- 1 Programmatic implementation of depression screening and remote mental health
- 2 support sessions for persons recently diagnosed with TB in Lima, Peru during the
- 3 COVID-19 pandemic

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- 5 Carmen Contreras^{1,2*}, Janeth Santa Cruz¹, Jerome Galea^{3,4}, Alexander L. Chu⁵, Daniela
- 6 Puma¹, Lourdes Ramos^{1,6}, Marco Tovar^{1,7}, Jesús Peinado^{1,7}, Leonid Lecca^{1,3,8}, Salmaan
- 7 Keshavjee^{3,9}, Courtney M. Yuen^{3,9}, Giuseppe Raviola^{3,8,10}

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- 9 ¹ Socios En Salud Sucursal Peru, Lima, Peru
- ² Harvard Global Health Institute, Harvard University, Cambridge, MA, USA
- ³ Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA,
- 12 USA
- ⁴ School of Social Work, University of South Florida, Tampa, FL, USA
- ⁵ Department of Medical Education, Dell Medical School at the University of Texas at
- 15 Austin, Austin, TX, USA
- ⁶ Escuela Profesional de Tecnología Médica, Universidad Privada San Juan Bautista, Lima,
- 17 Peru
- ⁷ Escuela de Medicina, Facultad de Ciencias de la Salud, Universidad Peruana de Ciencias
- 19 Aplicadas, Lima, Peru
- ⁸ Partners In Health, Boston, MA, USA

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21	⁹ Division of Global Health Equity, Brigham and Women's Hospital, Boston, MA, USA
22	¹⁰ Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA
23	
24	*Corresponding Author: Carmen Contreras Socios en Salud Sucursal Perú Jr. Puno 279
25	Cercado de Lima, Lima, Perú ccontreras ses@pih.org
26	Abstract
27	Background: Few studies have explored a stepped care model for delivering mental health
28	care to persons with TB. Here, we evaluated depression screening and remote low-intensity
29	mental health interventions for persons initiating TB treatment in Lima, Peru during the
30	COVID-19 pandemic.
31	Methods: We used the PHQ-9 to screen participants for depressive symptoms (PHQ-9≥5).
32	Participants with PHQ-9, 5-14 received remote Psychological First Aid (PFA) or Problem
33	Management Plus (PM+). Participants were re-evaluated six months after intervention
34	completion. We then compared the change in median PHQ-9 scores before and after
35	intervention completion. Those with PHQ-9≥15 were referred to higher-level care.
36	Findings: We found 62 (45.9%) of 135 participants had PHQ-9≥5 at baseline. Fifty-four
37	individuals with PHQ-9, 5-9 received PFA, of which 44 (81.5%) were re-evaluated. We
38	observed significant reductions in median PHQ-9 scores from 6 to 2 ($r = 0.98$; p<0.001). Four
39	participants with PHQ-9, 10-14 received PM+ but were unable to be re-evaluated. Four
40	participants with PHQ-9≥15 were referred to higher-level care.
41	Conclusions: Depressive symptoms were common among persons recently diagnosed with
42	TB. We observed improvements in depressive symptoms six months later for most
43	participants who received remote sessions of PFA.

44 **Key Words:** Depression, Mental Health, Tuberculosis, Psychological First Aid, Peru

Impact Statement

This report describes one of the first experiences incorporating depression screening and remote mental health support interventions as part of a wider community-based active TB screening program. Our findings reaffirm the high prevalence of depressive symptoms among persons recently diagnosed with TB in northern Lima as well as the urgent need to meet and address the psychosocial needs of members of this vulnerable patient population. Importantly, our observations also provide further practical insight into how depression screening and remote mental health interventions may be integrated into existing TB programs, including community-based active TB screening programs.

Introduction

Tuberculosis (TB) is a debilitating infectious disease caused by *Mycobacterium tuberculosis*, a human pathogen that affects the lungs and other organs, causing significant morbidity and mortality (World Health Organization 2022b). TB remains a leading cause of mortality due to a single infectious disease after the coronavirus disease (COVID-19) (World Health Organization 2022a). The World Health Organization (WHO) estimated that in 2022 roughly 10.6 million people acquired TB and 1.3 million - 167,000 of which were HIV positive - died from TB (World Health Organization 2023). In the Americas region, Peru has one of the highest TB burdens with an estimated annual TB incidence rate of 130 per 100,000 persons per year and is a hotspot for drug-resistant TB (World Health Organization 2022a).

Mental disorders such as depression are common among persons with TB. It is estimated that about 45% of persons with TB have depression with prevalence estimates exceeding 50% in persons with MDR-TB (Duko *et al.* 2020). Similar depression prevalence estimates have been previously reported among persons with TB and MDR-TB in Peru (Ugarte-Gil *et al.* 2013; Vega *et al.* 2004). Furthermore, comorbid mental disorders have adverse impacts on TB treatment outcomes. Recent systematic reviews and meta-analyses have reported that persons with TB and depressive symptoms have more than four times the odds of poor TB treatment outcomes compared with those without depressive symptoms (Ruiz-Grosso *et al.* 2020). Taken together, the current evidence base suggests that addressing comorbid mental disorders such as depression is integral to improving both mental well-being and treatment success rates among those with TB (Sweetland *et al.* 2018).

