


# BMJ Open Patient adherence to tuberculosis treatment in the Indian subcontinent: systematic review and meta-synthesis of qualitative research

Kalpita Shringarpure <sup>1</sup>, Meera Gurumurthy,<sup>2,3</sup> Karuna D Sagili,<sup>3</sup> Melissa Taylor,<sup>4</sup> Paul Garner,<sup>4</sup> Jamie Tonsing,<sup>3,5</sup> Raghuram Rao,<sup>6</sup> Kuldeep Singh Sachdeva<sup>3,6</sup>

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For numbered affiliations see end of article.

## Correspondence to

Dr Kalpita Shringarpure;  
kshringarpure@gmail.com

## ABSTRACT

**Objectives** How well patients adhere to their tuberculosis (TB) treatment influences their recovery and development of drug resistance, but influences on adherence are multiple and often competing. We synthesised qualitative studies from our setting in the Indian subcontinent to understand the dimensions and dynamics involved to help inform service provision.

**Design** Qualitative synthesis comprising inductive coding, thematic analysis and forming a conceptual framework.

**Data sources** Medline (OVID), Embase (OVID), CINAHL (EBSCOHost), PsycINFO (EBSCOHost), Web of Science Core Collection, Cochrane Library and Epistemonikos were databases searched on 26 March 2020 for studies published since 1 January 2000.

**Eligibility criteria for selecting studies** We included reports in English from the Indian subcontinent that used qualitative or mixed-methodology designs and reported findings around adherence to TB treatment. Full texts meeting eligibility were sampled based on ‘thickness’ (the richness of the qualitative data reported).

**Data extraction and synthesis** Two reviewers used standardised methods to screen abstracts and code. Included studies were assessed for reliability and quality using a standard tool. Qualitative synthesis was performed by inductive coding, thematic analysis and developing conceptual framework.

**Results** Of 1729 abstracts screened from initial search, 59 were shortlisted for full-text review. Twenty-four studies that qualified as ‘thick’ were included in the synthesis. Studies were set in India (12), Pakistan (6), Nepal (3), Bangladesh (1) or in two or more of these countries (2). Of the 24 studies, all but one included people who were taking TB treatment (1 study included only healthcare providers), and 17 included healthcare workers, community members or both.

We identified three themes: (1) personal influences on the people with TB include interconnections between their social role in the family unit, their own priorities in day-to-day living and their experience to date with the disease; (2) adherence is profoundly influenced by how individual healthcare providers interact with patients on treatment and address their needs; (3) adherence is influenced across communities by structural, social, economic and cultural factors related to treatment.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Our screening methods ensured we included studies that specifically addressed tuberculosis (TB) adherence in the region, and were also rich in terms of qualitative data.
- ⇒ The synthesis included data from those who had defaulted from treatment, which is important in understanding failed adherence.
- ⇒ The appraisal of the studies helps the reader understand the strengths and limitations of the data and studies included which ensure more robust interpretation and conclusions.
- ⇒ The synthesis includes only publications in the English language, therefore possibly losing out on some additional/important insights offered by studies published in the vernacular; however, most academic publications from the subcontinent relevant to this meta-synthesis were in English language.
- ⇒ Given the large number of hits obtained from the search strategy, abstracts were divided between reviewers and initial screening was done by a single reviewer only (although a rigorous screening tool with prespecified study inclusion/exclusion criteria used to avoid any subjectivity, and reasons for exclusion clearly documented in the screening software).

**Conclusion** Staff in TB programmes require an understanding of the various competing influences on individuals undergoing treatment. Programmes need to have more flexible and people-centred approaches to service provision in order to achieve adherence, and thus improve treatment outcomes.

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## INTRODUCTION

Although drugs for tuberculosis (TB) can be highly effective, taking these medicines is challenging. The duration of treatment is long (6 months for drug-sensitive TB and up to 2 years for drug-resistant TB) and side effects are common.<sup>1 2</sup> Adherence refers to the completeness with which those taking

treatment follow medical instructions.<sup>3</sup> Poor adherence can result in treatment failure, disease relapse, development or amplification of drug resistance, ill-health and / or in premature death.<sup>4</sup>

There is plenty of research on risk factors to treatment adherence in both low-income and middle-income<sup>5-8</sup> and high-income countries.<sup>9-19</sup> Age, gender, literacy, socio-economic and employment status are often cited as being associated with adherence. A recent systematic review protocol has hypothesised personal, sociocultural and structural factors as influencing adherence in high-income and middle-income settings, using published quantitative data from observational studies.<sup>20</sup> There are trials and reviews of particular, focused fixes for adherence including support mechanisms, reminders, incentives and directly observed therapy.<sup>20-26</sup> What is missing, however, is an understanding of the problems underlying adherence from the 'person on treatment' view and from the health system perspective. This helps formulate the problem in a more granular way, in order to plan more sophisticated strategies to improve adherence that take into account the healthcare provider-patient relationship, social structures and the sociocultural setting inhabited by the person taking the treatment,<sup>27 28</sup> reflecting that TB has been described as a 'social disease'.<sup>29</sup>

South Asia, 95% of whose population resides in the Indian subcontinent, contributes to 40% of the world's TB burden and has a disproportionate share of TB deaths.<sup>30</sup> In 2021, countries like India (28%), Indonesia (9.2%), China (7.4%), the Philippines (7.0%), Pakistan (5.8%), Nigeria (4.4%), Bangladesh (3.6%) and the Democratic Republic of the Congo (2.9%) accounted for two-thirds of the global TB burden.<sup>31</sup> The present review aims to understand the gap in addressing sociological influences on adherence to TB treatment in the Indian subcontinent by synthesising qualitative findings around the experiences of those receiving as well as those facilitating treatment for TB.

