Clinical management of combined TB and diabetes

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TANDEM

How to find TB-DM patients? **WP1**

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

How to manage TB-DM patients? **WP2**

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

What is the cellular / molecular basis of TB susceptibility in DM? **WP4**

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

What explains poor TB outcome in DM? **WP3**

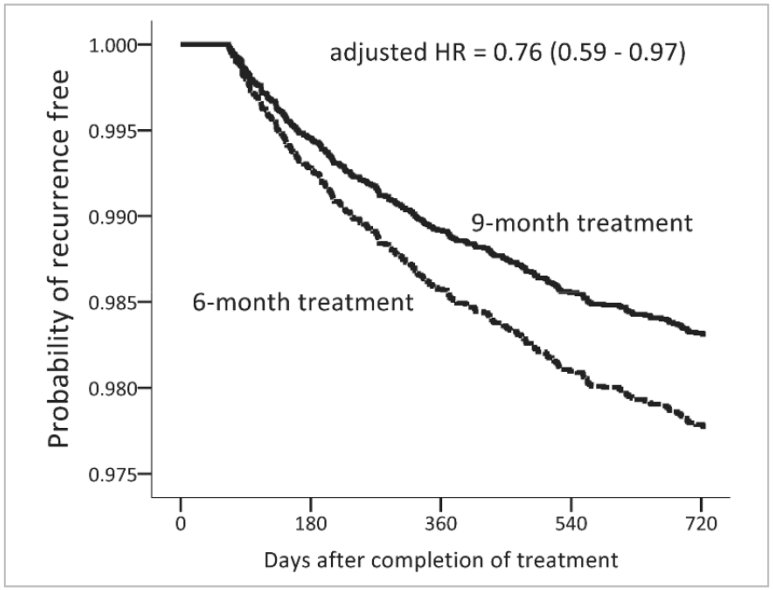
Bioprofiles in TB, DM and TB-DM:
gene expression; proteomics / metabolomics; leukocyte phenotyping
Effect hyperglycemia / TB treatment

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]).

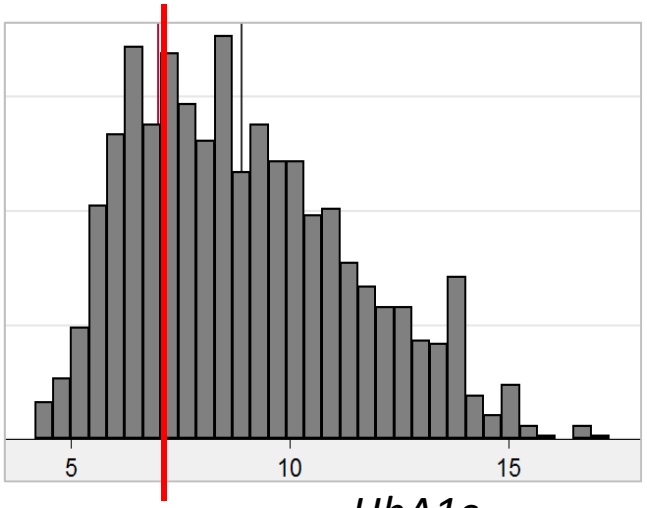


- higher dose?
  (~ body weight or per kg)

