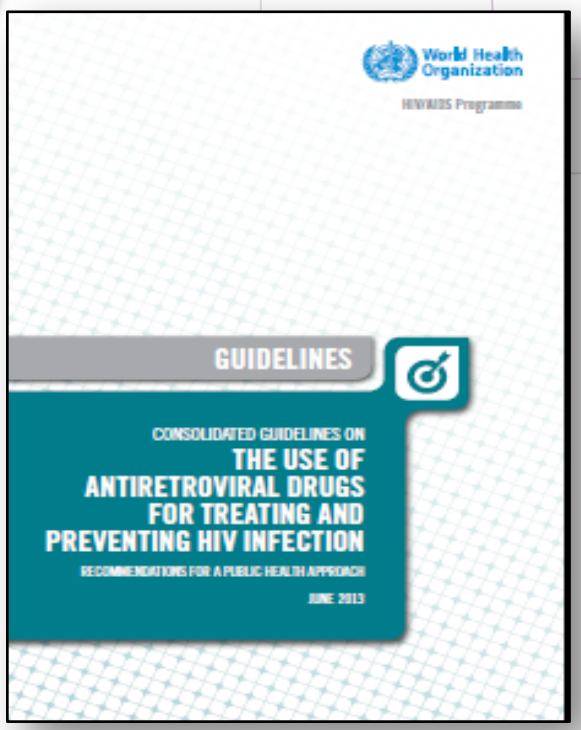
WHO Consolidated Guidelines on the use of ARV drugs for treating and preventing HIV infection

Dr. Gottfried Hirnschall
Director HIV Department WHO, Geneva



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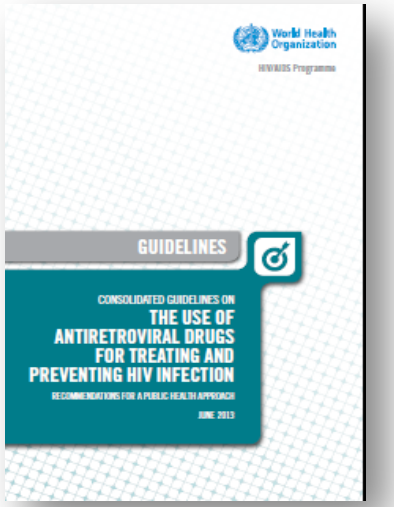
WHO 2013 Consolidated ARV Guidelines



WHAT TO DO?

- When to start or switch
- Which regimen to use
- How to monitor
- Co-infections & co-morbidities

HOW TO DO IT?

- Service delivery
- Diagnostics
- Drug supply

HOW TO DECIDE?

- Prioritization
- Equity and ethics
- Monitoring & Evaluation

Simplification and consolidation across:

- Continuum of HIV care
- Ages and populations
- Clinical, operational and programmatic
- Existing and new recommendations

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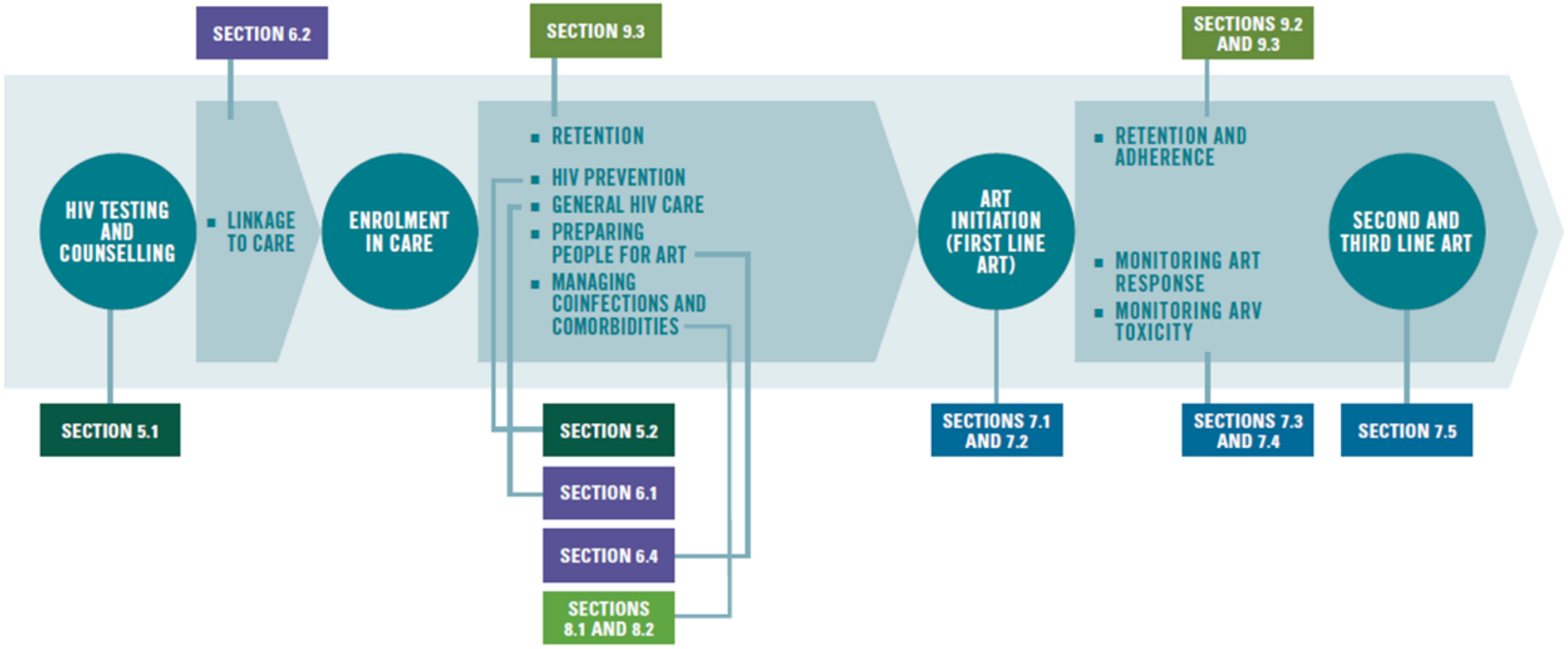
6 CHAPTERS: ALONG THE CONTINUUM OF CARE



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When to Start ART

World Health Organization

HIV TREATMENT

When to start ART

- Threshold moved to ≤ 500 CD4 NEW
- Priority for reaching all HIV+ symptomatic persons and those with CD4 ≤ 350
- More CD4-independent situations for ART initiation (in addition to HIV/TB coinfection and HBV advanced liver disease):
  - HIV serodiscordant couples NEW
  - Pregnancy NEW
  - Children less than 5 years of age NEW

GL are a "tool" for countries to produce their own guidelines: they will adapt the new threshold(s) with operational / programmatic local context

HIV TREATMENT

Populations With No Specific Recommendations

Insufficient evidence and/or favorable risk-benefit profile for ART initiation at CD4 > 500 cells/mm^3 (or regardless of CD4 count) in the following situations:

- ✓ **Individuals with HIV who are 50 years of age and older**
- ✓ **Individuals co-infected with HIV and HCV**
- ✓ **Individuals with HIV-2**
- ✓ **Key populations with a high risk of HIV transmission (e.g.: MSM, sex workers, IDU)**

These populations should follow the same principles and recommendations as for other adults with HIV

HIV TREATMENT

Recommendations

"Option B+"

"Option B"

All pregnant and breastfeeding women infected with HIV should initiate triple ARVs (ART), which should be maintained at least for the duration of mother-to-child transmission risk. Women meeting treatment eligibility criteria should continue lifelong ART .

