SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

RegioneEmilia-Romagna

Corso di aggiornamento

Tubercolosi: un impegno globale

venerdì 10 ottobre 2025

Percorso diagnostico e terapeutico della tubercolosi attiva e dell'infezione tubercolare: il paziente adulto

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UO Malattie Infettive,
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Dipartimento di Scienze Mediche e Chirurgiche
Alma Mater Studiorum Università di Bologna

stop TB

Outline

- Percorso diagnostico e terapeutico della TB attiva
  - Criteri diagnostici
  - Gestione TB polmonare: ricoverare o no?
  - Cenni di terapia
  - MDR-TB
- Percorso diagnostico e terapeutico dell'infezione tubercolare
  - Chi sottoporre a screening?
  - Infezione o malattia?
  - Terapia preventiva: regimi e indicazioni

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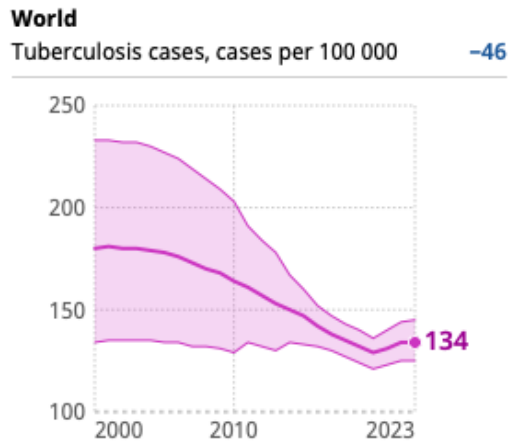
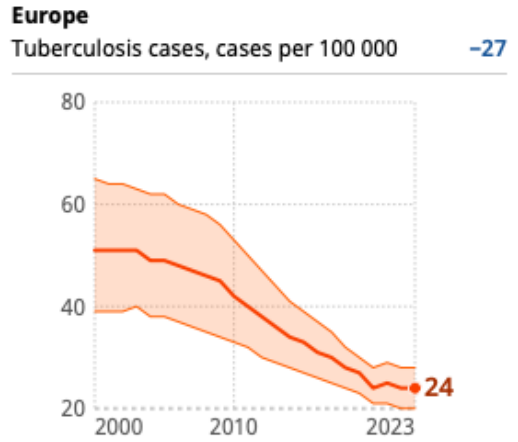
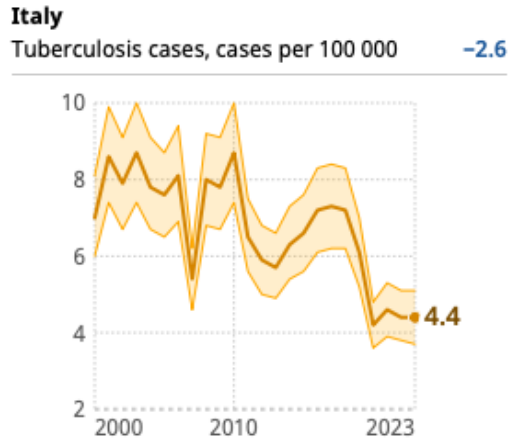
Casi di TB in Italia

- 2500-3000 casi totali
- M>F
- Età: qualsiasi (25-45; > 65)
- Nazionalità: >> paesi ad alta incidenza
- Attenzione a TB in pz italiani giovani (< 30)!!

- Forma polmonare >>
- Forma extra-polmonari (linfonodale/pleurica/ossea/SNC/genitourinaria/ addominale/oculare)





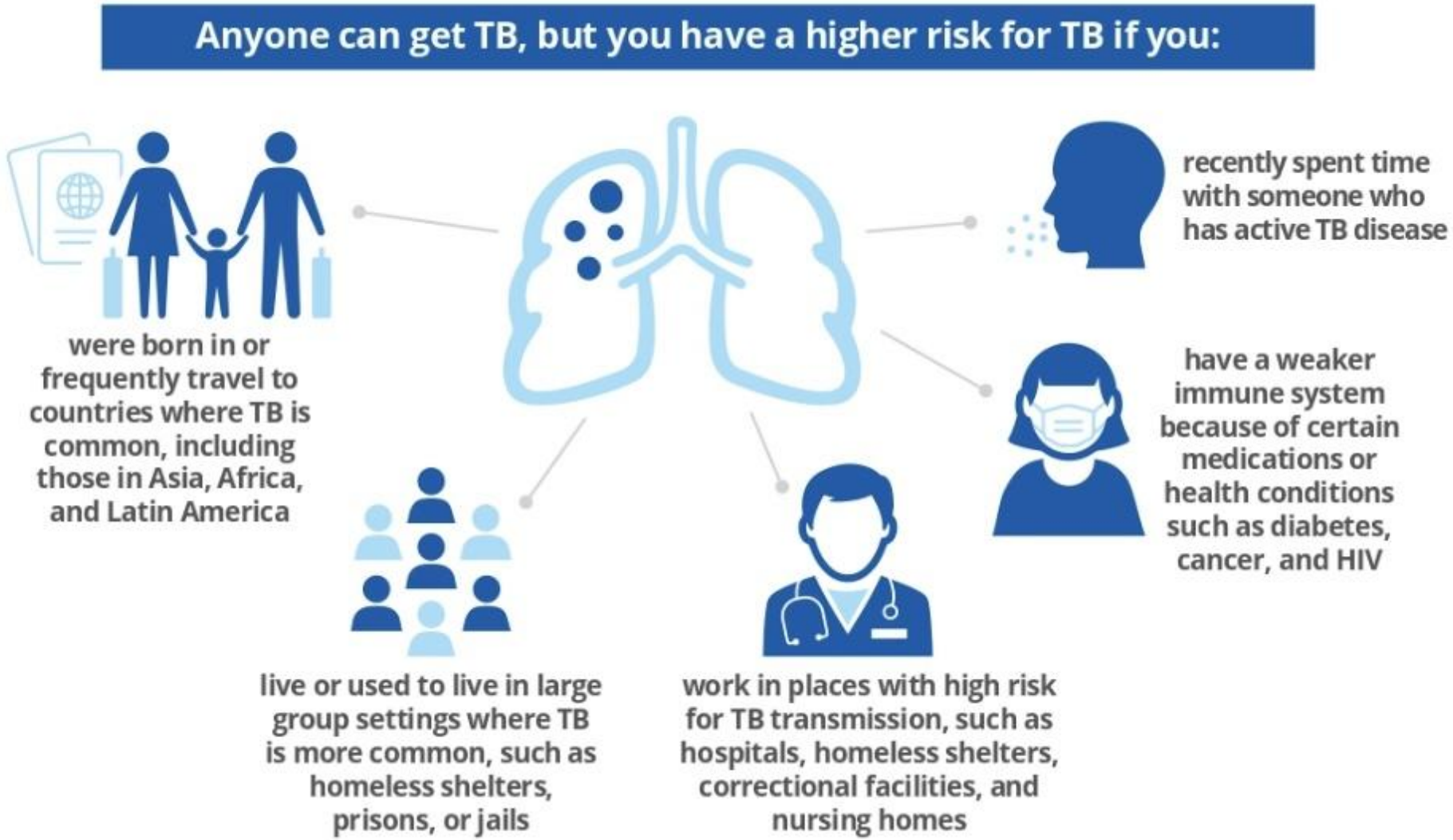


Criteri diagnostici

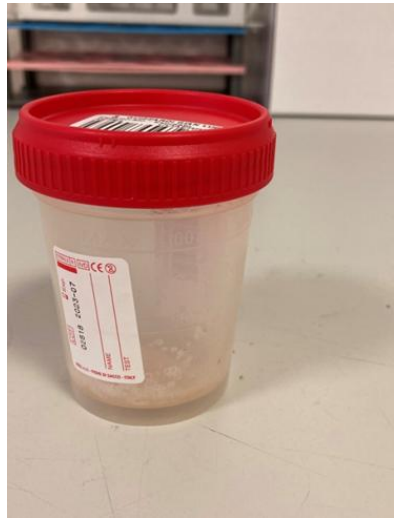
- Sintomi suggestivi di TB
  - Tosse da oltre due settimane (secca o produttiva), emoftoe
  - Sintomi costituzionali: febbre/febbricola, sudorazioni profuse, perdita di peso
  - Sintomi legati a localizzazione extrapolmonare

- Criterio epidemiologico (paese di provenienza, percorso migratorio, etc)
- Storia di pregressa TB, contatto di caso
- Comorbidità (HIV, immunosoppressione, etc)
- Altri fattori di rischio: TD, homeless
- Esami ematici: VES, PCR
- Imaging (Rx torace, HRCT, eco, RM, PET/TC)
- Anatomia patologica (flogosi granulomatosa cronica, necrosi caseosa)

Quando sospettare la TB?



