

Global Health Action



ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/zgha20

Depression among people living with tuberculosis and tuberculosis/HIV coinfection in Ukraine: a cross-sectional study

Anna Salnikova, Olena Makarenko, Yuliia Sereda, Tetiana Kiriazova, Karsten Lunze, Jack DeHovitz & Danielle C. Ompad

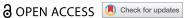
To cite this article: Anna Salnikova, Olena Makarenko, Yuliia Sereda, Tetiana Kiriazova, Karsten Lunze, Jack DeHovitz & Danielle C. Ompad (2025) Depression among people living with tuberculosis and tuberculosis/HIV coinfection in Ukraine: a cross-sectional study, Global Health Action, 18:1, 2448894, DOI: 10.1080/16549716.2024.2448894

To link to this article: https://doi.org/10.1080/16549716.2024.2448894

9	© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.
	Published online: 13 Feb 2025.
	Submit your article to this journal $oldsymbol{oldsymbol{\mathcal{C}}}$
ılıl	Article views: 838
Q ¹	View related articles 🗗
CrossMark	View Crossmark data ☑



RESEARCH ARTICLE



Depression among people living with tuberculosis and tuberculosis/HIV coinfection in Ukraine: a cross-sectional study

Anna Salnikova 60°, Olena Makarenko³, Yuliia Sereda³, Tetiana Kiriazova 60°, Karsten Lunze 60°, Jack DeHovitz od and Danielle C. Ompad od od

^aUkrainian Institute on Public Health Policy, Kyiv, Ukraine; ^bDepartment of Medicine, Boston Medical Center, Boston, MA, USA; Chobanian & Avedisian School of Medicine, Boston University, Boston, MA, USA; Department of Medicine, SUNY Downstate Health Sciences University, Brooklyn, NY, USA; Department of Epidemiology, New York University School of Global Public Health, New York, NY, USA; 'Center for Drug Use and HIV, HCV Research, New York University School of Global Public Health, New York, NY, USA

ABSTRACT

Background: Depressive disorders are associated with poor treatment outcomes, physical health, and quality of life among people living with TB (PLWTB) and TB/HIV (PLWTBHIV). Data on depression among PLWTB/HIV are limited in Ukraine.

Objectives: This cross-sectional study aimed to examine depression risk and its correlates and describe the willingness to seek depression treatment among PLWTB/HIV in Ukraine.

Methods: This secondary analysis included patients with and without HIV who initiated TB treatment within 30 days in two tertiary hospitals in Kyiv and Odesa. A survey was conducted from February 2021 to October 2022 and reviewed patients' health records. We used the Center for Epidemiological Studies-Depression Scale (CES-D) to indicate risk for clinical depression. Factors associated with depressive symptoms were identified using logistic regression.

Results: The sample included 209 participants (n = 100 with TB; n = 109 with TB/HIV). The mean age of participants was 43 (SD = 11) years; 66% of sample identified as male. Approximately 28% of participants were at risk for clinical depression; of whom 66% were willing to seek therapeutic or medical help. HIV coinfection (adjusted odds ratio [aOR] = 2.95, 95% confidence interval [CI]: 1.46,6.20), past 30 days illicit drug use (aOR = 3.57, 95% CI = 1.18,11.60), TB stigma (moderate stigma aOR = 7.40, 95% CI = 2.22,34.1; high stigma aOR = 15.50, 95% CI = 4.52,73.20), and unemployment status (aOR = 2.25, 95% CI = 1.12,4.60) were significantly associated with the odds of depressive symptoms among PLWTB.

Conclusion: Findings support integration of a brief depression screening tool into routine clinical care of PLWTB/HIV and highlight the importance of linking TB/HIV care with mental health services.

PAPER CONTEXT

- Main findings: The prevalence of risk for clinical depression (28%) was substantial among people with TB and TB/HIV coinfection in Ukraine and a majority was willing to seek for therapeutic or medical help. HIV, illicit drug use, TB stigma, and unemployment contributed to the risk of depression among this population.
- Added knowledge: This analysis supports the importance of a comprehensive approach to mental health and HIV/TB services in Ukraine.
- Global health impact for policy and action: Projects aimed at integration and linkage development of mental health services and clinical care for TB/HIV, accessibility to comprehensive services for people with TB and TB/HIV coinfection could be supportive for their health and well-being.

ARTICLE HISTORY

Received 24 September 2024 Accepted 29 December 2024

RESPONSIBLE EDITOR

Stig Wall

KEYWORDS

Depression; tuberculosis; HIV; mental health; Ukraine

Background

Tuberculosis (TB) remains one of the major public health threats globally. In 2023, an estimated 10.8 million people were diagnosed with TB and a total of 1.55 million people died from TB [1]. Ukraine has one of the highest TB incidence rates in the World Health Organization (WHO) European Region and ranks among the countries with the highest burden of multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB) [2]. Human immunodeficiency virus (HIV) coinfection accounted for approximately 20% of registered TB cases in Ukraine from 2015 to 2019 [3,4]. TB remains the main cause of death among adults living with HIV [5].

Depression is also a major public health burden and a leading cause of disability globally. The prevalence of depressive disorders in Ukraine was estimated to be 6.2% in 2019, which was higher than other countries in the region such as Poland (3.5%), Moldova (5.0%), and Estonia (6.0%) [6]. One in every eight Ukrainian adults reported symptoms consistent

New York, NY 10003, USA



CONTACT Danielle C. Ompad 🔯 dco2@nyu.edu 🗈 Department of Epidemiology, NYU School of Global Public Health, 708 Broadway, Room 718,

with clinical depression [7]; however, only one in four persons with potential depression had been informed by the healthcare professional or doctor that they had depression. In addition, only 0.4% of adults in Ukraine have been treated for depression with antidepressant medication or psychological therapy [7].

