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Supporting multidrug-resistant or rifampicin-resistant TB treatment adherence in people with harmful use of alcohol through person-centred care

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Background: TB is concentrated in populations with complex health and social issues, including alcohol use disorders (AUD). We describe treatment adherence and outcomes in a person-centred, multidisciplinary, psychosocial support and harm reduction intervention for people with multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) with harmful alcohol use.

Methods: An observational cohort study, including multilevel mixed-effects logistic regression and survival analysis with people living in Minsk admitted with MDR/RR-TB and AUD during January 2019–November 2021 who received this person-centred, multidisciplinary, psychosocial support and harm reduction intervention, was conducted.

Results: There were 89 participants enrolled in the intervention, with a median follow-up of 12.2 (IQR: 8.1–20.5) mo. The majority (n=80; 89.9%) of participants had AUD, 11 (12.4%) also had a dependence on other substances, six (6.7%) a dependence on opioids and three (3.4%) a personality disorder. Fifty-eight had a history of past incarceration (65.2%), homelessness (n=9; 10.1%) or unemployment (n=55; 61.8%). Median adherence was 95.4% (IQR: 90.4–99.6%) and outpatient adherence was 91.2% (IQR: 65.1–97.0%). Lower adherence was associated with hepatitis C, alcohol plus other substance use and outpatient facility-based treatment, rather than video-observed treatment, home-based or inpatient treatment support.

Conclusions: This intervention led to good adherence to MDR/RR-TB treatment in people with harmful use of alcohol, a group usually at risk of poor outcomes. Poor outcomes were associated with hepatitis C, other substance misuse and outpatient facility-based treatment support.

Keywords: alcohol use disorder, directly observed treatment, MDR/RR-TB, multidisciplinary, psychosocial care, treatment support.

Introduction

Multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) remains a global public health problem, with an estimated annual incidence of 0.5 million people affected globally and a treatment success rate of 59%.[1] The burden is particularly high in Eastern Europe and Central Asia. In Belarus, it is estimated there were >874 people with MDR/RR-TB in 2020, almost one-half of the

1778 people with TB. Despite improvements in diagnosis and care, Belarus remains one of the 30 highest ranked countries with a burden of MDR-TB.[1]

TB tends to be concentrated in groups with complex health and social issues, for example, homelessness, alcohol and substance misuse, and lack of access to healthcare or welfare.[2,3] In particular, people with alcohol use disorders (AUD) are at risk, with an estimated 740 000 incidents of TB attributable to alcohol disorders annually[1]; also, the risk of active TB is increased threefold.[4] In Minsk, approximately 40% of people with MDR/RR-TB present with AUD, and it is identified as one of the main barriers to adherence to treatment and a principal reason for people being sent to hospital for involuntary isolation.[5] Involuntary isolation is decreasing in Belarus, but remains a concern, and better outpatient approaches are needed.[6]

In 2014, Médecins Sans Frontières (MSF) opened a project to support the Belarus National Tuberculosis Programme to improve MDR/RR-TB treatment adherence and outcomes by providing a psychosocial support and harm reduction intervention for people with MDR/RR-TB using a person-centred approach through a multidisciplinary team of counsellors, educators, nurses, doctors, social workers and health promoters. The intervention includes patient education, counselling, mental health and social care. Person-centred care (PCC) is a way of delivering evidence-based, holistic, respectful healthcare tailored to an individual's changing needs. It respects an individual's autonomy to manage their own healthcare choices, based on advice from healthcare professionals.[7] PCC is pillar one of the End TB Strategy,[8] however, it is often restricted to pilot programmes only, while TB programmes tend to focus on case detection, treatment adherence and treatment outcomes.[9]

This study aimed to describe the characteristics and treatment outcomes of MSF's person-centred, multidisciplinary psychosocial support and harm reduction (PCMPS) intervention for people with MDR/RR-TB with a disorder due to the use of alcohol in Minsk.

Methods

Study setting and population

This study took place in Minsk, Belarus, where the estimated population is 2 100 000, and the number of people starting MDR/RR-TB treatment every year is around 200.

Study design

This was a cohort study using routinely collected data on people admitted to the PCMPS intervention. This was prospective for people enrolled after the study received approval (January 2020), and retrospective for those enrolled in 2019. A combined retrospective and prospective design was used for this study, as the care package was implemented before the study protocol and ethical approval could be finalised, and a fully prospective design would have resulted in too small a sample size for meaningful analysis. The full study protocol can be accessed on MSF's website at https://remit.msf.org/studies/973.

Inclusion criteria

People were included who:

- started treatment for MDR/RR-TB (pulmonary TB) during 1 January 2019–30 November 2021
- were aged >18 y
- lived in Minsk city
- had a confirmed or suspected alcohol disorder
- provided written informed consent to participate in the study (including people enrolled after the study received approval in January 2020).