(strong recommendation, moderate-quality evidence)

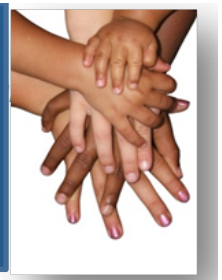
For programmatic and operational reasons, particularly in generalized epidemics, all pregnant and breastfeeding women infected with HIV should initiate ART as lifelong treatment.

(conditional recommendation, low-quality evidence)

In some countries, for women who are not eligible for ART for their own health, consideration can be given to stopping the ARV regimen after the period of mother-to-child transmission risk has ceased.

(conditional recommendation, low-quality evidence)

Children When to start ART



AGE GROUP	2010 RECOMMENDATIONS
<1 YEARS	Treat ALL Strong recommendation, moderate-quality evidence
1-2 YEARS	Treat ALL Conditional recommendation, very-low-quality evidence
2-5 YEARS	Initiate ART with CD4 count ⩽750 cells/mm3 or <25%, irrespective of WHO clinical stage
≥5 YEARS	Initiate ART with CD4 count ⩽350 cells/mm3 (As in adults), irrespective of WHO clinical stage AND WHO clinical stage 3 or 4

AGE GROUP	2013 RECOMMENDATIONS
< 1 YEAR	Treat ALL Strong recommendation, moderate-quality evidence
1-5 YEARS	Treat ALL Conditional recommendation, very-low-quality evidence Priority: children < 2 years or WHO stage 3-4 or CD4 count ≤ 750 cells/mm3 or < 25%
≥5 YEARS	CD4 ≤ 500 cells/mm3 Conditional recommendation, very-low-quality evidence CD4 ≤350 cells/mm³ as a priority (As in Adults) Strong recommendation, moderate-quality evidence

WHAT ART REGIMEN TO START

World Health Organization

Rationale: One Regimen For All

Preferred 1st line regimen:
TDF + 3TC (or FTC) + EFV

- **Simplicity:** regimen is very **effective, well tolerated** and available as a single, **once-daily FDC** and therefore easy to prescribe and easy to take for patients – facilitates adherence
- **Harmonizes regimens** across range of populations (Adults, Pregnant Women (1st trimester), Children >3 years, TB and Hepatitis B)
- **Simplifies drug procurement** and supply chain by reducing number of preferred regimens (phasing out d4T)
- **Safety in pregnancy**
- **Efficacy against HBV**
- **EFV is preferred NNRTI** for people with HIV and TB (pharmacological compatibility with TB drugs) and HIV and HBV coinfection (less risk of hepatic toxicity)
- **Affordability** (cost declined significantly since 2010)

HOW TO MONITOR AND WHEN TO SWITCH

World Health Organization

HIV TREATMENT

Recommendations: Monitoring for ART Response

RECOMMENDATION	STRENGTH
Viral load is recommended as the preferred monitoring approach to diagnose and confirm ARV treatment failure	***Strong recommendation, low-quality evidence*** NEW
If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure	***Strong recommendation, moderate-quality evidence***

HIV TREATMENT

Summary Adult MCH Guidelines

HIV/AIDS Department

Topic	2002	2003	2006	2010	2013
When to start	CD4 ≤200	CD4 ≤ 200	CD4 ≤ 200 - Consider 350 - CD4 ≤ 350 for TB	CD4 ≤ 350 -Irrespective CD4 for TB and HBV	**CD4 ≤ 500** -Irrespective CD4 for TB, HBV, PW and SDC - **CD4 ≤ 350 as priority**
1st Line	8 options - AZT preferred	4 options - AZT preferred	8 options - AZT or TDFpreferred - d4T dose reduction	6 options &FDCs - AZT or TDF preferred - d4T phase out	**1 preferred option & FDCs** - TDF and EFV preferred across all populations
2nd Line	Boosted and non-boosted PIs	Boosted PIs -IDV/r LPV/r, SQV/r	Boosted PI - ATV/r, DRV/r, FPV/r LPV/r, SQV/r	Boosted PI - Heat stable FDC: ATV/r, LPV/r	**Boosted PIs** - Heat stable FDC: ATV/r, LPV/r
3rd Line	None	None	None	DRV/r, RAL, ETV	**DRV/r, RAL, ETV**
Viral Load Testing	No	No (Desirable)	Yes (Tertiary centers)	Yes (Phase in approach)	**Yes** (preferred for monitoring, use of PoC, DBS)

