

The implementation of latent tuberculosis screening in Belgium's AIDS Reference Centers



CHLOÉ WYNDHAM-THOMAS

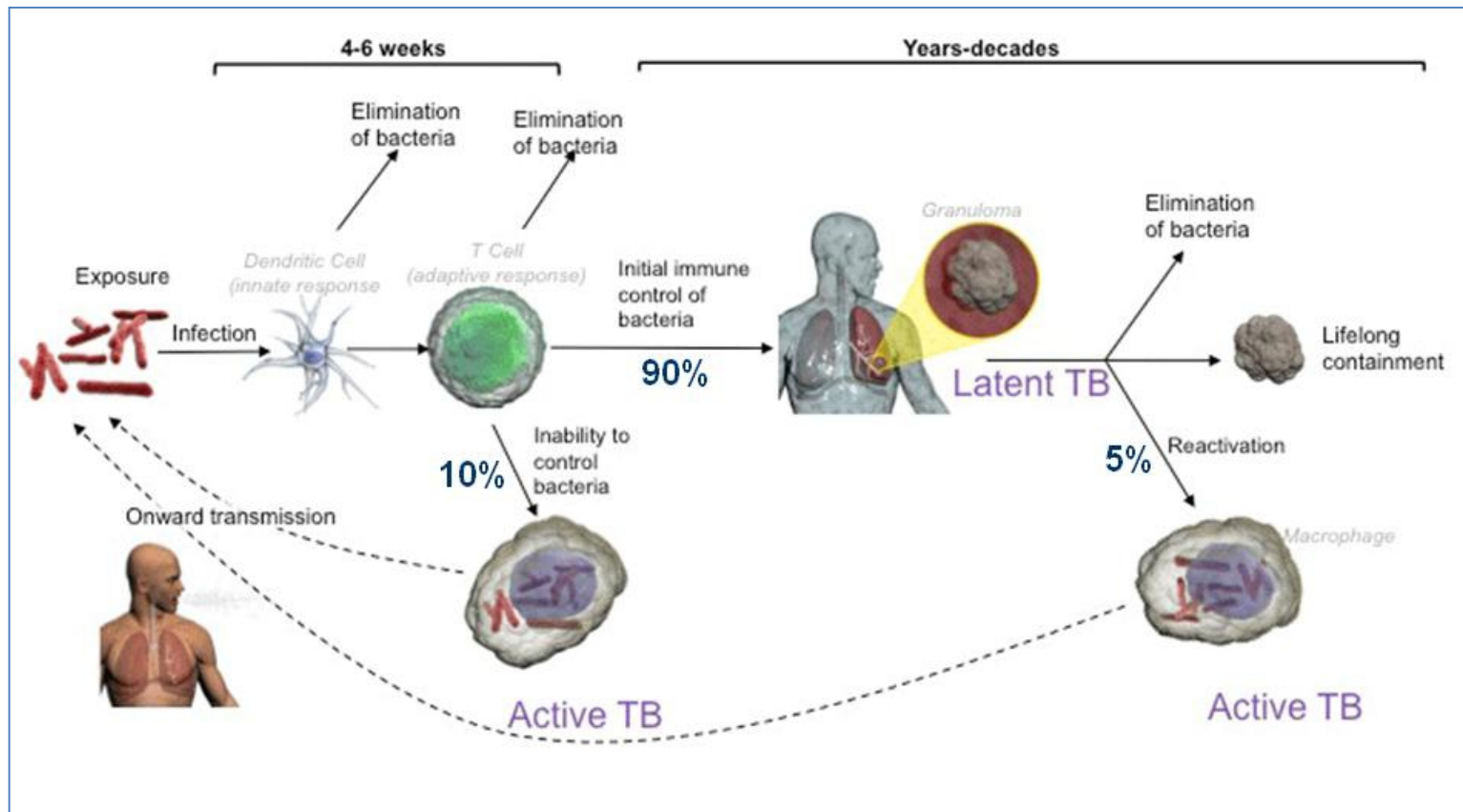
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Introduction



- Infection by *Mycobacterium tuberculosis* (Mtb):



Introduction



- Infection by *Mtb* in HIV+ patients
 - Reactivation of latent tuberculosis reaches 10%/year
 - 20-30x greater risk of developing active tuberculosis (TB)
 - In 2012:
 - 13% of the 8.600 000 cases of active TB were HIV+
 - 320.000 deaths due to HIV/TB co-infection were declared

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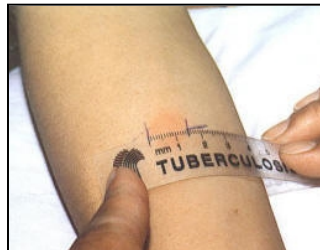
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 - In 2012:
 - 13% of the 8.600 000 cases of active TB were HIV+
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- **Screening and treatment of latent tuberculosis in HIV+ patients**
 - ➔ Decreases the risk of active TB by 30-60%
 - ➔ Strategy promoted by WHO



