

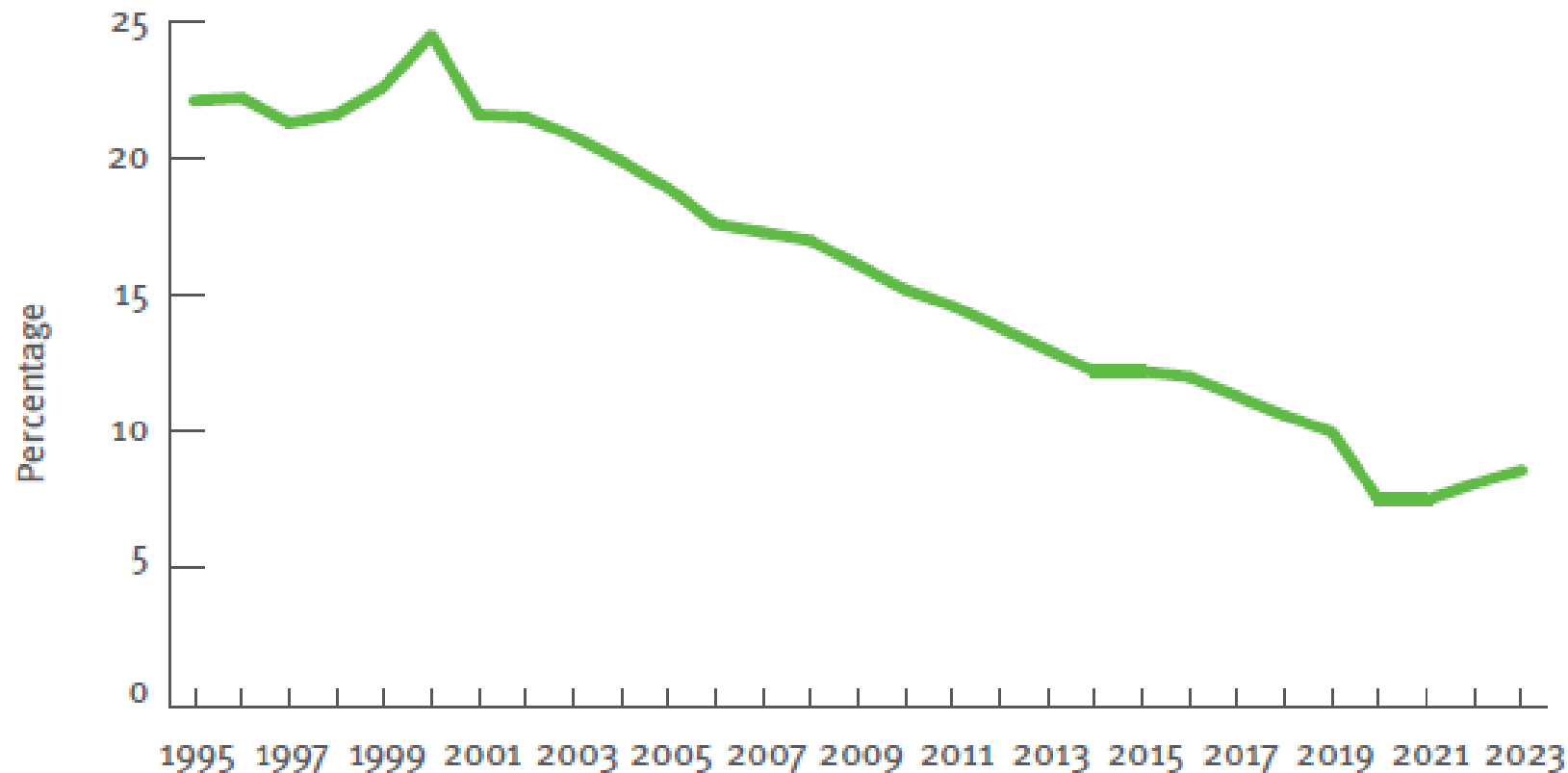


ELIMINATION DER TB: MISSION (IM)POSSIBLE?

CHRISTOPH LANGE

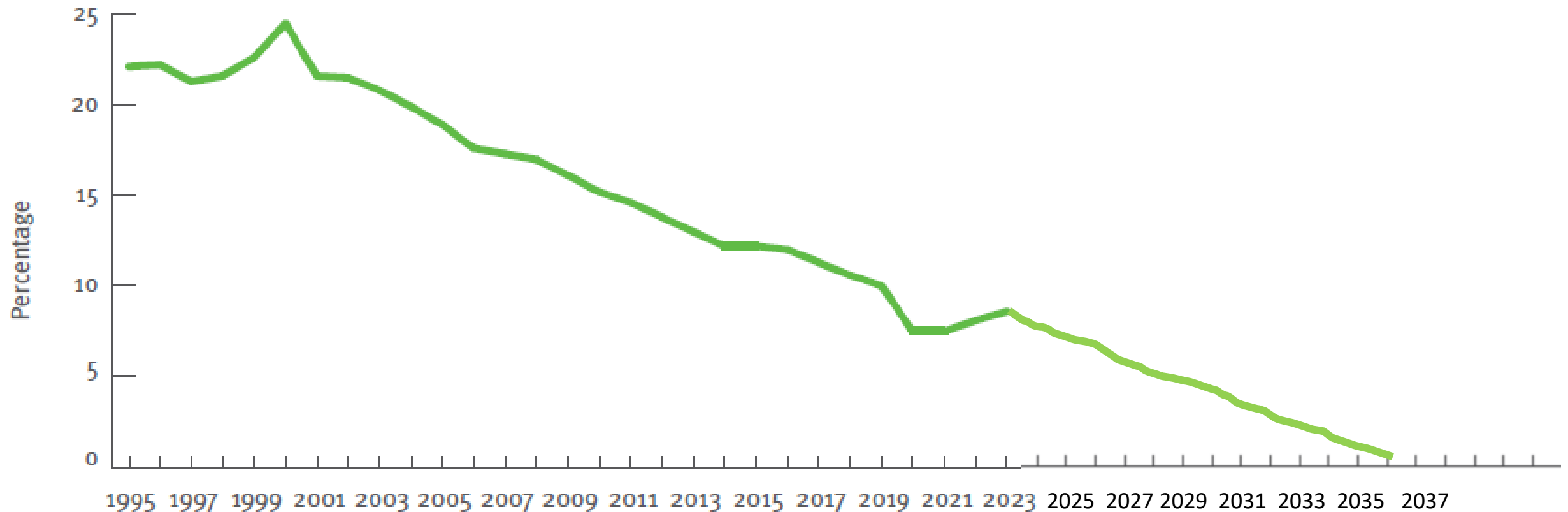
Inzidenz der TB in der EU/EEA

ECDC & WHO Europe, TB surveillance and monitoring in Europe 2025



Inzidenz der TB in der EU/EEA

ECDC & WHO Europe, TB surveillance and monitoring in Europe 2025



Herausforderungen für die TB Elimination

Kunst H et al. Eur Respir J 2025

Tuberculosis in adult migrants in Europe: a TBnet consensus statement

Odds ratio (95% CI) for migrant *versus* non-migrant populations by outcomes



**TB/HIV
co-infection**

OR 3.67 (1.81–7.43) in
people living with HIV
OR 0.89 (0.52–1.55) in
TB populations



MDR-TB

OR 3.16 (1.69–5.92)



**Extrapulmonary
TB**

OR 2.14 (1.53–3.02)

