

Scaling-up TB/HIV

HIV-TB SOTA
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Outline - key areas

- Global TB/HIV epidemiology/progress
- TB/HIV clinical management issues
- TB/HIV scale up – policies / evidence
- Summary / recommendations

Global situation 2007

TB/HIV

■ HIV/AIDS burden

- 33 million with HIV globally
- 2.7 million newly infected in 2007
- 3.4 million on ART
- In high prev. areas, five new HIV infections for every two people newly added on treatment

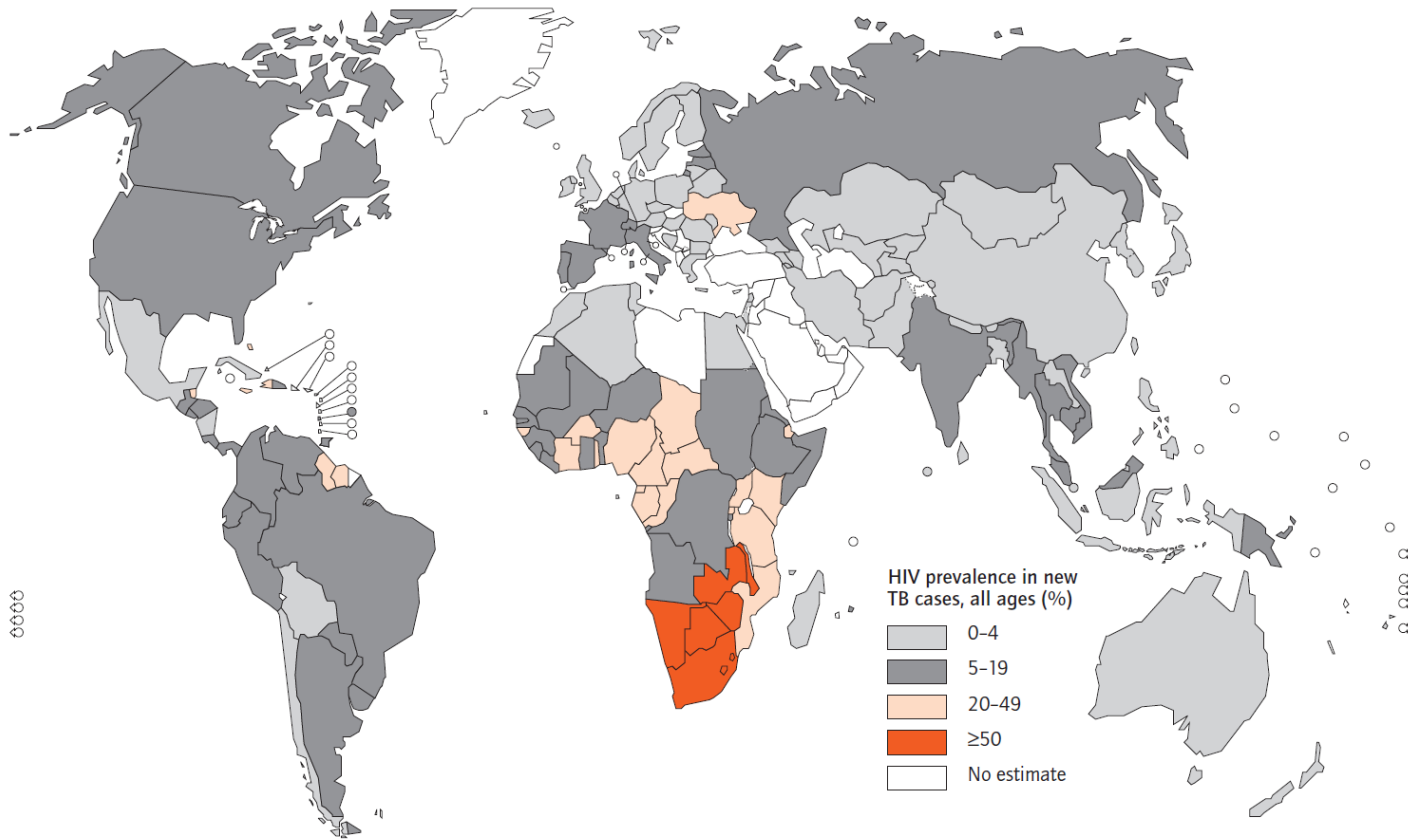
■ TB burden

- 9.27 million (139 per 100,000);
 - Estimated death 1.77 million (27 per 100,000)
- HIV-associated TB 1.4 million,
 - Estimated death 0.5 million (23% of all HIV deaths)

