# HIV-TB: Confronting the problem through an integrated research agenda

Recap… and more

# TB/HIV Collaborative Activities

**Establish mechanisms for collaboration**

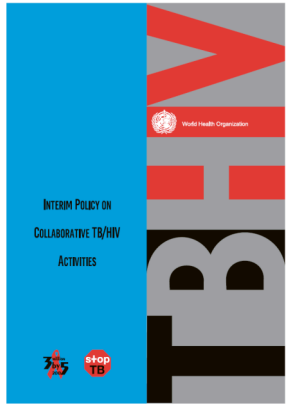
- Set up a coordinating body for TB/HIV activities
- Conduct surveillance of HIV prevalence among tuberculosis patients
- Carry out joint TB/HIV planning
- Conduct monitoring and evaluation

**Decrease the burden of TB in people with HIV/AIDS**

- Establish intensified tuberculosis case-finding
- Introduce isoniazid preventive therapy
- Ensure tuberculosis infection control in health care and congregate settings

**Decrease the burden of HIV in tuberculosis patients**

- Provide HIV testing and counselling
- Introduce HIV prevention methods
- Introduce co-trimoxazole preventive therapy
- Ensure HIV/AIDS care and support
- Introduce antiretroviral therapy



# The Policy-maker's Questions

1. What is the best solution to the TB/HIV problem?
   - WHO TB/HIV collaborative activities are best consensus to date, based on evidence available
2. What are the best ways to implement activities to solve the TB/HIV problem in my health system?
3. How can I bring about the necessary changes in the health system to implement TB/HIV activities?

*Lavis J et al. Use of research to inform public policymaking. Lancet 2004;364:1615-21*

# Program Issues

- Centralized and de-centralized programs
  - Rural vs. urban settings
  - “stigma” – barrier or excuse?
- Community involvement is crucial
  - Advocacy needs to be funded
  - Role of community in implementing new strategies

# 1. Assessment of the TB/HIV package

- What is the overall benefit of implementing the TB/HIV policy package?
  - Can it be implemented (process indicators)?
  - How much impact will it, or its components, have, if any (impact indicators)?
  - How much will it cost, relative to the other interventions we are, or could be doing?
- Build assessment into implementation
  - TB-side underway through annual survey
  - How to record and report "HIV-side" activities?
- More formal assessment would help, but costs

# 2. What are the best ways to implement TB/HIV activities?

- What governance, financial and delivery arrangements are the most conducive to the effectiveness of the package, in our setting?
  - Eg. Management by public sector, NGOs, both
  - Aid agency supported?
  - Community based care?

# Develop synergy

- Synergy between HIV and TB control programs
- Synergy between research and control programs
- Synergy between basic science and clinical science
- How can we maximize information gained?

# 3. What are the changes necessary in the health system to implement TB/HIV activities?

- What informational, educational and financial (incentive) approaches are needed to change behaviours to implement the package?
  - Eg. How to best promote productive collaboration between NTPs and NACPs?
  - Define most effective training approaches

# Conclusions

- From this crossroads we must choose the route where TB and HIV control travel together
- Current TB/HIV policy is a reasonable base
- Now we need to show what works and what does not - research
- Integrating the agenda demands researchers and controllers work together in high HIV, high TB countries

# Pathogenesis: Short term goals for discussion

***These goals are directed towards maximizing existing knowledge to discover novel and immediately applicable approaches for cure of TB and control of HIV in adults and children.***

- Determine the optimal timing of introduction of ARVs in TB/HIV co-infected adults and children receiving TB therapy

- Determine pediatric immune profiles that influence progression of HIV and TB/HIV outcome

- ***Maximize the global impact of clinical trials by integrating basic scientific discovery of host and pathogen factors correlated with or determining clinical outcome***