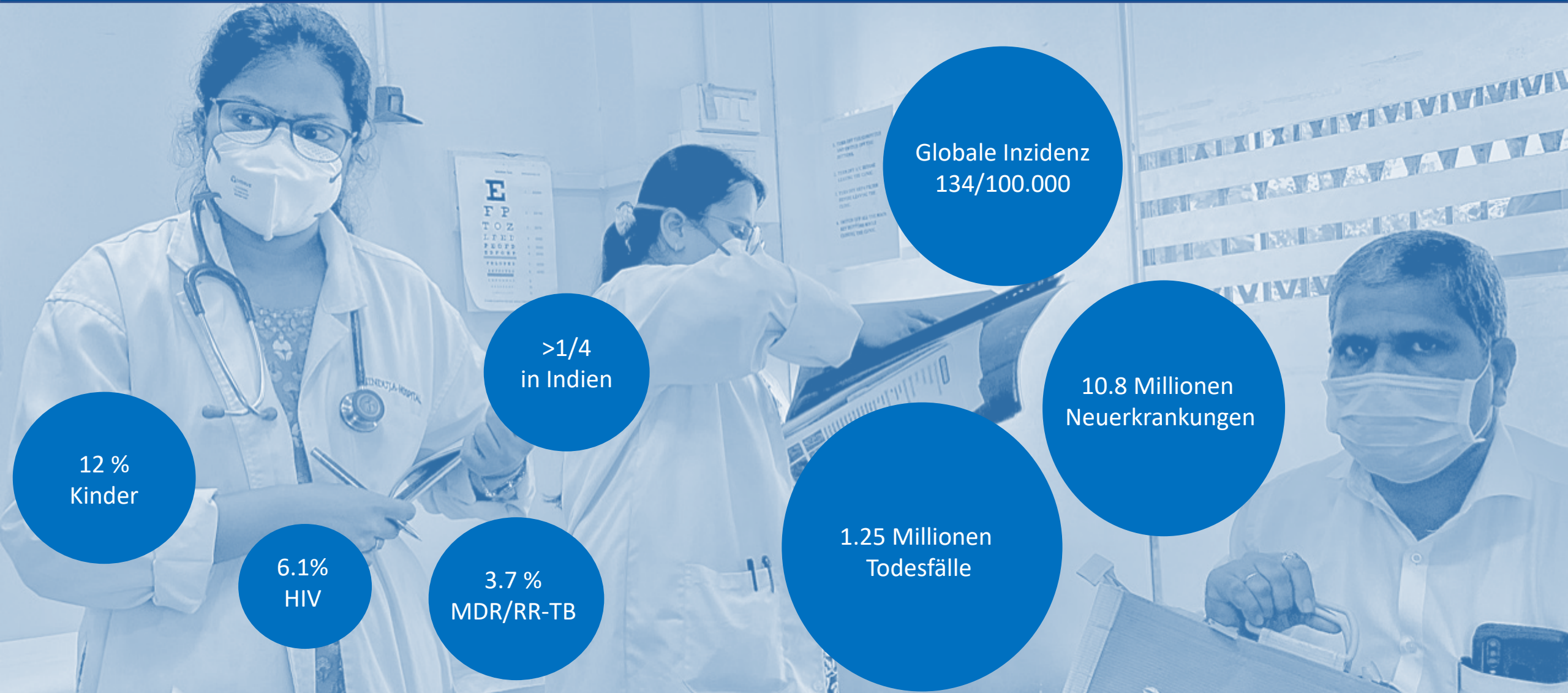


**Unfavourable
treatment**

OR 1.76 (1.01–3.05)

Tuberkulose aktuell

World Health Organization. Global tuberculosis report 2024. Geneva, Switzerland



Globale Inzidenz
134/100.000

>1/4
in Indien

10.8 Millionen
Neuerkrankungen

1.25 Millionen
Todesfälle

12 %
Kinder

6.1%
HIV

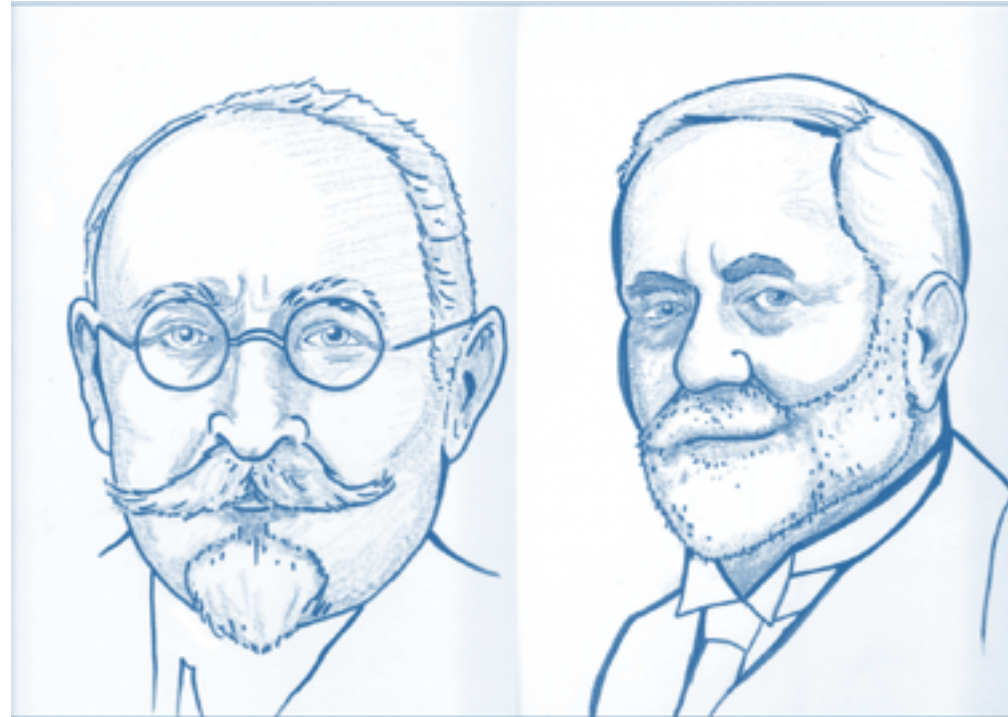
3.7 %
MDR/RR-TB

Prävention

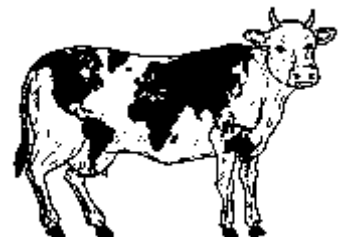


M. bovis bacille Calmette Guérin: BCG

Lange C et al. Lancet Infect Dis 2022, Martinez L et al. Lancet Glob Health 2022



All participants			
All ages	1309/49 686	473/18 866	0.82 (0.74–0.91)
<5 years	312/9225	80/1312	0.63 (0.49–0.81)
5–9 years	126/9936	36/1289	0.76 (0.51–1.14)
10–14 years	145/7847	34/1190	0.99 (0.66–1.48)
15–24 years	316/7984	69/2628	1.32 (0.98–1.75)
25–34 years	161/5159	57/3006	1.17 (0.83–1.64)
≥35 years	249/9535	197/9441	0.84 (0.67–1.06)



