

# **CDC Partnerships in TB Control in Africa**

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# Objectives

- To provide an overview of CDC's collaborative partnerships to support global efforts to combat TB and TB/HIV
- To identify challenges and opportunities to improve global TB control efforts

# Background

- >1.6 million TB deaths each year
- >9 million people develop active TB annually
- 1/3 of world's population have latent TB infection
- Leading cause of HIV/AIDS related deaths worldwide
- Most frequent infectious cause of death in women of child-bearing age in developing world

# Background

- Emergence of drug resistant TB complicating global TB landscape
- Multi-drug resistant (MDR) TB comprise 5% of all TB cases worldwide
- 4% to >20% of MDR B cases were actually extensively drug resistant (XDR) TB
- True incidence of MDR TB in the developing world, particularly Africa, is not known

# Areas of Focus

- Contribute to international efforts led by the Stop TB partnership:
  - To strengthen national TB control programs
  - To mitigate the impact of TB/HIV
  - To prevent emergence of and improve detection, diagnosis and treatment drug resistant TB
  - To address infection control in institutions and communities
- Decrease the incidence of US foreign-born TB cases

# Approach

- Conduct operational and epidemiological research and training that strengthens TB control efforts and builds capacity within national TB control programs (NTCPs)
- Provide technical assistance (TA) and program support to NTCPs
- Provide TA and scientific support to international organizations
- Conducts programmatically relevant clinical and diagnostic studies

# Approach

- Work in limited number of countries
  - Strategic interest (e.g., contributes to U.S. foreign-born TB cases )
  - High burden of TB (22 countries accounting for approximately 80% of TB cases globally)
  - Unique opportunities to conduct important research/training (e.g., *research that informs global policy*)

# Top 10 countries contributing foreign-born TB cases in the US, 2006

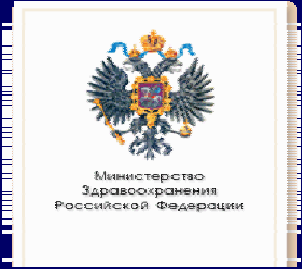
- Mexico\*
- Philippines\*
- Vietnam\*
- India\*
- China
- Haiti
- Guatemala
- South Korea\*
- Ethiopia\*
- Peru\*

\* countries with ongoing CDC projects/activities



# 22 TB High-burden Countries

Afghanistan	India	Russian Federation
Bangladesh	Indonesia	
Brazil	Kenya	South Africa
Cambodia	Mozambique	Tanzania
China*	Myanmar*	Thailand
Democratic Republic of Congo	Nigeria	Uganda
	Pakistan	Viet Nam
Ethiopia	Philippines	Zimbabwe



# Collaborations / Partnerships

- Ministries of Health in host countries
  - National TB Control Program
  - National AIDS Control Program
- In-Country institutions and non-governmental organizations
  - Community based organizations
  - Medical schools and schools of public health
  - Professional associations
  - Foundations

# Collaborations within CDC

- Global AIDS Program
- Division of Global Migration and Quarantine
- Division of HIV/AIDS Prevention
- International Emerging Infections Program
- Field Epidemiology and Laboratory Training Program
- Division of Health Care Quality Promotion
- Coordinating Office for Global Health



# Collaborations with other Federal Agencies

- US Agency for International Development
- National Institutes for Allergies and Infectious Diseases, NIH
- Department of State (OGAC/PEPFAR)
- Food and Drug Administration
- Department of Defense
- Department of Homeland Security

# Collaborations with International Agencies

- WHO (World Health Organizations: headquarter and regional offices)
- IUATLD (International Union Against TB and Lung Diseases)
- KNCV (Royal Netherlands TB Foundation)
- JICA (Japan International Cooperation Agency)
- GTZ (German Development Agency)
- FIND (Foundation for Innovative Diagnostics)
- FHI (Family Health International)
- MSH (Management for Science and Health)
- Bill and Melinda Gates Foundation

