



# New WHO recommendations on advanced HIV disease

Rapid overview of new guidance

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# Key global statistics for Advanced HIV disease and opportunistic infections

**630,000**

AIDS-RELATED  
DEATHS IN 2022

**30%**

AHD AT BASELINE,  
SOMETIMES HIGHER  
(UPTO 50%)

**187,000**

DEATHS FROM TB  
AMONG PLHIV IN  
2021

**112,000**

DEATHS FROM  
CRYPTOCOCCAL  
INFECTION IN 2021

**380,000**

AIDS-RELATED  
DEATHS IN THE WHO  
AFRICAN REGION

**1.5M**

CHILDREN LIVING  
WITH HIV

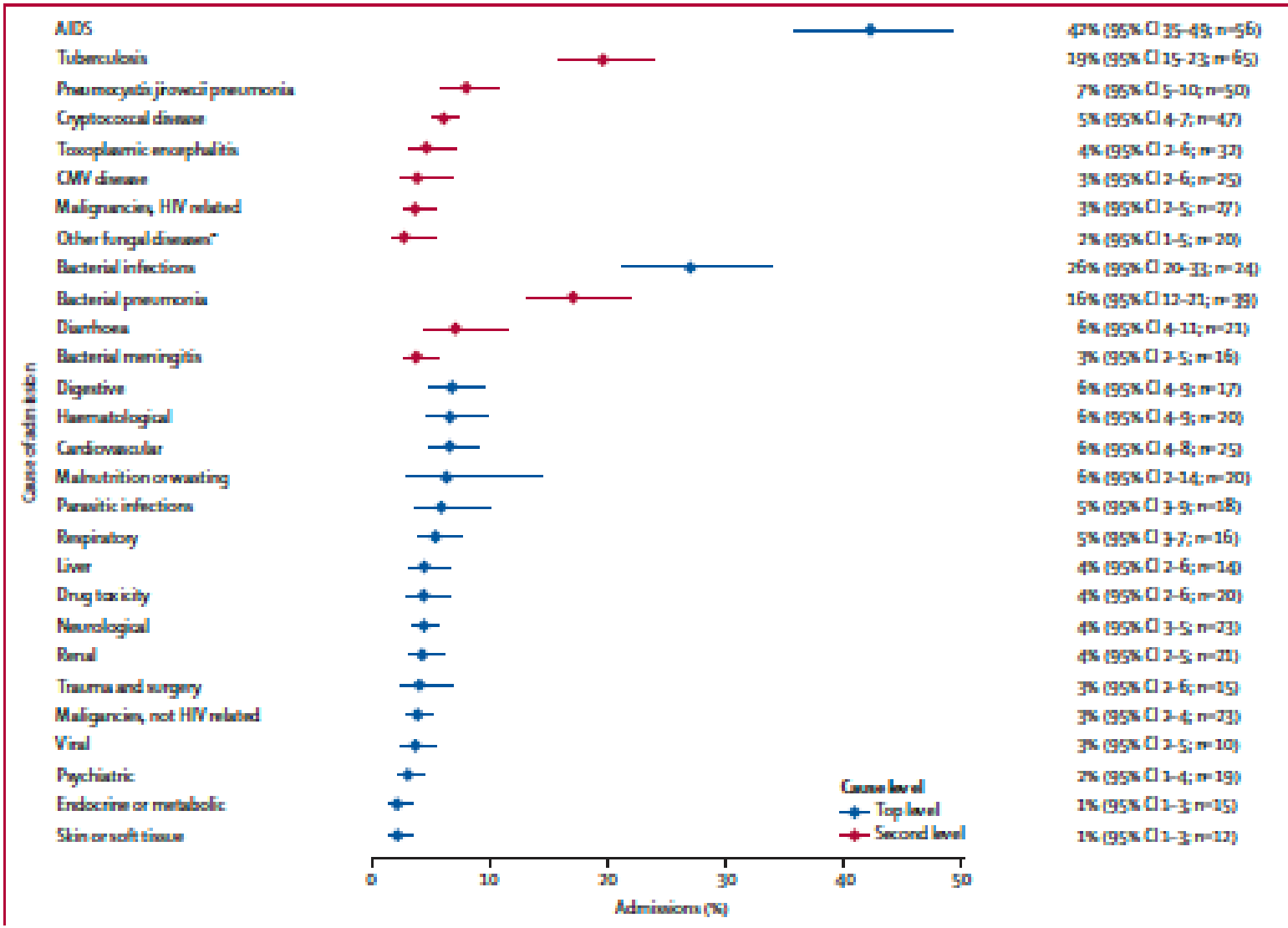
**84,000**

AIDS-RELATED  
DEATHS IN CHILDREN  
WITH HIV

**2.1M**

ADULTS LIVING WITH  
AHD in SSA

# Causes of hospitalisation 2014–23















- AIDS-related illnesses remained the most common cause of admission to hospital for people living with HIV.
- TB is the most common AIDS-related illness.
- 17% mortality in hospital

