Who Is Dying and Why?

AIDS Mortality as a Progress Metric

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MSF Access Campaign

90-90-90 Targets Workshop
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1. Trends in mortality
2. Finding the RIPs among the LTFU
3. Who is dying and why
4. Preventing senseless deaths
5. Why corrected mortality rates matter
1. Trends in mortality
FIGURE 2.1  Approaching a 2020 milestone

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

Source: UNAIDS 2018 estimates.
On mortality in EECA, Middle East, North Africa:
There has been no reduction in AIDS-related mortality in eastern Europe and central Asia since 2010, and deaths from AIDS-related illness increased by 11% in the Middle East and North Africa.
Mortality reductions remain higher among women than men. This gender gap is particularly notable in sub-Saharan Africa, ...more men living with HIV are dying
Outside of sub-Saharan Africa, 69% deaths from AIDS-related illness were among men and boys.

SOURCE: UNAIDS
Challenge: reach as many people as possible, as quickly as possible, as early in their disease progression as possible.

Number of patients receiving ART and number of deaths.

HIV deaths in South Africa, with and without ART

HIV-related deaths in adults for the years 1990–2014 by level of engagement in HIV care


2. Finding the RIPs among the LTFU
Tracing loss to follow up

4 years after the last clinic visit

- **21.8% known RIP**
  (95% CI, 20.8%–22.7%)

- **31.6% could not been found**
  (95% CI, 30.6%–32.7%)

- **22.6% alive but stopped ART**
  (95% CI, 21.6%–23.6%)

- **14.8% transferred out**
  (95% CI, 14.0%–15.6%)

- **9.2% remaining in care**
  (95% CI, 8.5%–9.8%)

9 studies tracing 7,377 PLWHA on ART considered LTFU across 8 sub-Saharan countries

Naïve and revised mortality estimates

(A) cumulative incidence of mortality among all ART users \((N = 165,464)\)

(B) Cumulative incidence of mortality among new ART users \((N = 49,129)\)

Findings

• 38.1% of deaths among PLWHA in first year on ART

• 61.8% among people on ART longer > 1 year
Intensive follow-up in Zambia corrects mortality figures

- Facilities reporting high 2-year LTFU rates (40–50%)
- “meaning that up to half of patients at particular sites had unknown outcomes.”
- “passive reporting of deaths” - average of 15–20% of deaths are known to the facility
- Found substantial underreporting of deaths. Revised numbers were 3 to 9 times higher.

Holmes CB, Sikazwe I, Geng E. We need to monitor mortality to improve public health programs: here’s why and how to do it. International Health [Online]. 2018 Jul 17.
3. Who is dying
Among 654,868 PLWHA entering care in 2016 in South Africa:

- Almost a third (32.9%) had advanced HIV disease
- 16.8% had very advanced HIV disease
- Men almost twice as likely as women (23.1% vs 12.6%) to enter care with very advanced HIV disease.

Proportion entering care with advanced and very advanced HIV disease (2004-2016) in RSA

Carmona S et al. Persistent High Burden of Advanced HIV Disease Among Patients Seeking Care in South Africa’s National HIV Program: Data From a Nationwide Laboratory Cohort. Clin Infect Dis. 2018;66(suppl_2)
(South Africa) Increased proportion of PLWHA presenting in 2016 with CD4<50 are **ART experienced**: from 14.3% in 2008 to 56.7% in 2017

Figure: Distribution of prior CD4 count testing, antiretroviral therapy (ART), ART retention, and recent virologic status in PLWHA presenting in 2016 with a CD4 count <50 cells/μL, Western Cape province, South Africa

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

** CHK, DRC (n=2210), 2015 - April 2017**
- Treatment naïve: 29%
- On ART < 6 M: 46%
- On ART > 6 M: 25%

** Donka Hospital, Guinea (n=588) Jan - Dec 2017**
- Treatment naïve: 38%
- On ART < 6 M: 43%
- On ART > 6 M: 19%

** Homa Bay Hospital, Kenya (n=244), Dec 2014 - March 2015**
- Treatment naïve: 40%
- On ART < 6 M: 47%
- On ART > 6 M: 13%