Wang, J. Y. et al, CHEST 2014

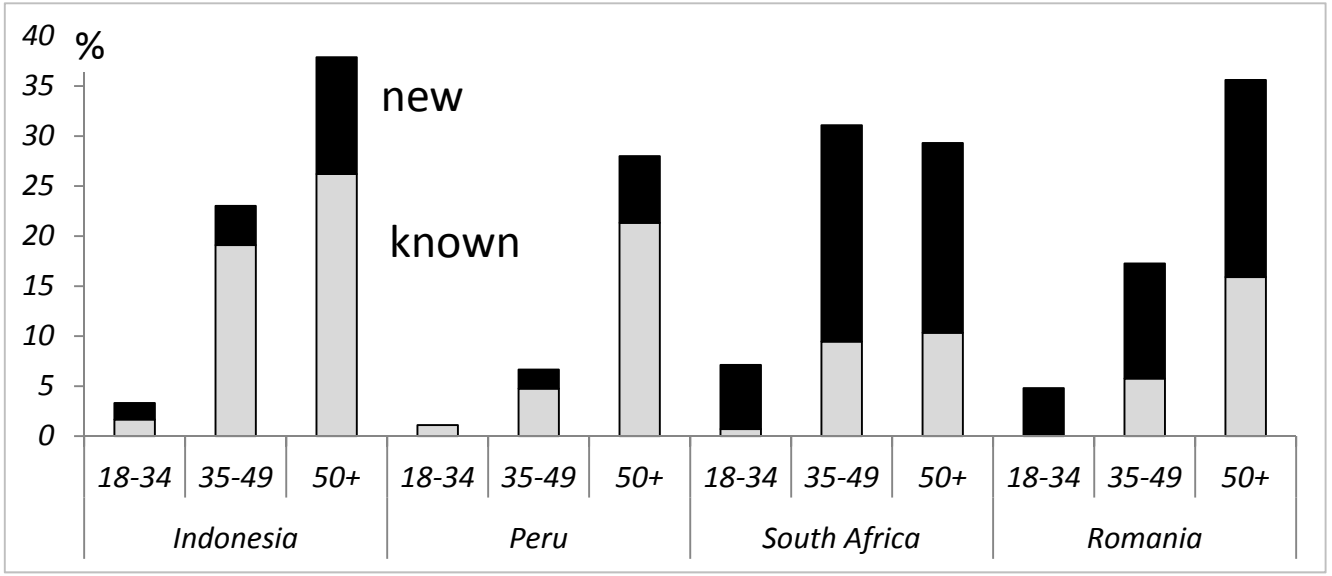
Glycemic control in TB-DM

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

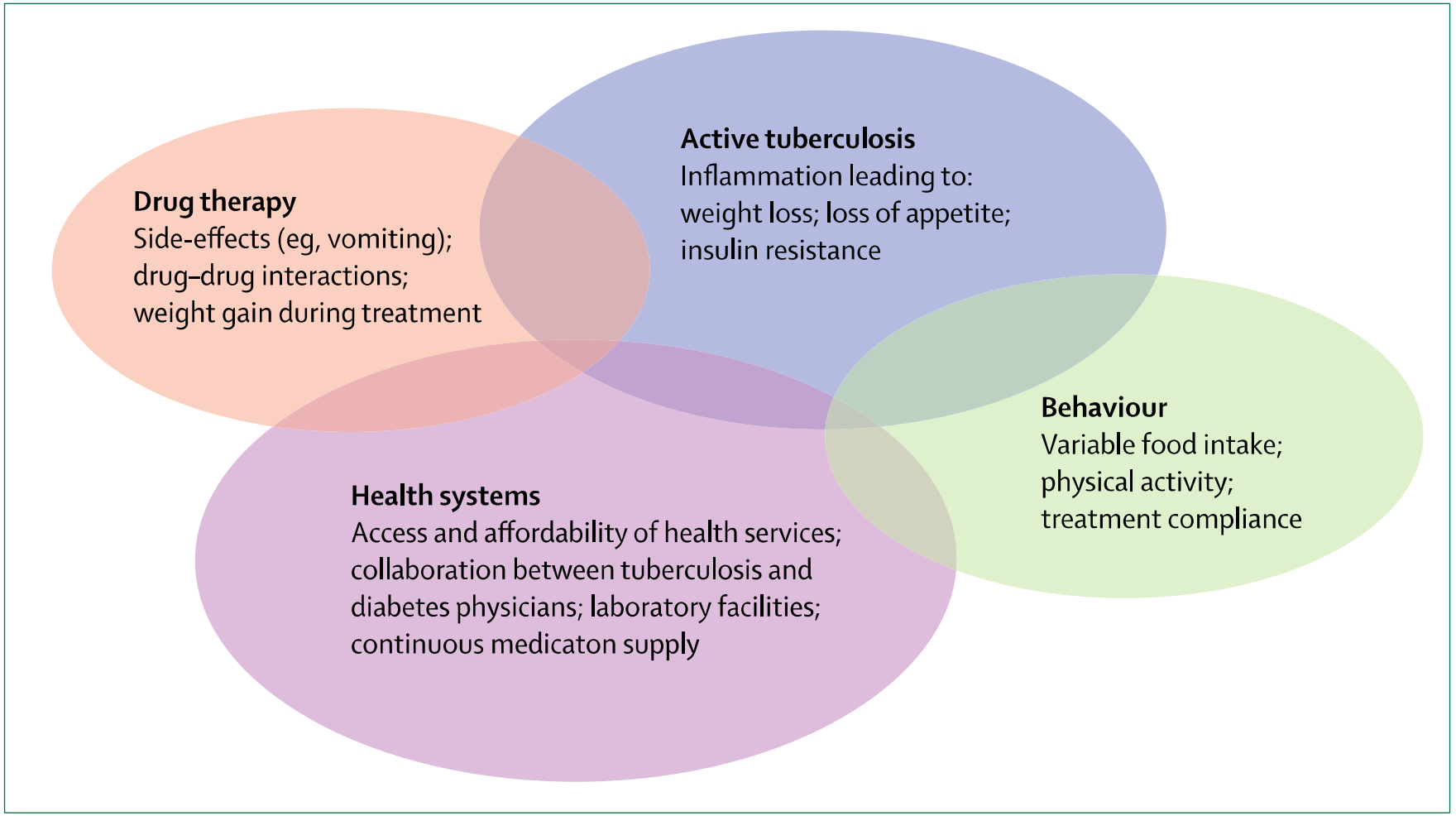


- When/ how should we aim for glycemic control?

TANDEM
(unpublished)



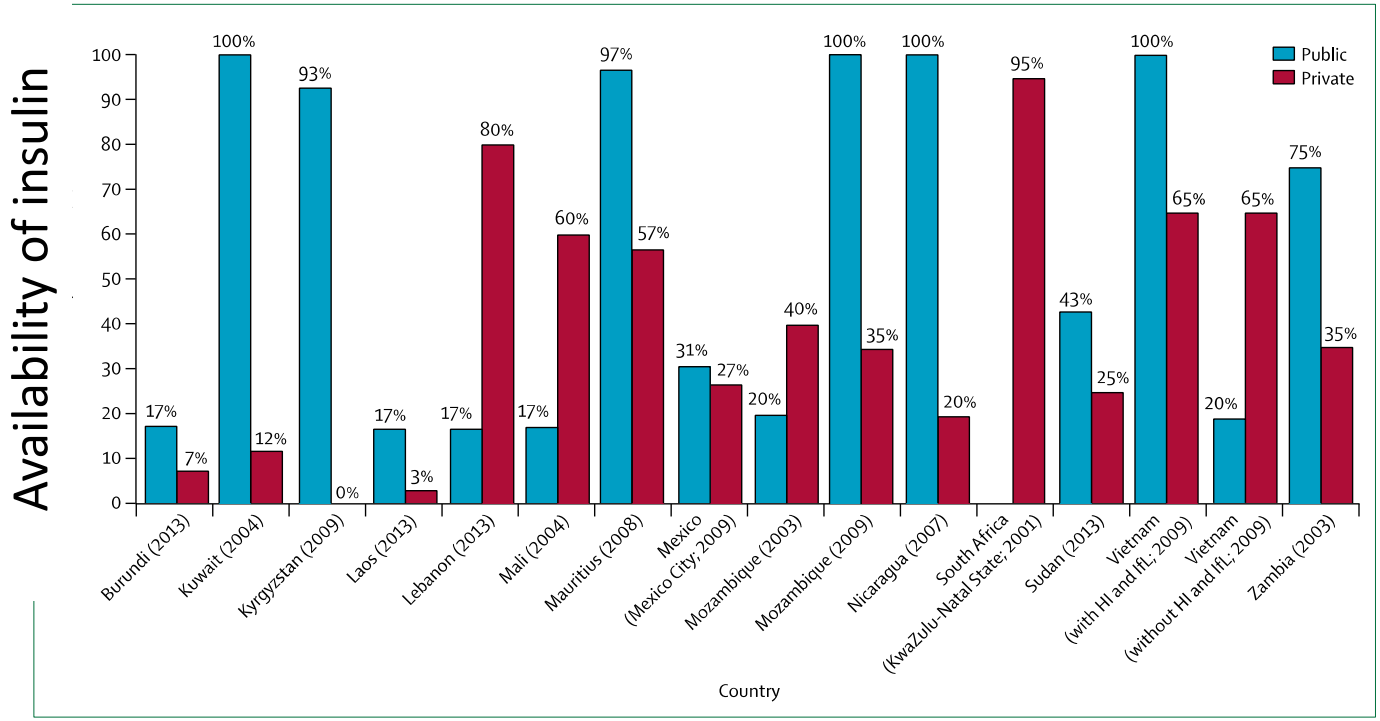
Glycemic control is difficult in TB-DM



Clinical Management of concurrent TB and DM and the implictions for patient services. Riza et al, Lancet Diabetes 2014;2:740-53

Constraints and challenges in access to insulin: a global perspective

David Beran, Margaret Ewen, Richard Laing



Beran et al. Lancet Diabetes 2016;4:275-285

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?

