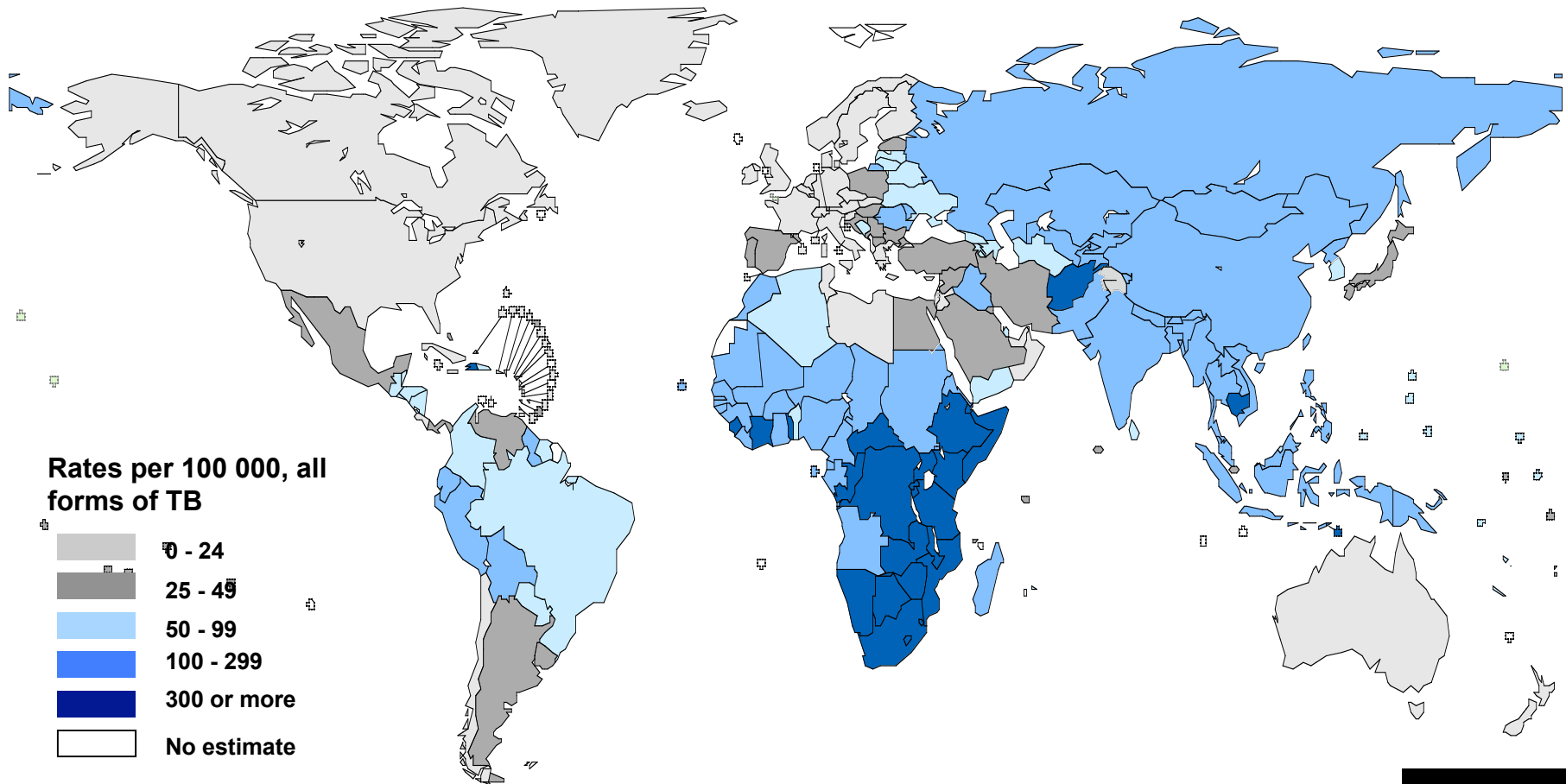


HIV Treatment as TB Prevention

Timothy Lahey, MD MMSc
Dartmouth Medical School

Estimated TB incidence rate, 2003