TB Vakzine in der Entwicklung

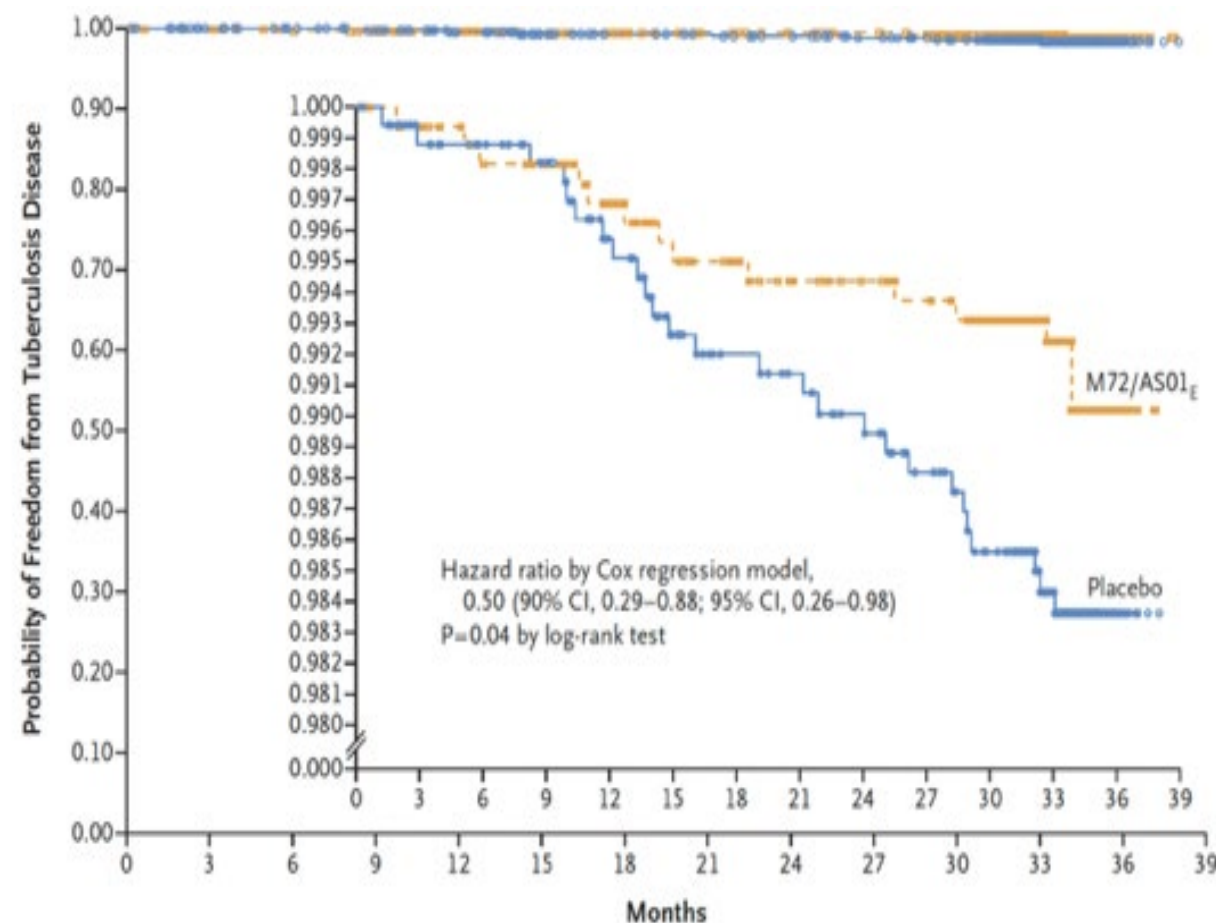
Lange C et al. Path Immun 2025

Name	Composition	Most advanced clinical stage	Representative clinical trial number
TB Protein: adjuvant formulations			
H56:IC31	Fusion protein of 2 antigens: IC31 as adjuvant ¹⁾	Phase IIb ongoing	NCT03512249
ID93:GLA-SE	Fusion protein of 4 antigens: GLA-SE as adjuvant ²⁾	Phase IIb ongoing	NCT03806686
M72:AS01 _E	Fusion protein of 2 antigens: AS01 _E as adjuvant ³⁾	Phase IIb completed	NCT01755598
M72:AS01 _E -4	Fusion protein of 2 antigens: AS01 _E as adjuvant ³⁾	Phase III ongoing	NCT06062238
AEC:BC02	Combination of 3 protein antigens: BC02 as adjuvant ⁴⁾	Phase IIa ongoing	NCT05284812
GamTBvac	Combination of 3 protein antigens: CpG as adjuvant ⁵⁾	Phase III ongoing	NCT04975737
Mtb-antigen encoding mRNA vaccines			
BNT164a1 / BNT164b1	mRNA expressing multiple Mtb antigens in lipid nanoparticles	Phase I ongoing	NCT05547464 NCT05537038
TB antigen expressing viral vectors			
ChadOx1.85A/MVA85A	ChadOx1 as carrier for prime, MVA as carrier for boost, both expressing same antigen ⁶⁾	Phase IIa completed	NCT0368160
TB/FLU-04L	Non-replicating influenza virus expressing 2 antigens ⁷⁾	Phase I completed	NCT02501421
Inactivated whole cell vaccines			
Immuvac	Killed <i>M. indicus pranii</i>	Phase III ongoing	CTRI/2019/01/017026
RUTI	Killed detoxified <i>M. tuberculosis</i>	Phase IIb ongoing	NCT04919239
DAR-901	Killed <i>M. obuense</i>	Phase IIb completed	NCT02712424
Viable attenuated whole cell vaccines			
MTBVAC	Genetically attenuated <i>M. tuberculosis</i> ⁸⁾	Phase III ongoing	NCT04975178
VPM1002	Genetically improved BCG ⁹⁾	Several phase III ongoing	NCT04351685

TB Vakzine in der Entwicklung

Tait DR et al. N Engl J Med 2019

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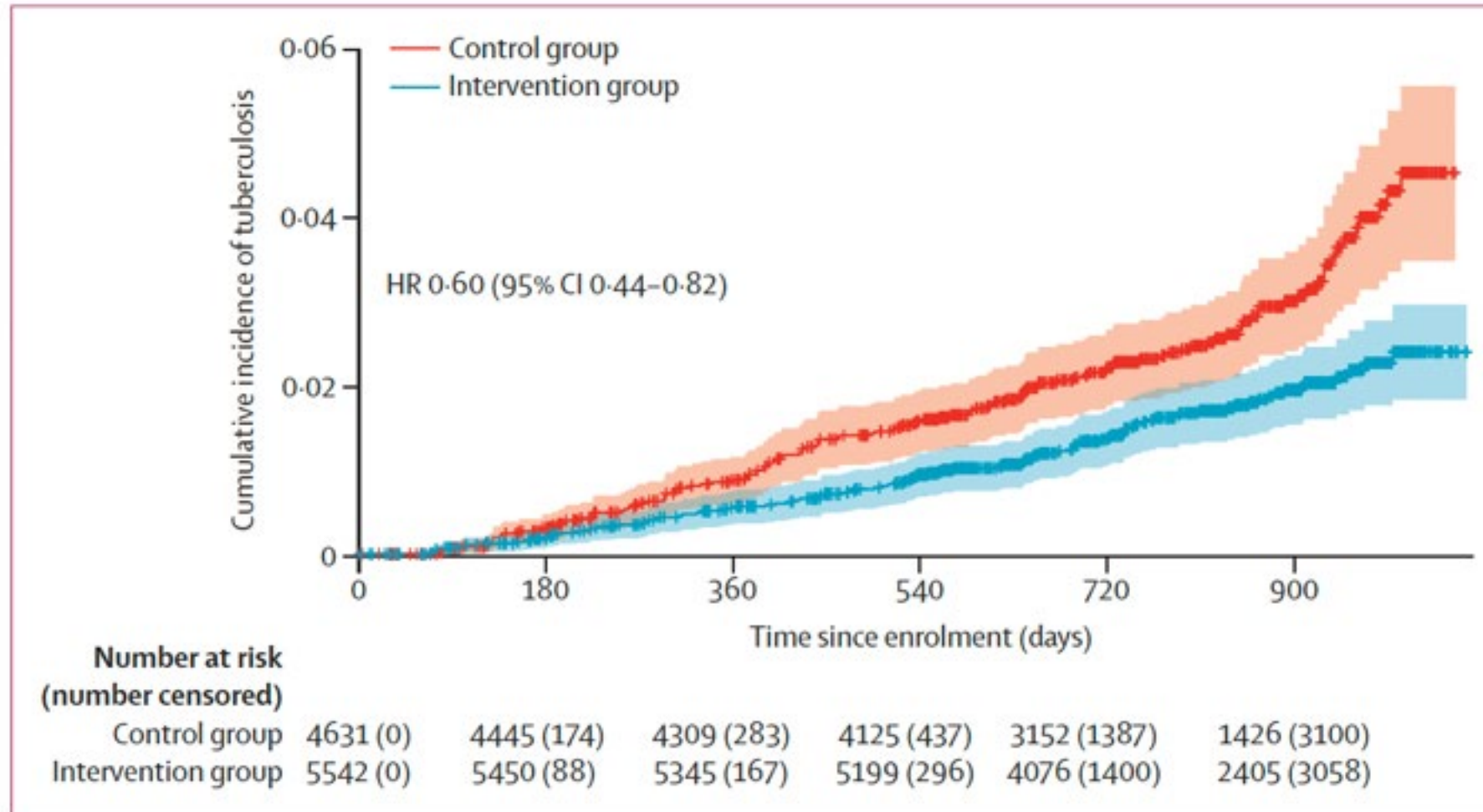