Introduction

1. Tuberculin skin test (TST)

- Measures *in vivo* the delayed hypersensitivity response to Purified Protein Derivative
- Lacks specificity (NTM, BCG)
- Lacks sensitivity in HIV+ patients



2. Interferon- γ release assay (IGRA)

- Measures *in vitro* the immune response to mycobacterial antigens RD-1/RD-11
- Greater specificity, in particular if BCG+
- Lacks sensitivity in HIV+ patients

QuantiFERON®-TB Gold In-Tube (QFT-GIT)
ESAT-6,CFP-10,TB 7.7

T-SPOT.TB®
ESAT-6,CFP-10

Introduction



- **Guidelines:**

- CDC: TST or IGRA, if negative, use the other
- ECDC: TST and IGRA
- NICE: TST and IGRA if $CD4+ < 200 \text{ cell/mm}^3$. If $> 200 \text{ cell/mm}^3$, TST or IGRA
- BHIVA: screening only in patients with high risk of progression to active TB (IGRA)
- Canada: TST → if negative and high risk of latent TB → IGRA (T-SPOT.TB suggested)



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- **Implementation of screening:**

- In 2011, screening and treatment of latent tuberculosis was made in 446,000 HIV+ patients
- Represents only 6% of all patients that know their HIV+ status
- Implementation in Belgium?

Objectives & Methods



1. **To evaluate the implementation of latent tuberculosis screening and treatment**
2. **To identify the barriers to its implementation**
3. **To investigate opinions with regards to different screening strategies:**
 - screening of all HIV-infected patients
versus
 - targeting screening to those at highest risk of active tuberculosis

Objectives & Methods



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→. **A multiple-choice questionnaire** was sent to 55 physicians working in an AIDS Reference Clinic or satellite clinic



BREACH
BEIJING RESEARCH AIDS & HIV COHORT STUDY

Results & Discussion



- Response rate: 34/55 (62%)
- Characteristics of participants:

	N	%
Place of main practice		
AIDS Reference Center	26	79
Satellite Center	7	21
Number of years working in the HIV field		
<5	7	21
5-10	7	21
>10	19	58
Estimated number of HIV-infected patients in practice		
<50	7	21
50-100	2	6
>100	24	73
Estimated number of active tuberculosis cases per year among HIV-infected patients followed		
0-1	15	45
2-5	11	33
>5	7	21

Results & Discussion



1. Implementation of latent tuberculosis screening and treatment:

	N
Use of latent tuberculosis screening (n=30)	
No	3
Yes, always	6
Yes, if <i>Mtb</i> exposition risk factors	9
Yes, in close contact cases	6
Other	6
Latent tuberculosis screening method applied (n=26)	
TST only	7
IGRA only	2
TST and IGRA	4
Adapted to CD4+ T-cell count	6
Other	7
Repetition of latent tuberculosis screening during follow-up (n=29)	
Yes	8
No	21

Results & Discussion



1. Implementation of latent tuberculosis screening and treatment:

	N
Exclusion of TB in HIV+ patients with a positive LTBI screen (n=33)	
Yes, always	25
Yes, in certain circumstances	4
No	1
Not applicable (screening not performed)	3
Management of HIV+ patients after contact with an infectious TB case (n=33)	
LTBI treatment in all cases	4
LTBI treatment only if screening positive	10
Dependent on patient's immune-deficiency	17
Other	2
Prescription of LTBI treatment in patients with a positive screen (n=32)	
All	14
Certain patients	17
Never	1

Results & Discussion



1. Implementation of latent tuberculosis screening and treatment:

→ Notable variability in the latent tuberculosis screening methods used in HIV-care

Results & Discussion



1. Implementation of latent tuberculosis screening and treatment:

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In low-tuberculosis incidence countries, WHO, WHEN and HOW to screen for latent tuberculosis in HIV+ patients remains unclear:

- < Lack of studies evaluating efficacy of different screening strategies
- < Discrepancies in the screening strategies recommended by alternative guidelines

Results & Discussion



2. Main barriers to latent tuberculosis screening and treatment

- Lack of sensitivity of screening tools (15)
- Poly-medication (13)
- Toxicity of treatment (13)

Results & Discussion



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- Lack of sensitivity of screening tools → no gold standard!
 - ✦ All the more in HIV+ patients (Van Zyl-Smit 2009)
 - ✦ Solutions? Combination of tools; Repetition of tests; New tools
- Poly-medication
 - ✦ Impact on adherence and toxicity (Edelman 2013)
- Toxicity of latent tuberculosis treatment
 - ✦ Liver toxicity: 0,001-0,15% (Norton 2012)

