The INDEPTH TB network – a research collaboration on TB suspects and risk factors

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History

• 2008: Osman shared a vision that INDEPTH would also contain a vibrant cross-site TB research arm

• 2009: The secretariat facilitated initial consultations and establishment of a TB interest group of sites to meet in Bissau
History

- 2010:
  - First meeting of the TB working group, participating sites:
    - Ballabgarh, India
    - Dodalab, Vietnam
    - Filabavi, Vietnam
    - Karonga, Malawi
    - Kisumu, Kenya
    - Navrongo, Ghana
    - Vadu, India
    - Bandim, Guinea Bissau
    - Dodowa, Ghana
    - Kanchanaburi, Thailand
    - Kintampo, Ghana
    - Matlab, Bangladesh
    - Nouna, Burkina-Faso
History

• 2010: Consultations in Washington with the Gates sponsored CPTR initiative Critical Path to new TB Regimens to develop TB drug trial capacity within an INDEPTH based platform.

• 2010: AGM in Accra, agreement to pursue initial cross site activities within two areas:
  – TB risk factors
  – TB suspects
History

• 2010: Seed money grant from INDEPTH for these two areas

• Participating sites:
  – Risk factors: Vadu, Karonga, Bandim
  – Suspects: Karonga, KEMRI/CDC, Filabavi, Bandim (not funded)
Preliminary report

• Funds transferred spring 2011

• Field work just initiated

• Data collection ongoing
TB risk factors - background

- TB mortality is falling, but still high – 1.45 mil. 2010

- Important risk factors for TB transmission and mortality well known

- Some of these currently addressed, eg ART roll out for HIV

- Other risk factors are thought to be important, but limited data is available.
TB risk factors - background

- WHO has identified gaps in knowledge:
  - **Neglected** risk factors (pollution, mental illness, etc)
  - **Strength of association** for established risk factors – consistency, reliability
  - **Dose-response** relationships (e.g. alcohol, smoking)
  - Effects of **cumulative exposure**, and ceased exposure
  - **Interaction** between different risk factors, overlapping exposure / clustering of risk factors
  - **Effect modification** by setting / epidemiological situation
  - **SES gradient** in different settings

- HDSS’ can provide these data!
TB risk factors - objectives

- To collect TB burden data on patients residing in the HDSS using the TB registers
- To collect information on TB risk factors using data collected in the HDSS and link to TB burden and TB treatment outcome data
- To characterize TB patients who seek (and do not seek) TB care
- To compare these data across all participating HDSS sites
- To build capacity in collecting, managing and analyzing tuberculosis surveillance data
TB suspects - background

- TB diagnosis is difficult
- Many are suspected of TB - but never diagnosed or treated
- Case definition for a TB suspect is broad (productive cough > 2 weeks, weight loss)
- A study from Bandim showed that 4% of assumed TB negative died within one month after initial consultation, 69% of these had TB as primary cause of death on VA
TB suspects - background

- Through a household visit after one month, 7% of those still symptomatic could be diagnosed with TB.
- Another study in Zimbabwe showed that 18% of initially smear negative TB patients could be diagnosed with TB within one year of follow-up.
- Follow-up is difficult in routine TB diagnostic facilities.
- HDSS’ can provide the needed follow-up!
TB suspects - objectives

- To roll out routines of logging TB suspects in health facility books
- To ensure HDSS ID is captured for new TB suspects in study area
- To register clinical symptoms at first presentation
- To establish follow-up of aTBneg 1 month after initial visit at facility
- To ensure VA of all deceased adults in the study area
TB suspects

• Current study set up:
  – Doctors enroll TB suspects at regular adult consultations at health centres
  – Prompt HIV testing, x-ray and antibiotic treatment for all smear neg
  – Clinical description
  – Risk assessment with Bandim TBscore
TBscore

- **Symptoms**
  - Cough
  - Haemoptysis
  - Dyspnoea
  - Chest pain
  - Night sweats

- **Signs**
  - Anemia
  - Pulse > 90 beats/min
  - Positive finding at lung auscultation
  - Temperature > 37 (axillary)
  - BMI <18
  - BMI <16
  - MUAC <220 mm
  - MUAC <200 mm

*Wejse C et al. TBscore: Signs and symptoms from tuberculosis patients in a low-resource setting have predictive value and may be used to assess clinical course. Scand J Infect Dis 2008;40(2):111-20.*
Status report risk factors

- Protocol in place
- Common database under construction
- Studies conducted: Diabetes prevalence among TB patients and background population (Bandim)

- Planned risk factor associations to be assessed:
  - Pollution
  - Diabetes
  - Crowding
  - Migration
  - SES
  - Smoking
  - Mental health

<table>
<thead>
<tr>
<th>Site</th>
<th>Karonga</th>
<th>Vadu</th>
<th>Bandim</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB patients</td>
<td>45</td>
<td>322</td>
<td>107</td>
</tr>
<tr>
<td>Controls</td>
<td>-</td>
<td>-</td>
<td>700</td>
</tr>
<tr>
<td>New pts/year</td>
<td>?</td>
<td>106</td>
<td>100</td>
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</tbody>
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Status report TB suspects

- Protocol in place
- Common database established

Patients identified since 2009:

<table>
<thead>
<tr>
<th>Site</th>
<th>Karonga</th>
<th>Filabavi</th>
<th>Kisumu</th>
<th>Bandim</th>
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</thead>
<tbody>
<tr>
<td>TB suspects</td>
<td>162</td>
<td>322</td>
<td>-</td>
<td>506</td>
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<tr>
<td>aTBneg</td>
<td>145</td>
<td>-</td>
<td>-</td>
<td>470</td>
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<tr>
<td>New pts/year</td>
<td>90</td>
<td>106</td>
<td>100</td>
<td>400</td>
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Future plans

- Enrollment of patients throughout 2012

- Additional risk factor association studies to be initiated

- Abstract presentations at ISC 2012

- To expand the network of cross-site TB research

- To conduct multi-site clinical trials
## Focus areas

<table>
<thead>
<tr>
<th>Immediately possible</th>
<th>Long term goals</th>
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<tr>
<td>TB suspects</td>
<td>Compare incidences</td>
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<tr>
<td>Risk factors</td>
<td>Risk of poor outcome</td>
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<tr>
<td>Treatment delay</td>
<td>Prevalence surveys</td>
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<tr>
<td>Health seeking patterns</td>
<td>Access to treatment</td>
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<tr>
<td>TB cause of death (VA)</td>
<td>Rural case detection</td>
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<td>TB in HIV, ART effects</td>
<td>Health care system/staff influence on TB epidemic</td>
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<tr>
<td>Effects of TB on household health outcomes (eg. Child mortality)</td>
<td>Multi-site trials: New drugs Vaccine candidates Micronutrients</td>
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<td>Time trends</td>
<td>Evaluate new diagnostics</td>
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<td>Effects of DOTS</td>
<td>Geographical differences</td>
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Acknowlegements

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- INDEPTH Network
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- Hanif Shaikh, Vadu
- Hoa Nguyen, Filabavi
- Frauke Rudolf, Bandim