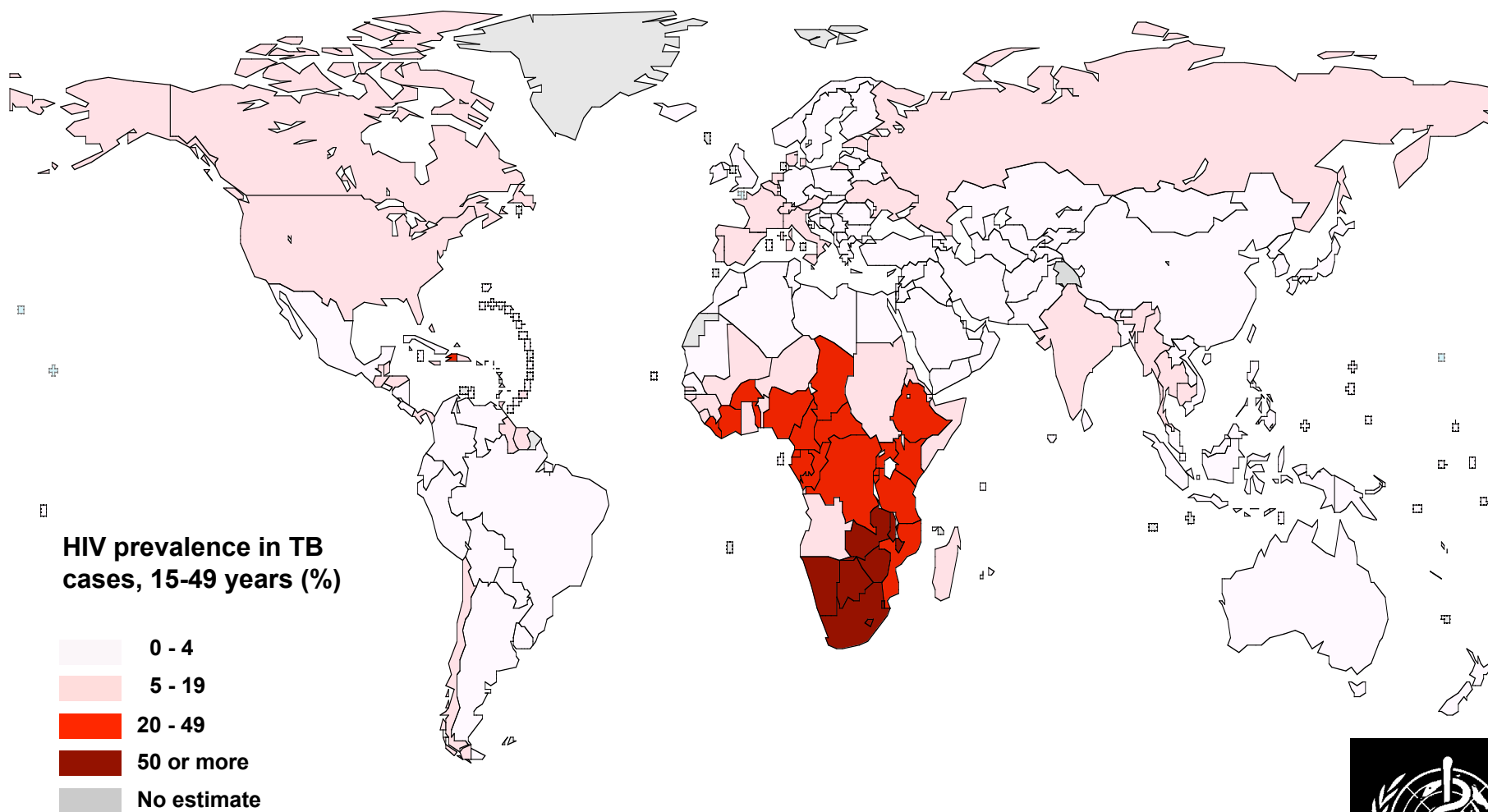


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Estimated HIV prevalence in TB cases, 2003