Results & Discussion



3. Opinions with regards to different screening strategies:

- 21 in favour of TARGET screening = *screening only HIV+ patients at highest risk of active tuberculosis*
- 4 in favour of screening for ALL HIV-infected patients
- 1 participant not in favour of latent tuberculosis screening

Results & Discussion



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➤ Target screening:

- ✦ Increase pre-test probability
- ✦ Decrease number exposed un-necessarily to latent tuberculosis treatment

- ✦ Attractive alternative for low tuberculosis incidence countries
- ✦ Already suggested in EACS and BHIVA guidelines

- ➔ But how to evaluate the risk of active tuberculosis in HIV+ patients?
 - ➔ BHIVA: algorithm based on (1) Country of origin (2) CD4+ T-cell count (3) Antiretroviral treatment
 - ➔ Not clinically validated!

Conclusions



1. **ONLY 25% of clinicians screen all their patients for latent tuberculosis**
2. **Methods used are variable**
3. **The majority of Belgium's HIV caregivers are in favour of limiting screening to patients at highest risk of active tuberculosis**

Conclusions



1. ONLY 25% of clinicians screen all their patients for latent tuberculosis
2. Methods used are variable
3. The majority of Belgium's HIV caregivers are in favour of limiting screening to patients at highest risk of active tuberculosis

Perspectives:

Results has been reported to the Belgian Latent tuberculosis working group

→ If this TARGET screening strategy is adopted, it must be associated with a large-scale prospective study

Acknowledgements

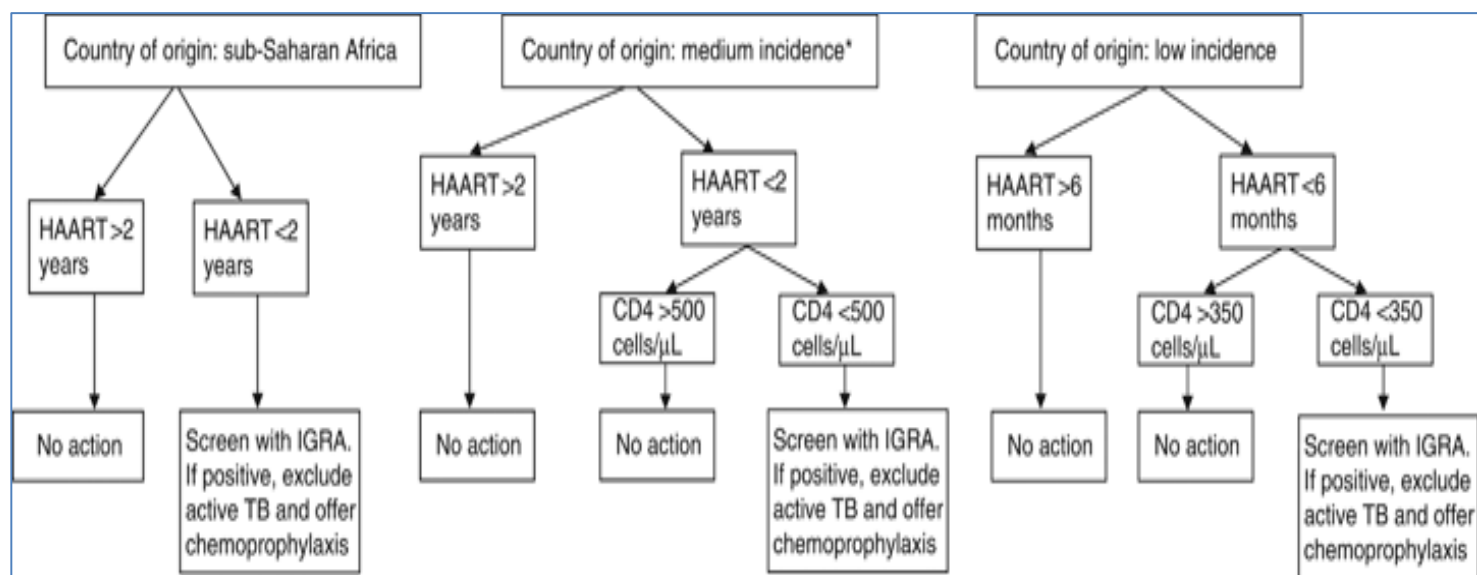


- K Schepers
- V Dirix
- JC Goffard
- F Mascart
- JP Van Vooren
- Fonds Erasme
- Les participants

Discussion



- BHIVA guidelines:



*Eastern Europe, Central Asia, North Africa and the Middle East, South Asia, East Asia, and the Caribbean