Conferma microbiologica



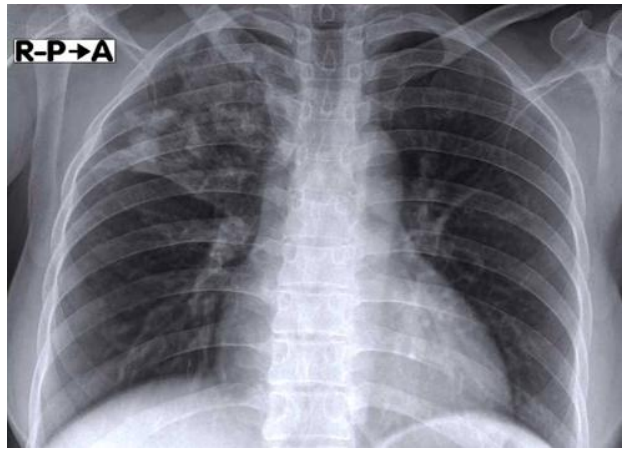
- Esame microscopico
- **Test molecolare (Xpert MTB/RIF o altri WRD)**
- **Esame colturale per MTb** (su campione a fresco!) -> **DST**

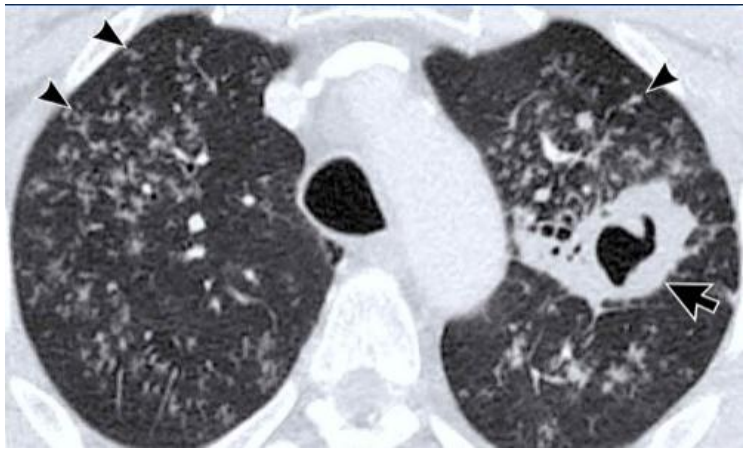
La conferma microbiologica deve sempre essere perseguita,
anche nelle forme extrapolmonari!

Test Mantoux e/o IGRA non sono test diagnostici di malattia:
la loro positività non conferma, la loro negatività non esclude la diagnosi di TB attiva!

Nel paziente con TB
(accertata o diagnosticata clinicamente)

- Notifica di caso
- Indagare **sempre** eventuale localizzazione polmonare in caso di EPTB **(anche in assenza di sintomi respiratori!!)**
- Proporre test HIV
- Ricovero si/no?





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1998: Linee guida nazionali →
non tutti i casi di TB polmonare necessitano di ospedalizzazione

ASPETTO CLINICO

ASPETTO SOCIALE

CONDIZIONE ABITATIVA

STRUTTURE TERRITORIALI INTEGRATE → ISOLAMENTO DOMICILIARE FIDUCIARIO

Indicazioni al ricovero

- Malattia estesa, miliare o meningite tubercolare
- Condizioni cliniche severe
- Paziente immunocompromesso
- Presenza o sospetto di poliresistenze (es. MDR-TB)

- Motivi socio-economici (senza fissa dimora, residenza in dormitorio)

- Positività batteriologica dell'espettorato qualora non sia possibile un sicuro isolamento domiciliare
- Presenza al domicilio di persone immunocompromesse o bambini < 5 anni

Criteri per isolamento fiduciario domiciliare

1. Il paziente ha un domicilio certo e stabile
2. Paziente vive (o comunque può dormire) da solo
3. E’ in grado di assumere la terapia autonomamente
4. Non vi sono al domicilio persone immunodepresse
5. Tutti i conviventi (compresi i bambini) sono stati presi in carico per lo screening dei contatti
6. Sono disponibili servizi territoriali e di supporto per garantire la prosecuzione della cura e l’isolamento stesso

Criteri per la sospensione dell'isolamento respiratorio

L'isolamento respiratorio può essere sospeso quando il paziente è da considerarsi non più contagioso ovvero quando nei pazienti inizialmente bacilliferi si verificano le seguenti condizioni:

1. scomparsa della febbre e riduzione della tosse (se presenti); e
2. il paziente ha assunto regolarmente la terapia con almeno 3 farmaci per la quale *M. tuberculosis* è sensibile o probabilmente tale per un periodo di almeno 2 settimane; e
3. si hanno **tre esami microscopici negativi per BAAR ottenuti in giorni diversi**, di cui uno del primo mattino

Nella TB MDR/XDR i tre esami microscopici negativi per BAAR (o due esami negativi se da espettorato indotto) devono essere ottenuti nell'arco di almeno una settimana.

Criteri per la sospensione dell'isolamento respiratorio

- Nei pazienti con TB attiva ed **esami microscopici negativi per BAAR**, che hanno iniziato il trattamento antitubercolare su base clinica o sulla base della positività dei soli test molecolari, ai fini della sospensione dell'isolamento respiratorio sono necessarie solo una documentata risposta clinica al trattamento (p.e. scomparsa della febbre) e l'assunzione della terapia antitubercolare efficace per un periodo **di almeno 2 settimane**

- Infine, l'isolamento respiratorio può essere sospeso quando la diagnosi di TB è stata esclusa, oppure quando il clinico ha posto una diagnosi alternativa che giustifica la sintomatologia del paziente

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IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

Duration of Effective Tuberculosis Treatment, Not Acid-Fast Bacilli (AFB) Smear Status, as the Determinant for De-isolation in Community Settings

Neela Goswami and Caitlin Reed

Many public health TB programs, extrapolating from national healthcare facility guidelines, have required that individuals with TB have negative acid-fast bacilli (AFB) sputum smears prior to discontinuation of isolation in community settings.

…….. **It is not unusual for persons with TB, particularly those with extensive or cavitary pulmonary disease, to have persistently positive AFB sputum specimens for weeks to months**.

Consequently, persons with TB often cannot work for prolonged periods and may be separated from their families.

persons undergoing treatment for TB disease face negative con sequences from isolation due to **stigma, mental health impacts, loss or interruption of employment or schooling, and issues accessing and maintaining housing**.

published online 18 April 2024

Clinical Infectious Diseases
INVITED COMMENTARY

Duration of Effective Tuberculosis Treatment, Not Acid-Fast Bacilli (AFB) Smear Status, as the Determinant for De-isolation in Community Settings

Neela Goswami and Caitlin Reed

Table 1. Summary of Key Evidence That Effective TB Treatment Rapidly Renders Persons With TB Noninfectious

Type of Evidence	Brief Summary	Location and Date
Randomized trial	Persons with TB randomized to sanatorium versus home-based treatment with INH and PAS; no difference in LTBI or TB disease among household contacts over 5 y; "major risk to contacts resulted from exposure to patient before diagnosis"	Madras, India, 1956–1959 [16]
Retrospective cohort	Persons with TB discharged from the hospital on treatment while still TB culture positive (majority also AFB smear positive) compared with persons with TB who were AFB smear and culture negative at discharge from hospital; no difference in TST conversion among household contacts	Arkansas, 1967–1971 [17]
Experiment	Guinea pigs susceptible to TB infection exposed to air vented from a TB ward; treatment of persons with TB with INH, PAS, and SM reduced transmission to guinea pigs by 98% immediately compared with untreated persons with TB	Baltimore VA TB Ward, 1959–1961 [18]
Experiment	Guinea pigs susceptible to TB infection exposed to air vented from MDR TB ward; TST conversions in guinea pigs showed infection of 1 (1%) of guinea pigs after 3 mo of exposure to 27 persons with MDR (most AFB smear positive) on treatment with regimen of levofloxacin, kanamycin, ethionamide, and either ethambutol or prothionamide	South Africa, ~2007–2012 [19]
Transcriptomic analysis	Analysis of TB isolates from respiratory aerosols of 7 persons with drug-susceptible TB on TB treatment with rifampin, INH, PZA, and ethambutol showed immediate downregulation of transcription of genes involved in TB virulence and infectiousness after 1 d of treatment	Mumbai, India, 2018–2020 [20]

Abbreviations: AFB, acid-fast bacilli; INH, isoniazid; MDR, multidrug resistant; LTBI, latent tuberculosis infection; PAS, para-aminosalicyclic acid; PZA, pyrazinamide; SM, streptomycin; TB, tuberculosis; TST, tuberculin skin test.

- **After initiation of effective TB treatment, AFB smear grade in sputum**—relied on historically as a sole laboratory predictor of infectiousness for isolation discontinuation decisions—**is no longer a useful indicator of infectiousness**.

- Even the **presence of culturable Mycobacterium tuberculosis complex bacilli in sputum may not have the direct correlation with infectiousness previously assumed**.

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Neela Goswami and Caitlin Reed

The key conclusion of the evidence review used to formulate the NTCA guidelines is that most persons with pulmonary TB in US community settings

- likely have little or no infectious potential **after 5 days of effective treatment and therefore can be taken out of isolation** accordingly, **regardless of sputum AFB smear or culture status**.
- **Treatment duration prior to de-isolation may be extended beyond 5 days due to several factors that are known to be associated with transmission**.

These include circumstances of the person's living situation and workplace;

- presence of vulnerable contacts, such as children less than 5 years of age or immunocompromised persons;
- lack of adequate ventilation or crowding of environments; or
- plans to travel by public conveyance.
- Individual characteristics to consider in decisions to extend isolation are baseline burden of disease, clinical confidence that TB treatment is effective, adherence to therapy, and comorbid medical conditions that are associated with TB drug malabsorption.

published online 18 April 2024

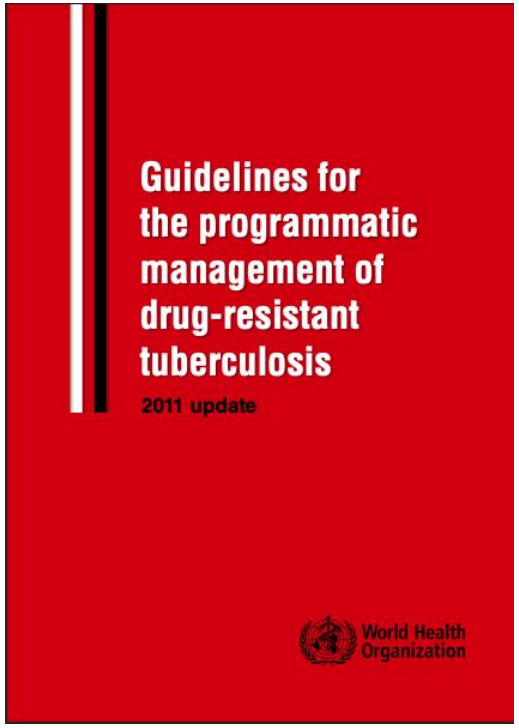
Clinical Infectious Diseases

GUIDELINES

National Tuberculosis Coalition of America (NTCA) Guidelines for Respiratory Isolation and Restrictions to Reduce Transmission of Pulmonary Tuberculosis in Community Settings

Maunank Shah,[1] Zoe Dansky,[1] Ruvandhi Nathavitharana,[2] Heidi Behm,[3] Shaka Brown,[4] Lana Dov,[5] Diana Fortune,[6] Nicole Linda Gadon,[4] Katelynne Gardner Toren,[7] Susannah Graves,[8] Connie A. Haley,[9] Olivia Kates,[1,10] Nadya Sabuwala,[11] Donna Wegener,[12] Kathryn Yoo,[13] and Joseph Burzynski[14]; on Behalf of the National TB Coalition of America

INVECE IL PAZIENTE CON MDR-TB VA SEMPRE RICOVERATO?



