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“ *You have to change your whole life* ”: a qualitative study of the dynamics of treatment adherence among adults with tuberculosis in the United Kingdom

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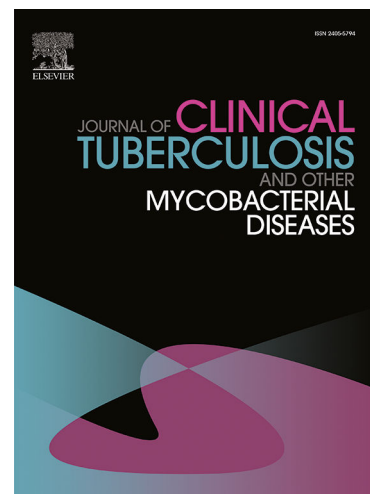
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1 ***“You have to change your whole life”:***
 2 **a qualitative study of the dynamics of treatment adherence among adults**
 3 **with tuberculosis in the United Kingdom**

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9 **Short title**

10 Dynamics of TB treatment adherence in the UK

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44 **Key words**

45 compliance; medication; outcomes; determinants; person-centred care; elimination

46

47 **Abstract**

48 Maintaining adherence to treatment for tuberculosis (TB) is essential if the disease is to be eliminated. As
49 part of formative research to develop an intervention to improve adherence, we documented the lived
50 experiences of adults receiving anti-TB treatment (ATT) in three UK cities and examined how personal, social,
51 and structural circumstances interacted to impact on individuals' adherence to treatment.

52 Using a topic guide that explored social circumstances and experiences of TB care, we conducted in-depth
53 interviews with 18 adults (six women) who were being or had been treated for TB (*patients*) and four adults
54 (all women) who were caring for a friend, relative, or partner being treated for TB (*caregivers*). We analysed
55 transcripts using an adapted framework method that classified factors affecting adherence as personal,
56 social, structural, health systems, or treatment-related.

57 Eleven of 18 patients were born outside the UK (in South, Central, and East Asia, and Eastern and Southern
58 Africa); among the seven who were UK-born, four were Black, Asian, or Minority Ethnic and three were
59 White British. TB and its treatment were often disruptive: in addition to debilitating symptoms and side
60 effects of ATT, participants faced job insecurity, unstable housing, stigma, social isolation, worsening mental
61 health, and damaged relationships. Those who had a strong support network, stable employment, a routine
62 that could easily be adapted, a trusting relationship with their TB team, and clear understanding of the need
63 for treatment reported finding it easier to adhere to ATT.

64 Changes in circumstances sometimes had dramatic effects on an individual's ability to take ATT; participants
65 described how the impact of certain acute events (e.g., the onset of side effects or fatigue, episodes of
66 stigmatisation, loss of income) were amplified by their timing or through their interaction with other
67 elements of the individual's life. We suggest that the dynamic and fluctuating nature of these factors
68 necessitates comprehensive and regular review of needs and potential problems, conducted before and
69 during ATT; this, coupled with supportive measures that consider (and seek to mitigate) the influence of
70 social and structural factors, may help improve adherence.

71 1. Introduction

72 Elimination of tuberculosis (TB) is a realistic prospect in low TB burden countries such as the United Kingdom
73 (UK), where incidence has declined from 15 per 100,000 population in 2011 to 8 per 100,000 in 2019.¹

74 Treating TB disease currently requires at least six months of daily therapy;^{2,3} non-adherence to anti-TB
75 therapy (ATT) worsens individual outcomes,⁴ increases the risk of drug-resistant TB (DR-TB),^{5,6} and may
76 prolong infectiousness.⁷ Optimising outcomes and maintaining adherence to treatment are essential if the
77 World Health Organization (WHO) 'pre-elimination' target of annual incidence <1 per 100,000 is to be
78 reached.^{8,9}

79 TB in the UK is predominantly present in people who are migrants,¹⁰ socioeconomically disadvantaged, or
80 both:^{11,12} 74% of people who developed TB in England in 2019 were born outside of the UK.¹³ Many
81 individuals diagnosed with TB in the UK also have so-called 'social risk factors' (SRFs: drug or alcohol misuse,
82 homelessness, or current or previous imprisonment). In 2019, 35% and 23% of people with TB who were
83 born in the UK and outside the UK, respectively, had at least one SRF.¹³

84 Formal adherence support for ATT in the UK is based on a standardised risk assessment conducted by a
85 specialist TB nurse (usually the individual's case manager) at treatment initiation. Individuals considered at
86 high risk of non-adherence are offered *enhanced case management*, which can include directly observed
87 therapy (DOT), video-observed therapy (VOT), and other forms of practical treatment support, such as a
88 weekly dosette box.¹⁴ Enhanced case management is offered most often to people with SRFs, though
89 individuals without recognised SRFs are also at risk of non-adherence: a study of nearly 13,000 people
90 treated for TB in London found that although the odds of non-adherence were highest in those with at least
91 one SRF, they were also high in some migrant communities, people who had previously had TB, those with
92 pulmonary disease, and those who were aged 16–24 years (versus those aged 25–34 years).¹⁵ Yet the
93 evidence around risk of non-adherence is inconclusive: a recent systematic review found that adherence to
94 treatment for DR-TB was no different in migrants and non-migrants (n = 8 studies, all in high-income
95 countries).¹⁶ Therefore, to focus supportive resources more efficiently on those with the greatest need (i.e.,

96 those most likely to have difficulty taking treatment), screening methods are required that categorise risk of
97 non-adherence by considering a wider range of criteria than simply 'static' demographics.