Various mental health interventions have demonstrated promise in improving treatment
outcomes in persons sick with TB. For example, across three randomized controlled trials,
psycho-emotional interventions (including counseling, self-help groups, and psychotherapy)
were associated with an increased likelihood of achieving successful TB treatment outcomes
(pooled RR, 95% CI, 1.37, 1.08 - 1.73); however, these studies considered all persons with
TB and included those without comorbid mental disorders (van Hoorn et al. 2016). A more
recently published systematic review by Farooq et al. considered two pharmacological and 11
psychosocial interventions for addressing common mental disorders such as depression
among persons with TB ($n = 4,326$) in various low- and middle-income countries (Farooq et
al. 2021). They reported that persons with TB who receive some kind of psychosocial
intervention generally have higher TB treatment adherence and cure rates compared with
those who do not receive the intervention or when compared with the pre-intervention period.
More recently, a large interventional study conducted by Pasha et al. in Pakistan evaluated
the implementation of screening for anxiety/depression and subsequent delivery of a series of
counseling sessions throughout the TB treatment period among 3,500 persons with TB
disease. They found that those who completed at least four sessions had significantly higher
rates of completing TB treatment compared with those who completed less than four sessions
(Pasha et al. 2021).

Even before the COVID-19 pandemic, there had been a significant interest in implementing remote mental health interventions for various common mental health issues in low-and middle-income countries (LMICs) (Fu *et al.* 2020). A recent systematic review and meta-analysis of randomized controlled trials (n = 4,104 across 22 trials) found that psychological interventions delivered across various digital modalities (e.g., websites, smartphone apps,

computers, audio-devices, and text messages) were moderately effective in addressing common mental disorders (pooled Hedges' g = 0.60, 95% CI 0.45 - 0.75) when compared with control interventions or usual care, and the vast majority of these interventions were used to address depression and substance use disorders (Fu *et al.* 2020). Since the start of the pandemic, systematic reviews of remote mental health interventions have reported adaptive transitions to implementing synchronous telemental health tools. However, the vast majority of studies were conducted in high-income countries, and commonly cited barriers to scaling up remote mental health interventions in LMICs include a lack of information technology resources and infrastructure in mental health services, socio-economic inequalities affecting access to remote mental health services, and reduced technological literacy (Witteveen *et al.* 2022).

Despite these challenges, research suggests that designing and delivering remote mental health interventions may be effective in addressing comorbid mental disorders among persons with TB. However, to our knowledge, none has evaluated the implementation of depression screening and delivery of remote mental health interventions embedded within the context of a wider community-based active TB screening program. Furthermore, few studies have reported on the use of a stepped care model for allocating different low-intensity mental health support interventions based on different depressive symptom severities at the time of initial screening (Bower and Gilbody 2005; Walker *et al.* 2018). Thus, the aim of this study was to evaluate remote low-intensity mental health interventions, specifically Psychological First Aid and Problems Management+, on depressive symptoms among people initiating treatment for pulmonary TB as part of a community-based active TB screening program in Lima, Peru during the COVID-19 pandemic.

Methods

Study design and context

We conducted a secondary analysis of data collected as part of a mental health program run by the non-profit organization Socios En Salud based in Lima, Peru. This program screened persons with active TB for depressive symptoms and subsequently provided low-intensity mental health interventions during their TB treatment period between 2019 and 2021. This mental health program was incorporated as part of a wider community-based active TB screening program called "TB Móvil" (TB-M), which SES first implemented in collaboration with the Ministry of Health (MINSA) of Peru in 2019 to identify persons with active TB across various districts of Metropolitan Lima (Galea *et al.* 2022; Yuen *et al.* 2021). Persons diagnosed with TB through the TB-M program were referred to participate in the SES mental health program. The mental health program was implemented remotely in parallel to the TB-M program between September 2020 and June 2021 during the early phases of the COVID-19 pandemic.

Intervention procedures

Participant enrollment and data collection

Participants were eligible for depressive symptom screening if they satisfied the following inclusion criteria: individuals were recently diagnosed with TB through the TB-M program and had subsequently initiated treatment; were referred by TB-M program staff members for further mental health evaluation; were 18 years or older; and were residents of communities and districts of northern Lima that were a part of the TB-M program catchment area. SES

psychologists contacted individuals who were referred by TB-M program staff by telephone
and then invited them to be screened for depressive symptoms within 30 days of initiating TB
treatment. Those who did not start TB treatment during this period were excluded. Participant
sociodemographic (e.g., age, sex, highest level of educational attainment, and region of
birth), clinical, and microbiological data (e.g., TB disease diagnosis, sputum smear
microscopy status, GeneXpert results, and rifampin resistance status) were obtained from the
TB-M program's database.
Data preparation and handling
For this secondary data analysis, we accessed non-identifiable information on TB-M program
participants from the SES informatics system. To describe the socio-demographic and
clinical characteristics, we considered the following variables among all participants
evaluated for depressive symptoms: age, sex, highest educational level attained, region of
birth, BK results, Gene Xpert results, chest radiography status, and rifampin resistance status.
We considered the age of participants as a continuous variable. The highest level of education
attained was categorized into three groups: primary, secondary, and post-secondary. We
defined region of birth as being born inside or outside of the Lima region. Clinical variables
like BK and GeneXpert results were considered as binary variables - negative or positive.
The main variables analyzed in this study were depressive symptoms at baseline and follow-
up as well as the type of remote mental health intervention provided by mental health
professionals.