## METHODS

### Inclusion criteria

We included studies that used qualitative or mixed-method designs in data collection and analyses to examine adherence to treatment for TB. Adherence in general refers to the completeness with which participants or patients follow medical instructions.<sup>3</sup> In this context, it refers to concordance or compliance to treatment, the extent to which the person on treatment continues taking the treatment regularly.<sup>28 32</sup> We included studies that describe perspectives of those undergoing treatment, of their caregivers, or of healthcare providers. All published studies between 1 January 2000 and 26 March 2020 that were reported in English and were set in the Indian subcontinent (Bangladesh, Bhutan, Maldives, Nepal, Pakistan and Sri Lanka in addition to India) were considered. Studies reporting findings on people with TB along with other

comorbidities (eg, HIV, diabetes) were included if they met the inclusion criteria.

### Search methods and study selection

We searched the following electronic databases on 26 March 2020 using the search terms and strategies described in online supplemental annexure 1: Cochrane Central Register of Controlled Trials published in the Cochrane Library; Medline (OVID), Embase (OVID); CINAHL; PsycINFO; Web of Science Core Collection and Epistemonikos.

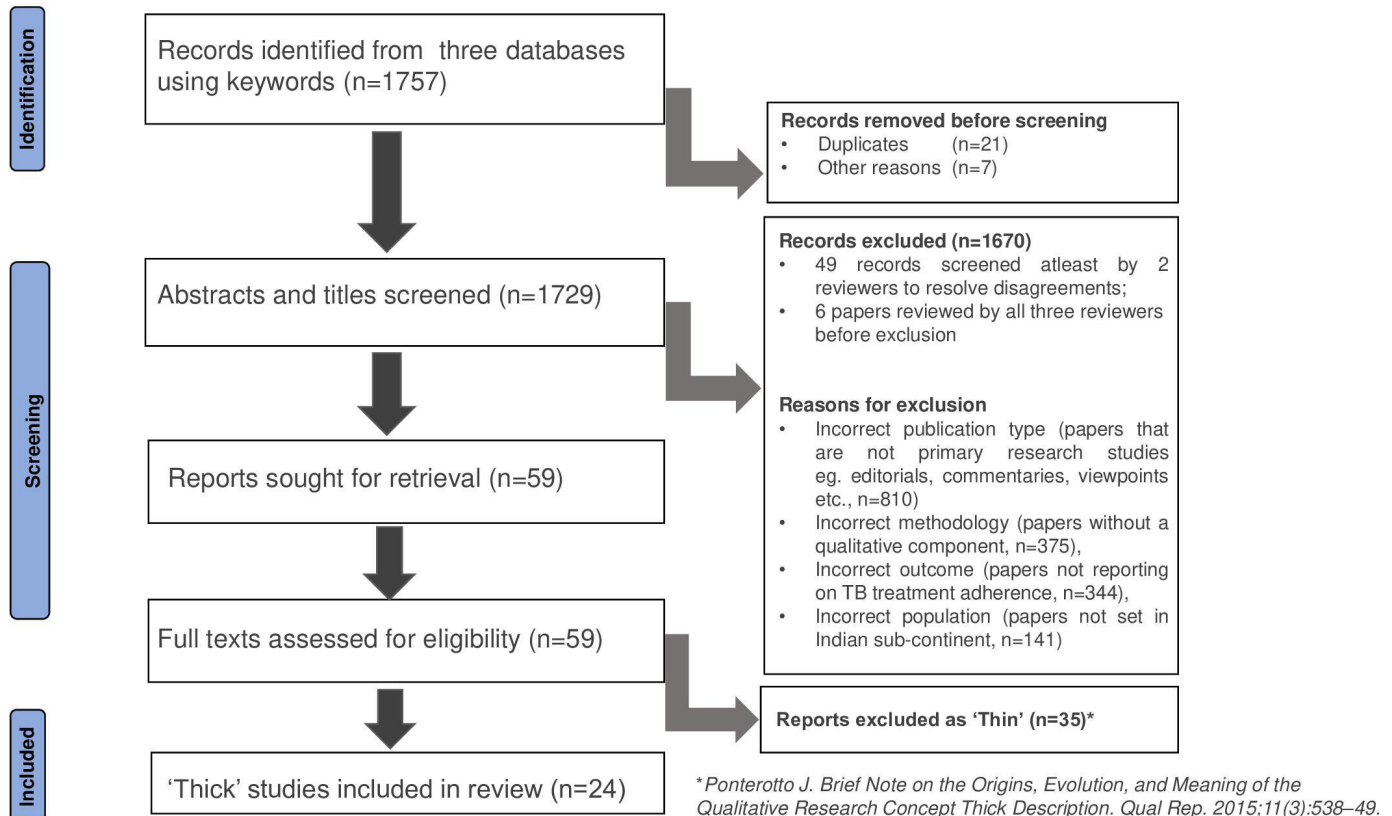
Given the large number of hits obtained from the search strategy, abstracts were divided between reviewers (KSS, MG, KDS) and initial screening was done by a single reviewer only (although a rigorous screening tool with prespecified study inclusion/exclusion criteria was used to avoid any subjectivity, and reasons for exclusion were clearly documented in the screening software, Rayyan.<sup>33</sup> When unsure at the screening stage, studies were included in full-text screening.

