

Tuberkulos

- om diagnostik, handläggning och smittrisk i låginkomstländer

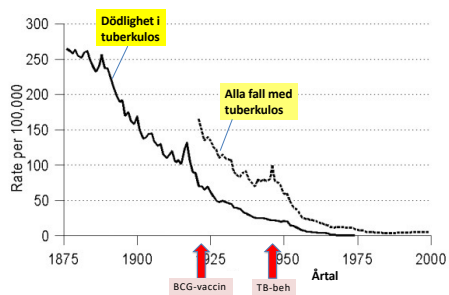


Workshop Holsbybrunn 22 april 2023
Leif Dotevall, infektionläkare Västra Götaland

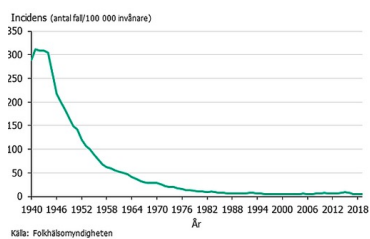


Hold your Breath™ (2015) Painting from WHO website - Paulina Siniatkina

Tuberkulos i Danmark 1875 - 2000



Incidens av TB i Sverige, 1940-2019



Who is most affected?

THE STOP TB DEPARTMENT

Poor, crowded & poorly ventilated settings

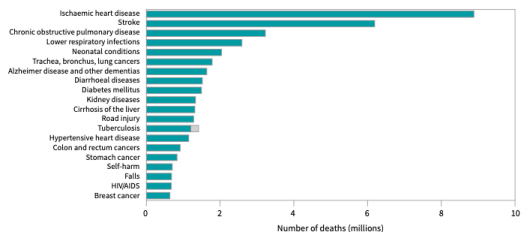
Half a million women and over 65,000 children die of TB each year; 10 million "TB" orphans

Migrants, prisoners, minorities, refugees face risks, discrimination & barriers to care

TB linked to HIV infection, malnutrition, alcohol, drug and tobacco use, diabetes

Top causes of death worldwide in 2019^{a,b}

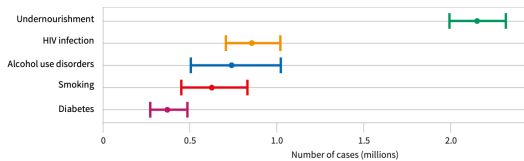
Deaths from TB among HIV-positive people are shown in grey.



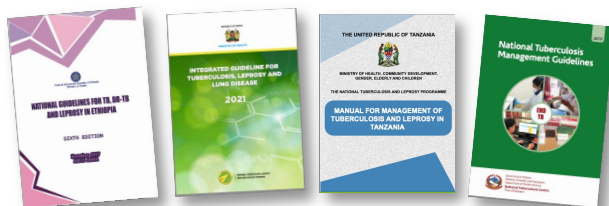
Global Tuberculosis Report 2022 (WHO)



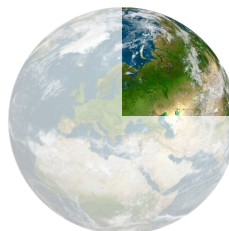
Global estimates of the number of incident TB cases attributable to selected risk factors, 2021*



Global Tuberculosis Report 2022 (WHO)



Process of care		Quality impact		
<p>2-month delay in diagnosis</p> <p>Only 1 in 2 patients with drug-susceptible tuberculosis, 1 in 5 patients with MDR tuberculosis, and 1 in 5 patients with latent tuberculosis infection are adequately diagnosed and treated</p> <p>Patients lost to follow-up: 4-38%</p>		<p>Delays in diagnosis results in</p> <p>High costs to patients (patients spend more than half of annual income on care)</p> <p>Increased waiting times for treatment</p> <p>Probably low patient satisfaction with care (although additional research is needed)</p>		
<p>50-60% patients begin seeking care in informal (eg, agencio or homeopathic doctors, and pharmacists) and private sectors</p>	<p>Governance</p> <p>52% HBCs recommend Xpert MTR/RIF as initial test. 47% have implemented this</p> <p>In 8 low-income HBCs, domestic funding represents <7% of NTP budget needs</p>	<p>Platforms</p> <p>1.1 microscopy labs per 100,000 population</p> <p>1.3 DST per 5 million population</p> <p>Limited accessibility to tuberculosis services at community level</p>	<p>Workforce</p> <p>3 health-care providers are seen before diagnosis</p> <p>28%-45% of providers correctly manage tuberculosis cases</p>	<p>Tools</p> <p>10 sputum smears for every Xpert test in HBCs</p> <p>20% of patients in need of bedaquiline have received it</p>