98 "Non-adherence" is a term that encompasses a spectrum of behaviours at various points throughout the
99 patient's journey and care pathway.¹⁷ The WHO's call for "*care and support, [that is] sensitive and responsive*
100 *to patients' educational, emotional and material needs*"¹⁸ reflects the increasing prominence of the
101 discussion around patient-centred care for TB,^{19–21} yet the most widely-used form of ATT adherence support,
102 DOT, has been criticised by patients as being inflexible and paternalistic; critics suggest that it seeks to
103 'enforce' treatment-taking, does not promote patient self-management, and focuses on pill-taking as the
104 defining feature of treatment adherence.^{22–25} Evidence-based, supportive approaches are needed that can
105 be adapted for use in all individuals starting ATT.

106 Globally, numerous qualitative studies have explored adherence to ATT: a 2007 systematic review by Munro
107 et al. synthesised qualitative data from 44 studies and classified the key determinants of adherence into four
108 categories: 1) *personal factors*, including knowledge and beliefs; 2) *structural factors*, including poverty,
109 gender, and law; 3) *social factors*, including family, community, and stigma; and 4) *health service-related*
110 *factors*, including the organisation of care and side effects.²⁶ However, assessing these dimensions as
111 distinct, though useful for analysis, risks over-simplification, as adherence behaviour is not constant²⁷ and
112 relationships between different dimensions can be dynamic and complex.²⁸

113 Despite these studies, there are few data available to help shape evidence-based, supportive approaches for
114 use across the highly diverse populations encountered in high-income, low incidence settings.^{29,30} The small
115 number of qualitative studies reporting on the experiences of individuals with TB in the UK have focused on
116 sub-populations living in extreme situations or within specific communities.^{31–34}

117 Using an adaptation of the Munro framework that includes greater consideration of the dynamic
118 relationships across different levels and types of determinants of adherence,²⁹ we conducted in-depth

119 interviews with a diverse group of adults receiving (and caring for those on) ATT in three cities in the UK. In
120 this analysis, we examine how individuals' experiences of the TB care trajectory, including their engagement
121 with the health system and their social networks, influenced how they felt about treatment and their ability
122 to take ATT. We use these data to map the relationships between and across factors that enabled and
123 impeded adherence to ATT and discuss the implications for assessing risk of non-adherence and intervening
124 to improve adherence.

125 **2. Methods**

126 Interviews were conducted from April to October 2019 as part of formative qualitative research for a study
127 seeking to develop, pilot, and evaluate an intervention to support patients taking ATT ("Intervening with a
128 Manualised Package to ACHieve treatment adherence in people with Tuberculosis" [IMPACT]).³⁵ Data from
129 qualitative interviews were used to shape the form and content of the intervention; all interviews were
130 conducted prior to the implementation of any part of the intervention.

131 **2.1. Sites of data collection**

132 Formative research was based in four National Health Service (NHS) Trusts: two in London and one each in
133 Edinburgh and Southampton; recruitment and interviews took place at eight physical sites across the three
134 cities. London overall has the highest TB incidence in the country, at 18.6 notifications per 100,000 in 2019;¹³
135 the two London Trusts involved in the study employed had slightly different modes of care, with, for
136 example, a dedicated social care team in one Trust, but not the other. Edinburgh (incidence 4.9 per 100,000
137 in 2018)³⁶ and Southampton (three-year average incidence 11.5 per 100,000)¹³ have fewer TB patients than
138 London and smaller dedicated services to deal with them. In both Trusts, people with TB are co-managed by
139 the Respiratory and Infectious Diseases teams, with two or three specialist TB nurses responsible for case
140 management.

141 2.2. Sampling and recruitment of participants

142 Adults (aged ≥ 18 years) who were taking or had taken ATT (*patients*) and adults who were caring for or had
143 cared for a friend, relative, or partner on ATT (*caregivers*) were asked to participate; formal inclusion and
144 exclusion criteria applied to patients and caregivers are described in Supplementary table 1. A purposive
145 sampling approach was adopted; it was attempted, throughout, to represent as fully as possible the wide
146 range of perspectives and backgrounds within the patient populations at each site. Further details of
147 recruitment and consent procedures are provided in Appendix 1.

148 2.3. Data collection

149 Interviews were conducted in confidential settings in hospitals or community health centres, often in
150 consultation rooms that also contained a workstation, examination couch, and sink. All interviews were
151 conducted in person, by one or two interviewers (one/two of ASK, KK, ASKJ, and MD), in English, and with
152 the help of a topic guide (Appendix 1) that covered the following topics: pathways to TB care; treatment
153 adherence issues; knowledge and perceptions of TB and treatment; adherence to ATT (experiences,
154 enablers, and barriers, and incidence of and reasons for non-adherence); social support; and structural and
155 health systems issues (interactions with and potential obstacles to care). During the interviewing process,
156 the lead interviewer (ASK) confirmed with each participant what was being said through short
157 summarisation at various points in the interview.

158 2.4. Data management and analysis

159 Interviews were audio recorded (using an Olympus DS-9500 [Olympus Corporation, Tokyo, Japan]), securely
160 encrypted, and transferred to a password-protected computer. Hand-written notes were scanned and
161 password protected, and the originals destroyed. Transcripts of interviews were used for analysis after being
162 checked for comprehensiveness and completeness.

