Reducing TB transmission in Europe

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GTN (Global Tuberculosis Network)

Introduction

OBJECTIVES: to discuss

- 5 core questions the WHO Euro IC document tries to answer
- Methods (rapid)
- Main answers to the questions
- Policy implications
- Need for a wider Regional perspective on infection control and reduction of transmission
- Conclusions and proposals for a WW WG

World Health Organization
REGIONAL OFFICE FOR Europe

Guiding Principles to Reduce Tuberculosis Transmission in the WHO European Region

Giovanni Battista Migliori, Lia D'Ambrosio, Rosella Centis,
Martin Van Den Boom, Soudeh Ehsani, Masoud Dara

WHO guidelines on tuberculosis infection prevention and control

2019 update

THE END TB STRATEGY

World Health Organization

Methods

Methods

Owing to the difficulty of summarising the five questions within an overarching research question, it was necessary to use a research methodology incorporating a wide search of scientific manuscripts using different search engines. It was particularly important to assess the current grey literature, along with studies preceding the internet era.

Relevant scientific documents published in English (in Google Scholar and other grey literature sources) were identified using the Google search engine and the following key words: "tuberculosis", "MDR-TB" (including extensively drug-resistant (XDR)-TB), "infectiousness", "contagiousness", "transmission" and "infection control". As a systematic review covering these topics was published in 2013 [5], the search focused on the 2013–2017 period. Historical articles were retrieved from World Health Organization (WHO) and International Union against Tuberculosis and Lung Disease documents [6, 7]. A nonsystematic approach was adopted because of the short period since the last published systematic review and the large time span from historical studies to the more recent ones.

All retrieved documents were evaluated, together with the references in the main articles, in order to answer the questions as fully possible.

- Non systematic review
- No time limitations, historical studies
- Grey literature

Number and size of organisms liberated

- Number of organisms liberated

Sneezing 4,500- 1,000,000 (~40,000 droplets)

Coughing 0-3,500 (~3,000 droplet nuclei)

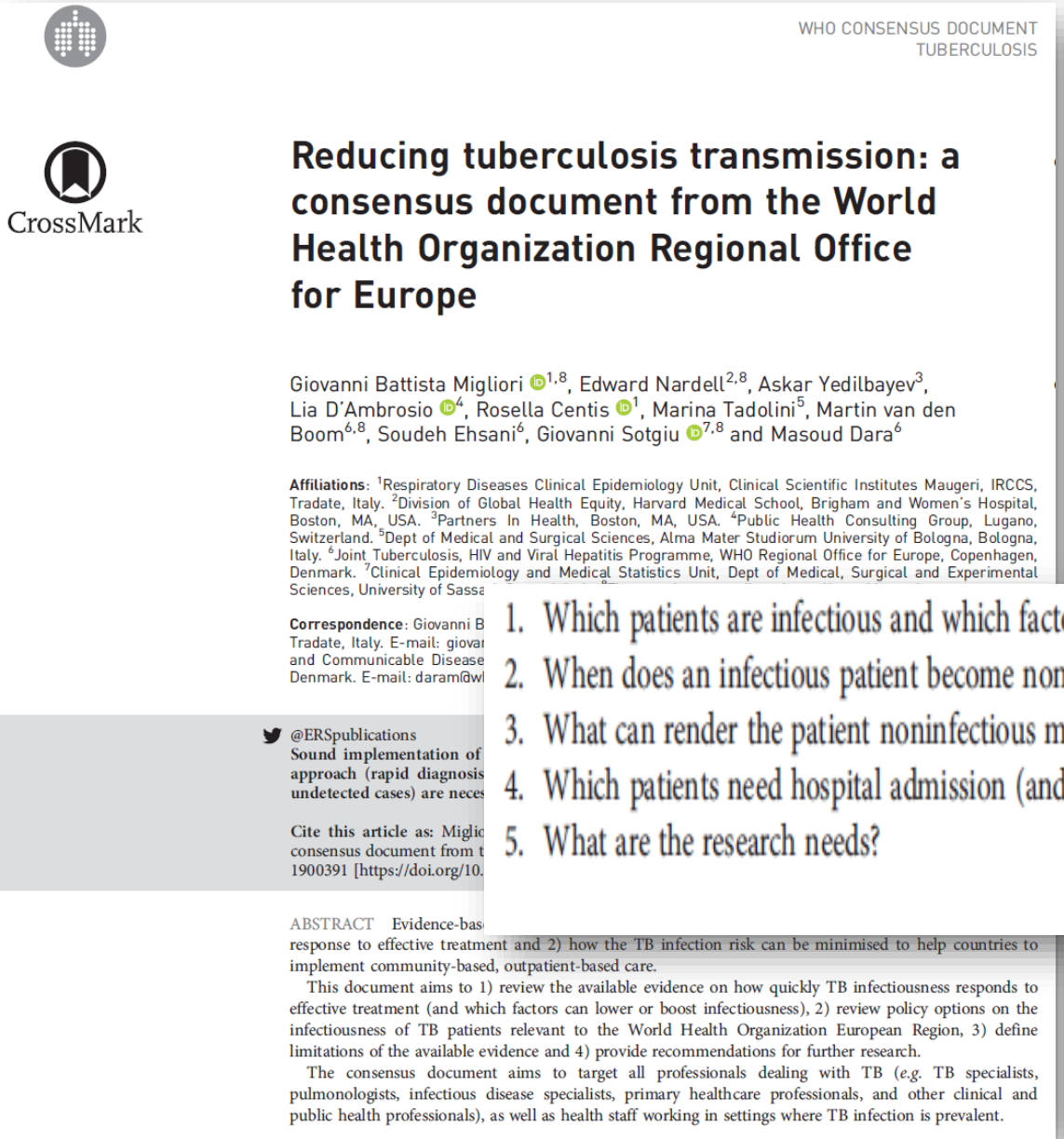
Talking 0-200 (in 5 min: ~3,000 droplet nuclei)