No. at Risk
M72/AS01_E
Placebo

1626	1621	1614	1609	1592	1580	1573	1566	1561	1557	1542	1468	12
1663	1650	1642	1632	1610	1586	1576	1571	1564	1553	1539	1460	19

Bessere Ernährung senkt TB-Inzidenz

Bharagva A. et al. Lancet 2023



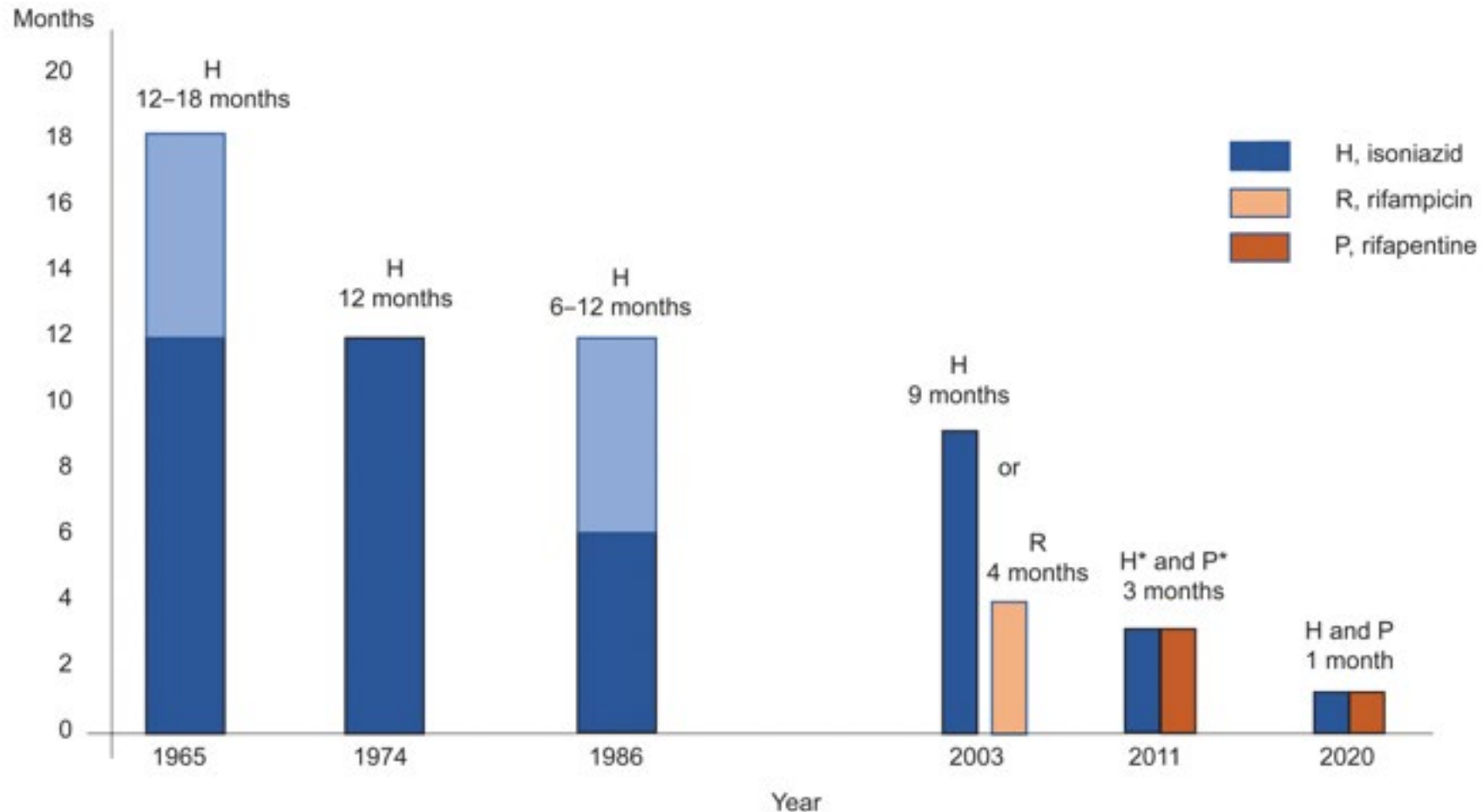
Das THT/IGRA Problem

Lange C et al. Pathog and Immun. 2017

Study	Country	Population	LTBI test	LTBI positive (%)	Number followed longitudinally	TB cases incident	Sensitivity %	Specificity %	PPV %	NPV %	NNT
Zellweger et al [36]	Europe	contacts	QFT-G-IT	1067 (27.4%)	3425	20	85.0	74.0	1.9	99.9	37
			T-SPOT.TB	299 (26.6%)	1061	4	50	73.6	0.7	99.7	37
Geis et al [47]	Germany	contacts	QFT-G-IT ^c	306 (19.3%)	254	6	100	n.d.	2.5	n.d.	34
Sloot et al [48]	Netherlands	contacts	TST/QFT-G-IT	739 (15.5%)	4716	17	76.5	85.8	1.9	99.9	89
		Close contacts	TST/QFT-G-IT		1622	10	90	79	2.6	99.9	30
Kik et al [51]	Netherlands	Migrant contacts	TST ^d	339	339	8	87.5	n.d.	3.8	n.d.	26
			QFT-G-IT	178	327	8	62.5	n.d.	2.8	n.d.	36
			T-SPOT.TB	181	299	8	75	n.d.	3.3	n.d.	30
Hermansen et al [49]	Denmark	Mixed ^a	QFT-G-IT	1703 (10.7%)	15980	40	50	88.7	1.32	99.9	68 ^e
Sester et al [8]	Europe	Immuno-compromised ^b	TST	212 (14.1%)	1404	6	50	86.2	1.5	99.8	50
			QFT-G-IT	239 (15.6%)	1342	4	50	84.1	0.9	99.8	80
			T-SPOT.TB	266 (17.7%)	1310	6	50	81.3	1.3	99.7	64
		HIV only	TST	55 (8.7%)	626	6	50	93.7	7.1	99.5	14
			QFT-G-IT	83 (13.1%)	621	4	50	92.1	3.9	99.6	26
			T-SPOT.TB	101 (15.9%)	561	6	50	89	4.7	99.4	21
		HIV positive HIV load	TST	24 (8.1%)	291	6	50	92.6	12.5	98.9	8
			QFT-G-IT	25 (8.4%)	289	4	50	91.9	8	99.2	13
			T-SPOT.TB	31 (10.4%)	255	6	50	88.8	9.7	98.7	10
Schablon et al [50]	Germany	HCW	QFT-G-IT	317 (8.3%)	3823	0	0	91.7	0	100	n.a. ^f
Slater et al [43]	USA	HCW	QFT-G-IT	853 (9.3%)	9153	0	0	90.7	0	100	n.a. ^f
Dorman et al [42]	USA	HCW	TST	125 (5.2%)	2418	0	0	94.8	0	100	n.a. ^f
			QFT-G-IT	118 (4.9%)	2418	0	0	95.1	0	100	n.a. ^f
			T-SPOT.TB	144 (6.0%)	2418	0	0	94	0	100	n.a. ^f

