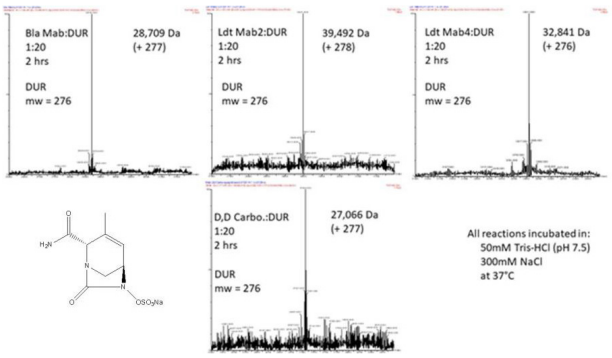
dextrose catalase and 0.05% (vol/vol) Tween 80. When more than 2 drugs were combined, Amox was added at fixed concentration of 8 μg/ml to serial dilutions of CEF-DUR or IMI-DUR. *Mab* isolates were incubated with test agents at 30°C for 48 h, and MIC was defined as lowest antibiotic concentration that prevented visible bacterial growth. Reaction intermediates in the inactivation pathway of $Bla_{Mab,}$ L,D-TP and D,D-TPs with DUR

Results. One hundred clinically derived and previously characterized isolates were tested in these assays. MIC_{50} and MIC_{90} of DUR alone was 4 and 8 μg/ml, demonstrating intrinsic activity. Combinations of DUR-IMI or DUR-CEF plus 8 μg/mL Amox lowered MIC_{50} to < 0.06 μg/ml in all 100 clinical isolates (Table). Mass spectrometry analyses of Bla_{Mab}, L,D-TP and D,D-$TPs_{Mab\ (2,4)}$ inactivated by DUR showed formation of stable adducts of DUR to Bla_{Mab}, L,D-TP and D,D-TPs (Fig.)

Chemical composition of durlobactam (DUR) and mass spectrometry of BlaMab, L,D TP and D,D TPs incubated with DUR



MIC50 and MIC90 of 100 Mab clinical strains against DUR alone and in combination with Amox, CEF and IMI

	DUR μg/mL	Amox μg/mL	Amox/DUR (1:1) μg/mL	CEF μg/mL	CEF/DUR (1:1) μg/mL	CEF/DUR + Amox 8 μg/mL	CEF/amox 8 μg/mL	IMI μg/mL	IMI/DUR (1:1) μg/mL	IMI/DUR + Amox 8 μg/mL	IMI/Amox (1:1) μg/mL
MIC50	4	>256	2	8	1	<0.06	4	2	2	<0.06	1
MIC90	8	>256	4	16	2	<0.06	8	4	2	0.25	2

DUR (durlobactam), CEF (Ceftaroxime), Amox (Amoxicillin), Imipenem (IMI)

Conclusion. We demonstrate that a novel DBO BLI, DUR, is an active agent with potent intrinsic activity against Bla_{Mab} and Mab L,D-TPs and D,D-TPs. We hypothesize that DUR improves b-lactam activity by protecting against the hydrolytic activity of Bla_{Mab} and by targeting multiple steps in PG synthesis

Disclosures. Alita Miller, PhD, Entasis Therapeutics (Employee) Robert A. Bonomo, MD, Entasis, Merck, Venatorx (Research Grant or Support)

1643. A scoping review of pediatric latent tuberculosis care cascades: Initial steps are lacking

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Each year an estimated 1 million children develop and ~200,000 die from tuberculosis (TB). The WHO has named identification and treatment of latent tuberculosis infection (LTBI) one of the cornerstones of efforts to eliminate TB by 2030. Identification and treatment of pediatric LTBI requires completion of a complex care cascade. While attention has been given to LTBI care cascades in adults, to date there has been no attempt to map literature on the pediatric LTBI care cascade.

Facilitators and barriers to retention in steps of the pediatric LTBI care cascade

Methods. We systematically searched PubMed, CINAHL, Cochrane and Embase databases for papers and abstracts describing screening, diagnosis, and treatment of pediatric LTBI. We categorized literature using seven step-offs in the pediatric LTBI care cascade, extrapolated from prior studies focused on adults: 1) intention to screen to initial test, 2) initial test to receipt of results, 3) receipt to referral for evaluation, 4) referral to completion of evaluation, 5) completion to treatment recommendation, 6) recommendation to treatment acceptance/initiation, and 7) initiation to treatment completion. Our aim was to assess factors that facilitated and inhibited completion of each cascade step, and to identify knowledge gaps in this literature.

Results. We identified 137 studies that met inclusion criteria. Most studies described multiple step-offs in the care cascade, although the focus of most (120/137 studies) was on initiation and completion of LTBI therapy (the final step in the care cascade). Several effective strategies to improve medication adherence were described, including selective use of nursing visits, directly observed therapy, shorter treatment regimens, and peer counseling. Reports of facilitators and barriers for retention in upstream step-offs in the cascade were scarce, revealing a lack of published evidence for how to retain children from pre-screening to treatment initiation (Table).