Earlier initiation

Simpler treatment

Less toxic, more robust regimens

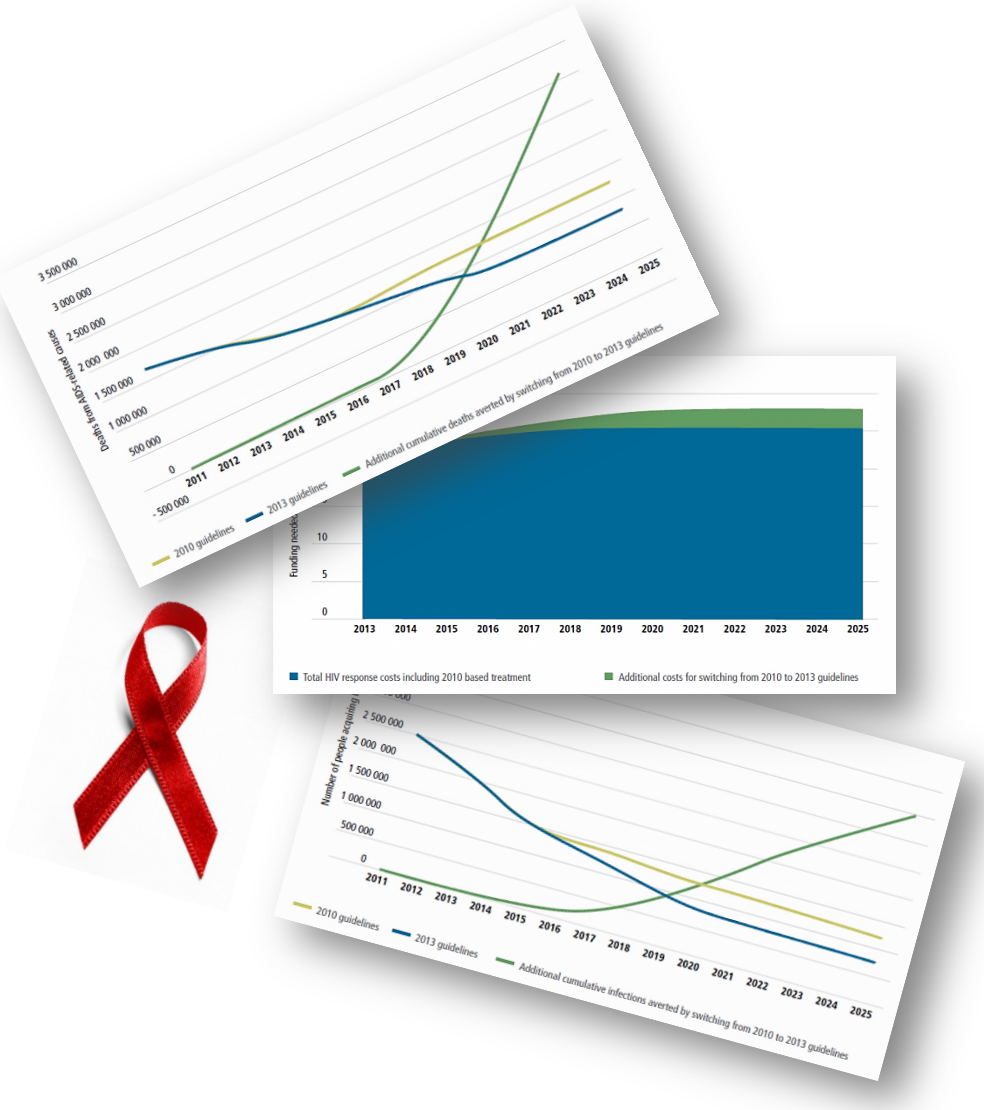
Better monitoring

Key WHO Operational and Service Delivery Recommendations

- Expanded testing scenarios
- Task shifting and decentralization
- Service integration
- Adherence support
- Retention in care

HIV TREATMENT

Projected impact of the new recommendations



- **Mortality**
- **Incidence**
- **Cost**

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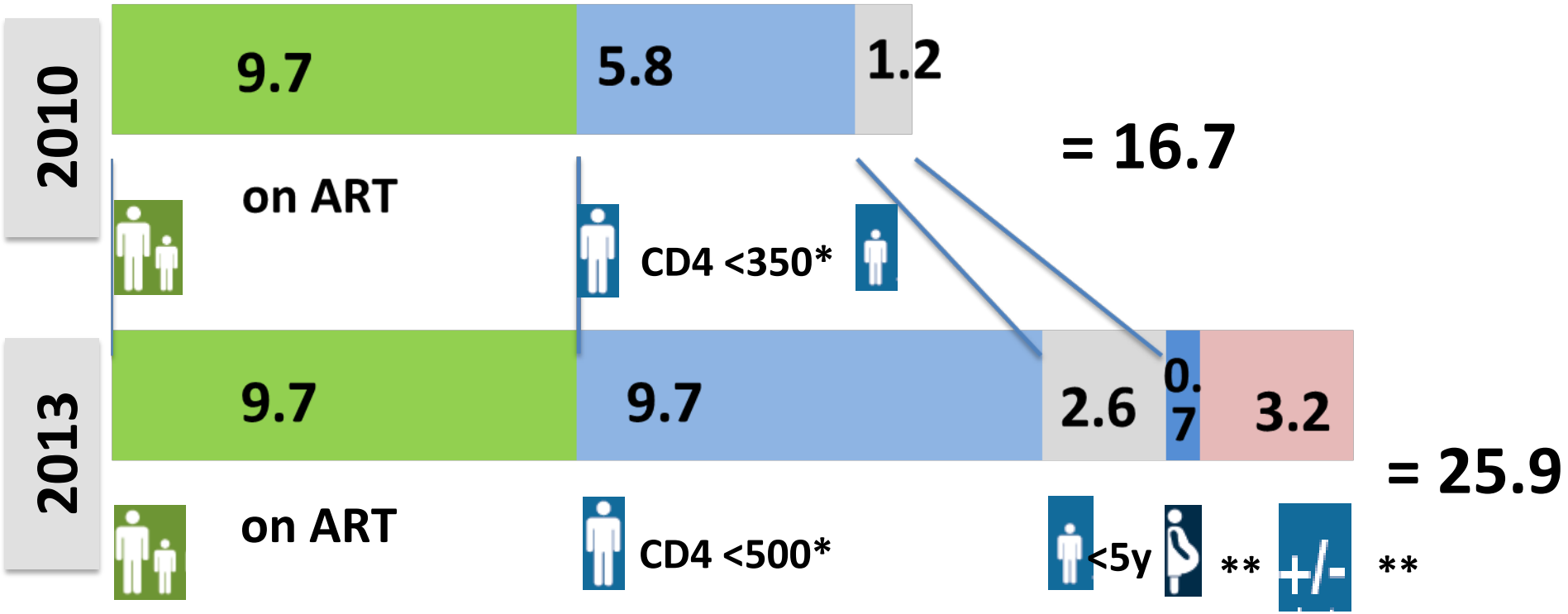
HIV TREATMENT

Estimated impact on ART eligibility of implementing the new recommendations



Number of people eligible for ART in low- and middle-income countries in million per WHO 2010 and 2013 ARV guidelines, based on end of 2012 epidemic situation