# New WHO Recommendations

| Interventions                                     | Disease area                                       |
|---|--|
| CD4 testing to identify Advanced HIV disease      | Advanced HIV disease                               |
| Clinical Staging to identify advanced HIV disease |  |
| Paclitaxel and LP-doxorubicin                     | Kaposi's Sarcoma                                   |
| Interventions at discharge                        | PLHIV who were hospitalized with serious illnesses |

# How were these questions prioritized?

Roadmap for WHO scoping and future guidelines on Advanced HIV disease

| Expected results/policy changes |   |   |   |
|---------------------------------|---|---|---|
| Topic area                      | 2024  | 2025–2026   | 2027–2028   |
| CD4 testing                     |    |   |   |
| Cryptococcal meningitis         |   |   |  |
| Severe Bacterial infections     |   |   |  |
| Tuberculosis                    |    |    |   |
| PCP                             |   |    |   |
| Toxoplasmosis                   |   |    |   |
| CMV                             |   |  |   |
| Talaromycosis                   |  |  |   |
| Histoplasmosis                  |   |  |   |
| Kaposi Sarcoma                  |  |   |   |



Included for WHO guidelines scoping



Study results expected



Pending new evidence, no changes expected

# Why is CD4 testing important?

**2006**

- ART initiation in PLHIV with a CD4 <200cells/mm<sup>3</sup>

**2010**

- Viral load if available
- ART initiation in PLHIV with a CD4<350cells/mm<sup>3</sup>

**2013**

- Viral load as preferred for treatment monitoring and identification of treatment failure