Depressive symptom screening and definitions

SES psychologists interviewed participants using the validated Spanish version of the Patient Health Questionnaire 9 (PHQ-9), a depression screening instrument widely used in clinical practice and research (Calderón *et al.* 2012). The score evaluates the number and frequency of nine depressive symptoms and ranges from 0 (i.e., experiencing no depressive symptoms none of the time) to 27 (i.e., experiencing all depressive symptoms nearly every day). The PHQ-9 uses different score ranges to classify different depressive symptom severities. They include: minimal (PHQ-9 ≤4), mild (PHQ-9, 5-9), moderate (PHQ-9, 10-14), moderately severe (PHQ-9, 15-19), and severe (PHQ-9 score ≥20) (Kroenke *et al.* 2001).

Mental health interventions

The mental health interventions offered as part of the SES mental health program were originally developed before the pandemic and subsequently underwent revisions at the onset of the pandemic. Here, we describe the mental health interventions that were delivered during the early phases of the pandemic period specifically. Between September 2020 and June 2021, remote mental health support sessions were offered to participants identified with signs and symptoms of depression. Those with PHQ-9 scores 5-9 received one session of Psychological First Aid (PFA), and those with PHQ-9 scores from 10-14 received five support sessions of Problem Management Plus (PM+) (Dawson *et al.* 2015). People with PHQ-9 scores ≥15 received one session of PFA before being promptly referred for higher-level mental health care at public health care institutions. The remote PFA and PM+ support sessions and referral process for patients with severe depressive symptoms are further described in detail below.

Psychological First Aid (PFA). The remote PFA sessions provided basic psychological support in emergent and stressful situations. The primary aim of the remote PFA support sessions was to help participants restore their emotional balance according to three principles: (1) observe the person's problem, needs, and possible solutions; (2) listen carefully to the person and help him/her feel supported and address his/her basic needs; (3) connect the individual to public or private mental health institutions if further specialized care was needed (International Federation of Red Cross and Red Crescent Societies 2020). This intervention was administered on an individual basis by SES psychologists via a telephone call, consisting of a single session lasting approximately 45 minutes.

Problem Management Plus (PM+). PM+ is a low-intensity, trans-diagnostic psychological intervention recommended by the WHO in treating common mental disorders in many resource-limited settings (Hamdani *et al.* 2018; World Health Organization 2016). Previous studies have shown that it is effective in reducing symptoms of anxiety and depression (Hamdani *et al.* 2018; Rahman *et al.* 2016). Its primary advantage is that it can be delivered widely by trained non-specialists such as community health workers, volunteers, and psychology students. The PM+ intervention has previously been adapted for use in the general Peruvian population (Coleman *et al.* 2021). The intervention consisted of five remote 90-minute sessions that were delivered on an individual basis every week. In the first session, participants were oriented and motivated to participate and receive psychoeducation and learn basic stress management and control strategies. In the second session, participants learned problem-solving techniques for life problems and were introduced to behavioral activation techniques. In the third and fourth sessions, they were introduced to techniques for strengthening social support and continued to practice problem-solving techniques,

221	behavioral activation procedures, and relaxation exercises. In the last session, all learned
222	strategies were reviewed and demonstrated by participants as a means of assessing
223	understanding for future use and application.
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225	Referral process and criteria for further specialized mental health care
226	SES psychologists referred participants with PHQ-9 ≥15 for higher-level mental health care
227	at public health care institutions. The referral process included identifying public health care
228	facilities closest to the participant's home, contacting the local facility, and arranging
229	appropriate follow-up to ensure that the referral process was successful. In areas without
230	access to mental health facilities, participants were referred to a nearby health care center
231	instead. Those experiencing mental health problems other than depression were referred to
232	specialized public mental health services operated by the MINSA of Peru.
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234	Depression re-evaluation
235	Among those who had received and completed remotely administered sessions of PFA or
236	PM+, SES psychologists contacted those same participants six months later and invited them
237	to be re-evaluated for depressive symptoms using the PHQ-9 questionnaire.
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239	Data collection and statistical analysis
240	SES psychologists uploaded data collected from participants to the SES electronic data
241	system. These included PHQ-9 scores at the time of enrollment/baseline and at the time of
242	follow-up, type of remote mental health support sessions received (PFA or PM+), and

whether participants were referred to primary care facilities or public health centers for higher-level mental health care. Continuous variables of characteristics of people with TB were reported as medians with interquartile ranges (IQR), and categorical variables were reported as frequencies with percentages. We reported the overall proportion of people initiating treatment for TB with PHQ-9≥5 at the time of study enrollment. For participants who were re-evaluated, we used the Wilcoxon's paired sign-rank test to compare the within-person change in median PHQ-9 scores between baseline and the six-month follow-up. We reported the relevant effect size ("r") estimate and accompanying p-value (Kerby 2014; Rosenthal 1994). All statistical analyses were conducted using Stata/SE 17.0 (Stata Corp., College Station, TX) with a significance level of 0.05.

