

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Patients' perspectives of tuberculosis treatment challenges and barriers to treatment adherence in Ukraine: A qualitative study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032027
Article Type:	Research
Date Submitted by the Author:	29-May-2019
Complete List of Authors:	Aibana, Omowunmi; University of Texas Health Science Center at Houston, Internal Medicine Dauria, Emily; University of California San Francisco, Psychiatry Kiriazova, Tetiana; Ukrainian Institute on Public Health Policy Makarenko, Olena; Ukrainian Institute on Public Health Policy Bachmaha, Mariya; PH Capital. Public Health Experts. Rybak, Natasha; The Miriam Hospital, Warren Alpert School of Medicine at Brown University, Infectious Diseases Flanigan, Timothy; The Miriam Hospital, Warren Alpert School of Medicine at Brown University, Infectious Diseases Petrenko, Vasyl; O O Bogomolets National Medical University, Phthiology (Tuberculosis) Becker, Anne ; Harvard Medical School, Department of Global Health and Social Medicine Murray, Megan; Harvard Medical School, Department of Global Health and Social Medicine
Keywords:	Tuberculosis < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES, QUALITATIVE RESEARCH

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **Patients' perspectives of tuberculosis treatment challenges and barriers to treatment**
4 **adherence in Ukraine: A qualitative study**
5
6
7

8 Omowunmi Aibana,¹ Emily Dauria,² Tetiana Kiriazova,³ Olena Makarenko,³ Mariya Bachmaha,⁴
9 Natasha Rybak,⁵ Timothy P. Flanigan,⁵ Vasyl Petrenko,⁶ Anne E. Becker,⁷ Megan B. Murray⁷
10

11 1 Department of Internal Medicine, McGovern Medical School at the University of Texas Health
12 Science Center, 6431 Fannin Street, MSB 1.122, Houston, Texas 77030, USA
13

14 2 Department of Psychiatry, University of California, San Francisco, 1001 Potrero Avenue
15 Room 7G21, San Francisco, CA 94110
16

17 3 Ukrainian Institute on Public Health Policy, 5 Mala Zhytomyrska Str., Office 61A, Kyiv 01001
18 Ukraine
19

20 4 PH Capital. Public Health Experts. 17 M. Zakrevskoho street, office 137, Kyiv 02217 Ukraine
21

22 5 Division of Infectious Diseases, The Miriam Hospital, Warren Alpert Medical School at
23 Brown University, 164 Summit Ave, Providence, Rhode Island 02906, USA
24

25 6 Department of Phthisiology (Tuberculosis), Bogomolets National Medical University, 13
26 Tarasa Shevchenka Boulevard, Kyiv 01601 Ukraine
27

28 7 Department of Global Health and Social Medicine, Harvard Medical School, 641 Huntington
29 Avenue, Boston, Massachusetts 02115, USA
30
31
32
33
34

35 **Corresponding Author**

36 Omowunmi Aibana, MD MPH
37 6431 Fannin Street, MSB 1.122
38 Houston, TX 77030
39 email: Omowunmi.aibana@uth.tmc.edu
40 Phone: 713 741 3918
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT

Objectives: To understand the challenges faced by tuberculosis (TB) patients and factors that influence TB treatment adherence in Ukraine.

Design: Qualitative Study

Setting: TB treatment facilities in Kyiv Oblast, Ukraine

Participants: Sixty adults who had undergone treatment for drug-sensitive TB between June 2012 and August 2015.

Methods: We conducted semi-structured, in-depth, individual interviews among a purposively selected clinical sample of patients previously treated for drug-sensitive TB. Interview content encompassed WHO's framework for barriers to adherence to long-term therapies and included questions about patients' preferences and motivators of treatment adherence. We examined treatment experience across strata defined by previously identified risk correlates of non-adherence.

Results: Among 60 participants, 19 (32.8%) were HIV-positive, 12 (20.3%) had substance use disorder, and 9 (15.0%) had not completed TB treatment. Participants described the financial toll of lost income during TB treatment, and this toll was exacerbated by the additional costs of ancillary medications and transportation to ambulatory TB clinics. Respondents discussed the psychological distress of long-term hospitalization and their associated depressed and anxious feelings during TB treatment. Participants also reported antagonistic interactions with TB providers as a challenge; in addition, high pill burden of TB treatment undermined adherence. These challenges were consistently endorsed among participants with and without major risk factors for non-adherence.

Conclusions: Our findings highlight critical barriers to TB treatment adherence in this study population and suggest specific interventions that may be beneficial in mitigating high rates of poor treatment outcomes for TB in Ukraine.

Strengths and limitations of this study

- There is increasing recognition that patient-centered approaches are crucial for successful implementation of TB programs.
- There are no published qualitative assessments of patients' experiences during TB treatment in Ukraine.
- To our knowledge, this represents the first qualitative study of TB patients' perspectives in Ukraine, highlighting opportunities to implement new patient-centered approaches as part of efforts to improve TB care in Ukraine.
- This study is limited by selective sampling of TB patients in only one region of Ukraine.

For peer review only

INTRODUCTION

Tuberculosis (TB) remains a significant global health problem with an estimated 10 million new cases diagnosed in 2017.[1] TB control is especially challenging in Eastern European countries like Ukraine, which has one of the highest burdens of multi-drug resistant TB (MDR-TB) worldwide with an estimated 28% of new TB cases being MDR.[2] Although Ukraine has adopted the World Health Organization (WHO) recommended Directly Observed Therapy Short-course (DOTS) program for TB management, the national treatment success rate for drug-sensitive TB (DSTB) in 2016 was 76%,[2] significantly less than the WHO recommended target of at least 90%:[3] and studies have reported MDR-TB treatment success rates below 25%.[4, 5]

Failure to complete TB treatment may result in poor patient outcomes, prolonged infectiousness and acquisition of drug resistance.[6-11] Previous studies have identified many patient-related risk factors for loss-to-follow up during treatment including unemployment, substance use disorder, and HIV.[12-23] Qualitative studies from diverse social settings across the economic spectrum have also described barriers to TB treatment adherence such as stigma, financial burden, inadequate TB knowledge, and treatment side effects.[18, 21, 24, 25] However, such qualitative evidence from Eastern Europe remains scarce.

Prior analyses of Ukraine's National TB Program (UNTP) have enumerated institutional and political barriers to successful DOTS implementation;[26-27] however, there are no published qualitative assessments of patients' experiences during TB treatment. Notably, the WHO highlights patient-centered approaches to TB care as a critical component of TB control efforts.[28] These approaches recognize patients as the principal figures in the care continuum and consider patients' personal and social circumstances in delivering care.[28]

We conducted a qualitative study exploring patients' experiences during TB treatment to identify patient perspectives regarding critical challenges and associated factors that influence TB treatment adherence in Ukraine.

METHODS

Ethics Statement

The study was approved by the Institutional Review Board at The Miriam Hospital, Lifespan, Providence, RI [204815 45CFR 46.110(7)] and the Research Ethics Committee at Bogomolets Medical University, Kyiv, Ukraine (No. 86). All participants provided written informed consent.

Study Setting

We conducted this study in the Kyiv Oblast, Ukraine where the notification rate for pulmonary TB in 2017 was approximately 79 per 100,000. Patients receive TB diagnostic evaluation and treatment free of charge according to UNTP guidelines.[29] All administrative regions of Ukraine have dedicated TB hospitals where, prior to 2014, all patients diagnosed with DSTB were admitted to receive two months of inpatient intensive phase therapy with four drugs (isoniazid, rifampin, pyrazinamide, ethambutol) followed by four months of outpatient therapy with two drugs (isoniazid and rifampin) daily. Although new guidelines disseminated in 2014 recommended complete outpatient management of DSTB,[29] many regions, including Kyiv

Oblast, continue to hospitalize patients for the initial two months of treatment. Guidelines further stipulate daily directly observed therapy in TB clinics during the outpatient phase of DSTB treatment. In Kyiv Oblast, some patients arrange to receive medication weekly to better accommodate their schedules.

Inclusion Criteria

Eligible participants included all adult patients (≥ 18 years) treated for DSTB in Kyiv Oblast between June 2012 and study initiation in August 2015. We excluded individuals younger than 18 years of age and those treated for drug-resistant TB because pediatric and resistant TB require different management protocols.

Sampling

From a literature review and preliminary quantitative analysis of Kyiv Oblast data, we identified HIV infection, alcohol use disorder, and substance use disorder as major determinants of loss-to-follow up during DSTB treatment. Therefore, we used a purposive sampling strategy to maximize variability regarding participants' HIV status and presence or absence of alcohol or substance use disorder. To achieve theme saturation, we aimed for 12 – 16 patients per stratum [30] for a total sample size of approximately 48 – 64. Within each stratum, we also attempted to purposively sample patients who had finished TB treatment and those who had not completed treatment in order to maximize the breadth of patient experience in enablers and barriers to treatment adherence. We did not pre-specify a target for patients who had not completed treatment because we anticipated they might be unreachable.

We reviewed 147 consecutive medical records from the Kyiv Oblast's Central TB Hospital to identify the first 80 eligible participants with available contact information. We operationalized substance use disorder (SUD) within the constraints of available data in the medical chart, which included either self-reported "high alcohol consumption" or intravenous drug use (IVDU) at the time of TB diagnosis. We ascertained HIV status and treatment outcomes from clinical records. TB providers, who were not study investigators, then contacted potential subjects to provide information about the study and request participation. Information provided to patients included study objectives and procedures and how results could potentially inform interventions to improve TB care. In order to reach the desired sample size for HIV and SUD strata, 11 additional eligible participants were identified from hospital records and invited for study participation to replace previously selected individuals with these characteristics who declined participation. We extracted additional demographic information from the medical records: age, sex, residence, and employment status.

Data Collection Procedures

A local research team of three members conducted in-person, semi-structured interviews in the Russian or Ukrainian language with study participants. Interviews were conducted according to patients' availability from August through October 2015 either at TB clinics or patients' preferred location. Participants were informed of their right to withdraw at any time before,

during or after data collection. Interviewers obtained written informed consent prior to beginning interviews, which lasted 45 to 60 minutes. Participants received telephone cards worth 3.50 USD upon interview completion. All interviews were audio recorded, transcribed verbatim, and translated into English by qualified translators independently from the interviewers.

We developed the interview guide content to align with the WHO framework for categorizing factors influencing adherence to long-term therapies into five dimensions: socio-economic, health system/health care team-related, therapy-related, patient-related, and condition-related factors.[31] (Table 1) Interview questions were open-ended and facilitated elaboration on this framework by exploring adherence motivators and patients' treatment preferences. We also included questions intended to capture patients' perceptions of their own adherence behavior and TB knowledge. Questions addressed patients' experiences during TB diagnosis as well as inpatient and outpatient phases of treatment (Supplementary Interview Guide). Interviewers asked follow-up questions when appropriate to elicit additional explanatory and experiential details. The semi-structured format was intended to encourage patients to speak broadly on their relevant experience.

Table 1. World Health Organization's five dimensions affecting adherence to long term therapy¹

Social- and economic-related	Characteristics related to the patient's economic and social position (e.g., poverty, illiteracy, education level)
Health care team- and system-related	Aspects of the system and group of individuals providing condition-related care for the individual (e.g., patient-provider relationship, medication distribution)
Therapy-related	Factors related to the treatment protocol (e.g., medical regimen, treatment length)
Patient-related	Resources, knowledge, attitudes, beliefs, perceptions, and expectations of the patient (e.g., self-efficacy), forgetfulness, psychosocial stressors
Condition-related	Particular illness-related demands faced by the patient (e.g., severity of symptoms, level of disability, rate of disease progression).

¹ Table adapted from content from World Health Organization (WHO) framework on adherence[31].

Data Analysis

We analyzed data to identify and examine thematic content corresponding to questions eliciting details within the aforementioned WHO framework[31] and additional relevant themes that emerged from participant narratives. The process began with familiarization by reading transcripts followed by identifying and operationalizing themes and subthemes and creating an initial codebook. To improve reliability and intercoder agreement, OA, ED and TK open coded

ten initial transcripts with subsequent comparison of coding patterns and revision of the codebook via consensus. We double-coded all interviews in a similar manner and refined the codebook throughout the analysis phase. We coded all transcripts using the finalized codebook and reconciled discordant codes via consensus. All transcripts text in coded segments were then reviewed with codes organized under major themes and subthemes identified from the data. To evaluate whether HIV and SUD were key drivers of treatment adherence, we examined the occurrence and frequency of themes and subthemes among respondents with HIV or SUD compared to respondents without these comorbidities. We separately compared themes based on participants' treatment completion status. Finally, we selected illustrative excerpts across strata to convey this content in the respondents' own words.

We used NVIVO 11 (QSR International, Cambridge, MA) to facilitate qualitative data analysis.

Patient and Public Involvement

Patients were not involved in development of the research questions, study design, interpretation of results or writing of the manuscript.

RESULTS

Among 91 eligible participants whom we attempted to contact, 60 (65.9%) agreed to participate, 16 (17.6%) declined, 12 (13.2%) could not be reached from available contact information, and 3 (3.3%) were unavailable for interview.

Table 2 lists demographic and clinical characteristics of study participants. Nineteen (32.8%) participants were HIV-positive and 12 (20.3%) had SUD; among HIV-positive participants, 6 (33.3%) had overlapping SUD. Nine (15.0%) individuals did not complete TB treatment and among them, one (11.1%) respectively had HIV and SUD.

Table 2. Demographic characteristics of study participants (N = 60)

	n (%) or mean (\pm SD)
Age	38.5 (\pm 12.4)
Male	42 (70.0)
Substance Use Disorder	
Intravenous drug use ¹	8 (13.5)
High Alcohol Consumption ¹	4 (6.8)
HIV-positive ²	19 (32.8)
Substance Use Disorder among HIV-positive ³	6 (33.3)
Marital Status	
Married or Live-in Partner	28 (46.7)
Single	15 (25.0)
Divorced	11 (18.3)
Widowed	6 (10.0)
Education	

Secondary	26 (43.3)
Secondary Specialized	20 (33.3)
College	14 (23.3)
Rural Residency	31 (51.7)
Unemployed	32 (53.3)
Did not complete TB treatment	9 (15.0)

1 N = 59

2 N = 58

3 N = 18

We organized the main themes identified as principal challenges faced by TB patients and factors influencing adherence to DSTB treatment according to the WHO framework for organizing barriers to long-term therapy adherence (Table 1). We also categorized themes related to facilitators of treatment adherence. We did not identify additional relevant themes that did not align with the WHO framework.

Socio-economic related factors

Financial cost of TB treatment

Although TB drugs are free in Ukraine, participants across our sampling strata and regardless of treatment completion status, discussed various dimensions of the aggregate economic toll of TB treatment. Over half of participants (N=36: 20 HIV-/no SUD, 16 HIV+/SUD; 30 completers, 6 non-completers) described a critical need for financial support, which they did not receive, during TB treatment. Generally, patients are unable to work while hospitalized during the intensive treatment phase. However, for 12 participants (5 HIV-/no SUD, 7 HIV+/SUD; 10 completers, 2 non-completers), the financial hardship of lost income was prolonged because they remained unemployed for the entire treatment duration.

