Title:

Perspectives and experiences of patients and health care workers on pre-treatment loss to follow up in adults with pulmonary tuberculosis: protocol for a qualitative evidence synthesis.

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Background

Tuberculosis (TB) remains a major cause of morbidity and mortality in many low- and middle-income countries (LMICs) (1). Despite numerous efforts, resources, and research directed towards TB, these endeavours do not translate to sufficient improvement in health outcomes. For instance, TB incidence has been decreasing globally at a rate of 2% per year; however the reduction was not fast enough to reach the 2020 milestone of the WHO End TB Strategy (2, 3). The global targets are a reduction in TB incidence and mortality of 20% and 35%, respectively, from 2015 to 2020. However, in 2020, these indicators were 9% and 14% respectively, below the half mark. Africa has been making good progress with reductions of 16% (incidence) and 19% (mortality), though these percentages are still below the 2020 milestone.

Factors that contribute to a decrease in controlling the disease and poor health outcomes are delayed diagnosis and delayed initiation of treatment (2, 4). Therefore, access to timely and effective diagnostics and treatment will play a key role in containing the infection and in turn reducing morbidity and mortality. From the TB care cascade described by Subbaraman and colleagues, studies have shown that many patients are lost before starting treatment, yet they have been diagnosed with TB (5). These patients continue to spread the disease in the community and most die because of the disease (6). In a systematic review including 23 studies, MacPherson et al. found that the overall percentage of pre-treatment loss to follow up (PTLFU) ranged from 4% to 38%, with studies from Africa ranging from 6% to 38% (7).

Given that many people diagnosed with TB experience PTLFU, it is important to understand the factors that contribute to this attrition to come up with effective interventions. Studies have highlighted reasons that lead to patients dropping out before starting treatment without looking at the challenges experienced during the linkage to care (5, 7, 8). Several studies suggest that patients face health system barriers that may interfere with their receiving care (7, 9, 10) that have made them experience PTLFU. Findings from one qualitative study have shown that health system barriers play a major role in contributing to PTLFU (10). Regarding the quality of the health care worker-patient interaction, addressing constraints that health

care workers face in providing patient-centred care will be key in reducing PTLFU. Therefore, it is important to get perspectives and experiences from both patients and health care workers about PTLFU to come up with evidence informed solutions.

Quantitative studies have been able to highlight different patient characteristics and health system barriers that contribute to PTLFU. However, there are limited qualitative data to provide more insight on PTLFU. Hence conducting this qualitative evidence synthesis (QES), where we will systematically search for qualitative primary studies and draw their findings together, will assist in generating evidence on the contributors to PTLFU and provide knowledge on effective approaches to reduce PTLFU. To our knowledge no other QES on perspectives and experiences of patients and health care workers has been conducted so far.

This review is set out to answer the question: What is the current best available evidence on perspectives and experiences of patients and health care workers on PTLFU in adults with pulmonary TB?

Objective

To identify, appraise and synthesize evidence on perspectives and experiences of patients and health care workers on PTLFU in adults with pulmonary TB.

Methods

We will collect, appraise, and synthesize evidence on the perspectives and experiences of health care workers and patients on PTLFU. We will use thematic analysis approach where we will aggregate data from different primary qualitative studies and summarize using emerging themes.

Criteria for considering studies for the review.

The following studies shall be considered for inclusion: primary studies that use qualitative study designs such as ethnography, phenomenology, case studies, grounded theory studies and qualitative process evaluations on experiences and perspectives of patients (adults aged ≥ 18 years with pulmonary tuberculosis) and health care workers on PTLFU and studies that focus on PTLFU. Studies that use both qualitative methods for data collection (e.g., focus group discussions, individual interviews, observation, diaries, document analysis, open-ended survey questions) and qualitative methods for data analysis (e.g., thematic analysis,

framework analysis, grounded theory) will be included. For studies that have used mixed methods, we will only include them if the data have been collected and analysed using qualitative methods. Studies from any geographical setting globally shall be included. Studies in English only will be considered due to time limitations. The following studies shall be excluded: studies that collect data using qualitative methods but do not analyse these data using qualitative analysis methods (e.g., open-ended survey questions where the response data are analysed using descriptive statistics only).

Identification of studies

We shall use the SPIDER (Sample, Phenomenon of interest, Design, Evaluation, Research Type) (11) framework to come up with our search strategy as shown in Table 1. A comprehensive search will be done in different databases using guidelines recommended by the Cochrane Qualitative and Implementation Methods Group (12).

