



***Une réponse scientifique au VIH en Afrique
de l'Ouest et Centrale:
Traduire les bonnes pratiques dans la mise en
place des politiques***

Abidjan, Côte d'Ivoire, 3-5 December 2017



FROM THE EVIDENCE OF SCIENCE TO THE REALITY IN THE FIELD

DES AVANCEES SCIENTIFIQUES A LA REALITE DU TERRAIN

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IAS TOOLKITS

TRACK C: PREVENTION SCIENCE

IAS 2017 HIGHLIGHTS

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OCTOBER 2017



Overview

Self-Testing

PopART
Zambia

Other African
Studies

eSTAMP
USA

Treatment as Prevention

Swaziland

Opposites
Attract

Oral PrEP

Roll out
of PrEP

On Demand
Regimen

On demand
or daily?

PlusPills

New PrEP Agents

Dapivirine
Vaginal
Ring

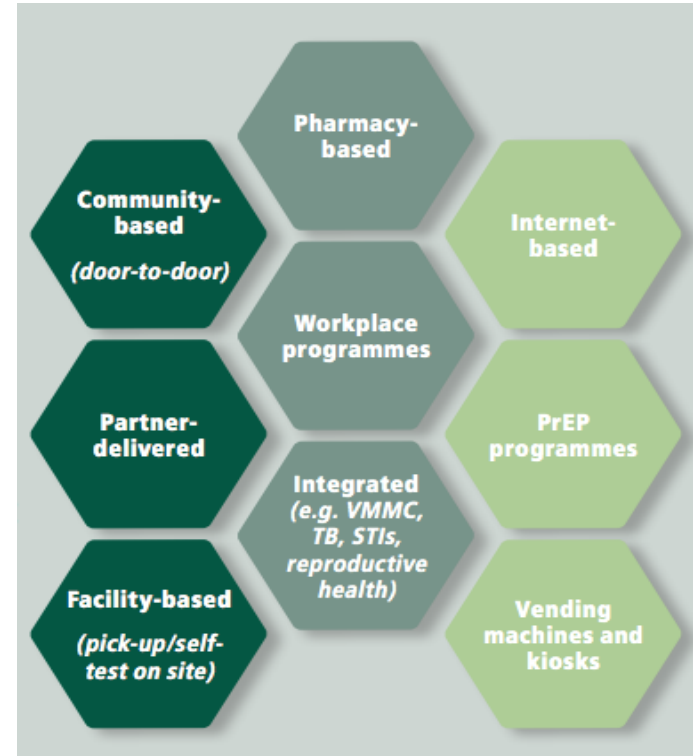
Injectable
Cabotegravir

Rilvipirine &
MK-8591



Other African Studies

- Numerous studies of self-testing (HIVST) in sub-Saharan Africa presented at IAS 2017
- Estimated size of the African self-testing market by 2020:
 - 3-5 million users with tests distributed through community channels
 - 11-15 million users with investment in distribution through pharmacies and healthcare facilities
- Secondary distribution to male partners by women attending antenatal services: randomised study in Uganda
 - Partners tested: 74% vs 36%
- **Self-testing feasible and acceptable for female sex workers in Zimbabwe and Zambia**
 - Linkage to care may be lower than in facility-based testing
 - No increase in intimate partner violence