Data collection

The data used for this study were collected through programme monitoring activities. Full details of the PCMPS intervention are provided in the supplementary material. Routinely collected data were used, including information on adherence, comorbidities, diagnoses of the 10th revision of the International Classification of Diseases (ICD-10),[10] TB treatment, mode of treatment support, TB outcome, sociodemographic information and screening tests (Patient Health Questionnaire-9 [PHQ-9] for screening of symptoms of depression; General Anxiety Disorder-7 [GAD-7] for screening of symptoms for anxiety; Alcohol Use Disorders Identification Test [AUDIT] to assess alcohol consumption and drinking behaviour;[11] Alcohol, Smoking and Substance Involvement Screening Test [ASSIST][12] to screen substance use and provide a self-motivation score).[13–16] All data were collected by health workers during sessions at baseline with patients, and the PHQ-9, GAD7, AUDIT, ASSIST and the self-motivation score were completed at 6-mo intervals for monitoring during follow-up. Written informed consent was obtained by counsellors for patients enrolling after January 2020.

Data analysis

Descriptive analysis of all variables (sociodemographic, clinical and mental health at cohort entry), stratified by the key outcome variables, was carried out. The outcome variables were being adherent or non-adherent, or having a positive treatment outcome. A positive treatment outcome was defined as being cured or completing treatment or being on treatment at study closure. Study closure was 28 February 2022, allowing at least 3 mo in care.

Confirmed or suspected alcohol disorder was defined as receiving an F10 ICD10 diagnosis from a psychiatrist or moderate or high scoring in the AUDIT or ASSIST screening tests. Adherent was defined as having taken >90% of the prescribed doses, ascertained through visits by a nurse or through video. Lost to follow-up (LTFU) was defined according to the WHO definition, whereby people interrupted their treatment for 2 consecutive months or longer. Any patient who was LTFU was classified as non-adherent. People who moved out of Minsk and continued TB treatment elsewhere were classified as 'not evaluated', but were included in this analysis until transfer. In the case of missing data, the study team would ask the data manager and clinicians to recheck files,

or if possible, to check with the patient to provide the missing data. Imputation was not carried out on any remaining missing data. Absolute counts, proportions, medians, IQRs and their respective 95% CIs are presented. Kaplan–Meier survival analysis was applied to calculate outcomes at 6, 12 and 18 mo. Multilevel mixed-effects logistic regression was applied to calculate the risk of non-adherence per treatment/month, whereby non-adherence was taking <90% of prescribed treatment in a calendar month. Patient ID was included as a random intercept and month of treatment was included as a random slope, where the correlation over time was modelled using an unstructured covariance. Fixed-effects variables were included in the multivariate model if there was an association with the method of treatment support and adherence by treatment/month by examining univariable models. A forward stepwise approach was used to determine which variables to include in the multivariable model. Variables that were colinear, or had large amounts of missing data, were not included in the multivariate model. An interaction term was applied between month of treatment and method of treatment support to examine time trends. An interaction term was applied between month of treatment and method of treatment support to examine time trends.

Ethics

Ethical approval for this study was received from the MSF Ethical Review Board (ref:1980) and from the ethics committee at the Republican Scientific and Practical Centre of Pulmonology and Tuberculosis (RSPCPT). All data were anonymised.

Results

Baseline characteristics of participants in the study

There were 89 people included, of whom 14 (15.7%) were female and 75 (84.3%) were male. Participants' baseline social characteristics, stratified by adherence status, are provided in Table 1A.

Table 1B shows the baseline medical characteristics stratified by adherence status. The most commonly recorded comorbidity was hepatitis C (n=32; 36.0%).

Table 1C shows the baseline mental health characteristics stratified by adherence status. The majority (n=83; 93.2%) of participants had an ICD10 mental health diagnosis. Eighty (89.9%) had an ICD10 alcohol diagnosis, while 11 (12.4%) had a dependency on other substances, including cathinones with/without opioids, while a further six (6.7%) had opioid and alcohol dependency.

ASSIST and AUDIT scores indicated that 40 (44.9%) self-reported moderate alcohol or other substance use, 20 (22.5%) high use and 29 (32.6%) low use.

A few participants had other mental health diagnoses; the most common were personality disorders (n=3; 3.4%). Two participants (2.2%) had a mental health disorder that was brought on by the effects of alcohol or other substances.[17] One patient reported mild intellectual difficulties, two people had an adjustment/anxiety disorder, six (6.8%) reported moderate or severe anxiety (GAD7) and 17 (19.3%) moderate or severe depression (PHQ9).

Table 1A. Baseline social characteristics of participants enrolled in the programme from January 2019 to November 2021, stratified by adherence status.