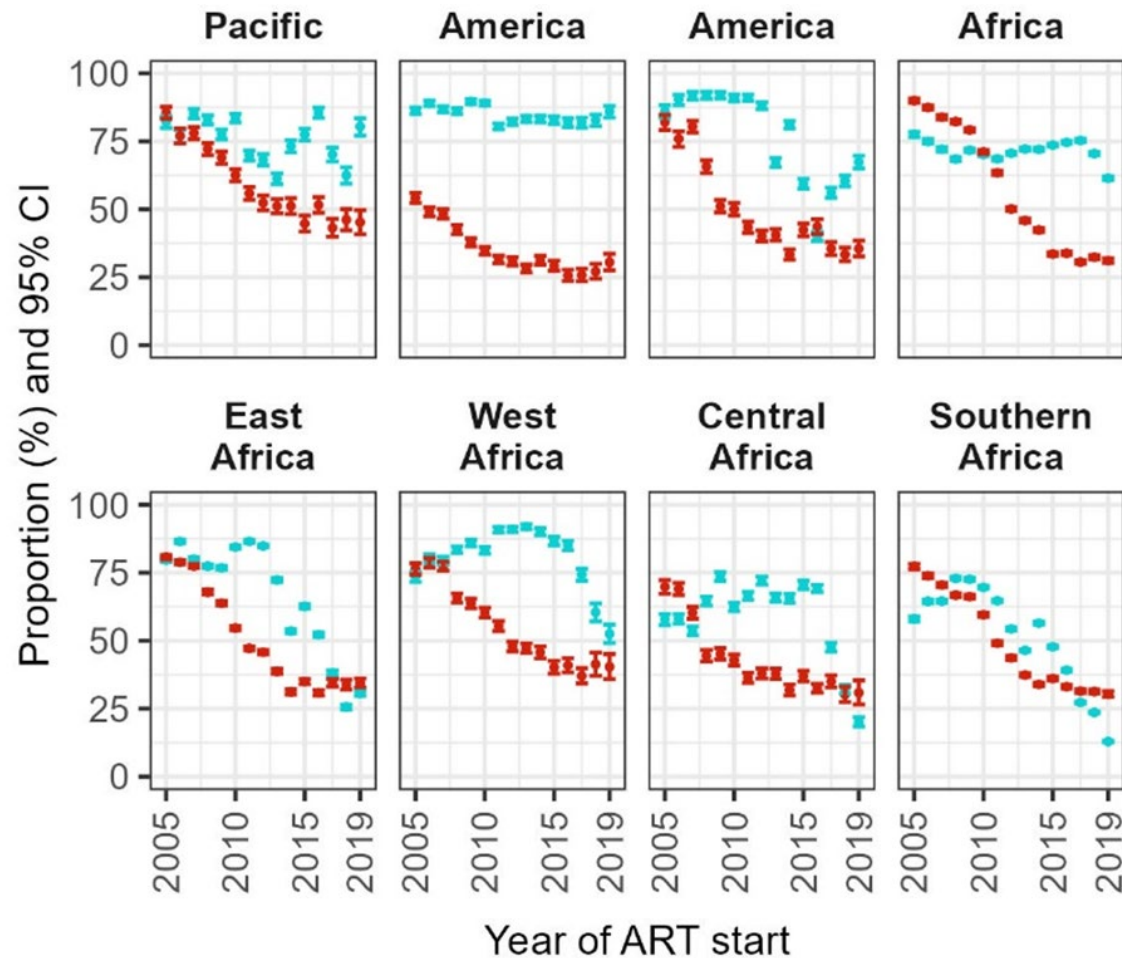
**2016**

- ART for all PLHIV regardless of CD4 cell count
- Consensus definition for advanced HIV disease (<200cells/mm<sup>3</sup>)

**2017**

- CD4 for identifying Advanced HIV disease

# Why is CD4 testing important?



- CD4 testing has had precipitous declines, despite AHD guidance in 2017
- AHD burden was unclear in many programmes owing to a focus on the triple 90's
- AHD burden stands at 30% of all PLHIV presenting to care, with proportions being around 44% in inpatient settings
- They have a very high risk of dying within the first 6-8 weeks, and ART alone is not sufficient to prevent opp. infections
- The systematic review for the guidelines estimated that approximately 25% of cases will be missed (at a prevalence of 30% AHD) if clinical staging was used- highlighting poor sensitivity of clinical staging



HIV-attributable KS



Non-HIV-attributable KS



## Why is Kaposi Sarcoma important?

- Declining greatly in most settings worldwide with scale-up of ART
- However, KS persists in several countries in Sub-Saharan Africa
  - Botswana, Mozambique, Kenya, Malawi, Rwanda, Tanzania, Zambia, Zimbabwe report cases ever year
- Mutilating disease –present in cases of severe immunosuppression –early ART and chemotherapy critical
- Treatment not well optimized - most countries simply use what is available

# Why focus on post-discharge care in PLHIV?

- Review in 2022 found that over 30% of PLHIV who were successfully discharged – either were readmitted(18%) or died (14%) within a year.
  - More recent studies confirmed these findings
- Multiple point of failure exist. HIV programmes designed primarily for outpatient settings, gaps in linkage to inpatient care services
- Modalities of linkage to care following discharge and support following discharge need to be assessed.

# Recommendations made

## **Advanced HIV disease**

**CD4 testing is recommended as the preferred method to identify advanced HIV disease among people living with HIV (new, 2025) (Strong recommendation, moderate-certainty evidence)**

**In settings in which CD4 testing is not yet available, WHO clinical staging can be used to identify advanced HIV disease among people living with HIV (Conditional recommendation, very-low-certainty evidence)**

**Hospitalized people with HIV may be provided interventions to support transitions to outpatient care and reduce avoidable readmissions. (Conditional recommendation, low-certainty evidence)**

**Interventions include:**

- **Pre-discharge goal setting**
- **Medication review**
- **Transitional care planning**
- **Telephone follow-up**
- **Home visits by a health-care provider and/or peer supporter**
- **Individualized support**

**WHO suggests paclitaxel or pegylated liposomal doxorubicin for the pharmacological treatment of Kaposi's sarcoma among people living with HIV (Conditional recommendation, low-certainty evidence)**

# Important implementation considerations (summarized)

| Recommendation area                 | Implementation considerations  |
|-------------------------------------|--|
| <b>CD4 testing</b>                  | Optimizing opportunities to use point of care tests, training and task-sharing, monitoring and quality assurance of tests, consider integration pathways with other disease programmes of primary healthcare   |
| <b>Clinical Staging</b>             | Adequate training of HCWs to conduct physical examinations and staging of disease, clear referral pathways, development of SOPs, resource prioritization   |
| <b>Post-discharge interventions</b> | Medical review, transitional care planning should be considered standard of care, identifying cadres for task-sharing, involvement of peer counsellors, volunteers, support groups, referral mechanisms and nutritional support to strengthen engagement |
| <b>Kaposi's sarcoma(KS)</b>         | Early diagnosis, provision of histopathological resources, HCW training, timely ART initiation, optimizing access to chemotherapeutics, capacity building and training   |