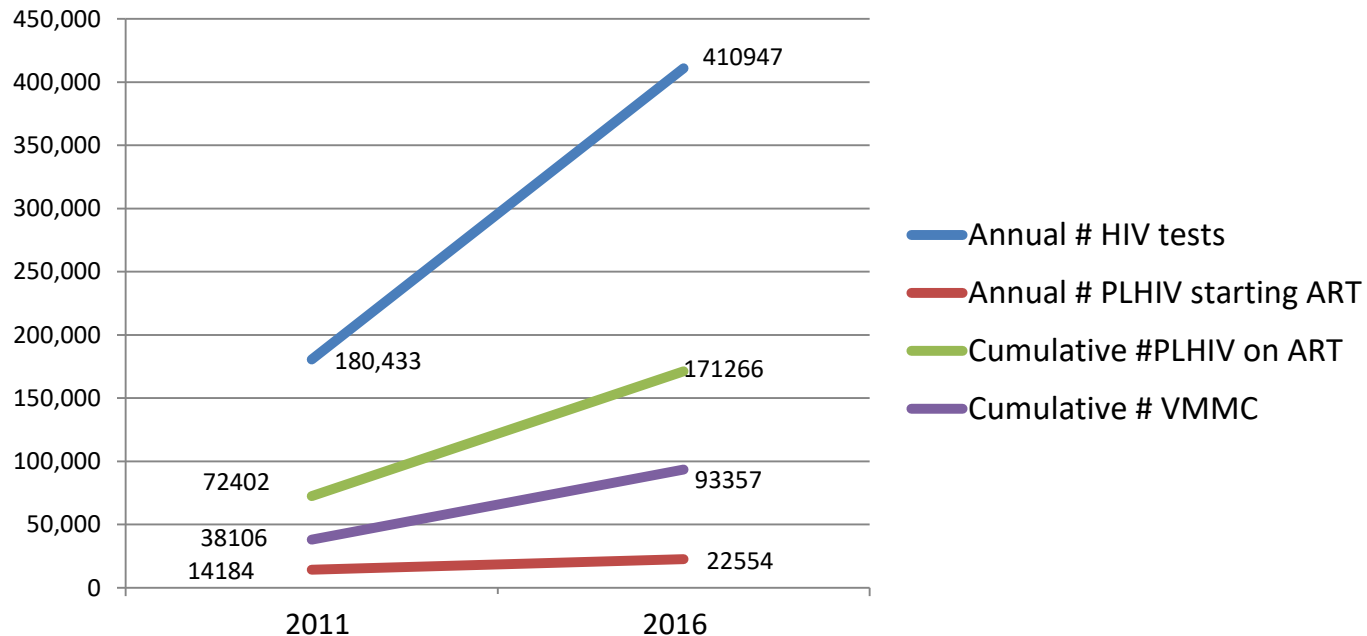




Treatment as Prevention

Swaziland

- **Convincing evidence that massively expanding HIV treatment coverage reduces new HIV infections (incidence) across the population**
- The study “shows that our efforts can pay off and is a proof of concept.”
 - Linda Gail-Bekker, International AIDS Society
- Swaziland: population 1.5 million, 79% rural, 32% living with HIV
- **Significant expansion of HIV testing, prevention and treatment services between 2011 and 2016:**

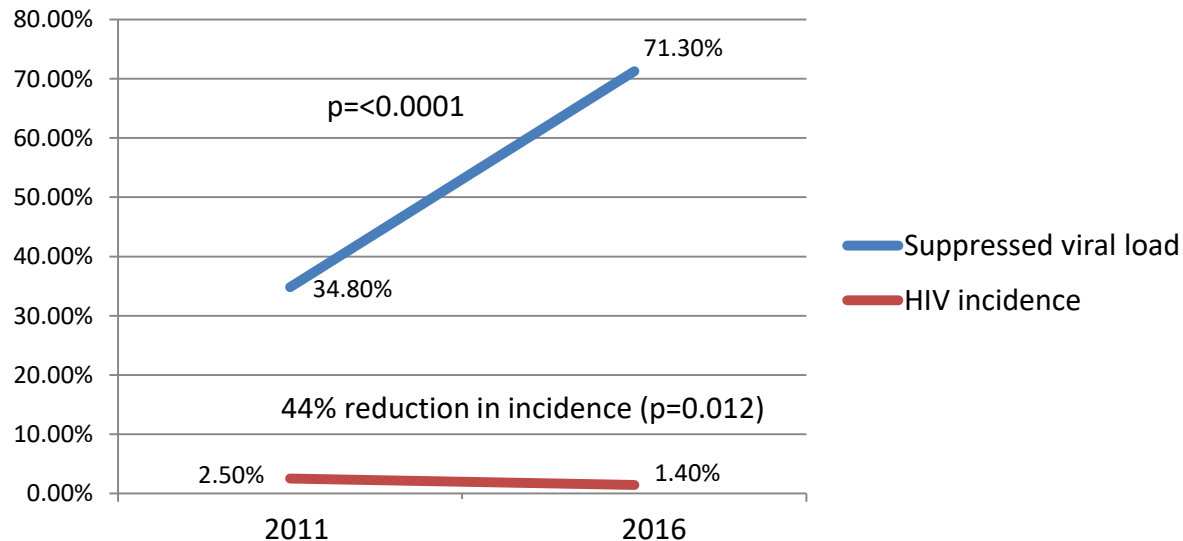




Treatment as Prevention

Swaziland

- Swaziland HIV Incidence Measurement Survey (nationally representative sample of the population) conducted in 2011 and 2016
- Progress to 90-90-90 targets: 85-87-92
- Remaining challenges:
 - Undiagnosed infection in 15-24 year olds (33.9% vs 12.9% in >25 years)
 - Unsuppressed viral load in 15-24 year olds on treatment (23.6% vs 6.7% in >25 years)
 - Undiagnosed infection in men (22.5% vs 11.4% in women)





Highlights

Promising developments

- Swaziland demonstrates that the ‘theory’ of treatment as prevention works in practice, at a population level
- Data to support a wider range of PrEP options, both agents and dosing schedules
- Self-testing helps individuals who do not engage with other testing services to learn their HIV status

Challenges

- Engaging younger people and men with HIV testing services and the treatment cascade
- Scaling up PrEP in the many countries where it is not currently available



Roll Out of PrEP

- PrEP is being effectively scaled up, mostly in countries where research was conducted (e.g. USA, France, Australia)
- Elsewhere much has been achieved without government support, through community and online mobilisation
- It's important to focus on what the 'consumer' wants
 - As seen in contraception, choice of method and choice of model of service delivery
- Urgently need to scale up PrEP implementation in at-risk populations
- “Give the power to the people, put the pill in their palms.” Sheena McCormack, UCL



*Yellow countries have some form of PrEP programming; blue countries do not.



