Challenge - Advanced HIV in Antiretroviral-Experienced Patients

Esther C. Casas
South African Medical Unit
Medecins Sans Frontieres

90-90-90 Targets Workshop

July 21-22, 2018 • Amsterdam

Sponsored by:

IAPAC INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

UNAIDS

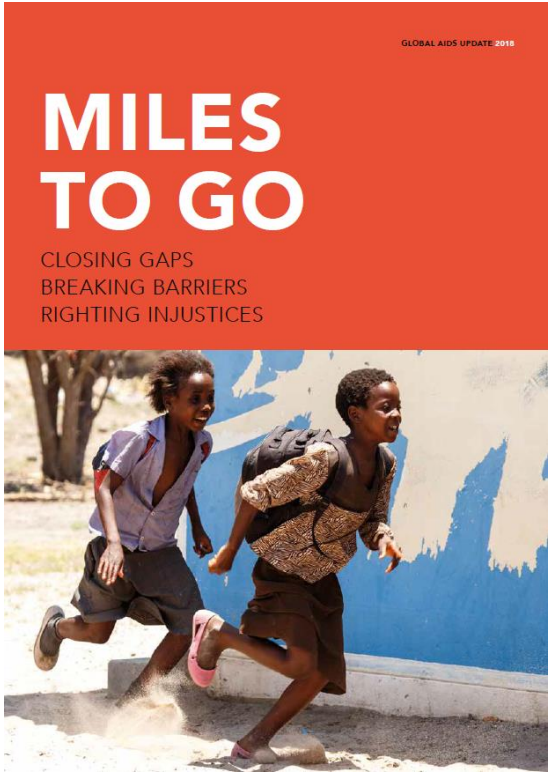
In partnership with:

BRITISH COLUMBIA CENTRE *for* EXCELLENCE *in* HIV/AIDS

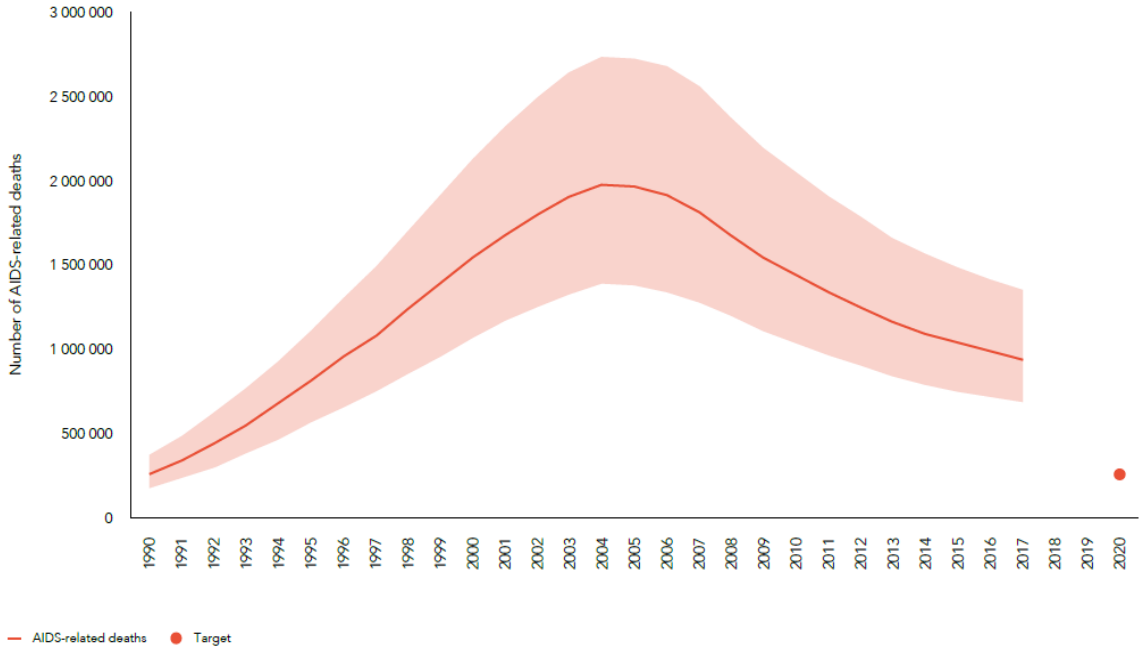
GNP+ GLOBAL NETWORK OF PEOPLE LIVING WITH HIV

IAS

The forgotten 4th 90: HIV related mortality plateauing



Number of AIDS-related deaths, global, 1990–2017 and 2020 target



Source: UNAIDS 2018 estimates.