Characteristic	≥90% adherence (N=67)	<90% adherent (N=22)	Total (N=89)
Gender			
Male	57 (76.0%)	18 (24.0%)	75
Female	10 (71.4%)	4 (28.6%)	14
Age group, y			
<35	11 (73.3%)	4 (26.7%)	15
35–55	42 (75.0%)	14 (25.0%)	56
>55	14 (77.8%)	4 (22.2%)	18
Marital status			
In union	27 (73.0%)	10 (27.0%)	37
Single	21 (84.0%)	4 (16.0%)	25
Widowed/divorced/ separated	19 (70.4%)	8 (29.6%)	27
Education level			
Did not finish school	3 (100.0%)	0 (0.0%)	3
Secondary	58 (73.4%)	21 (26.6%)	79
Graduate	6 (85.7%)	1 (14.3%)	7
Employment status			
Employed	24 (70.6%)	10 (29.4%)	34
Unemployed	43 (78.2%)	12 (21.8%)	55
History of incarceration			
Yes	44 (75.9%)	14 (24.1%)	58
No	23 (74.2%)	8 (25.8%)	31
Homeless status			
Homeless	7 (77.8%)	2 (22.2%)	9
Not homeless	60 (75.0%)	20 (25.0%)	80
Smoker			
Yes	52 (80.0%)	13 (20.0%)	65
No	2 (50.0%)	2 (50.0%)	4
IV illicit drug use			
Yes	9 (64.3%)	5 (35.7%)	14
No	45 (84.9%)	8 (15.1%)	53
Non-IV illicit drug use			
Yes	11 (68.8%)	5 (31.2%)	16
No	43 (84.3%)	8 (15.7%)	51
VOT			
No	41 (68.3%)	19 (31.7%)	60
Yes	26 (89.7%)	3 (10.3%)	29
Outpatient home-based support			
No	58 (73.4%)	21 (26.6%)	79
Yes	9 (90.0%)	1 (10.0%)	10
Outpatient facility support			
No	35 (97.2%)	1 (2.8%)	36
Yes	32 (60.4%)	21 (39.6%)	53
Inpatient only			
No	46 (68.7%)	21 (31.3%)	67
Yes	21 (95.5%)	1 (4.5%)	22

Abbreviations: IV, intravenous; VOT, video-observed treatment.

Table 1B. Baseline medical characteristics of participants enrolled in the programme from January 2019 to November 2021, stratified by adherence status.

Characteristic	≥90% adherence (N=67)	<90% adherent (N=22)	Total (N=89)
Regimen length			
Long (18–20 mo) regimen	30 (75.0%)	10 (25.0%)	40
Short regimen	9 (60.0%)	6 (40.0%)	15
Previous history of TB			
Yes	27 (73.0%)	10 (27.0%)	37
No	40 (76.9%)	12 (23.1%)	52
HIV status			
Positive	20 (80.0%)	5 (20.0%)	25
Negative	46 (73.0%)	17 (27.0%)	63
Hepatitis C status			
Yes	20 (62.5%)	12 (37.5%)	32
No	47 (82.5%)	10 (17.5%)	57
Hepatitis B status			
Yes	2 (50.0%)	2 (50.0%)	4
No	64 (76.2%)	20 (23.8%)	84
Diabetes status			
Yes	3 (75.0%)	1 (25.0%)	4
No	63 (75.0%)	21 (25.0%)	84
COPD			
Yes	3 (75.0%)	1 (25.0%)	4
No	63 (75.0%)	21 (25.0%)	84
Cirrhosis			
Yes	3 (100.0%)	0 (0.0%)	3
No	60 (74.1%)	21 (25.9%)	81
Renal illness			
Yes	2 (66.7%)	1 (33.3%)	3
No	64 (75.3%)	21 (24.7%)	85
Heart disease			
Yes	14 (82.4%)	3 (17.6%)	17
No	51 (72.9%)	19 (27.1%)	70

Abbreviation: COPD, chronic obstructive pulmonary disease.

TB treatment adherence

The median overall adherence for all people in the programme was 95.4% (IQR: 90.4–99.6%) and outpatient adherence was 91.2% (IQR: 65.1–97.0%). These are not the final data on adherence as 18 (20.2%) people have not completed treatment. Sixteen (72.7%) people who had adherence <90% were LTFU.

Factors associated with adherence

Tables 1A–1C show the proportion of people who adhered to treatment stratified by personal characteristics. Adherence <90% was more common in those with hepatitis C, certain psychiatric diagnoses and there was weak correlation with intravenous (IV) illicit drug use. Good adherence was associated with video-observed treatment (VOT); in inpatients, poor adherence was associated with facility-based treatment support.