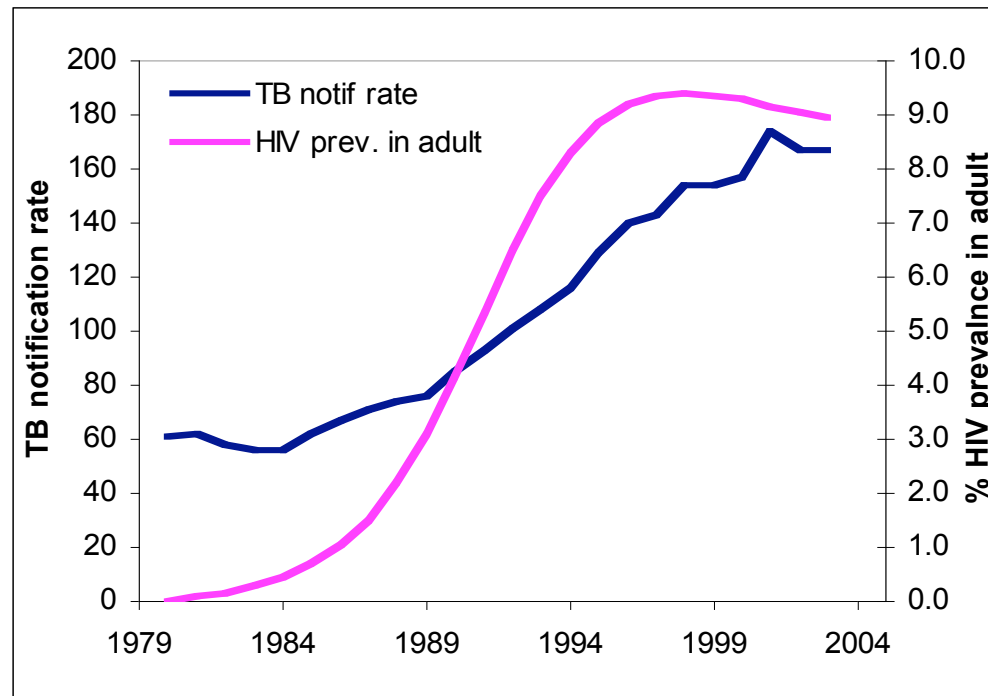


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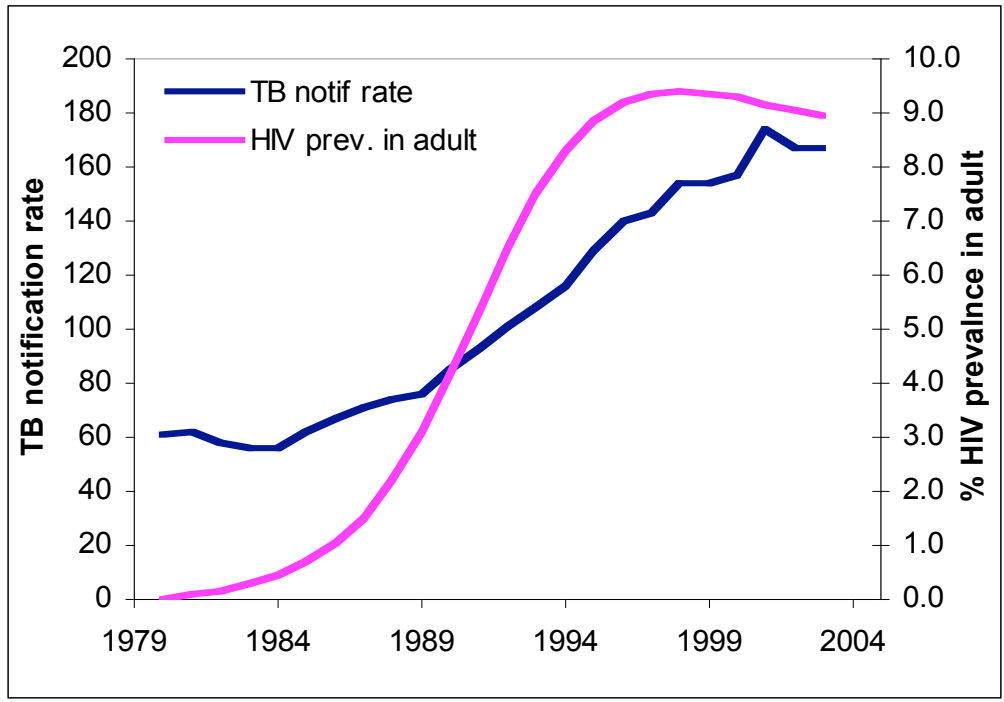
Tuberculosis Worldwide	Total Infected	Deaths
Total	16.1 million	1.77 million
HIV+	0.3 million (2%)	0.22 million (12%)