Depression is known to be associated with chronic diseases among adults [8-10], including TB. For people with TB and TB/HIV coinfection, depressive disorders have been associated with poor outcomes, including loss-to-follow-up, death during TB treatment, poor quality of life, and poor physical health [10–13]. The prevalence of depression is high among patients with TB [14]; however, data on depression and its correlates among patients with TB and TB/ HIV is limited in Ukraine.

This study was conducted in the cities of Kyiv and Odesa, Ukrainian regions with high TB and HIV prevalence. For example, in 2019, TB prevalence in Ukraine was the highest in Odeska Oblast, with 150.3 cases per 100,000 population; 46.4% of whom were co-infected with HIV. In Kyiv, the proportion of TB/ HIV coinfection among registered TB cases was the fourth highest (26.7%), exceeding the Ukrainian average (21.9%) [3]. The aim of the present study was to examine the risk for clinical depression and its correlates and describe willingness in treatment for depression among people living with TB (PLWTB) and TB/ HIV (PLWTBHIV) in Ukraine.

Methods

Study setting

The parent cohort study was conducted by the Ukrainian Institute on Public Health Policy (UIPHP) and aimed to examine unhealthy alcohol use and other comorbidities among TB and TB/HIV co-infected patients in Ukraine. Participants were recruited from two tertiary hospitals in Kyiv and Odesa cities: Kyiv City Tuberculosis Hospital No 1 and Odesa Regional Center for Socially Significant Diseases. Participants were surveyed at baseline and 3 months post-baseline.

Study design and duration

This analysis was a cross-sectional secondary data analysis of the baseline data that aimed to examine risk for depression among persons with diagnosed TB or TB/HIV co-morbidity. Data collection started in February 2021 and continued through October 2022. Data were collected through patient surveys and reviews of patients' health records. Of note, recruitment of participants started during the COVID-19

pandemic and data continued to be collected after the full-scaled invasion of Ukraine.

Study population and recruitment

The sample for this analysis consisted of 209 patients (100 PLWTB and 109 PLWTBHIV). We recruited adult patients (≥18 years) who had initiated outpatient TB treatment within the past 30 days. We enrolled patients in the study if they had initiated outpatient TB treatment following diagnosis (intensive phase) or if they had recently transitioned from inpatient to outpatient TB treatment (continuous phase). All consecutive patients who fit study criteria and provided informed consent were enrolled in the study.

Ethics approval and consent to participate

Ethics approval was obtained from the UIPHP Institutional Review Board. All participants were in the informed consent Confidentiality was ensured for the study participants by not including names and contact information in the final dataset. The electronic database was password protected and could be accessed only by the principal investigators and co-investigators.

Data collection

Medical providers at the study sites identified, informed, and referred eligible patients to research assistants. Research assistants informed participants about the study, requested informed consent, and conducted the interviews. Survey data were collected using intervieweradministered questionnaires. Physicians extracted patients' clinical data related to TB and HIV from their medical charts into a pre-defined form in Microsoft Excel. Survey questionnaires, screening forms, and informed consent were collected via the Research Electronic Data Capture (REDCap) platform [15,16] hosted on the UIPHP server. UIPHP researchers designed, developed, and maintained electronic data collection forms and implemented procedures for data quality control. Preventive quarantine measures against COVID-19 were followed throughout the study as required. Interviews with study participants were conducted either in-person or remotely via phone or internet-based communication technologies (e.g. Zoom, WhatsApp, etc.).

Demographic and socioeconomic variables included type of residence, age, sex, education, marital status, employment, income level, children in the family, housing stability, and history of imprisonment. Depression was assessed using the Center for Epidemiological Studies-Depression Scale (CES-D, 20-item scale with values ranging from 0 to 60) [17]. Participants with a CES-D score ≥ 16 points were considered at risk for depression, whereas CES-D score < 16 points implied no risk for depression. For those with a positive depression screening, willingness to be treated for depression was assessed with the question: 'Are you planning to seek medical or therapeutic help regarding your present complaints within the next 3 months?' Responses were categorized using a 5-point Likert scale from 1 - 'very unlikely' to 5 'very likely.' Participants unwilling to receive treatment for depressive symptoms were asked for the reasons.

TB stigma was measured with Van Rie et al.'s TB stigma scale [18] and categorized as very low (0-17), low (18-22), moderate (23-27), and high (28-44). Perceived social support was measured via a modified version of the Duke University-University of North Carolina Functional Support Questionnaire [19]. Illicit drug use items were from the European Monitoring Centre for Drugs and Drug Addiction bio-behavioral survey [20]; a dichotomous variable was created for illicit drug use in a past 30 days.

Clinical data extracted from the medical charts included HIV and TB diagnosis, dates of diagnosis, comorbidities at TB diagnosis, history of previously treated TB, TB drug resistance, social support during TB treatment, serious adverse events during TB treatment, and for patients with TB/HIV coinfection - date of HIV diagnosis, antiretroviral therapy (ART) regimens, and CD4 cell count and HIV viral load with dates of the diagnostic tests.