- Size of the droplets (function of air velocity)

Sneeze ~300 m/s (75% diameter ~10 µm=droplet nuclei).

Wells 1943, Duguid 1945, Wells/Riley 1953, et al.

The ERJ article version



WHO CONSENSUS DOCUMENT
TUBERCULOSIS

Reducing tuberculosis transmission: a consensus document from the World Health Organization Regional Office for Europe

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@ERSpublications
Sound implementation of
approach (rapid diagnosis
undetected cases) are neces

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ABSTRACT Evidence-bas
response to effective treatment and 2) how the TB infection risk can be minimised to help countries to implement community-based, outpatient-based care.

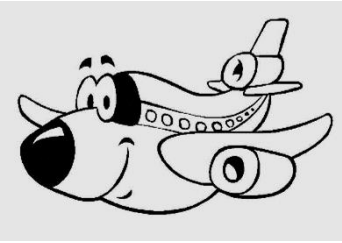
This document aims to 1) review the available evidence on how quickly TB infectiousness responds to effective treatment (and which factors can lower or boost infectiousness), 2) review policy options on the infectiousness of TB patients relevant to the World Health Organization European Region, 3) define limitations of the available evidence and 4) provide recommendations for further research.

The consensus document aims to target all professionals dealing with TB (*e.g.* TB specialists, pulmonologists, infectious disease specialists, primary healthcare professionals, and other clinical and public health professionals), as well as health staff working in settings where TB infection is prevalent.

1. Which patients are infectious and which factors favour disease transmission?
2. When does an infectious patient become noninfectious after starting treatment?
3. What can render the patient noninfectious more or less rapidly?
4. Which patients need hospital admission (and respiratory isolation) because of their infectiousness?
5. What are the research needs?

- several articles on IC exist
- focused on the 'traditional approach' (administrative c, environmental c, personal protection)
- some core questions still unanswered

Question 1: who is infectious?
Question 2: when the patient becomes non-infectious?
Question3: what can render the patient rapidly less infectious?