As we retrieved a large number of studies eligible for inclusion, we chose to sample the studies based on 'thickness'. Full texts included were classified as 'thick' or 'thin',<sup>34 35</sup> based on the depth of qualitative reporting for the scope of this review, and only 'thick' full texts were included in this synthesis (figure 1).

Studies were listed to have a 'thick description' when they accurately described and interpreted social actions within the appropriate context in which the social action took place. Other measures to evaluate 'thick description' were that the study captured the thoughts, emotions and web of social interaction among observed participants in their operating context. It should have had a central feature to interpret social actions assigning motivations and intentions for the said social actions. The context for, and the specifics of, the social action should be so well described that the reader experiences a sense of verisimilitude as they read the researcher's account. Verisimilitude means 'truth like statements that produce for readers the feeling that they have experienced, or could experience, the events being described'.<sup>36</sup> Therefore, for these thick studies also, a 'thick description' of social actions promoted 'thick interpretation', which lead to 'thick meaning' of the findings which could resonate with the investigators KSS, MG and KDS who reviewed them.

### Quality assessment

We used a quality assessment tool adapted from one developed by the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI centre).<sup>37 38</sup> Although non-validated, it was chosen for its detailed signalling questions, prior use within the author team and use in several other well-conducted qualitative evidence syntheses, including those published by Cochrane.<sup>39-41</sup> The Enhancing transparency in reporting the synthesis of qualitative research (ENTREQ) guideline for transparency was followed in the reporting of synthesis of qualitative research<sup>42</sup> (online supplemental annexure 2).



**Figure 1** Flow chart of studies included. RCT, randomised controlled trial. \*Ponterotto.<sup>36</sup>

### Qualitative data synthesis

Authors familiarised themselves with the qualitative data reported and used initial inductive coding (KSS, MG) that was subsequently refined (deductive coding) based on discussions (KSS, MG, KDS). Codes were grouped into analytical categories and subcategories from which overarching themes and subthemes were generated through an iterative process (KSS, MG) and checked for consistency and validity (KSS, MG, KDS). Disagreements, if any, were discussed and resolved between the reviewers. At a midway point, the core team (PG, MT) reviewed and discussed interpretations, to help identify the themes and subthemes. This was an iterative process conducted through team meetings at regular intervals (KSS, MG, KDS, PG, MT). We repeatedly refined our conceptual model and coding framework according to the preliminary themes. ATLAS.ti Qualitative software, Berlin, Germany was used for the qualitative analysis described.<sup>43</sup>

### Reflexivity statement

The reviewer team is experienced in diverse research skills, including both primary research in qualitative and quantitative methods, and evidence synthesis methods for quantitative study designs. They have a rich working as well as research experience in field of infectious diseases (KSS, MG, KDS, PG), clinical medicine (KSS), clinical trials (MG), TB and HIV management (KSS) and social science (KSS, KDS, PG, MT). The team reflected on personal biases or judgements throughout the process of the synthesis. This allowed them to reflect on emerging

themes through different perspectives and to construct meaning in the synthesis. To further increase reflexivity, 'negative' cases that is, findings that conflicted or offered alternate explanations to emerging themes or to the conceptual model, were carefully considered.

### Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

### RESULTS

We screened 1729 titles and abstracts from the outlined search and shortlisted 59 which met the inclusion criteria for full-text review. Full texts that met the eligibility criteria were sampled based on thickness: 35 were classified as 'thin' studies based on their qualitative construct, methodology and reporting; and 24 studies were qualified as 'thick' and were included in this qualitative synthesis.

The characteristics of the included studies are shown in online supplemental table 1. The earliest study was published in 2002 but most were published after 2012 (17/24). Studies were from India (12/24), Pakistan (6/24), Nepal (3/24), Bangladesh (1/24) and two in multiple countries, and were mostly purely qualitative (18/24). All studies used in-depth interview methods, and several studies also included focus group discussions. One study used an interesting method of 'photo-voice'—photographs taken by participants that were

followed by interviews and discussions. Of the 24 studies, all but one included people who were taking treatment for TB (1 study included *only* healthcare providers), and 17 included healthcare workers and/or community members in addition.

Participants taking treatment for TB ranged from those who had just commenced, to those who were well into treatment or had completed treatment and exited the programme. Importantly, there were also participants who had 'defaulted' treatment, therefore providing critical insights towards this synthesis' objective. Healthcare workers comprised doctors, pharmacists, nurses, community health workers and directly observed treatment (DOT) providers, traditional healers and other frontline health workers in the public or private sector. Number of female participants were reported by majority of the studies (20/24); the gender ratio, if not equal, was at least representative of that in the general population of those taking treatment for TB in those settings.

The quality assessment of shortlisted studies included in this synthesis is reported in online supplemental table 2. Quality of studies has been reported based on a tool adapted from a previously published review<sup>28</sup> (online supplemental table 2a) and on a tool adapted from the EPPI centre.<sup>37 38</sup> (online supplemental table 2b).

We identified the following three themes and seven subthemes. Barriers and facilitators of TB treatment in the Indian subcontinent with overarching themes, subthemes, associated categories and inductive codes have been depicted in table 1.