Präventive Therapie

Lange C et al. Int J Tuberc Lung Dis. 2022



Diagnostik



Neue TB Diagnostik

ClinTB; Deutsches Zentrum für Infektionsforschung (DZIF)



Sputum	LAM
Sputum	MBLA
Zungen/Wangen-Abstrich, Masken	PCR
Urin	LAM
Stuhl	PCR
Blut	CRISPR PCR
Blut	RNA Signaturen
Blut	Immunophänotypen

Genotypische Vorhersagen von AMR

Grobbel HP et al. Clin Infect Dis 2021



99%
korrekte Vorhersagen
für die Therapie

AMR-TB: Höchste Alarmstufe der WHO

World Health Organization. Bacterial Pathogens Priority List 2024. Geneva, Switzerland



Global Verteilung der AMR Tuberkulose

World Health Organization. Global tuberculosis report 2024. Geneva, Switzerland



AMR TB in der Ukraine

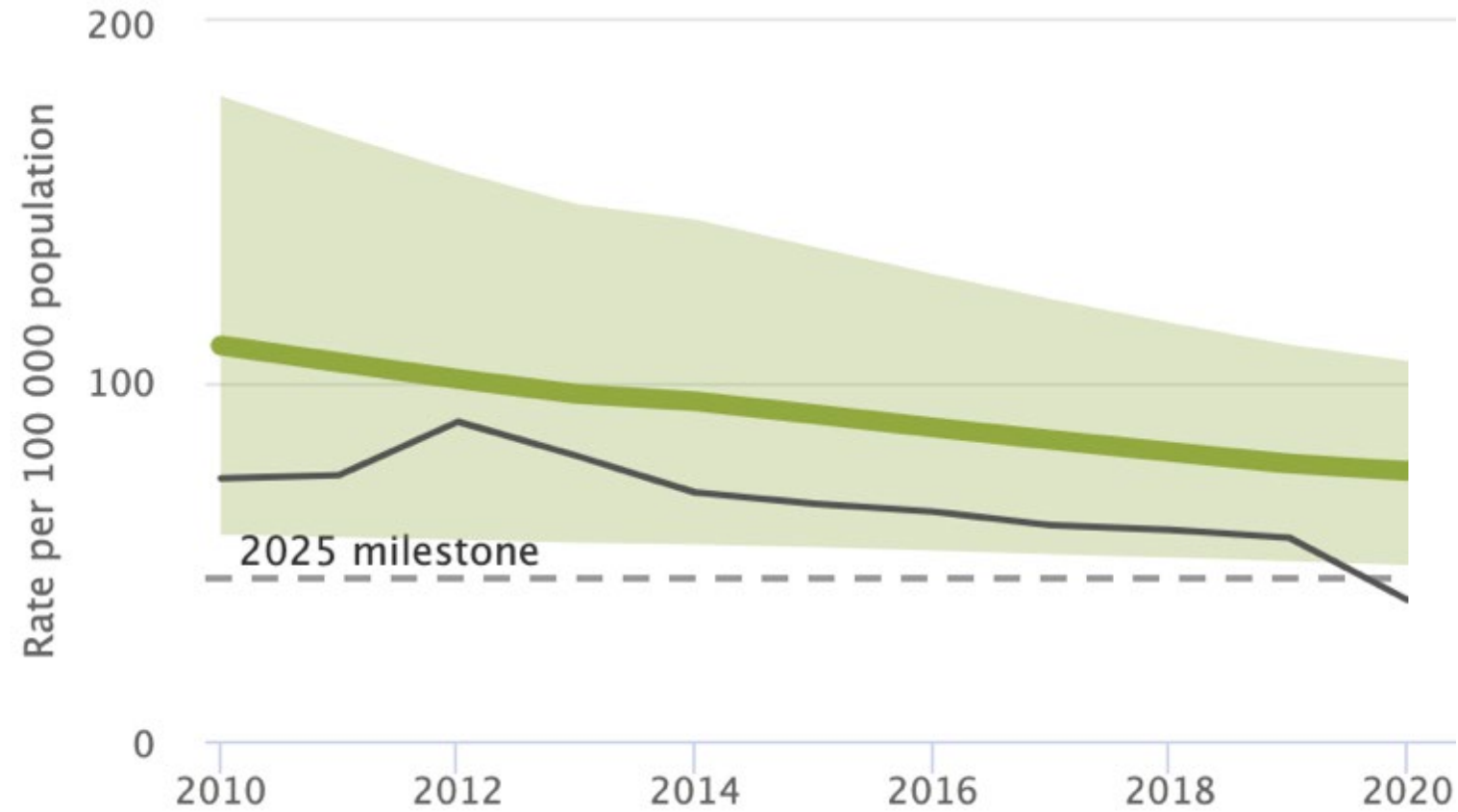
Butov D et al. Int J Tubercul Lung Dis 2020