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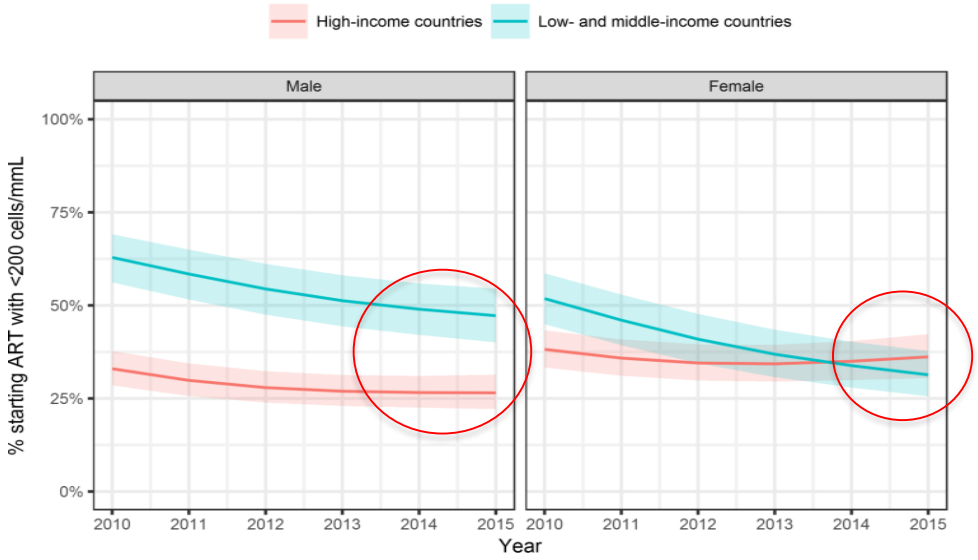
% of Advance disease in treatment experienced is increasing steadily



IeDEA-COHERE: Results based on 951 855 adults from 55 countries after imputation of missing data

Does not include "re-starters" after interruption

In 2015, 37% of people starting ART did so at CD4 cell count <200 cells/mm^3

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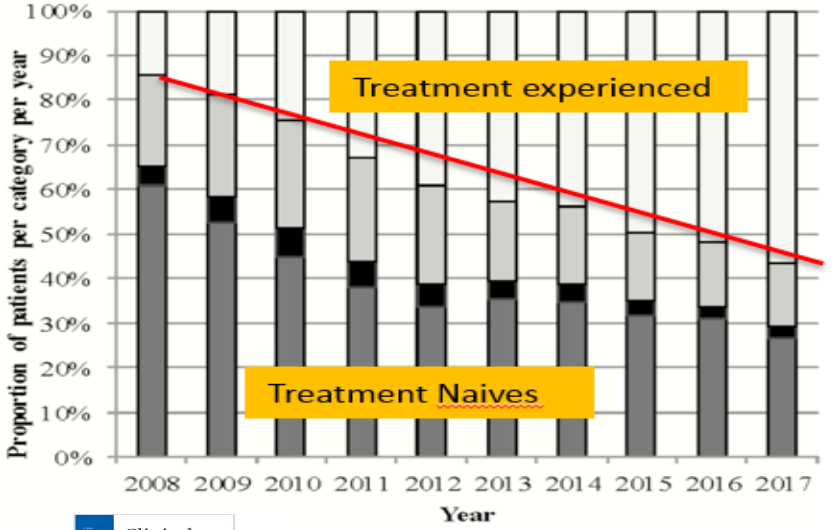
The Continuing Burden of Advanced HIV Disease Over 10 Years of Increasing Antiretroviral Therapy Coverage in South Africa
Meg Osler & all, CID 2018;66,suppl 2)



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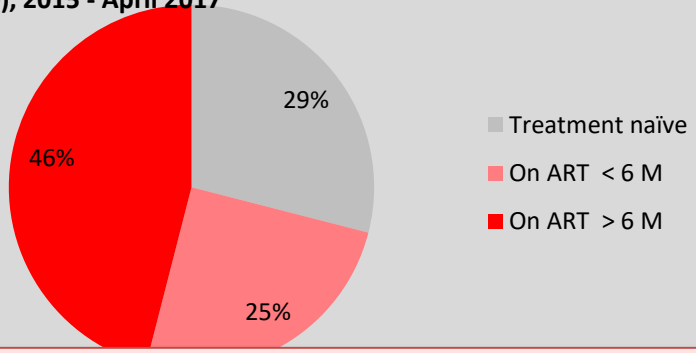
1 April 2018