Oral PrEP

On Demand or Daily?

- Qualitative study (AMPrEP) in Dutch MSM explored reasons why men chose on demand or daily regimens
- At baseline, 273 men chose daily and 103 chose on demand.
- Conclusion: give PrEP users a choice between regimens; allow choices to change as circumstances evolve

Reasons to choose daily or on-demand PrEP

	Daily PrEP (N=420)	n (%)	Event-driven PrEP (N=206)	n (%)
Expected adherence	Need for daily structure	133 (32%)	Issues with daily PrEP adherence	20 (10%)
	Issues with event-driven PrEP adherence	129 (31%)		
Perceived HIV risk	Unplanned/frequent sex	79 (19%)	Sex is planned	87 (42%)
			Low frequency of HIV risk	57 (28%)
Expected safety of the other regimen	Fear of side-effects related to event-driven PrEP reinitiation	5 (1%)	Toxicity and burden of daily medication	38 (19%)
	Fear of resistance development with event-driven PrEP	2 (<1%)		



Oral PrEP

PlusPills

- Early data on safety and acceptability of oral TDF/FTC PrEP in sexually active South African adolescents (15-19 years)
- 148 participants (99 female)
- Open-label demonstration study: daily PrEP + HIV prevention support
- PrEP was reasonably well tolerated with minimal safety concerns
- One HIV infection, in a 19 year old who had stopped PrEP 24 weeks previously
- Adherence decreased over time and with less frequent study visits:
 - Week 12 (monthly visits), 57% had detectable tenofovir
 - Week 48 (visits every 3 months), 38% had detectable tenofovir
- Side-effects and perceived side-effects were an important reason for PrEP discontinuations
- Conclusion: South African adolescents need access to PrEP with tailored adherence support and frequent clinic visits

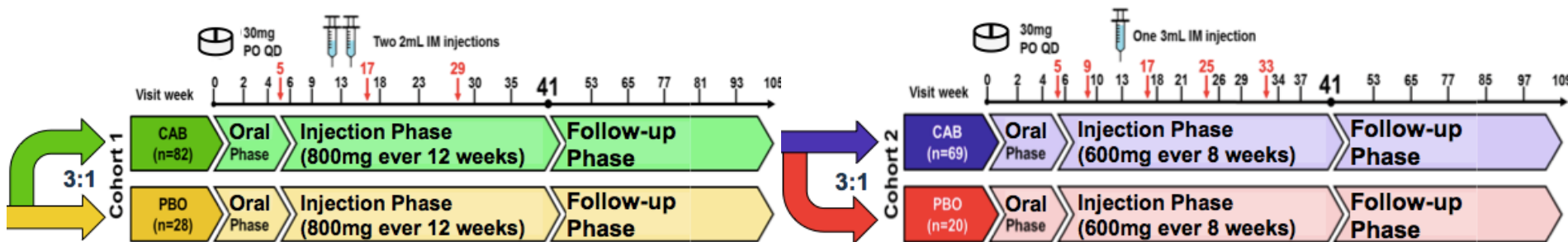
PLU  PILLS





Injectable Cabotegravir (strand-transfer integrase inhibitor)

- HPTN077: double-blind, randomised, placebo-controlled, phase II tolerability and pharmacokinetics study
- 199 male and female participants at low risk of HIV, assigned 3:1 to cabotegravir or placebo
 - Cohort 1: 800mg every 12 weeks
 - Cohort 2: 600mg every 8 weeks
- Adverse events: injection site pain (34% vs 2%) and headache (15% vs 2%)
 - Study withdrawals due to adverse events: 7.9% vs 2.1%
- Pharmacokinetic analyses: 600mg 8 week injections consistently met pre-specified pharmacokinetic targets for both sexes; are being evaluated in Phase 3 efficacy studies





IAS TOOLKITS

TRACK B: CLINICAL SCIENCE

IAS 2017 HIGHLIGHTS

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Overview

New Fixed Dose Combinations

Bictegravir/
FTC/TAF

Doravirine/
3TC/TDF

Darunavir/COBI/
FTC/TAF

Dual Therapy

Feasibility of
dual therapy

DTG/3
TC

DRV/r/
3TC

Other treatment
simplification strategies

Late Treatment Intensification

Epidemiology

Maraviroc treatment
intensification

Drug Resistance

Epidemiology

Hepatitis C
Co-Infection

Glecaprevir/
Pibrentasvir

Treatment in
West Africa



Do we need triple therapy for everyone for life?

