

TPT for Contacts of DR-TB:

what can we learn from TPT for contacts of DS-TB?

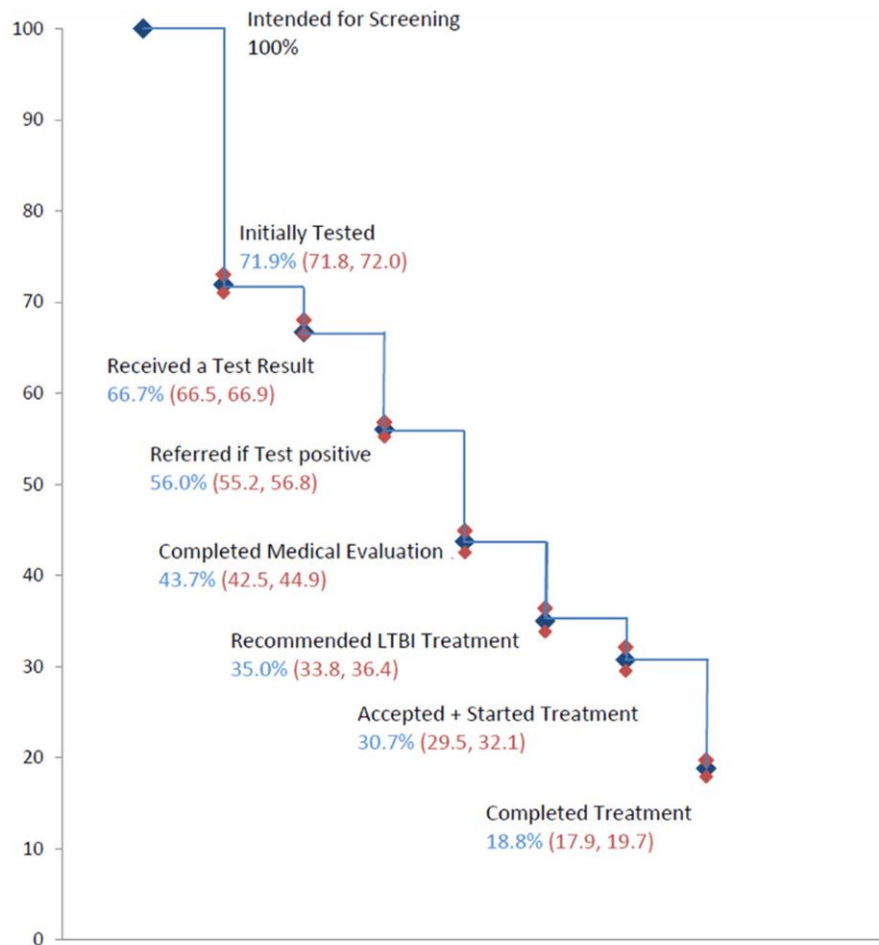
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TB prevention therapy (TPT)

- **TB could be avoided** through TB preventive therapy (TPT)
 - TPT is critical to the TB elimination plan
 - Significant scale-up is required to have a significant public health impact
- **Current situation (for DS-TB):** the uptake of TPT is still low, despite availability of shorter and safer treatment regimens (4 - 1 months) i.e., 4R, 3HR, 3HP and 1HP
- **Challenges/Barrier to scale-up:**
 - Regimens are “long” and potential to cause side effects - affect treatment completion → efficacy
 - Doctors and nurses reluctant to offer TPT *and* people reluctant to take TPT
- **Safety of TPT regimens** is absolutely essential, since it will be given to otherwise healthy persons.