Admission profile by ART status in 4 referral units hospitals supported by MSF

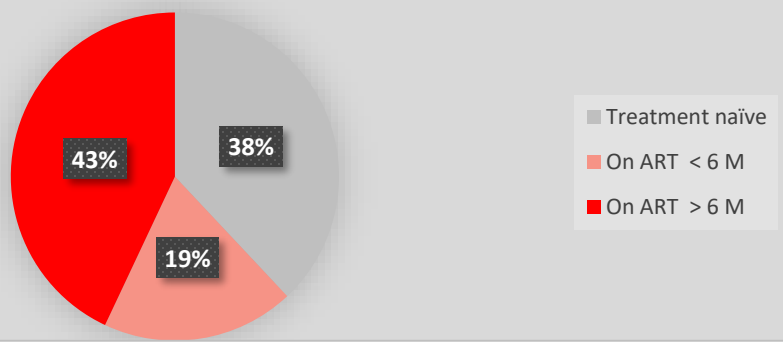
CHK, DRC (n=2210), 2015 - April 2017



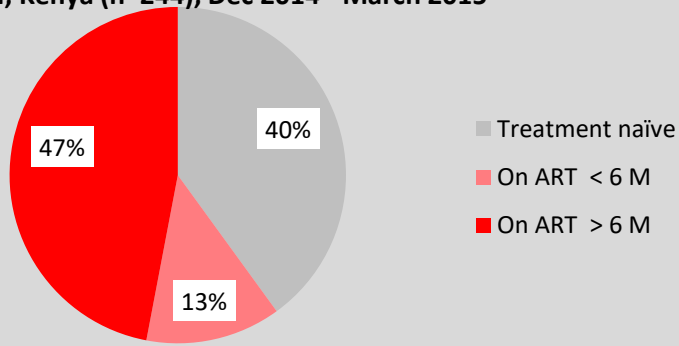
Amongst patients with VL≥1,000 cp/mL, **82% and 61% NNRTI DR in Kinshasa and Homa Bay respectively.**

High levels of drug resistance among ART-experienced hospitalized patients in Kenya and DRC, C. Bossard & all , Epicentre, submitted

Donka Hospital, Guinea (n=588) Jan -dec 2017



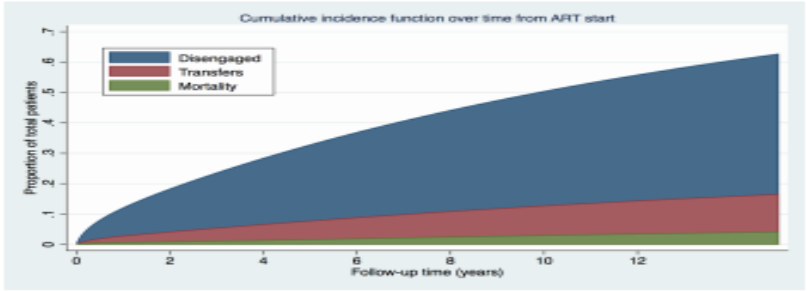
Homa Bay Hospital, Kenya (n=244), Dec 2014 - March 2015



Nsanje Hospital, Malawi (n=734, May 2016 - Dec 2017

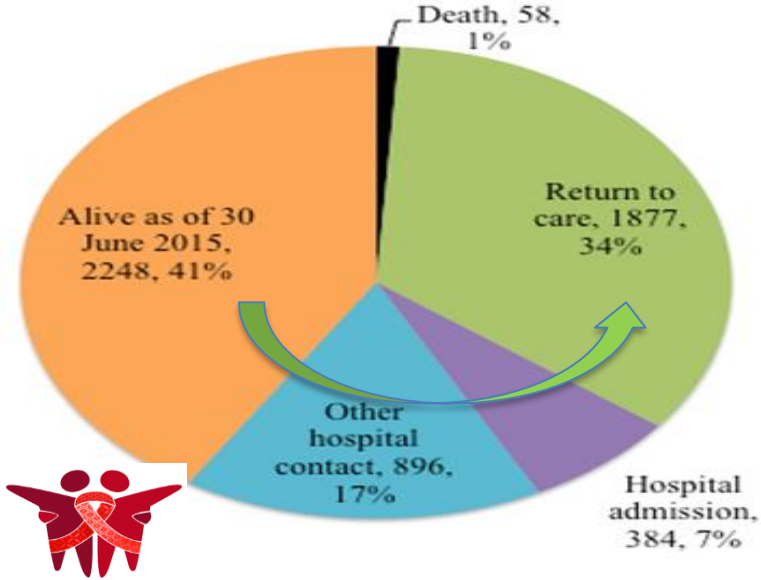
From linear to circular model

Khayelitsha: Retrospective cohort study of all patients ≥10yrs on ART visiting a Khayelitsha ART clinic, 2013