**Theme 1: personal influences include interconnections between a patient's social role in the family, their own priorities in day-to-day living and their experience of the disease**

**Subtheme 1.1: the influence of a patient's social role in the family**

A patient's social role in the family influenced priorities and adherence. Individuals who played the role of *primary*

**Table 1** Barriers and facilitators of TB treatment in the Indian subcontinent: overarching themes (OT), subthemes, associated categories and inductive codes

Overarching themes	Subthemes	Categories	Emergent codes	
<b>OT#1</b>	Influences include interconnections between a patient's social role in the family, their own priorities in day-to-day living and their experience of the disease	<ul style="list-style-type: none"> <li>▶ Influence of a patient's social role in the family</li> <li>▶ Influences of their own priorities in day-to-day living</li> <li>▶ Influence of their own experience of the illness</li> </ul>	<ul style="list-style-type: none"> <li>-Social role</li> <li>-Lifestyle factors</li> <li>-Disease experience</li> </ul>	Caregiver responsibilities, family obligations, marriageability, health-seeking behaviour, alcoholism, migration, confidentiality, fear of getting worse, improved health, not feeling better, motivation, weakness
<b>OT#2</b>	How providers treat patients profoundly influences adherence	<ul style="list-style-type: none"> <li>▶ Providers are overburdened with pressure to meet targets, straining their relationship with patients</li> <li>▶ People who do not adhere are labelled 'difficult' leading to further discrimination</li> </ul>	<ul style="list-style-type: none"> <li>-Programme structure</li> <li>-Provider constraints</li> <li>-Patient-centeredness</li> <li>-Healthcare Infrastructure</li> <li>-Treatment characteristics</li> </ul>	Programme targets, workload/burden, incentive-structures, training, provider motivation, caste-based discrimination, patient-profiling, previous 'defaulter', patient-provider relationship, confidentiality, private sector, delayed diagnosis, drugs stockouts, (un)friendly and (in)flexible treatment, side effect, medication burden, nutrition requirement, cost of treatment
<b>OT#3</b>	Beyond the individual-level, accessing service provision is also heavily determined by structural, social, economic and cultural factors pertaining to and influencing the treatment context	<ul style="list-style-type: none"> <li>▶ Although free, accessing TB services costs time and money</li> <li>▶ Information from health providers is often inadequate and confusing</li> <li>▶ Consequences of stigma and need for strong social supportive system</li> </ul>	<ul style="list-style-type: none"> <li>-Resource barriers</li> <li>-Knowledge and awareness</li> <li>-Social support</li> </ul>	Cost of treatment, nutrition requirement, financial issues, livelihood, transportation, time, access, TB awareness, trust/belief, misinformation, clarity of diagnosis or treatment, insufficient/inadequate information, family support, social support, stigma, marriageability

TB, tuberculosis.

*caregivers* had very different considerations and limitations compared with those who were (sometimes sole) breadwinners. The demands of young children or elderly in the house were a consideration for several women who were diagnosed with TB. They were either *not able to leave* the house unattended or did not find timings offered by the clinics or treatment supervisors conducive.<sup>44–50</sup> However, women were also terrified that they may pass the illness to their loved ones, so felt it was important to access treatment, and to recover so they were able to *protect their families, and feel stronger* in order to care for them sufficiently.<sup>46 47 51</sup>

### Subtheme 1.2: the influences of their own priorities in day-to-day living

For those who were the *main breadwinners* of their families, their nature of employment and the flexibility or understanding extended by their employers influenced their ability to access and continue treatment. Especially for daily-wage workers, this boiled down to having to *make a choice between going to work and getting treatment*.<sup>45–59</sup> Lack of livelihood impacted their entire families; lack of treatment was seen as something that only they needed to deal with. Long-term impact of the disease, and its consequent effect on the person and their families were not understood or considered in the context of the difficulties of their immediate realities. In such circumstances, several even *resorted to private sector for treatment* since it did not have the same restrictions in terms of accessing treatment as the public sector.<sup>45 51 52 55 60–62</sup> Contexts in which this was taken into account and *made flexible was seen as a great facilitator* for access and adherence to treatment.<sup>63</sup> Adding further complexity to an individual's motivation to access and continue taking treatment were factors that rendered their everyday lives unpredictable. The nature of jobs and lives for several participants reported by the studies were *migrant in nature*,<sup>45 50 58</sup> moving from place to place for as part of work or returning from urban centres to villages for personal and family reasons (including seeking support during illness and treatment). This combined with the fact that treatment for TB is several months (or sometimes even years)<sup>50 64</sup> long meant discontinuing treatment from the facility that they initiated their treatment under. The barriers of accessing treatment from another facility as they moved, or re-entering the system on their return were very high, and made for compelling factors in the discontinuation of treatment.<sup>47 50 54 58 60</sup>

Treatment taking for TB appeared to be a balancing act between the demands of the family, the disease and that of treatment itself but one in which those taking treatment stood to lose irrespective of which decision they made. Therefore, people ended up with the 'default' choice of continuing with the responsibilities of their social role. See [table 2](#) for illustrative examples and associated quote(s). Related to personal circumstances and influences, *alcoholism* was reported as a reason that contributed to individuals not being compliant with their

treatment and studies advocated treatment plans to take into account addictions in their provisions.<sup>50 52 54 58</sup>

### Subtheme 1.3: the influence of their own experience of the illness

Spanning across all these personal factors are the *experience of the disease itself and the response to treatment* in those taking it—this experience is critical in their motivation to adhering to the recommended regimen. While some felt better when on taking treatment and were therefore *motivated to recover and become stronger* to perform their social roles,<sup>56 59</sup> several did not see any impact of their treatment or even worse, the *side effects of the medications exacerbated* their weakness and their experience of the illness.<sup>44 46 50–54 64 65</sup> In some instances, those *feeling better also stopped taking treatment* as it could not justify the time or resources spent on taking the treatment further.<sup>44 45 50 54 57 58</sup> See [table 2](#) for illustrative quote.