* incl. co-infected with TB or HBV ** only CD4>500, others included in adults

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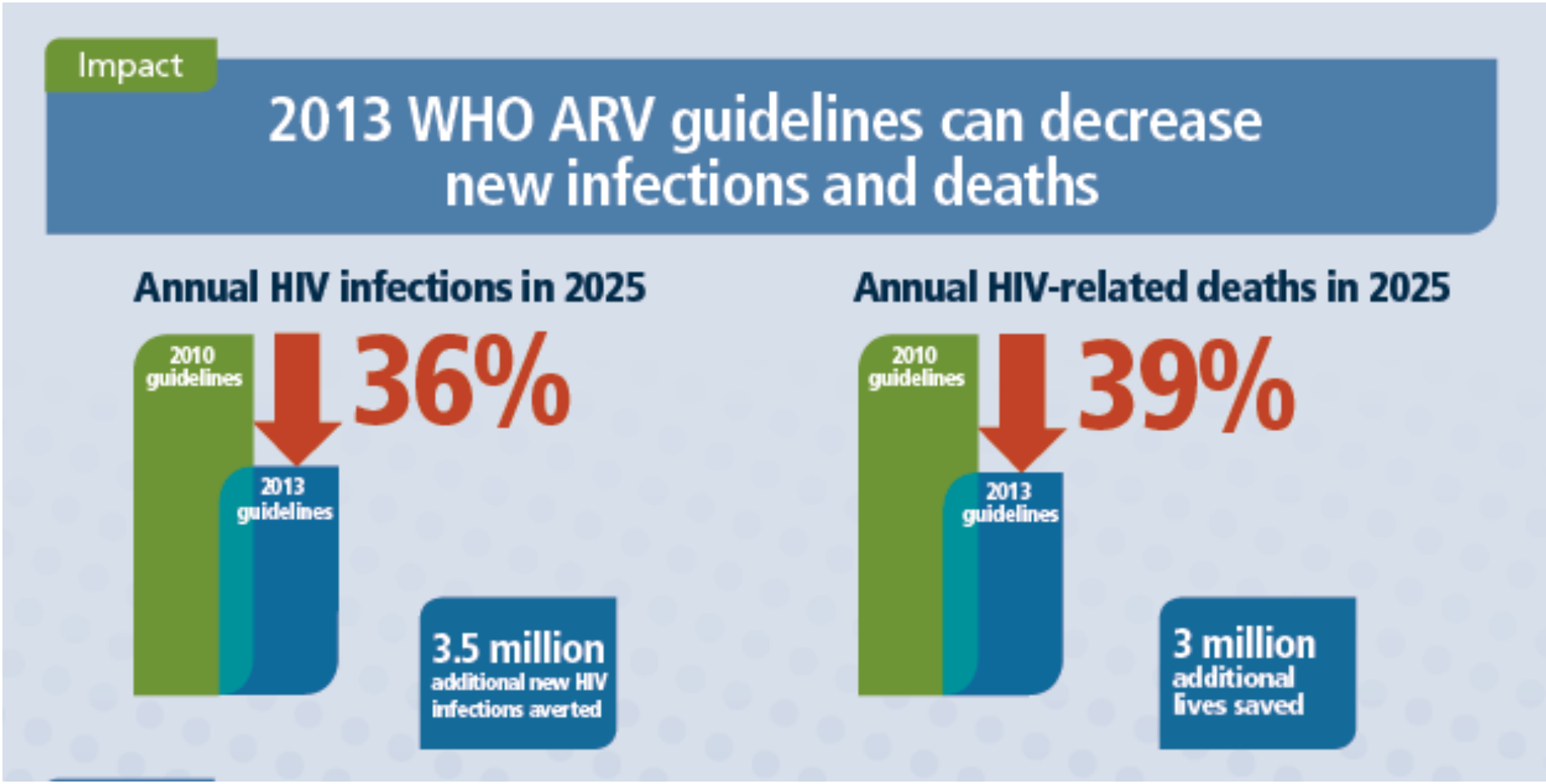
Estimated impact on incidence and deaths of implementing the new recommendations



WHO Global ART report, 2013

HIV TREATMENT

Summary Recommendations

Consolidation across:

- Continuum of HIV care
- Ages and populations
- Clinical, operational and programmatic guidance
- Existing and new recommendations

Key new recommendations:

- Earlier ART initiation ≤ CD4 500
- Single, preferred 1st line regimen (FDC)
- Lifelong ART for pregnant and breastfeeding women
- Immediate ART all children < 5 years
- Move to viral load monitoring
- Integration of ART into other services
- Decentralization and task-shifting
- Adherence support

Implications and impact (to 2015)

- Additional 3 million HIV-related deaths averted
- Additional 3.5 new HIV infections averted
- Cost - additional 10% on top of total resource needs

HIV TREATMENT

Next Steps

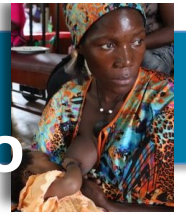
- Guidelines Dissemination meetings & opportunities to have regional and country level discussion around adaption:
  - Indonesia (SEARO) – July
  - South Africa (ESA) – July
  - Rwanda - August
  - Argentina (PAHO) - August
  - China (WPRO & SEARO) - September
  - Morocco (EMRO) - October
  - Ghana (WCA) – November
  - Europe (EURO) – November
  - Haiti / Carribean (PHCO) – TBD
  - ICAAP & ICASA meetings
- Opportunities to explore country level acceptability, feasibility, implications and costs of new guidelines

HIV TREATMENT

Extra Slides

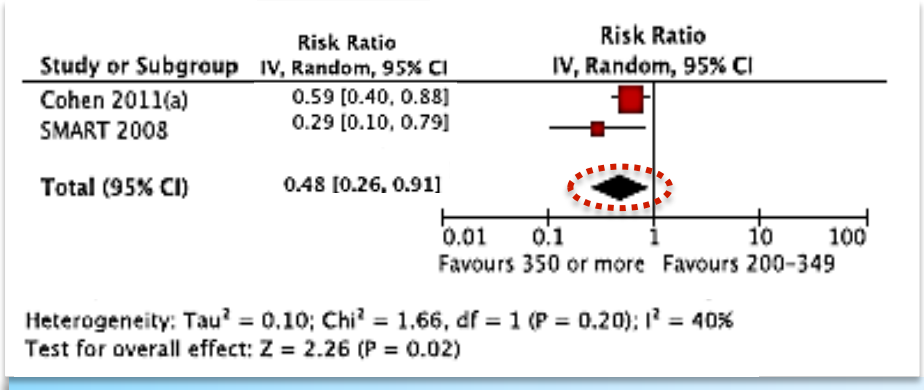
HIV TREATMENT

Evidence Summary: Risk of Death and/or Progression to



RCTs – SMART / HPTN 052

Risk of Death or Progression to AIDS



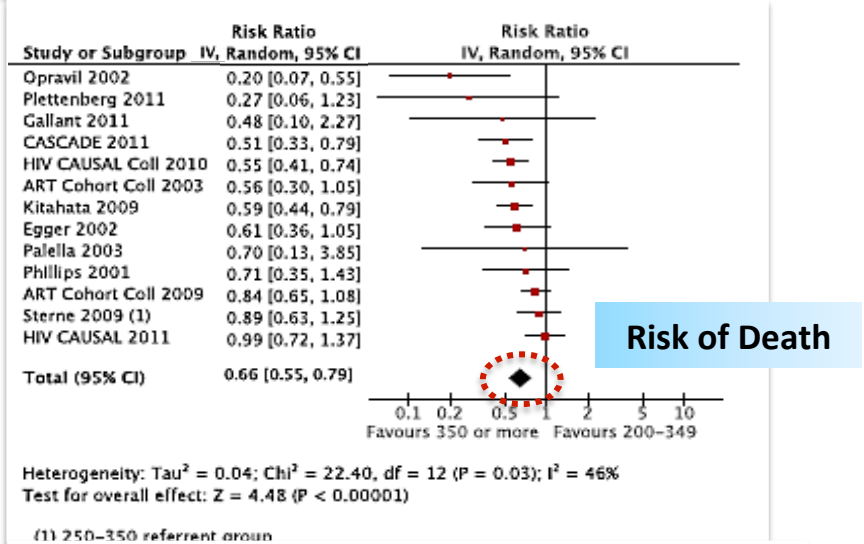
Clinical Trials (2 RCTs)