	Estimate at 5 years (95% CI)	Estimate at 10 years (95% CI)
Disengaged	0.251 (0.246-0.255)	0.377 (0.369-0.385)
Transfer	0.061 (0.058-0.063)	0.097 (0.093-0.102)
Dead	0.016 (0.014-0.017)	0.029 (0.026-0.032)

Figure 2. Cumulative incidence (competing risk analysis) of disengagement, transfer (including silent transfers), and mortality, as estimated by a flexible parametric survival model based on time to disengagement from ART start (as early as 2001) during the two-year window of analysis (Analysis 1)



Welcome Back services

[Kaplan et al CROI 2017 poster 990]

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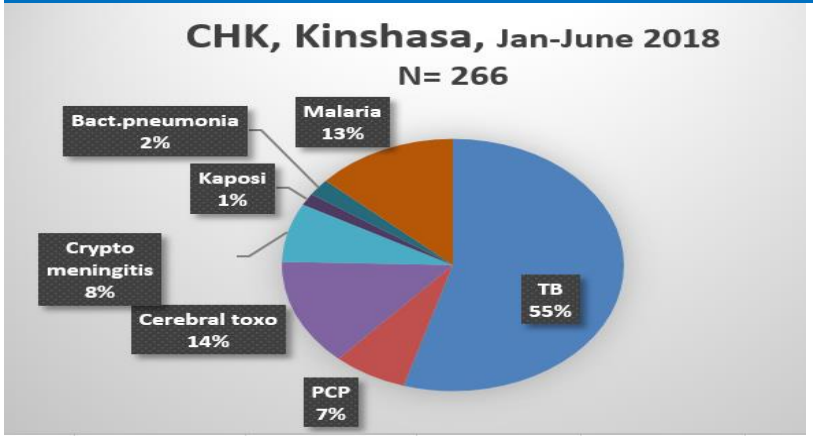
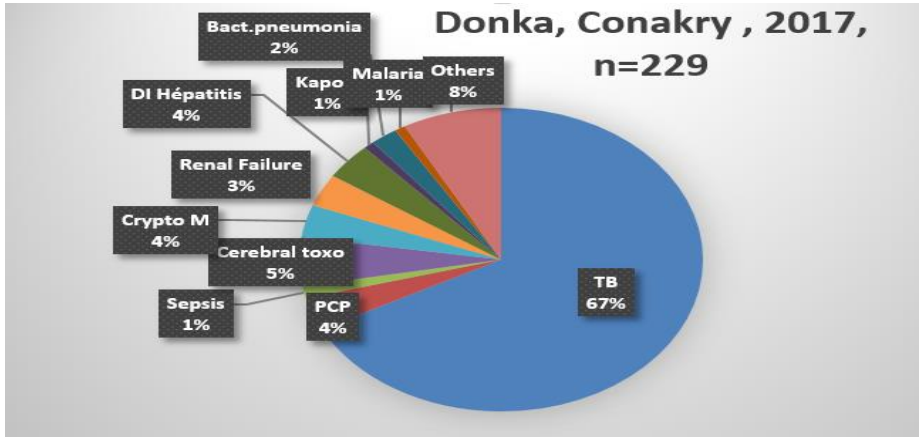
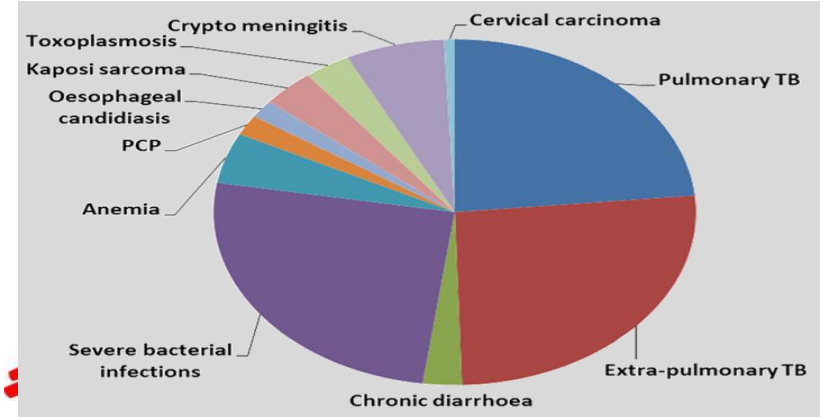
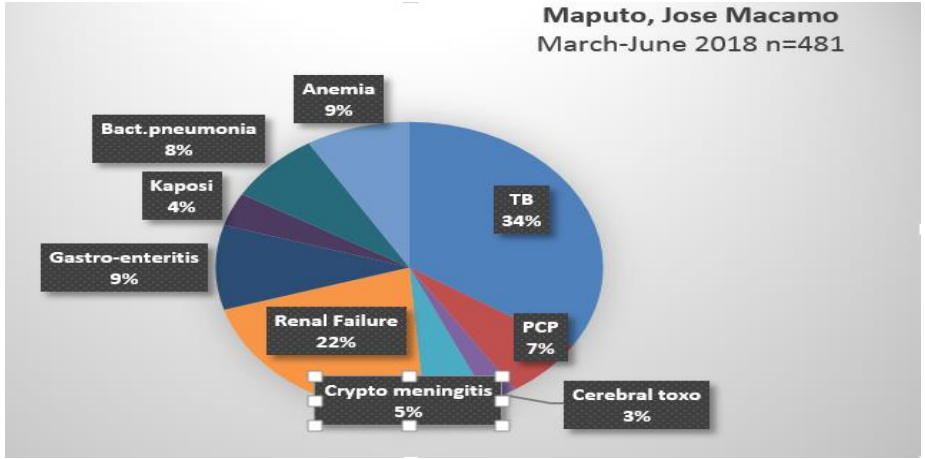
Most common causes of HIV related mortality (%) and CFR Kinshasa, Conakry, Maputo, 2018