# TB/HIV Programs / Activities

- HIV Testing of TB patients
  - Accelerating scale-up and coverage
  - Improving uptake of referrals to HIV care from TB settings
- Improving diagnosis of TB in HIV infected persons
  - Evaluation of different screening approaches in adults and children with HIV
  - WHO-CDC TB screening meta-analysis
  - *The ID-TB/HIV Study in Southeast Asia*
- Coordination/Integration of TB and HIV services

# TB/HIV Programs / Activities

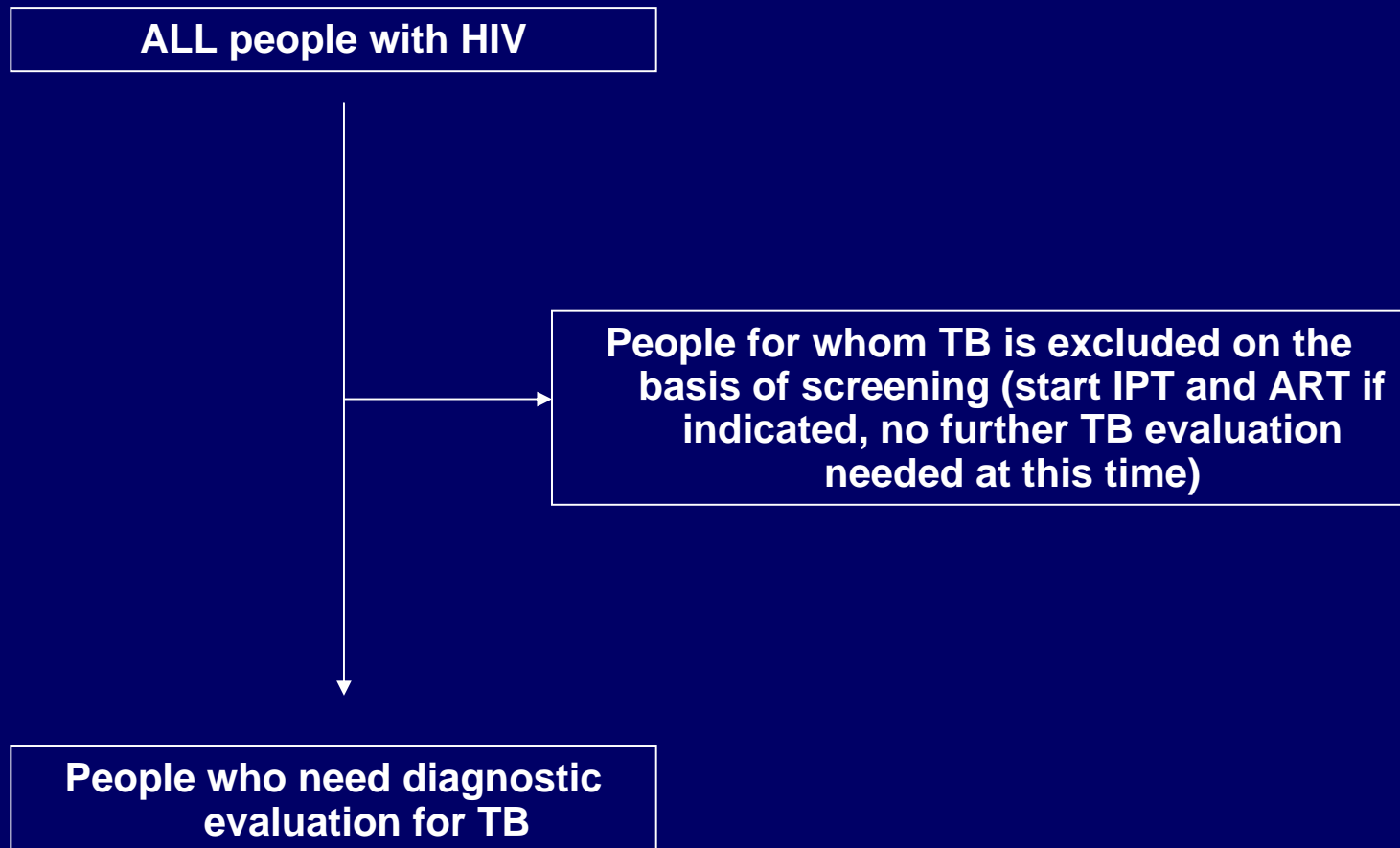
- TB/HIV Surveillance
  - TB/HIV surveillance modules for generic use
- Impact of ART and CPT on survival of patients with TB and HIV
- Participation in various national and international TB/HIV working groups (PEPFAR, WHO-headquarter and regional programs)
- Evaluating the impact of IPT on preventing active TB in patients with HIV
  - *IPT Clinical Trial in Botswana*