Furthermore, whereas there is disability/sick leave pay in Ukraine, only six patients described successfully navigating the system to obtain it. Two notable barriers were lack of patients' awareness about such program and failure of healthcare providers to inform patients. One participant explained:

There are doctors who do not inform you that you can perform all paperwork and register for disability group at once, just after starting treatment, and then you will receive some small pension. [S-15: Male, 24, HIV-/no SUD, Incomplete treatment]

Over half of participants (N=37: 21 HIV-/no SUD, 16 HIV+/SUD; 30 completers, 7 non-completers) described how the financial toll of lost income was exacerbated by additional costs incurred during TB treatment. These included imaging tests and ancillary medicines such as "hepatoprotectors," which are commonly prescribed in Ukraine to mitigate the toxic effects of TB drugs on the liver. For example, a participant described the financial burden of these additional medications as follows:

The prices of the medicines [. . .] are cosmic, incredible. You can't make it. Well, at least there is help, when they give TB pills for free; that is good. But the rest of it - the medicines for the liver,

1
2
3 *vitamins – I bought those myself [. . .] The ones for the liver are especially expensive [. . .], all*
4 *this hit my pockets a little bit. [S-30: Male, 30, HIV-/no SUD, Completed treatment]*
5

6 Distance and transportation costs to TB treatment facilities represented another major challenge.
7 Trips lasted several hours and cost up to 100.00 UAH (approximately 4.00 USD) daily. A patient
8 summarized his journeys as follows:
9

10 *[. . .] It's faster to get to the United States than to [the TB clinic]. [Laughs]. Here, transportation*
11 *is the end. Two or three buses! And try to get on one of them! [S-40: Male, 56, HIV-/no SUD,*
12 *Completed treatment]*
13

14 Assuming trips for TB services once weekly, transportation would cost approximately 16 USD
15 monthly, which represents 26% of the average monthly income of 61.40 USD per rural
16 household in Ukraine in 2014.[32] Two participants explicitly related transportation costs to their
17 treatment non-adherence. When asked about reasons for incomplete outpatient treatment, one
18 interviewee responded:
19

20
21 *I didn't have money to get to the [TB clinic]. [When the doctor asked] Well I told him, I don't*
22 *have money now to come, I'm in such a crisis, that I don't have any money, nothing. [S-53: Male,*
23 *57, HIV-/no SUD, Incomplete treatment]*
24

25 Fourteen participants (10 HIV-/no SUD, 4 HIV+/SUD; 11 completers, 3 non-completers) further
26 described how the financial burden of TB negatively affected their family either because they
27 were primary income earners who were no longer able to provide for their families or had to rely
28 on relatives for financial support.
29

30
31 *Well, 7 months, roughly speaking, I was treated for 7 months. [. . .] I didn't work anywhere. My*
32 *wife, she [was] on maternity leave. It was really hard financially. [S-15: Male, 24, HIV-/no SUD,*
33 *Incomplete treatment]*
34

35 *[. . .] And, of course, it had an impact, because all the money that was supposed to go to the*
36 *household, it all went to the hospital. [. . .] And my sister had to pull this all alone. And it was*
37 *hard. [. . .] Of course, the disease affected us. Hard. [S-41: Female, 34, HIV+, Completed*
38 *treatment]*
39
40
41

42 **Health system and health-care team related factors**

43 Psychological impact of hospitalization

44 Participants, irrespective of comorbidities or treatment completion status, broadly articulated the
45 challenges of hospital-based care. For instance, twelve participants (8 HIV-/no SUD, 4
46 HIV+/SUD; 11 completers, 1 non-completer) described the inpatient experience as
47 psychologically difficult due to boredom and prolonged isolation from family. This invoked a
48 sense of alienation likened to imprisonment, even though patients could leave the hospital
49 anytime.
50
51
52

53
54 *[. . .] it was difficult to stay in the hospital. You feel there like [you are] incarcerated [. . .] You*
55 *want to break free from there, well... You cannot go anywhere... Everything is the same... It was*
56 *difficult mentally. [S-35: Male, 29, HIV-/no SUD, Completed treatment]*
57
58
59

[. . .] You are just sitting and waiting [in the hospital room.], You can just become crazy. [. . .] Just sitting at this cage. That's the worst. [. . .] [S-7: Male, 45, SUD, Completed treatment]

Hospital conditions

The physical state of the TB hospital further contributed to the psychological toll of hospitalization. Twenty-four respondents (17 HIV-/no SUD, 7 HIV+/SUD; 20 completers, 4 non-completers) detailed the dehumanizing nature of the hospital setting, describing it as dilapidated, unsanitary, and lacking basic amenities.

There is nothing comfortable there. [Sighs]. It's just not possible. Well, it's unhuman. For a normal person who lives in a normal home [. . .] When there are holes in the walls. There are cockroaches everywhere [. . .], the building itself and all that - it's just terrible! All these things shocked me. [S-12: Female, 46, HIV+, Completed treatment]

I got [to the hospital] in winter, and there was no shower room at all. I mean, there is the large room with the cold water, where it is impossible to take a shower [. . .] This is the hell-hole. [S-52: Male, 36, HIV-/no SUD, Completed treatment]

One participant discussed how these conditions might shape patients' willingness to successfully complete TB treatment:

The buildings were awful inside. Surely, it's not unimportant. You know, when you get in a building, where everything is clean and okay, you know, you really want to take care of yourself. And when everything is in bad condition, I can understand some men who tried to go somewhere [else]. Because, you see, even tuberculosis people must have good buildings after all. [S-22: Female, 62, HIV-/no SUD, Completed treatment]

Ten respondents (4 HIV-/no SUD, 6 HIV+/SUD; 8 completers, 2 non-completers) highlighted incidents of drinking in the hospital, seemingly without staff repercussions, and this contributed to the psychological distress of hospitalization.

At first there were moments [Laughs]. I even wanted to escape [pause] I thought I would not be able to bear all this. Because people really were drinking and doing all possible things [pause] Well, it was very difficult [pause] I remember it as a nightmare, not that much the disease treatment itself as these conditions. [S-12: Female, 46, HIV+, Completed treatment]

One respondent explicitly mentioned substance use on the wards as a contributing factor to interrupting hospital treatment, recounting that:

[. . .] There is such a mess. And these [pause] drug users. It was impossible there both during day and night! It was terrible. A mess, in a word. But you can do nothing [to change the condition] - they are required to provide treatment. [S-31: Female, 47, SUD, Incomplete treatment]

Healthcare provider attitudes

Patient interactions with TB care providers were widely identified across sampling strata as another aspect of TB treatment experienced as a challenge to adherence. Just over one-third

(N=23: 14 HIV-/no SUD, 9 HIV+/SUD; 19 completers, 4 non-completers) of participants characterized interactions as disrespectful, antagonistic, and lacking compassion.

There were terrible characters [TB providers], who did not like anybody, no matter what kind of a person you are [. . .] Yes, I would like to improve the attitude, so that the staff treated the patients more like humans [. . .] [S-35: Male, 29, HIV-/no SUD, Completed treatment]

Among these, seven participants (1 HIV-/no SUD, 6 HIV+/SUD; 6 completers, 1 non-completer) described harsh reactions from healthcare providers after interrupting treatment. Notably, the same respondent who stopped treatment due to the hospital conditions illustrated her experience as follows:

They berated me [. . .] because I had no right to [stop treatment]. To escape from the hospital, especially as I live among the people [. . .] They said if I do not go through treatment – just die if you want to [. . .] They said, "If you want to get treatment – get it. It is in your best interest. If you do not want to – why would you occupy the [hospital] bed for nothing? You only waste products, let other people take your place." [S-31: Female, 47, SUD, Incomplete treatment]

Therapy-related factors

Pill burden and side effects

Over half (N=33: 22 HIV-/no SUD, 11 HIV/SUD; 26 completers and 7 non-completers) of participants discussed the physical challenge of swallowing 8 to 20 pills at once during the two-month intensive treatment phase. The pill burden had a negative impact on patients' experience. One participant recalled:

You do not want to take them because the amount of medicines – this is the bunch [shows with his hands][. . .] If to put them into plastic glass, it is half a glass of tablets. And it is difficult even physically to take them [at once]. Not speaking about moral difficulties. When a human sees such a number of pills for the first time, he is shocked. [. . .] It is terrible, it burns, it is unpleasant. You do not want to take them all the time. [S-52: Male, 36, HIV-/no SUD, Completed treatment]

Whereas participants widely described various TB treatment side effects, only one respondent discussed how providers' inattention to side effects was a barrier to adherence.

Patient-related factors

TB Knowledge

Respondents across our sampling strata expressed an adequate understanding of TB disease. However, whereas a majority of respondents (N=42: 25 HIV-/no SUD, 17 HIV+/SUD; 37 completers, 5 non-completers) knew that TB was transmitted via airborne droplets, many (N=20: 12 HIV-/no SUD, 8 HIV+/SUD; 17 completers, 3 non-completers) also erroneously believed TB transmission occurred via contact with bodily fluids. One participant exemplified this misconception by stating:

There are possible options that [TB] is transmitted through blood. Definitely. I suspect that it is also possible that it's sexually transmitted; if it's transmitted by airborne droplets, then why can't it be sexually transmitted as well. [S-6: Female, 37, HIV+, Completed treatment]

We found no discernible link between participants' misunderstanding of TB transmission and treatment non-adherence.

In addition, many participants (N=26: 15 HIV-/no SUD, 9 HIV+/SUD; 22 completers, 4 non-completers) conveyed their understanding that missing doses of TB medications could decrease treatment effectiveness or lead to acquisition of resistance. Only one patient expressed this was a motivator of treatment adherence.

I did not have any idea not to take pills. The doctor told me that if I did not take pills, the body would produce resistance to these pills, and the [treatment] would no longer work if I missed at least once. And I did not need this. I wanted effective treatment. [S-23: Male, 32, HIV+, SUD, Completed treatment]

Psychological state

Nineteen participants (13 HIV-/no SUD, 6 HIV+/SUD; 16 completers, 3 non-completers) broadly characterized their experience as psychologically difficult with eleven (7 HIV-/no SUD, 4 HIV+/SUD; 9 completers, 2 non-completers) specifying they experienced feelings of depression and anxiety. These feelings were largely associated with the TB diagnosis and often rooted in patients' fear for their own morbidity but were not clearly linked to treatment adherence.

As [with] every disease, it is some kind of stress for a person. More than that, it's not a flu, it's much more serious disease. Of course, psychologically it was hard. [S-48: Male, 48, HIV-/no SUD, Completed treatment]

Forgetfulness

Eight participants, all of whom completed treatment, (5 HIV-/no SUD, 3 HIV+/SUD) described instances of forgetting to take the pills amidst their daily routines. For example, a respondent explained:

I missed doses a little bit after the hospital. Because of my own fault. Sometimes simply - there was no time, I was busy [. . .] [S-47: Male, 18, HIV-/no SUD, Completed treatment]

Alcohol consumption

Four respondents with comorbid HIV or SUD (3 completers, 1 non-completer) described alcohol consumption as an individual-level factor that contributed to missed treatment doses. One participant disclosed:

[. . .] Well, honestly speaking, [. . .] my friends came to visit me [pause] I took [alcohol] with them and did not want to take the medicines [. . .] [I] did not take the pills. [S-60: Female, 33, SUD, Completed treatment]

Condition-related factors

TB-associated stigma

Participants across our comparison groups regarded TB as a shameful disease that only afflicts certain marginalized populations who engage in socially unacceptable behaviors (e.g. injection drug users and prisoners). Twelve participants (9 HIV-/no SUD, 3 HIV+/SUD; 10 completers, 2 non-completers) discussed how the perceived stigma associated with TB led to self-imposed withdrawal and isolation from social networks.

I thought that the people's attitude would change. [. . .] I have some friends who did not know but suspected that it may be [TB]. When I was at hospital, [. . .] I bought the new phone number that only my family knew [. . .]. [S-13: Male, 28, HIV-/no SUD, Completed treatment]

Other respondents (N=12: 8 HIV-/no SUD, 4 HIV+/SUD; 9 completers, 3 non-completers) described instances of feeling stigmatized and rejected by friends and family after disclosing their TB diagnosis. One participant described how his fear of rejection led him to attempt self-treatment after TB diagnosis.

[. . .] I just made a decision, because, well, I knew that this thing [TB] will pop up and everyone will abandon me. So, after all I decided to try [treatment] on my own, got into the Internet, found out how everything's done. [. . .] [S-37: Male, 37, HIV+, Completed treatment]

Facilitators of treatment adherence

When asked about motivation for continuing treatment, many participants (N=32: 19 HIV-/no SUD, 13 HIV+/SUD; 27 completers, 5 non-completers) described a desire to recover or stay healthy/alive, and some (N=12: 6 HIV-/no SUD, 6 HIV+/SUD; 11 completers, 1 non-completer) articulated their understanding of treatment necessity.

I had to overcome this crisis; it was necessary to be treated [. . .], otherwise – death. I had to get myself together, that's it. And this helped [. . .] [S-55: Male, 35, HIV-/no SUD, Completed treatment]

Only one respondent highlighted encouragement from providers as a facilitator of adherence.

Yes, the regimen. For me it's very hard [. . .] But thanks to the doctors, [. . .] they were coming, they were asking me – “did you take your pills?” And that's why I did not skip. [S-27: Female, 32, HIV+, SUD, Completed treatment]

Participants suggested various things that might have mitigated their negative treatment experience. Twenty-seven respondents (14 HIV-/no SUD, 13 HIV+/SUD; 24 completers, 3 non-completers) preferred the comfort of home-based treatment.

Well, everything is easier at home [. . .] Hospital is a hospital – everyone is sick there, and it's better to recover at home, with the family [. . .]. [S-2: Male, 43, SUD, Completed treatment]

Although psycho-emotional support was not routinely available, respondents (N=21: 13 HIV-/no SUD, 8 HIV+/SUD; 19 completers, 2 non-completers) broadly expressed an important need for such support, particularly during hospitalization.