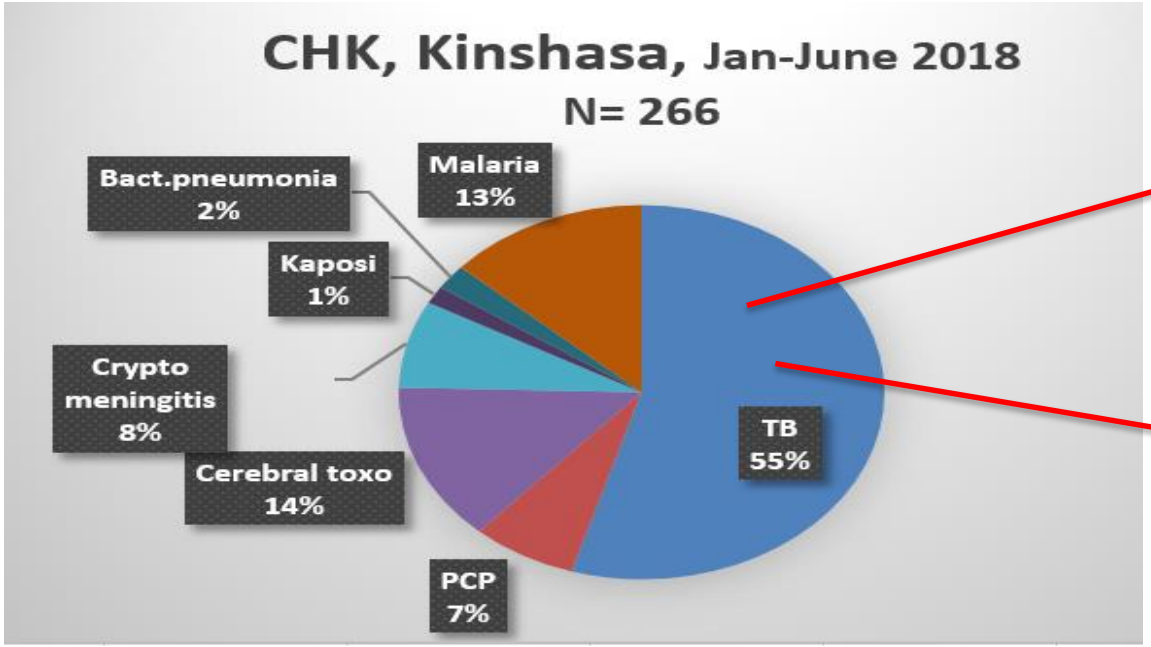


Nsanje, Malawi, **May2016-Dec 2017, n= 734**

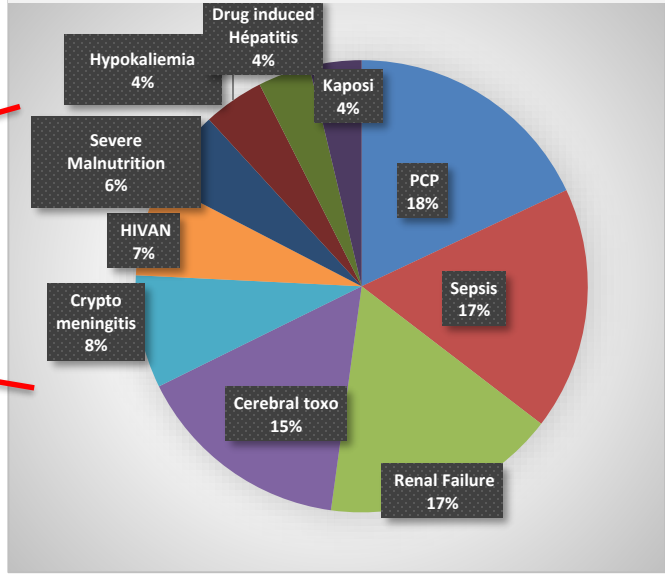




Mortality and co-morbidity IPD CHK, Kinshasa Jan-June 2018 n=266



Associated co-morbidities in HIV patient who died from TB , CHK Kinshasa Jan-June 2018 ,n= 161