# **ID TB/HIV Study**

## **Finding an Algorithm with High Sensitivity to Rule-out TB**



# General goal of screening



# Focus on clinical algorithms

- Primary goal to identify sensitive algorithms for ruling out TB disease, including assessment of predictive value of cough
  - This is a main barrier to early identification of TB and safe initiation of ART and IPT
- Secondary goal to identify algorithms which were specific for the diagnosis of TB disease

# Improving the Diagnosis of TB in HIV-infected Persons in SE Asia

- Objectives are to:
  - Develop an evidence-based clinical algorithm with high sensitivity to rule-out TB in HIV-infected persons
  - Develop an algorithm with high specificity to diagnose TB in HIV-infected persons
- Algorithm based on all patients, i.e. no assumptions about importance of cough or other symptoms
- Enroll broad cross-section of HIV-infected persons from multiple settings
- Use a sensitive combination of microbiological tests as the gold-standard

# Eligibility Criteria

- Documented HIV infection
- Age  $\geq 7$  years
- Not currently being treated for TB
- No TB treatment or IPT within one year
- No TB screening (x-ray or sputum smears) within previous 3 months
- No medications with anti-TB activity within past 1 month

# Enrollment Sites & Sample Size

- Total planned enrollment: 2,050 across 3 countries
  - 600 in one site in Bangkok, Thailand
  - 1,000 in four sites in Cambodia
  - 450 in three sites in Ho Chi Minh City, Vietnam



# Enrollment

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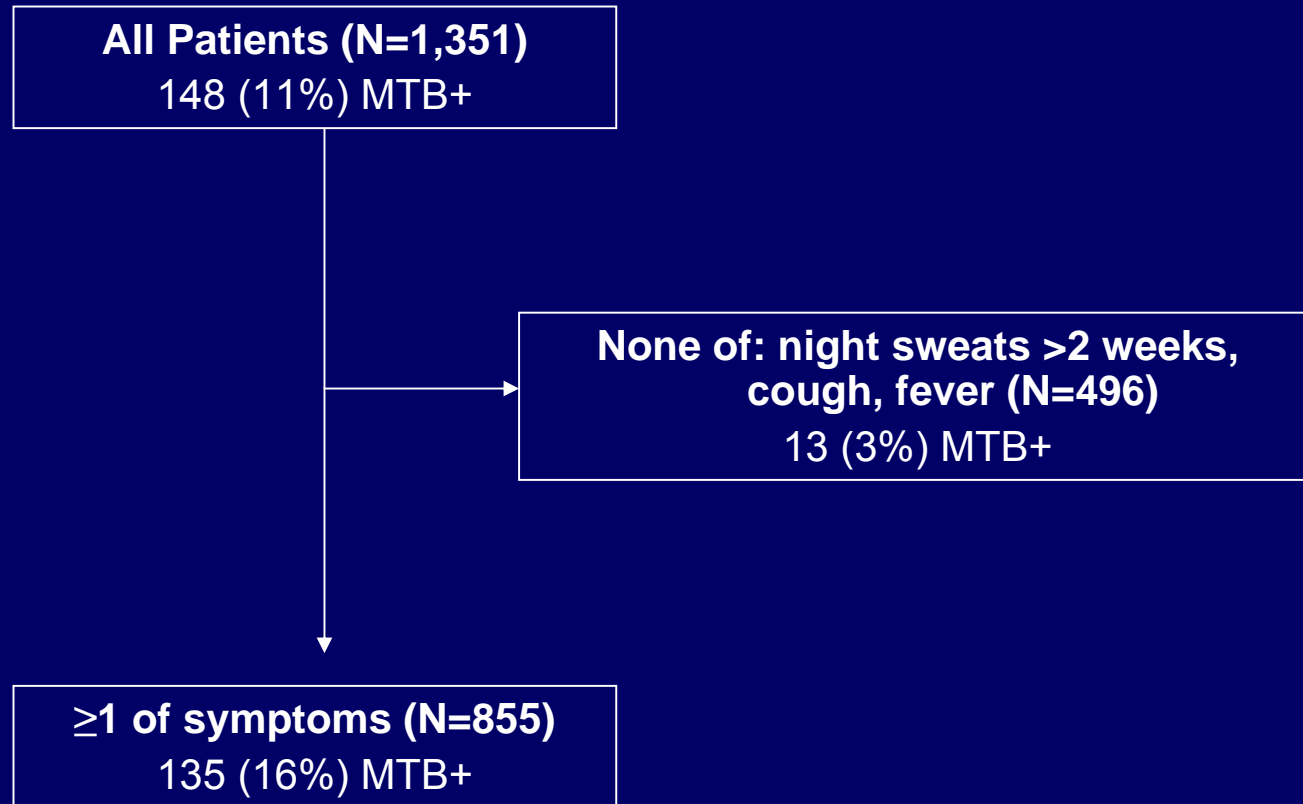
Country	Enrolled	Included in this analysis
Thailand*	669	657
Cambodia*	1009	561
Vietnam*	452	173
TOTAL*	2,130	1,391