1
2
3 *[. . .] psychological support, [. . .] is necessary by 100%. [In the TB hospital] it is very difficult*
4 *without it. If to remember, there is no one in the ward to speak to [pause] As you do not know*
5 *anyone [. . .] [S-13: Male, 28, HIV-/no SUD, Completed treatment]*
6
7
8

9 DISCUSSION

10
11 We identified the economic burden of TB, psychological toll of hospitalization, negative
12 healthcare provider attitudes, and treatment pill burden as prominent challenges faced by patients
13 treated for drug-sensitive TB in Ukraine. These challenges emerged as factors that undermine
14 treatment adherence and are consistent with identified adherence barriers in other social contexts,
15 thus suggesting that interventions implemented successfully elsewhere would be appropriate for
16 consideration in Ukraine. We also found commonalities in the challenges faced by TB patients
17 with and without risk factors for non-adherence. Hence, interventions to improve TB care in
18 Ukraine will likely have a broad impact on all TB patients.
19

20
21 First, there is a need for financial support for TB patients. Poverty is a risk factor for TB disease,
22 and TB treatment exacerbates existing financial hardships and impairs treatment adherence.[24,
23 25, 33-35] Studies have shown that cash transfers, and assistance with food and transport can
24 increase treatment success rates.[36, 37]. Recent evidence from Ukraine has demonstrated the
25 success of a pilot intervention of socio-economic support in reducing risk of loss-to-follow up
26 among high-risk TB patients.[38] Thus, scale-up of such programs can be considered in Ukraine.
27 Efforts to alleviate the financial consequences of TB in Ukraine can also focus on raising
28 awareness to increase access to existing sick/disability pay. We also note evidence from chronic
29 diseases, including HIV, indicate peer support groups can promote positive behaviors necessary
30 for retention in care.[31, 39, 40] Hence, in addition to direct economic support, establishing
31 social support networks using community members may represent a low-cost intervention that
32 could increase adherence to TB treatment in Ukraine.[31]
33
34
35
36

37 Participants described psychological distress associated with TB diagnosis, and many voiced
38 their desire for psychological support during treatment. Studies have similarly found high
39 prevalence of depression and anxiety among TB patients;[25, 41, 42] such negative emotional
40 states contribute to non-adherence.[43, 44] At the same time, treatment of psychiatric
41 comorbidities increases TB treatment adherence[41], and psychosocial support improves
42 treatment success rates.[37] Given TB diagnosis itself might render patients emotionally
43 distraught, integration of psycho-emotional care with TB treatment in Ukraine might help
44 patients better confront the challenges that undermine adherence. We further identified
45 hospitalization as a contributing source of emotional distress, and many participants expressed a
46 preference for home-based treatment. Prior analysis of UNTP have concluded that hospital-based
47 TB care contributes to poor outcomes[27] and the latest UNTP guidelines recommend outpatient
48 management of DSTB.[29] Ongoing reorganization of TB care in Ukraine will provide
49 opportunities to assess how full-scale implementation of home-based DSTB treatment influences
50 treatment outcomes.
51
52
53
54
55
56
57
58
59
60

We found that many TB patients reported strikingly negative provider attitudes. Studies have shown poor patient-provider interactions contribute to TB treatment non-adherence.[42, 44, 45] There is also ample evidence that patient-provider relationships characterized by trust and shared decision-making facilitate adherence to chronic disease therapy.[46-48] Raising awareness among TB providers about how patient-centered communication influences adherence should be a priority for TB control efforts in Ukraine. Given the psychological difficulties associated with TB, more supportive attitudes from providers might improve patients' willingness to remain in care. Targeted provider training on effective strategies (e.g. establishing reminder systems) that promote TB treatment adherence [37, 49] might also be useful in this setting.

Furthermore, we and others have found that pill burden represent an important barrier to TB treatment adherence.[18, 42] As fixed-dose combination (FDC) pills reduce TB treatment pill burden, the WHO recognizes higher patient satisfaction as an advantage of FDCs and recommend their use in TB programs.[50] Procurement of FDCs in Ukraine might improve patients' experience with TB treatment. We also note the lack of evidence supporting the benefit of hepatoprotective agents with TB therapy.[51] Their ongoing use in Ukraine adds to TB treatment pill burden and increases patients' expenses without a clear benefit.

Among individual-level factors assessed, we did not identify health literacy as a principal driver of adherence in this context, despite some evidence that low TB knowledge adversely affects treatment adherence.[21] We found low knowledge about TB transmission modes though could not directly link this to treatment adherence. Many participants also acknowledged the negative consequences of missing TB treatment doses, but this did not emerge as a main facilitator of treatment adherence.

Notably, we did not identify themes that distinguish non-completers nor illuminate unique reasons for incomplete treatment. Whereas certain factors, such as treatment cost and pill burden, were identified as barriers in majority of non-completers (7 of 9 for each), these factors were also identified by approximately half of completers. Indeed, each barrier to adherence identified affected both completers and non-completers. While participants were largely motivated to undergo treatment to remain healthy, we identified few facilitators of TB treatment adherence. Our findings suggest that TB patients, with and without risk factors for non-adherence, broadly encounter structural challenges within Ukraine's TB care delivery system that undercut their motivation for adherence.

Our study has notable limitations. It is possible our interviewers or interview guide did not sufficiently probe how patients' TB knowledge influence treatment adherence. We focused only on patients' perspectives about TB treatment without exploring providers' viewpoints. Future research efforts can investigate providers' experience to elucidate additional factors that influence TB treatment adherence in this context. Our study sample was purposively selected for maximal variation in factors known to impact TB treatment adherence within only one region of Ukraine and thus may not be representative of the full spectrum of TB patients in Ukraine or of patients who receive care from private providers. Nonetheless, we believe that our study sample represents a substantial portion of the TB patient population, including those at particular risk for

1
2
3 poor outcomes, and thus can inform approaches to support treatment adherence that are widely
4 applicable.
5
6
7

8 **Conclusion**

9

10 We document the first qualitative assessment of patients' experiences during TB treatment in
11 Ukraine and identify targets for interventions that may improve TB treatment outcomes.
12 Challenges that undermine treatment adherence were not unique to patients at highest risk for
13 non-adherence, thus incorporating patient-centered approaches into TB control efforts will likely
14 have a broad impact in Ukraine.
15
16
17

18 **Acknowledgements**

19

20 The authors are grateful to all the participating patients and TB staff in Kyiv Oblast. We also
21 wish to thank the interviewers, Olena Zublenko, Svitlana Gatchenko, and Oleg Kurdin, for their
22 contribution.
23

24 **Contributors:** MBM, OA, AEB, and TPF led the study design. VP oversaw acquisition of data
25 in conjunction with OA, TK, OM, MB, and NR. OA, ED and TK conducted analysis and
26 interpretation of data with supervision by AEB. OA and ED wrote the first draft of the
27 manuscript, and all authors contributed to revision of manuscript for important intellectual
28 content. All authors had full access to all of the data in the study and can take responsibility for
29 the integrity of the data and the accuracy of the data analysis.
30
31

32 **Funding:** This work was supported by the National Institute on Drug Abuse (NIDA)
33 [T32DA013911 to OA and ED; R25DA037190-04 to ED] and The National Institute of Mental
34 Health, The Brown Initiative in HIV and AIDS Clinical Research for Minority Communities
35 [R25MH083620 to OA]. The funding sources had no role in the study design, in the collection,
36 analysis, and interpretation of data, in the writing of the report or in the decision to submit the
37 manuscript for publication.
38
39

40 **Competing Interests:** None declared.
41
42

43 **Data sharing:** Given the sensitive nature of this qualitative research and the possibility of
44 identifying respondents, we are not able to make raw interview transcripts available in a public
45 repository. However, we are willing to make portions of translated transcripts (with any
46 identifying information redacted) available upon reasonable request. Interested persons should
47 contact the corresponding author.
48
49

50 The Submitting Author accepts and understands that any supply made under these terms is made
51 by BMJ to the Submitting Author unless you are acting as an employee on behalf of your
52 employer or a postgraduate student of an affiliated institution which is paying any applicable
53 article publishing charge ("APC") for Open Access articles. Where the Submitting Author
54 wishes to make the Work available on an Open Access basis (and intends to pay the relevant
55
56
57

1
2
3 APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence
4 – details of these licences and which Creative Commons licence will apply to this Work are set
5 out in our licence referred to above.
6
7
8

9 REFERENCES

- 10
11 1 World Health Organization. Global Tuberculosis Report 2018.
12 http://www.who.int/tb/publications/global_report/en/ (accessed 5 Mar 2019).
13
14 2 World Health Organization. Tuberculosis Country Profiles.
15 <http://www.who.int/tb/country/data/profiles/en/> (accessed 5 Mar 2019).
16
17 3 World Health Organization. The END TB Strategy. Global strategy and targets for tuberculosis
18 prevention, care and control after 2015.
19 https://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1 (accessed 5 Mar 2019).
20
21 4 Lytvynenko N, Cherenko S, Feshchenko Y, et al. Management of multi- and extensively drug-
22 resistant tuberculosis in Ukraine: how well are we doing? *Public Health*
23 *Action* 2014;4Suppl2:67–72.
24
25 5 Aibana O, Bachmaha M, Krasiuk V, et al. Risk factors for poor multidrug-resistant
26 tuberculosis treatment outcomes in Kyiv Oblast, Ukraine. *BMC Infect Dis* 2017;17(1):129.
27
28 6 Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of
29 drug resistance and relapse in tuberculosis. *N Engl J Med* 1994;330:1179–84.
30
31 7 Pablos-Mendez A, Knirsch CA, et al. Nonadherence in tuberculosis treatment: predictors and
32 consequences in New York City. *Am J Med* 1997;102:164–70.
33
34 8 Kolappan C, Subramani R, Karunakaran K, et al. Mortality of tuberculosis patients in Chennai,
35 India. *Bull World Health Organ* 2006;84:555–560.
36
37 9 Burman WJ, Cohn DL, Rietmeijer CA, et al. Noncompliance with directly observed therapy
38 for tuberculosis. Epidemiology and effect on the outcome of treatment. *Chest* 1997;111:1168–73.
39
40 10 Gelmanova IY, Keshavjee S, Golubchikova VT, et al. Barriers to successful tuberculosis
41 treatment in Tomsk, Russian Federation: non-adherence, default and the acquisition of multidrug
42 resistance. *Bull World Health Organ* 2007;85:703–711.
43
44 11 Franke MF, Appleton SC, Bayona J, et al. Risk factors and mortality associated with default
45 from multidrug-resistant tuberculosis treatment. *Clin Infect Dis* 2008;46:1844–1851.
46
47 12 Mishra P, Hansen EH, Sabroe S, et al. Socio-economic status and adherence to tuberculosis
48 treatment: a case-control study in a district of Nepal. *Int J Tuberc Lung Dis* 2005;9(10):1134–9.
49
50 13 Kliiman K, Altraja A. Predictors and mortality associated with treatment default in pulmonary
51 tuberculosis. *Int J Tuberc Lung Dis* 2010;14(4):454–63.
52
53
54
55
56
57
58
59
60

- 14 Jakubowiak WM, Bogorodskaya EM, Borisov SE, et al. Risk factors associated with default among new pulmonary TB patients and social support in six Russian regions. *Int J Tuberc Lung Dis* 2007;11(1):46–53.
- 15 Hasker E, Khodjikhonov M, Usarova S, et al. Default from tuberculosis treatment in Tashkent, Uzbekistan; who are these defaulters and why do they default? *BMC Infect Dis* 2008;8:97.
- 16 Mitruka K, Winston CA, Navin TR. Predictors of failure in timely tuberculosis treatment completion, United States. *Int J Tuberc Lung Dis* 2012;16(8):1075–82.
- 17 Jenkins HE, Ciobanu A, Plesca V, et al. Risk factors and timing of default from treatment for non-multidrug-resistant tuberculosis in Moldova. *Int J Tuberc Lung Dis* 2013;17(3):373–80.
- 18 Amuha MG, Kutuyabami P, Kitutu FE, et al. Non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara Hospital Uganda: prevalence and associated factors. *Afr Health Sci* 2009;9Suppl1:S8–15.
- 19 Caylà JA, Rodrigo T, Ruiz-Manzano J, et al. Tuberculosis treatment adherence and fatality in Spain. *Respir Res.* 2009;10:121.
- 20 Bhagat VM, Gattani PL. Factors affecting tuberculosis retreatment defaults in Nanded, India. *Southeast Asian J Trop Med Public Health* 2010;41(5):1153–7.
- 21 Muture BN, Keraka MN, Kimuu PK, et al. Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: a case control study. *BMC Public Health* 2011;11(1):696.
- 22 Burton NT, Forson A, Lurie MN, et al. Factors associated with mortality and default among patients with tuberculosis attending a teaching hospital clinic in Accra, Ghana. *Trans R Soc Trop Med Hyg* 2011;105(12):675–82.
- 23 Ifebunandu NA, Ukwaja KN. Tuberculosis treatment default in a large tertiary care hospital in urban Nigeria: prevalence, trend, timing and predictors. *J Infect Public Health* 2012;5(5):340–5.
- 24 Munro SA, Lewin SA, Smith HJ, et al. Patient adherence to tuberculosis treatment: A systematic review of qualitative research. *PLoS Med* 2007;4:e238.
- 25 Lohiniva AL, Mokhtar A, Azer A, et al. Qualitative interviews with non-national tuberculosis patients in Cairo, Egypt: understanding the financial and social cost of treatment adherence. *Health Soc Care Community* 2016;24(6):e164–e172.
- 26 Atun R, Olynyk I. Resistance to implementing policy change: the case of Ukraine. *Bull World Health Organ* 2008;86(2):147–54.
- 27 World Health Organization, Regional Office for Europe. Review of the National Tuberculosis Programme in Ukraine 10-22 October 2010.

1
2
3 [http://www.euro.who.int/en/countries/ukraine/publications3/review-of-the-national-tuberculosis-](http://www.euro.who.int/en/countries/ukraine/publications3/review-of-the-national-tuberculosis-programme-in-ukraine)
4 [programme-in-ukraine](http://www.euro.who.int/en/countries/ukraine/publications3/review-of-the-national-tuberculosis-programme-in-ukraine) (accessed 5 Mar 2019).

5
6 28 World Health Organization. A patient-centered approach to TB care. 2018.
7 <https://apps.who.int/iris/bitstream/handle/10665/272467/WHO-CDS-TB-2018.13-eng.pdf?ua=1>
8 (accessed 5 Mar 2019).

9
10
11 29 Ministry of Health of Ukraine, Unified Clinical Protocol for Primary, Secondary (Specialized)
12 and Tertiary (Highly Specialized) Medical Care for Adults with Tuberculosis. 04 September
13 2014. Available: https://phc.org.ua/uploads/files/dn_20141231_1039dod.pdf
14 (accessed 5 Mar 2019).

15
16
17 30. Guest G. How Many Interviews Are Enough?: An Experiment with Data Saturation and
18 Variability. *Field Methods* 2006;18(1):59–82.

19
20 31 The World Health Organization. Adherence to Long-term Therapies: Evidence for Action.
21 WHO, 2003. <http://whqlibdoc.who.int/publications/2003/9241545992.pdf> (accessed 5 Mar
22 2019).

23
24 32 Ukrainian State Statistical Services, Expenditures and Resources of Households of Ukraine in
25 year 2014, Kyiv, 2015. https://ukrstat.org/uk/druk/publicat/Arhiv_u/17/Arch_vrd_zb.htm
26 (accessed 18 March 2019).

27
28 33 Mauch V, Bonsu F, Gyapong M, et al. Free tuberculosis diagnosis and treatment are not
29 enough: patient cost evidence from three continents. *Int J Tuberc Lung Dis* 2013;17(3):381–7.

30
31 34 Chida N, Ansari Z, Hussain H, et al. Determinants of default from tuberculosis treatment
32 among patients with drug-susceptible tuberculosis in Karachi, Pakistan: A mixed methods study.
33 *PLoS One* 2015;10(11):e0142384.

34
35 35 Paz-Soldán VA, Alban RE, Jones CD, et al. The provision of and need for social support
36 among adult and pediatric patients with tuberculosis in Lima, Peru: a qualitative study. *BMC*
37 *Health Serv Res* 2013;13:290.

38
39 36 Andrade KVF, Nery JS, Souza RA, et al. Effects of social protection on tuberculosis
40 treatment outcomes in low or middle-income and in high-burden countries: systematic review
41 and meta-analysis. *Cad Saude Publica* 2018;34(1):e00153116.

42
43 37 van Hoorn R, Jaramillo E, Collins D, et al. The effects of psycho-emotional and socio-
44 economic support for tuberculosis patients on treatment adherence and treatment outcomes -
45 A systematic review and meta-analysis. *PLoS One* 2016;11(4):e0154095.

46
47 38 Priedeman Skiles M, Curtis SL, et al. Evaluating the impact of social support services on
48 tuberculosis treatment default in Ukraine. *PLoS One* 2018;13(8):e0199513.

49
50 39 Rachlis B, Naanyu V, Wachira J, et al. Identifying common barriers and facilitators to linkage
51 and retention in chronic disease care in western Kenya. *BMC Public Health*. 2016;16:741.