Adherence by type of treatment support

Most of the treatment (53%; 550/1038 treatment/months) received was as an inpatient. Median inpatient adherence was very good at 100% (IQR: 100–100%), with 96.2% of treatment months ≥90%. Twenty-two (24.7%) participants were treated only as inpatients. The proportions of treatment/months ≥90% for VOT, facility-based and home-based support were 80.3%, 58.8% and 90.0%, respectively. Figure 1A shows the proportion of people utilising each type of support over time. Inpatient care reduced over time while outpatient care, particularly VOT, increased over time. Figure 1B shows the linear line-of-best-fit for support method by treatment month. VOT adherence decreases over calendar time and treatment month, while outpatient facility support increases and the two other methods show no trend.

Table 2 shows a multilevel, mixed-effects logistic regression to assess the difference in adherence per treatment/month by type of support, controlling for selected characteristics. After adjustment, the odds of non-adherence for inpatients, home-based support and VOT were not statistically different, but facility-based support displayed the worst results. A table describing the differences in characteristics of the participants in each group is provided in the supplementary material.

TB treatment outcomes

Figure 2 shows the Kaplan–Meier curve for survival in the programme's cohort, with died, LTFU or failed as the outcome. Attrition is fastest in the first month, then remains fairly steady until month 14, and after that is static. Estimated outcomes at 6, 12 and 18 mo were 85.3% (95% CI 78.2 to 93.0%), 74.5% (95% CI 65 to 85.3%) and 67.1% (95% CI 56 to 80.3%), respectively. The median follow-up time on treatment was 12.2 (IQR: 8.1–20.5) mo. Not all participants in the study were followed up until treatment completion, with 18 (20%) of patients still on treatment in the programme and 13 (15%) not evaluated, due to being transferred to another facility and still being in treatment.

Factors associated with poor outcomes

Table 3 shows selected factors associated with LTFU, death or failure. The factors that were associated with poor outcomes were very similar to those for poor adherence: IV drug use, hepatitis C, a diagnosis of alcohol plus other substance misuse and facility-based support.

Discussion

TB treatment adherence and outcomes in a person-centred programme

Participants enrolled in the person-centred multidisciplinary psychosocial support and harm reduction intervention had good overall and outpatient adherence. While it was not possible to

Table 1C. Baseline mental health characteristics of participants enrolled in the programme from January 2019 to November 2021, stratified by adherence status.

Characteristic	≥90% Adherence (N=67)	<90% adherent (N=22)	Total (N=89)
Self-reported history of mental health issues			
Yes	2 (50.0%)	2 (50.0%)	4
No	65 (76.5%)	20 (23.5%)	85
Psychiatric diagnosis*			
F10.2 alcohol dependence	36 (73.5%)	13 (26.5%)	49
F10.0 acute alcohol intoxication	1 (33.3%)	2 (66.7%)	3
F10.1 harmful alcohol use	10 (100.0%)	0 (0.0%)	10
F19.2 alcohol plus other substance dependence	3 (37.5%)	5 (62.5%)	8
F11.2 opioid dependence and alcohol use or dependence	6 (100.0%)	0 (0.0%)	6
F70 mild intellectual difficulties and F10.2 alcohol dependence	1 (100.0%)	0 (0.0%)	1
F07.8/F06.8 disorder due to physical condition and F10.2 alcohol disorder	2 (100.0%)	0 (0.0%)	2
F60.3/F61 personality disorder and F10.2 alcohol or F19.2 substance dependence	3 (100.0%)	0 (0.0%)	3
F43.2 adjustment disorder and F10.2 alcohol dependence	0 (0.0%)	1 (100.0%)	1
None recorded	5 (83.3%)	1 (16.7%)	6
Baseline PHQ9			
<4 minimal	41 (74.5%)	14 (25.5%)	55
5–9 mild	12 (70.6%)	5 (29.4%)	17
10–14 moderate	10 (90.9%)	1 (9.1%)	11
≥15 moderately severe/severe	4 (66.7%)	2 (33.3%)	6
Baseline GAD7			
Minimal	54 (73.0%)	20 (27.0%)	74
Mild	8 (100.0%)	0 (0.0%)	8
Moderate or severe	4 (66.7%)	2 (33.3%)	6
Baseline ASSIST or AUDIT score			
Low	20 (69.0%)	9 (31.0%)	29
Moderate	33 (82.5%)	7 (17.5%)	40
High	14 (70.0%)	6 (30.0%)	20
Baseline risk for adherence issues			
Low risk	6 (85.7%)	1 (14.3%)	7
Moderate risk	44 (78.6%)	12 (21.4%)	56
High risk	17 (65.4%)	9 (34.6%)	26
Baseline self-motivation			
Low	6 (75.0%)	2 (25.0%)	8
Moderate	31 (73.8%)	11 (26.2%)	42
High	30 (76.9%)	9 (23.1%)	39

Abbreviations: ASSIST, Alcohol, Smoking and Substance Involvement Screening Test; AUDIT, Alcohol-use disorders identification test; GAD7, General Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.
*10th revision of the International Classification of Diseases.

formally compare the adherence in this cohort with another cohort, we collected information on adherence for other people with MDR/RR-TB in Minsk. Median overall adherence for 31 individuals not in the programme but attending the same facilities, who had completed MDR/RR-TB treatment, was 90% (IQR: 84–99%) compared with 95% who received the intervention (IQR: 90–100%). Median inpatient adherence for people with MDR/RR-TB not enrolled in this programme, but who had alcohol or substance use disorders, was identical at 100%. This suggests that this approach may have had a positive impact on outpatient adherence, in this risk group, without requiring involuntary hospitalisation.