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\*Enrollment completed



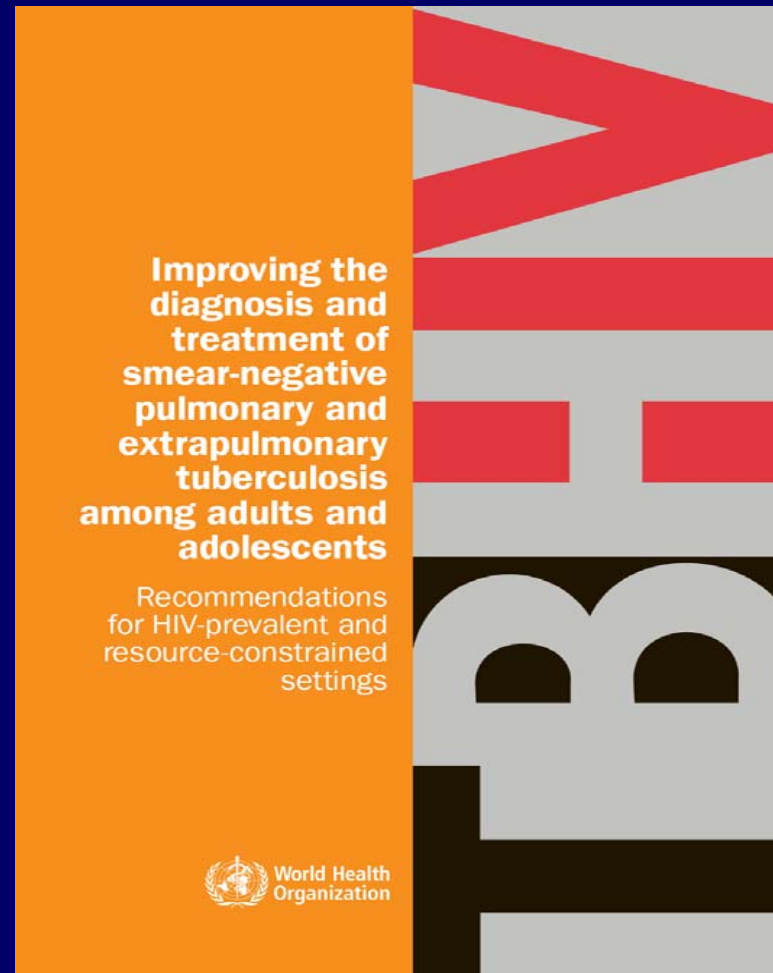
# Application of candidate approach to screening