163 Analysis was undertaken by ASK and KK (both of whom cross-checked transcripts, cross-checked themes
164 identified, and piloted the coding system) in a stepwise manner, using an adapted framework analysis
165 method. First, transcripts were read several times; narrative profiles of each patient were constructed that

166 included accounts of how patients presented themselves and their social networks; their TB diagnosis and
167 early experiences of care; and their experiences of being 'on treatment'. Attention was paid to the unique
168 trajectories of individuals and how demographic features such as gender, age, ethnicity, and social status
169 impacted on pathways to and experiences of care, and the effects of TB and ATT on their lives. Second, using
170 a conceptual framework of determinants of adherence derived from the systematic review by Munro et al.²⁶
171 and a previously described scoping review,²⁹ information was categorised from the profiles into a matrix to
172 compare and contrast data on the five key themes (personal, social, structural, health systems, and
173 treatment-related; Appendix 1) until theme saturation was reached. Third, the summarised information
174 allowed for the creation of separate files for each of the five thematic areas; retrieved data segments were
175 supplemented with information from the original transcripts and reviewed through a constant comparison
176 method to ensure that content and meaning of the themes were consistently applied.³⁷

177 To illustrate the ways in which various factors interacted with one another and the mechanisms by which
178 they might influence adherence behaviour, relationships between determinants and their potential effects
179 on an individual's ability to take ATT were mapped based on explicit descriptions by interviewees or through
180 inference by the authors after analysis of all interviews. Determinants were categorised as 'distal' when their
181 influence on adherence behaviour was indirect or mediated through intervening factors, or 'proximal' when
182 they exerted a more direct effect on adherence behaviour. Data were collated and analysed using NVivo
183 (v12, QSR International, Doncaster, Australia) and relationships were visually depicted using Vensim
184 (Ventana Systems UK; <https://www.ventanasystems.co.uk/>) and InkScape (<https://inkscape.org/>).

185 **2.5. Ethical considerations**

186 This study received approval from the Camberwell St Giles Ethics Committee (REC reference 18/LO/1818).
187 Written informed consent was obtained from each individual prior to data collection (further details in
188 Appendix 1). Pseudonyms are used in the manuscript to humanise accounts and quotes; no information that
189 could potentially identify a participant has been included.

190 **2.6. Funding**

191 This work was supported by the National Institute for Health Research (NIHR) Health Technology Assessment
192 Programme, UK grant number 16/88/06.

193 **3. Results**

194 **3.1. Participant characteristics**

195 Interviews were conducted with 18 patients and four caregivers. Participants varied widely in age,
196 ethnicity, migration status, level of education, profession, knowledge of TB, social support networks, disease
197 type and severity, experiences of treatment, adherence behaviour, and health literacy (Supplementary table
198 2).

199 Ages ranged from 20 to 65 years, but most participants were aged 20–35 years. The two youngest
200 individuals lived with their parents and siblings; others in their 20s and 30s had young children or lived alone.

201 Four of the six individuals aged 50 years or older had additional medical problems, including cancer and
202 depression. Two-thirds of patients were male; all four caregivers were female and had cared for a (male)
203 partner. Three patients were White British; four were born in the UK to Black and Asian families; and the
204 remaining 11 were migrants, originating from South, Central, and East Asia, and Eastern and Southern Africa.

205 TB disease severity varied widely and was not necessarily linked to age or comorbidities. One of the
206 youngest participants had disseminated, drug-resistant TB. Two participants had recurrent TB disease,
207 needing two courses of ATT in close succession, and another had re-started treatment several times (due to
208 non-adherence) and was waiting for surgery to address complications of TB. Other participants presented
209 with only neck swelling or experienced mild symptoms. Participants were at various stages of the treatment
210 journey at the time of interview: all had received at least three to four months of treatment and four
211 individuals had completed treatment a year or more prior to interview.

212 Six participants reported high levels of alcohol use, incarceration, emergency migration, or homelessness;
213 these individuals had usually been identified as ‘high risk’ for non-adherence soon after diagnosis and had

214 received some form of treatment support. Some patients who lived alone had parents available for support,
215 but others depended on employers, friends, and, in one case, a landlord. Three participants did not report
216 any strong social ties, and described interactions limited to colleagues or casual acquaintances.

217 **3.2. Lived experiences of illness and the care pathway**

218 **3.2.1. Symptom onset and entry into care**

219 *I coughed for probably, like, one, two weeks. ...I did some research online, it says it might be, you know,*
220 *even something like lung cancer. And I was so scared. I was so scared. I was so scared*
221 **– Zhen, a student in his 20s who lived alone and made several trips to his GP and to the Emergency**
222 **Department before he was diagnosed with TB.**

223 Experiences early in the treatment journey had lasting effects on individuals' attitude to their illness and
224 engagement with care. Care-seeking behaviour and the time taken to enter the TB care pathway were
225 influenced by disease severity and could be triggered by a dramatic event or acute deterioration in
226 wellbeing, but were also affected by the individual's priorities around their own health, which were
227 sometimes displaced by alcohol, insecure housing, or financial commitments; their sense of security (i.e.,
228 freedom to seek help); and their previous experiences of health care.

229 *...I started coughing blood. But I didn't take any notice. I said, '[inaudible], like, leave it'. And my sister*
230 *she's a nurse, she noticed that I'm losing weight, I'm not eating. She called the ambulance. I got to go to*
231 *[hospital], and they found I had TB.*
232 **– Yousuf, a patient in his 30s who consumed large amounts of alcohol and had been unwell for some**
233 **time before he sought care; he had persistent problems with adherence and developed DR-TB.**

234 The time between symptom onset and entry into care was often filled with anxiety, and participants
235 described feeling frightened and vulnerable. Delays sometimes occurred within the health system, through
236 early misdiagnosis or extended investigation. Some described losing trust in the system if a health care
237 provider (HCP) set expectations that were later not met.