## Theme 2: how providers treat patients profoundly influences adherence

### Subtheme 2.1: providers are overburdened with pressure to meet targets, straining their relationship with patients

The structure of the TB programmes across the Indian subcontinent *does not place patient priorities at its helm and heart*.<sup>46 49 53 66</sup> This was evident through programmatic algorithms, and through responses from persons taking treatment and treatment providers. This was exacerbated by inadequate infrastructure<sup>46 47 54 55 57 60 67</sup> and administration,<sup>49 50 53 55 57 67</sup> lack of access to care<sup>46 47 54 55 57 60 62 66 67</sup> as well as demanding treatments for TB<sup>57 58 63 67</sup> in terms of the duration,<sup>46 50 53 59 60 64</sup> pill burden,<sup>50 52 64</sup> adverse events from the medication,<sup>44 46 50 52–54 58 62 63</sup> lack of nutritional supplementation to support treatment<sup>45 46 50 54 59</sup> and the monetary deficit<sup>45 46 48 50 52 53 57</sup> to address some of these issues.

The TB treatment *programme incentivised or rewarded adherence*<sup>46 50 67</sup> measured through its daily DOT setup<sup>53 60 62</sup> and *penalised default*<sup>47 50 54 63</sup> at all levels—both the person undergoing treatment and the provider administering and therefore seen as responsible for it.<sup>46–48 50 53 54 59 60</sup> However, it failed to address and overcome the real and pressing challenges faced by the providers<sup>45–47 49 52 54 56 57 59–61 64 68</sup> and the persons taking treatment<sup>44 46 48–50 52–54 56 57 59 60 64 65</sup> to achieve adherence. For an illustrative example, see [table 2](#).

Programme staff reported *lack of training* related to programme implementation,<sup>50 55 57 60 64 67</sup> *insufficient human resources*<sup>50 51 53 56 60 66</sup> leading to inadequate monitoring of both treatment<sup>46 53 66 67</sup> and of adverse events following medication.<sup>52 54 55 58 63</sup> Staff reported being *overburdened with achieving 'targets'*,<sup>47 55 66 67</sup> which were always black-and-white vis-à-vis treatment outcome and in what was measured as a 'success'. In the competition to achieve this, healthcare providers often neglected the needs of patients and this led to strained relationships<sup>44 46 52 62–64 67</sup> and poor accountability towards those taking treatment.<sup>55 67</sup> In some of the DOT setups, monitoring adherence entailed the provider visiting

**Table 2** Barriers and facilitators of TB treatment in the Indian subcontinent: subthemes and illustrative quotes

Sub-themes	Illustrative quote
Sub-theme 1.1: The influence of a patient's social role in the family	My husband used to give me the medicines himself. Children and housework were being neglected and he was very concerned about that. (in-depth interview, control arm – female, Rawalpindi district) <sup>46</sup> They talk about me differently and gossip about my disease, I have a family to look after. My daughter is yet to be married.” [Patient 15, male, 47 years, urban slum] <sup>52</sup>
Sub-theme 1.2: The influences of their own priorities in day to day living	“He (another patient who came to take DOTS) is only 35 years old and has two small children. He comes to TB hospital by morning 9.30 and by the time he reaches his house it will be afternoon 2’ o clock. He will not have any time to go to work. He is in such a situation that if he does not go for his treatment, he will die and if he does not go for work, his children will die”(PP referred, M, U, 65 years)” <sup>62</sup>
Sub-theme 1.3: The influence of their own experience of the illness	A 27-year-old male TB patient shared a photograph of himself lifting up his young son and said: “This is that moment of happiness when I realised that I was getting better. So, in excitement, I picked up my son and threw him in the air. He had a habit (of saying) ‘Throw me up in the air!’ Before, I couldn’t even pick him up. I couldn’t even hold his hand to help him walk. When I threw him in the air, I was thrilled. This showed that I’m now getting better. I felt very happy.” <sup>59</sup>
Sub-theme 2.1: Providers are overburdened with pressure to meet targets, straining their relationship with patients	A volunteer health worker interviewed in Bangladesh was quite clear that the patient's right to confidentiality is not as great a priority for her as protecting the public's health by ensuring adherence to treatment. “Actually, patients should handle their family problems. I’m responsible for ensuring DOT is adhered to for the sake of other community members”. (Volunteer health worker, Bangladesh) <sup>49</sup>
Sub-theme 2.2: People who do not adhere are profiled as being ‘difficult’ leading to further discrimination	A DOT worker in one clinic approached the problem in this way: she starts a patient on treatment and if, after a few ‘test doses’, the patient experiences problems or does not come regularly for DOT, the health visitor discontinues the treatment. The patient is recorded as one who refused DOT. No further reference need be made to this patient. The TB treatment card is removed from the centre and so no record exists of this ‘enrolment.’ In other words, the patient is not recorded as a ‘defaulter’ and the clinic records (and therefore ‘results’) remain unaffected. <sup>47</sup> DL is a very old man who lives with his wife but no extended family. He was working until 1995 when he fell ill with TB. Eventually he was enrolled as a patient at one of the DOT centres and commenced treatment. Sometime into his treatment course, however, his wife fell ill and had to be hospitalised in a private hospital. During the period of her illness, DL was compelled to interrupt his TB treatment in order to look after her. Later, when he approached the DOT centre again, he was advised to go back to Moti Nagar chest clinic for another sputum examination. He borrowed Rs 50 from a neighbour to reach the clinic, but when he arrived and explained his situation (that he had previously been on treatment but had stopped), the staff there behaved rudely towards him. DL felt hurt and insulted. He returned home and refused to join back. <sup>54</sup>
Sub-theme 3.1: Although ostensibly free, accessing TB services costs time and money	A 30-year-old TB treatment supporter shared: “This is a picture of a patient's street where rain and sewage water have collected. We cross this with great difficulty to reach their house...We find it very difficult, and we worry that we may not be able to get their medication to them...She now has multi-drug resistant TB. If she misses her medication, I don’t know if she’ll get better or not.” <sup>59</sup>
Sub-theme 3.2: Information from health providers is often inadequate and confusing	“First, I could not afford the type of food recommended by the doctor. And even if once in a while there was something available, I could not bear to eat it in front of my children, who ate ordinary food, like chappaties and lentils. (focus group, family member arm – male, Gujranwala, district)” <sup>46</sup> “living in poverty is very challenging as it keeps changing our priorities...mostly in taking care of my family, I forget that keeping good health is also important...if I take leave from work then how will I feed my family” <sup>55</sup>
Sub-theme 3.3 Consequences of stigma and need for strong social supportive system	“My mother-in-law insisted on giving me the medicines herself. She was quite nasty to me during my illness and used to say that I had brought this infection from my parents’ house. She wanted me to get cured quickly, because the house work was being affected and also due to scare of spreading the disease in the family. (in-depth interview, control arm – female, Rawalpindi district)” <sup>46</sup>