"About one quarter of the world's population is infected with tuberculosis bacteria. Only a small proportion of those infected will become sick with TB"

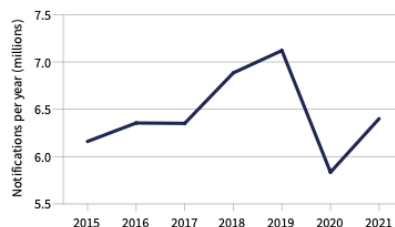
Building a tuberculosis-free world: The Lancet Commission on tuberculosis (Lancet 2019;393:1331-84)

WHO 12 Oct 2021

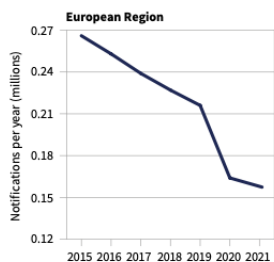
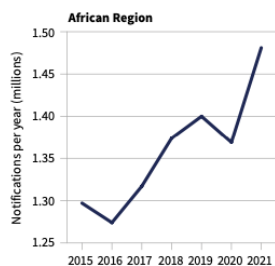


Free download

Global trend in case notifications of people newly diagnosed with TB, 2015–2021

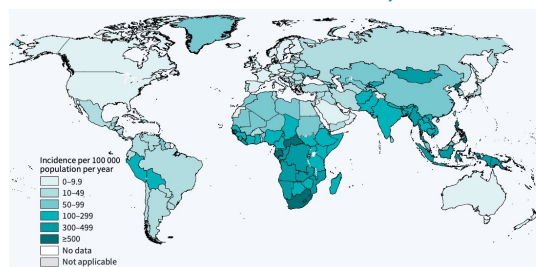


Global Tuberculosis Report 2022 (WHO)



Global Tuberculosis Report 2022 (WHO)

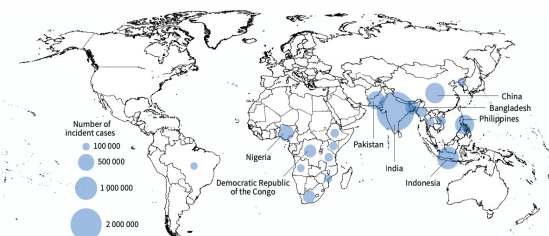
Estimated TB incidence rates, 2021



2021

Global Tuberculosis Report 2022 (WHO)

8 länder har två tredjedelar av alla nya TB-fall 2021



Global Tuberculosis Report 2022 (WHO)



2021

**1.2 million children fell ill with TB globally
196 000 child deaths due to TB**

(including among children with HIV)

11%

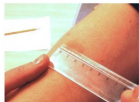
14%

Global Tuberculosis Report 2022 (WHO)

Latent tuberkulos

- Inga symtom. "Frisk"
- Ingen risk för smitta

Positiv tuberkulintest ("PPD", TST) eller positiv Quantiferon (IGRA)



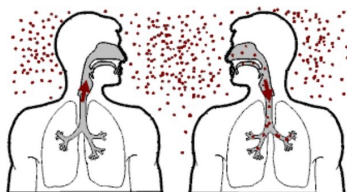
Aktiv tuberkulos

- "Sjuk", kliniska symtom
- Smittsamhet hos vissa med lung-TB
- Ingen smittsamhet vid extrapulmonell TB



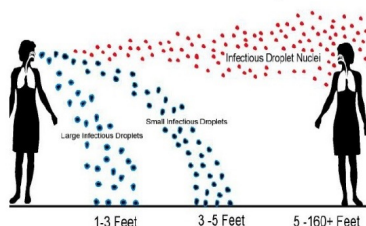
Hur smittar tuberkulos?