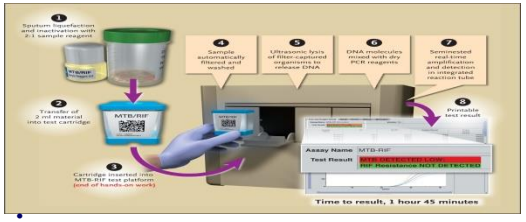
- *Transmission is 'probabilistic' and 'hyper-transmitters' account for much of it*
- *In the absence of better evidence, the cut-off value of 8-hour exposure is not useful to activate contact-tracing. In children and other vulnerable groups, a shorter time of exposure is likely to be sufficient to allow infection to occur. Criteria including intensity, frequency, and duration of exposure need to guide the contact-tracing plan following exposure to an infectious TB case based on the concentric circle approach.*

- *SS is a rapid and economic tool to assess pre-treatment infectiousness, although it has limitations. Up to one fifth of SS+ cases can transmit M. tuberculosis when un-treated. C is useful to demonstrate viability of bacilli, although the response takes 2-3 weeks: it cannot predict infectiousness once the treatment starts.*

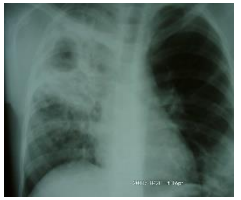
- *Although SS and C can remain positive for more than 2 weeks under treatment, the available evidence shows that infectiousness drops very rapidly if adequate treatment is implemented. This is easier when the strain is drug susceptible. The real risk is represented by undetected MDR- or XDR-TB cases*

Policy considerations: rapid diagnosis and isolation

- *New rapid diagnostic methods (Xpert, LPA) should be systematically used to identify promptly drug-resistant cases for whom adequate treatment can be rapidly started, thus reducing the patient's infectiousness.*



- *Stringent isolation criteria are necessary for suspected or confirmed XDR-TB cases for whom treatment does not rapidly prevent transmission. The experience of existing community-based programmes shows that MDR-TB cases can be managed also at home, as effective treatment reduces rapidly the patient's infectiousness.*



- *Although in principle out-patient management is recommended, a certain proportion of severe and/or social cases will still need hospital admission. Any hospital admitting TB cases should offer several services, including adequate infection control and quality patient-centred management.*

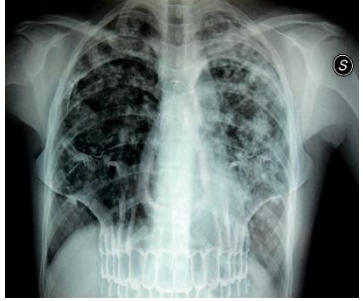
TABLE 5 Criteria for hospital admission

- **Main criteria [2, 105]**
- Complications of TB (*e.g.* respiratory failure and conditions requiring surgical interventions, such as haemorrhage, pneumothorax and pleural effusion)
- Severe forms of TB (*i.e.* TB meningitis) and/or severe clinical manifestations of comorbidities (*e.g.* liver disease, renal disease and uncontrolled diabetes)
- Life-threatening and serious medical events resulting from adverse reactions to anti-TB drugs (*e.g.* life-threatening arrhythmias, psychosis, renal failure and hearing loss)
- **Additional criteria [2, 128, 129]**
- Patients for whom effective and safe anti-TB treatment cannot be ensured in an outpatient, community or home setting (*i.e.* homelessness, overcrowding, exposure of children aged <5 years and pregnant women in the household)
- When there are accessibility problems (*i.e.* patient lives far from an outpatient facility)
- Where there is nonadherence to treatment (this can be considered in some settings as a last resort once all other care options have been used/applied exhaustively, based on the legal framework in force)

TABLE 6 Features of a hospital admitting tuberculosis (TB) and multidrug-resistant (MDR)/extensively drug-resistant (XDR)-TB patients

- Clinical expertise in TB and MDR/XDR-TB management (including for directly observed treatment)
- Laboratory results from laboratories with a robust external quality assurance system in place
- Respiratory isolation capacity and adequate infection control measures (including the recommended 12 air changes per hour)
- Personal protection measures (*i.e.* respirators) available within well-designed personal protection programmes, including staff awareness/education and respirator fit testing
- Open spaces that allow patients to socialise without the risk of *Mycobacterium tuberculosis* transmission [131]
- An adequate number of staff trained and supervised to adhere to administrative and personal protection measures of infection control
- A patient-centred approach (psychological support, palliative care, link with home care and social services for the post-discharge home care phase)