Continued

Table 2 Continued

Sub-themes	Illustrative quote
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DOT, directly observed treatment; TB, tuberculosis.

patients at their homes<sup>53 60 62</sup> which was not acceptable to several as this divulged their disease and treatment status.<sup>49 51 52 57 62 63 67</sup> In this context, phone reminders were considered better by the persons on treatment.<sup>44 46</sup>

### Subtheme 2.2: people who do not adhere are profiled as being 'difficult' leading to further discrimination

Central to the barriers to adherence is *discriminatory attitude* faced by the persons undergoing treatment.<sup>46 48–50 53 57 58 60 62 63 65 67</sup> This is partly due to *stigma prevalent around the disease* as well as due to *patients' own fears of transmitting TB* to other family members living with them. Furthermore, persons undergoing treatment for TB are subject to discrimination within the health system,<sup>46 57 62 65 67</sup> in that they are 'profiled' by health workers for their ability to continue and complete treatment—this results in the system neglecting those who need additional support in order to access and adhere to their treatment in favour of those who will provide successful outcomes and consequently incentives or recognition.

### Theme 3: beyond the individual-level, accessing service provision is also heavily determined by structural, social, economic and cultural factors pertaining to and influencing the treatment context

#### Subtheme 3.1: although ostensibly free, accessing TB services costs time and money

Studies in this synthesis reported that people needed multiple resources in order to access treatment, even though treatment itself is offered for free in the public sector health systems of all of the countries in which these studies were set. A person's livelihood, social setup and associated constraints have already been discussed as critical factors that influenced continuation of treatment under theme 1.

Even when these were conducive, and the medication was free of cost, taking treatment was still a resource-intensive process. Studies in this synthesis reported that individuals often needed to *travel long distances*—either by foot or using public or their own transport—to reach treatment centres and these journeys were often uncomfortable, expensive or time consuming.<sup>44–47 50 51 54 56 57 59 60 62 65</sup>

Those undergoing treatment were weak and demotivated to undertake these cumbersome journeys, even if it were to the homes of community health workers closer to their homes. Most of them (especially children, elderly or women), often also needed another *family member to accompany* them to the treatment centre.<sup>29 44 46 49 51 59</sup> Treatment taking was often according to rigid schedules of the treatment centres or personal schedules of community health workers, and seldom to the convenience of those taking treatment or others supporting them. To do this

on an everyday basis, and for long periods such as months or years proved to be draining on an individual or their family's resources in terms of people, their time and the costs involved in commute. This was also reported as a *deterrent by DOT providers who had to navigate similar terrains or logistical difficulties* in order to administer medicines to the homes of those taking treatment.<sup>46 57 59 67</sup> As described under theme 1, contexts in which *treatment provision was made flexible* was seen as a great facilitator for access and adherence to treatment.<sup>46 54 63</sup> See table 2 for an illustrative example.

Additionally, people taking treatment for TB were *advised to have nutritious food* which cost them more money, and needed resources such as time or access to another person preparing the food when they were too weak or ill to care for themselves. More often than not, there was also the issue of sharing with others in the household to consider since they could not afford to make this nutritious food for themselves alone.<sup>44–46 56</sup> See table 2 for an example.

