Clinical management of combined TB and diabetes

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How to find TB-DM patients?

Bidirectional screening:
- prevalence in 4 countries
- tools and algorithms
- health economic aspects

WP1

What is the cellular / molecular basis of TB susceptibility in DM?

In-vitro studies: macrophages, adipocytes
Patient genetic studies
Functional Genomics (linking genetics & in-vitro)

WP4

How to manage TB-DM patients?

DM management during TB treatment
Health economics
TB outcome
DM treatment needs after TB treatment

WP2

What explains poor TB outcome in DM?

Bioprofiles in TB, DM and TB-DM:
- gene expression; proteomics / metabolomics; leukocyte phenotyping
- Effect hyperglycemia / TB treatment

WP3
Clinical management of TB-DM

1. Should we adjust TB treatment in dose or duration?
2. Glycemic control: how important is it for TB?
3. Should we use insulin or metformin?
4. Is there more toxicity in TB-DM? should we monitor a TB-DM patient more intensively?
5. Can we explain the higher mortality in TB-DM? What other treatments should we consider?
6. What about lifestyle and smoking?
7. How to adjust counseling & education?
8. Where should patients be treated, how to coordinate care?
9. How to continue DM care after TB treatment?
10. ..
Longer duration TB treatment?

- Taiwan, insurance database, 12688 TB-DM, 43195 TB
- two-year TB recurrence rate: **2.20%** TB DM vs **1.38%** TB (*p*<0.001)
- 9 versus 6 months anti-TB treatment
  - lower recurrence rate in DM (**HR 0.76 [0.59-0.97]**) ,
  - under conditions of full DOTs (**HR 0.69 [0.43-1.11]**) .

- higher dose?  
  (~ body weight or per kg)

*Wang, J. Y. et al, CHEST 2014*
Glycemic control in TB-DM

• Range in dysglycemia
• How much is due to inflammation?
• Will it affect TB outcomes?

• When/ how should we aim for glycemic control?

TANDEM (unpublished)

HbA1c

18-34 35-49 50+
18-34 35-49 50+
18-34 35-49 50+
18-34 35-49 50+
Indonesia Peru South Africa Romania

%
Glycemic control is difficult in TB-DM

**Drug therapy**
Side-effects (e.g., vomiting); drug-drug interactions; weight gain during treatment

**Active tuberculosis**
Inflammation leading to: weight loss; loss of appetite; insulin resistance

**Health systems**
Access and affordability of health services; collaboration between tuberculosis and diabetes physicians; laboratory facilities; continuous medication supply

**Behaviour**
Variable food intake; physical activity; treatment compliance

Constraints and challenges in access to insulin: a global perspective

David Beran, Margaret Ewen, Richard Laing

Should we use insulin or metformin?

**Insulin:**
- No drug interaction
- More effective than oral

**But:**
- Need for self-monitoring
- Risk of hypoglycemia
- Access & availability
- Prescribed by TB doctors?
- Accepted by TB patients?

**metformin:**
- No drug interaction?
- No risk of hypoglycemia
- Widely available

**But:**
- Side effects
- Use in kidney dysfunction
- Safety?
How hard should we aim for glycemic control?

Pragmatic clinical trial in TANDEM

• Standard versus intensified management
• Intervention: counseling, more frequent measurement, adjustment of DM medication according to simple algorithms
• Frequent encounters with TB providers good opportunity for counseling, including lifestyle (smoking!)
DM care often substandard

- in ‘the South’ or those at highest TB risk in ‘the North’
- access
- retention
- glycemic control
- insufficient primary / secondary prevention cardiovascular disease
increased (early) mortality of TB-DM

**Diabetes is a strong predictor of mortality during tuberculosis treatment: a prospective cohort study among tuberculosis patients from Mwanza, Tanzania**

Daniel Faurschot-Jepsen, Nyagosya Range, George PrayGod, Kidola Jeremiah, Maria Faurschot-Jepsen, Martine G. Aabye, John Changalucha, Dirk L. Christensen, Harleen M. S. Grewal, Torben Martinussen, Henrik Krarup, Daniel R. Witte, Aase B. Andersen, and Henrik Friis

- 1250 pts, 51% HIV+, 17% DM
- death < 3 mths: RR 5.0 in HIV/DM; RR 2.2 in DM

**Impact of Diabetes and Smoking on Mortality in Tuberculosis**

George W. Reed, Hongjo Choi, So Young Lee, Myungsun Lee, Youngran Kim, Hyemi Park, Jongseok Lee, Xin Zhan, Hyeungseok Kang, SooHee Hwang, Matthew Carroll, Ying Cai, Sang-Nae Cho, Clifton E. Barry III, Laura E. Via, Hardy Kornfeld