- 1
2
3
4 40 Kanters S, Park JJ, Chan K, et al. Use of peers to improve adherence to antiretroviral therapy:
5 a global network meta-analysis. *J Int AIDS Soc* 2016;19(1):21141.
6
7 41 Pachi A, Bratis D, Moussas G, et al. Psychiatric morbidity and other factors affecting
8 treatment adherence in pulmonary tuberculosis patients. *Tuberc Res Treat* 2013;2013:489865.
9
10 42 Gebremariam MK, Bjune GA, Frich JC. Barriers and facilitators of adherence to TB
11 treatment in patients on concomitant TB and HIV treatment: a qualitative study. *BMC Public*
12 *Health* 2010;10:651.
13
14 43 Tola HH, Tol A, Shojaeizadeh D, et al. Tuberculosis treatment non-adherence and lost to
15 follow up among TB patients with or without HIV in developing countries: A systematic review.
16 *Iran J Public Health* 2015;44(1):1–11.
17
18 44 Jakubowiak WM, Bogorodskaya EM, Borisov SE, et al. Impact of socio-psychological factors
19 on treatment adherence of TB patients in Russia. *Tuberculosis (Edinb)* 2008;88(5):495–502.
20
21 45 Comolet TM, Rakotomalala R, Rajaonariora H. Factors determining compliance with
22 tuberculosis treatment in urban environment, Tamatave, Madagascar. *Int J Tuberc Lung Dis*
23 1998;2(11):891–7.
24
25 46 Young HN, Len-Rios ME, Brown R, et al. How does patient-provider communication
26 influence adherence to asthma medications? *Patient Educ Couns* 2017;100(4):696–702.
27
28 47 Schoenthaler A, Knafl GJ, Fiscella K, et al. Addressing the social needs of
29 hypertensive patients: The role of patient-provider communication as a predictor of
30 medication adherence. *Circ Cardiovasc Qual Outcomes*. 2017;10(9):e003659.
31
32 48 Sohal T, Sohal P, King-Shier KM, et al. Barriers and facilitators for type-2 diabetes
33 management in South Asians: A systematic review. *PLoS One* 2015;10(9):e0136202.
34
35 49 Liu Q, Abba K, Alejandria MM, et al. Reminder systems and late patient tracers in
36 the diagnosis and management of tuberculosis. *Cochrane Database Syst*
37 *Rev* 2008;(4):CD006594.
38
39 50 World Health Organization. Treatment of Tuberculosis: Guidelines for treatment of drug-
40 susceptible tuberculosis and patient care. 2017 update.
41 <https://apps.who.int/iris/bitstream/handle/10665/255052/9789241550000-eng.pdf?sequence=1>
42 (accessed 5 Mar 2019).
43
44 51 Saito Z, Kaneko Y, Kinoshita A, et al. Effectiveness of hepatoprotective drugs for anti-
45 tuberculosis drug-induced hepatotoxicity: a retrospective analysis *BMC Infect Dis* 2016;16(1):
46 668.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

INTERVIEW GUIDE

A. Introduction

- 1) Before starting the interview, I want to thank you for participating in the study. If you need any clarifications about any question, please feel free to ask me at any time. I would also like to remind you that you can choose not to answer questions if you are uncomfortable; and you can stop the interview at any time.

Interviewer: Remind patient that interview results will be anonymous; interviewer is not a doctor and does not work for the oblast/rayon TB hospital or polyclinic; information discussed will not be relayed to patients' doctors or family.

B. General question

Now, we're going to talk briefly about your health and healthcare in general.

- 2) What types of medical care do you think are important to have access to? Why?

C. TB Diagnosis: Healthcare team/system-related

Now, we're going to talk more about your Tuberculosis diagnosis.

- 3) Do you remember when you were diagnosed with Tuberculosis? Can you please tell me about that?

Try to get patient to talk about:

- How long did it take to receive the final diagnosis (days/months/number of visits to the clinic/hospital)?
- Setting of diagnosis (primary care clinic? Private doctor? TB ambulatory clinic? TB hospital?)
- If they recall how long it took them to contact the healthcare doctor/facility after symptoms started
- What was the final push to seek medical attention?

C. TB Diagnosis: Condition-related

- 4) Who did you disclose your TB diagnosis to?

Try to get patient to be specific:

- E.g. family, friends, co-workers, neighbors, employer/boss)?
- Were you worried about people finding out you have TB? And why?

- 5) How did the people react to the disclosure; did the relationship change?

D. TB Treatment: Therapy-Related Factors

- 6) How many months of TB treatment were you prescribed at first? How many months did you actually receive? Was this different from how long you expected? Why?

- 1 7) Can you please tell me some specifics about your treatment for TB? For example, how many
- 2 times a week did you take pills? Where did you take your pills (at home, at a clinic, in a hospital,
- 3 somewhere else)? How did your treatment change over time?
- 4
- 5 8) After you started taking TB medications, did your symptoms change? (e.g. improve? Worsen? Or
- 6 stay the same?) What was your expectation about that?
- 7
- 8 9) Did you have any concerns or questions about your treatment? What were they and how did you
- 9 address them?
- 10
- 11 10) Did you have any side effects? How did you cope with them?
- 12
- 13 11) What were the most challenging aspects of TB treatment for you? Probe patient to be specific
- 14

E. TB Treatment: Preferences

- 12) If you could choose, where would you prefer to get TB treatment? Why?
- 13) Are there some specific types of support you wish you had during TB treatment? (Probe the patient to be specific (e.g monetary or emotional support and from whom? Maybe family, friends, healthcare workers, government, NGO etc).

F. TB Treatment: Patient-related, Adherence Barriers and Motivators

- 14) Were there days or periods when you didn't take the TB medicine (or thought about not taking the medicines?) Can you please tell me about that?
Try to discuss:
 - Approximate number of days per month (or number of months) treatment was skipped
 - Why did patient stop taking medicines or why did they think about it?
 - a) If they stopped more than once, what were the reasons each time? (Explore issues that contributed to not taking the meds (e.g logistics? Side effects? Cost?))
 - b) Ask patient how they felt when this happened?
- 15) Were there times during your treatment where you thought about NOT taking the medicines but ultimately took them? Can you tell me more about what motivated you to do so?
- 16) What was the /reaction of healthcare workers when you stopped treatment? What did they tell you to do?

G. TB Treatment: Healthcare team- and system-related

- 17) How did you get to the facility to take your treatment? (Duration of travel, cost etc)
- 18) Can you please tell me about the facilities (dispensaries and hospitals) where you received your care? What do you think about the care provided to TB patients?
Talk about:
 - flexibility of hours
 - Medication stock-outs
 - Cleanliness
 - Privacy for consults/giving samples
 - Wait time to be seen
 - General patient-friendliness

19) Can you please tell me about the healthcare workers at the facilities where you received TB care?

Talk about:

- Impression of how healthcare workers interacted with patient
- Amount of time patient spent with doctor or nurse
- Did patient have time to ask questions and what did patient think of the responses to their questions

20) Did the healthcare workers explain your illness to you? Please tell me about that

Try to discuss the information patients received:

- At the time of diagnosis
- During the course of their treatment
- Regarding prognosis
- Regarding side effects

H. TB Knowledge: Patient-related

21) Did you have enough information about TB? Where did you get information regarding TB? (e.g. from healthcare workers, friends, family, or internet?)

Tell me please what you know about TB:

- Mode of transmission
- Effectiveness of treatment
- Impact of missing treatment

I. Impact of TB

22) Has TB changed your life or the life of your family in any way? Can you tell me more about that?

Talk about:

- Relationships with family/friends/others
- Mental health
- Work or School
- Overall financial impact of TB

23) At the time you had TB, did you have any other health problem? How did having TB affect your other illness? And vice versa?

J. Conclusion

24) If you could think about changes to the process of TB treatment, what would you want to be done differently?

Thank you again for your participation.

Standards for Reporting Qualitative Research (SRQR)*

<http://www.equator-network.org/reporting-guidelines/srqr/>

Page/line no(s).

Title and abstract

<p>Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended</p>	Page 1, Title
<p>Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions</p>	Page 2, Abstract

Introduction

<p>Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement</p>	Page 4, Intro (paragraphs 1-3)
<p>Purpose or research question - Purpose of the study and specific objectives or questions</p>	Page 4, Intro (paragraph 4)

Methods

<p>Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**</p>	Page 6, Data Analysis (paragraph 1)
<p>Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability</p>	NA
<p>Context - Setting/site and salient contextual factors; rationale**</p>	Pages 4-5, Study Setting
<p>Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**</p>	Page 5, Sampling
<p>Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues</p>	Page 4, Ethics Statement
<p>Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**</p>	Page 5, Sampling, (paragraph 2) Pages 5-6, Data Collection Procedures

1 2 3 4 5	Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	Pages 5-6, Data Collection Procedures
6 7 8	Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	Page 7, Results (Paragraph 1), Table 2
9 10 11 12	Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	Page 6-7, Data Analysis
13 14 15 16 17 18	Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	Pages 5-6, Data Collection Procedures Page 6-7, Data Analysis
19 20 21 22	Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	Pages 6-7, Data Analysis

Results/findings

25 26 27 28	Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	Pages 7-13, Results
29 30 31	Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Pages 7-13, Results

Discussion

34 35 36 37 38 39 40	Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	Pages 14-15, Discussion
41 42	Limitations - Trustworthiness and limitations of findings	Page 15, Discussion

Other

45 46 47 48	Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	Page 15, Competing Interests
49 50	Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	Page 16, Funding

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
DOI: 10.1097/ACM.0000000000000388

For peer review only

BMJ Open

Patients' perspectives of tuberculosis treatment challenges and barriers to treatment adherence in Ukraine: A qualitative study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032027.R1
Article Type:	Research
Date Submitted by the Author:	18-Nov-2019
Complete List of Authors:	Aibana, Omowunmi; University of Texas Health Science Center at Houston, Internal Medicine Dauria, Emily; University of California San Francisco, Psychiatry Kiriazova, Tetiana; Ukrainian Institute on Public Health Policy Makarenko, Olena; Ukrainian Institute on Public Health Policy Bachmaha, Mariya; PH Capital. Public Health Experts. Rybak, Natasha; The Miriam Hospital, Warren Alpert School of Medicine at Brown University, Infectious Diseases Flanigan, Timothy; The Miriam Hospital, Warren Alpert School of Medicine at Brown University, Infectious Diseases Petrenko, Vasyl; Bogomolets National Medical University Becker, Anne ; Harvard Medical School, Department of Global Health and Social Medicine Murray, Megan; Harvard Medical School, Department of Global Health and Social Medicine
Primary Subject Heading:	Global health
Secondary Subject Heading:	Health policy, Health services research, Infectious diseases, Patient-centred medicine, Public health
Keywords:	Public health < INFECTIOUS DISEASES, QUALITATIVE RESEARCH, Tuberculosis < INFECTIOUS DISEASES

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **Patients' perspectives of tuberculosis treatment challenges and barriers to treatment**
4 **adherence in Ukraine: A qualitative study**
5
6
7

8 Omowunmi Aibana,¹ Emily Dauria,² Tetiana Kiriazova,³ Olena Makarenko,³ Mariya Bachmaha,⁴
9 Natasha Rybak,⁵ Timothy P. Flanigan,⁵ Vasyl Petrenko,⁶ Anne E. Becker,⁷ Megan B. Murray⁷
10

11 1 Department of Internal Medicine, McGovern Medical School at the University of Texas Health
12 Science Center, 6431 Fannin Street, MSB 1.122, Houston, Texas 77030, USA
13

14 2 Department of Psychiatry, University of California, San Francisco, 1001 Potrero Avenue
15 Room 7G21, San Francisco, CA 94110
16

17 3 Ukrainian Institute on Public Health Policy, 5 Mala Zhytomyrska Str., Office 61A, Kyiv 01001
18 Ukraine
19

20 4 PH Capital. Public Health Experts. 17 M. Zakrevskoho street, office 137, Kyiv 02217 Ukraine
21

22 5 Division of Infectious Diseases, The Miriam Hospital, Warren Alpert Medical School at
23 Brown University, 164 Summit Ave, Providence, Rhode Island 02906, USA
24

25 6 Department of Phthisiology (Tuberculosis), Bogomolets National Medical University, 13
26 Tarasa Shevchenka Boulevard, Kyiv 01601 Ukraine
27

28 7 Department of Global Health and Social Medicine, Harvard Medical School, 641 Huntington
29 Avenue, Boston, Massachusetts 02115, USA
30
31

32
33
34 **Corresponding Author**

35 Omowunmi Aibana, MD MPH
36 6431 Fannin Street, MSB 1.122
37 Houston, TX 77030
38 email: Omowunmi.aibana@uth.tmc.edu
39 Phone: 713 741 3918
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT

Objectives: To understand the challenges faced by tuberculosis (TB) patients and factors that influence TB treatment adherence in Ukraine.

Design: Qualitative Study

Setting: TB treatment facilities in Kyiv Oblast, Ukraine

Participants: Sixty adults who had undergone treatment for drug-sensitive TB between June 2012 and August 2015.

Methods: We conducted semi-structured, in-depth, individual interviews among a purposively selected clinical sample of patients previously treated for drug-sensitive TB. Interview content encompassed WHO's framework for barriers to adherence to long-term therapies and included questions about patient preferences and motivators concerning treatment adherence. We examined treatment experience across strata defined by previously identified risk correlates of non-adherence.

Results: Among 60 participants, 19 (32.8%) were HIV-positive, 12 (20.3%) had substance use disorder, and 9 (15.0%) had not completed TB treatment. Respondents discussed the psychological distress associated with hospital-based TB care, as well as perceived unsupportive, antagonistic interactions with TB providers as major challenges to treatment adherence. An additional barrier to successful treatment completion included the financial toll of lost income during TB treatment, which was exacerbated by the additional costs of ancillary medications and transportation to ambulatory TB clinics. The high pill burden of TB treatment also undermined adherence. These challenges were endorsed among participants with and without major risk factors for non-adherence.

Conclusions: Our findings highlight important barriers to TB treatment adherence in this study population and suggest specific interventions that may be beneficial in mitigating high rates of poor treatment outcomes for TB in Ukraine.

Strengths and limitations of this study

- We analyzed qualitative data from semi-structured, individual interviews conducted among a large sample of patients with lived experience of TB in Kyiv Oblast.
- Study aimed to augment understanding of patient experiences to illuminate barriers to adherence to drug sensitive TB treatment in Ukraine.
- The study complements and contextualizes available evidence pointing to a high risk of lost to follow up among TB patients in this setting.
- This study is limited by selective sampling of TB patients in only one region of Ukraine.
- Additional studies are needed to explore provider perspectives on measures to improve adherence and TB treatment outcomes in Ukraine.