Several studies also reported that all of the above reasons made it *particularly harder for women*. It was unsafe for them to travel alone and therefore needed someone to accompany which meant that they had to risk stigma issues associated with family members or those in the community finding out that they had TB. Also, women especially found it difficult to accommodate nutrition requirements specified with TB treatment since they were the primary caregivers and caretakers of their families and more often than not, there was no one else to take care of and cook for them.<sup>29 44–46 51</sup>

#### Subtheme 3.2: information from health providers is often inadequate and confusing

Apart from the resource barriers, studies also reported *knowledge barriers* that contributed to lapses in treatment. Often individuals who needed to take treatment *did not understand what they had been diagnosed with, what caused the disease and the nature and duration of their treatment*.<sup>44–46 50 52 54–56 63 65 66</sup> Importantly, they were not aware of why a treatment with multiple antibiotics was important for their complete recovery, and how it would help in them not falling ill with a more severe form of the disease. They understood (incompletely) that after a certain duration, they would no longer be infective—this resulted in them stopping medication since they started to also feel better and taking further treatment did not justify the costs incurred in the process.

The lack of awareness or understanding that influenced treatment was at the level of the individual taking treatment, and at levels of their family/community, and

unfortunately also at the healthcare level (especially those administering or supervising treatment).<sup>58 67</sup>

In many occasions, individuals were provided insufficient information, or information received from the public sector was *contradicted by those from the private sector* and others that were first points of contact in the community such as traditional healers.<sup>50 51 66</sup> A combination of difficulty in access and inability to meet requirements of the public TB control programme, lack of awareness, misinformation and contradicting messaging lead to people *accessing other avenues of treatment* either as their first option or after dropping out of their treatment and supervision plans from the public sector.<sup>45 50 51 55 60 62 66 67</sup>

**Subtheme 3.3: consequences of stigma and need for strong social supportive system**

*Stigma associated with those diagnosed with TB and the availability (or lack) of support*—at the family and at the community levels—*influenced how and where people accessed treatment and the extent to which they were able to continue and complete.*<sup>29 44–52 56–60 62 63 65 67</sup> A person’s ability to access treatment and complete its duration was *heavily helped by a supportive family setup* that was able to contribute financially, in-kind or with moral encouragement.<sup>29 44 46 56–59 63 64</sup> This was further strengthened by a

*supportive social network* which was devoid of stigma and was able to reinforce efforts by the health system, and the person’s family.<sup>63 64 66</sup> See [table 2](#) for an example.

**DISCUSSION**

We developed a conceptual framework in order to appreciate how the three overarching themes—pertaining to those taking treatment (‘patient related’), to those providing treatment (‘provider related’) and to the context in which the treatment is situated (‘structural’)—related to and influenced each other ([figure 2](#)). This framework enhanced our understanding of the issues underlying adherence in the subcontinent and highlighted why existing interventions targeting adherence may not be successful in addressing them. The key take-away from this synthesis was that taking treatment for TB was very complex and that in the absence of a ‘*patient-centred*’<sup>62</sup> approach, those taking treatment had to navigate several personal, professional, provider-related as well as sociocultural and structural challenges in order for them to ‘adhere’.

Several studies highlighted limitations of DOTS in improving adherence be it due to access issues, loss of daily wages, lack of medication availability, experience

Conceptual framework



**Figure 2** Conceptual framework for adherence to tuberculosis (TB) treatment. DOT, directly observed treatment.



with DOT providers or problems associated with confidentiality.<sup>45 46 57 61 62 69</sup> These issues were also reported by studies that evaluated newer interventions such as mobile reminders or 99DOTS<sup>58 68</sup> highlighting that barriers to adherence could not be overcome by technology alone<sup>21 23 68 70</sup> and that more patient-friendly options like family DOTS with increased flexibility were required.<sup>24 47 66</sup> The synthesis reiterated a previous warning that a '*strict universal application of DOTS can jeopardise effectiveness of TB control*'<sup>71</sup> and more importantly, proved as a reminder that a '*patient can be trusted*'.<sup>63</sup> The existing system's structure and rigidity in terms of performance outputs also lent itself to the issues related to patient-provider interactions and experience.

This synthesis also clarified and confirmed our understanding of structural barriers to treatment in the context of the Indian subcontinent with a specific emphasis on stigma.<sup>62</sup> 'Gender' played a dynamic role in almost all aspects reported in this synthesis. Health-seeking behaviour was poor among women compared with men. The stigma and discrimination faced by women was more severe compared with men. Families and parents were more concerned when it came to the women having TB,<sup>49</sup> highlighting the importance of focusing on socio-cultural aspects of the disease.<sup>29 72</sup> Marriageability often presented itself as a double-edged sword, wherein on one hand, it prompted improved adherence so as to get fit soon and thereby eligible for marriage, while on the other hand, this led to stigma and thereby trying to hide the disease status and hence leading to non-adherence to treatment. Some marriages resulted in separation due to TB and its treatment.<sup>48 49 65 73</sup> Self-stigmatisation was also more in the women in that they felt that their disease may affect their kids and family. All of these pointed to the need for adapting interventions in a more nuanced and sensitive manner, especially for women taking treatment. A recent study that specifically looked at barriers to treatment adherence in female patients reported that TB had the potential to push female patients who worked in informal arrangements to poverty, and that the COVID-19 pandemic had particularly exacerbated these consequences.<sup>74</sup> The authors of this study urged health systems to recast frontline TB interventions, including prioritising access and care to marginalised or vulnerable populations.