Decentralized, Community-Based Treatment for Drug-Resistant Tuberculosis: Bangladesh Program Experience

Paul Daru,[a] Refiloe Matji,[b] Hala Jassim AlMossawi,[b] Krishnapada Chakraborty,[b] Neeraj Kak[b]

Shifting from hospital- to community-based management of drug-resistant TB, increased treatment enrollment, reduced treatment initiation delays, improved follow-up and adherence, and lowered treatment failure, and was associated with higher cure rates and lower mortality.

ABSTRACT

Background: Bangladesh is a highly populous country where the prevalence of drug-resistant tuberculosis (DR-TB) is growing. With the rapid increase in DR-TB notifications through GeneXpert technology, it was imperative to come up with a new treatment strategy that could keep up with the increase of patients diagnosed.

Intervention: Intervention was designed to support national transition of DR-TB management of World Health Organization-approved long course (20-to-24-month regimen) treatment from a hospital-based approach to the decentralized model of community-based programmatic management of DR-TB (cPMDT). In close coordination with the Ministry of Health and Family Welfare and National TB Program, patients were initiated into treatment at hospitals and then transferred to community-based care. A cadre of directly observed therapy providers supported treatment at the household level, supervised by the outpatient DR-TB teams.

Methods: We conducted a descriptive pre- and post-intervention study of all 1,946 DR-TB patients enrolled in treatment nationwide between May 2012 and June 2015. Data were collected from hospitals, patient cards, district records, and diagnostic laboratories through the National TB Program. Intervention results were assessed in comparison with the baseline (2011) indicators.

Results: During the intervention period, treatment enrollment of 1,946 diagnosed DR-TB patients through the national program increased from 50% in 2011 to 100% in 2015. The delay between diagnosis and treatment initiation decreased from 69 days in 2011 to 6 days in 2014. Most (95%) of the patients completed all scheduled follow-up smear and culture tests. By the sixth month of treatment, 99% of patients had negative smear conversion and 98% had negative culture conversion. The treatment success rate increased from 70% in 2011 to 76% in 2015 at the end of the intervention period. The results also indicate a decline between baseline and end line from 34% to 9% for patients died, 34% to 10% for loss to follow-up, and 1.7% to 0% for treatment failure.

Conclusions: Community-based management is an effective approach for increasing access to quality-assured DR-TB treatment. Using existing structures and resources, the intervention demonstrated that favorable treatment outcomes can be achieved and sustained by treating patients with DR-TB at their homes.

Published in final edited form as:
Int J Tuberc Lung Dis. 2012 August ; 16(8): 998–1004. doi:10.5588/ijtld.11.0713.

Integrated, Home-based Treatment for MDR-TB and HIV in Rural South Africa: An Alternate Model of Care

James C.M. Brust, MD[1], N. Sarita Shah, MD, MPH[1], Michelle Scott, MD[2], Krisda Chaiyachati, MD, MPH[3], Melissa Lygizos, MD[4], Theo L. van der Merwe, MBChB[5], Sheila Bamber, MBChB[5], Zanele Radebe, BA[6], Marian Loveday, MPhil[7,8], Anthony P. Moll, MBChB[5], Bruce Margot[9], Umesh G. Lalloo, MBChB[8], Gerald H. Friedland, MD[3], and Neel R. Gandhi, MD[1]

> PLoS One. 2018 Mar 29;13(3):e0194087. doi: 10.1371/journal.pone.0194087. eCollection 2018.

Community-based MDR-TB care project improves treatment initiation in patients diagnosed with MDR-TB in Myanmar

Pyae Phyo Wai [1], Hemant Deepak Shewade [2], Nang Thu Thu Kyaw [1], Saw Thein [3], Aung Si Thu [1], Khine Wut Yee Kyaw [1], Nyein Nyein Aye [1], Aye Mon Phyo [1], Htet Myet Win Maung [4], Kyaw Thu Soe [5], Si Thu Aung [4]

Affiliations + expand

PMID: 29596434 PMCID: PMC5875775 DOI: 10.1371/journal.pone.0194087

Free PMC article

Initiation, scale-up and outcomes of the Cambodian National MDR-TB programme 2006-2016: hospital and community-based treatment through an NGO-NTP partnership

Sophan Sam [# 1], Adrienne E Shapiro [# 1 2], Thim Sok [# 1], Sokhan Khann [1 3], Rassi So [1], Sopheap Khem [1], Sokhem Chhun [1], Sarith Noun [1], Bonamy Koy [4], Prum Chhom Sayouen [4], Chun Im Sin [5], Heng Bunsieth [1], Tan Eang Mao [4], Anne E Goldfeld [1 6]

Affiliations + expand

PMID: 29955361 PMCID: PMC6018896 DOI: 10.1136/bmjresp-2017-000256

Free PMC article

In Italia…

I pazienti con **nota o sospetta TB MDR vanno generalmente ricoverati in Ospedale**. Qualora non sussistano criteri clinici che motivino il ricovero, **può essere valutato se sussistano i criteri per l'isolamento domiciliare** (il paziente vive da solo, in grado di assumere la terapia, accetta l'isolamento domiciliare e sono disponibili servizi territoriali in grado di garantire la prosecuzione della cura e l'isolamento stesso).

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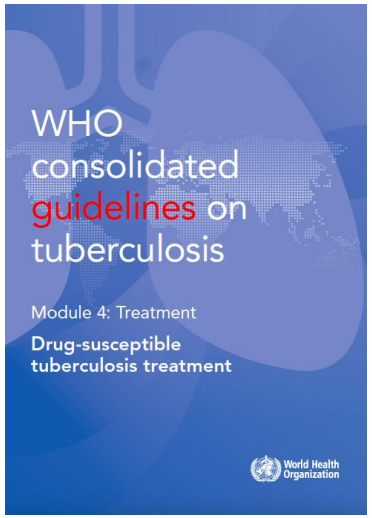
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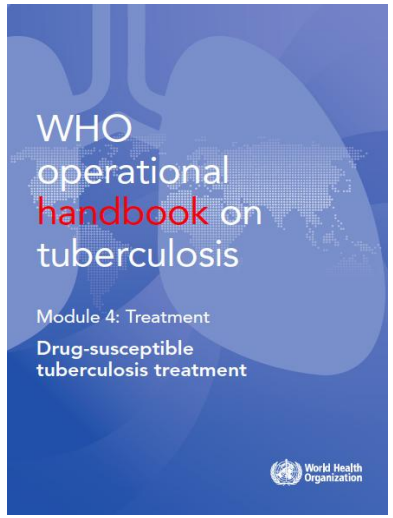
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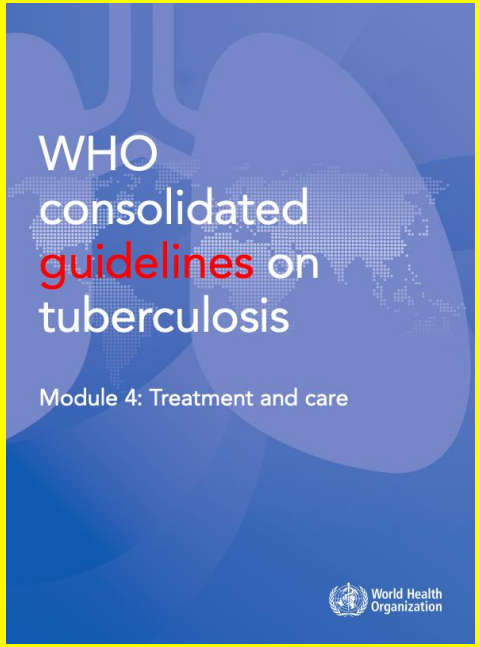
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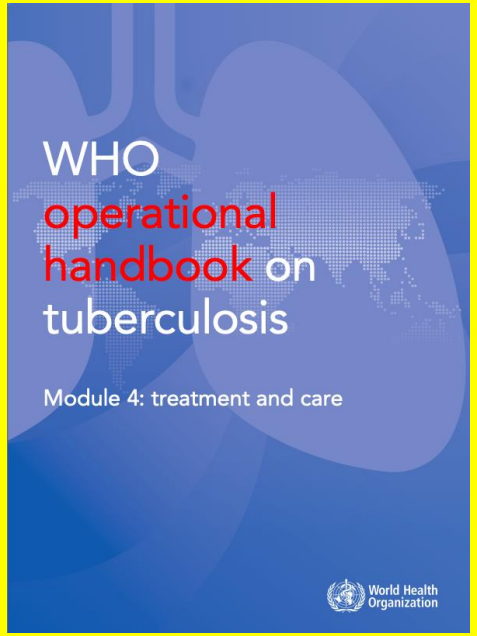
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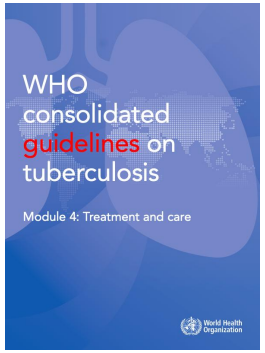
April 2025

1) Regime **tradizionale ≥ 6 mesi** (1980)



1. Treatment of drug-susceptible TB using a 6-month regimen

No.	Recommendation
1.1	New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR *(strong recommendation, high certainty of evidence).*
1.2	Wherever feasible, the optimal dosing frequency for new patients with pulmonary TB is daily throughout the course of therapy *(strong recommendation, high certainty of evidence).*
1.3	In all patients with drug-susceptible pulmonary TB, the use of thrice-weekly dosing is not recommended in both the intensive and continuation phases of therapy, and daily dosing remains the recommended dosing frequency *(conditional recommendation, very low certainty of evidence).*
1.4	The use of fixed-dose combination (FDC) tablets is recommended over separate drug formulations in treatment of patients with drug-susceptible TB *(conditional recommendation, low certainty of evidence).*
1.5	In new pulmonary TB patients treated with the regimen containing rifampicin throughout treatment, if a positive sputum smear is found at completion of the intensive phase, the extension of the intensive phase is not recommended *(strong recommendation, high certainty of evidence).*

No.	Recommendation
1.1	**New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR** ***(Strong recommendation, high certainty of evidence)***

This recommendation also applies to extrapulmonary TB

except TB of the **central nervous system, bone or joint**

for which some expert groups suggest longer therapy.