Data analysis

Descriptive analyses included the calculation of proportions for categorical variables and mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables. Bivariable associations for sociodemographic and clinical covariates and (1) HIV status and (2) risk for depression were estimated with logistic regression. Multivariable logistic regression models were constructed to identify correlates of depression risk. Variables were tested in the multivariable model based on findings from the bivariable analysis (i.e. association was significant at $p \le 0.05$) as well as based on theoretical considerations (i.e. age and sex are common correlates of depression). The Hosmer–Lemeshow goodness-of-fit test was used to assess model fit. Missing data were due to the refusals to answer the questions; these responses are reflected in Tables 1 and 2 in the 'Unknown' category. The level of significance was set at

Table 1. Sociodemographic characteristics of 209 patients with TB infection in Kyiv and Odesa, Ukraine, 2021–2022, stratified by HIV infection.

		TB	TB/HIV	
	Total	n = 100	n = 109	
Characteristic	N = 209	n (%)	n (%)	р
Type of residence				0.800
Rural	35 (17)	16 (16)	19 (18)	
Urban	174 (83)	84 (84)	90 (82)	
Sex				0.700
Female	72 (34)	36 (36)	36 (33)	
Male	137 (66)	64 (64)	73 (67)	
Age, years				0.007
Mean (SD)	43 (11)	46 (14)	41 (8)	
Median (IQR)	42 (36, 49)	46 (35, 54)	41 (37, 45)	
Range	19, 84	19, 84	21, 67	
Marital status				0.500
Married or partnered	97 (46)	49 (49)	48 (44)	
No partner	112 (54)	51 (51)	61 (56)	
Education				0.600
Secondary/vocational school or less	158 (76)	74 (74)	84 (77)	
Incomplete higher/higher	51 (24)	26 (26)	25 (23)	
Employment				0.400
Working ^a	131 (63)	60 (60)	71 (65)	
Not working ^b	78 (37)	40 (40)	38 (35)	
Household monthly income				0.600
<6000 UAH ^c	89 (46)	47 (48)	42 (44)	
≥6000 UAH	104 (54)	51 (52)	53 (56)	
Unknown	16	2	14	
Have children under 18 years old				0.200
No	145 (69)	74 (74)	71 (65)	
Yes	64 (31)	26 (26)	38 (35)	
Homeless				0.100
No	190 (91)	88 (88)	102 (94)	
Yes	18 (9)	12 (12)	6 (6)	
Unknown	1	0	1	
History of incarceration				0.016
No	161 (78)	85 (85)	76 (71)	
Yes	46 (22)	15 (15)	31 (29)	
Unknown	2	0	2	

^aFull or part time job.

^bUnemployed, disabled, homemaker, retired, or student.

cEquivalent to ~\$198-228 USD across the study period.

Table 2. Clinical characteristics of 209 patients with TB infection in Kyiv and Odesa, Ukraine, 2021–2022, stratified by

		ТВ	TB/HIV	
	Total,	n = 100	n = 109	
Characteristic	N = 209	n (%)	n (%)	р
TB diagnosis (from the beginning of study)				0.069
Less than 1 month (=<30 days)	176 (84)	89 (89)	87 (80)	
More than 1 month (>30 days)	33 (16)	11 (11)	22 (20)	
TB treatment during intensive phase				0.003
Inpatient	16 (8)	2 (2)	14 (13)	
Outpatient	192 (92)	98 (98)	94 (87)	
Unknown	1	0	1	
Comorbidities except HIV infection				0.006
No	165 (79)	87 (87)	78 (72)	
Yes	44 (21)	13 (13)	31 (28)	
TB treatment history				0.400
New	166 (79)	82 (82)	84 (77)	
Previously treated	43 (21)	18 (18)	25 (23)	
MDR/XDR-TB				0.200
No	191 (91)	94 (94)	97 (89)	
Yes	18 (9)	6 (6)	12 (11)	
Social support from NGOs during TB treatment				0.600
No	11 (5)	6 (6)	5 (5)	
Yes	198 (95)	94 (94)	104 (95)	
Perceived social support, score				0.001
Mean (SD)	24 (7)	26 (5)	23 (8)	
Median (IQR)	27 (22, 30)	27 (24, 30)	25 (19, 28)	
Range	0, 30	4, 30	0, 30	
Serious adverse events				0.200
No	206 (99)	100 (100)	106 (97)	
Yes	3 (1)	0 (0)	3 (3)	
Illicit drug use in a past 30 days				0.023
No	191 (91)	96 (96)	95 (87)	
Yes	18 (9)	4 (4)	14 (13)	
Depression				< 0.001
At risk for clinical depression (CESD \geq 16 scores)	58 (28)	16 (16)	42 (39)	
No risk	151 (72)	84 (84)	67 (61)	
HIV diagnosis (from the beginning of study)				
Less than 1 month			33 (30)	
From 1 month to 12 months			27 (25)	
More than a year			49 (45)	
Initiated ART therapy				
Yes			107 (98)	
No			2 (2)	
CD4 cells at TB diagnosis				
≥200 cells/m3 blood			37 (34)	
<200 cells/m3 blood			72 (66)	
Viral load at TB diagnosis				
No viral suppression			80 (77)	
Viral suppression (<200)			24 (23)	
Unknown			5	

p < 0.05. Data analyses were conducted in R version 4.2.2 (The R Foundation for Statistical Computing).

Results

Table 1 presents the socioeconomic and demographic characteristics of the sample, stratified by HIV status. The mean age of participants was 43 years (SD = 11), the median age was 42 (IQR = 36), 49). The sample was majority male 66% (n = 137) and lived in urban areas 83% (n = 174). Almost half 46% (n = 97) were married or had a partner and 24% (n = 51) had equivalent to college or higher education (incomplete Bachelor's degree or higher). Approximately 63% (n = 131) were employed and 46% (n = 89) had a monthly household income below Ukraine's minimum salary, equivalent to approximately \$198-228 USD across the study period [21]. The majority 91% (n = 190) of participants

were stably housed (i.e. not homeless). Almost onefourth of participants (22%, n = 46) had a history of incarceration. PLWTBHIV were significantly younger and more likely to have a history of incarceration than PLWTB.