Results

During the pandemic, we identified a total of 161 individuals who were referred for mental health evaluation after being assessed by the TB-M program (Figure 1). After excluding 26 participants, a total of 135 (83.9%) eligible participants underwent depressive symptom screening at baseline. Among all persons with TB who had undergone depressive symptom screening at baseline, the median age was 38.9 years (IQR: 28.4 years) and the majority were male (76 of 135 participants, 56.3%) (Table 1). Most participants were born in the Lima region (101 of 130 participants, 77.7%) and completed secondary education (91 of 129 participants, 70.5%). Microbiologically, 106 (81.5%) of 130 participants were tested for TB using sputum samples. Of those who had available GeneXpert MTB complex results (n = 100), 90 (90.0%) were positive; 10 (11.1%) of 90 participants with information on rifampicin resistance were resistant to rifampin.

Among 135 participants who underwent screening for depression at baseline, 62 (45.9%) had PHQ-9 \geq 5 (Table 1). Persons with TB and PHQ-9 \geq 5 at baseline tended to be younger compared with those with PHQ-9 \leq 5; albeit the comparison was not statistically significant (median age and IQR for participants with depressive symptoms vs. without at baseline: 37.2 years [22.0 years] vs. 41.6 years [30.5 years], p = 0.581) (Table 1). Furthermore, we did not find any statistically significant difference in the proportion of participants with PHQ-9 \geq 5 at baseline neither by sex (p = 0.055) nor by education level (p = 0.816; Table 2). However, those with PHQ-9 \geq 5 at baseline were more likely to be born within Lima compared with those with PHQ-9 scores \leq 5 (PHQ-9 \geq 5 vs. \leq 5 for the region of birth within Lima: 50 [70.4%] vs. 51 [86.4%], p = 0.035). We did not find a statistically significant difference in baseline depression status for those who had microbiological confirmation of their TB compared with those diagnosed based on clinical/radiological findings (p = 0.652).

Of the 62 participants who were found to have PHQ-9≥5 at baseline, almost all had PHQ-9, 5-9 (54 [87.1%]); 4 (6.5%) participants had PHQ-9, 10-14; 3 (4.8%) had PHQ-9, 15-19; and 1 (1.6%) had PHQ-9≥20 (Table 2; Figure 1). Among the 54 participants who were found to have PHQ-9, 5-9, 44 (81.5%) were re-evaluated six months after completing remote PFA support sessions. The majority of participants re-evaluated six months later no longer had clinically significant depressive symptoms, as evidenced by PHQ-9 scores <5 (n = 38 [86.4%]); only 6 (13.6%) had PHQ-9, 5-9. We observed a statistically significant reduction in the within-person change in the median PHQ-9 scores at baseline and during the six-month follow-up after completing the remote PFA support sessions (median PHQ-9 score and IQR

at baseline and at follow-up: 6 [3] and 2 [3], respectively, (r = 0.98; p<0.001; Table 3). Remote PM+ support sessions were delivered to four participants who were initially found to have PHQ-9, 10-14; however, they all refused re-evaluation six months later, and, therefore, a comparison could not be made. All participants who were found to have PHQ-9≥15 successfully received a single remote session of PFA and were immediately referred to higher-level mental health care.

Discussion

During the COVID-19 pandemic, we found that almost half of all persons recently diagnosed with TB as part of a community-based active TB screening program exhibited depressive symptoms (PHQ-9≥5). Furthermore, our findings also indicate that implementing a stepped care model for mental health screening and care delivery was associated with overall improvements in median PHQ-9 scores six months later.

Overall, we found that 45.9% of all persons with TB in our sample had depressive symptoms at the time of TB treatment initiation. We recognize that this prevalence estimate was determined using a liberal PHQ-9 cutoff score of 5. Nonetheless, our prevalence estimate is much higher than that recently reported in the general Peruvian population during the pandemic period (~20%) (Zegarra-López *et al.* 2022). Our estimate is consistent with the pooled depressive symptom prevalence estimate among persons with TB (Duko *et al.* 2020). In our program, most participants with depressive symptoms exhibited mild depression, defined by PHQ-9, 5-9 (54/62 [87.1%]). Most were contacted by SES psychologists within

the first 30 days following TB diagnosis, a period that also coincides with the initiation of TB treatment. The high prevalence at baseline may be related to an increased incidence of new depressive symptoms or an acute worsening of pre-existing depression or some other unassessed mental disorders within our study population. While our data limits our ability to differentiate between these two possibilities, the high prevalence of depressive symptoms may be due to a variety of acute psychosocial stressors related to receiving a TB diagnosis and/or transitioning to receiving TB treatment (Sweetland *et al.* 2017). In particular, the perceived stigma associated with a TB diagnosis is notably high among persons with TB, and its sequelae (e.g., discrimination) are common means by which persons with TB may develop and experience depressive symptoms (Chen *et al.* 2023; Lee *et al.* 2017; Mohammedhussein *et al.* 2020; Sweetland *et al.* 2017). Thus, our findings suggest that the integration of early depression screening within TB screening programs could be useful in identifying a large sample of patients who may benefit from concurrent mental health care during their TB treatment, especially around the time of TB diagnosis and initiation of TB treatment.