# Long term goals for discussion

***These goals are directed towards understanding host and pathogen factors that will allow:***

***(i) targeted drug development including immunotherapeutic approaches to co-infection***

***(ii) Identification of patients who will benefit from specific therapeutic approaches or who are at risk for adverse events***

Determine the impact of ethnic specific host genetic factors in TB/HIV pathogenesis and clinical outcome in adults and children

Determine the impact of HIV-1 clade specificity upon HIV/TB pathogenesis and clinical outcome

Determine the impact of MTb strain specificity upon HIV/TB pathogenesis and clinical outcome

# Tools for Treating and Preventing TB in HIV-infected People

| Tools | Currently Available | In Development |
|---|---|---|
| Diagnostics | Sputum smear (ZN, auramine)<br>Culture (LJ)<br>Rapid culture (MGIT, BACTEC)<br>NAA tests (TMA, RT-PCR) | Simple rapid cultures<br>Immunodiagnostics<br>Antigen-based detection |
| Treatment | First line drugs (IRZES)<br>Second line drugs for MDR TB (Fluoroquinolones) | Fluoroquinolones<br>Diarylquinolines<br>Nitroimadazopyrans<br>Ethambutol analogues<br>Others |
| Preventive therapy | INH, INH/RIF | Rifapentine/INH |
| Other | ARVs<br>Infection Control | ? |

Strategies for Controlling HIV-Related Tuberculosis:
How are tools applied to reduce burden of disease?

| Tools | Current Strategies | Future Strategies |
|---|---|---|
| Diagnostics | Diagnose symptomatic patients who present to health services.<br>Rely on test (ZN) with 50% sensitivity<br>Algorithm for smear negatives | Active case finding<br>Contact evaluations<br>Use of new technologies<br>Joint TB/HIV case finding |
| Treatment | DOTS with first line drugs<br>INH/EMB continuation phase in many settings | Shortened treatment<br>Intermittent treatment<br>Avoid drug interactions |
| Preventive therapy | Primary INH PT for limited time | New regimens (e.g., RPT)<br>Continuous INH<br>Secondary PT<br>Mass PT |
| Other | ARVs for advanced disease<br>No infection control | Earlier ARVs<br>Enhanced infection control |

# Impact of Rapid Diagnostics, Active Case Finding and HAART on TB in High HIV Prevalence Areas: A Mathematical Model

| Intervention | % Reduction TB Prevalence | % Reduction TB Incidence | % Reduction TB Mortality |
|---|---|---|---|
| Standard | 0 | 0 | 0 |
| Molecular | 20 | 3 | 20 |
| Culture | 21 | 3 | 21 |
| Comm ACF | 25 | 10 | 21 |
| HIV ACF | 19 | 6 | 22 |
| HAART | 8 | 10 | 9 |

Dowdy, Dorman et al., 2005

# Preventive Therapy of HIV-Related TB
# Unresolved Issues and Opportunities

- What is optimal duration of INH?
- Who should get INH PT?
  - TST+ only, or high prevalence populations?
  - Patients starting ARVs?
  - Patients with prior treatment for TB?
- What are alternative regimens?
  - —Rifapentine/INH weekly x 3 months
  - —INH/Rifampin twice weekly or daily x 2-3 months
- What are alternative public health approaches?
  - —Mass preventive therapy?

# Strategies to Reduce TB/HIV in Addition to DOTS

- Active or intensified case finding
  - to identify cases transmitting infection, and who may die without treatment
- Treatment of latent TB infection
  - to prevent disease in HIV+ (and HIV-) persons
- Household HIV/TB interventions linked to cases
  - to promote active case finding, identify candidates for TB preventive therapy (and antiretroviral drugs), and reduce HIV transmission
- Combined ARV and IPT treatment programs
  - to reduce probability of developing primary or reactivation TB

# Where do we go from here?

- Put TB on center-stage of HIV agenda
- Funding commitment for TB diagnostics and drugs
- Commitment to streamline process for maximum efficiency of translating research into practice