Table 2 presents the clinical and behavioral characteristics of the sample, stratified by HIV status. One-fifth of the patients (21%, n = 43) had a previously treated TB infection. Eighteen (9%) had MDR-TB or extensively drug-resistant tuberculosis (XDR-TB). Most of the patients with MDR-TB or XDR-TB (67%, n = 12) were coinfected with HIV and 39% (n = 7) had depression risk. High TB stigma was significantly more common among people with MDR- or XDR-TB compared to those who did not have resistant TB (50% vs. 18%, p = 0.021; data not shown), while very low and low TB stigma were less common among those with MDR- or XDR-TB (11% vs. 27% for both categories). PLWTBHIV were

significantly more likely to receive inpatient TB treatment (13% [n = 14] vs. 2% [n = 2], p = 0.003) and were more likely to have a comorbidity compared to PLWTB (28% [n = 31] vs. 13% [n = 13], p = 0.006). Besides HIV coinfection, a variety of comorbidities were reported among the sample including hepatitis 10% (n = 20), anemia 9% (n = 19), hypertension 2% (n = 5), candidiasis 2% (n = 5), mycobacteriosis 1% (n = 5)= 3), cancer 1% (n = 2), diabetes 1% (n = 2), and osteochondrosis 1% (n = 2). Less than 1% (n = 1) reported each of the following: coronary heart disease, cytomegalovirus infection, peptic ulcer, and depression. Some participants had more than one comorbidity. Only 1% (n = 3) experienced serious adverse events during TB treatment. Illicit drug use within past 30 days was reported by 9% (n = 18); PLWTBHIV were more likely to report illicit drug use as compared to those with TB infection only (13% [n = 14] vs. 4% [n = 4], p = 0.023).

Almost all participants (95%, n = 198) received social support from non-governmental organizations during TB treatment, as indicated in the medical records. Perceived social support among participants was high with the median score of 27 (IQR = 22, 30). More than half of PLWTBHIV were diagnosed with HIV within the year prior to study enrollment 55% (n = 60). Almost all PLWTBHIV (98%, n = 107) initiated ART for HIV infection. Two-thirds of PLWTBHIV had CD4 cells counts less than 200 cells/mm³ (66%, n = 72) and 77% (n = 80) had detectable viral loads (i.e. equal or more than 200 copies/ ml); Table 2).

Approximately 28% (n = 58) of the participants were at risk for depression based on a CES-D cut-off score (Table 2). Females were more likely to be at risk for depression as compared to males (35% [n = 25] vs. 24% [n = 33]); however, this difference was not significant (p = 0.10; data not shown). There were also no significant differences in mean (41 [SD = 10] vs. 44 years [SD = 12],t-test p = 0.148) and median age by risk of depression (40 vs. 43 years, ranksum p = 0.136). Depression risk was more common among PLWTBHIV compared to PLWTB (39% [n = 42] vs. 16% [n = 16], p < 0.001). Among those at risk for depression, 66% (n = 37) were willing to seek either therapeutic or medical help for it (data not shown). For the 34% (n = 19) who were not willing to seek help, reasons for not seeking help included: not very serious complaints 63% (n = 12), unwillingness to take more pills 21% (n = 4), not affordable depression treatment 16% (n = 3), lack of awareness of where to apply for help 10% (n = 2), lack of time to visit a doctor 10% (n = 2), no regular complaints 10% (n = 2) = 2), possible side effects of treatment 5% (n = 1), embarrassed to apply to the doctor 5% (n = 1), and other reasons 21% (n = 4). Among the written in explanations, participants reported a low level of confidence in doctors, symptoms probably related to TB, and no sense in

seeking treatment. Some participants reported more than one reason for not seeking help. Both patients who reported pill load as the reason for not seeking for help for depressive symptoms were on ART in addition to TB treatment.

Multivariable models

In bivariate analyses (Table 3), HIV coinfection, time since TB diagnosis, illicit drug use in a past 30 days, TB stigma, perceived social support, and employment status were significantly associated with the odds of depressive symptoms. These variables, along with sex and age, were included in the full model for multivariable analysis.

Full and parsimonious logistic models were constructed to estimate the associations between key covariates and risk for depression. In the final parsimonious model (Table 3), HIV coinfection (adjusted odds ratio [AOR] = 2.95, 95% confidence interval [CI]: 1.46–6.20), illicit drug use in a past 30 days (AOR = 3.57, CI: 1.18-11.60), TB stigma (low stigma: AOR = 6.32, CI: 1.81-29.9, moderate stigma: AOR = 7.40, CI: 2.22-34.1, high stigma: AOR = 15.5, CI: 4.52–73.2), and unemployment status (AOR = 2.25, CI: 1.12-4.60) were significantly associated with the risk for depression among people with TB. The Hosmer-Lemeshow goodness-offit test for the parsimonious model was non-significant (p = 0.12), indicating that the model fit the data well.

Discussion

The proportion of PLWTB at risk for depression in this sample was higher than general adult population estimates for adults before the full-scale invasion of Ukraine (28% vs. 6%, respectively) [7,22], yet lower than what has been observed among PLWTB elsewhere. According to a 2020 meta-analysis that included 25 studies across low- and middle-income countries, the pooled prevalence of depression among TB patients was 45.2% (95% CI 38.04-52.55) [14], which was considerably higher than the present study. Of note, the meta-analysis did not contain data from any countries in the Eastern European or Central Asian region [23]. The difference in the prevalence of the risk for depression in the present versus prior studies could be explained by differences in the instruments used to collect data, cut-off scores applied to estimate prevalence, populations studied, type of TB (e.g. MDR-TB vs. non-MDR-TB), or sample size. Despite these differences, the findings suggest that PLWTB in Ukraine experience a substantial burden of depression symptomology.