Previous studies addressing comorbid mental and health concerns among persons with TB disease have primarily focused on delivering mental health interventions to those who screen positive for depressive symptoms, regardless of their symptom severity at the time of initial screening (Farooq *et al.* 2021). However, few studies have implemented a stepped care model of first screening for mental disorders and subsequently delivering severity-appropriate mental health interventions. In Nepal, Walker et al. conducted a feasibility and acceptability pilot study for a psychosocial support package among patients with MDR-TB (Walker *et al.* 2018). Their package involved providing all patients with information and educational materials and initially screening them for symptoms of anxiety and depression using the

Johns Hopkins Symptom Checklist. For those who screened positive for either anxiety or
depression, they were subsequently referred for depressive symptom screening using the
PHQ-9. Those who had PHQ-9 scores less than 10 were re-screened on a monthly frequency.
Those who had PHQ-9, 10-19 received a series of counseling sessions based on behavioral
activation originally evaluated in India for treating depression. Those who had PHQ-9>19 or
who expressed suicidal intent were referred for higher-level psychiatric and medical care.
Although this study concluded that, overall, it was feasible to design and implement a
stepped care model for mental health care within a National Tuberculosis Program, it
suffered a couple of key limitations, including (a) utilization of a complex two-step screening
system that likely resulted in fewer number of patients receiving the counseling intervention;
and (b) inability to evaluate the potential impact of the mental health intervention on changes
in depression and anxiety severity in relation to the time of initial screening. Our present
study utilized the PHQ-9 as the only standardized screening tool and implemented a stepped
care model with different severity-appropriate virtual mental health support sessions.
Although we were unable to re-evaluate enough participants who received remote PM+
sessions, we were able to re-evaluate a high proportion (~80%) of those who completed
remote PFA sessions and gain a sense of the possible mental health impact associated with
providing severity-specific mental health interventions.

More broadly speaking, our findings and programmatic experience are consistent with overall global patterns of shifting toward remote means of delivering mental health care and support at the onset of the COVID-19 pandemic. This shift has been described by a recent umbrella review of 38 systematic reviews of studies on remote mental health interventions and care delivery during the pandemic (Witteveen *et al.* 2022). In particular, there was a greater shift

toward synchronous modalities of remote mental health care delivery (e.g., use of videoconferencing platforms and telephone calls) than asynchronous means (e.g., self-help apps, websites, or digital tools) (Witteveen *et al.* 2022). This shift is also consistent with our programmatic approach with the use of telephone calls and videoconferencing means to deliver remote PFA sessions and PM+ sessions. However, despite these adaptive changes, these reviews also highlighted limited access to remote mental health care and services among members of vulnerable populations and communities as a chief barrier and disparity; this included a paucity of studies reporting on remote mental health interventions from LMICs, particularly during the early phase of the pandemic (Witteveen *et al.* 2022). Our study adds to a growing need for research that evaluates innovative and integrated ways of meeting the psychosocial needs of vulnerable patient populations like those with TB in resource-limited settings.

Our programmatic experience and findings have implications for integrating mental health care and TB care. We show that low-intensity mental health interventions such as PFA and PM+ support sessions can be administered virtually to persons recently diagnosed with TB during the pandemic era. This type of care delivery modality is in line with the wider and accelerated shifts toward adapting and utilizing telehealth-based technologies during the pandemic (Moreno *et al.* 2020; Witteveen *et al.* 2022). Low-intensity psychosocial interventions such as PFA are first-line psychosocial interventions that can be administered in high-stress mental health crises and delivered by trained non-specialist personnel. This may greatly expand service coverage in settings with limited resources and fewer formally-trained mental health professionals (Pollock *et al.* 2020); these lessons may also be applicable in high-income settings. Furthermore, integrated TB and mental health screening in high-risk

populations, settings, or communities offers an opportunity to detect a higher number of individuals with both TB and mental health issues. This may be particularly important during times when acute psychosocial stressors and TB-associated stigma are likely to be most severe.

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Our study has several notable limitations. First, although we observed statistically significant reductions in the median PHQ-9 scores from baseline to six months following completion of PFA sessions, we are limited in our ability to infer to what extent the mental health interventions may have contributed to these reductions. On one hand, remote PFA sessions could have improved depressive symptoms by providing immediate psychosocial support to persons with newly diagnosed TB during what is often a significant and traumatic life event and transition (Hermosilla et al. 2023). On the other hand, we also considered other plausible explanations, which include but are not limited to natural improvements in depressive symptoms with time, improvements in TB disease because of ongoing treatment, the beneficial impacts of other unmeasured psychosocial and/or clinical factors (i.e., residual confounding), or a combination of these factors. In a similar vein, we were unable to compare changes in median PHQ-9 scores over time with a control group, as every participant who had PHQ-9≥5 at baseline was offered mental health support. Second, we were unable to reevaluate slightly less than 20% of those who had PHQ-9 scores 5-9 at baseline six months after completing PFA support sessions. Assuming those with higher PHQ-9 scores are less likely to follow-up, this could have led to an overestimation of the change in median PHQ-9 scores between baseline and follow-up. Finally, we were unable to assess the association between completing the mental health interventions and TB treatment outcomes, including known mediators such as treatment adherence. Previous studies have demonstrated a positive

correlation between emotional support during TB treatment and improved treatment adherence and success rates (Ruiz-Grosso *et al.* 2020). Therefore, future mental health interventions could include regular, monthly follow-up depression assessments throughout the TB treatment period, particularly at the start of TB treatment when depressive symptoms are likely to be most severe.