HIV Prevalence in New TB Cases- 2007

■ **FIGURE 1.3**

Estimated HIV prevalence in new TB cases, 2007



Management of TB/HIV co-infection

- High mortality during first 2 months
 - ART should be initiated earlier ($CD4 < 350$ cells/mm³), if possible **during the intensive phase of TB treatment**
- Early ART initiation has challenges
 - High pill burden
 - Drug-drug interaction
 - Toxicity
 - IRIS

Recommended ART for patients with active TB (WHO)

- First-line ART regimen
 - 2 NRTIs plus 1 NNRTI (EFV)
 - Use of triple NRTIs
- Second-line ART: Limited PI options for pts on TB regimen with R.
 - Use of additional amounts of boosted ritonavir with some PIs (SQV/r or LPV/r)
 - Replacement of rifampicin with rifabutin.

Rifabutin

- Added on WHO EML for use in HIV+ TB pts on 2nd line ART - ritonavir-boosted PIs
- Equally safe / effective as rifampicin
- Little effect on PI serum concentration
- cost-effective in combination with the standard dose of boosted-PIs.

IRIS

■ Paradoxical TB-IRIS

- Pts on TB treatment and start ART
- 1-4 weeks after ART initiation
- Major risk factors:
 - Low CD4 count, Disseminated TB
 - Short interval between TB treatment and ART

■ Unmasking TB-IRIS (ART Associated TB)

- High incidence during first 3 months of ART.
- Severe pulmonary TB, TB abscess, neurological manifestations...
- High mortality (>20%) during first year of ART.

WHO 2009 TB guidelines - draft

Treatment of TB (TB/HIV)

- New TB (PTB and EP) cases: 2HRZE / 4HR
- 2HRZE/6HE regimen should be phased out
- Optimal dosing is daily throughout the course
- In high INH resistance continuation phase: 4HRE
- All previously treated patients: culture and DST
- Failures with DR likelihood: empiric MDR regimen

Collaborative TB/HIV activities

A. Establish the mechanism for collaboration

- A.1. TB/HIV coordinating bodies
- A.2. HIV surveillance among TB patient
- A.3. TB/HIV joint planning
- A.4. TB/HIV monitoring and evaluation

B. To decrease the burden of TB in PLWHA- 3 I's

- B.1. Intensified TB case finding (ICF)
- B.2. Isoniazid preventive therapy (IPT)
- B.3. TB infection control in health care and other settings (IC)

C. To decrease the burden of HIV in TB patients

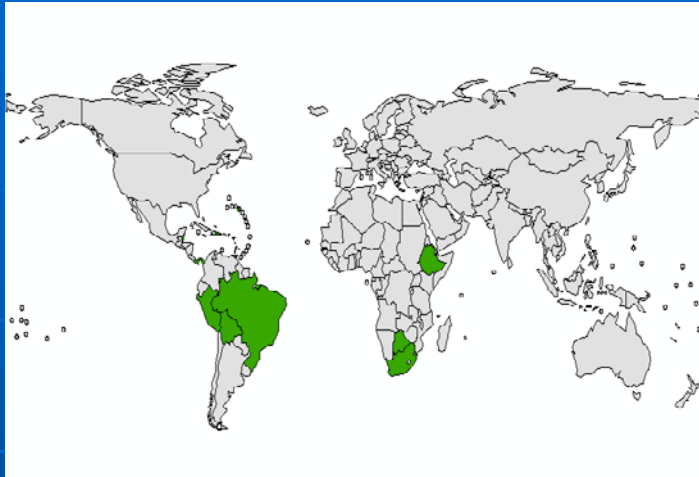
- C.1. HIV testing and counselling
- C.2. HIV preventive methods
- C.3. Cotrimoxazole preventive therapy
- C.4. HIV/AIDS care and support
- C.5. Antiretroviral therapy to TB patients.