European policy: hospitalization criteria



- *Complicated forms of TB (i.e. respiratory failure and conditions requiring surgical interventions such as haemorrhage, pneumothorax and pleural effusion);*
- *Severe forms of TB disease (TB meningitis) and/or severe clinical manifestations of co-morbidities (e.g. liver disease, renal disease and uncontrolled diabetes);*
- *Life-threatening and serious medical events resulting from adverse events of anti-TB drugs (i.e. life-threatening arrhythmias, psychosis, renal failure and hearing loss).*

Additional arguments (to be applied in rare and exceptional cases) include:

- *Cases for whom effective and safe anti-treatment cannot be ensured in outpatient, community or home settings (i.e. in severe cases of homelessness, overcrowding, exposure of children aged less than 5 years and pregnant women in the household) and/or having accessibility problems (living far from an out-patient facility).*
- *As the last resort measure only, involuntary isolation of non-adherent patients once all the other care options have been used/applied exhaustively can be considered in some settings.*

European policy: hospital requirements to admit

- *Clinical expertise on TB and MDR-/XDR-TB management (DOT!!)*
- *Quality controlled laboratory*
- *Respiratory isolation capacity and adequate infection control measures in place (including the recommended 12 ACH).*
- *Personal protection measures (i.e. respirators) available within well designed personal protection programmes including staff awareness/education and respirator fit-testing.*
- *Open spaces allowing patients to socialize without risk of TB transmission*
- *Adequate number of staff trained and supervised to adhere to administrative and personal protection measures of infection control*
- *Patient-centred approach (psychological support, palliative care, link with home care and social services for the post-discharge home-care phase; etc).*

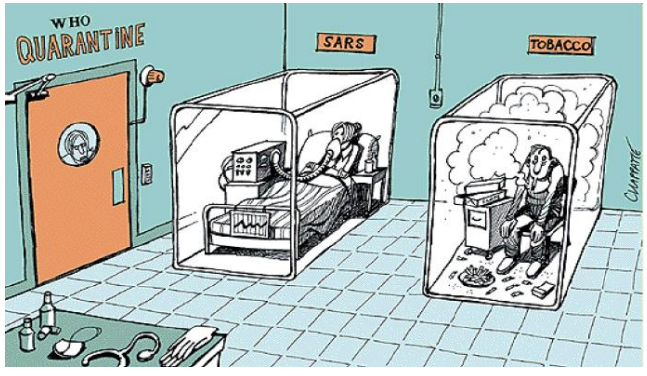


TABLE 7 Main policy elements derived from the present review

- Infection control planning is needed at the national/subnational and facility levels.
- Three groups of actors should be considered: patients, health staff and visitors.
- The cut-off value of 8 h exposure is not useful to activate contact-tracing. Criteria related to the intensity, frequency and duration of exposure should guide the contact-tracing plan following exposure to an infectious TB patient based on the concentric circle/"stone-in-the-pond" approach.
- Sputum smear microscopy is a quick, cheap tool for assessing pre-treatment infectiousness, although it has limitations. Sputum culture is useful to demonstrate the viability of bacilli, although results take 2–3 weeks. Neither sputum nor culture can used to predict infectiousness once the treatment starts.
- Although sputum smear and culture tests can still be positive >2 weeks after treatment starts, the available evidence shows that infectiousness drops very rapidly if adequate treatment is implemented; however, this is difficult to quantify.
- It is easier to provide adequate treatment when the *Mycobacterium tuberculosis* strain is drug susceptible. The real risk is infection from undetected MDR-TB or XDR-TB cases.
- New rapid molecular diagnostic techniques (*i.e.* Xpert MTB/RIF and line probe assays) should be systematically used to promptly identify drug-resistant patients so that adequate treatment can be rapidly started, thus reducing the period of infectiousness.
- Stringent isolation criteria are necessary for presumed and confirmed XDR-TB patients for whom treatment does not rapidly prevent transmission. Existing community-based programmes have shown that MDR-TB patients can also be managed at home because effective treatment rapidly reduces their infectiousness.
- Although outpatient management is recommended in principle, a proportion of TB patients (*e.g.* clinically severe cases) will need hospital admission. Any hospital admitting TB patients should offer adequate infection control and quality patient-centred management.
- FAST (Find cases Actively by cough surveillance and rapid molecular sputum testing, Separate safely, and Treat effectively based on rapid drug susceptibility testing) is the strategy recently proposed to minimise the risk that undetected TB cases further transmit *M. tuberculosis*.