238 *Yeah, so I didn't take it [the medication] - so that hospital, so eventually I moved out, so I wasn't there no*
 239 *more. And then I had to sign up in a new hospital, then start the whole, sort of, treatment again. (...) So I*
 240 *was there for about six months without taking no meds and knowing I've got TB.*

241 – **Eunice, a patient in her 20s who had spent time in prison and was living in social housing; she**
 242 **described a tenuous relationship with her TB team.**

243 The way an individual responded to diagnosis was shaped by their knowledge and beliefs about TB. These, in
 244 turn, were often tied to age, culture, class, country of origin, and previous knowledge of the disease. For
 245 example, some UK-born participants thought of TB as something of ‘the past’ or associated it with
 246 ‘foreigners’, whereas participants from high TB burden countries were more likely to consider it a disease of
 247 ‘the poor’ or of marginalised communities.

248 *...no one actually in my family, my relatives have ever been diagnosed with TB. So I was quite surprised*
 249 *when I was first diagnosed. It's like, back in [South Asian country], the number of reported cases are*
 250 *really high but then usually people who suffer from malnutrition, or belonging to, probably, not so well-*
 251 *to-do families, especially the nutrition part, would get affected, and that's how the illness was probably*
 252 *triggered.*

253 – **Rita, a patient in her 30s who moved to the UK to pursue her career.**

254 **3.2.2. Time on treatment**

255 **3.2.2.1. Relationships with immediate family**

256 By the time they started ATT, many individuals had depleted physical and emotional resources, having been
 257 through weeks of illness and investigation. For those whose lives were supported by ‘fragile’ infrastructure
 258 (tenuous relationships, insecure housing, or irregular employment), TB and its treatment were sometimes
 259 seen as additional burdens (“*a hell crisis*”) to be shouldered by both the patient and their family.

260 *TB medication being started last year in November I think - that was a horrible experience. So he has to*
 261 *leave his job because he couldn't cope, like you know he can't sleep. Every time he is feeling hungry, so*
 262 *he wants to eat something, he is getting up from that, so even I couldn't sleep sometimes. I went*
 263 *upstairs to sleep because I had to sleep - I can't break my sleep - I will get headache because I need to*
 264 *wake up early morning to drop my children.*

265 – **Jaya speaking about her husband Arif, who resigned from his job a short time after starting ATT,**
 266 **making her the family's main breadwinner.**

267 The existence of at least one stable, close relationship was important in allowing the patient to continue to
 268 function, often by relieving them of some of their normal responsibilities.

269 *She's been a rock, to be honest. She's... I could just share everything, you know what I mean - we don't*
 270 *hide anything from each other. If I come to any consultants or consultations, she comes with me. I prefer*
 271 *that because, as I say, I've got a bad memory, and she remembers everything.*

272 – **Alastair, a patient in his 50s, talking about his wife, Aileen**

273 *I always put on a face to Alastair and my family, and I don't think they realised how depressed I was*
 274 *after the cancer thing. But I know exactly - that's the - you know the worst thing, it's probably that I*
 275 *know how he's feeling, you know? (...) So that's helped him as well. I think if he hadn't been through that,*
 276 *I don't think he'd be coping.*

277 – **Aileen, Alastair's wife, speaking about her previous illness and how it helped with her husband's TB**
 278 **care**

279 In contrast, participants whose families were overseas felt the absence of a local support network acutely,
 280 and often felt conflicted about how much they could divulge to or ask from family who were far away.

281 *My folks back home didn't even know that I was diagnosed because I didn't want to upset them. (...) Both*
 282 *of my parents are pretty old, I didn't want to stress them out.*

283 – **Rita, who lived alone**

284 In some cases, the stability provided by relationships worked to counter the 'chaos' introduced by drugs or
 285 alcohol, or the disruption caused by multiple hospital visits. However, TB could also put strain on existing
 286 relationships (e.g., through stigma or changes in power relations), in some cases leading to lasting changes in
 287 their character.

288 *The first week I stayed at the hospital, my mum was like, 'Don't come home – you're full of TB, I don't*
 289 *want you to come home. I don't want to take care of you.'*

290 – **Janella, a patient in her 20s who became tearful recounting this experience.**

291 **3.2.2.2. Wider interactions**

292 Relationships beyond the immediate family were also important to many participants; for those without
 293 partners, social groups sometimes formed their primary support network, with friends stepping in to help
 294 with cooking, shopping, and other day-to-day tasks.

295 *They said to me, 'For the first two weeks, try to have as little contact with the general public.' (...) So I*
 296 *just phoned up one of my mates and said, 'Get us this from the shop, or whatever, and I'll sort out the*
 297 *money when you come up'. They'd do that.*

298 – **Michael, a patient in his 50s who lived alone but had a circle of close, supportive friends.**

299 Interactions with others could also prove difficult, and many patients experienced discrimination. Several
 300 participants did not disclose their diagnosis to their employers, and one even resigned without giving TB as a
 301 reason, hoping that this would boost his chances of re-employment once he recovered. Episodes of
 302 discrimination and rejection, even if fleeting, sometimes had substantial negative effects on individual's
 303 confidence and sense of identity.

304 *He offered me a job... He said, 'If you wanna come down, you can stay in the caravan on the holiday park*
 305 *and do a bit'. I said, 'I can't. Got TB'. (...) He said, 'You know, no one will touch you - if this gets out, that*
 306 *you've got it, then most firms... because you're public liability'. That's his attitude and mentality. If you're*
 307 *working with other people, then they'll all just, 'Oh, what happens if they catch it?'*

308 – **Michael describing a conversation with a previous employer that made him feel suicidal.**

309 **3.2.2.3. Health care professionals**

310 Relationships with HCPs were frequently cited as important to patients and caregivers, and the person with
 311 whom patients had the most contact was usually their TB case manager (a nurse) or DOT care worker. Trust
 312 in these relationships was strengthened by clear, easily accessible two-way communication (e.g., a phone
 313 number to use out of hours); early demonstrations of confidence and competence; a willingness to adapt,
 314 including flexibility in communication style and acknowledgment of difficult life circumstances; a sense of
 315 'completeness' of the information received; and collaborative decision-making.