HIV testing and treatment

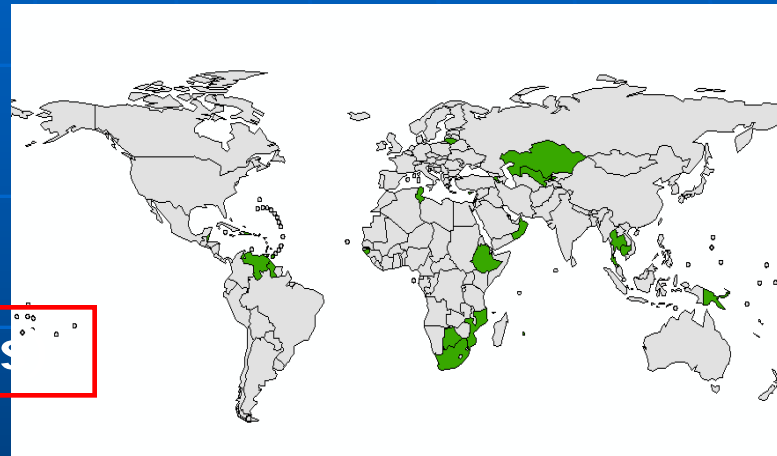
Global 2007 (WHO)

Region	TB patients tested for HIV, thousands (%)	% of tested TB patients HIV +	% of identified TB patients on CPT	% of identified TB patients on ART
AFR	492 (37)	51	66	29
AMR	114 (49)	13	36	77*
EMR	4.2 (1.1)	12	35	65*
EUR	169 (35)	2.5	52	16
SEAR	122 (5.5)	15	37	17
WPR	95 (6.6)	7	45	28
Global	996 (16)	30	63	30

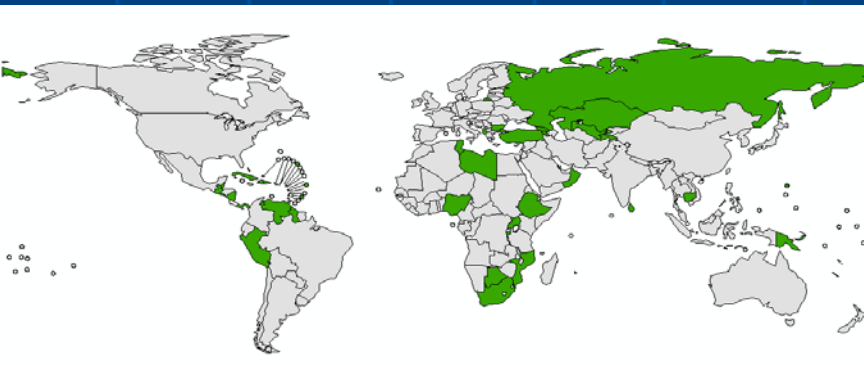
Implementation of IPT 2005-2007



2005 (10 countries, 26000 cases)



2006 (25 countries, 27000 cases)



2007 (45 countries, 29000 cases)

Scaling up the 3 I's

ICF, IPT, IC

Cross-cutting challenges (global consensus)

- Policies and guidelines (3 I's)
- HR capacity - trained staff.
- Weak M&E system – Ownership? R&R?
- Tools/strategy to scale up ICF & IPT
- TB-IC policy and implementation
- Laboratory/Health systems capacity
- Committent/collaboration NTP/NACP
 - Priority setting
- Integration - centralized ART services vs decentralized TB services

Intensified TB Case Finding

- High CFR for HIV-infected TB pts
 - 25-50% during TB treatment
 - >50% deaths occur within 2 months
- Early diagnosis vital
 - Reduces transmission and case-fatality
 - Improve safety of ART initiation
 - Improve uptake of IPT
- Challenges:
 - Diagnosis difficult (AFB, X-ray, clinical)
 - Evidence-based approach to TB screening

WHO policy on TB case finding

- TB screening of PLHIV using at least a simple set of questions
- A referral system between HIV and TB services.
- TB screening among PLHIV at health facilities, contacts, those at high risk for HIV, and congregate settings.