- Taiwan, 657 pts, 20% DM, 80% smoking (HIV+ excluded)
- 1-year mortality 6% in non-DM, 13% in DM
- DM plus smoking: one-year TB-ass mortality: HR 5.78
<table>
<thead>
<tr>
<th>Rank</th>
<th>Status</th>
<th>Study</th>
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<tbody>
<tr>
<td>1</td>
<td>Recruiting</td>
<td><strong>Pulmonary Tuberculosis Patients With Diabetes Mellitus</strong></td>
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<td><strong>Conditions:</strong> Diabetes Mellitus; Pulmonary Tuberculosis</td>
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<td><strong>Intervention:</strong> Procedure: intensive monitoring</td>
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<td>2</td>
<td>Not yet recruiting</td>
<td><strong>Effect of Supplementary Vitamin D in Patients With Diabetes Mellitus and Pulmonary Tuberculosis</strong></td>
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<td><strong>Conditions:</strong> Type 2 Diabetes Mellitus; Pulmonary Tuberculosis</td>
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<td><strong>Interventions:</strong> Dietary Supplement: Vitamin D; Dietary Supplement: Calcium; Dietary Supplement: Placebo Vit D; Dietary Supplement: Placebo Calcium</td>
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<td>3</td>
<td>Terminated</td>
<td><strong>Immunobiology of Diabetes and Tuberculosis</strong></td>
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<td><strong>Conditions:</strong> Tuberculosis; Diabetes Mellitus</td>
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<td><strong>Intervention:</strong> Biological: BCG</td>
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<td>4</td>
<td>Completed</td>
<td><strong>Nutrition, Diabetes and Pulmonary TB/HIV</strong></td>
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<td><strong>Conditions:</strong> Tuberculosis; HIV; Diabetes</td>
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<td><strong>Interventions:</strong> Dietary Supplement: Multimicronutrients; Dietary Supplement: Energy and proteins</td>
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<td>5</td>
<td>Active, not recruiting</td>
<td><strong>Risk of Hospitalized Infections Among Patients With Type 2 Diabetes Exposed to Oral Antidiabetic Treatment</strong></td>
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<td><strong>Condition:</strong> Diabetes Mellitus, Type 2</td>
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# Tuberculosis and HIV

315 studies found for: HIV AND tuberculosis

Modify this search | How to Use Search Results

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<tr>
<td>1</td>
<td>Recruiting</td>
<td>Effect of HIV and/or Active Tuberculosis on the Immune Responses to Trivalent Influenza Vaccine (TIV) in Adults</td>
<td>Influenza; HIV; Tuberculosis</td>
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<td>Intervention: Biological: Trivalent Inactivated Influenza Vaccine</td>
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<td>2</td>
<td>Completed Has Results</td>
<td>Tuberculosis and Human Immunodeficiency Virus (HIV) Immune Reconstitution Syndrome Trial (THIRST)</td>
<td>HIV; Tuberculosis</td>
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<td></td>
<td>Intervention: Drug: Fixed dose combination zidovudine/lamivudine/abacavir</td>
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<tr>
<td>3</td>
<td>Unknown †</td>
<td>Impact of HIV Infection on Latent Tuberculosis (TB) Among Patients With HIV-TB Co-infection</td>
<td>Latent Tuberculosis Infection; HIV Infections; Tuberculosis</td>
</tr>
<tr>
<td>4</td>
<td>Terminated Has Results</td>
<td>Daily Isoniazid to Prevent Tuberculosis in Infants Born to Mothers With HIV</td>
<td>HIV Infection; Tuberculosis; Pneumocystis Jiroveci Pneumonia</td>
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<td>Interventions: Drug: Isoniazid (INH); Drug: Trimethoprim/Sulfamethoxazole (TMP/SMX); Drug: Isoniazid Placebo (PL)</td>
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Clinical management of TB-DM

• TB treatment: longer? Higher dose rifampicin?
• Glycemic control: how important is it for TB?
• Should we use insulin or metformin?
• Is there more toxicity in TB-DM? should we monitor a TB-DM patient more intensively?
• Can we explain the higher mortality in TB-DM? What other treatments should we consider?

• Need for studies ‘beyond screening’ for TB-DM
• including (pragmatic) clinical trials