There are several strengths to this synthesis. The findings reported here reiterate those reported by previous qualitative synthesis in context of treatment adherence (TB or other diseases), therefore offering further validation. In addition to supporting findings from previous syntheses,<sup>28 32</sup> our report also highlights nuances around sociocultural issues specific to the Indian subcontinent that need to be accounted for with sensitivity.<sup>45 48–50 62 65 75–78</sup> The robust screening process ensured that only studies that addressed treatment adherence in sufficient depth with rich qualitative data were included. Importantly, this synthesis included data from those who had 'defaulted' from treatment, an important

voice and source of information for the topic. Insights gained from the perspective of those who could not adhere to treatment and presented in this synthesis were corroborated by recent studies including similar participants.<sup>79 80</sup> Studies from four of the seven countries in the Indian subcontinent were included—therefore the findings reported here are generalisable to this region, especially with studies from countries that were in the list of top 10 high-burden countries for TB and multidrug-resistant-TB. Importantly, studies included in this review were of the recent genre, that is, they were conducted after the revised TB control programme was introduced in India, and similar programmatic reforms were implemented in others. Therefore, questions addressed by the qualitative studies about interventions affecting adherence—why they were needed, what were the challenges in implementing them and how they were overcome, and finally the appropriateness of these interventions and their acceptability—are topical and relevant. Our rigorous qualitative assessment offers transparency to the readers on the strengths and limitations of the studies included in this synthesis, and consequently on any risk of bias in the interpretations presented and in conclusions drawn.

There are, however, some limitations to this work too. Given the large number of hits obtained from the search strategy, abstracts were divided between reviewers and initial screening was done by a single reviewer only (although a rigorous screening tool with prespecified study inclusion/exclusion criteria used to avoid any subjectivity, and reasons for exclusion clearly documented in the screening software). Also, the synthesis includes only publications in the English language, therefore possibly losing out on some additional insights offered by studies published in the vernacular.

Several recommendations can be suggested based on this review. TB programmes should be made accountable to those taking treatment, placing 'patient-centeredness' at their helm. Success measures should therefore additionally include qualitative indicators based on patient feedback, in support of achieving better quantitative indicators such as percentage adhered or defaulted, and therefore improved treatment outcomes. Similarly, interventions introduced to improve adherence should not be assessed purely on quantitative metrics but should be evaluated thoroughly for how they were enabling patients and providers access and deliver treatments in a better fashion that is, how they address underlying sociological challenges such as those highlighted in this synthesis. Importantly, a flexible, patient-friendly treatment structure needs to evolve—persons taking treatment may be given a 'menu' of options to select from ranging from conventional health-facility DOTS to family or community DOTS and opt for counselling arrangements that suit their social and cultural contexts and that is sensitive to the gender issues identified. The socio-economic and cultural context in which the treatment is taken is as important a factor to be considered as the individual limitations of the person undergoing treatment or those



of the provider administering. A cafeteria approach may therefore prove beneficial in improving adherence as well as outcomes to treatment.

At a larger level, public-private partnerships may be essential to deliver services around treatment such as supervision, support and counselling. Frequent and consistent awareness campaigns are required to improve knowledge at an individual as well as community level, and to reduce stigma. Social security schemes should be introduced that can be accessed by those affected by TB and their families to lessen the financial strains associated with taking treatment. These welfare schemes must consider the challenges and constraints faced by individuals and their families during treatment and in the period following. Persons on treatment should be made aware of existing social security schemes. Towards this, it would be critical for the TB control programme to work with other social welfare departments and ministries (eg, Women and Child Development) in order to maximise benefit as well as their reach in terms of the different demographics of patients with TB.

In summary, this review highlights several sociological issues that are faced by those taking treatment as well as those providing treatment in the Indian subcontinent and re-iterates that an inflexible approach to improve adherence will not work. Modifying health-seeking behaviour is no doubt necessary but is far from being sufficient in achieving treatment adherence and completion. Issues underlying adherence need to be understood and resolved at an individual level. It is imperative to also consider the healthcare provider perspective and requirements to achieve such an individualised, patient-centric approach in administering treatment. This evidence synthesis points to a much-needed paradigm shift in our approach to adherence. Political will and large-scale advocacy efforts will be required to mobilise actions that can address the gamut of challenges identified here.

#### Author affiliations

<sup>1</sup>Department of Community Medicine, Medical College Baroda, Baroda, Gujarat, India

<sup>2</sup>Research Division, Vital Strategies, Singapore

<sup>3</sup>TB Department, International Union Against Tuberculosis and Lung Disease (The Union), South East Asia Office, New Delhi, India

<sup>4</sup>Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK

<sup>5</sup>The Global Fund to Fight AIDS Tuberculosis and Malaria, Grand-Saconnex, Geneva, Switzerland

<sup>6</sup>National Tuberculosis Elimination Programme (NTEP), Central TB Division, India Ministry of Health and Family Welfare, New Delhi, India

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review. PG: definition of intellectual content, data analysis, manuscript preparation, manuscript editing, manuscript review. JT: concept, definition of intellectual content, manuscript review. RR: concept, definition of intellectual content, manuscript review. KS: concept, definition of intellectual content, manuscript review.

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#### ORCID iD

Kalpita Shringarpure <http://orcid.org/0000-0003-2203-9419>

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