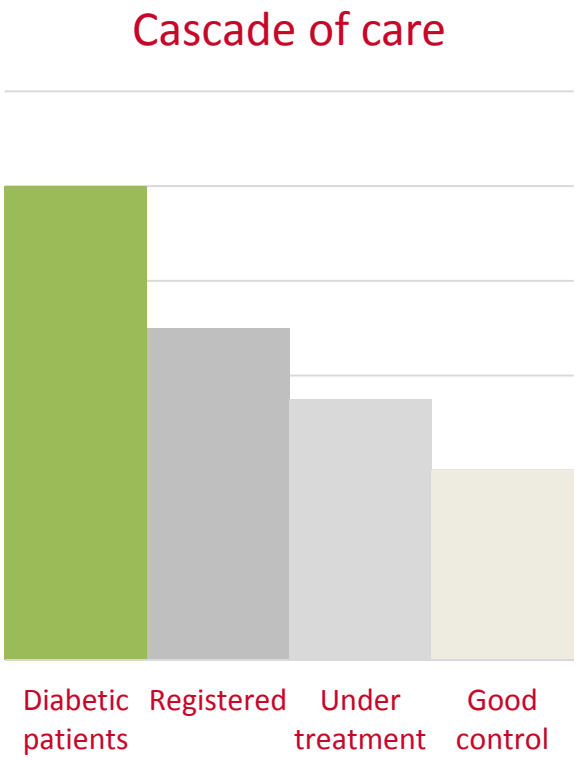
How hard should we aim for glycemic control?

Pragmatic clinical trial in TANDEM

- Standard versus intensifed 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 Faurholt-Jepsen[1], Nyagosya Range[2], George PrayGod[3], Kidola Jeremiah[3], Maria Faurholt-Jepsen[1], Martine G. Aabye[4], John Changalucha[3], Dirk L. Christensen[5], Harleen M. S. Grewal[6], Torben Martinussen[7], Henrik Krarup[8], Daniel R. Witte[9], Aase B. Andersen[10] and Henrik Friis[1]

Trop Med Int Health '13

- 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[1], Hongjo Choi[2], So Young Lee[2], Myungsun Lee[2], Youngran Kim[2], Hyemi Park[2], Jongseok Lee[2], Xin Zhan[4], Hyeungseok Kang[5], SooHee Hwang[5], Matthew Carroll[6], Ying Cai[6], Sang-Nae Cho[2,3], Clifton E. Barry III[6], Laura E. Via[6], Hardy Kornfeld[7]*

Plos One '13

- 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

Clinicaltrials.gov

18 studies found for: Diabetes AND tuberculosis

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Rank	Status	Study
1	Recruiting	**Pulmonary Tuberculosis Patients With Diabetes Mellitus** **Conditions:** Diabetes Mellitus; Pulmonary Tuberculosis **Intervention:** Procedure: intensive monitoring
2	Not yet recruiting	**Effect of Supplementary Vitamin D in Patients With Diabetes Mellitus and Pulmonary Tuberculosis** **Conditions:** Type 2 Diabetes Mellitus; Pulmonary Tuberculosis **Interventions:** Dietary Supplement: Vitamin D; Dietary Supplement: Calcium; Dietary Supplement: Placebo Vit D; Dietary Supplement: Placebo Calcium
3	Terminated	**Immunobiology of Diabetes and Tuberculosis** **Conditions:** Tuberculosis; Diabetes Mellitus **Intervention:** Biological: BCG
4	Completed	**Nutrition, Diabetes and Pulmonary TB/HIV** **Conditions:** Tuberculosis; HIV; Diabetes **Interventions:** Dietary Supplement: Multimicronutrients; Dietary Supplement: Energy and proteins
5	Active, not recruiting	**Risk of Hospitalized Infections Among Patients With Type 2 Diabetes Exposed to Oral Antidiabetic Treatment** **Condition:** Diabetes Mellitus, Type 2

Tuberculosis and HIV

315 studies found for: HIV AND tuberculosis

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

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