# Preliminary Conclusions from Study

- Cough > 2 or 3 weeks insensitive (21-25% sensitivity), should not be used alone as initial screening
  - WHO algorithm for diagnosing smear-negative TB should be modified
- No other single symptom sufficiently sensitive
- Combination of symptoms (“m of n”)
  - Can be highly sensitive
  - Example – any 1 of: night sweats >2 weeks, fever, cough
  - Simple, performs as well as or better than other approaches that we evaluated

# WHO TB Screening and Diagnosis Algorithm



# Conclusions from study

- Using the WHO algorithm, 81% of TB patients would be missed
- Compared to use of sputum smears + chest radiography, using the algorithm we have defined:
  - Decreases number of smears performed by 37%
  - Decreases number of x-rays performed by 39%
  - Decreases number of people needing further diagnostic evaluation (e.g. culture) by 72%
- Number of false negatives and false positives low

# Impact to Date

- Cambodia has initiated IPT and modified ICF guidelines. They are awaiting final analysis to inform exact algorithm
- Thailand and Vietnam are awaiting the final algorithm to inform their guidelines
- WHO/WPRO has incorporated findings into revised TB/HIV regional framework
- WHO HQ is collaborating with CDC on a TB screening meta-analysis to inform global guidelines, expected completion during Q2 2009
- Studies of implementation of this revised approach planned for Kenya, Cambodia, Vietnam, and Thailand



# **Isoniazid Preventive Therapy in HIV-infected Adults Accessing Anti-retroviral Therapy in Botswana**

# Botswana IPT Trial Objectives

- **Primary question:**
  - Is lifetime IPT superior to 6 months IPT to prevent active TB, hospitalization, illness and/or death?
- **Some of the secondary questions:**
  - How long after 6 months IPT does the effect last?
  - Do differences in CD4 or TST affect IPT efficacy?
  - Do ARVs in addition to IPT result in added TB prevention?
  - Estimate subject adherence with limited vs. continuous INH

# IPT Trial Study Design

Study Type: Randomized Double-Blind Placebo Controlled

Setting: Eight government clinics where IPT & ARV care provided

Participants: 2,000 PLWH - 1,000 per study arm



# Screening for the IPT Trial

Nov 2004 – Jun 2006

Screen1\*

4331

Declined

313

(7%)

Ineligible

1084

(25%)

Screen2 \*\*

2934

(68%)