Table 1: SPIDER framework for the search strategy

S- Sample	PI- Phenomenon of interest	D- Design	E- Evaluation	R- Research type
Adults with pulmonary TB and Health care workers working with patients diagnosed with TB	Pre-treatment loss to follow up	Qualitative methods of data collection: interviews, FGDs, observations and qualitative methods of analysis: thematic analysis, framework analysis, ground theory	Perspectives, attitudes, and experiences on pre-treatment to loss to follow up	Qualitative studies
Key search terms	Key search terms	Key search terms	Key search terms	Key search

				terms
Adult* OR patient* OR “person with tuberculosis” OR ‘person with TB’ OR tuberculosis OR TB “health care worker” [MeSH] OR “health personnel” [MeSH]	“Pre-treatment loss to follow up” [MeSH] OR “loss to follow up” OR “PTLFU” OR “Default treatment”	“qualitative research” [MeSH] qualitative OR interview* OR FGD OR “focus group*” OR observation* OR ethnography OR survey	Perce* OR experience* OR attitude* OR behaviour OR know* OR belie* OR understand* OR feel* OR view* OR opinion*	qualitative

The search will be done without date restrictions but will be restricted to studies in English only, in the following electronic databases: MEDLINE (OVID), Cochrane library, EMBASE(OVID), CINAHL (Cumulative Index to Nursing and Allied Health Literature), Global Index Medicus, LILACS, HERDIN, Science Citation Index and Social science citation Index. The search strategy will include the following key terms and their associated synonyms: ‘Pre-treatment loss to follow up’, ‘tuberculosis’, ‘health care workers’, ‘patients’, ‘experiences’ ‘perspectives’, ‘survey’, ‘interview’, ‘focus group’ and ‘qualitative research’. The reference list of the included studies will also be reviewed to identify additional studies. Medical Subject Headings (MeSH) terms will be used when implementing the search in PubMed and Boolean operators such as ‘OR’ and ‘AND’ will also be incorporated in the search to refine and expand the search. The search output will be entered into the EndNote reference management software to delete the duplicates. The duplicates not identified by EndNote, will be manually removed. Thereafter, Covidence, a screening and data extraction tool for authors conducting systematic reviews, will be used for study selection (13).

Selection of studies

Study selection will involve initial screening of title and abstracts to filter the studies that satisfy the inclusion criteria. Thereafter, full texts for titles and abstracts will be obtained. Then formal eligibility assessment on all full texts will be done to come up with the final list of the included studies. Two review authors will independently do the screening. Any disagreement will be resolved through discussion and consensus building. The results of the study selection process will be presented in a flow diagram according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidance (14).

Sampling of studies

Purposeful sampling will be considered depending on the number of studies included to reach data saturation. This is to ensure a greater variation of concepts is achieved without having a very large volume of primary data overwhelming the analysis. A three-step sampling framework will be used as described by Ames and colleagues (15). The framework will mainly consider studies that: are conducted in low- and middle-income settings, score three or more on a 5-point scale of data richness (Table 2) and have study objectives that closely match our synthesis objectives.

Data collection and management

Data abstraction will be conducted using a structured format to retrieve information. For this process, one review author will extract data using predesigned form (Table 3), from the included studies and a second review author will verify the information. To ensure validity, the predesigned form will be piloted by extracting data from 10% of the included studies. The form will then be updated accordingly. The following data will be extracted: first author, date of publication, setting, study design, type of participant (patient or health care worker), method of data collection, type of data analysis such as (thematic and framework), reported experiences, and perspectives. Disagreements will be resolved through discussion and consensus building.

Table 2:Data richness table(15)

Score	Measure	Example
1	Very little qualitative data presented that relate to the synthesis objective. Those findings that are presented are descriptive	For example, a mixed methods study using open ended survey questions or a more detailed qualitative study where only part of the data relates to the synthesis objective

2	Some qualitative data presented that relate to the synthesis objective	For example, a limited number of qualitative findings from a mixed methods or qualitative study
3	A reasonable amount of qualitative data that relate to the synthesis objective	For example, a typical qualitative research article in a journal with a smaller word limit and often using simple thematic analysis
4	A good amount and depth of qualitative data that relate to the synthesis objective	For example, a qualitative research article in a journal with a larger word count that includes more context and setting descriptions and a more in-depth presentation of the findings
5	A large amount and depth of qualitative data that relate in depth to the synthesis objective.	For example, from a detailed ethnography or a published qualitative article with the same objectives as the synthesis

Assessment of Methodological Quality

Included studies will be assessed for methodological quality using the Evidence for Policy and Practice Information (EPPI) center tool which has been used in other qualitative reviews (16, 17). The following domains of qualitative studies will be assessed using the tool: rigor in the sampling, rigor in data collected, rigor of data analysis, support of the findings from the data, breadth and depth of the findings, reliability of the study findings and relevance of the study findings to the aims of the synthesis. However, studies will not be excluded based on quality. Two review authors will apply the EPPI center tool independently and any disagreements will be resolved through discussion and consensus building.