Cascade step	Facilitators of retention†	Barriers to retention ‡	Knowledge gaps
1) Intended for screening à initial testing (n = 42 studies)*	• Contact tracing programs	• Concurrent infections • Fear of testing procedures • "Parental avoidance"	• Populations at risk for low testing uptake • Strategies to optimize testing uptake
2) Initially testing à received test result (n = 43)	• Younger age	• Non-specific loss to follow-up	• Comparison of TST and IGRA in loss to follow up • Reasons for loss to follow up
3) Received test result à referral for evaluation (n = 22)	• No analytic studies	• Non-specific loss to follow-up	• Reasons for loss to follow up • Strategies to optimize referral
4) Referral for evaluation à completion of evaluation (n = 26)	• No analytic studies	• Non-specific loss to follow-up • Refusal of TB clinic visit	• Comparison of referral to TB/health department versus primary care clinics • Reasons for loss to follow up
5) Completion of evaluation à recommendation for treatment (n = 61)	• No analytic studies	• Medical contra-indications • Moving away/transferred care before starting therapy • Parent/parent non-acceptance of therapy	• Prevalence of medical contra-indications • Strategies to shorten time between completion of evaluation and recommendation for treatment
6) Recommendation for treatment à initiation of treatment (n = 77)	• Knowledge about TB transmission, treatment and policy • Relationships with TB patients	• Lack of knowledge about LTBI therapy • Older age • Parental or patient refusal of treatment	• Reasons for parental refusal • Strategies to improve initial treatment uptake
7) Initiation of treatment à completion of treatment (n = 120)	• Close relationship and close contact with TB index case • Established record of follow-up prior to LTBI screening • Knowledge about TB spread and prevention • Location of treatment, and use of health department clinic • Peer counseling and contingency contracting programs • Psychological states (mastery, self-esteem) • Shorter period between screening and medical evaluation • Shorter therapy regimens • Selective use of nurse-led outreach programs and DOT • Socioeconomic and demographic features (income, younger age, recent immigration)	• Distance or lack of transportation to clinic • Forgetfulness • Lack of cooperation from children • Lack of insurance • Lack of understanding of how or how long to take therapy • Longer treatment regimens • Lower parental education • Parental work conflicts • Pregnancy • Psychological states (engaging in high risk behaviors) • Side effects • Socioeconomic and demographic features (older age, lack of insurance) • Stigma about TB and links to HIV • Treatment at non-TB clinics	• Location of treatment (primary care clinics, health department clinics) • Scalability or durability of effective pilot programs • Socioeconomic and demographic features associated with adherence • Timing of therapy discontinuation • Use of novel adherence strategies (e.g. mHealth)

Table. Summary of facilitators, barriers, and knowledge gaps in literature about the pediatric LTBI care cascade.
*Most studies described multiple steps of the cascade. Therefore, study totals do not sum to 137.
† Factors identified in literature as significantly associated with completing steps in the cascade.
‡ Factors listed in literature as preventing completion of steps in the cascade (assessment of statistical significance not required)
Abbreviations: TST = tuberculin skin test; IGRA = interferon-gamma release assay; DOT = directly-observed therapy; HIV = human immunodeficiency virus

Conclusion. While existing literature describes LTBI treatment initiation and completion in children, our analysis reveals a lack of data guiding retention of children from LTBI screening through treatment initiation. This review highlights the need to further understand early steps of the care cascade, in order to help alleviate the burden of TB in children.

Disclosures. Jessica Haberer, MD, MS, Merck (Consultant)

1644. "And the stick to fight TB is IPT": Perspectives on TPT Implementation Among Senior Nurses in Rural South Africa

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Tuberculosis (TB) disproportionately affects people living with HIV (PLH). The World Health Organization (WHO) has endorsed tuberculosis preventative therapy (TPT) in resource-limited settings with high HIV and TB burdens. South Africa has led global TPT efforts, yet implementation remains sub-optimal.

Methods. In a rural, impoverished region of South Africa with high TB and HIV prevalence, primary care clinic-based senior nurses were asked to participate in anonymous, semi-structured interviews assessing TPT knowledge, beliefs, and attitudes. The currently available regimen is isoniazid preventive therapy (IPT) for 12 months. Through an iterative process, a code list was generated and applied to each transcript. The data were analyzed using thematic analysis and Nvivo 12 software to identify facilitators and barriers to IPT prescribing.

Results. Among 22 nurses at 14 primary health clinics, 86% were female, median age 39 (IQR 31-54.8) years, with median 10.5 (IQR3-18) years of health care experience. Nurses felt that TPT was effective at preventing TB. Barriers to implementation included limited time to counsel patients due to understaffing in high-volume clinics and lack of documentation of IPT prescription in patients' charts, which limited effective follow-up. Nurses certified in Nurse-Initiated Management of Antiretroviral Therapy (NIMART) expressed confidence in their IPT knowledge, but those not certified wanted additional training. Nurses identified patient-level factors impeding TPT implementation, including transportation, HIV-related stigma, mobility, particularly among men, and pill burden associated with length of IPT (12 months) with concurrent daily chronic medications. Facilitators included availability of IPT in both hospitals and primary care clinics, and capacity for task-shifting to other healthcare professionals (counselors, staff nurses). The impending rollout of 3HP (12 weeks of isoniazid-rifapentine) was viewed favorably.

Conclusion. Nurses identified limited time to counsel PLH and lack of standardized training programs as the main barriers to implementation of TB preventative therapy. Addressing these barriers will be critical to successful implementation of new TPT regimens.

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1647. Breast Tuberculosis: A Diagnostic Challenge

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