316 *I think the nurses done really, really well here. They are on the ball and they get to know you and they*
 317 *know their patients and if someone is going to mess around with the tablets. They know who would be*
 318 *committed and who wouldn't, as they do get to know you on that level, which is - I can't fault the team*
 319 *here at all. (...) I've still got their numbers. They text, say 'How are you?'*

320 – **Naomi, a patient in her 50s who spoke to us a year after completing treatment.**

321 *Yeah, because couple of times I was running out the medicine and then I had to call her; when I called*
 322 *her she made sure that she got the medicine ready for me to come and pick it up. Basically what I think -*
 323 *they know what they're doing. That's it.*

324 – **Aalok, a patient in his 40s, describing his confidence in his TB nurses.**

325 Interactions with the health service could be challenging for participants with serious comorbidities, who
 326 sometimes received conflicting advice from different specialties, leading to a disjointed experience and
 327 mistrust. Previous experience of illness sometimes proved useful, providing pre-established medication
 328 routines or familiarity with the health system. However, for those who were unfamiliar with the system
 329 (usually migrants with no family support), obtaining adequate support could be an all-encompassing activity,
 330 requiring weeks of correspondence, multiple visits to relevant authorities, and, in some cases, legal action.
 331 These individuals often had to rely on assistance from members of their TB team.

332 *I don't blame the doctor or medical system - they are so kind. But I don't understand why they make*
 333 *problem with sickness person. Make hard, difficult, complicated. Like, I don't have energy to do that. I*
 334 *run to - they said, "Go to [institution]". I run to them, they say, "We don't do this, we don't do that." (...)*
 335 *Sometimes, when I pop in, they see my face - not English - they said, "Oh, we don't do this, we don't*
 336 *that." And they never ask, sit down, explain. And I went around, they say, "Go there!" I went there, they*
 337 *say, "Go this!"*

338 – **Suchin, a patient in her 60s who lived alone and received support from the TB social care team to**
 339 **fight her eviction in court**

340 **3.2.2.4. Routines**

341 An established routine or the ability to quickly adopt a new routine was described by some participants as
 342 'the secret' of adherence. This was more difficult for people with relatively unstructured lives, in uncertain
 343 housing situations, or with serious alcohol or drug habits. Some participants found the externally imposed

344 routine in hospital to be useful in building a treatment-taking habit. Though many found hospital isolating
 345 and alienating, it was seen by others as a respite from daily life, allowing time for reflection and rest.

346 *It wasn't terrible but it gives you a lot of time to think (...) You think you are going to lose your life, to be*
 347 *honest, so it's given me a bigger incentive to do more - but I was at my lowest point.*
 348 **– Naomi, describing the two months she spent in hospital at the start of her treatment.**

349 Even in those who managed to establish robust routines, the number of pills and associated side effects
 350 could make it difficult to maintain regularity. Many individuals developed 'adjunct' systems to help keep
 351 track of the different tablets, such as keeping a written log, organising them within a cupboard or box, or
 352 setting reminders.

353 *I think when I was first taking it, I didn't really fully understand, and some of my questions weren't*
 354 *answered properly. So, I had like a sheet with all the medicines that I'm supposed to have - I think that*
 355 *was kind of confusing. So what I did when I first got home, was I write it down myself, just to make it*
 356 *easy to understand.*
 357 **– Imran, a patient in his early 20s who lived with his parents and siblings**

358 Side effects could be debilitating, and for some participants occurred daily for several months. Patients often
 359 had to rearrange their lives around periods when they knew they would be "out of it".

360 *"It's so depressing. You're having to sit indoors for about four hours before - you're waiting for the*
 361 *person to come round with the tablets, and then, you know, you can't go out. Cos I don't want to be*
 362 *walking on the high street and vomit coming up - people will look at you, and next thing you know they*
 363 *get the police on you. So I'm like, 'No, I gotta wait until I feel right'. It's soul-destroying."*
 364 **– Michael, speaking about the effects of treatment, side effects, and DOT on his daily routine and**
 365 **mental state**

366 **3.3. Dynamic interactions and turning points in adherence behaviour**

367 Only a few of the processes, relationships, and events discussed above, particularly those with a more direct
 368 effect on adherence, fit cleanly into one of the 'personal', 'social', 'structural', 'health systems', or
 369 'treatment-related' categories, and often the combined effects of two or more factors (from different

370 spheres of an individual's life) were cited as influencing adherence-related behaviour. The dynamic nature of
371 these interactions was illustrated most clearly when participants described changes in circumstances that
372 occurred while they were taking ATT, and how 'ripples' from these events led to sometimes profound
373 changes in other aspects of their lives, including their ability to maintain a medication habit. Some changes
374 were more predictable, such as a latent alcohol habit that became more prominent a few months into
375 treatment, or employment that was already unstable but ended after starting treatment. Others were less
376 predictable, such as the loss of a foundational relationship (due to TB-related or other reasons) or, most
377 commonly, fluctuations and deteriorations in mental health. Several patients described feeling profoundly
378 anxious and depressed, sometimes suicidal, and some described dramatic changes in their personality or a
379 loss of identity after starting ATT.