Tuberculosis in Tanzania	HIV prevalence	HIV prevalence in TB patients
	7%	34%



June 2005

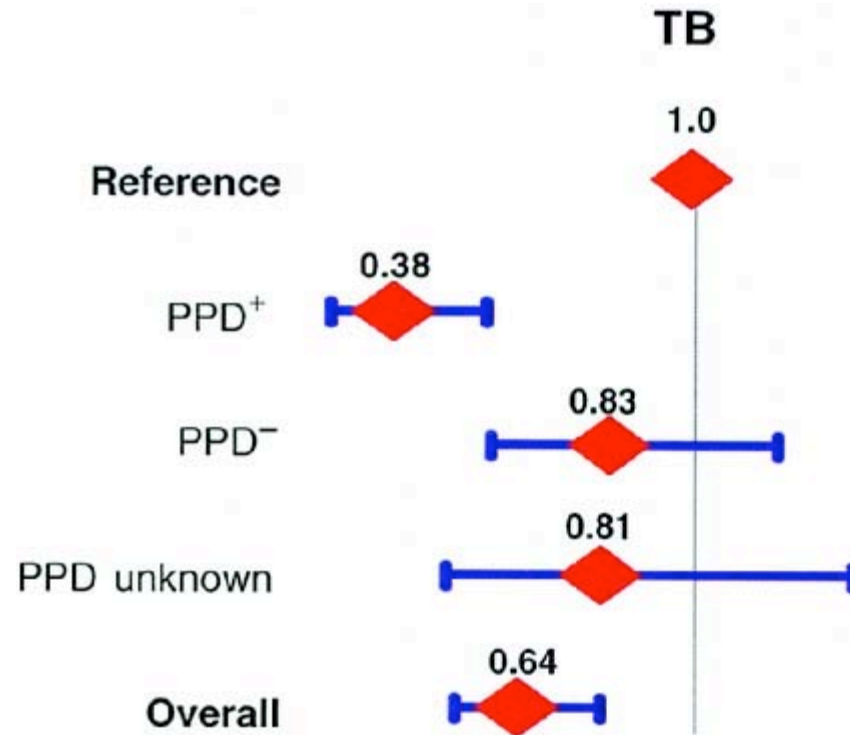


Tuberculosis in Tanzania	HIV prevalence	HIV prevalence in TB patients
	7%	↑%



June 2005

Isoniazid Prevention of TB (IPT)



IPT Drawbacks during HIV

- ↓ **TST sensitivity during HIV**

– Graham *JAMA* 1992

- ↑ **risk of TB during HIV**

– Range *Int J Tuberc Lung Dis* 2001

- ↑ **risk of TB with falling CD4**

– Moore *AIDS* 2007



**Potential for
missed
treatment
opportunities**

- **Risk of subclinical TB**

- **IPT doesn't fix immune system → future TB risk**



Does treating HIV prevent TB?