In conclusion, we found that depressive symptoms were common among people with TB who were identified by a community-based active TB screening program. We also observed significant improvements in depressive symptoms six months later among most participants who received remote sessions of PFA. Future studies are needed to rigorously evaluate the feasibility and utility of frequent depression assessments during the TB treatment period as well as the impact of severity-appropriate, low-intensity psychosocial interventions on TB treatment outcomes regarding cost, programmatic scalability, and acceptability among persons with TB.

Author Contribution Statement

CC is the corresponding author. CC, JS, and JG designed and oversaw the implementation of the mental health interventions. DP, MT, JP, LL, SK, and CY designed and oversaw the implementation of the community-based active TB case finding program "TB Móvil." LR devised the analytical approach and carried out the data analysis. CC and JS drafted the primary version of the manuscript. ALC, CC, JS, DP, MT, JP, LL, SK, CY, and GR revised

428	and edited subsequent versions of the manuscript. All authors reviewed and approved the
429	final version of the manuscript.
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434	
435	Conflict of Interest Statement
436	All authors have no conflicts of interest to declare.
437	
438	Ethics Statement
439	The study was reviewed and approved by the Ethics Review Committee of SES.
440	Confidentiality was maintained throughout the study. All collected data were kept
441	confidential and used only for study purposes.
442	
443	Data Availability Statement
444	The anonymized version of the data analyzed in this study is available upon request.
445	
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452	Bower, P, and Gilbody, S (2005) Stepped care in psychological therapies: access,
453	effectiveness and efficiency: Narrative literature review. British Journal of
454	Psychiatry, 186 (1), 11–17. doi:10.1192/bjp.186.1.11.
455	Calderón, M, Gálvez-Buccollini, JA, Cueva, G, Ordoñez, C, Bromley, C, and Fiestas, F
456	(2012) Validación de la versión peruana del PHQ-9 para el diagnóstico de depresión.
457	Revista Peruana de Medicina Experimental y Salud Pública, 29 (4), 578–579.
458	doi:10.1590/S1726-46342012000400027.
459	Chen, X, Chen, Y, Zhou, L, and Tong, J (2023) The role of self-esteem as moderator of the
460	relationship between experienced stigma and anxiety and depression among
461	tuberculosis patients. Scientific Reports, 13(1), 6889. doi:10.1038/s41598-023-34129-
462	4.
463	Coleman, SF, Mukasakindi, H, Rose, AL, Smith, SL (2021) Adapting Problem
464	Management Plus for Implementation: Lessons Learned from Public Sector Settings
465	Across Rwanda, Peru, Mexico and Malawi. Intervention (Amstelveen, Netherlands),
466	19 (1), 58–66.
467	Dawson, KS, Bryant, RA, Harper, M, van Ommeren, M (2015) Problem Management
468	Plus (PM+): a WHO transdiagnostic psychological intervention for common mental
469	health problems. World Psychiatry, 14(3), 354–357. doi:10.1002/wps.20255.
470	Duko, B, Bedaso, A, and Ayano, G (2020) The prevalence of depression among patients with
471	tuberculosis: a systematic review and meta-analysis. Annals of General Psychiatry,
472	19 , 30. doi:10.1186/s12991-020-00281-8.
473	Farooq, S, Tunmore, J, and Comber, R (2021) Pharmacological or non-pharmacological
474	interventions for treatment of common mental disorders associated with Tuberculosis:

451

References

475	A systematic review. Chronic Respiratory Disease, 18, 147997312110039.
476	doi:10.1177/14799731211003937.
477	Fu, Z, Burger, H, Arjadi, R, and Bockting, CLH (2020) Effectiveness of digital psychological
478	interventions for mental health problems in low-income and middle-income countries:
479	a systematic review and meta-analysis. The Lancet. Psychiatry, 7(10), 851–864.
480	doi:10.1016/S2215-0366(20)30256-X.
481	Galea, JT, Puma, D, Tzelios, C, Keshavjee, S (2022) A structured community engagement
482	strategy to support uptake of TB active case-finding. <i>Public Health Action</i> , 12 (1), 18–
483	23. doi:10.5588/pha.21.0059.
484	Hamdani, SU, Ahmed, Z, Sijbrandij, M, Minhas, FA (2018) Correction to: Problem
485	Management Plus (PM+) in the management of common mental disorders in a
486	specialized mental healthcare facility in Pakistan; study protocol for a randomized
487	controlled trial. International Journal of Mental Health Systems, 12(1), 53.
488	doi:10.1186/s13033-018-0231-1.
489	Hermosilla, S, Forthal, S, Sadowska, K, Magill, EB, Watson, P, and Pike, KM (2023) We
490	need to build the evidence: A systematic review of psychological first aid on mental
491	health and well-being. <i>Journal of Traumatic Stress</i> , 36 (1), 5–16.
492	doi:10.1002/jts.22888.
493	International Federation of Red Cross and Red Crescent Societies (2020) Remote
494	Psychological First Aid during the COVID-19 outbreak Interim guidance - March
495	2020 (Technical Guidelines). Retrieved from
496	https://reliefweb.int/report/world/remote-psychological-first-aid-during-covid-19-
497	outbreak-interim-guidance-march-2020
498	Kerby, DS (2014) The Simple Difference Formula: An Approach to Teaching Nonparametric
499	Correlation. Comprehensive Psychology, 3, 11.IT.3.1. doi:10.2466/11.IT.3.1.