380 *I was just so afraid that my heart will get something wrong. And [nurse] said, 'Do you have anxiety'?*
381 *Now I started to think about it - probably, because of all those kind of issues, I might have some level of*
382 *anxiety.*

383 **– Zhen, who described persistent anxiety about his health several months after completing ATT**

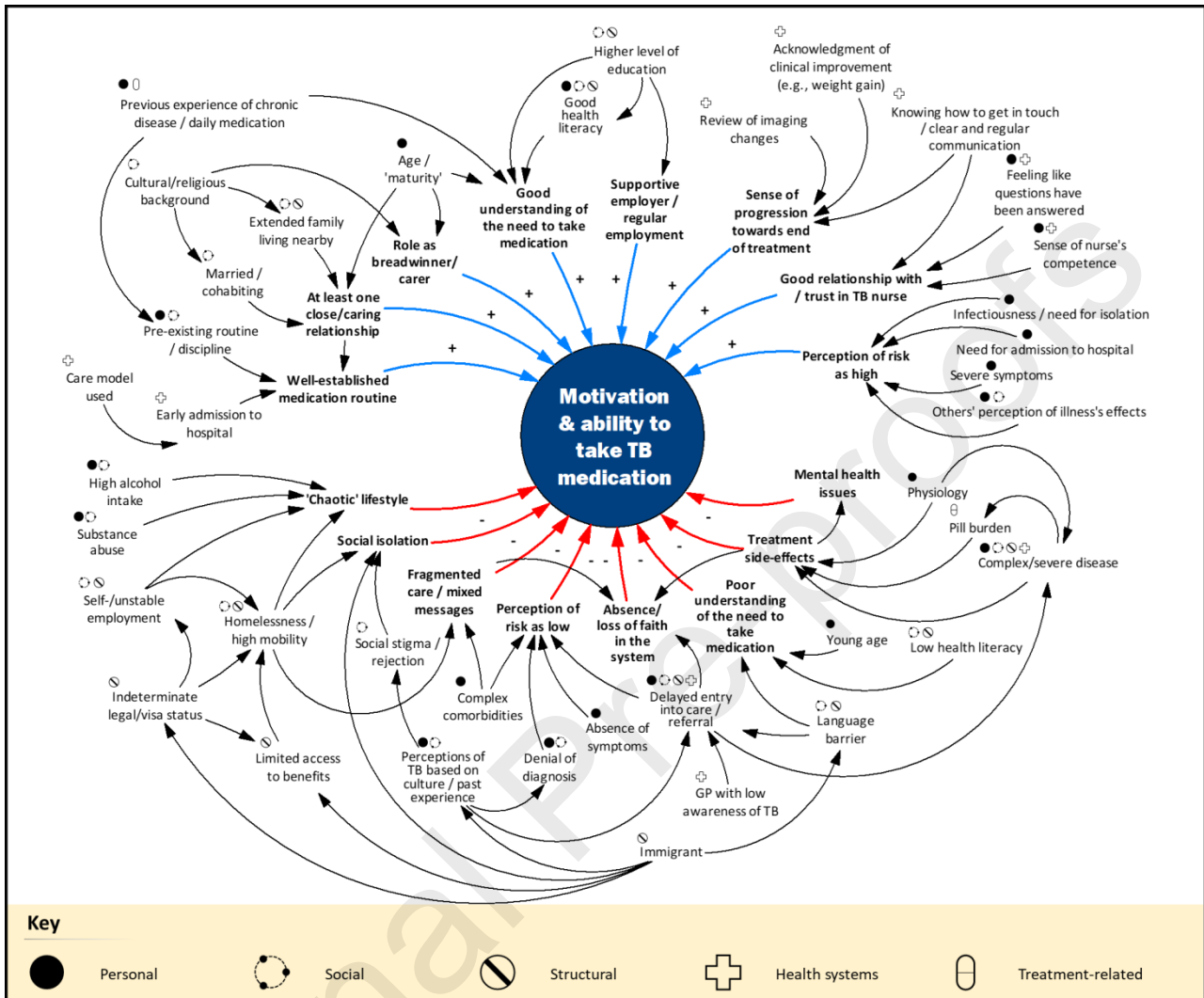
384 Changes could occur slowly over the course of illness, for example, a progressive increase in the amount of
385 alcohol consumed or a gradual reduction in mental wellbeing, or could be triggered by specific events or
386 phenomena, such as severe side effects (e.g., leading to a sudden deterioration in function or hospital
387 admission), pain, fatigue (such that someone who was previously able to work had to stop), social or physical
388 isolation, episodes of stigmatisation or rejection, eviction, a loss of income, or setbacks in treatment. For
389 example, one participant experienced worsening fatigue and side effects that meant he could no longer
390 work; unemployment then created financial pressure for his family and led to the re-emergence of a
391 previous alcohol habit, which strained relationships with his wife and children and worsened his previous
392 mild cognitive impairment, culminating in him stopping ATT entirely. Reduced mental wellbeing, in
393 particular, often put a strain on existing relationships, which in turn led to worsening anxiety, isolation, and
394 difficulties maintaining a treatment-taking routine.

395 *When I take the medication, four, five months, my behaviour also is changing... Other people are saying,*
396 *'What kind of behaviour are you doing?' ...I asked one of the colleagues, 'What happened? I don't know*
397 *what I am doing.' He told me, 'Your head is going crazy.'*

398 **– Gopal, a patient in his 30s who described a progressive loss of identity and confidence over several**
399 **months of treatment, to where he was reluctant to venture out of the house after dark.**

400 Using data from all individuals interviewed, Figure 1 illustrates some of the key factors identified and maps
401 their interactions and the mechanisms through which they might affect adherence. Sixteen 'proximal'
402 characteristics (eight 'positive' [top of the figure] and eight 'negative' [bottom of the figure]) were identified
403 that had a more direct effect on an individual's ability to take treatment: positive characteristics included an
404 ability to create and maintain a medication routine, the existence of at least one caring or close relationship,
405 and regular employment and/or a supportive employer; and negative characteristics included a 'chaotic'
406 lifestyle, fragmented care, and severe treatment side effects.