Durata complessiva di **9 mesi** se:

→ Cavitazione all'Rx torace iniziale

→ Se regime standard non include pirazinamide o isoniazide (per intolleranza o resistenza)

→ Se lenta risposta clinica o radiologica al 6 mese di terapia

Nelle forme ossee o del SNC-> durata terapia almeno **12 mesi**

Pill-burden: Fixed-dose combinations (FDCs)

1998 introduzione delle combinazioni fisse
2017 raccomandazione dell'OMS

RIFINAH(INH, RIF)

RIFATER (INH, RIF, PZA)

RIMSTAR®(INH, RIF, PZA, and EMB)

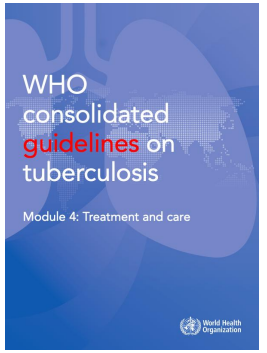
Vantaggi:

Sanità pubblica: ridotto rischio di "errore" da parte del paziente

Paziente: Semplificazione del trattamento

Operatore sanitario: Più agevole la supervisione del trattamento

2) Regime 4 mesi



2. Treatment of drug-susceptible TB using 4-month regimens

No.	Recommendation
2.1	People aged 12 years or older with drug-susceptible pulmonary TB may receive a 4-month regimen of isoniazid, rifapentine, moxifloxacin and pyrazinamide (2HPMZ/2HPM) *(conditional recommendation, moderate certainty of evidence).*
2.2	In children and adolescents between 3 months and 16 years of age with non-severe TB (without suspicion or evidence of MDR/RR-TB), a 4-month treatment regimen (2HRZ(E)/2HR) should be used *(strong recommendation, moderate certainty of evidence).*

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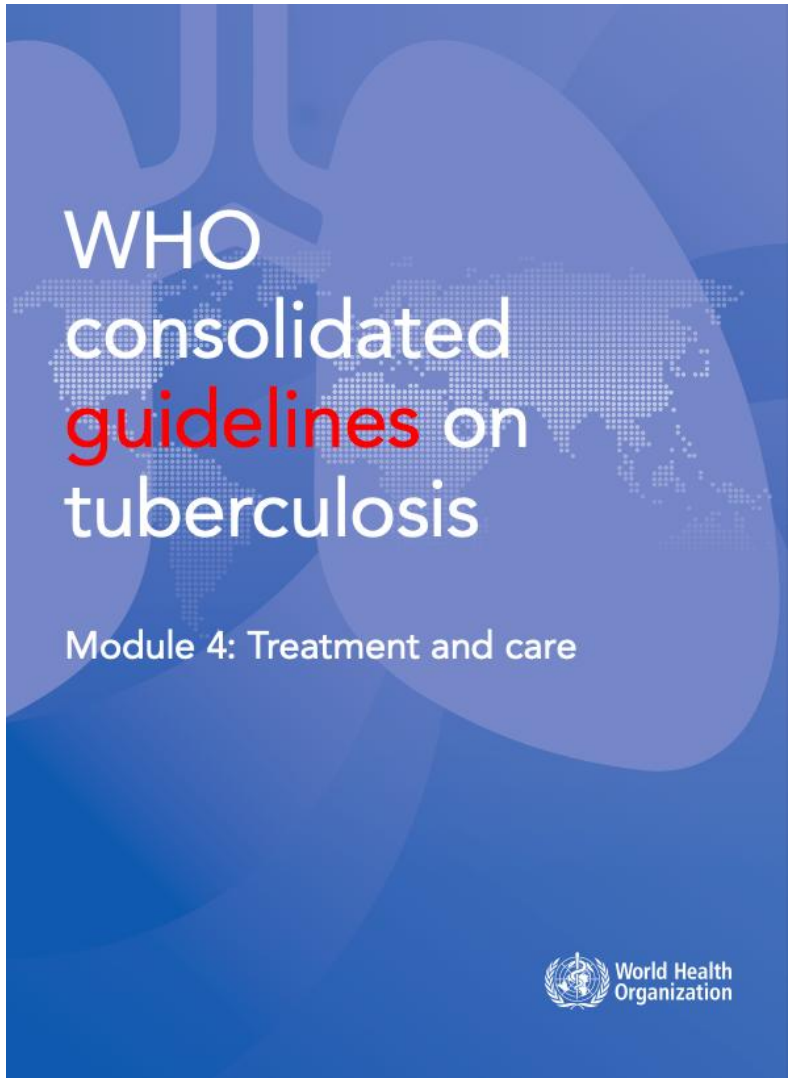
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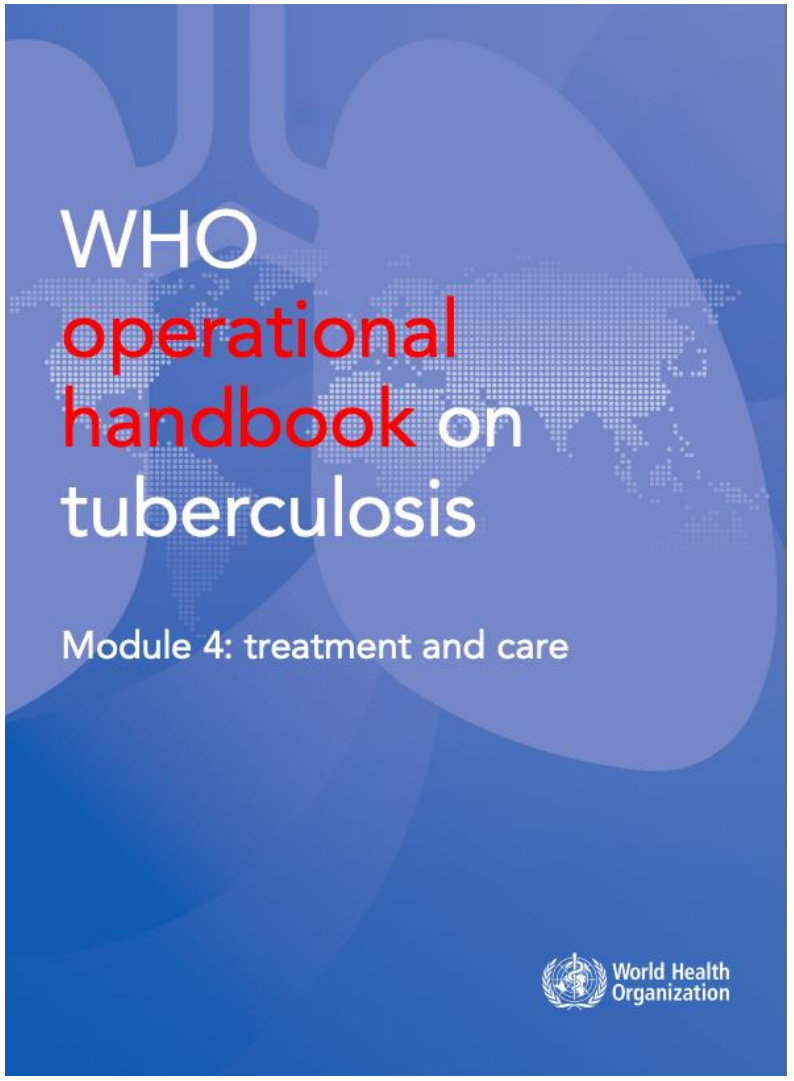
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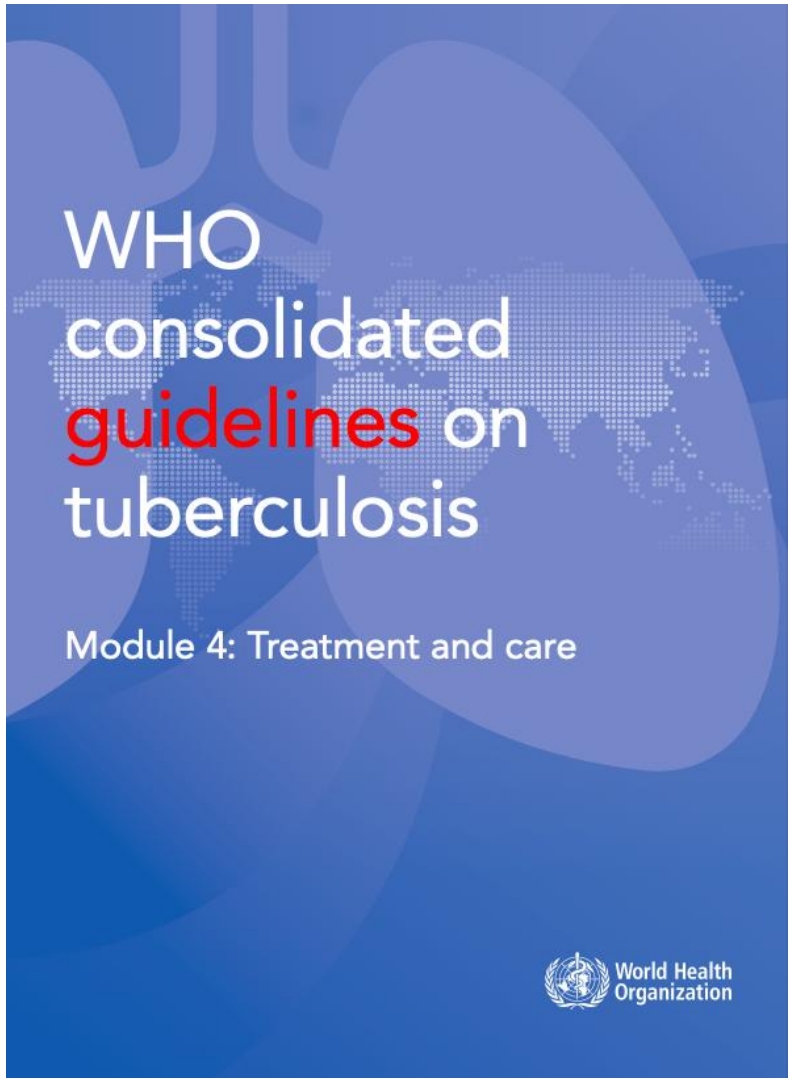
World Health Organization