This study highlights the potential for depression screening to identify patients in need of treatment in Ukraine. The patients who screened positive for

Table 3. Bivariate analysis and multivariable logistic regression models of depression among 209 patients with TB infection in Kyiv and Odesa, Ukraine, 2021-2022.

	Depression (CESD ≥ 16 scores)				
	Yes n = 58	No n = 151		Full model	Parsimonious model
Characteristic	n (%)	n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Group					
TB	16 (28)	84 (56)	1.0	1.0	1.0
TB/HIV	42 (72)	67 (44)	3.29 (1.73, 6.51)	2.32 (1.09, 5.08)	2.95 (1.46, 6.20)
Sex					
Female	25 (43)	47 (31)	1.0	1.0	-
Male	33 (57)	104 (69)	0.60 (0.32, 1.12)	0.49 (0.23, 1.06)	-
Age, years, mean (SD)	41 (10)	44 (12)	0.98 (0.95, 1.01)	0.97 (0.93, 1.00)	-
Employed					
Working ^a	30 (52)	101 (67)	1.0	1.0	1.0
Not working ^b	28 (48)	50 (33)	1.89 (1.02, 3.50)	2.11 (0.98, 4.61)	2.25 (1.12, 4.60)
Time since TB diagnosis					
Less than 30 days	54 (93)	122 (81)	1.0	1.0	-
More than 30 days	4 (7)	29 (19)	0.31 (0.09, 0.84)	0.36 (0.09, 1.12)	-
Illicit drug use in a past 30 days					
No	47 (81)	144 (95)	1.0	1.0	1.0
Yes	11 (19)	7 (5)	4.81 (1.79, 13.8)	3.98 (1.23, 13.9)	3.57 (1.18, 11.6)
TB stigma score					
Very low (0–17 scores)	3 (5)	51 (34)	1.0	1.0	1.0
Low (18–22 scores)	15 (26)	38 (25)	6.71 (2.04, 30.5)	5.20 (1.42, 25.4)	6.32 (1.81, 29.9)
Moderate (23–27 scores)	19 (33)	39 (26)	8.28 (2.59, 37.1)	7.80 (2.19, 37.9)	7.40 (2.22, 34.1)
High (28–44 scores)	21 (36)	23 (15)	15.5 (4.77, 70.5)	11.8 (3.07, 60.6)	15.5 (4.52, 73.2)
Perceived social support score, median (IQR)	24 (14, 28)	27 (24, 30)	0.92 (0.88, 0.96)	0.96 (0.91, 1.01)	-

OR = Odds ratio; CI = Confidence interval.

depression in this study did not have a diagnosis of depression in their medical charts, suggesting missed opportunities for screening and referral to treatment. Only one patient had depression recorded in the medical chart at baseline; this person had a low CESD score suggesting that the depression may have been treated or had resolved at the time of the study. These findings were consistent with the WHO survey on the main risk factors for noncommunicable diseases (NCDs), which reported that only one in four adults with suspected depression were told about it by a doctor or healthcare professional [7].

In this sample, PLWTBHIV had approximately three times the odds of depression compared to PLWTB after controlling for employment status, past 30-day illicit drug use, and TB stigma. This is consistent with prior studies; for example, two studies in Ethiopia found co-morbid HIV infection to increase the odds of depression four to six-fold [24,25]. One study of PLWTB in South Africa found high rates of psychiatric disorders, but no differences in prevalence by HIV status [26]; they did not assess depression by HIV status specifically but did find high prevalence of major depressive episodes (40.6%), unipolar depression (37.6%), and bipolar spectrum conditions (19.3%). Depression may be elevated among PLWHIV coinfection because of HIV stigma [26-28]. Furthermore, psychiatric symptoms, including depression, could occur as a side effect of specific antiretroviral therapies for HIV [29]. In this study, some patients' ART regimens included dolutegravir and efavirenz, medications associated with increased risk for depression [30,31].

Unemployment was significantly associated with depression. This is consistent with prior studies that have shown unemployment to be associated with depression and anxiety, including among PLWTB [32,33]. Remarkably, in the present study, around half of participants with depression were unemployed (48%), and onefifth (21%) had permanent or temporary disability.

TB stigma was also a significant correlate of depression. TB stigma has previously been shown to be associated with depression [24,34-36] as well as a barrier to positive TB treatment outcomes [37]. Educational programs aimed at supporting specialized healthcare providers to identify and address patients' concerns about TB stigma could mitigate stigma impact. Support from the family and communities could also alleviate stigma [37].

Approximately two-thirds of those who screened positive for depression risk were willing to seek medical or therapeutic help. Among participants unwilling to seek help, the reasons for not doing so were consistent with the barriers to seeking care reported in the Mental Health Assessment for Ukraine [22]. Of note, the full-scale invasion of Ukraine is likely to exacerbate mental health issues, including depression and other mood disorders in this population. Recent evidence has demonstrated an increase in depression, anxiety, and stress among Ukrainians [38].

This study has several limitations to consider. The study population is limited to TB patients in Odesa and

^aFull or part time job.

^bUnemployed, disabled, homemaker, retired, or student.