INTRODUCTION

Tuberculosis (TB) remains a significant global health problem with an estimated 10 million new cases diagnosed in 2018.[1] TB control is especially challenging in Eastern European countries like Ukraine, which has one of the highest burdens of multi-drug resistant TB (MDR-TB) worldwide with an estimated 29% of new TB cases being MDR.[2] Following the dissolution of the Soviet Union, many former Soviet Union countries experienced significant reduction in health care financing with a concomitant substantial rise in individual out-of-pocket healthcare costs.[3] Amidst this post-Soviet era decline in public health and safety net programs, many countries faced rising poverty levels, high incarceration rates, skyrocketing injection drug use, and a rapid rise in HIV incidence, all of which fueled the TB epidemic in Eastern Europe in the 1990s.[4-9]

Whereas TB incidence is now declining in parts of Eastern Europe, Ukraine remains among countries in this region with ongoing rise in TB incidence, which has increased from 41.7 per 100,000 in 1995 to 80 per 100,000 in 2018.[1, 2, 10] TB burden is unevenly distributed with the highest incident rates in the penitentiary system throughout Ukraine and in the South-eastern region.[11] In virtually all parts of Ukraine, rate of incident TB among rural residents is 20-30% higher than among urban residents.[11] TB incidence as well as associated mortality remains higher for men compared to women,[11] and rising rates of HIV and TB co-infection indicate a convergence of HIV and TB epidemics in Ukraine.[2, 11]

The Ukrainian National TB program (UNTP) issues standard procedures and guidelines for TB program activities.[12] TB service is organized as a centralized, vertical system made up of specialized hospitals and outpatient clinics. The system relies heavily on passive case finding with diagnosis and management of TB primarily undertaken by TB specialists. Although Ukraine has adopted the World Health Organization (WHO) recommended Directly Observed Therapy Short-course (DOTS) program for TB management, the national treatment success rate for drug-sensitive TB (DSTB) in 2017 was 76%, [2] significantly lower than the WHO recommended target of at least 90%; [13] and studies have reported MDR-TB treatment success rates below 25% among TB patients treated in Kyiv, the capital of Ukraine.[14, 15]

Failure to complete TB treatment may result in poor patient outcomes, and previous studies have identified many patient-related risk factors for loss-to-follow up during treatment including unemployment, substance use disorder, and HIV.[16-24] Qualitative studies from diverse social settings across the economic spectrum have also described barriers to TB treatment adherence such as stigma, financial burden, inadequate TB knowledge, and treatment side effects.[19, 22, 25, 26] Qualitative evidence from Eastern Europe has revealed additional factors such as hospital-based treatment, lack of social support and poor patient-provider communication as drivers of poor treatment adherence, particularly among MDR-TB patients.[27-29]

Prior analyses of Ukraine's National TB Program (UNTP) have enumerated institutional and political barriers to successful DOTS implementation; [10, 30] however, only one qualitative study to-date has assessed patient perspectives concerning barriers to treatment adherence in the specific context of TB care delivery in Ukraine.[31] Notably, the WHO highlights patient-

centered approaches to TB care as a critical component of TB control efforts.[32] These approaches recognize patients as the principal figures in the care continuum and consider patients' personal and social circumstances in delivering care.[32]

We conducted a qualitative study exploring patients' experiences during TB treatment to identify patient perspectives regarding critical challenges and associated factors that influence TB treatment adherence in Ukraine.

METHODS

Ethics Statement

The study was approved by the Institutional Review Board at The Miriam Hospital, Lifespan, Providence, RI [204815 45CFR 46.110(7)] and the Research Ethics Committee at Bogomolets Medical University, Kyiv, Ukraine (No. 86). All participants provided written informed consent.

Study Setting

We conducted this study in the Kyiv Oblast, Ukraine where the notification rate for pulmonary TB in 2017 was approximately 79 per 100,000. Patients receive TB diagnostic evaluation and treatment free of charge according to UNTP guidelines.[12] All administrative regions of Ukraine have dedicated TB hospitals where, prior to 2014, all patients diagnosed with DSTB were admitted to receive two months of inpatient intensive phase therapy with four drugs (isoniazid, rifampin, pyrazinamide, ethambutol) followed by four months of outpatient therapy with two drugs (isoniazid and rifampin) daily. Although new guidelines disseminated in 2014 recommended complete outpatient management of DSTB,[12] many regions, including Kyiv Oblast, continue to hospitalize patients for the initial two months of treatment. Guidelines further stipulate daily directly observed therapy in TB clinics during the outpatient phase of DSTB treatment. In Kyiv Oblast, some patients arrange to receive medication weekly to better accommodate their schedules.

Inclusion Criteria

Eligible participants included all adult patients (≥ 18 years) treated for DSTB in Kyiv Oblast between June 2012 and study initiation in August 2015. We excluded individuals younger than 18 years of age and those treated for drug-resistant TB because pediatric and resistant TB require different management protocols.

Sampling

From a literature review and preliminary quantitative analysis of Kyiv Oblast data, we identified HIV infection, alcohol use disorder, and substance use disorder as major determinants of loss-to-follow up during DSTB treatment. Therefore, we used a purposive sampling strategy to maximize variability regarding participants' HIV status and presence or absence of alcohol or substance use disorder. To achieve theme saturation, we aimed for 12 – 16 patients per stratum for a total sample size of approximately 48 – 64. Within each stratum, we also attempted to

1
2
3 purposively sample patients who had finished TB treatment and those who had not completed
4 treatment in order to maximize the breadth of patient experience in enablers and barriers to
5 treatment adherence. We did not pre-specify a target for patients who had not completed
6 treatment because we anticipated they might be unreachable.
7

8
9 We reviewed 147 consecutive medical records from the Kyiv Oblast's Central TB Hospital to
10 identify the first 80 eligible participants with available contact information. We operationalized
11 substance use disorder (SUD) within the constraints of available data in the medical chart, which
12 included either self-reported "high alcohol consumption" or intravenous drug use (IVDU) at the
13 time of TB diagnosis. We ascertained HIV status and treatment outcomes from clinical records.
14 TB providers, who were not members of the study team, then contacted potential subjects to
15 provide information about the study and refer interested individuals to the study team. Study
16 staff informed interested individuals about study objectives and procedures and how results
17 could potentially inform interventions to improve TB care. In order to reach the desired sample
18 size for HIV and SUD strata, 11 additional eligible participants were identified from hospital
19 records and invited for study participation to replace previously selected individuals with these
20 characteristics who declined participation. We extracted additional demographic information
21 from the medical records: age, sex, residence, and employment status.
22
23
24
25

26 **Data Collection Procedures**

27
28 A local research team of three members conducted in-person, semi-structured interviews in the
29 Russian or Ukrainian language with study participants. Interviews were conducted according to
30 patients' availability from August through October 2015 either at TB clinics or patients'
31 preferred location. Participants were informed of their right to withdraw at any time before,
32 during or after data collection. Interviews lasted 45 to 60 minutes. Participants received
33 telephone cards worth 3.50 USD upon interview completion. All interviews were audio recorded,
34 transcribed verbatim, and translated into English by qualified translators independently from the
35 interviewers.
36
37

38
39 We developed the interview guide content to align with the WHO framework for categorizing
40 factors influencing adherence to long-term therapies into five dimensions: socio-economic,
41 health system/health care team-related, therapy-related, patient-related, and condition-related
42 factors.[33] (Table 1) Interview questions were open-ended and facilitated elaboration on this
43 framework by exploring adherence motivators and patients' treatment preferences. We also
44 included questions intended to capture patients' perceptions of their own adherence behavior and
45 TB knowledge. Questions addressed patients' experiences during TB diagnosis as well as
46 inpatient and outpatient phases of treatment (Supplementary Interview Guide). Interviewers
47 asked follow-up questions when appropriate to elicit additional explanatory and experiential
48 details. The semi-structured format was intended to encourage patients to speak broadly on their
49 relevant experience.
50
51
52
53
54
55
56
57
58
59
60

Table 1. World Health Organization's five dimensions affecting adherence to long term therapy¹

Social and economic-related	Characteristics related to the patient's economic and social position (e.g., poverty, illiteracy, education level)
Health care team and system-related	Aspects of the system and group of individuals providing condition-related care for the individual (e.g., patient-provider relationship, medication distribution)
Therapy-related	Factors related to the treatment protocol (e.g., medical regimen, treatment length)
Patient-related	Resources, knowledge, attitudes, beliefs, perceptions, and expectations of the patient (e.g., self-efficacy), forgetfulness, psychosocial stressors
Condition-related	Particular illness-related demands faced by the patient (e.g., severity of symptoms, level of disability, rate of disease progression).

1 Table adapted from content from World Health Organization (WHO) framework on adherence[33].

Data Analysis

We analyzed data to identify and examine thematic content corresponding to questions eliciting details within the aforementioned WHO framework[33] and additional relevant themes that emerged from participant narratives. The process began with familiarization by reading transcripts followed by identifying and operationalizing themes and subthemes and creating an initial codebook. To improve reliability and intercoder agreement, OA, ED and TK open coded ten initial transcripts with subsequent comparison of coding patterns and revision of the codebook via consensus. We double-coded all interviews in a similar manner and refined the codebook throughout the analysis phase. We coded all transcripts using the finalized codebook and reconciled discordant codes via consensus. All coded segments in the transcript text were organized under major themes and subthemes identified from the data. To evaluate whether HIV and SUD were key drivers of treatment adherence, we examined the occurrence and frequency of themes and subthemes among respondents with HIV or SUD compared to respondents without these comorbidities. We separately compared themes based on participants' treatment completion status. Finally, we selected illustrative excerpts across strata to convey this content in the respondents' own words.

We used NVIVO 11 (QSR International, Cambridge, MA) to facilitate qualitative data analysis.

Patient and Public Involvement

Patients were not involved in development of the research questions, study design, interpretation of results or writing of the manuscript.

RESULTS

Among 91 eligible participants whom we attempted to contact, 60 (65.9%) agreed to participate, 16 (17.6%) declined, 12 (13.2%) could not be reached from available contact information, and 3 (3.3%) were unavailable for interview.

Table 2 lists demographic and clinical characteristics of study participants. Nineteen (32.8%) participants were HIV-positive and 12 (20.3%) had SUD; among HIV-positive participants, 6 (33.3%) had overlapping SUD. Nine (15.0%) individuals did not complete TB treatment and among them, one (11.1%) respectively had HIV and SUD.

Table 2. Demographic characteristics of study participants (N = 60)

	n (%) or mean (\pm SD)
Age	38.5 (\pm 12.4)
Male	42 (70.0)
Substance Use Disorder	
Intravenous drug use ¹	8 (13.5)
High Alcohol Consumption ¹	4 (6.8)
HIV-positive ²	19 (32.8)
Substance Use Disorder among HIV-positive ³	6 (33.3)
Marital Status	
Married or Live-in Partner	28 (46.7)
Single	15 (25.0)
Divorced	11 (18.3)
Widowed	6 (10.0)
Education	
Secondary	26 (43.3)
Secondary Specialized	20 (33.3)
College	14 (23.3)
Rural Residency	31 (51.7)
Unemployed	32 (53.3)
Did not complete TB treatment	9 (15.0)

1 Missing observations, N = 1

2 Missing observations, N = 2

3 Missing observations, N = 1

Overview of participants' experiences with accessing TB care

Participants had experienced various symptoms prior to TB diagnosis (e.g., poor sleep and appetite, fevers, malaise, weight loss, cough). For several, these symptoms had persisted for months prior to seeking care. Participants noted a variety of reasons for delayed healthcare seeking including lack of funds for out-of-pocket expenses, a perception that healthcare workers were not competent, and prior experience with lack of resources in healthcare facilities. Several

respondents described the need for consistent access to affordable medical care in Ukraine; such access was deemed necessary for timely identification of TB and receipt of relevant care.

[We need access] to all [medical services]. [. . .] especially to emergency ones. And access should be free, so it does not happen that when you need something urgent in the hospital, they tell you - this much money or that much money. [S-35: Male, HIV-/no SUD, Completed treatment]

Nearly half of respondents described severe or debilitating symptoms as the final push for seeking care.

I was coughing for rather long time. Probably for half a year. I was coughing, but I thought it would disappear. I didn't take it seriously [. . .] Only when it became obvious, [when the bleeding started], then we called an ambulance and went to the hospital. [S-10: Female, HIV-/no SUD, Completed treatment]

I felt bad. Well, I had to solve this problem, because it was impossible to continue living and working like that. [. . .] I physically could not, well... perform my duties anymore. [S-6: Female, HIV+/no SUD, Completed treatment]

Notably, for majority of participants, once they sought care for their TB-specific symptoms, they received prompt referral to appropriate TB facilities for diagnosis and treatment initiation.

I was diagnosed immediately [. . .] and I was immediately given the documents and was told to go to [TB hospital] the next day. That is, I was diagnosed in one day. In the ambulatory [clinic]. [S-17: Male, HIV-/no SUD, Completed treatment]

For a few patients, their path to final TB diagnosis and treatment was lengthy, as exemplified by one participant who described prolonged treatment course for pneumonia prior to TB treatment.

At first, I was taken to the hospital and was told that I had pneumonia. [. . .] They were treating me in a wrong way [for two months] and I threw a lot of money down the drain. [S-25: Female, HIV-/no SUD, Completed treatment]

We organized the main themes identified as principal challenges faced by TB patients and factors influencing adherence to DSTB treatment according to the WHO framework for organizing barriers to long-term therapy adherence (Table 1). We also categorized themes related to facilitators of treatment adherence. We did not identify additional relevant themes that did not align with the WHO framework.

Socio-economic related factors

Financial cost of TB treatment

Although TB drugs are free in Ukraine, participants across our sampling strata and regardless of treatment completion status, discussed various dimensions of the aggregate economic toll of TB treatment. Over half of participants (N=36: 20 HIV-/no SUD, 16 HIV+/SUD; 30 completers, 6 non-completers) described a critical need for financial support, which they did not receive, during TB treatment. Generally, patients are unable to work while hospitalized during the intensive treatment phase. However, for 12 participants (5 HIV-/no SUD, 7 HIV+/SUD; 10

completers, 2 non-completers), the financial hardship of lost income was prolonged because they remained unemployed for the duration of their treatment.

Furthermore, whereas there is disability/sick leave pay in Ukraine, only six patients described successfully navigating the system to obtain it. Two notable barriers were lack of patient awareness about how to access this support and failure of healthcare providers to inform patients. One participant explained:

There are doctors who do not inform you that you can perform all paperwork and register for disability group at once, just after starting treatment, and then you will receive some small pension. [S-15: Male, HIV-/no SUD, Incomplete treatment]

Over half of participants (N=37: 21 HIV-/no SUD, 16 HIV+/SUD; 30 completers, 7 non-completers) described how the financial toll of lost income was exacerbated by additional costs incurred during TB treatment. These included imaging tests and ancillary medicines such as “hepatoprotectors,” which are commonly prescribed in Ukraine to mitigate the toxic effects of TB drugs on the liver. For example, a participant described the financial burden of these additional medications as follows:

The prices of the medicines [. . .] are cosmic, incredible. You can't make it. Well, at least there is help, when they give TB pills for free; that is good. But the rest of it - the medicines for the liver, vitamins – I bought those myself [. . .] The ones for the liver are especially expensive [. . .], all this hit my pockets a little bit. [S-30: Male, HIV-/no SUD, Completed treatment]

Distance and transportation costs to TB treatment facilities represented another major challenge. Trips lasted several hours and cost up to 100.00 UAH (approximately 4.00 USD) daily. A patient summarized his journeys as follows:

[. . .] It's faster to get to the United States than to [the TB clinic]. [Laughs]. Here, transportation is the end. Two or three buses! And try to get on one of them! [S-40: Male, HIV-/no SUD, Completed treatment]

Assuming trips for TB services once weekly, transportation would cost approximately 16 USD monthly, which represents 26% of the average monthly income of 61.40 USD per rural household in Ukraine in 2014.[34] Two participants explicitly related transportation costs to their treatment non-adherence. When asked about reasons for incomplete outpatient treatment, one interviewee responded:

I didn't have money to get to the [TB clinic]. [When the doctor asked] Well I told him, I don't have money now to come, I'm in such a crisis, that I don't have any money, nothing. [S-53: Male, HIV-/no SUD, Incomplete treatment]

Fourteen participants (10 HIV-/no SUD, 4 HIV+/SUD; 11 completers, 3 non-completers) further described how the financial burden of TB negatively affected their family either because they were primary income earners who were no longer able to provide for their families or had to rely on relatives for financial support.