nur **45 %** Heilung



TB Inzidenz in der Ukraine

World Health Organization 2025: Tuberculosis profile Ukraine

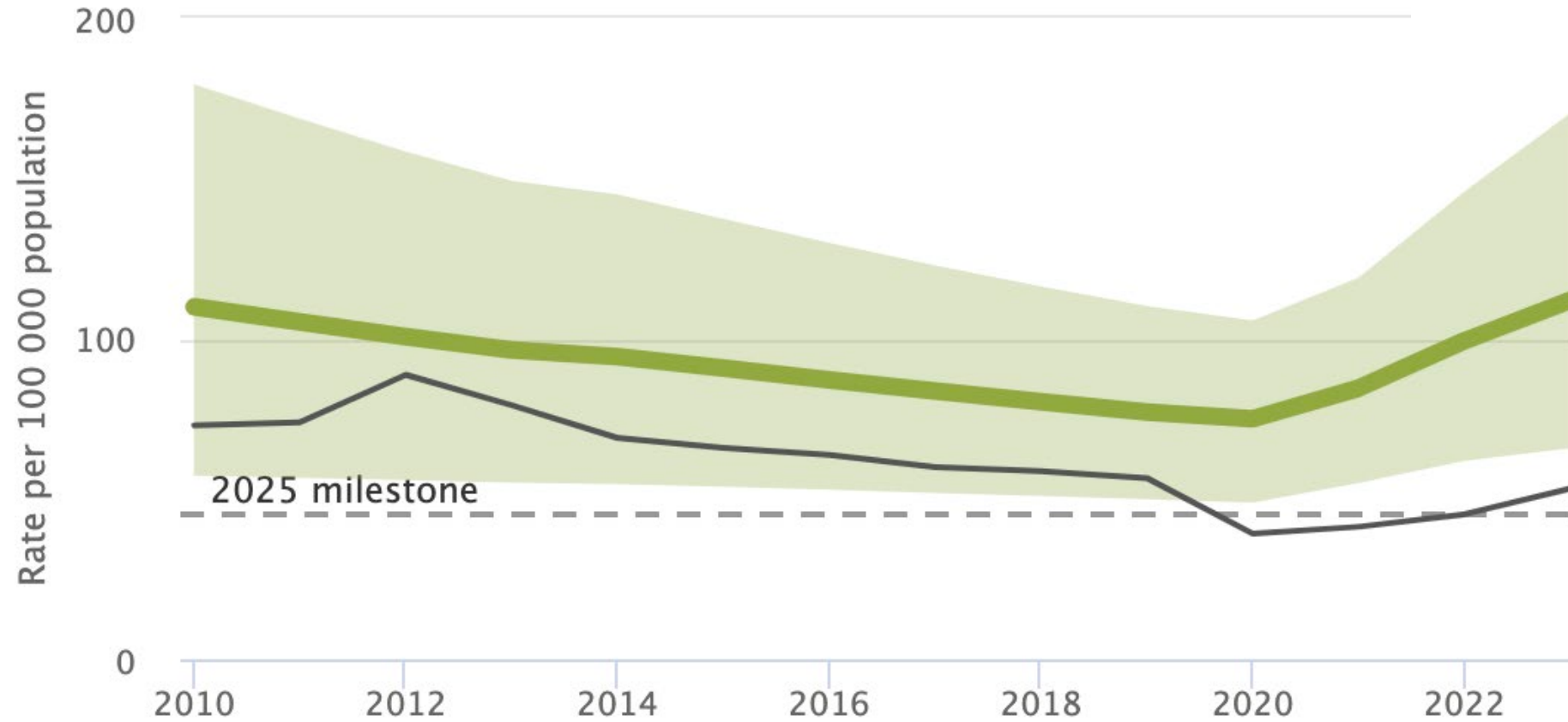


U-Bahn in Kyjiv, Frühjahr 2022



TB Inzidenz in der Ukraine

World Health Organization 2025: Tuberculosis profile Ukraine



Zunahme der AMR-TB in der Ukraine

Konstantynovska O et al. Emerg Infect Dis 2025

FQ-Resistenz **10%**  **30%**
2014 2023



Zunahme der AMR-TB in Europa

Stoycheva K et al. Euro Surveill. 2024



Anteil Ukrainer an MDR/RR-TB in der EU/EWR

5 %  **20 %**
2021 2022

Zunahme der AMR-TB in Europa

Vasiliu A et al. Euro Surveill. 2025