Of participants in this cohort, 85% and 67% are either still in treatment or were cured and completed treatment at 6 and 18 mo, respectively. Treatment success may therefore be slightly lower in this cohort than the average in Belarus, of 74% and 80%, in 2018 and 2019.

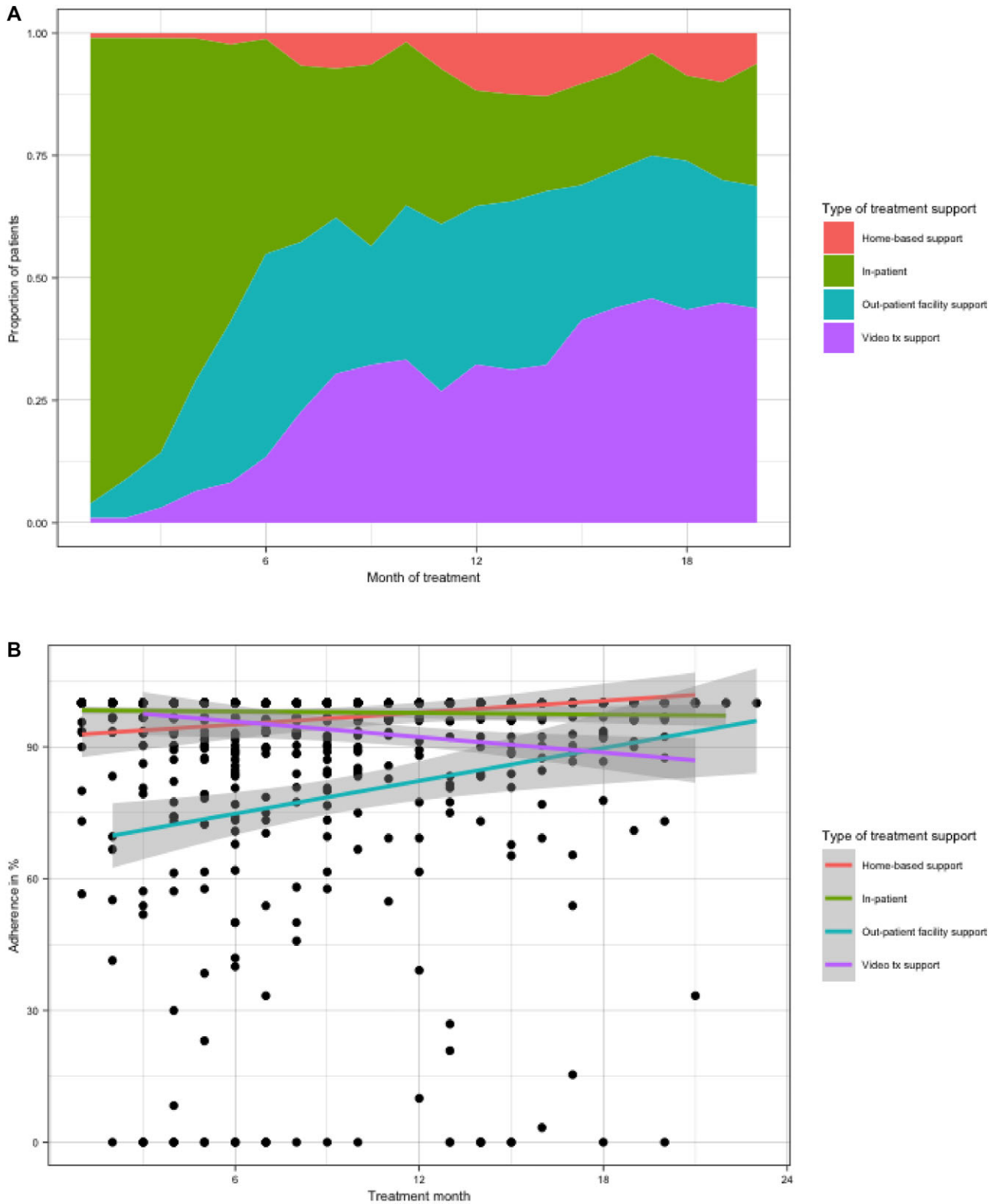

Figure 1. (A) Proportion of 89 participants enrolled in the programme utilising each method of treatment support per treatment month. (B) Monthly adherence for 89 participants in the programme by method of treatment support over treatment month, with a linear trend.