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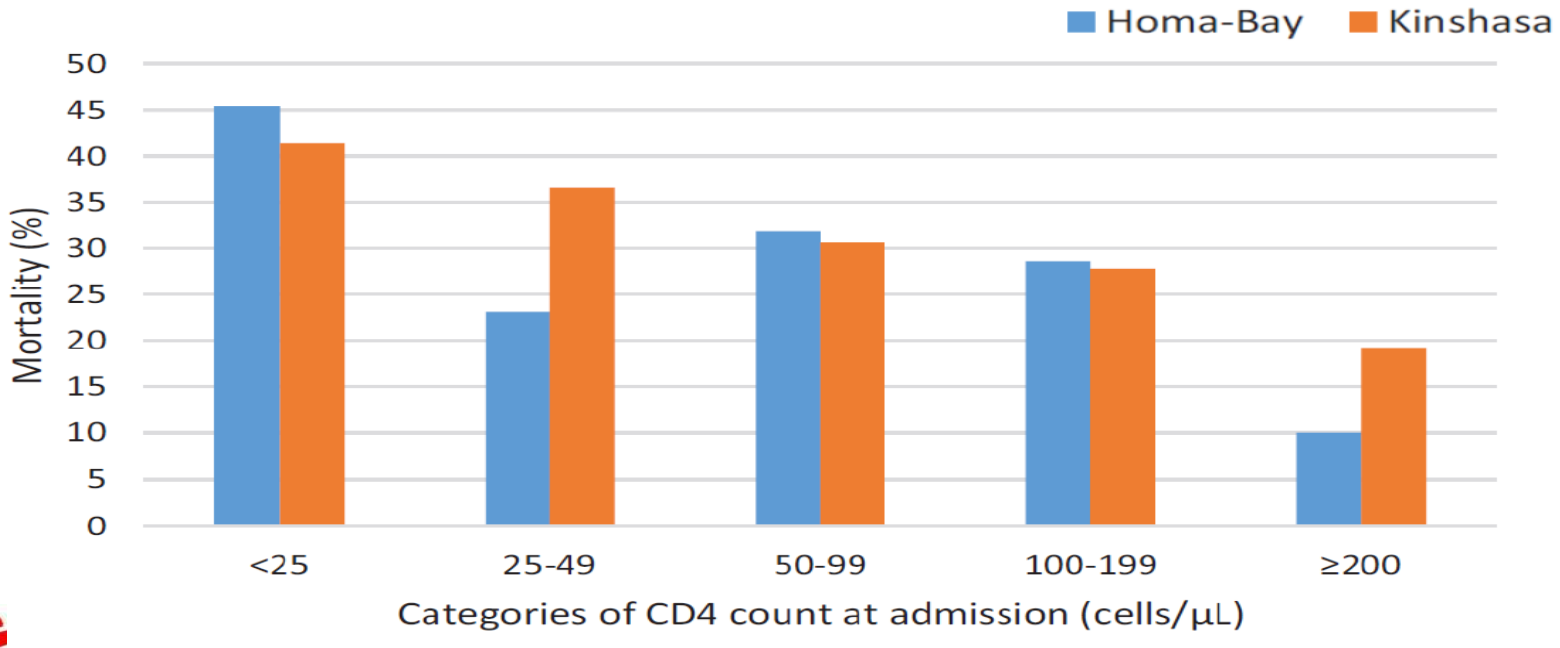
CD4 & IPD mortality
CD4 as single independent risk factor of mortality

Figure 1. Mortality among patients diagnosed with tuberculosis, stratified by CD4 cell count at admission, Homa-Bay, Kenya (n = 80) and Kinshasa, Democratic Republic of Congo (n = 248).