TB preventive therapy

- IPT – effective, safe and feasible (WHO)
- The role of ART & IPT in TB prevention has become more evident
- But concerns
 - Durability of protection
 - Effectiveness of TB screening
 - Drug resistance risk
 - Adherence

Widespread ART is associated with decline in TB prevalence

Cape Town IAS 2009

	HIV Negative			HIV Positive		
	2005n=584	2008n=899	p-value	2005 n=174	2008n=306	p-value
Current Notified TB	0.7%	0.7%	0.97	4.0%	2.3%	0.24
Previously Undiagnosed TB	0.5%	0.4%	0.84	5.2%	1.3%	0.01
TOTAL	1.2%	1.1%	0.98	9.2%	3.6%	0.02

Middelkoop K et al. *Widespread ART is associated with decline in TB prevalence.* 5th IAS Conference on HIV Treatment, Pathogenesis and Prevention, Cape Town, abstract WeLBB105, 2009.

TB incidence in HIV infected patients in Rio – impact of ART and IPT

Incidence rate of tuberculosis for primary exposure categories.

Exposure category	IR (per 100 PY)	Incidence rate ratio
Naive	4.01 (3.40–4.69)	1.0 (REF)
ART only	1.90 (1.66–2.17)	0.48 (0.39–0.59)
IPT only	1.27 (0.41–2.95)	0.32 (0.10–0.76)
Both	0.80 (0.38–1.47)	0.20 (0.09–0.91)
Total	2.28 (2.06–2.52)	

Golub J et al, AIDS 2007, 21:1441–1448

IPT, HAART and TB risk in HIV infected adults in SA – prospective study

Incidence rate of tuberculosis for primary exposure categories.

IPT & HAART history	IR (per 100 PY)	Incidence rate ratio
Naive	7.1 (6.2–8.2)	REF
HAART only	4.6 (3.4–6.2)	0.65 (0.46–0.91)
IPT only	5.2 (3.4–7.8)	0.73 (0.44–1.13)
IPT and HAART	1.1 (0.2–7.6)	0.15 (0.004–0.85)

Golub J etal AIDS 2009, 23:631–636

TB drug susceptibility after IPT

IAS 2009 - Thibela TB*

	First episode			Re-treatment episode	
	TB after IPT group	Control cluster	Laboratory sub-study	TB after IPT group	Control cluster
Any INH resistance	7/58 (12.1%)	12/182 (6.6%)	32/270 (11.8%)	1/13 (7.7%)	12/67 (17.9%)
MDR-TB	1.58 (1.7%)	6/182 (3.3%)	21/269 (7.8%)	1/13 (7.7%)	8/67 (11.9%)

- TB episode with drug resistance in TB after IPT group not significantly different from those in comparison group

- Most TB episodes after IPT have good treatment outcome.

- Data don't support concerns about drug resistance following IPT

*TB treatment outcomes and drug susceptibility in individuals previously exposed to INH preventive therapy in a high HIV prevalent setting – South Africa. Poster + oral presentation IAS 2009

ICF and IPT scaling up HIV/AIDS implementers - ICAP Moz

TB screening for ICF - ART facilities

- Used active TB symptom screening tool.
- Progressive increase in the proportion of HIV patients **screened for TB** at enrollment:
 - **26%** (587/2,219) patients at 5 facilities in Q1 2007
 - **58%** (4,614/8,023) patients at 32 facilities in Q4 2008

Conclusion

- Enhancing TB case finding using TB screening at ART facilities is feasible.
- Screening tool improves **data collection** as well as management and **follow-up** of co-infected patients.
- Challenge was high number of suspects – sensitivity??
- Recommend - screening tools evaluation and validation