Table 2. Regression on treatment non-adherence by method of treatment support with outcome adherence <90% in a calendar month.

	Univariable model	Multivariable model	
	OR* (95% CI)	AOR* (95% CI)	p value
Fixed effects			
Method type			
VOT	Reference	Reference	
Facility based	3.8 (1.7–8.7)	13.0 (1.9–90.3)	<0.0001
Home based	0.3 (0.1–1.5)	5.7 (0.1–228.0)	
Inpatient	0.1 (0.0–0.2)	0.2 (0.0–1.4)	
Month of treatment	1.2 (1.0–1.3)	1.1 (0.9–1.3)	
Interaction with month of treatment and method			
VOT	Interaction not presented in univariate	Reference	
Facility based		0.8 (0.7–1.0)	
Home based		0.7 (0.5–1.0)	
Inpatient		0.9 (0.7–1.2)	
Hepatitis C			
No	Reference	Reference	
Yes	2.0 (0.7–5.3)	2.5 (0.9–6.8)	0.0718
Baseline motivation			
High	Reference	Reference	
Moderate	1.7 (0.6–4.6)	1.9 (0.8–4.5)	0.1332
Low	2.3 (0.4–12.5)	3.9 (0.9–16.6)	
Psychiatric diagnosis			
Alcohol disorder	Reference	Reference	
Alcohol and other substance dependence	1.6 (0.4–6.7)	2.1 (0.5–9.8)	0.0522
Disorder due to physical condition and alcohol dependence	0.1 (0.003–4.3)	0.2 (0.01–3.3)	
Acute alcohol intoxication	4.0 (0.5–31.9)	2.3 (0.3–16.4)	
Mild intellectual difficulties and alcohol dependence	2.4 (0.1–66.0)	1.9 (0.1–36.0)	
Harmful alcohol use	0.3 (0.1–1.6)	0.5 (0.1–2.0)	
None recorded	0.2 (0.001–2.3)	0.2 (0.0–3.4)	
Opioid and alcohol dependence or use	0.0 (0.002–0.6)	0.04 (0.004–0.5)	
Personality disorder and alcohol and substance dependence	0.9 (0.1–9.2)	0.5 (0.1–4.3)	
Adjustment and alcohol disorder	3.2 (0.1–103.8)	6.1 (0.1–249.0)	

Abbreviations: AOR, adjusted OR; VOT, video-observed treatment.
*OR and AOR presented with person and month of treatment included as random effects with participant as a random intercept and month of treatment as a random slope with an unstructured covariance. For AOR adjustments are made for all other variables presented as fixed effects.

People in this study are particularly vulnerable, and experience a high level of marginalisation, and high levels of distrust towards others.[18] The intervention worked through building a trusting relationship, allowing the provision of multidisciplinary, holistic support, which has been previously described.[18]

This study presents the findings of the PCMPS intervention in a cohort of participants with MDR-TB and with AUD. There is limited evidence published on interventions to support people experiencing these comorbidities. The study depicts findings from a cohort in one geographical region and this could potentially limit its generalisability. However, we believe that all people experiencing MDR-TB and AUD face similar challenges from these conditions and similar interventions would impact them positively, regardless of geographical location.

Risk factors for poor adherence

Levels of adherence and treatment outcomes were worst among people with hepatitis C. Healthcare providers reported that this may be because people with hepatitis C self-monitor damage to their liver caused by the combination of alcohol, other substances, hepatitis C treatment and MDR/RR-TB treatment, so skip doses to protect their livers.

In a systematic review, mental health disorders were shown to be associated with twice the odds of a poor TB treatment outcome,[19] and harmful alcohol and substance use are well-reported risk factors for TB outcomes.[20,21] The majority of participants in this cohort were diagnosed with a mental health disorder, most commonly an alcohol disorder. Levels of depres-