# TB preventive treatment in people living with HIV, global context



- PLHIV receiving TPT decreased: 2019-2022 with slight increase in 2023
- Aim to reach 90% of PLHIV provided with TPT by 2025 & 95% by 2030\*
- UN target:
  - Reach at least 90% of people at high-risk of developing TB with TPT
  - providing TPT to ~45 mln people with TB, including ~ 15 million PLHIV (by 2027)

Data source: Global TB Report 2024, WHO&GAM UNAIDS estimates

\*Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030

\*\* Second United Nations high-level meeting on TB:  
<https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/featured-topics/un-declaration-on-tb>

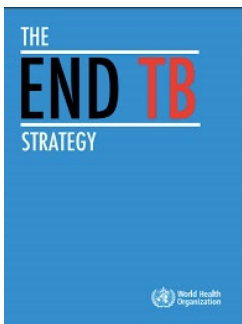
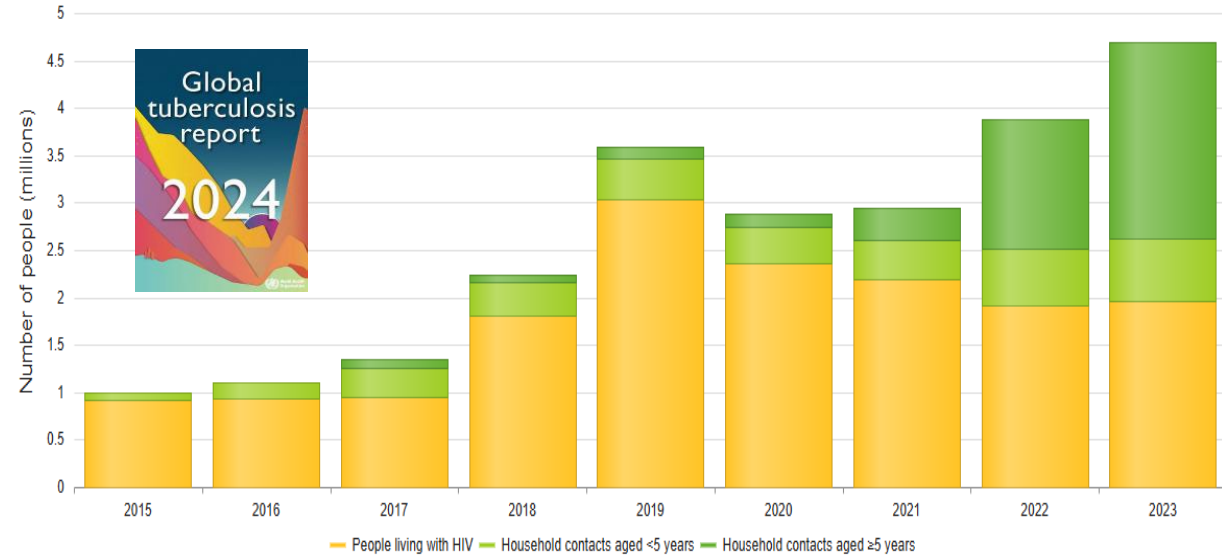
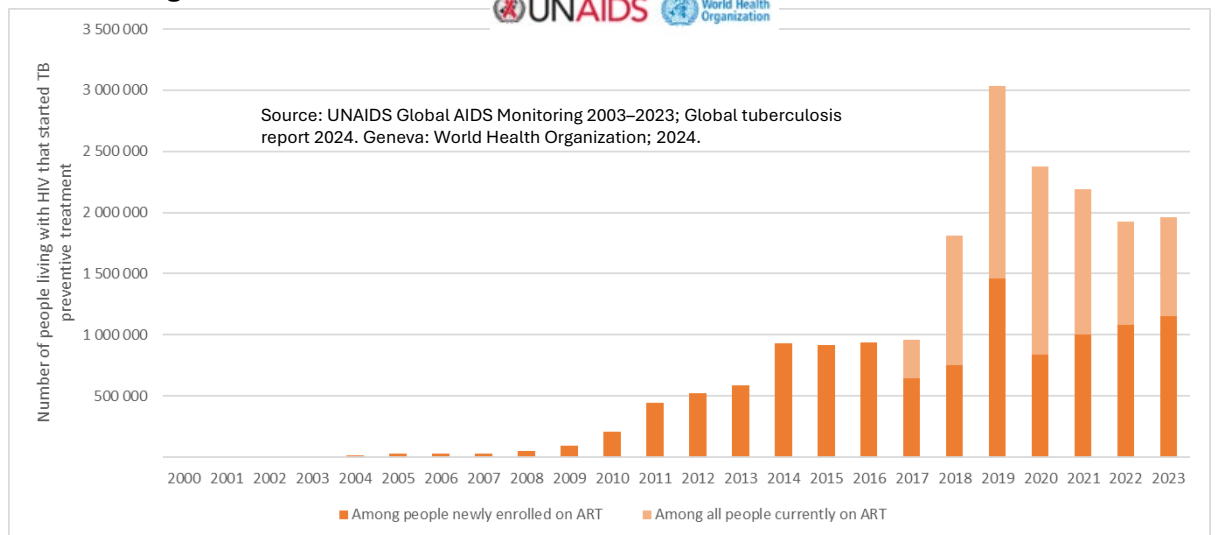