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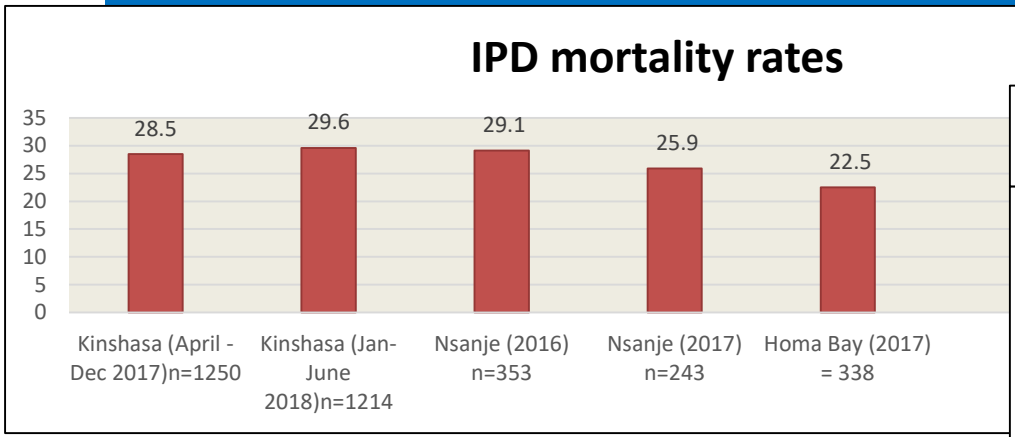
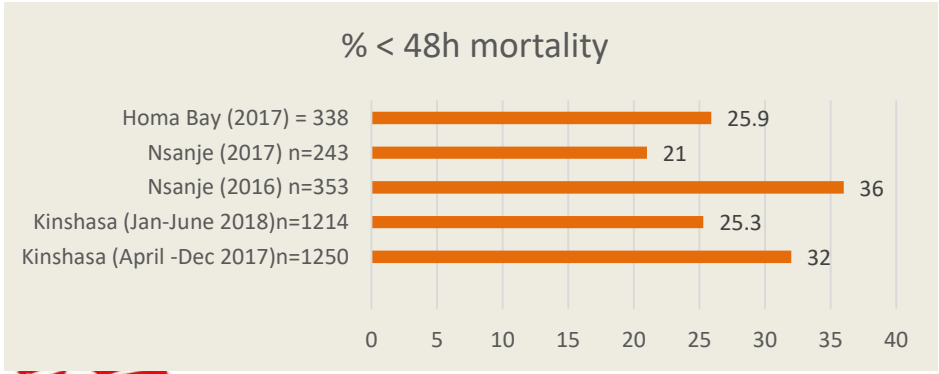
Can we improve HIV mortality with an IPD focused strategy ?





But also, high post-discharge mortality

Homa Bay, Kenya:

PHC level f/up @12 weeks after hospital discharge 234 patients with Advanced HIV, May 2016 – Dec 2017:

- **39 negative outcome (died or LTFU at PHC level) (16.7%)**
- **101 no outcome (43.2%),**
- **94 alive (40.2%),**

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Objective: identify patients with advanced disease earlier
3 levels of intervention

community

Adapt treatment literacy
(failures, interruptions..)

Welcome Back Service

Primary Health Facility

Screening package

Post admission discharge

Where: PHC level with CHW back up
What : management plan ,up-referral criteria

Adapt referal criteria

Hospital

Rapid assesment unit

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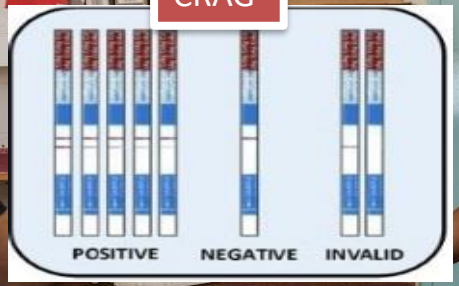
At PHC level : comprehensive screening package

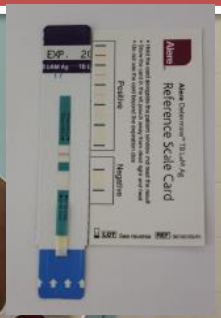
Semi –quant CD4 LFA

(CD4<100)

CRAG



TB –LAM



Triage Danger signs | CD4 | LAM Xpert | CrAg LFA | Referral criteria | VL POC or near POC

PHC level: triage

Pico: feasibility in overcrowded nurse based PHC clinic ?