Responding to adherence challenge to IPT

Urban ART facility - ICAP Mozambique

- IPT implementation
 - INH made available at general pharmacy
 - ART facility chosen for IPT
 - National TB screening tools used
 - Doctors: prescribe IPT
 - Nurses: focal point + monthly followup
 - First month – only **38%** (13/34) went to IPT follow-up, but 57% defaulters returned for ART not IPT
- Response:
 - Strengthened **counseling** of patients pre-IPT and during follow-up
 - “IPT” recorded on **patient card and file envelope** in addition to the IPT register
 - **More healthcare staff involved** in patient follow-up – patients better tracked

Responding to adherence challenge to IPT Cont'd

First 6 months of IPT implementation July – December 2008

	Patients adherent + follow up	Defaulters to follow-up visit
Month 2	38% (13/34)	62% (21/34) 57% (12/21) to ART visit not IPT visit
Month 3	78% (42/54) 45% with delay	22% (12/54)
Month 6	91% (99/109) 32% with delay	9% (10/109)

Lessons Learnt

- IPT in ART facility is feasible
- Intensive patient counseling improves adherence
- If pts return for first follow-up visit, rarely miss further visits
- Combining IPT & ART visits can reduce IPT missed visits and delays

WHO policy on TB prevention

- HIV services should provide IPT as essential package of care for PLHIV when active tuberculosis is safely excluded for 6-9 months
 - Mandatory CXR (WHO/UNAIDS 1998 policy)
 - PPD skin test is not a requirement
- Rifampicin and pyrazinamide containing regimens are contraindicated
- Information about isoniazid preventive therapy should be made available to all people living with HIV

TB preventive therapy / IPT summary

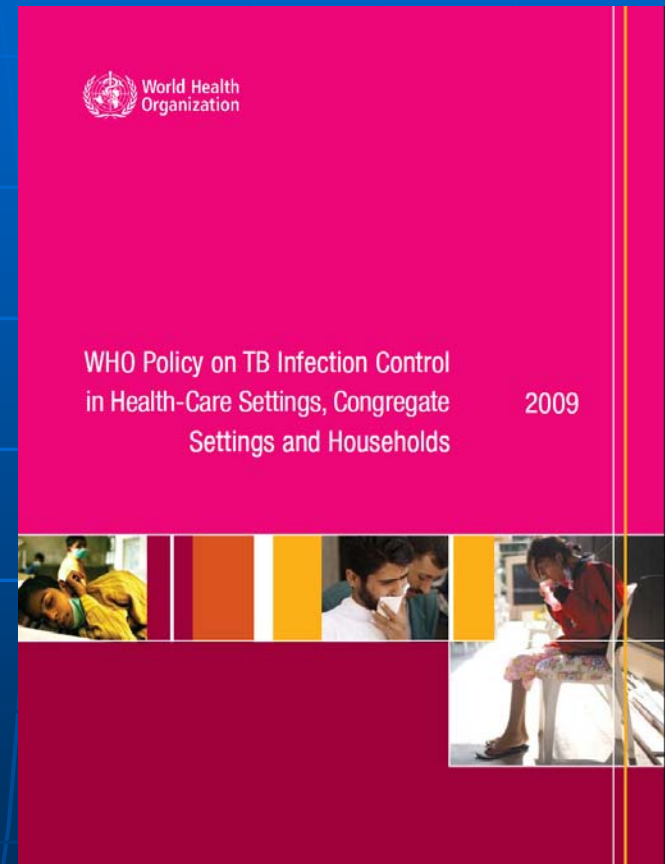
- ART reduces TB incidence, but TB remains high after ART.
- IPT reduces TB incidence (also during ART) and is cost-effective and safe.
- Strategies to implementation and adherence need to be enhanced.
- New drugs for shorter treatment and porbably longer protection?
- New tools for more accurate Dx of latent TB and to exclude active disease.