Fig. 3.1 The global number of people provided with TB preventive treatment (TPT), 2015-2023



Number of people living with HIV enrolled on ART that started TB preventive treatment, global, 2002-2023



Source: UNAIDS Global AIDS Monitoring 2003-2023; Global tuberculosis report 2024. Geneva: World Health Organization; 2024.

# WHO Recommendation (2025)

## TPT in people living with HIV

### ✓ TPT options for PLHIV (adults and adolescents):

❖ **Preferred:** 3 months rifapentine + isoniazid (3HP)

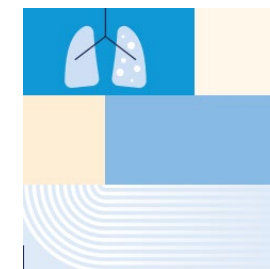
❖ **Alternatives:** 6 or 9 months isoniazid (6H or 9H)

*(conditional recommendation, low certainty evidence)*

➤ Other WHO recommended regimens such as 3HR, 1HP, 4R and 6Lfx may be used in special circumstances)\*

\* WHO consolidated guidelines on tuberculosis Module 1: prevention - tuberculosis preventive treatment, 2nd edition  
<https://www.who.int/publications/i/item/97892400961961>

| Population             | Preferred  | Alternative  | Other (special circumstances)   |
|------------------------|--|--|---|
| Adults and adolescents | <b>3HP</b><br>(Isoniazid + Rifapentine, weekly for 3 months) | <b>6H</b><br>(Isoniazid, daily for 6 months) <sup>1</sup><br><b>9H</b><br>(Isoniazid, daily for 9 months) <sup>2</sup> | <b>3HR</b> (Isoniazid + Rifampicin, daily for 3 months) <sup>3</sup><br><b>1HP</b> (Isoniazid + Rifapentine, daily for 1 month) <sup>4</sup><br><b>4R</b> (Rifampicin, daily for 4 months) <sup>5</sup><br><b>6Lfx</b> (6 months of daily levofloxacin) <sup>6*</sup> |



# Policy and Practice Implications



## Benefits

- Shorter duration → improved adherence
- Effective & accessible → cost savings
- Fewer AEs & lower hepatotoxicity
- Compatible with dolutegravir-based ART
- Comparable efficacy to 6-9H



## Programmatic relevance

- Simplifies logistics
- Supports the targets of WHO End-TB and Global health sector strategies on HIV/HEP/STIs
- Feasible in low-resource settings / LMIC

## Examples of Country Implementation of 3HP for TPT in PLHIV

| Country      | Implementing/ Supporting Entity        | Description   | Coverage/Results   |
|--------------|--|---|--|
| South Africa | IMPAACT4TB                             | National scale-up of 3HP with focus on PLHIV; supported by IMPAACT4TB.                            | ≥80% treatment completion; high patient and provider acceptability.  |
| Uganda       | CHAI, Unitaid                          | Integration of 3HP into routine HIV care; emphasis on healthcare worker training and drug supply. | ~70% adherence; improved outcomes while using 3HP as compared to 6H. |
| India        | National TB Elimination Program (NTEP) | Pilot studies in high-burden districts; evaluating feasibility, adherence, and safety.            | Pilot data shows high adherence and minimal adverse effects.         |
| Brazil       | Ministry of Health                     | National guideline inclusion of 3HP; integration in primary care and provider training.           | Wide acceptance: early implementation showed high tolerability.      |