Kyiv and therefore is not representative of all PLWTB in Ukraine. The study was initiated during the second year of the COVID-19 pandemic and the last 5 months of baseline enrollment coincided with Russia's invasion of Ukraine. The COVID-19 pandemic and the full-scale invasion of Ukraine did not affect the willingness of participants to join the study (interviews were remote). However, recruitment of newly diagnosed patients, the target group, was likely negatively affected as people may have delayed treatment due to the pandemic or military conflict, or may have been displaced to other parts of Ukraine, or out of Ukraine. Therefore, the primary study extended the sample by recruiting TB patients without HIV comorbidity (not only with TB/HIV coinfection as initially was planned). It is also plausible that mental health was negatively affected by both the pandemic and the invasion. Due to the limited sample size, confidence intervals are wide for some associations and estimates should be interpreted with caution.

Conclusions

The WHO recommends integrating screening for NCDs, including mental health conditions, into infectious disease programs [39]. In 2023, the Ukrainian government stipulated that screening should be provided to patients with sensitive and multidrug-resistant TB with the PHQ-9 and Hospital Anxiety and Depression Scale (HADS) [40]. Similar provisions were made by the government for PLHIV, where the PHQ-2 should be used to screen for depression and anxiety and those with a positive answer to at least one of the PHQ-2 questions being further evaluated with the PHQ-9 [41]. These results suggest that Ukrainian patients with TB and/or HIV would benefit from the integration of brief mental health screenings and referrals to treatment in tuberculosis care, whether it is provided in primary, secondary, or tertiary care settings and regardless of whether the TB infection is MDR or XDR. Additional research is needed to determine how to effectively integrate and implement such tools into these settings.

Linkage of clinical care for TB/HIV with mental health services should continue to be established, in light of the substantial depression risk among this population. For PLWTB and comorbidities such as HIV, depression, and substance use in the context of challenging social determinants of health such as stigma and unemployment, accessibility of comprehensive services is critical for supporting their health and well-being.

Authors' contributions

OM and KL were PIs of the survey and responsible for development, coordination, and implementation of the parent study. TK, KL, and OM were responsible for overall

coordination of the survey implementation. YS conducted all parent study data management and analysis. TK, JD, and AS conceptualized the current analysis. AS led this manuscript, conducted the data analysis, and drafted the final paper. DCO coordinated the manuscript development, data analysis, drafting, and submission. YS, JD, KL, DCO reviewed the manuscript before submission and provided comments. All authors reviewed and approved manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethics and consent

Ethics approval was obtained from the Ukrainian Institute on Public Health Policy Institutional Review Board. All participants were engaged in the informed consent process. Confidentiality was ensured for the study participants by not capturing names, contacts, dates in the final dataset. The electronic database was password protected and could be accessed only by the principal investigators and coinvestigators.

Funding information

This study was supported with grants from the Fogarty International Center of the National Institutes of Health [D43TW010562 and D43TW012491]. JD secured funds for the current analysis. DCO was supported, in part, by the Center for Drug Abuse and HIV research [CDUHR; NIDA P30DA011041]. The parent survey was funded by the Providence/Boston Centers for AIDS Research [CFAR; P30AI042853].

ORCID

Anna Salnikova b http://orcid.org/0009-0004-5687-6359 Tetiana Kiriazova http://orcid.org/0000-0002-8480-6591 Karsten Lunze http://orcid.org/0000-0001-8495-0350 Jack DeHovitz http://orcid.org/0000-0001-7307-0614 Danielle C. Ompad http://orcid.org/0000-0003-0240-0393

References

- [1] World Health Organization. Global tuberculosis report 2024. Geneva: World Health Organization; 2024 [cited 2024 Nov 22]. Available from: https:// iris.who.int/bitstream/handle/10665/379339/ 9789240101531-eng.pdf?sequence=1
- [2] World Health Organization. Global tuberculosis report 2021. Geneva: World Health Organization; 2021 [cited 2022 Feb 1]. Available from: https:// www.who.int/tb/publications/global_report/en/
- [3] Ukrainian Ministry of Health, Public Health Center. Tuberculosis in Ukraine: analytical and statistical reference book. Kyiv: Ukrainian Ministry of Health; 2019. [cited 2022 Feb 16]. Available from: https://phc. org.ua/sites/default/files/users/user90/TB_surveil lance statistical-information 2019 dovidnyk.pdf
- [4] Ukrainian Ministry of Health, Public Health Center. Tuberculosis in Ukraine: analytical and statistical