Well, 7 months, roughly speaking, I was treated for 7 months. [. . .] I didn't work anywhere. My wife, she [was] on maternity leave. It was really hard financially. [S-15: Male, HIV-/no SUD, Incomplete treatment]

[. . .] And, of course, it had an impact, because all the money that was supposed to go to the household, it all went to the hospital. [. . .] And my sister had to pull this all alone. And it was hard. [. . .] Of course, the disease affected us. Hard. [S-41: Female, HIV+/no SUD, Completed treatment]

Health system and health-care team related factors

For many participants, systems-level factors related to the TB treatment facilities and the TB care team occurred in tandem and emerged as notable barriers to treatment adherence.

Psychological impact of hospitalization

Participants, irrespective of comorbidities or treatment completion status, broadly articulated the challenges of hospital-based care. For instance, twelve participants (8 HIV-/no SUD, 4 HIV+/SUD; 11 completers, 1 non-completer) described the inpatient experience as psychologically difficult due to boredom and prolonged isolation from family. This invoked a sense of alienation likened to imprisonment, even though patients could leave the hospital anytime.

[. . .] You are just sitting and waiting [in the hospital room.], You can just become crazy. [. . .] Just sitting at this cage. That's the worst. [. . .] [S-7: Male, HIV-/SUD, Completed treatment]

One male respondent explored how the psychological impact of hospitalization influenced his willingness to remain in treatment and credited his ultimate compliance with treatment to intermittent opportunities to communicate with family members.

[. . .] it was difficult to stay in the hospital. You feel there like [you are] incarcerated [. . .] You want to break free from there, well... You cannot go anywhere... Everything is the same... It was difficult mentally. [. . .] The only thing that saved me was communication with relatives [pause] on the phone. And sometimes, on the weekends [pause] they came. But besides that – everything is the same, within these four walls, with pills. [S-35: Male, HIV-/no SUD, Completed treatment]

Hospital conditions

The psychological toll of hospitalization was further exacerbated by physical state of the TB hospital for many participants. Twenty-four respondents (17 HIV-/no SUD, 7 HIV+/SUD; 20 completers, 4 non-completers) detailed the dehumanizing nature of the hospital setting, describing it as dilapidated, unsanitary, and lacking basic amenities.

There is nothing comfortable there. [Sighs]. It's just not possible. Well, it's unhuman. For a normal person who lives in a normal home [. . .] When there are holes in the walls. There are cockroaches everywhere [. . .], the building itself and all that - it's just terrible! All these things shocked me. [S-12: Female, HIV+/no SUD, Completed treatment]

I got [to the hospital] in winter, and there was no shower room at all. I mean, there is the large room with the cold water, where it is impossible to take a shower [. . .] This is the hell-hole. [S-52: Male, HIV-/no SUD, Completed treatment]

One participant discussed how these conditions might shape patients' willingness to successfully complete TB treatment:

The buildings were awful inside. Surely, it's not unimportant. You know, when you get in a building, where everything is clean and okay, you know, you really want to take care of yourself. And when everything is in bad condition, I can understand some men who tried to go somewhere [else]. Because, you see, even tuberculosis people must have good buildings after all. [S-22: Female, HIV-/no SUD, Completed treatment]

Ten respondents (4 HIV-/no SUD, 6 HIV+/SUD; 8 completers, 2 non-completers) highlighted incidents of drinking in the hospital, seemingly without staff repercussions, and this contributed to the psychological distress of hospitalization.

At first there were moments [Laughs]. I even wanted to escape [pause] I thought I would not be able to bear all this. Because people really were drinking and doing all possible things [pause] Well, it was very difficult [pause] I remember it as a nightmare, not that much the disease treatment itself as these conditions. [S-12: Female, HIV+/no SUD, Completed treatment]

One respondent with a substance use disorder explicitly mentioned substance use on the wards as a contributing factor to interrupting hospital treatment, recounting that:

[. . .] There is such a mess. And these [pause] drug users. It was impossible there both during day and night! It was terrible. A mess, in a word. But you can do nothing [to change the condition] - they are required to provide treatment. [S-31: Female, HIV-/SUD, Incomplete treatment]

Healthcare provider attitudes

Patient interactions with TB care providers were widely identified across sampling strata as another aspect of TB treatment experienced as a challenge to adherence. Just over one-third (N=23: 14 HIV-/no SUD, 9 HIV+/SUD; 19 completers, 4 non-completers) of participants characterized interactions as disrespectful, antagonistic, and lacking compassion.

There were terrible characters [TB providers], who did not like anybody, no matter what kind of a person you are [. . .] Yes, I would like to improve the attitude, so that the staff treated the patients more like humans [. . .] [S-35: Male, HIV-/no SUD, Completed treatment]

It's hostile. Awfully hostile. The doctor is just an overseer. Actually, she insults people. [Once], a young girl came with two little children – and [the doctor] was yelling at her so loudly, that, in front of her children, probably the hair rose on her head with fright. This is not a conversation of a doctor and a patient. It is just scary. [S-20: Female, HIV-/no SUD, Completed treatment]

Among these, seven participants (1 HIV-/no SUD, 6 HIV+/SUD; 6 completers, 1 non-completer) described harsh reactions from healthcare providers after interrupting treatment. Notably, the same respondent who stopped treatment due to the hospital conditions illustrated her experience as follows:

They berated me [. . .] because I had no right to [stop treatment]. To escape from the hospital, especially as I live among the people [. . .] They said if I do not go through treatment – just die if you want to [. . .] They said, "If you want to get treatment – get it. It is in your best interest. If you

do not want to – why would you occupy the [hospital] bed for nothing? You only waste products, let other people take your place." [S-31: Female, HIV-/SUD, Incomplete treatment]

The rigid implementation of facility-based DOT daily, as prescribed by UNTP guidelines, coupled with the authoritative style of TB providers in Ukraine seemed to further strain interactions between providers and patients. Some participants perceived providers as unaccommodating of patient needs related to the difficulties associated with daily clinic visits and other challenges faced by TB patients. One participant who had undergone TB treatment twice and struggled with substance use disorder recalled how his negative experience with the TB specialist contributed to his reluctance to complete his first course of treatment.

The most difficult was when I was on out-patient treatment. I had to go every day to see a doctor, to get pills. [. . .] Well, I did not want to go every day. I had other problems [substance use disorder] [. . .] Well, for the addicted man, yes. I did not have time. And I had at that time tuberculothapist, she was still from the Soviet Union. Everything had to be according to schedule – “You must come every day to see me.” And so every day I had quarrels with her. That I was late, then something else. [. . .] I did not work out relations with the doctor, that’s all. Well, she had a quite different approach. [. . .] Oh, she considered me a garbage. And I with such pride – [went] away. [S-18: Male, HIV+/SUD, Completed treatment].

Therapy-related factors

Pill burden and side effects

Over half (N=33: 22 HIV-/no SUD, 11 HIV/SUD; 26 completers and 7 non-completers) of participants discussed the physical challenge of swallowing 8 to 20 pills at once during the two-month intensive treatment phase. The pill burden had a negative impact on patients’ experience. One participant recalled:

You do not want to take them because the amount of medicines – this is the bunch [shows with his hands][. . .] If to put them into plastic glass, it is half a glass of tablets. And it is difficult even physically to take them [at once]. Not speaking about moral difficulties. When a human sees such a number of pills for the first time, he is shocked. [. . .] It is terrible, it burns, it is unpleasant. You do not want to take them all the time. [S-52: Male, HIV-/no SUD, Completed treatment]

Whereas participants widely described various TB treatment side effects, for one respondent, her provider’s unsupportive response to side effects compounded her negative experience with treatment and served as a barrier to adherence.

The first month, when a severe allergy appeared, [I] even came to the doctor and said – “I’m not going to take it. I will not take it, because well, it’s unbearable.” I have already reached the point that I had a nervous breakdown [. . .] I came, I was not given any reasonable answer. I said I’m not going to take it at all, then I called, they told me to take it anyway. I took... four and a half (months). Then for two weeks I did not take any medicine [S-4: Female, HIV+/SUD status unknown, Completed treatment]

Patient-related factors

TB Knowledge

Respondents across our sampling strata expressed an adequate understanding of TB disease. However, whereas a majority of respondents (N=42: 25 HIV-/no SUD, 17 HIV+/SUD; 37 completers, 5 non-completers) knew that TB was transmitted via airborne droplets, many (N=20: 12 HIV-/no SUD, 8 HIV+/SUD; 17 completers, 3 non-completers) also erroneously believed TB transmission occurred via contact with bodily fluids. One participant exemplified this misconception by stating:

There are possible options that [TB] is transmitted through blood. Definitely. I suspect that it is also possible that it's sexually transmitted; if it's transmitted by airborne droplets, then why can't it be sexually transmitted as well. [S-6: Female, HIV+/no SUD, Completed treatment]

In addition, many participants (N=26: 15 HIV-/no SUD, 9 HIV+/SUD; 22 completers, 4 non-completers) conveyed their understanding that missing doses of TB medications could decrease treatment effectiveness or lead to acquisition of resistance. Only one patient expressed this was a motivator of treatment adherence.

I did not have any idea not to take pills. The doctor told me that if I did not take pills, the body would produce resistance to these pills, and the [treatment] would no longer work if I missed at least once. And I did not need this. I wanted effective treatment. [S-23: Male, HIV+/SUD, Completed treatment]

Notably, the unsupportive communication style of providers adversely influenced the amount and quality of information patients received about TB. We identified five instances of participants discussing how the negative interpersonal relationship with providers discouraged them from seeking information from doctors. Highlighting this experience, one participant noted:

I had bad relations with the doctor. So, I did not always consult with her. Yes, she was rude sometimes [. . .] she was mean to me [. . .] She spoke with asperity. Well, she produced an impression - she was not talking with patients, but with passers-by, with the ordinary people from the street. [S-49: Female, HIV+/no SUD, Completed treatment]

Negative patient-provider interactions also led these participants to pursue other avenues for information about their TB diagnosis and treatment plan. These negative interactions occurred in the context of other challenges to engaging and completing TB treatment. For example, one female respondent who experienced various painful treatment side-effects and initially refused inpatient treatment due to the poor hospital conditions, described seeking out TB-related information from other sources to avoid interactions with her healthcare providers.

[. . .] when I ask a question, I'd like to get an answer from doctors. Without negativity [. . .] My doctor perceived me with so much negativity. And I don't know why, I treated her fine. [. . .] I got home, I started reading things myself [on the internet] and got interested. [S-56: Female, HIV-/no SUD, Completed treatment]

Psychological state

1
2
3 TB diagnosis itself further compounded the psychological challenges associated with hospital-
4 based TB care. Nineteen participants (13 HIV-/no SUD, 6 HIV+/SUD; 16 completers, 3 non-
5 completers) broadly characterized their experience as psychologically difficult with eleven (7
6 HIV-/no SUD, 4 HIV+/SUD; 9 completers, 2 non-completers) specifying they experienced
7 feelings of depression and anxiety. These feelings were largely associated with the TB diagnosis
8 and often rooted in patients' fear for their own morbidity but were not clearly linked to treatment
9 adherence.

10
11
12 *As [with] every disease, it is some kind of stress for a person. More than that, it's not a flu, it's*
13 *much more serious disease. Of course, psychologically it was hard. [S-48: Male, HIV-/no SUD,*
14 *Completed treatment]*

15 16 Forgetfulness

17
18 Eight participants, all of whom completed treatment, (5 HIV-/no SUD, 3 HIV+/SUD) described
19 instances of forgetting to take the pills amidst their daily routines. For example, a respondent
20 explained:

21
22 *I missed doses a little bit after the hospital. Because of my own fault. Sometimes simply - there*
23 *was no time, I was busy [. . .] [S-47: Male, HIV-/no SUD, Completed treatment]*

24 25 Alcohol consumption

26
27 Four respondents with comorbid HIV or SUD (3 completers, 1 non-completer) described alcohol
28 consumption as an individual-level factor that contributed to missed treatment doses. One
29 participant disclosed:

30
31 *[. . .] Well, honestly speaking, [. . .] my friends came to visit me [pause] I took [alcohol] with*
32 *them and did not want to take the medicines [. . .] [I] did not take the pills. [S-60: Female, HIV-*
33 */SUD, Completed treatment]*

34 35 Condition-related factors

36 37 TB-associated stigma

38
39 Participants across our comparison groups regarded TB as a shameful disease that only afflicts
40 certain marginalized populations who engage in socially unacceptable behaviors (e.g. injection
41 drug users and prisoners). Twelve participants (9 HIV-/no SUD, 3 HIV+/SUD; 10 completers, 2
42 non-completers) discussed how the perceived stigma associated with TB led to self-imposed
43 withdrawal and isolation from social networks.

44
45 *I thought that the people's attitude would change. [. . .] I have some friends who did not know but*
46 *suspected that it may be [TB]. When I was at hospital, [. . .] I bought the new phone number that*
47 *only my family knew [. . .]. [S-13: Male, HIV-/no SUD, Completed treatment]*

48
49 Other respondents (N=12: 8 HIV-/no SUD, 4 HIV+/SUD; 9 completers, 3 non-completers)
50 described instances of feeling stigmatized and rejected by friends and family after disclosing
51 their TB diagnosis. One participant described how his fear of rejection led him to attempt self-
52 treatment after TB diagnosis.
53
54
55
56
57
58
59
60

[. . .] I just made a decision, because, well, I knew that this thing [TB] will pop up and everyone will abandon me. So, after all I decided to try [treatment] on my own, got into the Internet, found out how everything's done. [. . .] [S-37: Male, HIV+/no SUD, Completed treatment]

Facilitators of treatment adherence

When asked about motivation for continuing treatment, many participants (N=32: 19 HIV-/no SUD, 13 HIV+/SUD; 27 completers, 5 non-completers) described a desire to recover or stay healthy/alive, and some (N=12: 6 HIV-/no SUD, 6 HIV+/SUD; 11 completers, 1 non-completer) articulated their understanding of treatment necessity.

I had to overcome this crisis; it was necessary to be treated [. . .], otherwise – death. I had to get myself together, that's it. And this helped [. . .] [S-55: Male, HIV-/no SUD, Completed treatment]

Only one respondent highlighted encouragement from providers as a facilitator of adherence.

Yes, the regimen. For me it's very hard [. . .] But thanks to the doctors, [. . .] they were coming, they were asking me – “did you take your pills?” And that's why I did not skip. [S-27: Female, HIV+, SUD, Completed treatment]

Participants suggested various things that might have mitigated their negative treatment experience. Twenty-seven respondents (14 HIV-/no SUD, 13 HIV+/SUD; 24 completers, 3 non-completers) preferred the comfort of home-based treatment.

Well, everything is easier at home [. . .] Hospital is a hospital – everyone is sick there, and it's better to recover at home, with the family [. . .]. [S-2: Male, SUD, Completed treatment]

Although psycho-emotional support was not routinely available, respondents (N=21: 13 HIV-/no SUD, 8 HIV+/SUD; 19 completers, 2 non-completers) broadly expressed an important need for such support, particularly during hospitalization.