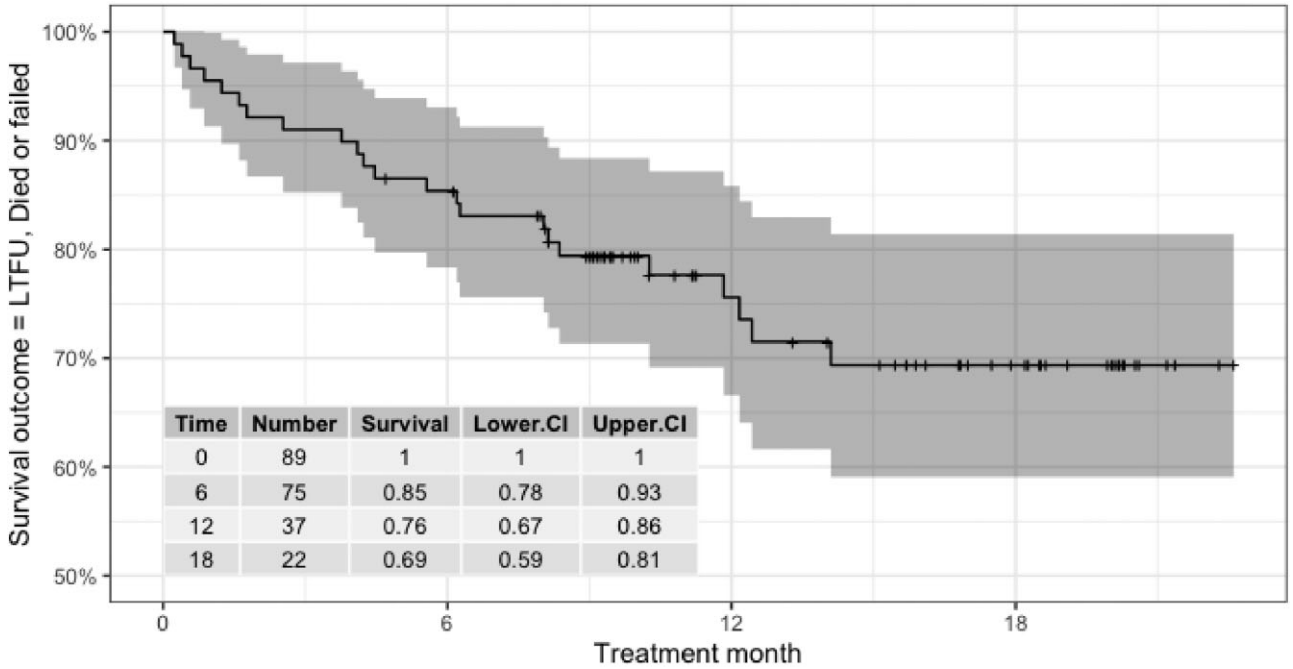

Figure 2. Kaplan–Meier survival curve on attrition from care (outcome=LTFU, failed or died) for the 89 participants in the programme with a survival table showing the number in the cohort at 0, 6, 12 and 18 mo and the survival proportion. LTFU, lost to follow-up.

sion and anxiety in this cohort were similar to other published studies,[22,23] although neither depression nor anxiety were risk factors in this group. Poor adherence was associated with dependence on other substances (cathinones with/without opioids) and weakly with IV-drug use. However, the six participants who had opioid and not cathinone dependency had good adherence and positive treatment outcomes. This may be due to strategies used by people for withdrawal after cathinone use that decrease the chance of taking TB medication. Alternatively, according to project psychiatric reports, low adherence in substance users may be due to undiagnosed personality disorders.

Comparison with other studies on psychosocial support or PCC

The evidence for psychosocial support or person-centred interventions that impact adherence to MDR/RR-TB for people with/without AUD is mixed, and studies with a comparison group are scarce. A review of mental health and TB in low- to-middle-income and emerging economies found only one 'person-centred' intervention.[24] This study in Nepal found that counselling and financial support improved the MDR-TB cure rate.[25] A study in Kazakhstan found that psychosocial support increased MDR/RR-TB adherence to 97%, compared with 48% prior to the introduction of the intervention.[26] Preliminary evidence from South Africa indicated that brief motivational interviewing and relapse prevention led to moderate adherence in people with MDR-RR/TB and problematic substance misuse.[27] However, a study in Ukraine that analysed the impact of mental health interventions for people with AUD and MDR/RR-TB did not report a difference in adherence or treatment outcomes associated with either AUD or mental health interventions, despite reporting high levels of adherence across all arms, as well as gains in the well-being of participants.[28] Similarly, integrated management of physician-delivered alcohol treatment for people with TB in Russia reported no impact on treatment outcomes.[29] A more recent study in South Africa indicated that naltrexone alone was insufficient to improve adherence to TB treatment and called for more person-centred approaches.[30]

Location and method of treatment support

Good adherence was possible in people who received VOT, home-based and inpatient treatment support. There were differences in the characteristics of people who used VOT, facility- or home-based treatment support; most notably, home-based support was only available to people who had health problems, which made VOT or travel to a facility difficult. Adherence through VOT decreased over time and over the course of treatment. This may be because the number of people who used VOT increased, due to changes in eligibility criteria during the COVID-19 pandemic. A systematic review of adherence interventions for all people with TB found that community/home-based support led to greater treatment success, and that VOT was equivalent to in-person support.[31] Previous research in Belarus found that VOT was preferable, as adherence levels were high, people with TB were at a reduced risk of infecting others, and people with TB and providers saved time or money.[32] More recently, a randomised controlled trial in Moldova in participants with drug-sensitive

Table 3. Participant characteristics by treatment outcome presented with univariate hazard ratios from a Cox model.