APRIL 2025



2. WHO recommendations on DR-TB treatment

Treatment of drug-resistant TB using 6-month regimens	
1.1	WHO suggests the use of the 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM) rather than 9-month or longer (18-month) regimens in MDR/RR-TB patients. *(Conditional recommendation, very low certainty of evidence)*
1.2	WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance. *(Conditional recommendation, very low certainty of evidence)*
Treatment of drug-resistant TB using 9-month regimens	
2.1	WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. *(Conditional recommendation, very low certainty of evidence)*
2.2	WHO suggests using the 9-month all-oral regimens (**BLMZ, BLLfxCZ and BDLLfxZ**) over currently recommended longer (>18 months) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. Amongst these regimens, using BLMZ is suggested over using BLLfxCZ, and BLLfxCZ is suggested over BDLLfxZ. *(Conditional recommendation, very low certainty of evidence)*
2.3	WHO suggests against using 9-month DCLLfxZ or DCMZ regimens compared with currently recommended longer (>18 months) regimens in patients with fluoroquinolone-susceptible MDR/RR-TB. *(Conditional recommendation, very low certainty of evidence)*
Longer regimens for MDR/RR-TB	
3.1	In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, all three Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of the treatment if bedaquiline is stopped. If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it. *(Conditional recommendation, very low certainty of evidence)*

6 months

1. Treatment of drug-resistant TB using 6-month regimens

1.1 The 6-month bedaquiline, pretomanid, linezolid and moxifloxacin (BPaLM) regimen for MDR/RR-TB and pre-XDR-TB (b)

WHO suggests the use of the 6-month treatment regimen composed of bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM) rather than 9-month or longer (18-month) regimens in MDR/RR-TB patients.

(Conditional recommendation, very low certainty of evidence)

1.2 The 6-month bedaquiline, delamanid, linezolid, levofloxacin and clofazimine (BDLLfxC) regimen (a)

WHO suggests the use of a 6-month treatment regimen composed of bedaquiline, delamanid, linezolid (600 mg), levofloxacin, and clofazimine (BDLLfxC) in MDR/RR-TB patients with or without fluoroquinolone resistance.

(Conditional recommendation, very low certainty of evidence)

WHO consolidated guidelines on tuberculosis. Module 4: treatment and care. Geneva: World Health Organization;2025

9 months

2. Treatment of drug-resistant TB using 9-month regimens

2.1 The 9-month all-oral regimen for MDR/RR-TB (b)

WHO suggests the use of the 9-month all-oral regimen rather than longer (18-month) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded.

(Conditional recommendation, very low certainty of evidence)

2.2 The modified 9-month all-oral regimens for MDR/RR-TB (a)

WHO suggests using the 9-month all-oral regimens (**BLMZ, BLLfxCZ and BDLLfxZ**) over currently recommended longer (>18 months) regimens in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded. Amongst these regimens, using BLMZ is suggested over using BLLfxCZ, and BLLfxCZ is suggested over BDLLfxZ.

(Conditional recommendation, very low certainty of evidence)

2.3 WHO suggests against using 9-month DCLLfxZ or DCMZ regimens compared with currently recommended longer (>18 months) regimens in patients with fluoroquinolone-susceptible MDR/RR-TB.

(Conditional recommendation, very low certainty of evidence)

WHO consolidated guidelines on tuberculosis. Module 4: treatment and care. Geneva: World Health Organization;2025

18+ months

3. Treatment of drug-resistant TB using longer regimens (b)

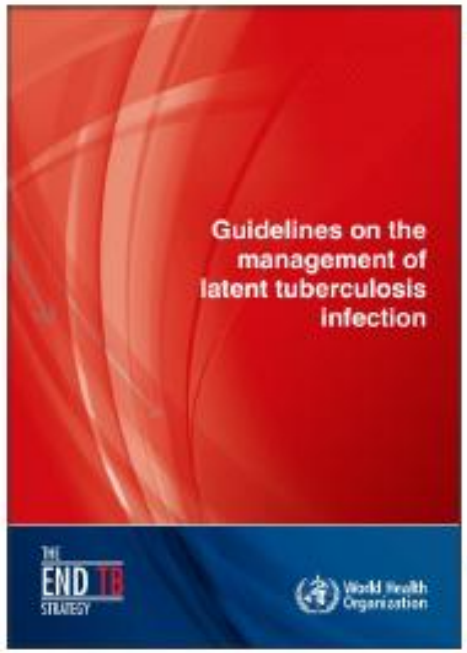
3.1 In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, all three Group A agents and at least one Group B agent should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of the treatment if bedaquiline is stopped. If only one or two Group A agents are used, both Group B agents are to be included. If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it.

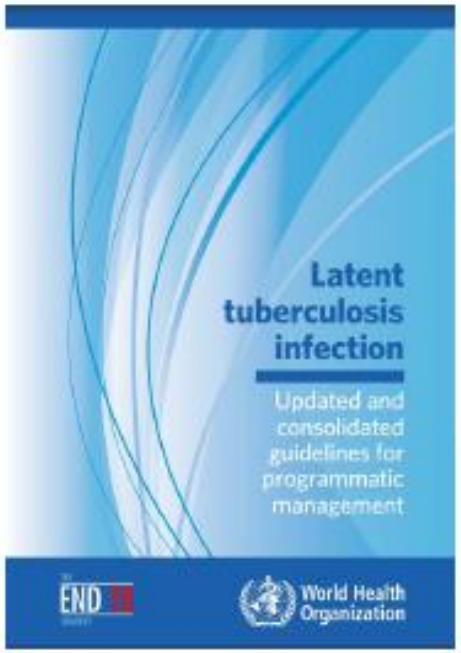
(Conditional recommendation, very low certainty of evidence)

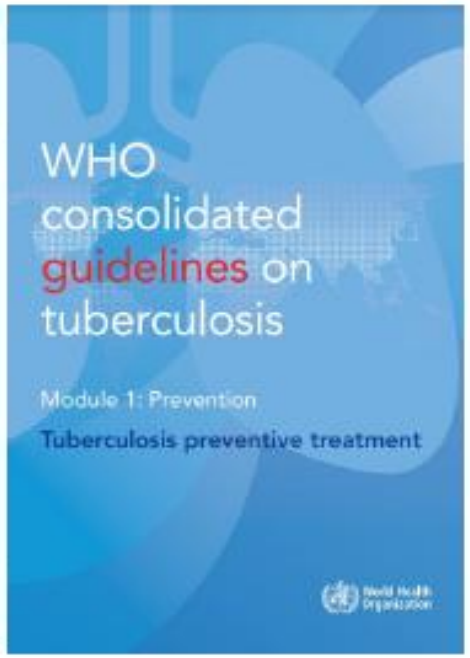
Outline

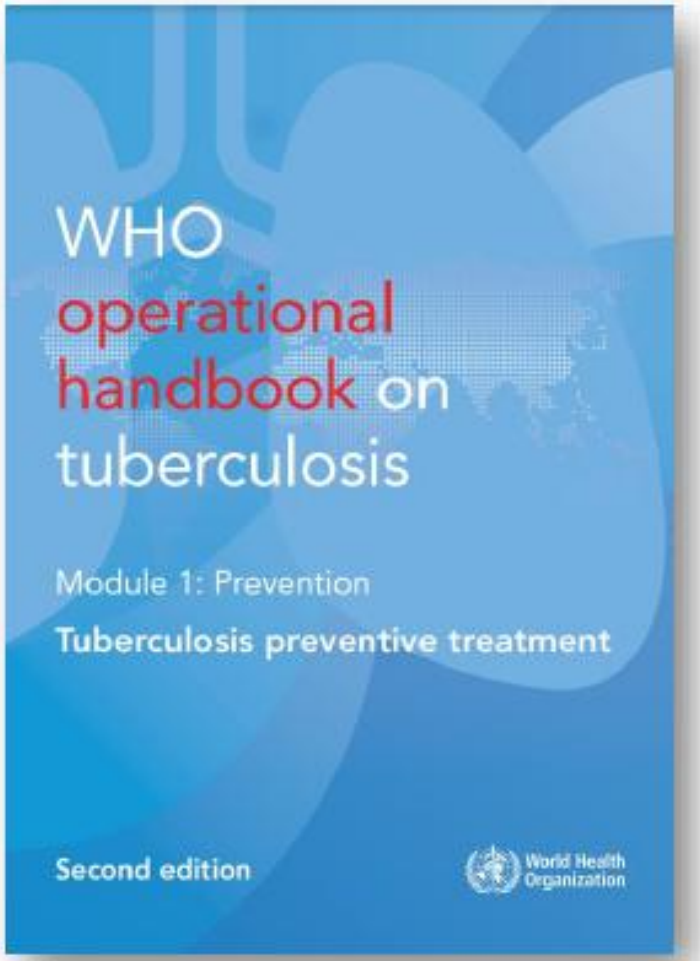
- Percorso diagnostico e terapeutico della TB attiva
  - Criteri diagnostici
  - Gestione TB polmonare: ricoverare o no?
  - Cenni di terapia
  - MDR-TB
- Percorso diagnostico e terapeutico dell'infezione tubercolare
  - Chi sottoporre a screening?
  - Infezione o malattia?
  - Terapia preventiva: regimi e indicazioni