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PERSPECTIVE

F-A-S-T: a refocused, intensified, administrative tuberculosis transmission control strategy

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transmission control that we call *FAST*: Find cases Actively by cough surveillance and rapid molecular sputum testing, Separate safely, and Treat effectively based on rapid drug susceptibility testing (DST).

IMPLEMENTATION OF F-A-S-T

In a TB hospital in Veronesh, Russia, 932 patients with suspected pulmonary TB were hospitalized from May 2013 to March 2014; 923 underwent Xpert testing, of whom 863 (93.5%) were tested within 2 days of admission: 407 were positive and 161 (study participants) were rifampin-resistant, of whom 159 were started on MDR-TB treatment within 3 working days of receiving the result. Under normal operating conditions before the pilot implementation of FAST, as in most Russian TB hospitals, treatment failure, often identified months after admission, was the usual criterion for DST. If DST was performed using conventional means, results were obtained after several more months.[5] Under usual practice, other

Russia
93% of suspected cases tested within 2 days (n:863)

Over the first 21 weeks of implementation, a total of 1891 sputum samples from discrete patients admitted to one of the in-patient departments at NIDCH were tested using Xpert. Of these 1891 samples, approximately 11% and 1% unsuspected cases of TB and MDR-TB were identified, respectively. Of the 1453 patients admitted to the facility as non-TB patients with other respiratory diseases, about 9% actually had TB and had been misclassified upon admission. The unsuspected TB rate was more than twice as high among patients with a previous history of TB. Furthermore, of the 60 TB patients on treatment admitted to the facility, approximately 8% were identified as unsuspected, Xpert-confirmed MDR-TB cases. All 1891 samples were processed

Bangladesh
11% TB and 1% MDR unsuspected cases identified;
9% respiratory cases with TB misclassified

Research needs

More information is needed on how drugs stop transmission, apart from their bactericidal effects. It is also important to discover effective (and cost-effective) screening approaches for undetected TB (*e.g.* active screening through cough surveillance, digital radiology and breathe tests that do not require sputum). Host-directed therapy is also an emerging area of research, *e.g.* evaluating the role of statin or metformin-like drugs in preventing or limiting TB in the household contacts of highly drug-resistant patients.

Finally, MDR-TB treatment will inevitably generate XDR-TB cases among treatment failures; unfortunately, some of these patients will be incurable and need palliative care. More research is needed to identify models to ensure that untreatable XDR-TB patients receive the necessary level of comfort (while preventing transmission) at home or in palliative care institutions [107].

- How drugs/effective treatment stop transmission?
- How to detect the dangerous cases (undetected ones) and implement the FAST approach?
- How host-directed therapy can help?
- How palliative care needs to be organised?
- What NTPs can do to support reserach and implementation of sound IC?

Conclusions

- Although well established, core questions on IC are partially answered by the WHO EURO document.
- However, more needs to be known…
- A better understanding of how transmission occurs and how rapidly effective treatment renders the patient ‘non infectious’ as well as on how NTPs implement established IC principles are priorities in the WHO European Region
- WHO Euro in collaboration with partners will continue to work into this direction, further building on the short survey we have distributed here.
- The creation of an IC WG within the WW initiative could be useful

"La casa storta", a Sopot (Polonia). Costruita nel 2004, è stata progettata dagli architetti Szotyński e Zaleski. Loro stessi si erano ispirati ai disegni dei grafici Jan Marcin Szancer e Per dahlberg.

Let's build a strong IC house!!!

Thank you!!!
Spacibo!!!