- Requirements for dual therapy agents:
 - Potent, long half life, once daily, minimal side-effects, low primary resistance rates
- Treatment-naïve patients: dual ART with robust drugs is a realistic ART option for individuals with low to moderate viral load and good immune status
- Some guidelines now include dual therapy as an alternative option, when other therapies cannot be used
- Switching studies for treatment experienced patients - only two types of reduced drug regimens have matched the efficacy of triple therapy:
 - Boosted protease inhibitor + lamivudine
 - Dolutegravir + rilpivirine
- Rather than only assessing dual therapy by viral suppression, evaluation should also be based on residual viremia, persistent inflammation and immune activation, penetration in reservoirs, toxicity, and cost



Dual Therapy

DTG/3TC

- 120 participants in single-arm phase II study (ACTG A5353)
- Eligibility criteria: treatment naïve, viral load < 500,000 cpm, no major resistance mutations
- Interim analysis at 24 weeks
- **High rate of virologic suppression regardless of baseline viral load**
- 3 cases of virological failure, including one patient with emergent integrase resistance (M184V)

	Baseline HIV-1 RNA		Total N=120
	> 100,000 cpm N=37	≤ 100,000 cpm N=83	
Virologic success HIV-1 RNA < 50 cpm [95% CI]	33 (89%) [75%,97%]	75 (90%) [82%,96%]	108 (90%) [83%,95%]
Virologic non-success HIV-1 RNA ≥ 50 cpm	3 (8%) 3	2 (2%) 0	5 (4%) 3
Discontinued study treatment for other reasons while HIV RNA ≥ 50*	0	2	2

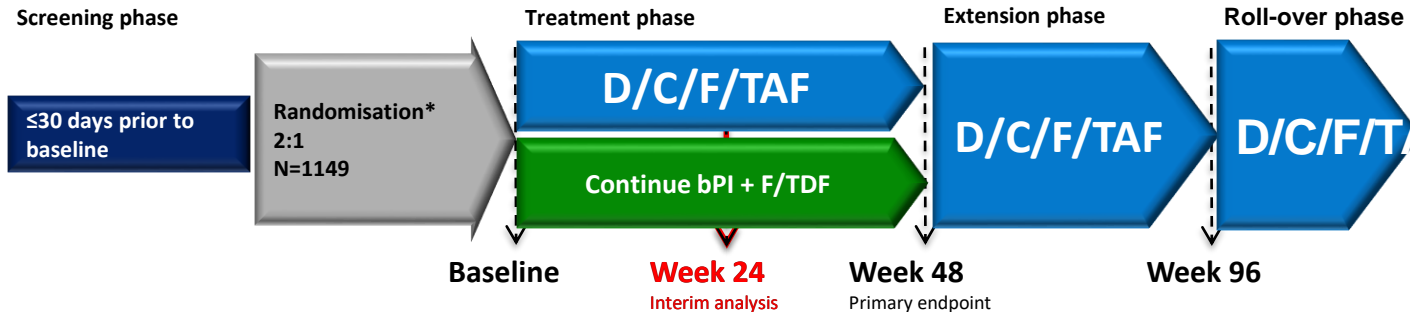
- Data from larger, comparative studies with longer follow-up are needed to confirm these findings - two phase III studies are ongoing

- Efficacy and safety of switching from boosted-protease inhibitors plus emtricitabine/tenofovir disoproxil fumarate regimens to the single-tablet regimen (STR) of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in virologically suppressed, HIV-1-infected adults through 24 weeks: EMERALD Study

- Jean-Michel Molina¹, Joel Gallant², Chloe Orkin³, Eugenia Negrodo⁴, Laveeza Bhatti⁵, Joseph Gathe⁶, Erika Van Landuyt⁷, Erkki Lathouwers⁷, Veerle Hufkens⁷, Simon Vanveggel⁷, Magda Opsomer⁷

¹Department of Infectious Diseases, St-Louis Hospital, University of Paris Diderot, Paris, France; ²Southwest CARE Center, Santa Fe, New Mexico, USA; ³Barts and Health NHS Trust, London, UK; ⁴Germans Trias i Pujol University Hospital, Badalona, Spain; ⁵AIDS Healthcare Foundation, Beverly Hills, California, USA; ⁶Therapeutic Concepts, Houston, Texas, USA; ⁷Janssen Pharmaceutica NV, Beerse, Belgium

EMERALD: Open-label, Randomised, Multicentre, Parallel-group, Non-inferiority Phase III Trial



Objective: Non-inferiority and safety of switching to D/C/F/TAF vs continuing bPI + FTC/TDF regimens in virologically suppressed HIV-1-infected adults at Week 48

Key inclusion criteria:

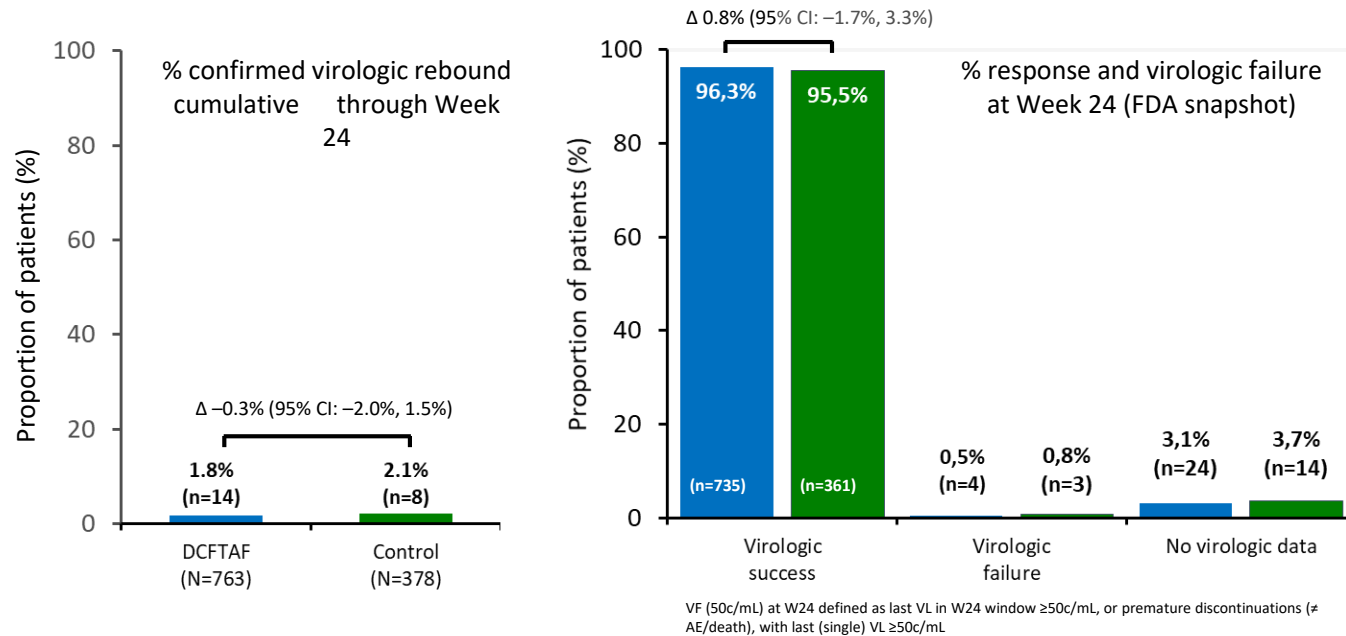
- Previous ART VF allowed
- Absence of history of VF on DRV, and if historical genotype available, absence of DRV RAMs[†]
- Viral load (VL) <50 c/mL for ≥2 months before screening; one VL ≥50 and <200 c/mL within 12 months prior to screening allowed
- Creatinine clearance (by Cockcroft-Gault) ≥50 mL/min

*Stratified by bPI (protease inhibitor boosted with low-dose ritonavir or COBI) at screening; [†]DRV RAMs: V111, V321, L33F, I47V, I50V, I54L or M, T74P, L76V, I84V or L89V (IAS-USA)

Molina JM, IAS 2017



Week 24 Efficacy



- Most rebounders (10/14 D/C/F/TAF and 5/8 control) resuppressed (<50 c/mL) by Week 24
- No confirmed rebounds ≥ 200 c/mL
- No discontinuations for VF
- **No DRV/primary PI or NRTI RAMs were observed** (2 patients genotyped in each group)

Molina JM, IAS 2017



**Safety of 400 mg Darunavir/100 mg Ritonavir with
TDF/FTC or ABC/3TC in Virologically Suppressed HIV-1 Infected Adults:
An Open-label Study – ANRS 165 Darulight
Molina JM¹, and the ANRS Darulight Study Group**

Pts (n, %)	N= 95
Treatment success	87 (91.6%)
Treatment failure	8 (8.4%)
Changed DRV dose without virologic failure	2
Virologic failure > 50 c/ml	6 (6.3%)
Virologic failure > 200 c/ml	2
Successful genotypic resistance test	3
Primary NRTI-RAMs	0
Primary PI-RAMs	0

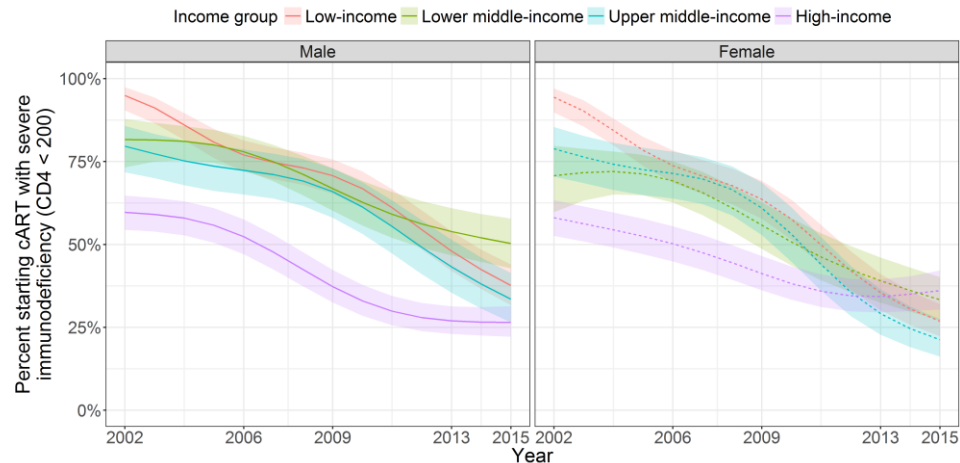
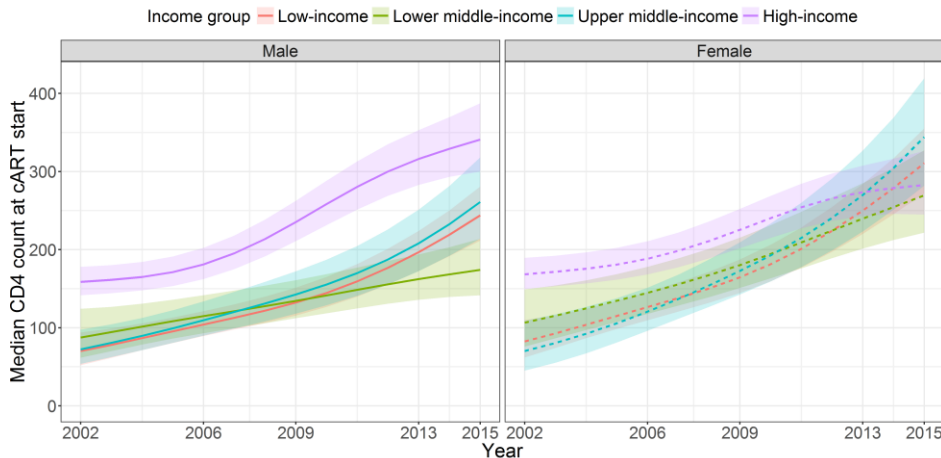
Molina JM, IAS 2017