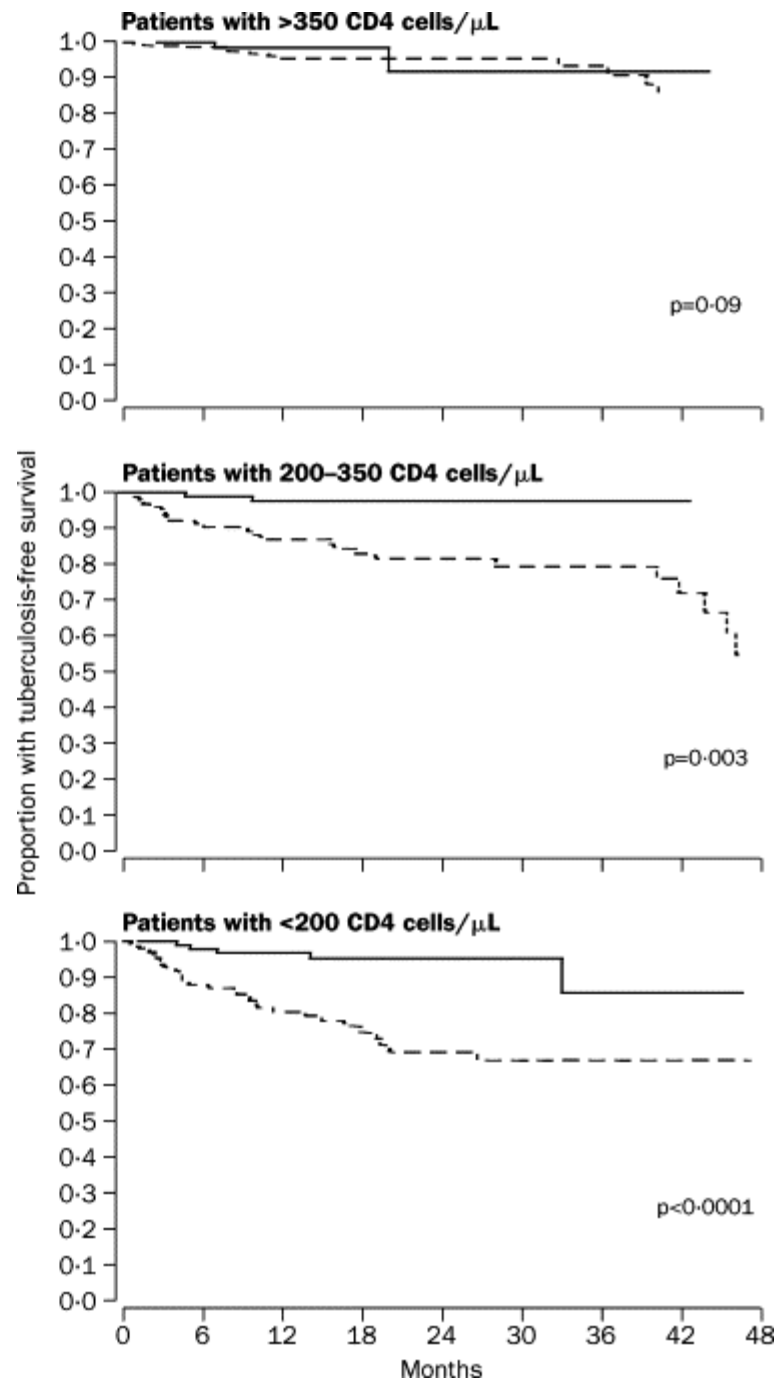
Treated HIV Pts Have Less TB

- **60-80% reduction in risk in developed world HIV cohorts**

- Jones *Int J Tuberc Lung Dz* 2000 - US
- Elzi *Clin Infect Dis* 2007 - Switzerland

264 on
HAART, 770
not on
HAART in
South
Africa

4x lower
incidence of
TB in those
with HAART



Better HIV Therapy = Better TB Prevention

- 2160 HIV patients in Italy
- Risk of TB characterized according to antiretroviral regimen
- Two drugs: 84% less risk of TB
- HAART: 92% less risk of TB

How Fast Does HAART Work?

