratamiento de 90/90/90 para poner fin a la epidemia mundial del VIH
  - Alcanzar las metas fijadas para el 2020 y el 2030
  - Clave para recordar, es que las metas de tratamiento están basadas sobre la presunción de que el tratamiento de VIH no solo mantiene vivas a las personas, mejoran su calidad de vida, sino también previenen la transmisión del VIH.

PEPFAR

Treatment for All: 28M on ART by 2020



PEPFAR
U.S. President's Emergency Plan for AIDS Relief

Source: Stover, 2015

Retos para lograr el 90/90/90

- Limitado espacio físico e infraestructura de laboratorio
- Limitado personal de salud?
- Brechas en la Cascada persisten, oportunidades perdidas y falta de seguimiento.
- Introducir nuevos e innovadores modelos de entrega de servicios, para alcanzar una masiva cobertura en servicios de TARV.

Metas para mejorar la entrega de servicios

- Optimizar el uso de la actual infraestructura y recurso humano
- Reducir las barreras al tratamiento (medicas, administrativas, estigma, etc.) y centrar el cuidado en el paciente a través de un algoritmo simplificado de atención.
- **Incrementar la adherencia y retención a la TARV a través de modelos innovadores**
- Mantener/mejorar la calidad de los servicios de atención.

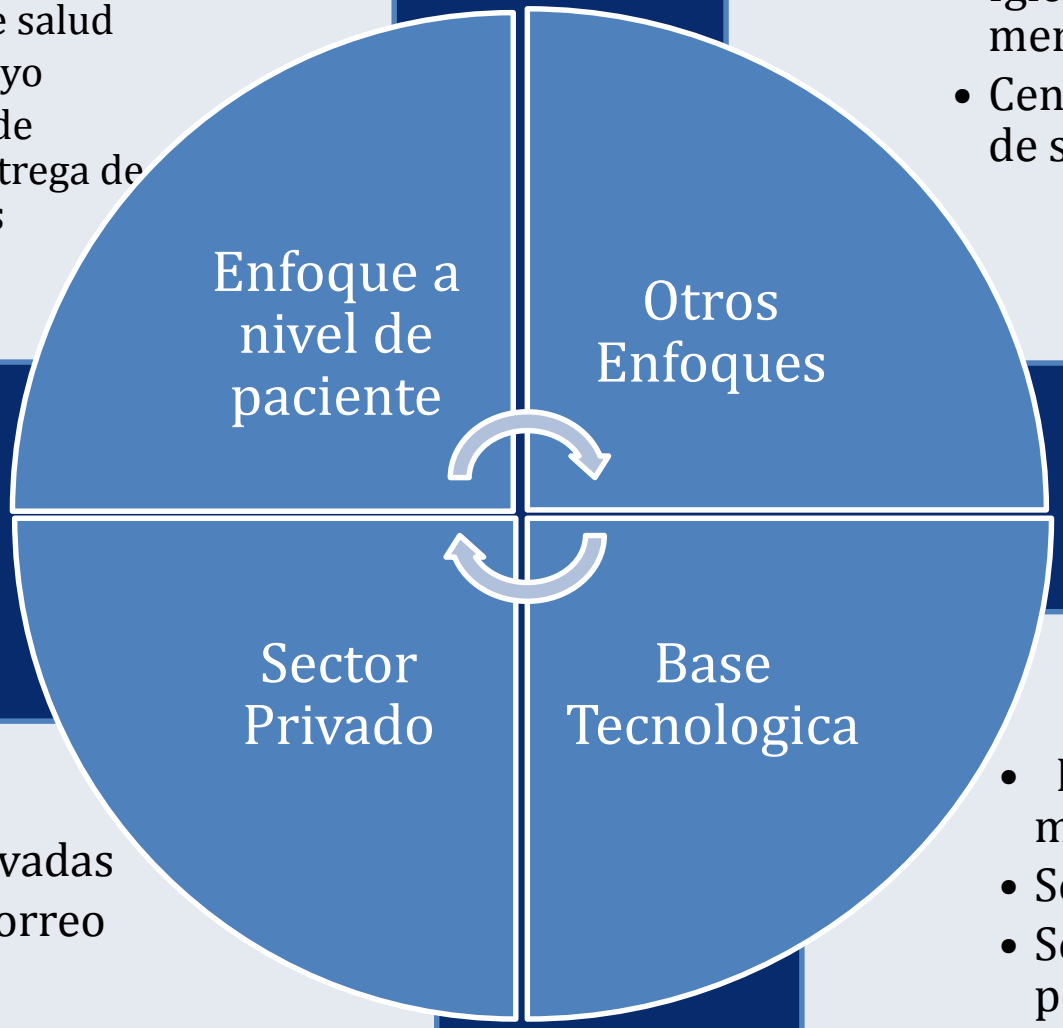
Modelos diferenciados de entrega de servicios

- Eficientar la entrega de servicios fuera de un establecimiento de salud?
  - Modelos comunitarios deben ser considerados y discutidos
  - Modelo de MSF esta siendo evaluado, principalmente en paises con epidemia generalizada
- Entrega de servicios de atención diferenciados por paciente?
  - Por ejemplo, enfermos, saludables, estables, en TARV por años, adherentes: promover entregas para varios meses, reducir las visitas a las clinicas, promover la visita domiciliaria, etc.

Modelos de entrega de servicios de ART

- Clubs de adherencia comunitarios.
- Promotores de salud
- Grupos de apoyo
- Rastreadores de pacientes y entrega de medicamentos
- TAES

- Clinicas moviles
- Iglesias y mercados
- Centros-puestos de salud



- Farmacias privadas
- Entrega por correo

- Kioscos medicos
- Sector privado
- Seguimiento por SMS

Apoyo de PEPFAR para Prueba/Tratamiento

- Promover como un medio para aumentar el tratamiento y poner fin a la epidemia del SIDA

- Sobre la base de apoyo de los objetivos de tratamiento, PEPFAR va a colaborar con la OPS, ONUSIDA, FM para apoyar acciones a nivel de la política

- Asegúrese de que las lagunas financieras y de los costos de tratamiento son identificadas y tratadas

Apoyo de PEPFAR para Prueba/Tratamiento

- Apoyar el análisis de los costos y la rentabilidad de proporcionar un tratamiento más temprano

- Abogar por una financiación innovadora de fuentes nacionales

- Promover nuevos modelos de prestación de servicios que sean mas eficientes