Triage

Screening package

DANGER SIGNS

- Respiratory rate > 30/mi
- Temperature > 39°C
- Heart rate > 120/min
- Systolic BP < 90mm Hg
- Saturation < 90%
- Moderate/severe dehydration

Refer to hospital

- ble to walk unaided
- red mental state: confusion, nge behaviour, reduced level of sciousness
- Any other neurological problem: new onset severe headache, seizures, paralysis, difficulty talking, cranial nerve problems, rapid deterioration in vision

ART-naïve or ART <6 months	**STABLE** and ART-naïve or on ART for <6 months	**UNSTABLE** and ART-naïve or on ART for <6 months
ART >6 months	**STABLE** and on ART for >6 months; still on it or interrupted	**UNSTABLE** and on ART for >6 months; still on it or interrupt

Refer to hospital

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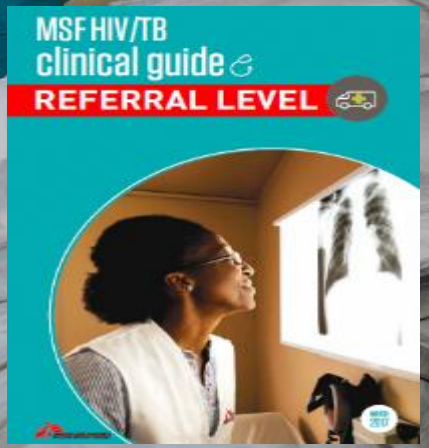
Referral hospital level
Rapid assesment unit (RAU)

Quick assesment : 25 to 35 % death within 48 hours



- Patients triage -> danger signs
- POC tests: CD4, CrAg, **VL**, LAM, Creatinine, RDT, Hb, glucose, urine Package of medication for Advanced HIV
- Referral network and SOP’s
- Specific management algorithms

POC diagnostic tools needed for management of advanced disease

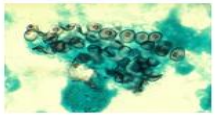
Currently Available

- POC CD4
- TB-LAM
- CrAg LFA

Challenges

- Slow uptake (e.g. TB-LAM and CrAg LFA)
- Not in national algorithms (e.g. TB-LAM)
- More costly than lab-based (e.g. POC CD4)
- Maintenance needed (e.g. POC CD4)

Currently Lacking

- POC CD4 LFA
- PCP LFA 
- Toxoplasma
- Severe Bacterial Infections

Challenges

- Under development (e.g. CD4 LFA)
- Lack of innovation (e.g. PCP)
- Lack of validation (e.g. Toxoplasma)
- Too complex (e.g. SBI)

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Advanced HIV care management : ongoing operational research

- **Modified VL algorithms to switch to 2nd line:**
  - After 1 VL>1000 if **CD4 <100:**
    - Unstable patient / stage 4
    - Failing for more than 6 months
  - Empirical switch (if no VL available within 48 hrs)
- **DTG on optimized back bone**
  - Re-challenging TLD in patient failing TLE or switch to ZLD
  - DTG in second line ART
- **Empiric TB treatment**
  - Priority for CD4 < 100
  - Decision to take at admission
  - If TB-LAM negative => clinical decision
- **Empiric treatment for other OI, if CD4<100**
  - High dose CTX for:
    - Toxo if neurological symptoms
    - PCP: if respiratory rate > 30 min
    - Isospora belli
  - Normal LP and neurological symptoms
    - DD Toxo/Tuberculome

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Conclusion

- HIV advance disease will not disappear
- Failure and Resistance is replacing late presentation in Advance disease
- Early identification/screening is crucial -> all levels of care
  - Advance disease and OIs
  - ART experience and Failure
- Readiness to welcome back experience ART patients
- Referral system
  - Improvement of detection and case management at referral level (RAU)
- R & D : new POC diagnostics needed

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Acknowledgements

MSF field teams and stakeholders

MSF field teams in Kinshasa, Maputo, Conakry, Nsanje

SAMU colleagues, Emmanuel Fajardo(Access campaign), Claire Bossard (Epicentre)

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