Characteristic	Cured, completed or on treatment (N=66)	Died, LTFU or failed (N=23)	Total (N=89)	Hazard ratio (univariable)	Hazard ratio (multivariable)
IV illicit drug use					
Yes	9 (64.3%)	5 (35.7%)	14	Reference	
No	47 (88.7%)	6 (11.3%)	53	0.3 (0.08–0.9)	0.3 (0.08–1.2)
Hepatitis C status					
Yes	20 (62.5%)	12 (37.5%)	32	Reference	
No	46 (80.7%)	11 (19.3%)	57	0.5 (0.2–1.2)	0.4 (0.1–1.4)
Psychiatric diagnosis					
Alcohol dependence	38 (77.6%)	11 (22.4%)	49	Reference	
Harmful alcohol use	10 (100.0%)	0 (0·0%)	10	0.0 (NA**)	0.03 (0.0–1.7)
Acute alcohol intoxication	1 (33.3%)	2 (66.7%)	3	4.4 (1.0–20.1)	
Alcohol plus other substance dependence	3 (37.5%)	5 (62.5%)	8	3.5 (1.2–10.1)	2.4 (0.6–10.2)
Opioid dependence and alcohol use or dependence	6 (100.0%)	0 (0.0%)	6	0.0 (NA**)	0.02 (0.0–207.2)
Mild intellectual difficulties and alcohol dependence	1 (100.0%)	0 (0.0%)	1	0.0 (NA**)	0.03 (NA**)
Disorder due to physical condition and alcohol dependence	1 (50.0%)	1 (50.0%)	2	2.1 (0.3–15.9)	0.05 (NA**)
Personality disorder and alcohol or substance dependence	3 (100.0%)	0 (0.0%)	3	0.0 (NA**)	0.01 (0.0–22.2)
Adjustment disorder and alcohol use or dependence	0 (0.0%)	1 (100.0%)	1	10.5 (1.3–86.3)	99.6 (12.9–768.6)
None recorded	3 (50.0%)	3 (50.0%)	6	4.4 (1.2–16.2)	0.19 (NA**)
Baseline risk for adherence issues					
Low risk	6 (85.7%)	1 (14.3%)	7	Reference	
Moderate risk	42 (75.0%)	14 (25.0%)	56	2.3 (0.3–17.3)	0.06 (0.01–0.2)
High risk	18 (69.2%)	8 (30.8%)	26	2.9 (0.4–23.1)	0.01 (0.0–0.05)
VOT					
No	39 (65.0%)	21 (35.0%)	60	Reference	
Yes	27 (93.1%)	2 (6.9%)	29	0.2 (0.03–0.6)	0.25 (0.05–1.3)
Outpatient facility support					
No	33 (91.7%)	3 (8.3%)	36	Reference	
Yes	33 (62.3%)	20 (37.7%)	53	4.1 (1.22–13.9)	24.7 (1.2–524.9)

**Insufficient number of outcomes to calculate a 95% CI.
Abbreviations: IV, intravenous; LTFU, lost to follow-up; NA, not available; VOT, video-observed treatment.

TB found that VOT had a higher adherence than clinic-based support.[33]

Limitations

Participants who did not consent for their data to be used in the study made up 12.7% (n=13) of the potential cohort. Those who did not consent may have been more likely to have died or LTFU early in the programme and have worse adherence, so the outcomes of this study may have been different if they were included. Our study did not have a comparison group so it is impossible to precisely assess the intervention´s impact, or to allow for any conclusions regarding causation. Not all participants in the study were followed up until treatment completion, with 20% of patients (n=18) still on treatment in the programme and 13 (15%) not evaluated, due to being transferred to another facility and still being on treatment, which introduces bias in the survival analysis. There is a risk of false positive results due to multiple statistical testing, and a risk of false negative statistical testing due to the small sample size. The small overall sample size, and size of certain subgroups, make it difficult to draw firm statistical conclusions, but we believe the study remains useful due to the unique and vulnerable nature of the study population.

Conclusions

People receiving person-centred, multidisciplinary care achieved good levels of adherence to MDR/RR-TB treatment, despite having complex health and social needs. People with hepatitis C or cathinone and alcohol users appeared to be at a greater risk of poor treatment outcomes. The findings from this and other studies indicate that VOT or home-based support may be preferable for people with known and documented risk factors for

non-adherence. We recommend that the findings from this study are used to encourage and guide multidisciplinary PCC to be scaled up for people with MDR/RR-TB and AUD across Belarus, or similar settings.

Supplementary data

Supplementary data are available at *International Health* online.

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Data availability: The datasets generated and/or analysed during the current study are not publicly available due to a risk of participants being identified, but a deidentified version of the data can be made available from the corresponding author upon reasonable request.

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