[. . .] psychological support, [. . .] is necessary by 100%. [In the TB hospital] it is very difficult without it. If to remember, there is no one in the ward to speak to [pause] As you do not know anyone [. . .] [S-13: Male, HIV-/no SUD, Completed treatment]

DISCUSSION

We identified structural barriers related to centralized, facility-based TB services and economic impacts of treatment, provider communication styles, the psychological toll of TB, as well as treatment pill burden as prominent challenges faced by patients treated for drug-sensitive TB in Ukraine. These challenges emerged as factors that undermine treatment adherence and are consistent with identified adherence barriers in other socio-political contexts, thus suggesting that interventions implemented successfully elsewhere would be appropriate for consideration in Ukraine. A recent qualitative study among TB patients in Ukraine similarly identified the inconvenience and cost of clinic-based DOT during the ambulatory phase of treatment as major challenges to treatment adherence.[31] Our study provides additional insights into how hospitalization and patient interactions with TB providers adversely influences adherence in the

context of TB services in Ukraine. We also found commonalities in the challenges faced by TB patients with and without risk factors for non-adherence. Hence, interventions to improve TB care in Ukraine will likely have a broad impact on all TB patients.

We identified various dimensions of TB care in Ukraine that undermine patient commitment to TB treatment. Many participants described their negative experience of hospitalization, including the degrading infrastructure and the isolating hospital environment, as a major source of distress and deterrent to treatment, and nearly half of participants expressed a preference for home-based TB treatment. A recent study from Latvia, with similar organization of TB services, revealed that initiating TB treatment in a demoralizing hospital setting adversely affected patients' willingness to adhere to a prolonged treatment course.[29] The rigid expectation of facility-based DOT throughout the ambulatory phase of treatment in Ukraine further compromised patients' ability to complete treatment. This expectation disregards associated barriers that undermine healthcare seeking behavior, such as time and cost of daily transport. A prior analysis of UNTP has concluded that hospital-based TB care contributes to poor outcomes,[30] and the latest UNTP guidelines recommend outpatient management of DSTB.[12] Moreover, a pilot study in Ukraine recently reported home-based DOT facilitated retention in TB care.[31] Ongoing reorganization of TB care in Ukraine will provide opportunities to assess how full-scale implementation of home-based DSTB treatment influences patients' experiences and treatment outcomes.

We also found that many TB patients reported strikingly negative attitudes toward providers. The harsh, rigid style of TB providers in Ukraine compromised patient willingness to continue treatment and led to missed opportunities for providers to convey information about TB and the importance of TB therapy. Studies in other socio-political contexts have shown poor patient-provider interactions contribute to TB treatment non-adherence.[27, 28, 35] Notably, studies from former Soviet Union countries have specifically demonstrated that the authoritative communication styles of TB providers in these settings can undermine patient autonomy and readiness to comply with treatment recommendations.[27, 28] There is ample evidence that patient-provider relationships characterized by trust, mutual respect, and shared decision-making facilitate adherence to chronic disease therapy.[27, 36-38] A recent evaluation of a social support program for TB patients in Ukraine reported that excellent rapport and communication marked by respect and empathy from nurses was a key driver of success in patient retention.[31] Given the psychological difficulties associated with TB, more supportive attitudes from providers might improve patient willingness to remain in care.

Participants described psychological distress associated with TB diagnosis, and many voiced their desire for psychological support during treatment. Studies have similarly found high prevalence of depression and anxiety among TB patients;[25, 35, 39] such negative emotional states contribute to non-adherence.[40] At the same time, treatment of psychiatric comorbidities increases TB treatment adherence[39], and psychosocial support improves treatment success rates.[41, 42] Given TB diagnosis itself might render patients emotionally distraught, integration of psycho-emotional care with TB treatment in Ukraine might help patients better confront the challenges that undermine adherence.

1
2
3 Many participants discussed the economic burden of TB treatment. Poverty is a risk factor for
4 TB disease, and TB treatment exacerbates existing financial hardship and impairs treatment
5 adherence.[25, 27, 31 43-45] Studies have shown that cash transfers, and assistance with food
6 and transport can increase treatment success rates.[41, 46]. Recent evidence from Ukraine has
7 demonstrated the success of a pilot intervention of socio-economic support in reducing risk of
8 loss-to-follow up among high-risk TB patients.[31, 47] Efforts to alleviate the financial
9 consequences of TB in Ukraine can also focus on raising awareness to increase access to existing
10 sick/disability pay. We also note evidence from chronic diseases, including HIV, indicate peer
11 support groups can promote positive behaviors necessary for retention in care.[33, 48, 49] A
12 previous qualitative study among TB patients in Uzbekistan found support and encouragement
13 from peers and family members was a motivating factor to remain in treatment.[27] Hence, in
14 addition to direct economic support, establishing social support networks using community
15 members may represent a low-cost intervention that could increase adherence to TB treatment in
16 Ukraine.[33]

17
18 Furthermore, our study findings are consistent with other research that pill burden represents an
19 important barrier to TB treatment adherence.[19, 35] As fixed-dose combination (FDC) pills
20 reduce TB treatment pill burden, the WHO recognizes higher patient satisfaction as an advantage
21 of FDCs and recommend their use in TB programs.[50] Procurement of FDCs in Ukraine might
22 improve patients' experience with TB treatment. We also note the lack of evidence supporting
23 the benefit of hepatoprotective agents with TB therapy.[51] Their ongoing use in Ukraine adds to
24 TB treatment pill burden and increases patients' expenses without a clear benefit.

25
26 Among individual-level factors assessed, we did not identify health literacy as a principal driver
27 of adherence, despite evidence in similar contexts that low TB knowledge adversely affects
28 treatment adherence.[27, 28] We found low knowledge about TB transmission modes though
29 could not directly link this to treatment adherence. Many participants also acknowledged the
30 negative consequences of missing TB treatment doses, but this did not emerge as a main
31 facilitator of treatment adherence. In contrast, qualitative studies among TB patients in Eastern
32 Europe have found that incorrect information about TB treatment, disseminated through lay
33 community networks, contributed to non-adherence whereas knowledge and belief in the
34 effectiveness of TB therapy as well as increased patient awareness about importance of treatment
35 facilitated adherence.[27, 28]

36
37 Notably, we did not identify themes that distinguish non-completers nor illuminate unique
38 reasons for incomplete treatment. Whereas certain factors, such as treatment cost and pill burden,
39 were identified as barriers in majority of non-completers (7 of 9 for each), these factors were also
40 identified by approximately half of completers. Indeed, each barrier to adherence identified
41 affected both completers and non-completers. While participants were largely motivated to
42 undergo treatment to remain healthy, we identified few facilitators of TB treatment adherence.
43 Our findings suggest that TB patients, with and without risk factors for non-adherence, broadly
44 encounter structural challenges within Ukraine's TB care delivery system that undercut their
45 motivation for adherence.

46 **Policy and Practice Implications**

Our findings highlight two major opportunities for changes in Ukraine's TB program targeted at delivering patient-centered care and improving TB treatment outcomes. First, similar to other assessment of TB services in this region [29], we found that highly centralized care and facility-based DOT undermine patient ability to remain in treatment. Whereas DOT focuses on medical care to achieve TB cure, there is increasing recognition of the need to integrate such medical services with financial and psychosocial support. Low socioeconomic status broadly undermines healthcare seeking behavior and it is well known that poverty elevates risk of TB disease, which in turn renders patients poorer.[25, 27, 31, 43-45] Thus, TB control efforts in this setting must address socio-economic factors that put patients at higher risk for TB and undercut their will to remain in care. Successful programs of socioeconomic and psycho-emotional support for TB patients have been documented in Ukraine and similar contexts in Eastern Europe [31, 41, 52]. Hence scale-up of such programs can be considered for broad adoption in Ukraine.

Second, we identified how negative provider-patient relationships adversely impacts treatment adherence. Raising awareness and training TB providers on patient-centered communication styles and collaborative approaches that promote patient ownership in treatment should be a priority for TB control efforts in Ukraine. Targeted provider training on effective strategies (e.g. establishing reminder systems) that promote TB treatment adherence [31, 41, 48] might also be useful in this setting. Efforts should also include support for providers to mitigate challenges that might influence their interpersonal communication with patients.

Limitations

Our study has notable limitations. It is possible our interviewers or interview guide did not sufficiently probe how patients' TB knowledge influence treatment adherence. We focused only on patients' perspectives about TB treatment without exploring providers' viewpoints. Future research efforts can investigate providers' experience to elucidate additional factors that influence TB treatment adherence in this context. TB providers approached eligible patients to provide them with study information and interviews frequently occurred in clinical settings despite offering participants their preferred choice of interview location. Although study staff informed participants that their decision to participate would not impact their future receipt of healthcare services and that the TB care providers would not be granted access to interview details, it remains possible that hospital-based recruitment and data collection may have resulted in selection bias. Our study results reflect a range of positive and negative descriptions of treatment settings and patient-provider interactions suggesting that patients did not feel obliged to only present a positive portrayal of their TB treatment experience. Lastly, our study sample was purposively selected for maximal variation in factors known to impact TB treatment adherence within only one region of Ukraine and thus may not be representative of the full spectrum of TB patients in Ukraine or of patients who receive care from private providers. Nonetheless, we believe that our study sample represents a substantial portion of the TB patient population, including those at particular risk for poor outcomes, and thus can inform approaches to support treatment adherence that are widely applicable.

Conclusion

We document a qualitative assessment of patients' experiences during TB treatment in Ukraine and identify targets for interventions that may improve TB treatment outcomes. Challenges that undermine treatment adherence were not unique to patients at highest risk for non-adherence, thus incorporating patient-centered approaches into TB control efforts will likely have a broad impact in Ukraine.

Acknowledgements

The authors are grateful to all the participating patients and TB staff in Kyiv Oblast. We also wish to thank the interviewers, Olena Zublenko, Svitlana Gatchenko, and Oleg Kurdin, for their contribution.

Contributors: MBM, OA, AEB, and TPF led the study design. VP oversaw acquisition of data in conjunction with OA, TK, OM, MB, and NR. OA, ED and TK conducted analysis and interpretation of data with supervision by AEB. OA and ED wrote the first draft of the manuscript, and all authors contributed to revision of manuscript for important intellectual content. All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Funding: This work was supported by the National Institute on Drug Abuse (NIDA) [T32DA013911 to OA and ED; R25DA037190-04 to ED] and The National Institute of Mental Health, The Brown Initiative in HIV and AIDS Clinical Research for Minority Communities [R25MH083620 to OA]. The funding sources had no role in the study design, in the collection, analysis, and interpretation of data, in the writing of the report or in the decision to submit the manuscript for publication.

Competing Interests: None declared.

Data sharing: Given the sensitive nature of this qualitative research and the possibility of identifying respondents, we are not able to make raw interview transcripts available in a public repository. However, we are willing to make portions of translated transcripts (with any identifying information redacted) available upon reasonable request. Interested persons should contact the corresponding author.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

REFERENCES

- 1 World Health Organization. Global Tuberculosis Report 2019.
2 http://www.who.int/tb/publications/global_report/en/ (accessed 28 Oct 2019).
- 3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- 2 World Health Organization. Tuberculosis Country Profiles.
<http://www.who.int/tb/country/data/profiles/en/> (accessed 28 Oct 2019).
- 3 Rechel B, Richardson E, McKee M, editors. Trends in health systems in the former Soviet countries. Observatory Studies Series, No. 35. Copenhagen (Denmark): European Observatory on Health Systems and Policies 2014. <https://www.ncbi.nlm.nih.gov/books/NBK458305/> (accessed 28 Oct 2019).
- 4 Koch E. Local Microbiologies of Tuberculosis: Insights from the Republic of Georgia. *Medical Anthropology* 2011;30(1):81–101.
- 5 Koch E. Tuberculosis Is a Threshold: the Making of a Social Disease in Post-Soviet Georgia. *Medical Anthropology* 2013;32(4):309–24.
- 6 Altice FL, Azbel L, Stone J, et al. The perfect storm: incarceration and the high-risk environment perpetuating transmission of HIV, hepatitis C virus, and tuberculosis in Eastern Europe and Central Asia. *Lancet* 2016;388(10050):1228–48.
- 7 Droznin M, Johnson A, Johnson AM. Multidrug resistant tuberculosis in prisons located in former Soviet countries: A systematic review. *PLoS One* 2017;12(3):e0174373.
- 8 Jolley E, Rhodes T, Platt L, et al. HIV among people who inject drugs in Central and Eastern Europe and Central Asia: a systematic review with implications for policy. *BMJ Open* 2012;2(5):e001465.
- 9 Gökengin D, Oprea C, Uysal S, et al. The growing HIV epidemic in Central Europe: a neglected issue?. *J Virus Erad* 2016; 2(3):156–161.
- 10 Atun R, Olynik I. Resistance to implementing policy change: the case of Ukraine. *Bull World Health Organ* 2008;86(2):147–54.
- 11 Public Health Center of the Ministry of Health of Ukraine. Tuberculosis in Ukraine Analytical and Statistical Reference Book. 2017.
https://www.phc.org.ua/sites/default/files/uploads/files/PATH_booklet_003-4.pdf (accessed 28 Oct 2019).
- 12 Ministry of Health of Ukraine, Unified Clinical Protocol for Primary, Secondary (Specialized) and Tertiary (Highly Specialized) Medical Care for Adults with Tuberculosis. 04 September 2014. Available: https://old.phc.org.ua/uploads/files/dn_20141231_1039dod.pdf (accessed 28 Oct 2019).
- 13 World Health Organization. The END TB Strategy. Global strategy and targets for tuberculosis prevention, care and control after 2015.
https://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1 (accessed 28 Oct 2019).