Low quality evidence for lower risk of progression to AIDS or death with early ART

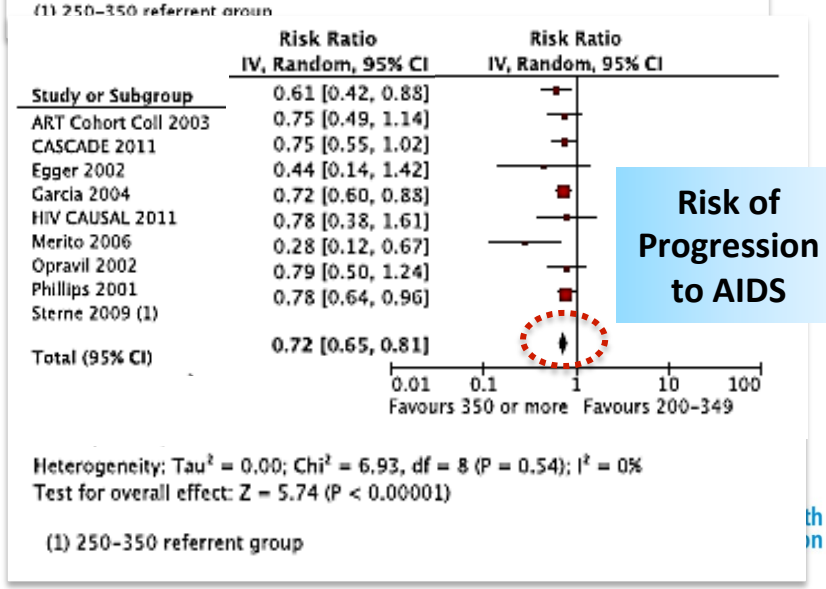
Observational studies

Moderate quality evidence for lower risk of death (**13 studies)** or progression to AIDS (**9 studies**) with early ART

Observational data



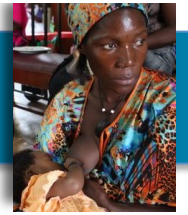
Risk of Death



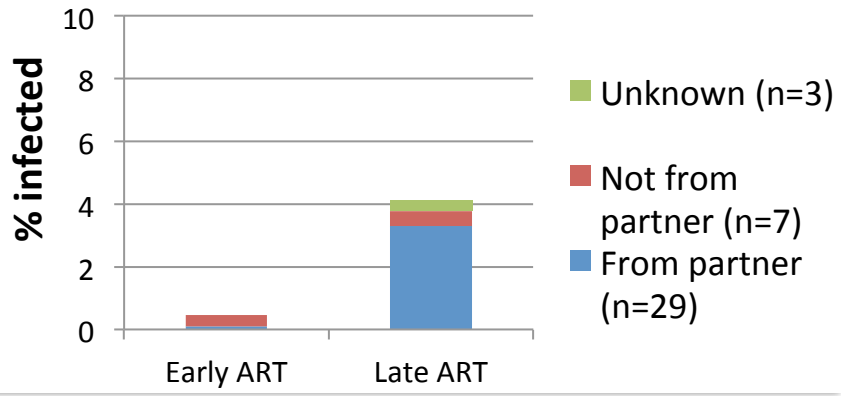
Risk of Progression to AIDS

HIV TREATMENT

Evidence Summary: Risk of HIV Sexual Transmission

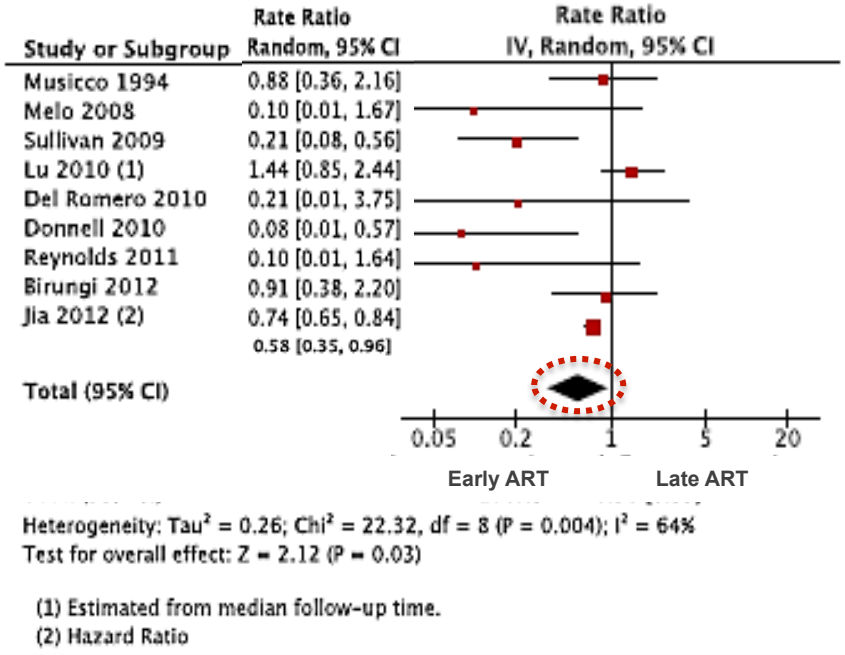


Clinical Trial - HPTN 052



- RCT on efficacy of ART to prevent HIV transmission between discordant couples
- HIV+ partner with CD4 ≥ 350-550 cells/µL randomized to early vs. delayed ART
- Significant HIV prevention benefit – **a 96% reduction** in transmission.
- 1 genetically linked infection in early ART arm versus 29 infections in delayed arm.

Observational data



RCT and Observational data

- High to moderate quality evidence that treatment prevents sexual transmission of HIV (**1 RCT and observational data**)

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What's the evidence?