WHO guidelines on TPT





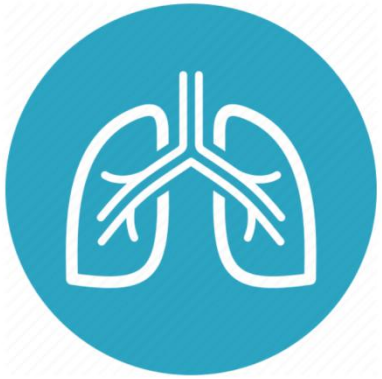




2015 2018 2020 2024

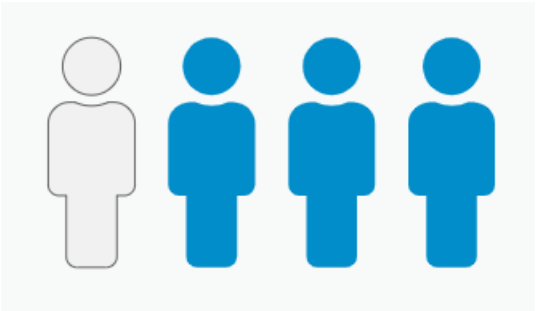
September

Infezione tubercolare

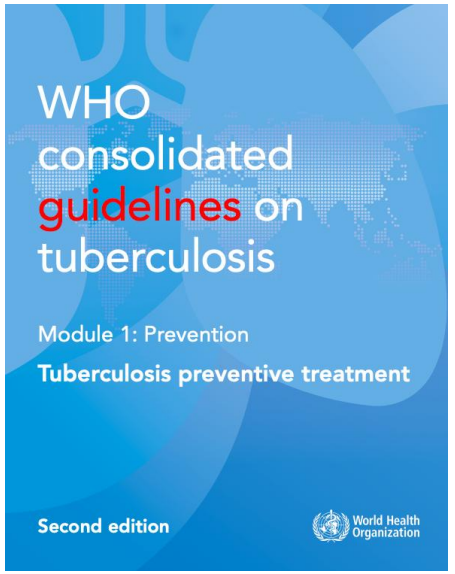


L'infezione tubercolare (ITB) è definita uno stato di persistente risposta immunitaria nei confronti della stimolazione da parte degli antigeni del *Mycobacterium tuberculosis* senza evidenza di malattia clinicamente manifesta.

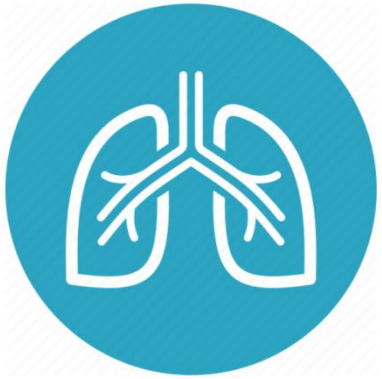
Gli individui con ITB non hanno malattia attiva ma possono ammalarsi in futuro



Si stima che un quarto della popolazione mondiale sia **affetto** da ITB. NON PIU' VERO!!!



Infezione tubercolare



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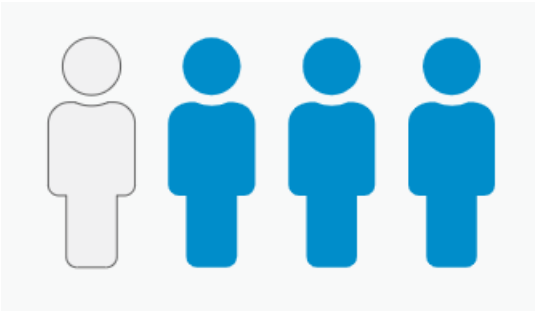
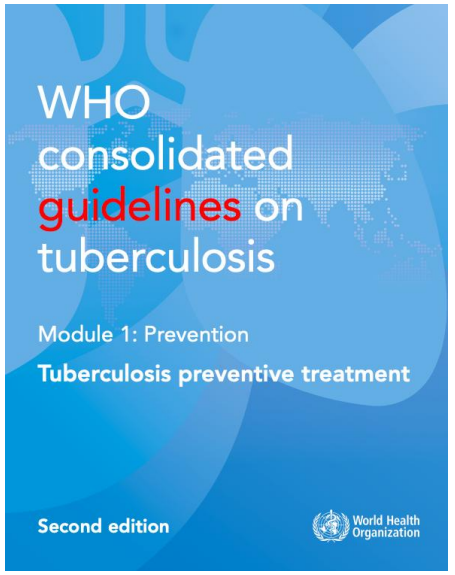
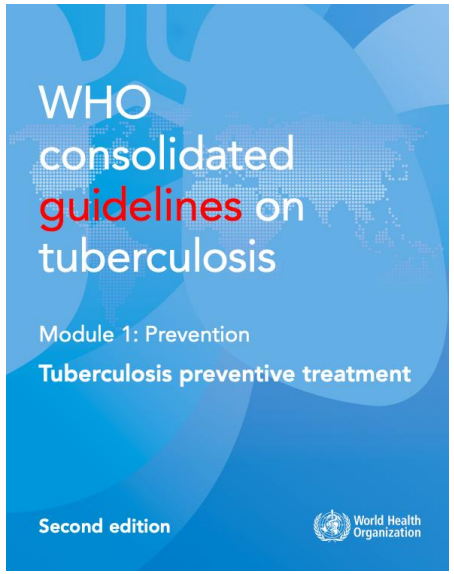


Si stima che un quarto della popolazione mondiale sia entrato in contatto con il MTb (ma che solo una % non ancora nota ma molto inferiore, rimane "infetta" con bacilli vivi e vitali e dunque corre il rischio di riattivazione)



Tubercolosi: gruppi a rischio

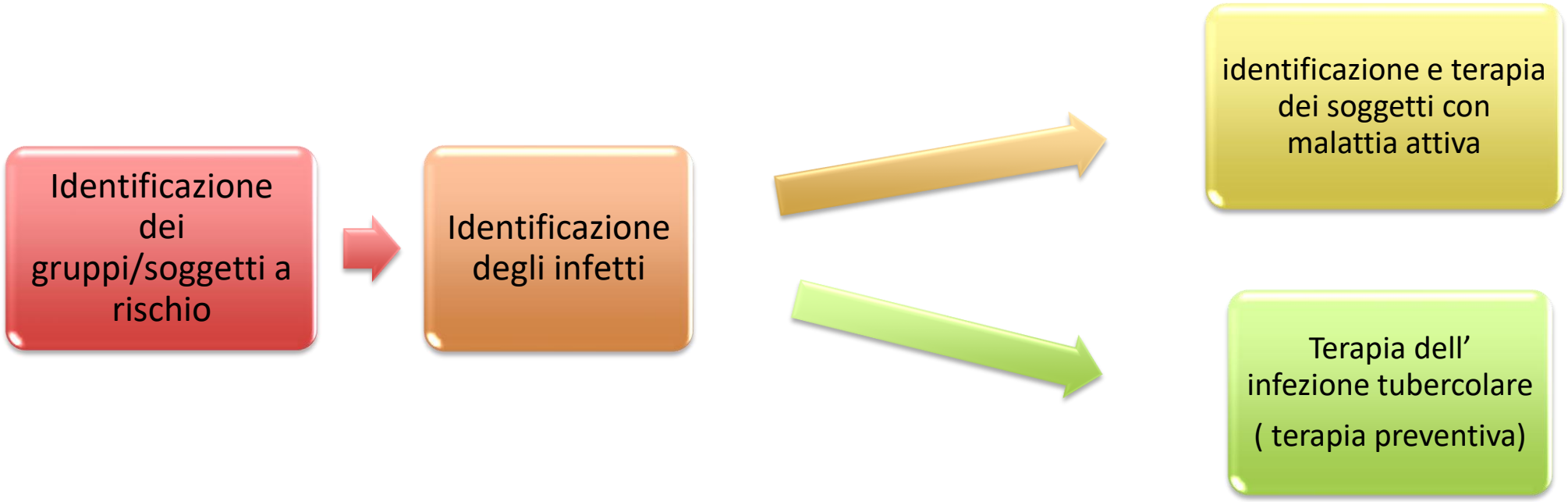


- Persone HIV+
- Contatti di persone affette da TB
- Pazienti candidate a anti-TNF
- Pazienti candidati a trapianto d'organo
- Dializzati
- Pazienti affetti da silicosi

In Paesi a bassa incidenza, testare e trattare l'infezione TB può essere considerato anche per:

- Carcerati
- Operatori sanitari
- Immigrati da paesi ad alta incidenza di TB (>100/100,000)
- Persone senza fissa dimora
- Persone che fanno uso di sostanze stupefacenti

Prevenzione della tubercolosi



Nessuna attività di screening dei gruppi a rischio deve essere intrapresa se non con lo scopo di identificare i soggetti cui prescrivere la terapia preventiva

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Ruling out TB

	Adults and adolescents living with HIV[b]	Children living with HIV[a]	HIV-negative household / close contacts of TB patients	Clinical at-risk populations
Clinical symptom-based screening[a]	Current cough, fever, weight loss or night sweats	Absence or poor weight gain, fever or current cough or history of contact with a case of TB, reduced playfulness, night sweats	Cough of any duration, haemoptysis, fever, night sweats, weight loss, chest pain, shortness of breath, fatigue	
Frequency of symptom screening	At every visit to a health facility or contact with a health worker			

Excluding TB disease before initiating TPT is one of the critical steps in the TBI care pathway

WHO four-symptom screening rules

11. Among adults and adolescents living with HIV, chest X-ray may be used to screen for TB disease.

12. Among adults and adolescents living with HIV, C-reactive protein at a cut-off of > 5 mg/L may be used to screen for TB disease.