Table 3: Data extraction form for qualitative synthesis on perspectives and experiences of patients and health care workers on PTLFU (18)

Author
Country
Aims of the study.
Ethics – how ethical issues were addressed.
Study setting

Theoretical background of study

Sampling approach

Participant characteristics

Data collection methods

Data analysis approach

Key themes identified in the study (1st order interpretations)

Key themes related to data extraction.

Authors' explanations of the key themes (2nd order interpretations)

Authors' recommendations

Assessment of study quality

Data synthesis and analysis

Data will be analysed separately for patients and health care workers as we expect to find differences between these two groups. The analysis will be done using the thematic framework analysis approach (12, 19). Synthesis of data will be done using five stages of the framework synthesis as follows.

- **Familiarisation with the data**

One review author will familiarize herself with the data against the objective of the review and note the recurrent themes across the studies.

- **Identifying a thematic framework**

A pre-determined thematic framework developed using Supporting the Use of Research Evidence (SURE) guidelines (20) will be used to guide the thematic analysis. The framework will be adopted based on the emerging themes from the included studies. The framework will provide a list of factors that could contribute to PTLFU and possible strategies to reduce PTLFU.

- **Indexing**

Two review authors will independently read through the extracted data to look for themes according to the predetermined thematic framework and additional emergent themes. As new

themes emerge, the framework will be modified. This will be done by discussion and consensus by the two review authors. All included studies will be read until there are no new emerging themes. Based on the themes identified, coding of the data will be done where each primary study will be given a code. Parts of the studies will be indexed with one or more codes where applicable.

- Charting

Data will be sorted by themes and presented in the form of an analysis table (Chart). Studies and related themes will be presented in columns and rows of the table hence enabling the review authors to compare findings of the studies across different themes and subthemes.

- Mapping and interpretation

The charts will be used by the review authors to define the identified concepts and map the range and nature of the phenomena. Associations will be explored between themes to help clarify our findings. Mapping and interpretations of the findings will be done in accordance with the review objectives and emerging themes. Presentation of findings will be done using a 'Summary of Qualitative Findings' table where the key findings, judgements, and related explanations of the assessment will be summarized.

Assessing our confidence in the review findings

Assessment of our confidence in each finding will be done by two review authors independently using the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) approach (21). The assessment will be done on the following four key components: methodological limitations of included studies; coherence of the review findings; adequacy of the data contributing to a review finding; and relevance of the included studies to the review question. After the assessment, the review authors will make a judgement about the overall confidence in the evidence supporting the review findings and categorize the confidence into high, moderate, low, or very low. This will be done through discussion and consensus building. The CERQual assessment and the explanations will be presented in a summary of findings table.

Review author reflexivity

The review author team has a range of research experience and expertise in clinical research and evidence synthesis in TB. This could influence their input in conducting the QES,

therefore the following measures will be factored in to moderate their influence. During the study selection process, the review authors will resolve conflicts through discussion and aim to achieve a consensus as a team. Two review authors who will be involved in data coding, data extraction and writing up the findings will repeatedly discuss how their backgrounds may influence their data analysis and writing of the findings. They will also question each other's interpretations of the findings to assess their fit with the existing findings. The other review authors will also be consulted to verify that the findings are reflections of the supporting data.

Ethics and dissemination

For this systematic review, a formal ethical review will not be pursued since the data collected will be retrospective and data are available to the public. The title will be registered with the International Prospective Register of Systematic Reviews (PROSPERO). This protocol has been prepared using Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols (PRISMA-P) (22). Findings of the systematic review will be prepared using Enhancing transparency in reporting the synthesis of qualitative research ENTREQ statement - (23) using relevant items for the qualitative synthesis. We will submit the manuscript to a peer reviewed, open access biomedical journal, ensuring that the study findings can be accessed worldwide through the internet. We also anticipate disseminating our findings through conference meetings and presentations.

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CONTRIBUTIONS OF AUTHORS

MM developed the concept of the study and drafted the initial protocol. MM, EO, KRS, TY gave input to the versions of the protocol. MM, EO, KRS, TY contributed to the final draft of the protocol.

DECLARATIONS OF INTEREST

None declared.

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