- reference book. Kyiv: Ukrainian Ministry of Health; 2017 [cited 2022 Feb 16]. Available from: https://www. phc.org.ua/sites/default/files/uploads/files/PATH_ booklet_003-4.pdf
- [5] UNAIDS. Global AIDS monitoring 2018: Ukraine. Geneva: UNAIDS; 2018 [cited 2024 Nov 19]. Available from: http://www.unaids.org/sites/ default/files/country/documents/UKR_2018_coun tryreport.pdf
- [6] Global Health Data Exchange [Internet]. 2019 [cited 2023 Jul 10]. Available from: https://vizhub.health data.org
- [7] STEPS. Prevalence of noncommunicable disease risk factors in Ukraine 2019. Copenhagen: WHO Regional Office for Europe; 2020 [cited 2023 Aug 16]. Available from: https://www.phc.org.ua/sites/default/files/users/ user90/2019_STEPS_report_eng.pdf
- [8] Herrera PA, Campos-Romero S, Szabo W, Martinez P, Guajardo V, Rojas G. Understanding the relationship between depression and chronic diseases such as diabetes and hypertension: a grounded theory study. Int J Environ Res Public Health. 2021;18:12130. doi: 10.3390/ijerph182212130; Epub 20211119; PubMed 34831886; PubMed Central PMCID: PMID: PMC8618720.
- [9] Njie GJ, Khan A. Prevalence of tuberculosis and mental disorders comorbidity: a systematic review and meta-analysis. J Immigr Minor 2022;24:1550-1556. doi: 10.1007/s10903-021-01312-6; Epub 20211118; PubMed PMID: 34796457; PubMed Central PMCID: PMC9114162.
- [10] Ruiz-Grosso P, Cachay R, de la Flor A, Schwalb A, Ugarte-Gil C. Association between tuberculosis and depression on negative outcomes of tuberculosis treatment: a systematic review and meta-analysis. PLOS ONE. 2020;15:e0227472. doi: 10.1371/journal.pone. 0227472; Epub 20200110; PubMed PMID: 31923280; PubMed Central PMCID: PMC6953784.
- [11] Grenard JL, Munjas BA, Adams JL, et al. Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Intern Med. 2011;26:1175-1182. doi: 10.1007/s11606-011-1704-y; Epub 20110501; PubMed PMID: 21533823; PubMed Central PMCID: PMC3181287.
- [12] Deribew A, Deribe K, Reda AA, et al. Change in quality of life: a follow up study among patients with HIV infection with and without TB in Ethiopia. BMC Public Health. 2013;13:408. doi: 10.1186/1471-2458-13-408; Epub 20130429; PubMed PMID: 23627925; PubMed Central PMCID: PMC3649920.
- [13] Deribew A, Tesfaye M, Hailmichael Y, et al. Tuberculosis and HIV co-infection: its impact on quality of life. Health Qual Life Outcomes. 2009;7:105. doi: 10.1186/1477-7525-7-105; Epub 20091229; PubMed PMID: 20040090; PubMed Central PMCID: PMC2809048.
- [14] Duko B, Bedaso A, Ayano G. The prevalence of depression among patients with tuberculosis: a systematic review and meta-analysis. Ann Gen Psychiatry. 2020;19:30. doi: 10.1186/s12991-020-00281-8; Epub 20200507; PubMed PMID: 32419837; PubMed Central PMCID: PMC7206806.
- [15] Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform. 2019;95:103208. doi: 10.1016/j.jbi.2019.103208; Epub

- 20190509; PubMed PMID: 31078660; PubMed Central PMCID: PMC7254481.
- Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)-a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42:377–381. doi: 10.1016/j.jbi.2008.08. 010; Epub 20080930; PubMed PMID: 18929686; PubMed Central PMCID: PMC2700030.
- [17] Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas. 1977;1:385-401. doi: 10.1177/ 014662167700100306 PubMed PMID: 1979-10129-
- [18] Van Rie A, Sengupta S, Pungrassami P, et al. Measuring stigma associated with tuberculosis and HIV/AIDS in southern Thailand: exploratory and confirmatory factor analyses of two new scales. Trop Med Int Health. 2008;13:21-30. doi: 10.1111/j.1365-3156.2007.01971.x PubMed PMID: 18290998.
- [19] Broadhead WE, Gehlbach SH, de Gruy FV, Kaplan BH. The duke-unc functional social support questionnaire. Measurement of social support in medicine patients. Med Care. 1988;26:709-723. doi: 10.1097/00005650-198807000-00006 PubMed PMID: 3393031.
- [20] European Monitoring Centre for Drugs and Drug Addiction. DRID guidance module: example questionnaire for bio-behavioral surveys in people who inject drugs. Lisbon: European Monitoring Centre for Drugs and Drug Addiction; 2013 [cited 2024 Nov 19]. Available from: http://drogfokuszpont.hu/wpcontent/uploads/DRID_module_example_question naire_final.pdf
- [21] Verkhovna Rada of Ukraine. Zakon Ukrainy: Pro derzhavnyi biudzhet Ukrainy [Law of Ukraine: on the state budget of Ukraine]. 2021 [cited 2024 Nov 22]. Available from: https://zakon.rada.gov.ua/laws/ show/1082-20#Text
- [22] World Bank Group. Mental health in transition. Assessment and guidance for strengthening integration of mental health into primary health care and community-based service platforms in Ukraine. Washington (DC): World Bank Group; 2018 [cited 2024 Nov 19]. Available from: https://documents1. worldbank.org/curated/en/310711509516280173/pdf/ 120767-WP-Revised-

WBGUkraineMentalHealthFINALwebvpdfnov.pdf

- [23] Stoichita A, Dumitrescu A, Ciobanu A, et al. Depression and anxiety symptoms among people rifampicin-resistant tuberculosis receiving in-patient care in the national pulmonology reference institute in Romania. Monaldi Arch Chest Dis. 2021;91. doi: 10.4081/monaldi.2021.1704; Epub 20210114; PubMed PMID: 33470090.
- [24] Duko B, Gebeyehu A, Ayano G. Prevalence and correlates of depression and anxiety among patients with tuberculosis at WolaitaSodo University Hospital and sodo health center, WolaitaSodo, South Ethiopia, cross sectional study. BMC Psychiatry. 2015;15:214. doi: 10.1186/s12888-015-0598-3; Epub 20150914; PubMed PMID: 26370894; PubMed Central PMCID: PMC4570612.
- [25] Yohannes K, Mokona H, Abebe L, et al. Prevalence of depressive symptoms and associated factors among patients with tuberculosis attending public health institutions in Gede'o zone, South Ethiopia. BMC