- **CHER trial (young infant)**

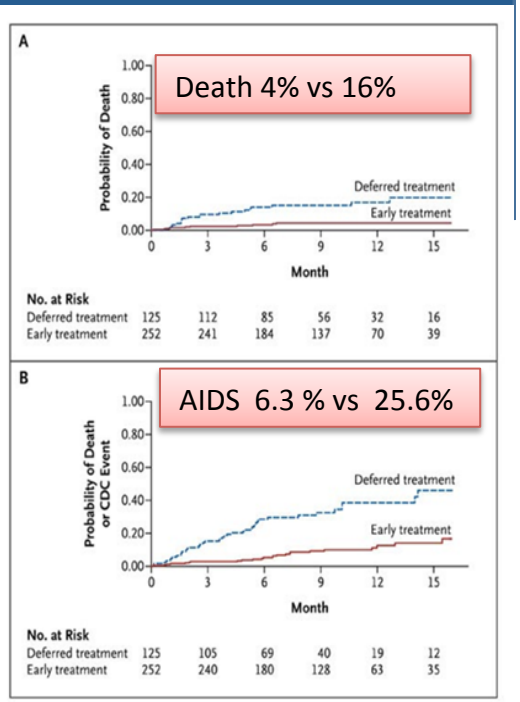
Early ART reduces mortality and HIV progression by 75%

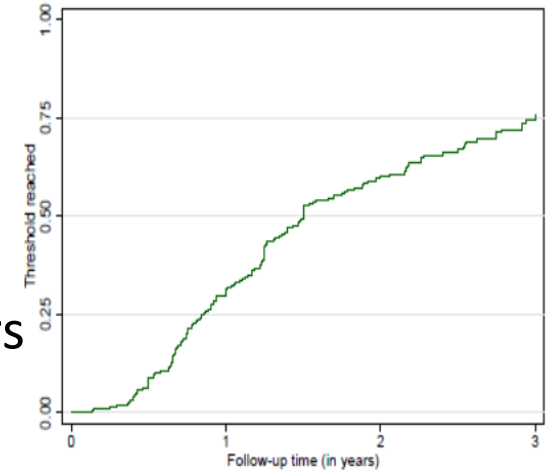
- **PREDICT trial (1-12 years)**

AIDS-free survival did not differ between deferred and early treatment group (median age 6.4 years).

- **IeDea SA: (2-5 years)**

Modelling of observational data showed no difference in mortality between early and starting ART based on current CD4 threshold. However, 75% of children with CD4 > 25% (or 750 cells/mm3) become eligible by 3 years from enrolment.





1 *Violari A. NEJM 2008;359:2233-44.*
2 *Puthanakit T.* Lancet Infect Dis 2012:933-941.
3 Schomaker M. IeDEA Southern Africa Collaboration 2012

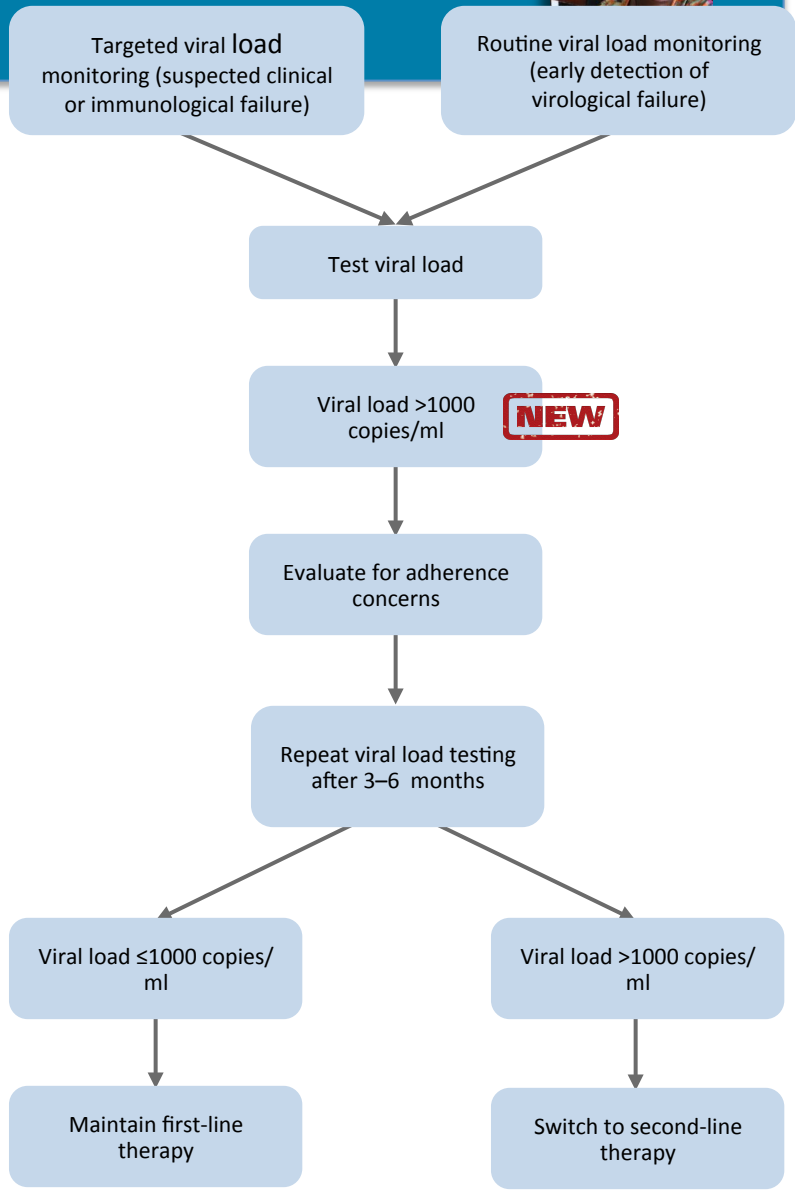
IAS 2013 KUALA LUMPUR, MALAYSIA

World Health Organization

HIV TREATMENT

Rationale: for VL

- Lack of viral load or CD4 capacity should not prevent starting ART
- If VL availability limited, phase in use of targeted approach (or CD4/ clinical monitoring)
- Same for adults & children
- Earlier capture of treatment failure & reducing HIVDR
- Help discriminate between treatment failure & non-adherence



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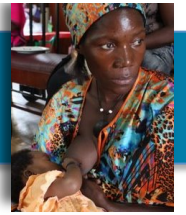
HIV TREATMENT

ARVs and breastfeeding



2013 (no change from 2010)

National agencies should decide between promoting mothers with HIV to either breastfeed and receive ARV interventions or to avoid all breastfeeding

Where the national choice is to promote BF, mothers whose infants are HIV uninfected or of unknown HIV status should:

- exclusively breastfeed their infants for the first six months of life
- introduce appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life
- breastfeeding should then only stop once a nutritionally adequate and safe diet without breast-milk can be provided
  (strong recommendation, high-quality evidence for the first 6 months; low-quality evidence for the recommendation of 12 months)

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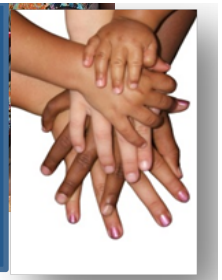
What ART to start in Children



< 3 Years	Prior PMTCT ARV's	2013 recommendations
<12 months	Exposed	LPV/r plus 2 NRTIs If LPV/r not available, NVP-based Plus NRTI backbone: • AZT or ABC + 3TC • (d4T+3TC*)
	Not Exposed	
	Exposure unknown	
12 to <36 months	Regardless of exposure	

