

Lindsay McKenna, TB Project Co-Director at Treatment Action Group (TAG)

Engaging communities in the development and introduction of long-acting TB technologies

Community engagement in R&D of long-acting TB technologies

Rationale is inherent and instrumental.

- Participation in research as more than a trial participant is an international human right.
- Community engagement ensures social value, a pre-requisite for ethical research.
- Communities can inform product development, helping to ensure that new LA technologies (LATs) address the priorities and needs of those affected by TB.

CABs have a role at every stage of development.



- Questions community engagement can help answer at the current stage of LATs for TB (Red box):
 - Do new technologies address the priorities and needs of those affected by TB?
 - What is the role of LATs in TB prevention and treatment?
 - What challenges in TB would LATs ideally solve?
 - What is the acceptability of LAI formulations?

The TB community has opinions

Global TBCAB position papers (Public Health Action 2023).

- Five papers responding to the scientist- and funder-driven TB research agenda without considering community input.
 - Presented as a symposium at The Union Conference 2023: *Flipping the Script: Communities Sharing Perspectives on TB Treatment and Vaccines Research*.
- Two papers are particularly relevant to the development of new TB treatment regimens and the research agenda for LA TB treatment.
 - **Paper 1: Balancing toxicity and duration.** Response to the perceived outsized focus on duration without considering other aspects that affect treatment completion, outcomes, & QoL (e.g., Pill burden, safety, tolerability, side effects, and healthcare system engagement).
 - **Paper 3: Choices for TB prevention and treatment.** Response to the push for one-size-fits-all TB treatment.
- Key points (Paper 1).
 - Even mild/moderate AEs and side effects matter. The experience of AEs is at least as important as treatment duration in determining treatment completion. **Need to optimize safety and tolerability alongside efficacy and duration.**
 - Acceptable trade-offs depend on perspective. Researchers & stakeholders may accept similar side effects for shorter duration, whereas affected communities may not. **Meaningful community consultation is needed to understand perspectives.**
 - Treatment duration has been narrowly defined by clinical researchers. Focusing on treatment duration overlooks time spent engaging in all aspects of care (Feeling unwell, waiting for test results, monitoring visits, out-of-pocket expenses). **Measures of time spent in the clinic could be co-primary endpoints** (e.g., Home Time: number of days without in-person healthcare interactions).
- Proposals and conclusions (Paper 1).
 - Person-centered endpoints and deeper examination of treatment non-completion.

- Co-primary and secondary endpoints for future TB trials. Cure with no significant AEs; Amount of time spent feeling unwell; Required toxicity monitoring schedule (HCP visits, waiting time for results); Relative impact of any grade AE on QoL; Out-of-pocket expenses.
- There is a real concern about toxicity. Shorter therapeutic duration is not always better, especially if individual drugs have increased toxicity or require more intensive monitoring for toxicity.

Other CABs are promoting TB community perspectives.

- Growing interest in documenting patient and community needs and priorities regarding TB treatment to inform TB trial design.
 - Unite4TB community survey aims to develop and prioritize a list of core outcomes.
- Growing realization that understanding community perspectives is essential for translation to policy.
 - Informs discussions of values, preferences, and equity in development of national and global guidelines.
- Growing urgency to think beyond non-inferiority to SOC.
 - Novel person-centered outcomes that articulate the benefits of other aspects of treatment regimens and are increasingly important as new regimens perform better and make gains in safety and efficacy.

Community acceptability is critical for development of LAIs for TB

Change the narrative around injectables.

- Difficult side effects (e.g., pain & permanent disability) led to a years-long campaign to remove injectable agents from global SOC TB regimens.
- New LAI agents are not the same, but negative associations may carry over and need to be overcome.

Begin a robust community engagement program now – not when final LAI product is available.

- Forum to address myths and misinformation and build trust.
- Qualitative research to understand values and preferences.
 - **Structured community consultations** to inform TPP and PPC documents.
 - **Patient preference surveys** to inform product design (dosing interval, route, privacy/stigma).
 - **Normalize inclusion of qualitative acceptability work in clinical trials and application of high evidentiary standards for patient preference and acceptability:** UNMC/LONGEVITY patient & provider acceptability surveys for specific products; ATLAS & FLAIR trials included acceptability studies of LAIs for HIV.

Cautionary advice

Avoid LAT take over – the research agenda needs to maintain a diverse portfolio.

- Because there are few funders of TB R&D, a shift in one donor’s priorities would impact the entire field.
- Determine the role of LATs (define issues that LAT would address), but acknowledge oral options are needed & may be preferred by some.

Consider access earlier in development.

- New formulations can come with new IP protections, even drugs with expired primary patents.
- Leverage public and philanthropic funding and resources to: Ensure availability, accessibility, acceptability, & quality (AAAQ) and improve transparency of R&D costs, commercialization, voluntary license terms, etc.

Community engagement resources

LAT CAB	Cross-disease CAB sponsored by TAG and AfroCAB. Assists with all stages of R&D, demand creation, and access expansion.
TAG Publications	Communities as actors in the R&D process (https://www.treatmentactiongroup.org/publication/communities-as-actors-in-the-research-and-development-process/). Developing acceptable LA formulations for TB amidst a push for all-oral treatment (https://www.treatmentactiongroup.org/resources/tagline/tagline-october-2021/injectables-redux-developing-acceptable-long-acting-formulations-for-tb-prevention-amidst-a-push-for-all-oral-treatment/). TBCAB community position papers (Public Health Action 2023).