Anteil Ukrainer bei im Ausland
geborenen in der EU/EWR mit
MDR/RR-TB

10 %  **50%**
2020 2023

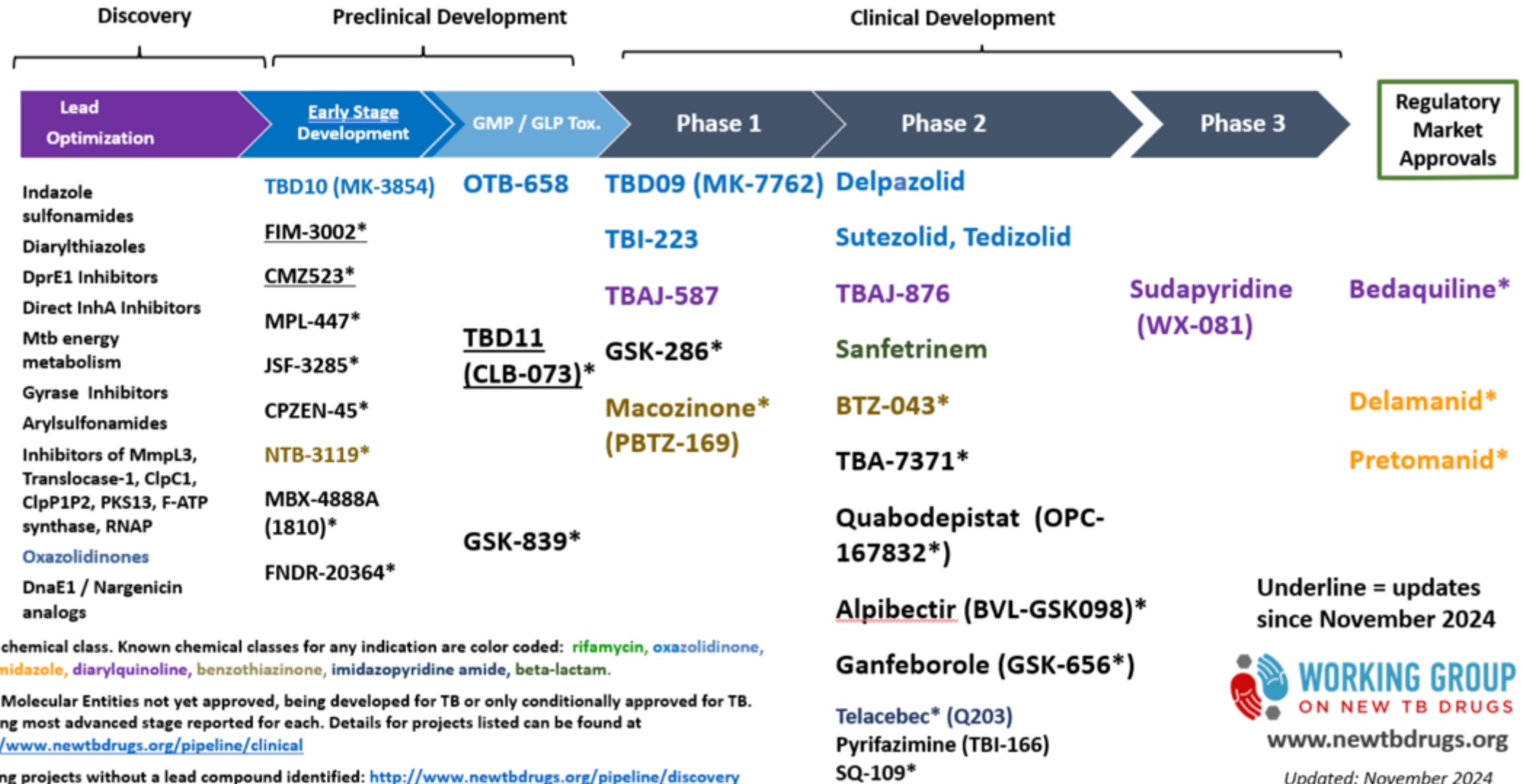


Therapie



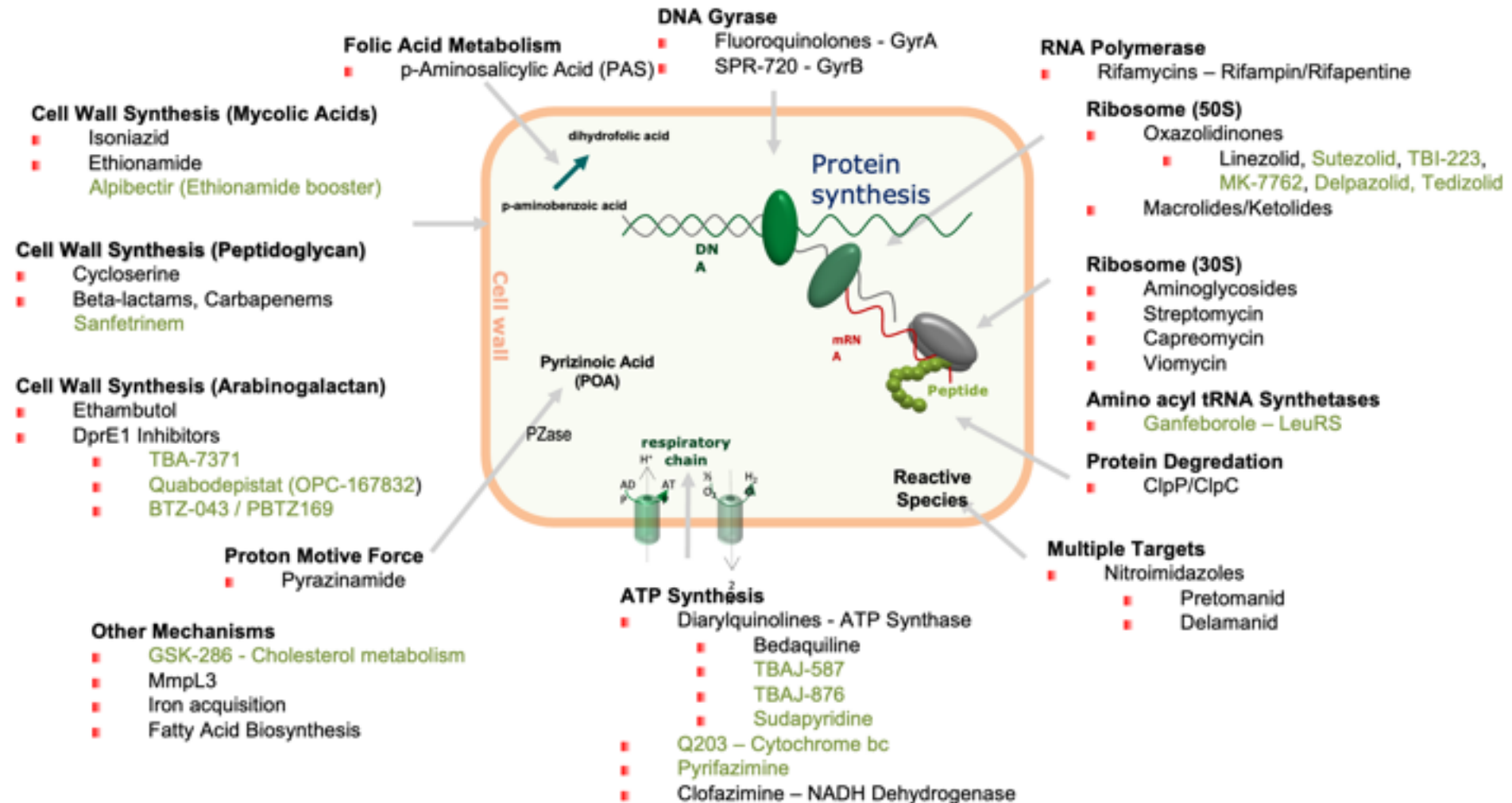
18 Substanzen in Phase I-III

Working group on new TB drugs: www.newtbdrugs.org



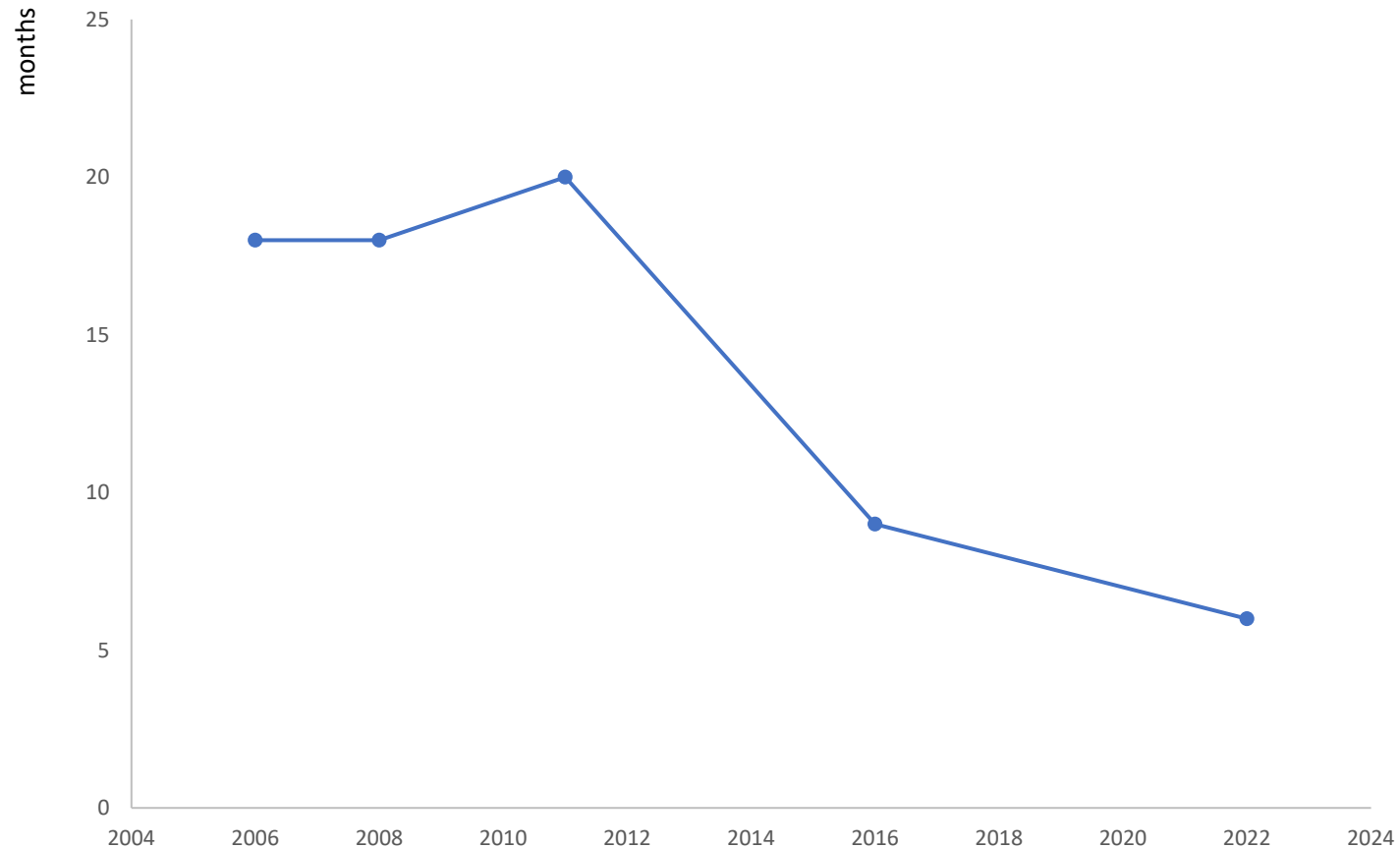
Neue Zielstrukturen für die Therapie

Hoelscher M et al. Clin Microbiol Infect. 2024



6 Monate Therapie der AMR-TB

Dheda K et al. Lancet Respir Med. 2024



Unzureichender Zugang zu Medikamenten

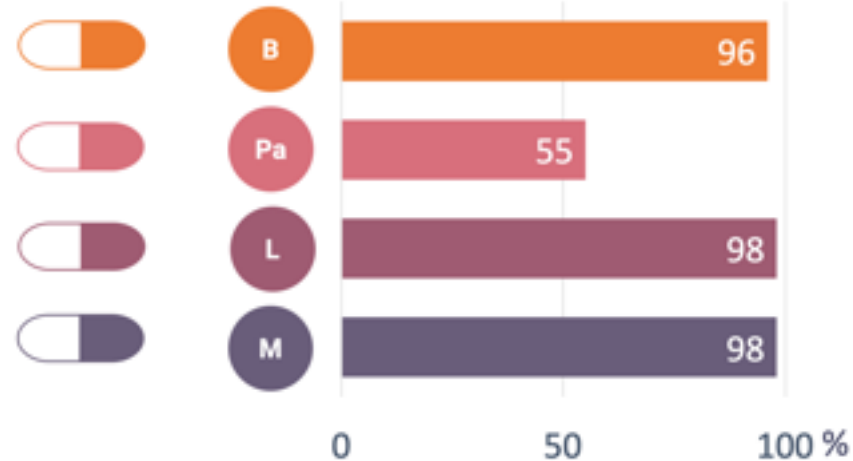
Günther G et al. Clin Microbiol Infect. 2024