≥ 3 Years	2013 recommendations	
3-10 years (Including > 10 yrs who weighing <35kg)	NNRTI	EFV is preferred NVP as alternative
	2NRTIs	In preferential order: ABC + 3TC AZT or TDF + 3TC or FTC
10-19 years (weighing ≥35 kg) (align with adults)	NNRTI	EFV is preferred NVP as alternative
	2NRTIs	In preferential order: TDF + FTC or 3TC ABC + 3TC AZT + 3TC

- When HIV RNA monitoring is available, consider to substitute LPV/r with NNRTI after virological suppression is sustained (conditional, low quality)

IAS 2013 KUALA LUMPUR MALAYSIA

World Health Organization

Expanded testing and linkage to care

WHO 2013 Recommendations:

- Generalized epidemics: community-based HIV testing in addition to PITC

- Concentrated epidemics: community-based HIV testing for key populations in addition to PITC

- provider-initiated testing & counselling (PITC)
- Adolescent testing & counselling

HIV TREATMENT

Decentralization: Bringing ART closer to communities

WHO 2013 Recommendations:

- Initiation and maintenance of ART in peripheral primary facilities

- Initiation of ART in peripheral primary facilities and maintenance at community level between clinic visits.

HIV TREATMENT

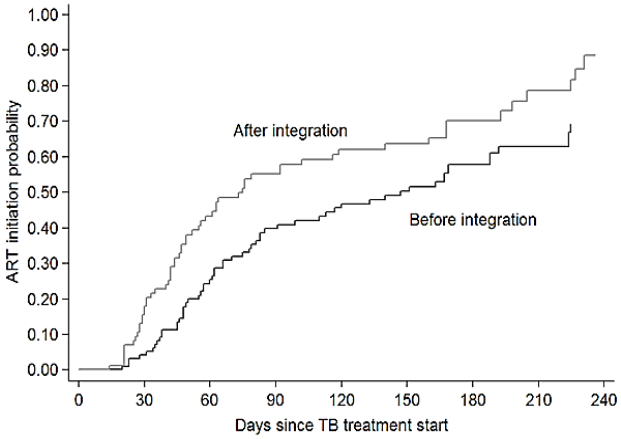
Task shifting: nurses and non-physician clinicians providing care and treatment

WHO 2013 Recommendations:

- Trained non-physician clinicians, midwives and nurses can **initiate** first-line ART and **maintain** treatment
- Trained and supervised community health workers can **dispense** ART between clinic visits.

HIV TREATMENT

Service integration: Responding to co-morbidities and multiple needs



WHO 2013 Recommendations:
Initiate and maintain ART in :

- TB care settings
- MCH/ANC settings
- OST settings with linkage to continued HIV care and treatment

World Health Organization

HIV TREATMENT

Adherence support: combinations of interventions

WHO 2013 Recommendations: Combination of interventions

- Minimizing out of pocket payments
- Use of fixed-dose combinations
- Strengthening drug supply system
- Patient counselling and education
- Peer support
- Nutritional support in food insecure settings

- **Mobile phone text messages**

Global Advocates' Call to Discuss the WHO Consolidated Guidelines on ART

Community Perspectives on the 2013 WHO Consolidated Guidelines & the Community Guide on ART for Treatment and Prevention

Moono Nyambe (GNP+)

Overview

I. Community Voices that informed the 2013 Guidelines

II. Community Response to the 2013 Guidelines

III. Community Guide on ART for Treatment and Prevention

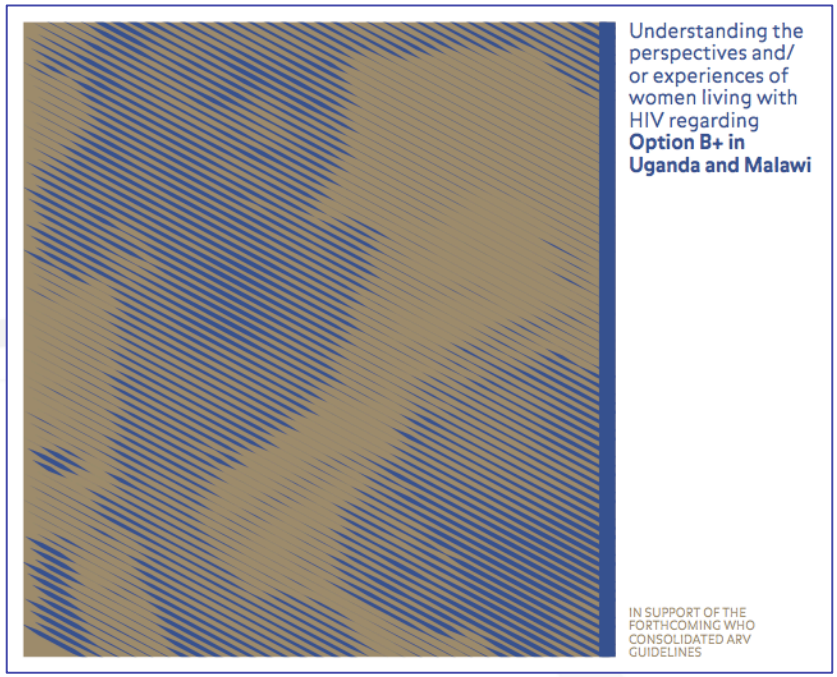
I. Community Voices that informed the 2013 Guidelines

I. Community Voices: Community Consultation

- E-Survey
  - 1088 Responses
  - 6 Languages
- E-Forum Discussion
  - 155 Responses
  - 5 Languages
- Held in November & December 2012

- Topics included:
  - **Clinical** - Testing and Counseling, When to start, What to start (for adults, adolescents, pregnant and breastfeeding women, children, people with co-infections)
  - **Operational** – Access to ARV treatment, Decentralization, Community Roles
  - **Programmatic** – criteria for national decision-making

I. Community Voices: Focus Group Discussions



- Held in Malawi and Uganda (November 2012)
- WLHIV and their partners
  - 8 Groups (n=88)
  - Characteristics: rural/ urban, Muslim, young, leadership/professionals
- Focused on "Option B+"

ICW Global
International Community of Women Living With HIV/AIDS

COWLHA
Coalition of Women Living with HIV and AIDS

International Community of Women Living with HIV & AIDS Eastern Africa


Universal access to
treatment, care, and support saves lives!
LAMIVUDINE & STAVUDINE TABLETS
LAMISTAR - 40
Aspen Lamivudine Tablets
NEVIRAPINE TABLETS 200 mg
Nevivir
60 Tablets
EFAVIRENZ CAPSULES 200 mg
ESTIVA
90 Capsules
STOCRIN
600
ZIDOVUDINE TABLETS USP 300 mg
Zido - H
STOCRIN
aspen
ARV DISP

II. Community Response: In General

- Supportive of initiating treatment when CD4<500 cells/mm^3
- Country conditions matter
- Concerned about recommendations made based on low quality evidence

II. Community Response

- Will these recommendations become a reality for people living with HIV?
  - Inconsistent supply causing inadvertent resistance
  - Lack of access to food, water, refrigeration, all needed for ARVs to be effective
  - Unprepared health systems
  - Inadequate support families to adhere to regimens

III. Community Role in 2013 Guidelines Implementation

Rationale for the *Community Guide on ART for Treatment and Prevention*

I. Community Voices (#1)

ARV programming for treatment and prevention should employ a ***human rights based approach***, including rights assessments and monitoring and the mitigation and repeal of harmful policies and laws.