500	Kroenke, K, Spitzer, RL, and Williams, JB (2001) The PHQ-9: validity of a brief depression
501	severity measure. Journal of General Internal Medicine, 16(9), 606–613.
502	doi:10.1046/j.1525-1497.2001.016009606.x.
503	Lee, L, Tung, H, Chen, S, and Fu, C (2017) Perceived stigma and depression in initially
504	diagnosed pulmonary tuberculosis patients. Journal of Clinical Nursing, 26(23-24),
505	4813–4821. doi:10.1111/jocn.13837.
506	Mohammedhussein, M, Hajure, M, Shifa, JE, and Hassen, TA (2020) Perceived stigma
507	among patient with pulmonary tuberculosis at public health facilities in southwest
508	Ethiopia: A cross-sectional study. PloS One, 15(12), e0243433.
509	doi:10.1371/journal.pone.0243433.
510	Moreno, C, Wykes, T, Galderisi, S, Arango, C (2020) How mental health care should
511	change as a consequence of the COVID-19 pandemic. The Lancet Psychiatry, 7(9),
512	813–824. doi:10.1016/S2215-0366(20)30307-2.
513	Pasha, A, Siddiqui, H, Ali, S, Brooks, MB, Maqbool, NR, and Khan, AJ (2021) Impact of
514	integrating mental health services within existing tuberculosis treatment facilities.
515	Medicine Access @ Point of Care, 5, 23992026211011314.
516	doi:10.1177/23992026211011314.
517	Pollock, A, Campbell, P, Cheyne, J, Maxwell, M (2020) Interventions to support the
518	resilience and mental health of frontline health and social care professionals during
519	and after a disease outbreak, epidemic or pandemic: a mixed methods systematic
520	review. Cochrane Database of Systematic Reviews, 2020(11).
521	doi:10.1002/14651858.CD013779.
522	Rahman, A, Riaz, N, Dawson, KS, Farooq, S (2016) Problem Management Plus (PM+):
523	pilot trial of a WHO transdiagnostic psychological intervention in conflict-affected
524	Pakistan. World Psychiatry, 15(2), 182–183. doi:10.1002/wps.20312.

525	Rosenthal, R (1994) Parametric Measures of Effect Size. The Handbook of Research
526	<i>Synthesis</i> , 231–244.
527	Ruiz-Grosso, P, Cachay, R, de la Flor, A, Schwalb, A, and Ugarte-Gil, C (2020) Association
528	between tuberculosis and depression on negative outcomes of tuberculosis treatment:
529	A systematic review and meta-analysis. PloS One, 15(1), e0227472.
530	doi:10.1371/journal.pone.0227472.
531	Sweetland, AC, Jaramillo, E, Wainberg, ML, Dua, T (2018) Tuberculosis: an opportunity
532	to integrate mental health services in primary care in low-resource settings. The
533	Lancet. Psychiatry, 5(12), 952–954. doi:10.1016/S2215-0366(18)30347-X.
534	Sweetland, AC, Kritski, A, Oquendo, MA, Wainberg, ML (2017) Addressing the
535	tuberculosis-depression syndemic to end the tuberculosis epidemic. <i>The International</i>
536	Journal of Tuberculosis and Lung Disease, 21(8), 852–861.
537	doi:10.5588/ijtld.16.0584.
538	Ugarte-Gil, C, Ruiz, P, Zamudio, C, Seas, C (2013) Association of Major Depressive
539	Episode with Negative Outcomes of Tuberculosis Treatment. PLoS ONE, 8(7),
540	e69514. doi:10.1371/journal.pone.0069514.
541	van Hoorn, R, Jaramillo, E, Collins, D, Gebhard, A, and van den Hof, S (2016) The Effects
542	of Psycho-Emotional and Socio-Economic Support for Tuberculosis Patients on
543	Treatment Adherence and Treatment Outcomes - A Systematic Review and Meta-
544	Analysis. <i>PloS One</i> , 11 (4), e0154095. doi:10.1371/journal.pone.0154095.
545	Vega, P, Sweetland, A, Acha, J, Shin, S (2004) Psychiatric issues in the management of
546	patients with multidrug-resistant tuberculosis. The International Journal of
547	Tuberculosis and Lung Disease: The Official Journal of the International Union
548	Against Tuberculosis and Lung Disease, 8(6), 749–759.