** Nsanje Hospital, Malawi (n=734), May 2016 - Dec 2017**
- Treatment naïve: 16%
- On ART < 6 M: 42%
- On ART > 6 M: 25%
- Unknown: 17%
Among newly starting treatment deaths:
50.3% no history of missed visits
14.0% while late
31.7% while lost

Among longer on ART deaths:
8.8% always in care, at RIP
13.7% late history (but in care at RIP)
29.1% in care but lost history
11.7% while late
36.7% while lost

Fig 3. Proportion of patients who died after starting antiretroviral therapy (ART) by engagement status, with left truncation for individuals on ART before the study observation period (N = 165,464).

4. Preventing senseless deaths
Lessons

- Associated with mortality
  - Male gender
  - Low CD4 count at initiation
  - Advanced disease
  - Shorter time on ART
  - Stopping ART (even with less advanced disease and longer ART)

- What’s needed
  - INTENSIVE CASE FINDING
  - Outreach and early HIV diagnosis
  - Better and rapid linkage to ART
  - Men into early ART initiation
  - Advanced HIV package of care
  - Better adherence support
  - POC tools
  - INTENSIVE ACTIVE TRACING
  - Welcome back to care...
TB FAIL

• Between 2000 and 2016, “Among HIV-positive people, TB treatment supported by ART averted an additional 9 million deaths.” (Source WHO Global TB report)

• In 2017 3 out of 5 people starting HIV treatment are not screened, tested or treated for TB (UNAIDS Miles to Go)

• Globally, just 42% of people newly registered in HIV care were receiving tuberculosis preventive therapy.

• Among the 124 countries that reported data to UNAIDS in 2016, only 39% of the estimated number of people living with HIV who had incident tuberculosis received treatment for both HIV and tuberculosis
Non-negotiable package of OI/advanced HIV care at **PHC and inpatient facilities** to **test/treat/prevent**

- tuberculosis
- severe bacterial infections (SBI)
- cryptococcal meningitis
- toxoplasmosis
- Pneumocystis jirovecii pneumonia (PCP)

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>CD4</th>
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<tr>
<td>Sputum Xpert MTB/RIF</td>
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<tr>
<td>Urine TB-LAM</td>
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<tr>
<td>Cryptococcal antigen screening (CrAg)</td>
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<tr>
<td>Preventive</td>
<td>Cotrimoxazole</td>
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<td>TB prophylaxis</td>
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<td>- CTX, isoniazid, &amp; pyridoxine in FDC</td>
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<tr>
<td>-3HP (3 months of weekly INH + rifapentine)</td>
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<tr>
<td>Antifungal preemptive therapy for CrAg positive</td>
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5. Why corrected mortality matters
“Young paediatric patients were at greater risk of early death, being almost twice as likely to die within 90 days. Males were at greater risk of early death once initiated on ART (HR 1.35, 95% CI 1.09, 1.66))

Females in late adolescence were at greatest risk of death > 90 days after entering pre-ART/ART (HR 2.44 [1.60, 3.74] <0.01).

Late adolescents demonstrated greater non-engagement in care (RR 1.21 (95% CI 1.16, 1.26)).

Among both males and females, early paediatric and late adolescent groups experienced significantly greater loss to follow-up.”
Why corrected mortality matters

• Systemic changes needed in measuring mortality
  • Civil registration and vital statistics systems

• Not “LTFU prevention,” but rather “death prevention”

• Highlights gaps in equity, services, to inform better policy and corrective action
  • “mortality across facilities ranged from 0 per 100 person years to 13.4 per 100 person years, even though the facilities in theory receive similar support”
  • Needs of populations - Young paediatric and late adolescent age groups at increased risk of late diagnosis, early death, delayed treatment initiation and loss of continuity of care