- 1
2
3 14 Lytvynenko N, Cherenko S, Feschenko Y, et al. Management of multi- and extensively drug-
4 resistant tuberculosis in Ukraine: how well are we doing? *Public Health*
5 *Action* 2014;4Suppl2:67–72.
6
7 15 Aibana O, Bachmaha M, Krasiuk V, et al. Risk factors for poor multidrug-resistant
8 tuberculosis treatment outcomes in Kyiv Oblast, Ukraine. *BMC Infect Dis* 2017;17(1):129.
9
10 16 Kliiman K, Altraja A. Predictors and mortality associated with treatment default in pulmonary
11 tuberculosis. *Int J Tuberc Lung Dis* 2010;14(4):454–63.
12
13 17 Mitruka K, Winston CA, Navin TR. Predictors of failure in timely tuberculosis treatment
14 completion, United States. *Int J Tuberc Lung Dis* 2012;16(8):1075–82.
15
16 18 Jenkins HE, Ciobanu A, Plesca V, et al. Risk factors and timing of default from treatment for
17 non-multidrug-resistant tuberculosis in Moldova. *Int J Tuberc Lung Dis* 2013;17(3):373–80.
18
19 19 Amuha MG, Kutuyabami P, Kitutu FE, et al. Non-adherence to anti-TB drugs among TB/HIV
20 co-infected patients in Mbarara Hospital Uganda: prevalence and associated factors. *Afr Health*
21 *Sci* 2009;9Suppl1:S8–15.
22
23 20 Caylà JA, Rodrigo T, Ruiz-Manzano J, et al. Tuberculosis treatment adherence and fatality
24 in Spain. *Respir Res.* 2009;10:121.
25
26 21 Bhagat VM, Gattani PL. Factors affecting tuberculosis retreatment defaults in Nanded, India.
27 *Southeast Asian J Trop Med Public Health* 2010;41(5):1153–7.
28
29 22 Muture BN, Keraka MN, Kimuu PK, et al. Factors associated with default from treatment
30 among tuberculosis patients in Nairobi province, Kenya: a case control study. *BMC Public*
31 *Health* 2011;11(1):696.
32
33 23 Burton NT, Forson A, Lurie MN, et al. Factors associated with mortality and default among
34 patients with tuberculosis attending a teaching hospital clinic in Accra, Ghana. *Trans R Soc Trop*
35 *Med Hyg* 2011;105(12):675–82.
36
37 24 Ifebunandu NA, Ukwaja KN. Tuberculosis treatment default in a large tertiary care hospital in
38 urban Nigeria: prevalence, trend, timing and predictors. *J Infect Public Health* 2012;5(5):340–5.
39
40 25 Lohiniva AL, Mokhtar A, Azer A, et al. Qualitative interviews with non-national tuberculosis
41 patients in Cairo, Egypt: understanding the financial and social cost of treatment adherence.
42 *Health Soc Care Community* 2016;24(6):e164–e172.
43
44 26 de Vries SG, Cremers AL, Heuvelings CC, et al. Barriers and facilitators to the uptake of
45 tuberculosis diagnostic and treatment services by hard-to-reach populations in countries of low
46 and medium tuberculosis incidence: a systematic review of qualitative literature. *Lancet Infect*
47 *Dis* 2017;17(5):e128–e143.
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 27 Horter S, Stringer B, Greig J, et al. Where there is hope: a qualitative study examining
4 patients' adherence to multi-drug resistant tuberculosis treatment in Karakalpakstan, Uzbekistan.
5 *BMC Infect Dis* 2016;16:362.
6

7
8 28 Stringer B, Lowton K, Tillashaikhov M, et al. 'They prefer hidden treatment': anti-
9 tuberculosis drug-taking practices and drug regulation in Karakalpakstan. *IJTL*
10 *2016;20(8):1084–90.*
11

12 29 Kielmann K, Vidal N, Riekstina V, et al. "Treatment is of primary importance, and social
13 assistance is secondary": A qualitative study on the organisation of tuberculosis (TB) care and
14 patients' experience of starting and staying on TB treatment in Riga, Latvia. *PLoS One*
15 *2018;13(10):e0203937.*
16

17
18 30 World Health Organization, Regional Office for Europe. Review of the National
19 Tuberculosis Programme in Ukraine 10-22 October 2010.
20 [http://www.euro.who.int/en/countries/ukraine/publications3/review-of-the-national-tuberculosis-](http://www.euro.who.int/en/countries/ukraine/publications3/review-of-the-national-tuberculosis-programme-in-ukraine)
21 [programme-in-ukraine](http://www.euro.who.int/en/countries/ukraine/publications3/review-of-the-national-tuberculosis-programme-in-ukraine) (accessed 28 Oct 2019).
22

23
24 31 Charyeva Z, Curtis S, Mullen S, et al. What works best for ensuring treatment adherence.
25 Lessons from a social support program for people treated for tuberculosis in Ukraine. *PLoS*
26 *One* 2019;14(8):e0221688.
27

28 32 World Health Organization. A patient-centered approach to TB care. 2018.
29 <https://apps.who.int/iris/bitstream/handle/10665/272467/WHO-CDS-TB-2018.13-eng.pdf?ua=1>
30 (accessed 28 Oct 2019).
31

32
33 33 The World Health Organization. Adherence to Long-term Therapies: Evidence for Action.
34 WHO, 2003. <http://whqlibdoc.who.int/publications/2003/9241545992.pdf> (accessed 28 Oct
35 2019).
36

37 34 Ukrainian State Statistical Services, Expenditures and Resources of Households of Ukraine in
38 year 2014, Kyiv, 2015. https://ukrstat.org/uk/druk/publicat/Arhiv_u/17/Arch_vrd_zb.htm
39 (accessed 28 Oct 2019).
40

41 35 Gebremariam MK, Bjune GA, Frich JC. Barriers and facilitators of adherence to TB
42 treatment in patients on concomitant TB and HIV treatment: a qualitative study. *BMC Public*
43 *Health* 2010;10:651.
44

45
46 36 Young HN, Len-Rios ME, Brown R, et al. How does patient-provider communication
47 influence adherence to asthma medications? *Patient Educ Couns* 2017;100(4):696–702.
48

49 37 Schoenthaler A, Knafl GJ, Fiscella K, et al. Addressing the social needs of
50 hypertensive patients: The role of patient-provider communication as a predictor of
51 medication adherence. *Circ Cardiovasc Qual Outcomes*. 2017;10(9):e003659.
52

53
54 38 Sohal T, Sohal P, King-Shier KM, et al. Barriers and facilitators for type-2 diabetes
55 management in South Asians: A systematic review. *PLoS One* 2015;10(9):e0136202.
56
57

- 1
2
3 39 Pachi A, Bratis D, Moussas G, et al. Psychiatric morbidity and other factors affecting
4 treatment adherence in pulmonary tuberculosis patients. *Tuberc Res Treat* 2013;2013:489865.
5
6 40 Tola HH, Tol A, Shojaeizadeh D, et al. Tuberculosis treatment non-adherence and lost to
7 follow up among TB patients with or without HIV in developing countries: A systematic review.
8 *Iran J Public Health* 2015;44(1):1–11.
9
10 41 van Hoorn R, Jaramillo E, Collins D, et al. The effects of psycho-emotional and socio-
11 economic support for tuberculosis patients on treatment adherence and treatment outcomes -
12 A systematic review and meta-analysis. *PLoS One* 2016;11(4):e0154095.
13
14 42 Gelmanova IY, Taran DV, Mishustin SP, et al. 'Sputnik': a programmatic approach to
15 improve tuberculosis treatment adherence and outcome among defaulters. *Int J Tuberc Lung Dis*
16 2011;15:1373–1379.
17
18 43 Mauch V, Bonsu F, Gyapong M, et al. Free tuberculosis diagnosis and treatment are not
19 enough: patient cost evidence from three continents. *Int J Tuberc Lung Dis* 2013;17(3):381–7.
20
21 44 Chida N, Ansari Z, Hussain H, et al. Determinants of default from tuberculosis treatment
22 among patients with drug-susceptible tuberculosis in Karachi, Pakistan: A mixed methods study.
23 *PLoS One* 2015;10(11):e0142384.
24
25 45 Paz-Soldán VA, Alban RE, Jones CD, et al. The provision of and need for social support
26 among adult and pediatric patients with tuberculosis in Lima, Peru: a qualitative study. *BMC*
27 *Health Serv Res* 2013;13:290.
28
29 46 Andrade KVF, Nery JS, Souza RA, et al. Effects of social protection on tuberculosis
30 treatment outcomes in low or middle-income and in high-burden countries: systematic review
31 and meta-analysis. *Cad Saude Publica* 2018;34(1):e00153116.
32
33 47 Priedeman Skiles M, Curtis SL, et al. Evaluating the impact of social support services on
34 tuberculosis treatment default in Ukraine. *PLoS One* 2018;13(8):e0199513.
35
36 48 Rachlis B, Naanyu V, Wachira J, et al. Identifying common barriers and facilitators to linkage
37 and retention in chronic disease care in western Kenya. *BMC Public Health*. 2016;16:741.
38
39 49 Kanters S, Park JJ, Chan K, et al. Use of peers to improve adherence to antiretroviral therapy:
40 a global network meta-analysis. *J Int AIDS Soc* 2016;19(1):21141.
41
42 50 World Health Organization. Treatment of Tuberculosis: Guidelines for treatment of drug-
43 susceptible tuberculosis and patient care. 2017 update.
44 <https://apps.who.int/iris/bitstream/handle/10665/255052/9789241550000-eng.pdf?sequence=1>
45 (accessed 28 Oct 2019).
46
47 51 Saito Z, Kaneko Y, Kinoshita A, et al. Effectiveness of hepatoprotective drugs for anti-
48 tuberculosis drug-induced hepatotoxicity: a retrospective analysis *BMC Infect Dis* 2016;16(1):
49 668.
50
51
52
53
54
55
56
57
58
59
60

1
2
3 52 Garden B, Samarina A, Stavchanskaya I, et al. Food incentives improve adherence to
4 tuberculosis drug treatment among homeless patients in Russia. *Scand J Caring Sci*
5 2013;27:117–122.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

INTERVIEW GUIDE

A. Introduction

- 1) Before starting the interview, I want to thank you for participating in the study. If you need any clarifications about any question, please feel free to ask me at any time. I would also like to remind you that you can choose not to answer questions if you are uncomfortable; and you can stop the interview at any time.

Interviewer: Remind patient that interview results will be anonymous; interviewer is not a doctor and does not work for the oblast/rayon TB hospital or polyclinic; information discussed will not be relayed to patients' doctors or family.

B. General question

Now, we're going to talk briefly about your health and healthcare in general.

- 2) What types of medical care do you think are important to have access to? Why?

C. TB Diagnosis: Healthcare team/system-related

Now, we're going to talk more about your Tuberculosis diagnosis.

- 3) Do you remember when you were diagnosed with Tuberculosis? Can you please tell me about that?

Try to get patient to talk about:

- How long did it take to receive the final diagnosis (days/months/number of visits to the clinic/hospital)?
- Setting of diagnosis (primary care clinic? Private doctor? TB ambulatory clinic? TB hospital?)
- If they recall how long it took them to contact the healthcare doctor/facility after symptoms started
- What was the final push to seek medical attention?

C. TB Diagnosis: Condition-related

- 4) Who did you disclose your TB diagnosis to?

Try to get patient to be specific:

- E.g. family, friends, co-workers, neighbors, employer/boss)?
- Were you worried about people finding out you have TB? And why?

- 5) How did the people react to the disclosure; did the relationship change?

D. TB Treatment: Therapy-Related Factors

- 6) How many months of TB treatment were you prescribed at first? How many months did you actually receive? Was this different from how long you expected? Why?

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
- 7) Can you please tell me some specifics about your treatment for TB? For example, how many times a week did you take pills? Where did you take your pills (at home, at a clinic, in a hospital, somewhere else)? How did your treatment change over time?
 - 8) After you started taking TB medications, did your symptoms change? (e.g. improve? Worsen? Or stay the same?) What was your expectation about that?
 - 9) Did you have any concerns or questions about your treatment? What were they and how did you address them?
 - 10) Did you have any side effects? How did you cope with them?
 - 11) What were the most challenging aspects of TB treatment for you? Probe patient to be specific

E. TB Treatment: Preferences

- 16
17
18
19
20
21
22
23
24
25
26
- 12) If you could choose, where would you prefer to get TB treatment? Why?
 - 13) Are there some specific types of support you wish you had during TB treatment? (Probe the patient to be specific (e.g monetary or emotional support and from whom? Maybe family, friends, healthcare workers, government, NGO etc).

F. TB Treatment: Patient-related, Adherence Barriers and Motivators

- 27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
- 14) Were there days or periods when you didn't take the TB medicine (or thought about not taking the medicines?) Can you please tell me about that?
Try to discuss:
 - Approximate number of days per month (or number of months) treatment was skipped
 - Why did patient stop taking medicines or why did they think about it?
 - a) If they stopped more than once, what were the reasons each time? (Explore issues that contributed to not taking the meds (e.g logistics? Side effects? Cost?))
 - b) Ask patient how they felt when this happened?
 - 15) Were there times during your treatment where you thought about NOT taking the medicines but ultimately took them? Can you tell me more about what motivated you to do so?
 - 16) What was the /reaction of healthcare workers when you stopped treatment? What did they tell you to do?

G. TB Treatment: Healthcare team- and system-related

- 47
48
49
50
51
52
53
54
55
56
57
58
59
60
- 17) How did you get to the facility to take your treatment? (Duration of travel, cost etc)
 - 18) Can you please tell me about the facilities (dispensaries and hospitals) where you received your care? What do you think about the care provided to TB patients?
Talk about:
 - flexibility of hours
 - Medication stock-outs
 - Cleanliness
 - Privacy for consults/giving samples
 - Wait time to be seen
 - General patient-friendliness

1 19) Can you please tell me about the healthcare workers at the facilities where you received TB care?

2
3 Talk about:

- 4
- 5 • Impression of how healthcare workers interacted with patient
 - 6 • Amount of time patient spent with doctor or nurse
 - 7 • Did patient have time to ask questions and what did patient think of the responses to their
 - 8 questions
 - 9

10
11 20) Did the healthcare workers explain your illness to you? Please tell me about that

12
13 Try to discuss the information patients received:

- 14
- 15 • At the time of diagnosis
 - 16 • During the course of their treatment
 - 17 • Regarding prognosis
 - 18 • Regarding side effects
 - 19

20
21
22 **H. TB Knowledge: Patient-related**

23
24
25 21) Did you have enough information about TB? Where did you get information regarding TB? (e.g.
26 from healthcare workers, friends, family, or internet?)

27
28 Tell me please what you know about TB:

- 29
- 30 • Mode of transmission
 - 31 • Effectiveness of treatment
 - 32 • Impact of missing treatment
 - 33

34
35 **I. Impact of TB**

36 22) Has TB changed your life or the life of your family in any way? Can you tell me more about that?

37
38 Talk about:

- 39
- 40 • Relationships with family/friends/others
 - 41 • Mental health
 - 42 • Work or School
 - 43 • Overall financial impact of TB
 - 44

45
46 23) At the time you had TB, did you have any other health problem? How did having TB affect your
47 other illness? And vice versa?

48
49 **J. Conclusion**

50
51 24) If you could think about changes to the process of TB treatment, what would you want to be done
52 differently?

53
54
55 *Thank you again for your participation.*

Standards for Reporting Qualitative Research (SRQR)*

<http://www.equator-network.org/reporting-guidelines/srqr/>

	Page/line no(s).
Title and abstract	
Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	Page 1, Title
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	Page 2, Abstract
Introduction	
Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	Pages 4-5, Intro
Purpose or research question - Purpose of the study and specific objectives or questions	Page 5, Intro (paragraph 6)
Methods	
Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	Page 7, Data Analysis (paragraph 1)
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	NA
Context - Setting/site and salient contextual factors; rationale**	Page 4, Introduction Page 5, Study Setting
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	Page 5, Sampling
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	Page 5, Ethics Statement
Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	Page 5, Sampling, (paragraph 2) Pages 6, Data Collection

	Procedures
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	Pages 6, Data Collection Procedures
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	Page 8, Results (Paragraph 1), Table 2
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	Page 7, Data Analysis
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	Pages 6, Data Collection Procedures Page 7, Data Analysis
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	Pages 7, Data Analysis

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	Pages 8-16, Results
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Pages 8-16, Results

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	Pages 16-18, Discussion
Limitations - Trustworthiness and limitations of findings	Page 19, Limitations

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	Page 20, Competing Interests
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	Page 20, Funding

1 *The authors created the SRQR by searching the literature to identify guidelines, reporting
2 standards, and critical appraisal criteria for qualitative research; reviewing the reference
3 lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to
4 improve the transparency of all aspects of qualitative research by providing clear standards
5 for reporting qualitative research.
6
7

8 **The rationale should briefly discuss the justification for choosing that theory, approach,
9 method, or technique rather than other options available, the assumptions and limitations
10 implicit in those choices, and how those choices influence study conclusions and
11 transferability. As appropriate, the rationale for several items might be discussed together.
12

13
14 **Reference:**

15 O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative**
16 **research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
17 DOI: [10.1097/ACM.0000000000000388](https://doi.org/10.1097/ACM.0000000000000388)
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60