Cascade of Care of TPT



- **Gaps in each steps**
 - ~ 30% initiated TPT
 - ~19% completed TPT
- **Gaps in each steps, why?**
 - knowledge and understanding about TPT
 - both the community and health care workers
 - quality of care in each steps
- **Health system strengthening is needed**
 - to close the gaps
 - addressing local specific situation
 - involving all stakeholders in decision making

Alsdurf, Lancet ID, 2016, Oxlade, Lancet GH,

DR-TB Preventive Therapy

- Results from the TB-CHAMP and the V-QUIN trials (n=)
 - Children and adults
 - 6-months of Levofloxacin vs placebo
 - 45% reduction of microbiologically-confirmed TB.
 - Safe and well-tolerated
- SR-MA (Zhou et al, CMI, 2024):


Study	TPT		No TPT		Risk Ratio	RR	95%-CI	Weight
	Events	Total	Events	Total				
Adler-Shohet et al 2014	0	26	0	5		0.21	[0.00; 9.38]	3.9%
Bamrah et al 2014	0	104	3	15		0.02	[0.00; 0.39]	6.6%
Chang et al 2021	0	18	1	44		0.80	[0.03; 18.79]	5.7%
Denholm et al 2012	0	11	2	38		0.67	[0.03; 12.97]	6.4%
Garcia-Prats et al 2014	0	24	0	10		0.43	[0.01; 20.19]	3.8%
Gureva et al 2022	0	58	1	14		0.08	[0.00; 1.93]	5.7%
Kritski et al 1996	2	45	13	145		0.50	[0.12; 2.11]	26.8%
Malik et al 2021	2	172	0	43		1.26	[0.06; 25.79]	6.2%
Schaaf et al 2002	2	41	13	64		0.24	[0.06; 1.01]	27.3%
Trieu et al 2015	0	50	0	166		3.30	[0.07; 164.07]	3.7%
Williams et al 2013	0	8	0	4		0.53	[0.01; 22.50]	4.0%
Random effects model	557	548				0.34	[0.16; 0.72]	100.0%

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.69$

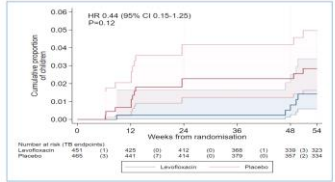
- Shorter (and safer) regimens?
 - Trials to find other regimens, head-to-head comparison (with 6-m LFX) (courtesy of A. Hesselning, Greg J Fox, Rapporteur Session, The Union World Conference, 2023)
- Candidates of the regimens? Esp. for FQ-resistant-TB contacts

The Union **WORLD CONFERENCE ON LUNG HEALTH 2023** Paris, November 15-19
TRANSFORMING EVIDENCE INTO PRACTICE

A phase III cluster randomised placebo-controlled trial to assess the efficacy of preventive treatment in child contacts of multidrug-resistant TB: The TB-CHAMP Trial, by Hesselning et al (LB02-107-16)




- 922 children in South Africa were enrolled: 453 in LFX arm and 469 in placebo arm.
- Evidence of LFX efficacy with substantial effect size: 1.1% in LFX-arm vs 2.6% in placebo-arm (HR 0.44 [95% CI 0.15-1.25])
- LFX was extremely safe in children
- Data of VQUIN and TB-CHAMP are shared with WHO.



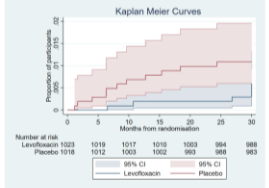
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TRANSFORMING EVIDENCE INTO PRACTICE

The effectiveness of levofloxacin for the treatment of latent TB infection among household contacts of patients with multidrug-resistant TB: The VQUIN trial, by Fox et al (LB02-106-16)



- 2041 children and adults in Vietnam were enrolled: 1023 in LFX arm and 1018 in placebo arm.
- 6 months LFX was associated with a 45% reduction in microbiologically-confirmed incident TB at 30 months.
- LFX was well-tolerated among adults and children and no acquired drug resistance.



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Summary

- TPT is critical for TB elimination plan (also for contacts of DR-TB)
- Cascade of care of TPT:
 - Comprehensive effort to close the gaps in each steps → increase the uptake of TPT
 - Addressing all possible barriers
 - **Approaching the close contacts with a better way: empathy, respect and give choices**
 - **Quality of care**
- Finding shorter and safer regimens is substantial (also relevant for DR-TB)
- Treatment regimen for fluoroquinolone-resistant-TB contacts
- Comprehensive approach (research) - multidisciplinary, i.e., patient and provider perceptions on TPT - better acceptability

Thank you