Late Treatment Initiation

Epidemiology

- WHO guidelines say treat all regardless of CD4 count, but what is actually happening?
- Cohort data from 2002 to 2015: 16 low-income countries, 11 lower-middle countries, 9 upper-middle countries, 19 high-income countries
- **Median CD4 count at treatment initiation has increased over time, but remained below 350 in 2015 in all income brackets**
- In 2015, >25% of people in all income brackets began treatment with CD4 below 200, i.e. severe immunodeficiency



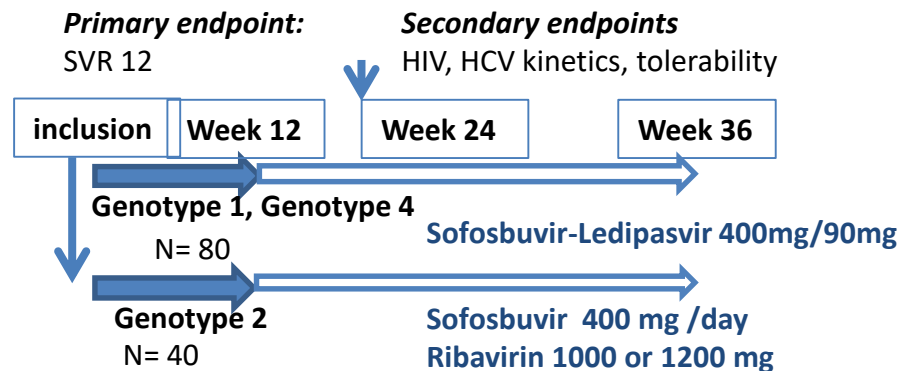
- **"Substantial additional efforts and resources are needed to increase testing coverage with the aim of achieving earlier diagnosis, linkage to care, and initiation of ART globally."**



Hepatitis C Co-Infection

Treatment in West Africa

- Almost all studies of hepatitis C treatment have been conducted in high income countries - very little research in resource-limited settings
- Do different health systems have an impact on outcomes?
- TAC ANRS 12311 trial assessed the feasibility, efficacy and safety of interferon-free direct-acting antivirals (DAA) treatment in Cameroon, Ivory Coast and Senegal
- 110 treatment-naïve adults, 10% with compensated liver cirrhosis
- 12 week therapy:



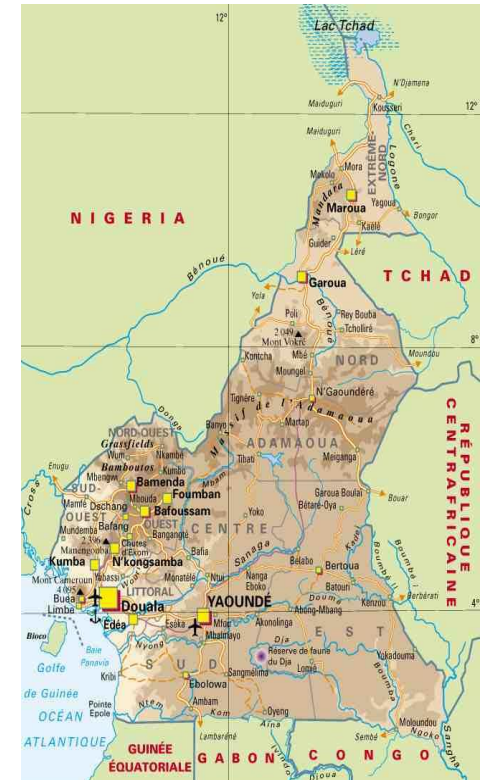
- **89% sustained virological response (SVR12), similar to studies in high-income countries and 78% in those with cirrhosis; treatment safe and well tolerated**
- “This is very good proof that when treatment is available, patients are adherent and keen on taking treatment – this is the time to advocate for larger access to DAAs in Africa.” – Karine Lacombe, Saint-Antoine Hospital, Paris.