13. Among adults and adolescents living with HIV, molecular WHO-recommended rapid diagnostic tests may be used to screen for TB disease.

14. Among HIV-negative household contacts aged ≥ 5 years and other risk groups, the absence of any symptoms of TB and the absence of abnormal chest radiographic findings may be used to rule out TB disease before TB preventive treatment.

15. Among individuals aged ≥ 15 years in populations in which TB screening is recommended, systematic screening for TB disease may be conducted with a symptom screen, chest X-ray or molecular WHO-recommended rapid diagnostic tests, alone or in combination.

16. Among individuals < 15 years who are close contacts of a person with TB, systematic screening for TB disease should be conducted with a symptom screen of any one of cough, fever or poor weight gain; or chest radiography; or both.

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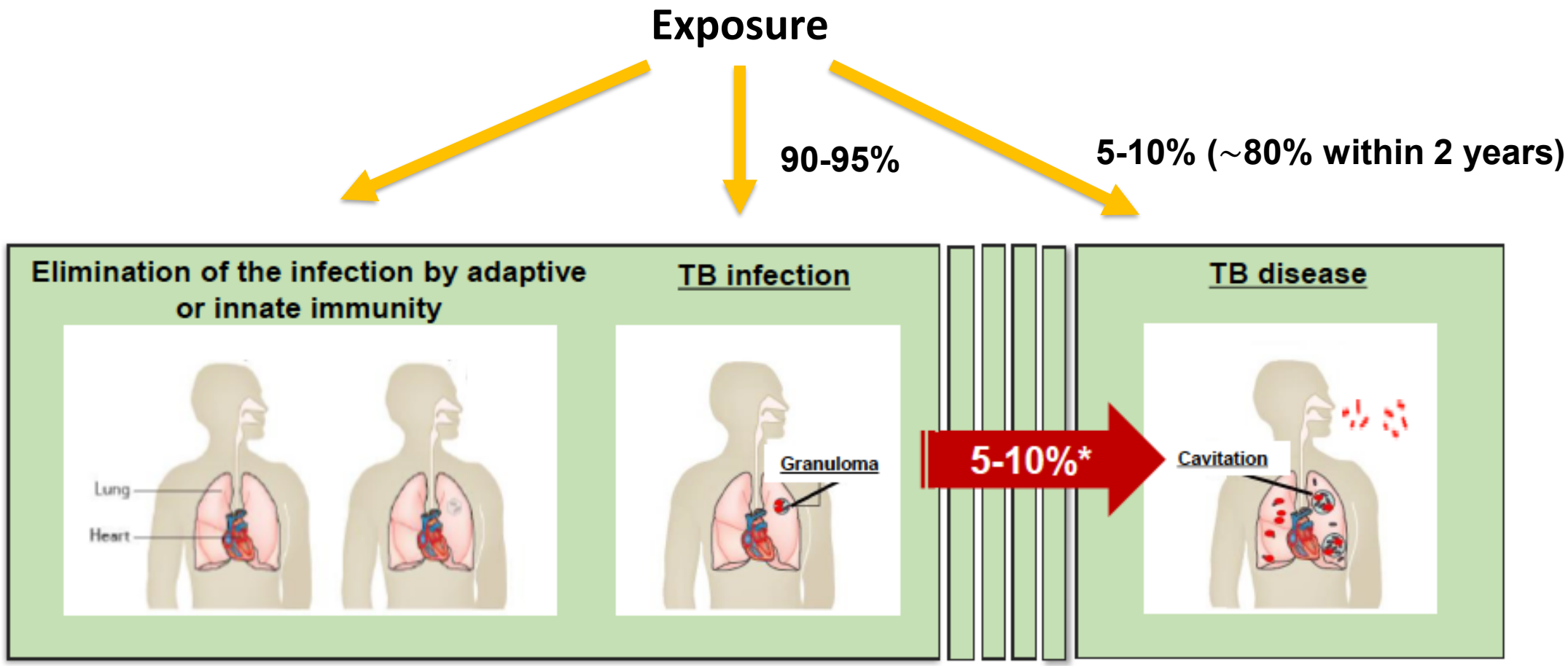
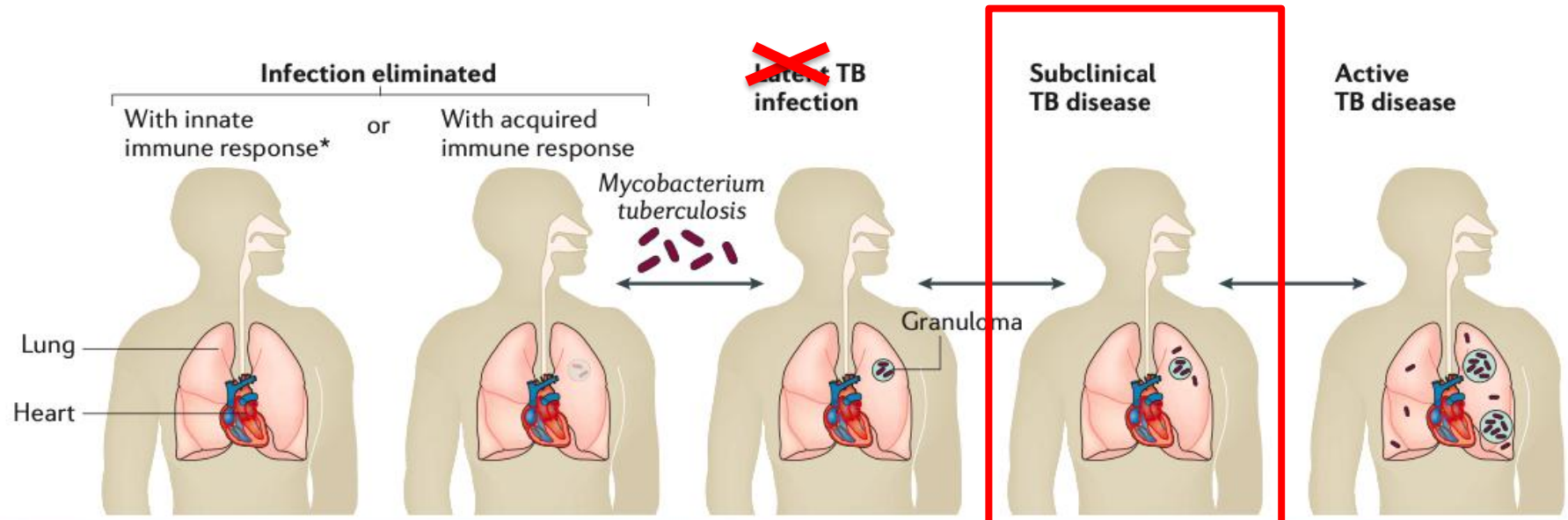
Natural history of TB



* In the lifetime

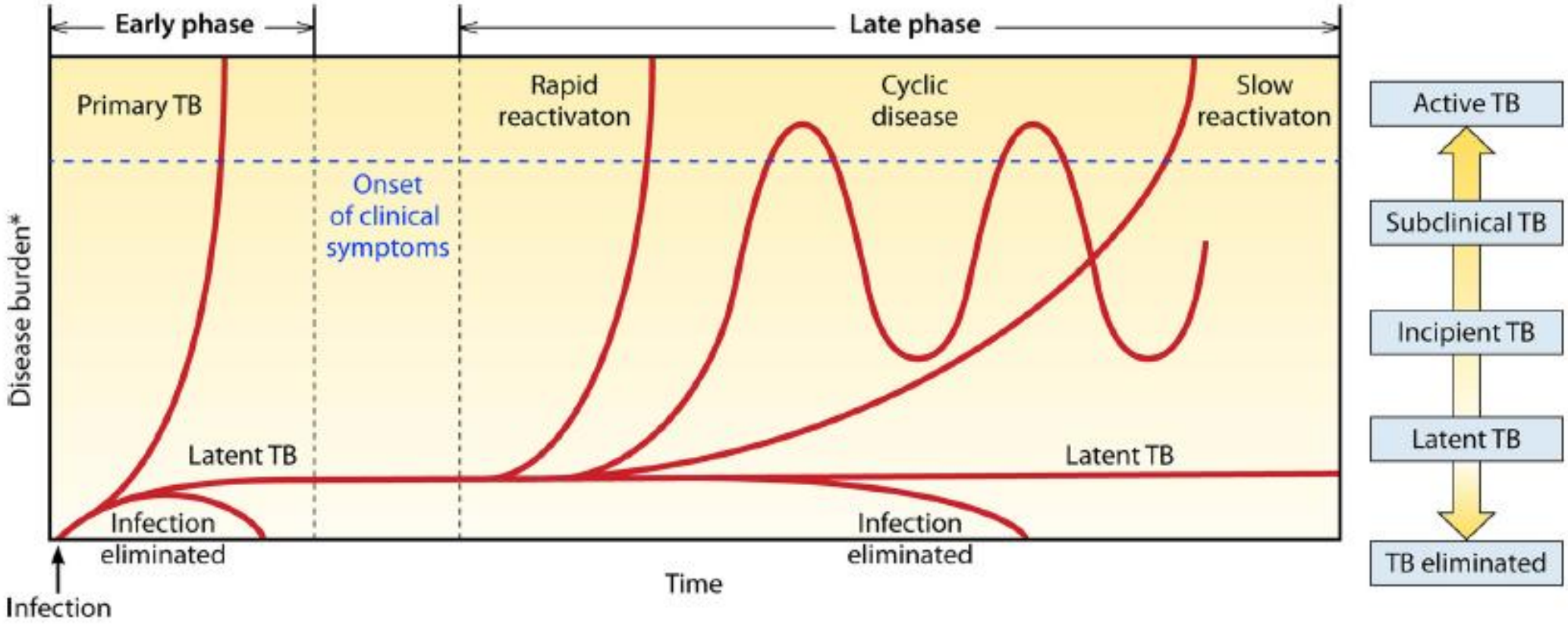
Tuberculosis



TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Sputum smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventive therapy	Multidrug therapy	Multidrug therapy

M Pai, MA Behr, D Dowdy, K Dheda, et Al. Nature Reviews 2016

Incipient and subclinical tuberculosis: a clinical review of early stages and progression of infection



Drain PK et Al. Clinical Microbiology. October 2018

How to find those with subclinical TB?