1. Luftburen smitta via droppkärnor
2. Peroral (via opastöriserad mjölk)
3. Hematogen – placentär spridning (mor- barn)



- Smitta via upphostningar, aeroliserade genom hosta, nysning, utandning och krymper genom torkning...
- Oftast relativt låg smittsamhet
- Närhet ökar risk
- Vissa patienter "superspridare"
- Tuberkulos smittar inte utomhus

Infectious Droplets & Droplet Nuclei travel lengths

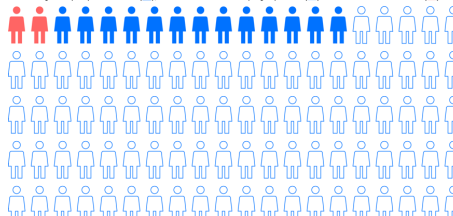


Tuberkulosens förlopp efter smitta...

Outcomes

Not everyone who has tuberculosis will get sick, or die, from it

For every 100 people with TB (□), five to 15 will develop symptoms (■) and one to two will die (■)



Source: World Health Organization's Global Tuberculosis Report 2017

BloombergOpinion

Latent tuberkulos

- hur stor är risken att reaktivera och insjukna i aktiv tuberkulos?

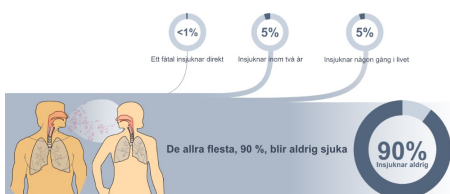
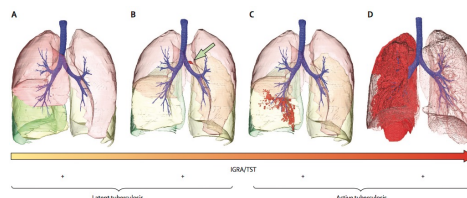


Bild: Henrik Mellström Dahlgren, Smittskydd Västra Götaland



Latent tuberkulos → Aktiv tuberkulos
- en glidande skala....

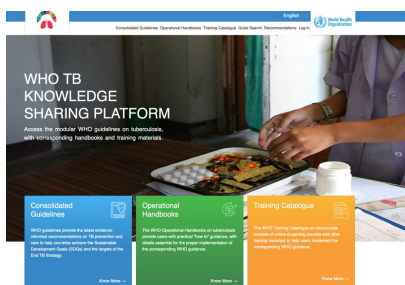
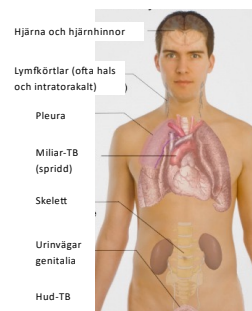
Riskfaktorer för progress av LTBI till aktiv TB (Källa: ECDC)

Riskfaktor	Relativ risk hos person med LTBI och riskfaktor jämfört med befolkning i stort (LTBI-status okänt)
Hiv-positiv *	183.0 (41.7-803.4)
Silikos	170.3 (137.9-210.2)
Dialys	41.4 (37.9-44.8)
Behandling med TNF-alfa-hämmare	16.2 (14.6-18.0)
Diabetes	10.3 (5.9-17.6)