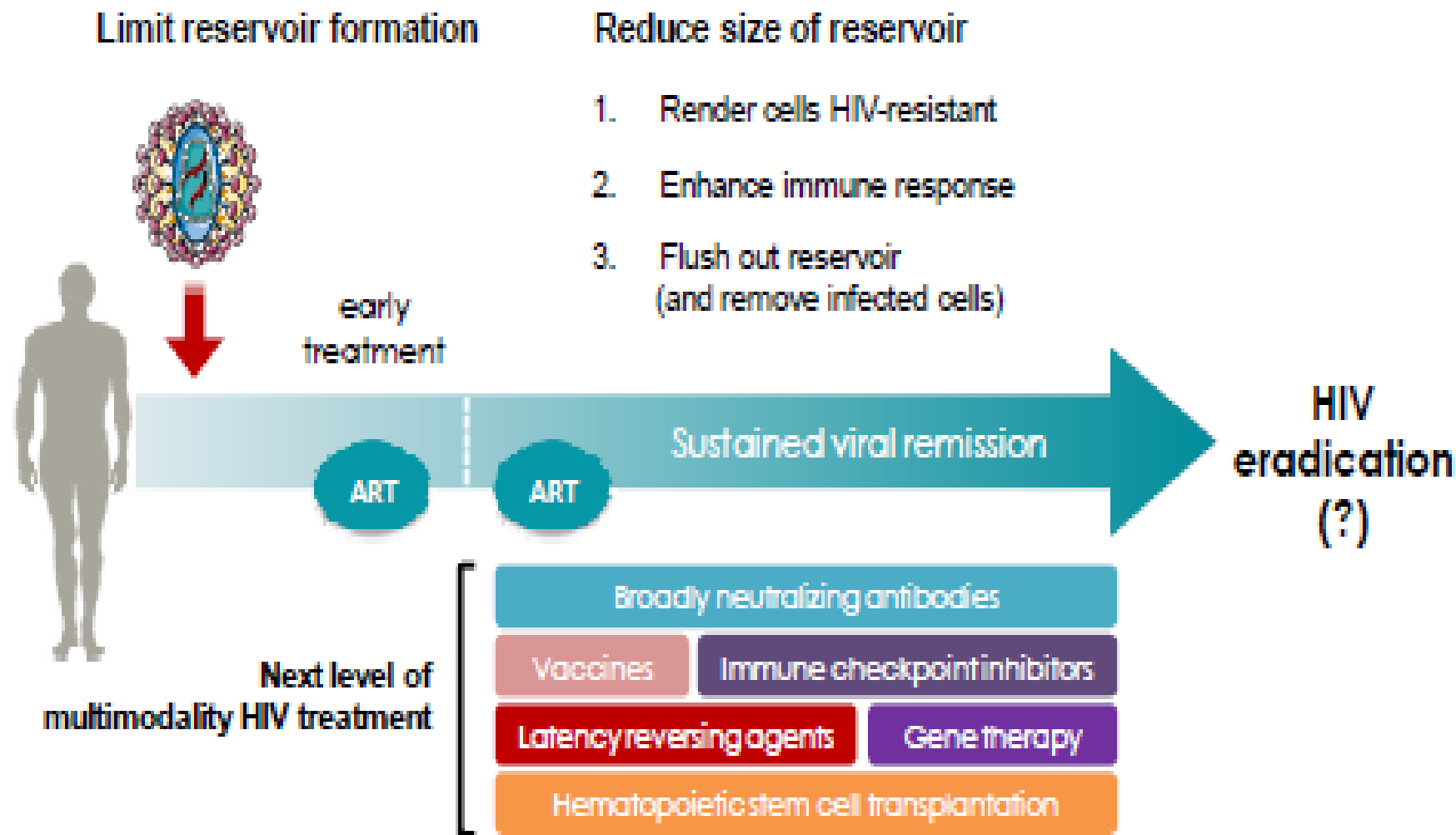
Hepatitis C Co-Infection

Treatment in West Africa

- Cameroon was presented as an example of good practice
 - The government treats hepatitis C as a public health priority
- Co-operative agreement with pharmaceutical companies to obtain DAAs at reduced prices
- Ten treatment centres established
 - a demonstration project evaluating feasibility, efficacy and cost effectiveness is on its way
- Challenges: implementing screening programmes, sustainable financing mechanisms



1. ART will not cure HIV, novel strategies needed





Highlights

Promising developments

- New fixed dose combinations will increase treatment options for patients and allow for increasingly individualised therapy.
- Approaches to simplify treatment, such as dual therapy, dose reduction and short cycle therapy, may improve the quality of life for people with HIV and lower costs.
- Success of providing direct-acting antivirals for hepatitis C in West Africa.