Active TB

Passive case finding

(patients self-presenting to HFs)

Entry point:

- TB suggestive symptoms
- CXR -> HRCT -> Sputum
- Other imaging/samples for EPTB
- Decision to start anti-TB treatment

Subclinical TB

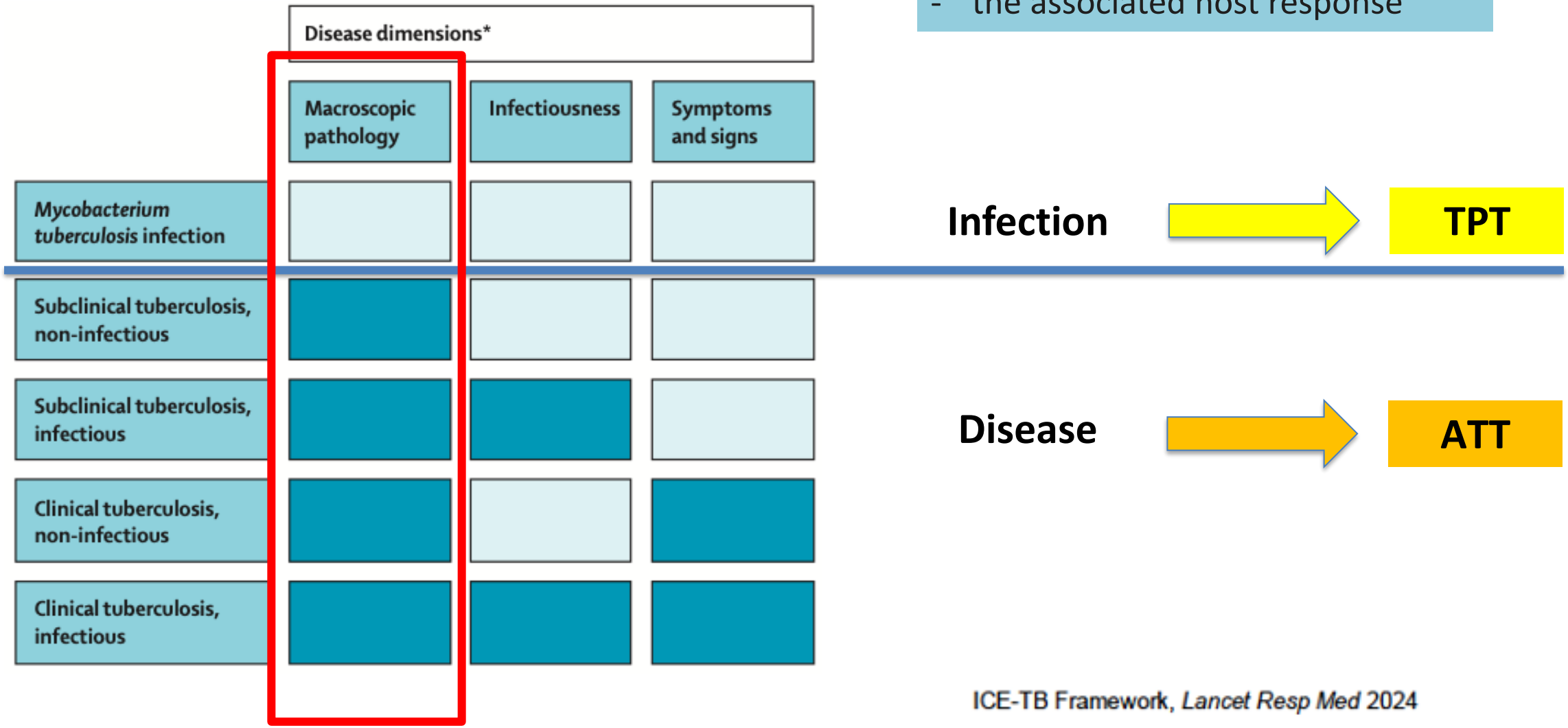
Active case finding or screening programmes for high risk groups

Entry point:

- Positive TST/IGRA and/or abnormal CXR
- HRCT/PET -> Sputum/Induced sputum/BAL
- Decision to start anti-TB treatment **(or TPT is subclinical TB is ruled out)**

Classification of early tuberculosis states to guide research for improved care and prevention: an international Delphi consensus exercise

Anna K Coussens, Syed M A Zaidi, Brian W Allwood, Puneet K Dewan, Glenda Gray, Mikashmi Kohli, Tamara Kredo, Ben J Marais, Guy B Marks, Leo Martinez, Morten Ruhwald, Thomas J Scriba, James A Seddon, Phumeza Tisile, Digby F Warner, Robert J Wilkinson, Hanif Esmail*, Rein M G J Houben*, on behalf of the International Consensus for Early TB (ICE-TB) group†*



Pre-requisites for all the states of infection and disease:
- presence of viable Mtb
- the associated host response

Infection → **TPT**

Disease → **ATT**

ICE-TB Framework, *Lancet Resp Med* 2024

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Terapia Preventiva

- L’efficacia della terapia preventiva è tale da ridurre significativamente il rischio di riattivazione della infezione TB (60-85% se ben eseguita e a secondo della durata prescelta).

WHO consolidated guidelines on TB. Module 1 preventive treatment. 2020

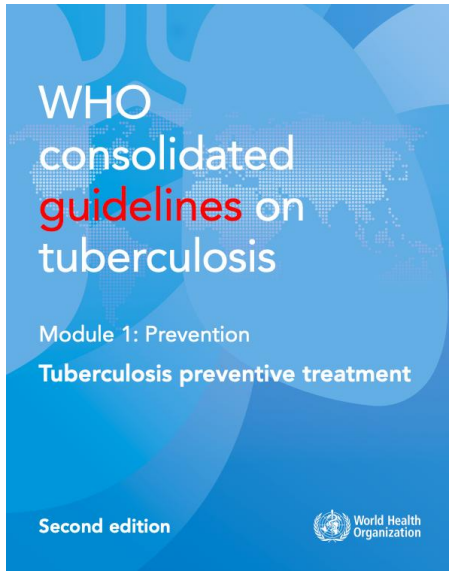
Terapia Preventiva. Il fattore età

Il fattore età (> o ≤ di 35/50 anni) può essere preso in considerazione secondo il seguente schema:

- **TPT indipendentemente dall'età (e in tempi più rapidi) per**:
  - contatti di casi contagiosi
  - HIV+
  - Soggetti in terapia con farmaci o affetti da patologie immunosoppressive

- **TPT solo in soggetti ≤ di 35/50 anni**
  - Tutti gli altri gruppi a rischio

2020 guidelines – TPT options



6 or 9 months of daily isoniazid*

3 months regimen of daily isoniazid plus rifampicin*

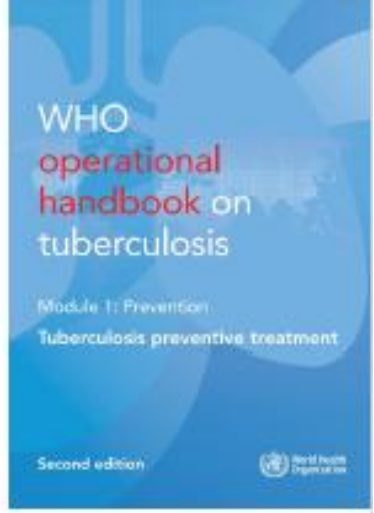
4 months of daily rifampicin alone

3 months regimen of weekly rifapentine plus isoniazid*

1 month regimen of daily isoniazid plus rifapentine

** Strong recommendation*

TB preventive treatment (TPT) options



1.4. TB preventive treatment options

TB preventive treatment with isoniazid or rifamycins

19. The following TB preventive treatment options are recommended regardless of HIV status: 6 or 9 months of daily isoniazid, or a 3-month regimen of weekly rifapentine plus isoniazid, or a 3-month regimen of daily isoniazid plus rifampicin.

20. The following alternative TB preventive treatment options may be used regardless of HIV status: a 1-month regimen of daily rifapentine plus isoniazid or 4 months of daily rifampicin.

TB preventive treatment with levofloxacin

21. In contacts exposed to multidrug- or rifampicin-resistant tuberculosis, 6 months of daily levofloxacin should be used as TB preventive treatment. **(Strong recommendation, moderate certainty of the estimates of effect)**

Age >14 years, by body weight: < 46 kg, 750 mg/day; >45 kg, 1g/day

Age <15 years (range, approx. 15–20 mg/kg/day), by body weight:
5–9 kg: 150 mg/day;
10–15 kg: 200–300mg/day;
16–23 kg: 300–400mg/day;
24–34 kg: 500–750mg/day

WHO 2024

Conclusioni

- Importante pensare alla TB e porla in diagnosi differenziale in base a criteri diagnostici
- Cercare sempre la conferma batteriologica
- Attenzione a localizzazione polmonare, anche in assenza di sintomi!
- Se possibile, trattare il paziente in regime ambulatoriale!!
- La gestione della TB richiede lavoro di equipe e collaborazione tra servizi intra- ed extraospedalieri
- Individuare e trattare l'infezione TB è una priorità nel controllo della tubercolosi
- La terapia preventiva è efficace nel prevenire la riattivazione dell'infezione TB
- La terapia preventiva deve essere individualizzata e monitorata
- …FORMAZIONE FORMAZIONE FORMAZIONE!!

THANKS TO

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https://stoptb.it