*inga uppgifter om antiretroviral behandling eller inte

Lung-TB
- ca 60 %

Extrapulmonell tuberkulos
- ca 40 %



<https://tbkso.org/>

Diagnostik - aktiv TB

Val av primära diagnostiska metoder vid misstanke om aktiv tuberkulos

Lokalisation	Mikrobiologi	Radiologi	Övrigt
Lungor	Mikroskopi, PCR och odling x 3 på sputum	Lungtg (ev DT thorax)	Minst ett morgonprov. Infuserat sputum vid svårighet att få bra prov.
Lymfkörtlar	PCR och odling på punktat/biopsi	Lungtg (ev DT thorax)	PAD (DBS, separata rör)
Pleurit	PCR och odling på pleurabiopsi och pleuravätska (best <100 ml)	Lungtg (ev DT thorax)	Kontakt med lungmedicin för biopsi/PAD (DBS, separata rör)
Spondylodisk	PCR och odling på biopsi (punktat)	MR halsrygg	Nedre thoraxal eller övre lumbalnivå vanligtast.
Intraabdominell	PCR och odling på feces (>1 ml) x 2-3 och punktat/biopsi (konst, peritonium, sams)	DT buk med kontrast	PAD (DBS, separata sterila rör)
Urogenital	PCR och odling på morgonurin (100 ml) x 3.	DT buk med kontrast	Ev kontakt med urolog/gynekolog
Meningit	PCR och odling på likvor (minst 1 ml och best <50)	MR hjärna	
Miljår	PCR och odling på saccum, urin, feces. Biodödning och benvägsbiopsi för mykobakterier	DT thorax	Likvort med LP och MR hjärna. Särskilda flaskor används för blododling av mykobakterier (kontakta närmaste mykobakterielab).

SILF Vårdprogram Tuberkulos 2023

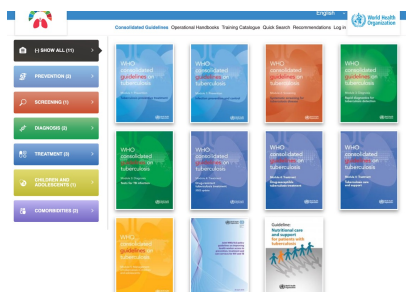
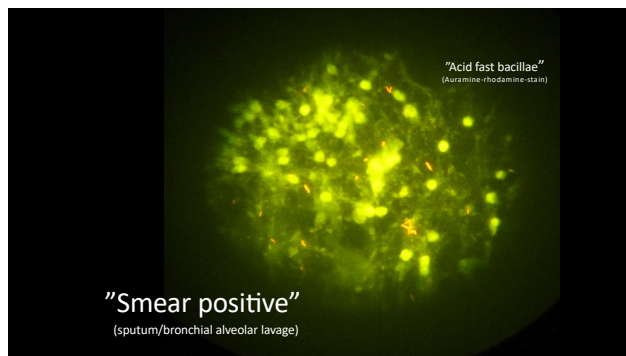


Mycobakterie-odling

– särskilda odlingsrör eller tomma rör

Direkt-mikroskopi

Limit of detection of 5000-10 000 bacilli per millilitre of sputum



<https://tbksp.org/en/implementation-books-soil>



Fig. 2. WHO-recommended rapid diagnostic testing platforms to be used as initial tests for TB, 2022



<https://www.who.int/news/item/20-05-2022-tuberculosis-fast-cure-drug-resistance-universal-access-to-diagnosis>

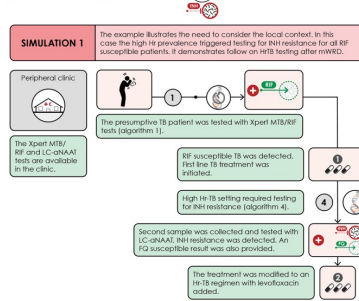
Fig. 2.1. Summary of testing procedures for the newly endorsed moderate complexity automated NAATs (14)