- Public Health. 2020;20:1702. doi: 10.1186/s12889-020-09794-z; Epub 20201113; PubMed PMID: 33187488; PubMed Central PMCID: PMC7666498.
- [26] Thungana Y, Wilkinson R, Zingela Z. Comorbidity of mental ill-health in tuberculosis patients under treatment in a rural province of South Africa: a cross-sectional survey. BMJ Open. 2022;12:e058013. doi: 10.1136/bmjo pen-2021-058013; Epub 20221121; PubMed PMID: 36410818; PubMed Central PMCID: PMC9680183.
- [27] Felker-Kantor EA, Wallace ME, Madkour AS, et al. HIV stigma, mental health, and alcohol use disorders among people living with HIV/AIDS in New Orleans. J Urban Health. 2019;96:878-888. doi: 10.1007/ s11524-019-00390-0 PubMed PMID: 31520231; PubMed Central PMCID: PMC6904691.
- [28] Rueda S, Mitra S, Chen S, et al. Examining the associations between hiv-related stigma and health outcomes in people living with HIV/AIDS: a series of meta-analyses. BMJ Open. 2016;6:e011453. doi: 10. 1136/bmjopen-2016-011453; Epub 20160713; PubMed PMID: 27412106; PubMed Central PMCID: PMC4947735.
- [29] Fettiplace A, Stainsby C, Winston A, et al. Psychiatric symptoms in patients receiving dolutegravir. J Acquir Immune Defic Syndr. 2017;74:423-431. doi: 10.1097/ qai.0000000000001269 PubMed PMID: 27984559; PubMed Central PMCID: PMC5321108.
- [30] Preta LH, Chroboczek T, Treluyer JM, et al. Association of depression and suicidal behaviour reporting with HIV integrase inhibitors: a global pharmacovigilance study. J Antimicrob Chemother. 2023;78:1944-1947. doi: 10.1093/jac/dkad187 PubMed PMID: 37311223.
- [31] Checa A, Castillo A, Camacho M, et al. Depression is associated with efavirenz-containing treatments in newly antiretroviral therapy initiated HIV patients in Ecuador. AIDS Res Ther. 2020;17:47. doi: 10.1186/ s12981-020-00303-1; Epub 20200729; PubMed PMID: 32727488; PubMed Central PMCID: PMC7391584.
- [32] Amiri S. Unemployment associated with major depression disorder and depressive symptoms: a systematic review and meta-analysis. Int J Occup Saf Ergon. 2022;28:2080-2092. doi: 10.1080/ 10803548.2021.1954793; Epub 20210805; PubMed PMID: 34259616.
- [33] Ahmed A, Saqlain M, Umair MM, et al. Stigma, social support, illicit drug use, and other predictors of anxiety and depression among HIV/AIDS patients in Pakistan: a cross-sectional study. Front Public Health. 2021;9:745545. doi: 10.3389/fpubh.2021. 745545; Epub 20210930; PubMed PMID: 34660521; PubMed Central PMCID: PMC8514983.

- [34] Gong Y, Yan S, Qiu L, et al. Prevalence of depressive symptoms and related risk factors among patients in China: a multistage tuberculosis cross-sectional study. Am J Trop Med Hyg. 2018;98:1624-1628. doi: 10.4269/ajtmh.17-0840; Epub 20180405; PubMed PMID: 29637878; PubMed Central PMCID: PMC6086169.
- [35] Assefa S, Boru B, Gebeyehu DA, Terefe B. Depression, anxiety and their associated factors among patients with tuberculosis attending in Gondar city health facilities, North West Ethiopia. BMC Psychiatry. 2023;23:91. doi: 10.1186/s12888-023-04573-7; Epub 20230206; PubMed PMID: 36747183; PubMed Central PMCID: PMC9900546.
- [36] Shen R, Zong K, Liu J, Zhang L. Risk factors for depression in tuberculosis patients: a meta-analysis. Neuropsychiatr Dis Treat. 2022;18:847-866. doi: 10. 2147/ndt.S347579; Epub 20220411; PubMed PMID: 35431546; PubMed Central PMCID: PMC9012238.
- [37] Aibana O, Dauria E, Kiriazova T, et al. Patients' perspectives of tuberculosis treatment challenges and barriers to treatment adherence in Ukraine: a qualitative study. BMJ Open. 2020;10:e032027. doi: 10.1136/bmjo pen-2019-032027; Epub 20200202; PubMed PMID: 32014870; PubMed Central PMCID: PMC7044979.
- [38] World Health Organization. Scaling-up mental health and psychosocial services in war-affected regions: best practices from Ukraine. Geneva: World Health Organization; 2022 [cited 2024 Nov 22]. Available from: https://www.who.int/news-room/feature-stories /detail/scaling-up-mental-health-and-psychosocialservices-in-war-affected-regions-best-practices-fromukraine
- [39] World Health Organization. Integrating the prevention and control of noncommunicable diseases in HIV/AIDS, tuberculosis, and sexual and reproductive programmes: implementation guidance. Geneva: World Health Organization; 2023 [cited 2024 Nov 19]. Available from: https://www.who.int/ publications/i/item/9789240061682
- [40] Ministry of Health of Ukraine. On the approval of the procedure for the provision of medical and psychosocial support services for patients with sensitive and multidrug-resistant tuberculosis. 2023 [cited 2024 Nov 22]. Available from: https://zakon.rada.gov.ua/laws/ show/z0973-23#Text
- [41] Ministry of Health of Ukraine. On the approval of the procedure for the provision of HIV prevention services among representatives of some key groups regarding HIV infection. 2023 [cited 2024 Nov 22]. Available from: https://zakon.rada.gov.ua/laws/show/ z0332-24#Text