Global efforts – ongoing

- WHO-CDC meta-analysis: sensitive clinical algorithm to screen TB in PLHIV
- Standardized evidence-based guidelines to TB screening and prevention (IPT) among PLHIV.
- Research on shorter and effective TB preventive regimens. (CREATE...)
- Community case finding strategy for TB (Eg. ZAMBART Project)

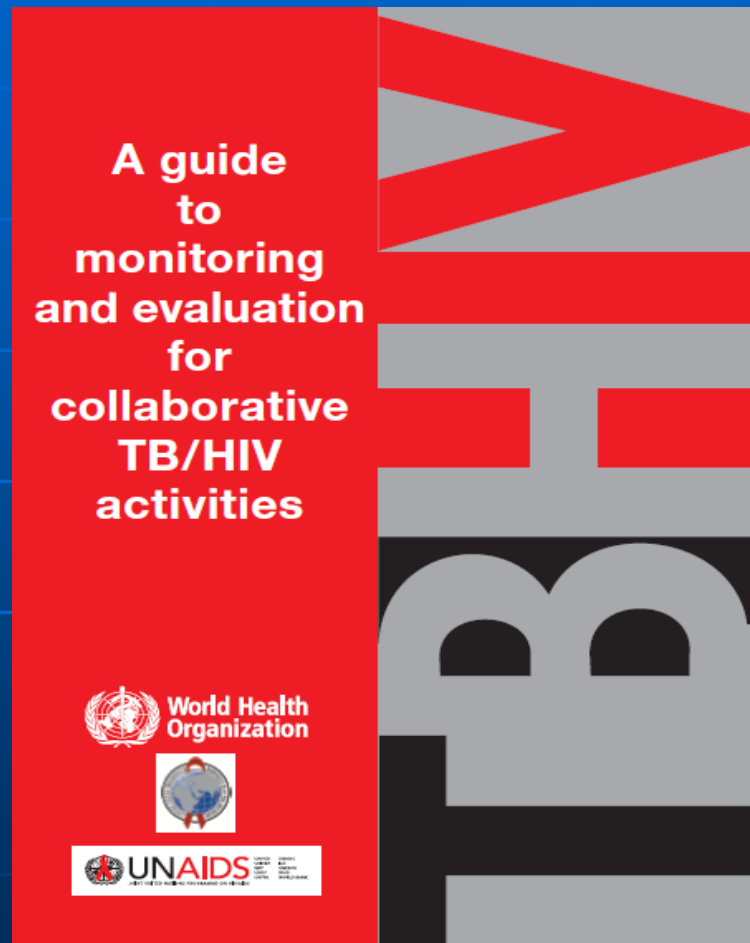
TB-IC policy in health care facilities (WHO 2009)

- Organisation and systems
- Administrative controls
 - Triage, cough etiquette, minimise hospital stay
- Environmental controls
 - Ventilation (natural and mechanical)
 - UV radiation
 - Health facility design and renovation
- Personal protective interventions
 - Respirators
 - Prevention and care package for HIV positive health workers



TB/HIV M&E

- Revised 2009
- Indicators (2004) reduced from 20 to 12
- Including 2 new indicators



TB/HIV research agenda

Cape Town July'09

- Clinical challenges of Dx & Rx of TB in PLHIV:
 - TB IRIS, PI+Rifamycins
 - TB and early mortality in PLHIV
- MDR-TB/HIV
 - Early DR diagnostic strategy and tools
 - Best treatment models – community or hospital
 - TB-IC strategies and tools
- Pediatric TB in HIV infected children
 - Better diagnostic tools for TB in co-infected children
 - Maternal interventions to reduce risk in children
 - Safe and effective vaccine for TB in HIV+ and HIV-
- Preventing TB in PLHIV
 - Impact of ART on TB prevention
 - Community case finding for TB
 - TB-IC effectiveness of strategies

Conclusions/Recommendations

- Scaling up TB care in HIV/AIDS settings a gap
- ICF: priority and gateway to TB care for PLHIV
- IPT: feasible/effective but has to be linked to ICF
- TB-IC: comm. & CHW and congregate settings.
- Engage HIV stakeholders to scale up TB/HIV.
- ART scale up key to reducing TB and mortality
- Enhance effectiveness - "evidence based"
- Define benchmarks and targets for countries
- Focus on efficiency and sustainability of programs