	Absolc baseline MTB and MTB RIF/INH	BD MAX MTB/IS	Truenat Fluorotype MTB/IS	Roche cobas MTB and MTB RIF/INH
Maximum # of samples per run	N = 94	N = 24	N = 94	N = 94
Specimen receipt to result and turnaround for all samples	7 hrs	4.4 hrs	4.4 hrs	5.6 hrs
Inactivation	3 x 30 sec Invert several times Vortex 30/30 sec	2 x 90 mins TB Shake 10 times Pre-incubate 5 min Shake 10 times	2 x 10 min TB Vortex	2 x Cobas MTB Vortex 30/30 sec
Incubation	1 h Vortex 30/30 sec at 20 min	25 min	30 min	1 h
DNA extraction, amplification & detection	DNK extraction <15 min m2000 kit Solid phase and transfer to instrument Amplification and detection 20/30 min	3 x 41 min run time 16 results	DNK extraction 2 x 10 min Send plate and transfer to instrument Amplification and detection 1 x 6 min	Sanitize 1 min per sample Centrifuge all and 2 x 32 min run time 16 results

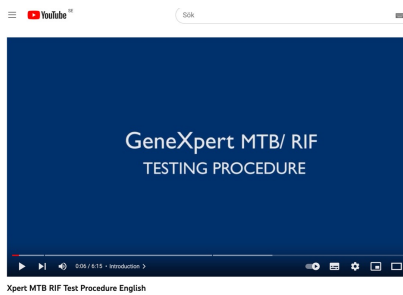
DNK, deoxyribonucleic acid; NAAT, nucleic acid amplification test.

<https://tbksp.org/node/538>

Fig. 4.8. Scenario 2: High Hr-TB setting



<https://tbksp.org/en/node/744>



Xpert MTB RIF Test Procedure English

<https://www.youtube.com/watch?v=wmcjEb8tPaY>

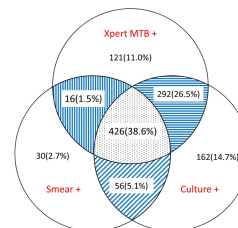
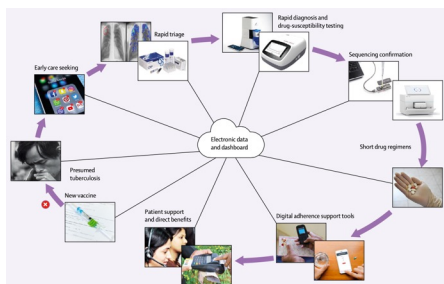


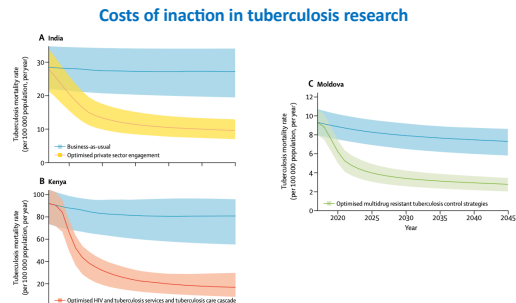
Fig. 1 Agreement of sputum smear, culture and Xpert MTB in 1103 pulmonary tuberculosis patients with all tests in Shanghai, China, in the first half of 2018. Smear + = smear positive. Culture + = culture positive. Xpert MTB + = Xpert MTB positive. The blue lines represent the agreement between two diagnostic techniques used, and the dot area shows the agreement among all three tests.

Wu et al. BMC Infectious Diseases (2020) 20:153



Schematic for a modern tuberculosis care delivery system

Lancet, vol 393 April 20, 2019



Building a tuberculosis-free world: The Lancet Commission on tuberculosis (Lancet 2019;393:1331-84)

BCG vaccination



- The bacille Calmette-Guérin (BCG) vaccine has existed for **80 years**
- One of the **most widely used of all current vaccines**
 > 80% of neonates and infants in countries where it is part of the national childhood immunization programme
- BCG vaccine has a documented protective effect **against meningitis and disseminated TB in children**
- It does **not prevent primary infection** and, more importantly, does **not prevent reactivation** of latent pulmonary infection, the principal source of bacillary spread in the community
- The impact of BCG vaccination on transmission of Mtb is therefore **limited**.

Waning BCG vaccine efficacy - A childhood vaccine