407 **Figure 1. Mechanisms* by which personal, social, structural, health systems, and treatment-related**
 408 **factors† influenced individuals' motivation and ability to take anti-TB treatment, based on interviews with**
 409 **18 patients and four caregivers**



410 'Positive' influences are depicted in the top half of the figure (blue arrows, '+' notation) and 'negative' influences in the
 411 bottom half (red arrows, '-' notation)

412 *Only key mechanisms have been included for clarity. Additional relationships are undoubtedly present but not
 413 represented.

414 †Although for some composite factors both the 'positive' and 'negative' are described explicitly (e.g., good
 415 understanding and poor understanding), the same holds true for most of the elements included in the figure. For
 416 example, the *absence* of a medication routine was likely to make it more difficult to take treatment, and *more*
 417 integrated (i.e., less fragmented) care was likely to make it easier to take treatment.

418 GP: general practitioner; TB: tuberculosis

420 4. Discussion

421 In three UK cities, we conducted in-depth interviews with 22 people who had taken or cared for someone
 422 taking ATT. TB and being 'on treatment' were often experienced as disruptive: in addition to debilitating
 423 symptoms, side effects, and stigma, many participants also had to balance income loss or reduction,

424 unstable housing, social isolation, worsening mental health, and damaged relationships. Those who had a
425 strong support network, stable employment, an adaptable routine, a trusting relationship with their TB
426 team, and clearly understood the need for treatment reported being more easily able to adhere to ATT,
427 whereas those with a 'chaotic' lifestyle, who were socially isolated, experienced severe side effects, or faced
428 structural barriers (such as language or recourse to public funds) reported finding it more difficult to adhere.

429 Based on these data, we frame adherence as a complex, dynamic phenomenon that spans a longer
430 timeframe than conventionally examined. Rather than focusing on static determinants or conceptualising
431 adherence as the act of taking or not taking pills as prescribed, we suggest the adoption of a relational view
432 (Arkelyan et al., in preparation) that sees an individual's life in the context of its complex social and
433 structural connections; recognises that health-related behaviour is intertwined with other aspects, such as
434 identity, community, and relationships; and allows for the examination of how medicine-taking patterns
435 reflect the temporal and socio-spatial fluctuations inherent to many individuals' experience of having TB and
436 receiving care. In exploring the mechanisms that may facilitate or impede adherence, we demonstrate the
437 extensive *potential* for non-adherence, even in people with so-called ordinary lives.

438 Experiences of social exclusion, the detrimental effects of reduced social support and stigma, and the
439 importance of routine were important themes in our data and were also highlighted by a 2015 study
440 conducted among mostly homeless individuals in London.³² Though our participants had fewer 'established'
441 risk factors for non-adherence than those in the 2015 study, many of the same issues were encountered by
442 people with more 'ordinary' lives, suggesting that these factors occur along a spectrum and defy simplistic
443 binary assessment (as does non-adherence itself).¹⁷ Two studies among African migrants in Sheffield (Somali
444 adults, 2013) and London (African adults, 2015) discussed experiences that were shared by many of our
445 participants, including frustration with the diagnostic process in primary care, difficulties in maintaining
446 relationships while receiving treatment, the positive effect of a supportive social network on adherence, and
447 the toll on mental health over the course of treatment.^{33,34} Similar themes were also identified by a recent
448 critical synthesis of barriers to TB care among migrants, which placed 'relationships' at the centre of a

449 theoretical model of experiences relating to adherence, with ‘cumulative vulnerability’ (the compounding of
450 difficulties faced by migrants across multiple systems), ‘acculturation’ (balancing one’s identity with
451 relationships with society), and ‘interpretations of illness’ (individual understanding of the disease and the
452 experience) exerting important effects on those relationships.³⁸

453 **4.1. Assessment and intervention**

454 In the absence of robust routine data on adherence,³⁹ there remains a need for consistent, widespread use
455 of contextually modifiable, nuanced methods to assess for the likelihood of non-adherence in every person
456 starting treatment for TB, as well as socially and culturally sensitive, sustainable approaches to support them
457 through treatment.⁴⁰ The current TB adherence landscape in the UK is encouraging: the need to ensure a
458 “high treatment completion rate” is part of the national TB strategy;⁴¹ most NHS Trusts follow the case
459 management model, where one specialist TB nurse coordinates an individual’s care from diagnosis to
460 discharge;¹⁴ and adherence policy (across conditions) is based loosely around the ‘Perceptions and
461 Practicalities’ (PAPA) framework, which considers individual motivation and ability, as well as a number of
462 intrinsic and extrinsic factors, to specify the ‘minimum ingredients’ of adherence support, targeted to the
463 needs of the patient.⁴² Although DOT remains the mainstay of adherence support in most Trusts, VOT⁴³ is
464 increasingly available, as are medication aids (e.g., dosette boxes) and a range of ‘softer’ measures, such as
465 occasional home visits or additional phone contact. However, our data suggest that despite the emphasis
466 placed by the health system on medicine-taking, for many people it remains only one aspect of being ‘on
467 treatment’ and may not be prioritised by those trying to balance numerous other issues. Some of the major
468 challenges faced by our participants (unstable housing and income, restricted access to common resources,
469 and social exclusion and isolation) are likely to affect a high proportion of those with TB in the UK, given the
470 disproportionate burden of disease in people who are migrants, socially deprived, or both.¹³ Although some
471 TB services (e.g., North Central London) have a dedicated ‘social care’ team to help respond to these
472 issues,⁴⁴ most do not, leading to disparities in the care available to patients in different parts of the country.