Enrolled in IPT Trial

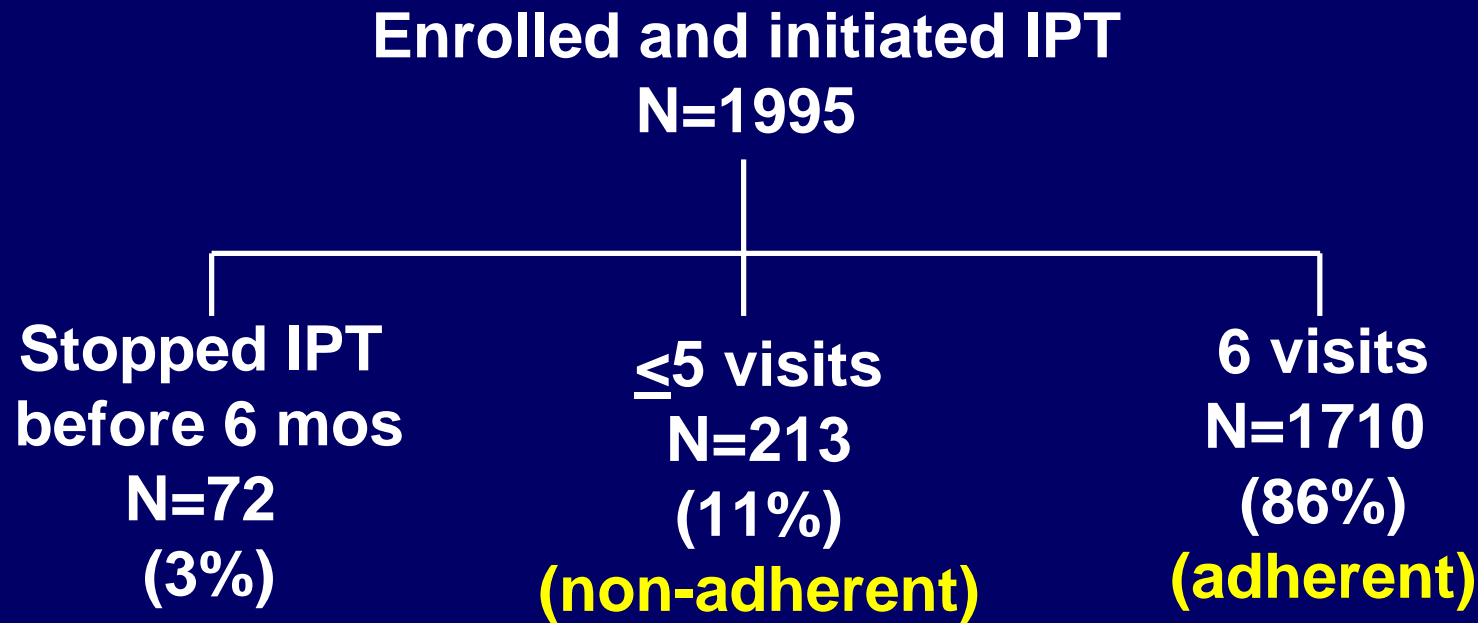
n=1995

\* National IPT program screening criteria

\*\* Specific clinical trial screening criteria



# Outcomes and adherence for IPT Trial enrollees during 6 months of observation



\* National IPT program screening criteria

\*\* Specific clinical trial screening criteria

# Summary of IPT Trail findings during 6 months of observations

- 7 (0.4%) developed TB disease
- 28 (1.4%) had severe adverse events: 19 (69%) hepatitis, 5 (18%) rash
- 21 died (59% from and AIDS defining illness)
- 22% initiated highly active anti-retroviral treatment (HAART)
- Overall IPT adherence was 89% and being on HAART improved adherence

# IPT Trial Progress

- Completed enrolment in July 2006
- Last person to take the last pill will be in June 2009
- Code will be broken after that time

# Challenges and Opportunities

- Inadequate capacity at national level to plan and implement quality TB programs
- Urgent need to expand laboratory coverage and strengthen laboratory capacity
  - Quality assured smear microscopy
  - Culture and drug susceptibility testing
  - New rapid techniques for detecting drug resistant TB
- Urgent need for new and improved diagnostic tools
  - Field testing and introduction of new rapid and reliable diagnostic tools
  - Testing algorithms to improve speed and accuracy of diagnosis

# Challenges and Opportunities

- Improved surveillance for TB disease, TB/HIV and drug resistance
- Critical need for new drugs → safer, shorter and more effective regimens
- Improve case management of TB patients and patients co-infected with HIV
- Accelerate response to MDR and XDR-TB
  - Prevalence surveys to measure the magnitude of the problem and geographic spread
  - Rapid diagnosis and effective management and treatment

# Challenges and Opportunities

- Implement and facilitate appropriate infection control practices in health care settings and communities
- Develop local workforce expertise through training and education
- Establish regional “Centers of Excellence” for TB diagnosis, treatment and public health.