Challenges

- Late diagnosis and poor linkage to care means that a quarter of people with HIV have severe immunodeficiency when they start treatment.
- The increasing prevalence of drug resistance makes it harder to control the epidemic.



IAS TOOLKITS

TRACK D: IMPLEMENTATION SCIENCE

IAS 2017 HIGHLIGHTS

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Overview

Differentiated Service Delivery

Why do we need DSD?

Paediatric Services

Implementation Challenges

Urban vs Rural

Integrated Services for PWID

Costs and Funding

\$90 \$90 \$90

US Funding Decisions

Economic Incentives

Introduction

Punto Seguro

Couples Testing

Stigma

Stigma in Healthcare

Reducing Stigma

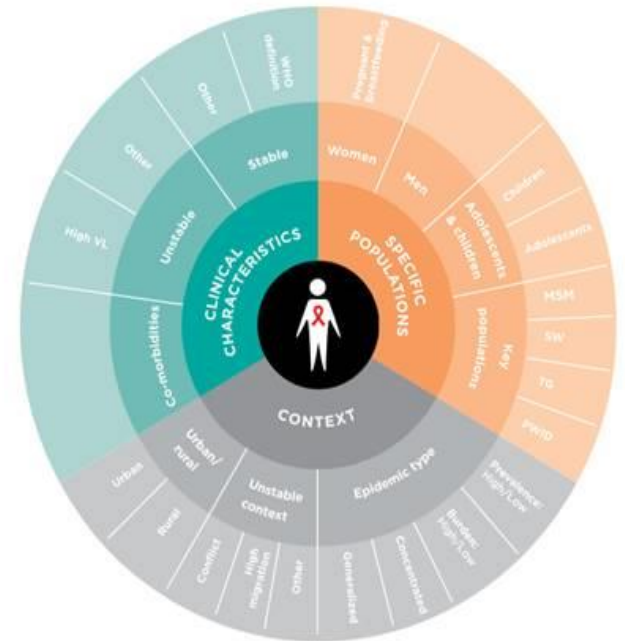
Providing Stigma-Free Services



Differentiated Service Delivery

Why do we need DSD?

- Progress towards HIV epidemic control:
 - 19.5 million individuals accessing ART worldwide
 - 1.8 million new HIV infections each year
 - 1 million deaths from HIV-related disease each year
- Our successes are due to the public health approach (consistent package of care, decentralised delivery model) enabling scale-up of services
- Challenges to reaching 90-90-90 goals:
 - Expanding ART coverage
 - Achieving high quality care
 - Improving efficiency
- There are structural, psychosocial and behavioural obstacles to successful engagement in care
- DSD can address these challenges and reduce gaps in outcomes





Differentiated Service Delivery

Why do we need DSD?

- DSD is a client-centred approach that simplifies and adapts HIV services
 - Tailor services to recipients of care: modulate the frequency, location and content of service provision
- For example, multi-month prescribing (MMP): people with less complex care needs are prescribed several months ARVs at a time
 - Monthly clinic visits can be difficult to manage for patients: transport costs, time away from education/work, etc.
 - Frees up staff capacity for patients who are starting treatment, have co-morbidities, or are unwell





Differentiated Service Delivery

Why do we need DSD?

- DSD implementation studies should focus on adapting DSD to specific populations
 - For example, poor engagement of men with services and worse clinical outcomes for men. Could tailored interventions for men help reduce gender disparities?



- “We have to evolve our public health approach into a new model, a model of ‘precision public health’. Let’s stick with what has worked, what’s served us well thus far, but let’s make it precise and tailored so in the end we’re responsive to the people we aim to serve.”
 - Wafaa El-Sadr, Columbia University



Couples Testing

- Cluster randomised trial in Zimbabwe: use of incentives to encourage participation in couples HIV testing and counselling
- 68 rural communities
- Non financial incentives worth \$1.50 - a grocery item such as bar of laundry soap, petroleum jelly, cooking oil
- Incentive for couples testing *versus* standard community mobilisation
- Participation in testing:
 - People tested per day: 70 vs 56
 - Proportion couple testers: 55.7% vs 10.0%
 - HIV prevalence: 8.8% vs 6.5%
- Economic analysis: incentives added little to the cost of the intervention, the main cost in both arms was human resources
 - Cost per person tested: \$7.96 vs \$8.18
- Cost per HIV-positive diagnosis: \$93.10 vs \$128.10



Implementation Science Highlights

Promising developments

- The client centred approach of differentiated service delivery is more responsive to the needs of different groups of patients and may boost their engagement with care
- Economic incentives can help engagement with existing services and technologies

Challenges

- Less commitment to the global HIV/AIDS response from its largest donor
- Stigma against key populations in healthcare settings remains an important barrier to access to care
- Attention needs to be given to appropriate implementation of differentiated service delivery models



CONCLUDING THOUGHTS

“This was the first conference in which we can see the combination of prevention and treatment at the population level and see how it works... It works beautifully.”

François Dabis, French National Agency for Research on AIDS and Viral Hepatitis (ANRS)

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