473 The need for including social support in TB care has been discussed for some time, particularly in lower
474 income settings,⁴⁵ but there is limited evidence available around the use of supportive interventions in
475 higher income settings upon which to base policy. A systematic review of psycho-emotional and socio-
476 economic support interventions for TB (which found an association between the use of these interventions
477 and better treatment outcomes) included only six studies from high income settings published between
478 1990 and 2015,⁴⁶ and in a scoping review we found that 70% of the included TB adherence interventions
479 targeted only one aspect of adherence, most often a personal or health systems component.²⁹ This is
480 partially reflective of the fragmented disciplinary assumptions about when, why, and how people take
481 medicines, resulting in the view that knowledge, beliefs, and practices around medicine-taking form the crux
482 of adherence (premised on a definition that centres on maintaining behaviour that meets HCP
483 recommendations),^{47,48} and that this is the domain most amenable to intervention. This is not restricted to
484 TB: a meta-analysis of theories underpinning adherence interventions (n = 124 studies across a range of
485 conditions) found that 65% were based around motivation, cognition, or beliefs,⁴⁹ and others have
486 suggested that interventions that do not consider wider influences on adherence or that target only one
487 aspect of behaviour are likely to be variably effective.⁵⁰

488 In considering approaches to intervention, it may help to conceptualise an individual's life as a complex
489 system,^{28,51-53} with the person at the centre and their actions framed in the context of the multiple,
490 relationships with their environment and the people around them. This would also allow us to describe the
491 introduction of disease and care into that system in energetic terms: complex systems require energy to
492 maintain their organisation or 'order',⁵⁴ and an approach that demands the taking of tablets at all costs (i.e.,
493 the imposition of 'rigid order')⁵⁵ will likely require the input of a large amount of energy from the patient,
494 their family, and/or the health system. This is particularly the case in patients whose lives are already
495 chaotic, or who have less robust support structures. A supportive approach that looks more broadly at the
496 'system' (i.e., the patient, their relationships, their environment), harnesses existing strengths, identifies

497 vulnerabilities, and focuses on improving capability, instead of concentrating interventions primarily on the
498 act of medicine-taking, is likely to be more efficient and therefore easier to scale and sustain.

499 In addition, if we consider the system to be 'adaptive' (that each element within the system has the
500 potential to change or evolve based on its interactions), every contact between patient and HCP then has
501 the potential to be an 'intervention'. Thus the act of risk assessment, if conducted in a way that engages the
502 patient in their own care, could itself reduce the risk of non-adherence by improving the individual's
503 awareness of their vulnerabilities and enabling collaborative strategies to be developed that can improve
504 treatment-taking ability. Critically, our data suggest that assessments should be repeated at regular intervals
505 throughout treatment to account for changes in circumstance or capability.

506 It is also important to state that many experienced clinicians, particularly specialist TB nurses, already work
507 in this patient-centred way, though this often requires them to go beyond what the health service expects
508 (or supports) them to do. If the universal standard of care for people with TB is to be truly "sensitive and
509 responsive"¹⁸ to their needs, we cannot rely on the compassion of individual HCPs, but must adopt person-
510 centredness throughout the health system.⁵⁶

511 **4.2. Limitations and strengths**

512 This study has limitations. Interviews were conducted in health care facilities by a medical doctor, which may
513 have influenced the information volunteered by participants, though this was not explicitly discussed with
514 participants, the interviewer was not involved in routine care provision, and one other non-clinician was
515 present for most interviews. Despite reassurances of anonymity, participants who were still receiving care
516 may have moderated their criticisms of the health service out of fear of repercussions. Individuals with DR-
517 TB are likely under-represented in our data, though many of the issues we discuss are likely to be relevant to
518 them, given the longer and more arduous treatment regimens. Interviews were conducted in English, and
519 some migrant experiences will not have been captured; however, many of our participants had limited
520 English and several described challenges around language and communication. Qualitative data were not

521 linked to empirical estimates of adherence in any of the patients interviewed and the designation of factors
522 as 'key determinants' as well as the relationships between factors depended on self-report by participants
523 and interpretation by authors. Our study also has strengths: participants were recruited from four NHS
524 Trusts in three cities, reflecting some of the variation in care models and resources available in different
525 parts of the country; and participants were not recruited from any particular risk group, and their common
526 experiences may be closer to those of the 'average' person treated for TB in the UK.

527 **5. Conclusions**

528 'Taking tablets' is only one aspect of treatment for TB. Supportive measures that are truly patient-centred
529 will need to be grounded in a deep, contextual understanding of patients' experiences of, views towards,
530 and behaviours associated with TB and its care. Improving adherence among all persons treated for TB, as
531 part of efforts towards elimination in low TB incidence countries, will require supportive approaches that
532 consider not only an individual's beliefs about TB and ATT, but also social and structural circumstances and
533 changes in them over time, and look to improve capability, rather than enforce medicine-taking. Policy and
534 guidelines need to acknowledge the need for regular assessment during treatment if we are to reduce non-
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544 The views expressed are those of the authors and not necessarily those of the National Health Service, UK,
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546 8. Declaration of interests

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565 engagement and patient support programmes to healthcare policy makers, providers, and industry.

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698 **“You have to change your whole life”: a qualitative study of the dynamics of treatment adherence among**
699 **adults with tuberculosis in the United Kingdom**

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701 Robert Horne, Heinke Kunst, Mike Mandelbaum, Ben G Marshall, Ceri McSparron, Ananna Rahman, Helen R Stagg, Jacqui White,
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703 **Ethical statement**

704 This study received approval from the Camberwell St Giles Ethics Committee (REC reference 18/LO/1818).
705 Written informed consent was obtained from each individual prior to data collection. Pseudonyms are used
706 to refer to participants; care has been taken to disclose no information that could reveal participants'
707 identities.

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