- 1044 Ugandan adults starting ART
- TB incidence highest in first 6 months of ART
- 48% lower risk by 7 months after ART
- 39% lower risk by 18 months


How Long Does HAART Work?

- 1044 Ugandan adults starting ART
- TB incidence highest in first 6 months of ART
- **48%** lower risk by 7 months after ART
- **39%** lower risk by 18 months

IPT and ART: Synergy

- 11,026 HIV+ pts in Brazil

Treatment	TB incidence (per 100 PY)
None	4.01
IPT	1.27
ART	1.9
Both	0.8 (Cox hazard 0.24; P < 0.001)

A stack of gold coins is the central focus, set against a deep red background. The coins are stacked vertically, with several more coins scattered around the base of the stack. The lighting is warm, highlighting the metallic texture of the coins. A semi-transparent yellow box with a thin black border is positioned on the right side of the image, containing the text.

**What's the cost
of ART to
prevent TB?**

Overlapping Side Effects



Side Effect	TB rx	HIV rx
Rash	Pyrazinamide, rifampin, rifabutin, isoniazid	Nevirapine, efavirenz, abacavir
Nausea/vomiting	Pyrazinamide, rifampin, rifabutin, isoniazid	Zidovudine, PI's
Hepatitis	Pyrazinamide, rifampin, rifabutin, isoniazid	Nevirapine, PI's, immune reconstitution with viral hepatitis
Bone marrow toxicity	Rifabutin, rifampin	Zidovudine

Drug Interactions

Class	Agent	ART
Anti-Mycobacterials	Rifabutin	All PIs with RTV boosting: standard dose PI/r + RBT 150 mg qod or 150 mg 3x/wk
		FPV 1400 mg bid + RBT 150 mg/d or 300 mg 3x/wk
		ATV 400 mg/d + RBT 150 mg qod or 150 mg 3x/wk
		EFV 600 mg/d + RBT 450-600 mg/d or 600 mg 3x/wk
		IDV 1000 mg q 8h + RBT 150 mg/d or 300 mg 3x/wk
		LPV/r 400/100 mg bid + RBT 150 mg qod or 150 mg 3x/wk
		NFV 1000 mg tid + RBT 150 mg/d or 300 mg 3x/wk
		NVP standard + RBT standard (no adjustment)
		RTV 600 mg bid + RBT 150 mg qod or 150 mg 3x/wk
		TPV/r 500/200 mg + RBT 150 mg qod or 150 mg 3x/wk
	Rifampin	All PIs & NNRTIs contraindicated except EFV (600 or 800 mg/day) using standard doses of rifampin. NVP - if necessary, use with caution and monitor LFTs



Immune Reconstitution Disease
(IRD)

TB Immune Reconstitution Dz

- **Wide array of incidence estimates**
 - ~15%
- **Likely relates to**
 - Prevalence of TB
 - Population immune compromise
 - Case definition

TB Immune Reconstitution Dz


- 160 on TB rx, then ART in South Africa
- Median CD4 68
- IRD 12%
- Usually pulmonary (84%), 1% death rate
- Low CD4 a risk for IRD

HAART days after TB rx	0-30	31-60	61-90	91-120	>120
% with IRD	100	33	14	7	0

Summary: ART ↓ TB

- It works
- Works ~ 6 months
- Durability of benefit?
- Better + IPT
- Beware drug toxicity and, <2 mo, IRD





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