**Thank you for your Attention**



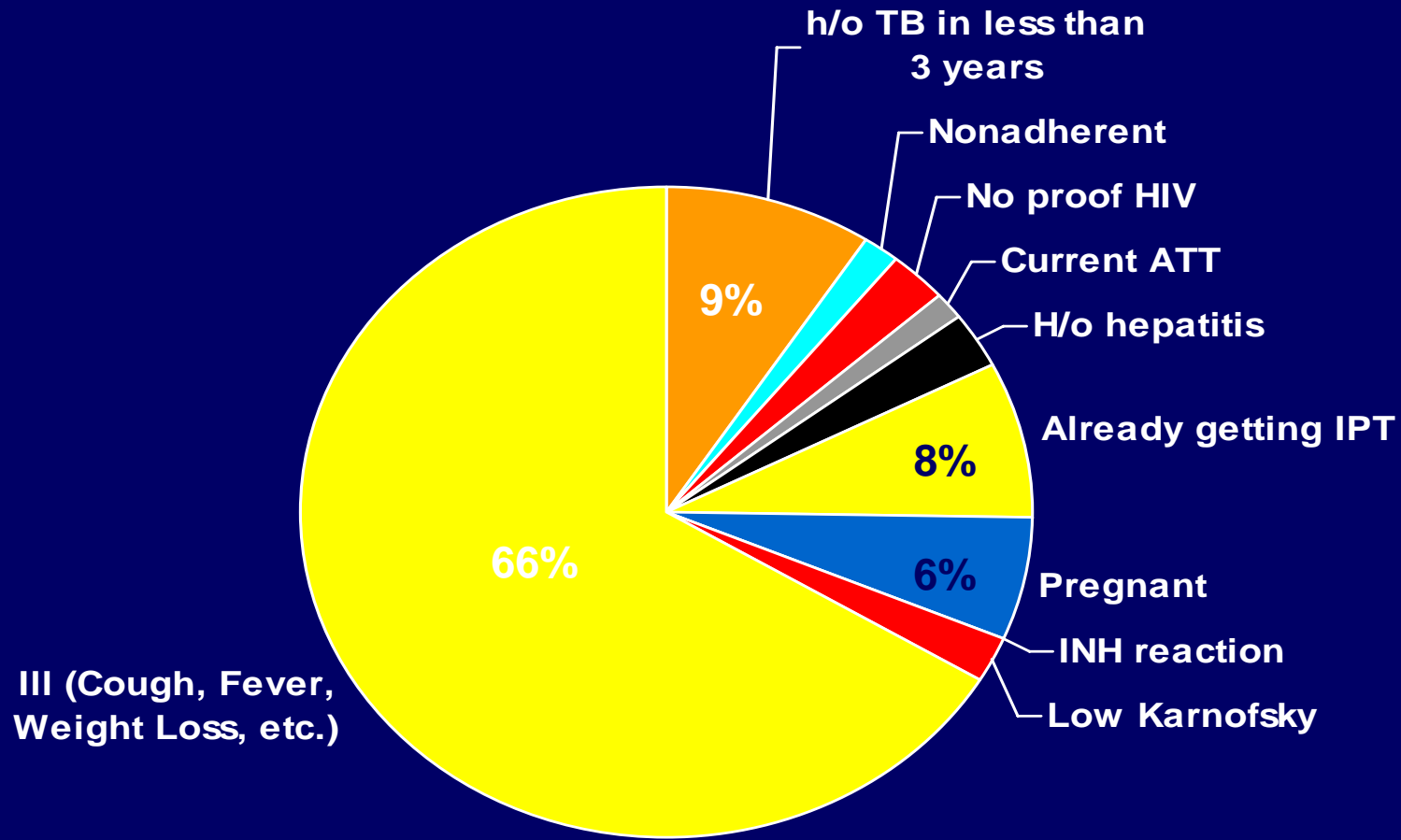
# Strengthening National TB Programs

- TA to evaluate program quality and performance
- Operational research training and mentoring
  - Applied epidemiological methods
  - Data analysis
  - Synthesis and scientific writing
- TB and TB/HIV surveillance and surveys
- TB disease prevalence surveys

# Strengthening National TB Programs

- Epidemiological Studies
  - TB screening practices among pediatric TB suspects/patients
  - Assessment of Guidelines for Diagnosis of Smear-Negative TB
- Laboratory capacity development
  - Expansion of quality-assured culture and DST
  - Evaluation and implementation of new rapid diagnostics

# Reasons for Exclusion (1084 Ineligible on Screen1)



# Reasons for Stopping IPT before 6 months

- TB cases (n=7)
  - 3 definite, 2 possible and 2 possible TB deaths
- Deaths (n=21)
  - 6 each due to CNS and GI, 2 respiratory, 4 others, 3 unknown
- Severe adverse events (n=28)
  - 19 hepatitis, 5 rash, 2 seizure, 2 others
- Others (n=16)
  - 9 moved too far, 2 “too ill”, 3 started warfin, 2 doctor stopped