• More accurate reflection of the state of ART within the health system at national, provincial, and facility levels
• Mbeki’s denialism and inaction resulted in more than 330,000 deaths in South Africa from 1999 to 2007

• In the 2000–2014 period, if South Africa had moved swiftly to implement WHO guidelines
  • 2.20 million (95% CI: 2.00 million–2.37 million) fewer HIV-related deaths
  • 6.15 million life years that were actually saved and the 8.80 million life years that could have been saved

• Model-based comparison of different “scale-back strategies” based on hypothetical reduction of international funding for HIV in South Africa and Côte d’Ivoire
  • No New ART
  • Late Presentation
  • ART 0.350*10^9 cells/L
  • reduced retention
  • no viral load monitoring
  • no 2nd line ART

• For example, although a strategy of decreased case identification (Late Presentation) reduces the HIV program budget (RSA 13%, CI 13%), deaths are projected to increase (RSA 22%, CI 15%).

• “reverse enormous strides made over the last 20 years in curbing the global HIV epidemic and in improving HIV-related survival.”

• “Our findings suggest that reduced HIV foreign aid will produce modest savings to donors at the expense of HIV epidemic revival and massive loss of life among recipient nations.”

Thank you

For latest MSF reports, go to:
www.msf.org/aids-2018,
www.msfaccess.org/stopping-deaths
sharonann.lynch@msf.org

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HIV deaths

- **2017**
  - 940,000 deaths
  - (670,000–1.3 mn)

- **1980 to 2016**
  - 1980
    - 4,224 deaths
  - 2005
    - peak at 1.91 million deaths
  - 2016
    - 1.03 million deaths

- **2005 to 2016**
  - HIV deaths decreased by 45.8%
  - TB-related PLWHA deaths decreased 20.9%
Number of deaths as ART increases

Low CD4 at initiation

- South Africa
- PLWHA presenting with advanced HIV disease has remained unchanged over the last 5 years
- More than a third of patients enter care with a CD4 cell count <200 cells/µL.
  - Men almost twice as likely as women (23.1% vs 12.6%) to enter care with very advanced HIV disease
- Need to support rapid identification and treatment initiation

Diagnosing TB in HIV+ pregnant women

- Symptom screening not good enough for HIV+ pregnant women
  - Symptom screening 90.1% sensitivity
  - But among HIV+ pregnant women (RSA) dropped to 28%
- A cluster-randomised trial to compare universal sputum TB testing with standard symptom-based testing in this population.
- The majority of women with previously undiagnosed prevalent TB were asymptomatic.
- Universal TB screening of all HIV+ pregnant women increased case detection 10-fold
- MGIT identified more TB than Xpert in women whose pregnancy may mask TB symptoms.
- Our data support sputum testing all HIV-infected pregnant women for TB in high burden
- Xpert detected one third the rate of TB compared with MGIT


Swaziland: TB decreased as ART coverage increased
Most common causes of HIV related mortality (%) and CFR. Kinshasa, Conakry, Maputo 2018

CHK, Kinshasa, Jan-June 2018
N=266

- Bact.pneumonia 2%
- Malaria 13%
- Cerebral toxo 14%
- PCP 7%
- TB 55%

Donka, Conakry, 2017, n=229

- TB 67%
- Others 8%
- Malaria 1%
- Kaposi 1%
- Renal Failure 3%
- Cerebral toxo 5%
- Sepsis 1%
- Crypto M 4%
- PCP 4%
- Bact.pneumonia 2%

Maputo, Jose Macamo
March-June 2018 n=481

- TB 34%
- Renal Failure 22%
- Anemia 9%
- Bact.pneumonia 8%
- Gastro-enteritis 9%
- Crypto meningitis 5%
- Cerebral toxo 3%
- Severe bacterial infections
- Anemia
- Chronic diarrhoea
TB-related deaths among people living with HIV concentrated in eight countries

Distribution of tuberculosis-related deaths among people living with HIV, global, 2016