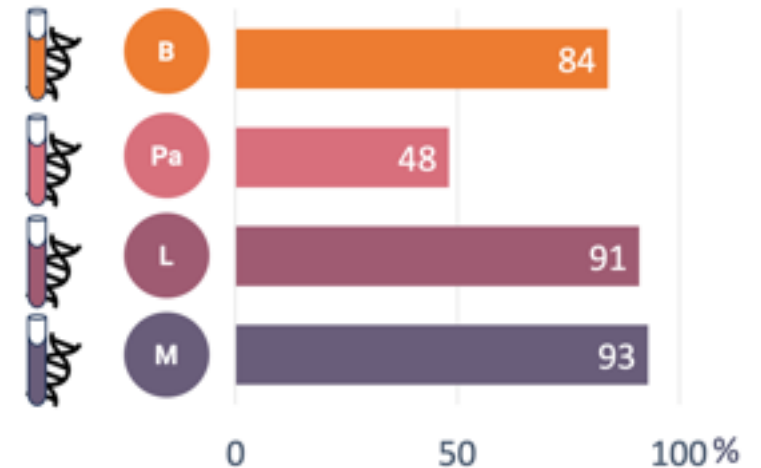
Representatives from 44/54
countries of the WHO
Europe region



52% of participating countries
have access to all the drugs



48% have access to
DST for all the drugs



DODGE Impact auf die EndTB Strategie

<https://tb.impactcounter.com> 24. März 2025



Estimated impact associated with the funding discontinuation

between January 24th, 2025 at 12:00 PM EST and present

Additional TB Deaths

11.045

Incrementing every 7.72 minutes

Additional TB Cases

14.024

Incrementing every 7.72 minutes

1-Year

2025-2030

If funding resumes within 3 months

Deaths: **28.936**
Cases: **51.458**

Deaths: **99.860**
Cases: **634.736**

If funding resumes within 1 year

Deaths: **55.342**
Cases: **79.014**

Deaths: **268.579**
Cases: **1.660.036**

If funding is never resumed

Deaths: **71.348**
Cases: **92.279**

Deaths: **2.243.717**
Cases: **10.676.456**

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Cases: **10.676.456**

Shanghai Pulmonary Hospital (TB ward)

März 2025



1.800 stat. Patienten
150.000 ambulante Patienten

4 % MDR/RR-TB
40% FQ-R

BPaLM

Keine DST für:

- Bedaquiline
- Pretomanid
- Linezolid
- Delamanid
- Clofazimin

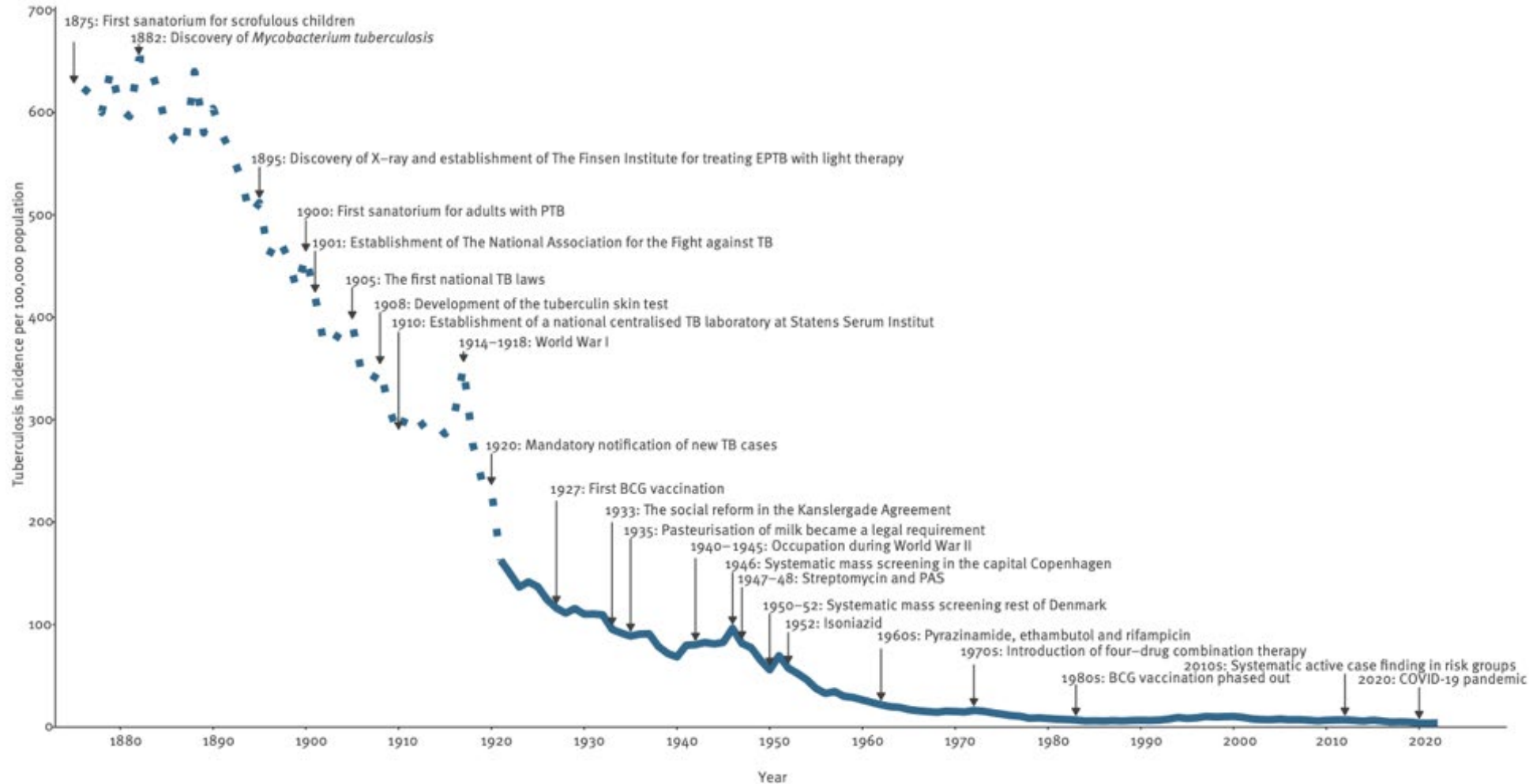
Neulich in Brandenburg...

Ehem. Tuberkuloseklinik Sommerfeld (Kremmen)



Brilliant: TB Inzidenz in DK über 140 Jahre

Nordholm C et al. Euro Surveill. 2024



Elimination der TB: Mission impossible

Trotz **innovativer Diagnostik**

Trotz **neuer Medikamente**

Noch nie so **viele Fälle** berichtet, wie heute

Es gibt **kein Problem** in der **Forschung und Entwicklung**

Es gibt **ein Problem** in der **Implementierung**

Soziale Determinanten sind entscheidend

Eine **Elimination** der Tuberkulose ist aktuell **unrealistisch**

Eine **Kontrolle** der Tuberkulose **wäre** schon ganz **schön**

Wichtigste Faktoren dafür sind **Wohlstand und Frieden**



You never walk alone.... DANKE!

Alberto Garcia Basteiro
Alexander Kay
Andreas Diacon
Andrew DiNardo
Anna Mandalakas
Anca Vasiliu
Askar Yedilbayev
Barbara Kalsdorf
Berit Lange
C. Robert Horsburgh
Christina Maier
Clifton Barry III
Collins Kidake
Cristian Coarfa
Cristina Popa
Dagmar Schaub
Dariusz Woelk
David Barros Aguire
Debrah Vambe
Derek Sloan
Doris Hillemann
Dumitru Chesov

Elena Chesov
Elmira Ibrahim
Erwin Schurr
Florian Maurer
Frank van Leth
Franziska Daduna,
Gunar Günther
Guy Thwaties
Hans-Peter Grobbel
Harald Hoffmann
Helmut Salzer
Henry Welsh
Inna Friesen
Ioana Olaru
Jakob Lange
Jan Heyckendorf
Jan Rybniker
Jessica Hofmeister
Johanna Eggeling
Joel Lelievre
Karoline Gaede
Katharina Budde

K.C. Chang
Keertan Dheda
Kelly Dooley
Krista Stoycheva
Lasse Möller
Laura Böttcher
Liga Kuksa
Lorenzo Guglielmetti
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Marylyn Addo
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Matthias Merker
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Stefan Niemann
Stefan Schmiedel
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