549	Walker, IF, Khanal, S, Hicks, JP, Newell, JN (2018) Implementation of a psychosocial
550	support package for people receiving treatment for multidrug-resistant tuberculosis in
551	Nepal: A feasibility and acceptability study. PLOS ONE, 13(7), e0201163.
552	doi:10.1371/journal.pone.0201163.
553	Witteveen, AB, Young, S, Cuijpers, P, Sijbrandij, M (2022) Remote mental health care
554	interventions during the COVID-19 pandemic: An umbrella review. Behaviour
555	Research and Therapy, 159, 104226. doi:10.1016/j.brat.2022.104226.
556	World Health Organization (2016) Problem management plus (PM+): individual
557	psychological help for adults impaired by distress in communities exposed to
558	adversity (Manual), Geneva: World Health Organization. Retrieved from
559	https://www.who.int/publications/i/item/WHO-MSD-MER-16.2
560	World Health Organization (2022a) Global tuberculosis report 2022, Geneva. Retrieved
561	from https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-
562	tuberculosis-report-2022
563	World Health Organization (2022b, October 27) Tuberculosis Fact Sheet., World Health
564	Organization. Retrieved from https://www.who.int/news-room/fact-
565	sheets/detail/tuberculosis
566	World Health Organization (2023) Global tuberculosis report 2023, Geneva: World Health
567	Organization. Retrieved from https://www.who.int/teams/global-tuberculosis-
568	programme/tb-reports/global-tuberculosis-report-2023
569	Yuen, CM, Puma, D, Millones, AK, Keshavjee, S (2021) Identifying barriers and
570	facilitators to implementation of community-based tuberculosis active case finding
571	with mobile X-ray units in Lima, Peru: a RE-AIM evaluation. BMJ Open, 11(7),
572	e050314. doi:10.1136/bmjopen-2021-050314.

573	Zegarra-López, AC, Florentino-Santisteban, B, Flores-Romero, J, Delgado-Tenorio, A, and
574	Cernades-Ames, A (2022) A Cross-Sectional Study on the Prevalence of Depressive
575	Symptoms and Its Associated Sociodemographic Factors in Peru during the COVID
576	19 Pandemic. International Journal of Environmental Research and Public Health,
577	19 (21), 14240. doi:10.3390/ijerph192114240.
578	
579	

Table 1. Baseline participant characteristics, by baseline depressive symptom status (N = 135)

		Baseline depre	p-value	
Characteristics	Total no. (%),	PHQ-9 scores	PHQ-9 scores ≥5	
	$N = 135^{a}$	(n = 73)	(n = 62)	
Age, years, median (IQR) $(n = 135)$	135 (100.0)	41.6 (30.5)	37.2 (22.0)	0.581
Gender (n = 135)				0.501
Male	76 (56.3)	47 (64.4)	29 (46.8)	0.055
Female	59 (43.7)	26 (35.6)	33 (53.2)	1
Highest educational level achieved (n = 129)	, ,	, ,	,	
Primary or less	24 (17.8)	14 (20.6)	10 (16.4)	0.816
Secondary	91 (70.5)	46 (67.7)	45 (73.8)	1
Post-secondary	14 (10.9)	8 (11.8)	6 (9.8)	
Region of birth $(n = 130)$		· · · · · · · · · · · · · · · · · · ·		
From Lima	101 (77.7)	50 (70.4)	51 (86.4)	0.035
Outside of Lima	29 (22.3)	21 (29.6)	8 (13.6)	
TB diagnosis methodology (n = 130)				
Microbiological confirmation	106 (81.5)	54 (79.4)	52 (83.9)	0.652
Clinical/radiological criteria	24 (18.5)	14 (20.6)	10 (16.1)	
BK results (n = 100)				
Negative	53 (53.0)	33 (60.0)	20 (44.4)	0.159
Positive	47 (47.0)	22 (40.0)	25 (55.6)	
GeneXpert MTB Complex Detection Status (n = 100)				0.021
Negative/not detected	10 (10.0)	9 (16.4)	1 (2.2)	0.021
Positive/detected	90 (90.0)	46 (83.6)	44 (97.8)	1
Rifampin resistance status ^b (n = 90)				
Sensitive	49 (54.4)	25 (54.3)	24 (54.5)	0.076
Resistant	31 (34.4)	19 (41.3)	12 (27.3)	1
Indeterminant	10 (11.1)	2 (4.3)	8 (18.2)	1

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Table 2. Breakdown of depressive symptom severity at baseline among persons with TB

Baseline depressive symptom severity	PHQ-9 score range	No. (%)
None/ minimal	0 - 4	73 (54.1)
Mild	5 – 9	54 (40.0)
Moderate	10 – 14	4 (3.0)
Moderately severe	15 – 19	3 (2.2)
Severe	≥20	1 (0.7)
Total		135 (100.0)

^a Total number may be less than 135 due to missing data

^b Numbers and percentages reported only among participants with a positive GeneXpert test result

Table 3. Comparisons of median PHQ-9 scores at baseline and six months following completion of remote PFA support sessions in persons with TB (n = 44)

Baseline PHQ-9				PHQ-9 at Re-evaluation (Six Months Follow-up)			Change in Median PHQ-9		
Median	Min	Max	IQR	Media n	Min	Max	IQR	Effect size (r)	p-value
6	5	9	3	2	0	5	3	0.98	<0.001

590 Figure 1. Study flow chart