I. Community Voices (#2)

ARV programming for treatmetn and prevention must recognize the importance of the ***full involvement of people living with HIV and key affected communities*** in operational research and in planning, implementing, and evaluating high-quality, rights-based HIV combination prevention, treatment and care programmes

I. Community Voices (#3)

To be effective and appropriately meet the comprehensive needs of people living with HIV, their sexual partners and family members, treatment programmes need to ***include behavioural and structural interventions***

I. Community Voices (#4)

Prioritize addressing social and legal impediments to ARV programming for treatment and prevention, including addressing stigma and discrimination, safe disclosure, gender-based violence, criminalization of HIV exposure, forced sterilization, among others

I. Community Voices (#5)

Guaranteed access (i.e. assured, available, and affordable) to ARVs, regular monitoring, addressing service and lab quality and capacity constraints, and plugging the leaks in the treatment cascade are critical factors determining the success of ARV programming for treatment and prevention in many countries.

I. Community Voices (#6)

ARV programming for treatment and prevention that requires task-shifting/sharing must ***effectively involve communities as service providers*** and ***ensure sustainable task-shifting strategies***

I. Community Voices (#7)

Implementation of ARV for treatment and prevention requires consensus at all levels (e.g. national, district and local) and across all sectors on ***communication and messaging around the programmes' changes and implications***, based on proven principles of communication, including robust field-testing

III. Community Guide: Goal

- Support in-country partners to be in the best position to meet community demands stemming from ARV programming and research at country and regional level.

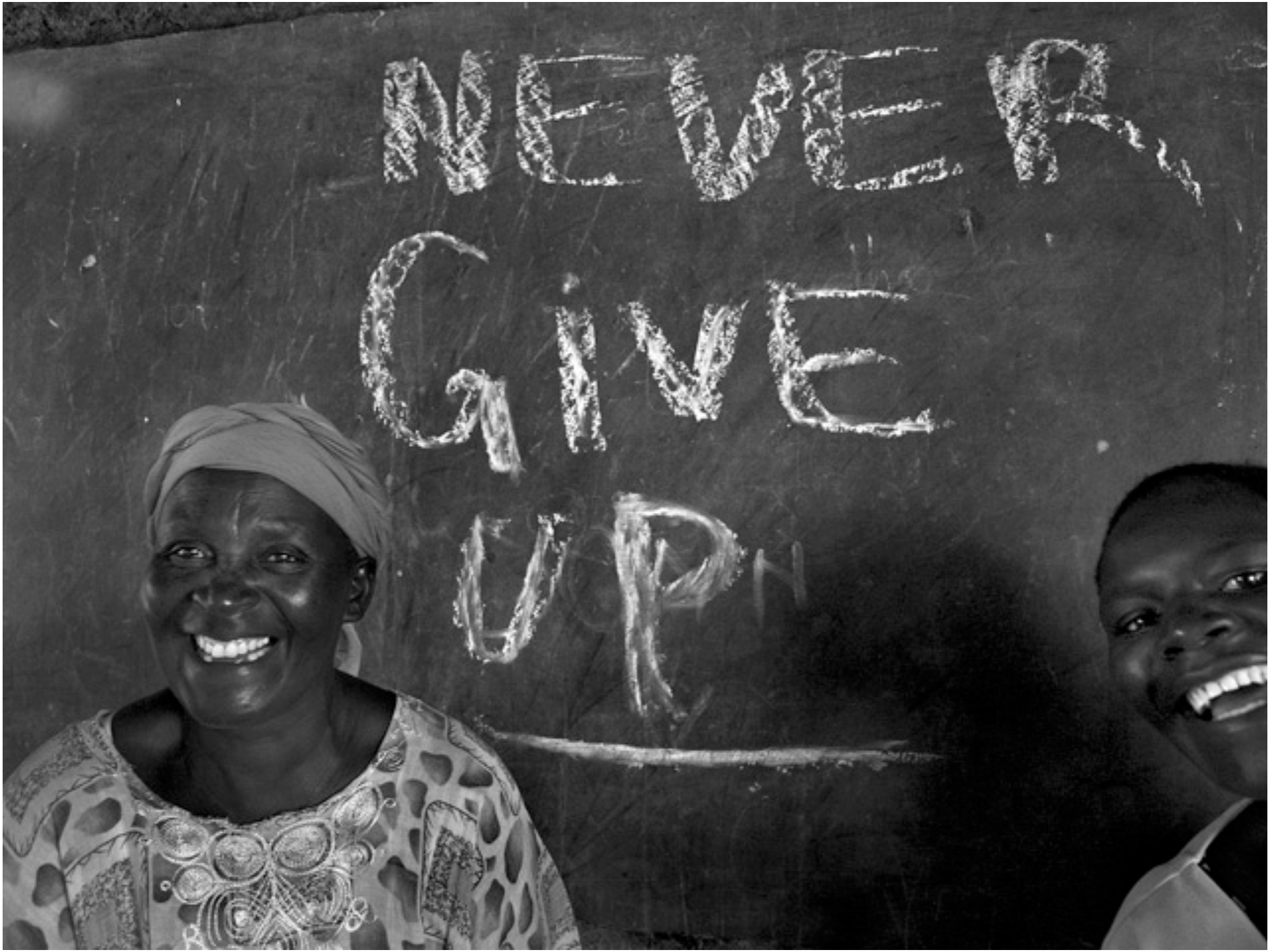
III. Community Guide: Objectives

1. Help our partners to understand what the 2013 WHO Consolidated ARV Guidelines
2. Prepare our partners for the roles they may need to play as ARV programming is discussed (at the policy level), planned for (at the programmatic level), rolled-out in their context (at the operational level), and researched/ evaluated (at the research/M&E level).
3. Support our partners to demonstrate the communities' added value in terms of health outcomes and integrated health and community systems strengthening when they contribute to service provision in ARV programming.

III. Community Guide Survey

We seek your input to identify the most important topics and the most effective means of sharing this Community Guide with you and your communities!

http://www.research.net/s/CommunityGuideSurvey


NEVER
GIVE
UP!!

Thank You!

For more information about the Community Consultations or the Community Guide, email:
ahsieh@gnpplus.net

To complete the Community Guide Survey, visit:

http://www.research.net/s/CommunityGuideSurvey