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**Effectiveness of a WHO self-help psychological intervention for preventing mental disorders among Syrian refugees in Turkey: a randomized controlled trial**

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Refugees are at high risk of developing mental disorders. There is no evidence from randomized controlled trials (RCTs) that psychological interventions can prevent the onset of mental disorders in this group. We assessed the effectiveness of a self-help psychological intervention developed by the World Health Organization, called Self-Help Plus, in preventing the development of mental disorders among Syrian refugees experiencing psychological distress in Turkey. A two-arm, assessor-masked RCT was conducted in two Turkish areas. Eligible participants were adult Syrian refugees experiencing psychological distress (General Health Questionnaire  $\geq 3$ ), but without a diagnosis of mental disorder. They were randomly assigned either to the Self-Help Plus arm (consisting of Self-Help Plus combined with Enhanced Care as Usual, ECAU) or to ECAU only in a 1:1 ratio. Self-Help Plus was delivered in a group format by two facilitators over five sessions. The primary outcome measure was the presence of any mental disorder assessed by the Mini International Neuropsychiatric Interview at six-month follow-up. The presence of mental disorders at post-intervention, and psychological distress, symptoms of post-traumatic stress disorder and depression, personally identified psychological outcomes, functional impairment, subjective well-being, and quality of life at post-intervention and six-month follow-up were secondary outcome measures. Between October 1, 2018 and November 30, 2019, 1,186 refugees were assessed for inclusion. Five hundred forty-four people were ineligible, and 642 participants were enrolled and randomly assigned to either Self-Help Plus (N=322) or ECAU (N=320). Self-Help Plus participants were significantly less likely to have any mental disorders at six-month follow-up compared to the ECAU group (21.69% vs. 40.73%; Cramer's  $V=0.205$ ,  $p<0.001$ , risk ratio: 0.533, 95% CI: 0.408-0.696). Analysis of secondary outcomes suggested that Self-Help Plus was not effective immediately post-intervention, but was associated with beneficial effects at six-month follow-up in terms of symptoms of depression, personally identified psychological outcomes, and quality of life. This is the first prevention RCT ever conducted among refugees experiencing psychological distress but without a mental disorder. Self-Help Plus was found to be an effective strategy for preventing the onset of mental disorders. Based on these findings, this low-intensity self-help psychological intervention could be scaled up as a public health strategy to prevent mental disorders in refugee populations exposed to ongoing adversities.

**Key words:** Refugees, prevention, common mental disorders, Self-Help Plus, psychological intervention, public health strategy, randomized controlled trial

In 2020, the number of forcibly displaced people in the world, 80 million, was the highest since World War II<sup>1</sup>. Among them, 26 million fled their countries due to violence or persecution<sup>1</sup>. The largest group of refugees was from Syria, accounting for 6.6 million people. Around 3.6 million Syrian refugees are in Turkey, making Turkey the world's top refugee hosting country<sup>1</sup>.

Many Syrian refugees have been exposed to potentially traumatic experiences such as bombings, threats, captivity, torture, injury, and witnessing death or injury of loved ones<sup>2</sup>. Moreover, they are at risk of discrimination, economic problems, and social isolation. In 2020, the COVID-19 pandemic exacerbated Syrian refugees' hardship in Turkey because of a sudden and severe deterioration in income generation opportunities and access to services and social supports<sup>3</sup>.

Owing to potentially traumatic events, major losses and other stressors before, during and after migration, refugees are at high risk of developing common mental disorders<sup>4</sup>. The World Health Organization (WHO) estimates that rates of depression, post-traumatic stress disorder (PTSD) and any mental disorder among people exposed to conflict in the previous 10 years are 10.8%, 15.3% and 22.1% respectively<sup>5</sup>. Evidence suggests that Syrian refugees are at high risk of developing these disorders<sup>6</sup>.

A significant component of consensus-based humanitarian mental health policy and practice involves psychological interventions that aim to have preventive and health promotion effects<sup>2</sup>. However, evidence for such effects has been limited, and a recent Cochrane review did not identify any randomized studies assessing whether preventive psychological and social interventions can reduce the frequency of mental disorders in people affected by a humanitarian crisis<sup>7</sup>.

In recent years, the WHO has developed a series of brief transdiagnostic psychological interventions, including Problem Management Plus<sup>8</sup> and Self-Help Plus<sup>9</sup>, which have been tested for treatment of mental health problems among people affected by adversity<sup>10-13</sup>. However, they have never been evaluated as indicated preventive interventions – i.e., they have not been tested among people who are distressed, but who do not meet the criteria for any mental disorder, to see whether they can prevent the onset of mental disorders.

In the present study, we examined the effectiveness of Self-Help Plus as an indicated intervention to prevent the onset of mental disorders among distressed Syrian refugees in Turkey.

## **METHODS**

### **Study design**

The study was an assessor-masked, parallel-group randomized controlled trial (RCT). The trial protocol was published and registered at [clinicaltrials.gov](https://clinicaltrials.gov) (NCT03587896)<sup>14</sup>. The study was approved by the WHO Ethics Review Committee and the Ethics Committees of Istanbul Sehir University and Koc University. Written informed consent was provided by all participants.

Participant recruitment occurred from October 1, 2018 to November 30, 2019 in Istanbul and Mardin, Turkey. Six-month follow-up assessments ended in June 2020.

Local non-governmental organizations (NGOs) implementing projects for refugees in Turkey were approached to identify potentially eligible participants. These NGOs provide integrated reception services that include food, housing; legal, educational, health care and social guidance and support; and programmes to promote socioeconomic inclusion and integration. Participants were consecutively invited to participate by members of the research team, in agreement with local service staff, who facilitated contacts.

All research team members were Arabic-speaking. They were trained in conducting the interviews, administering the rating scales, and performing follow-up assessments, so that they were able to assist the persons in a culturally appropriate manner. Research team members followed a code of conduct, complying with the principles of neutrality, impartiality, confidentiality, demeanor, and avoiding activities that might lead to a conflict of interests. All research-related training activities were coordinated by the WHO Collaborating Centre of the University of Verona, Italy.

### **Randomization and masking**

Participants were randomly assigned either to the Self-Help Plus arm (consisting of Self-Help Plus combined with Enhanced Care as Usual, ECAU) or to ECAU only, in a 1:1 ratio. Randomization was centralized and coordinated by the Verona Collaborating Centre.

The randomization schedule was generated by Castor Electronic Data Capture (EDC) software<sup>15</sup>, employing variable block randomization. Research team members involved in recruitment were able to access the web-based software to randomize each newly enrolled participant, but were not able to access the randomization list, and were not aware of the block size. Castor EDC software allowed random allocation only after the main information

on the enrolled participant was entered, upon verification of the inclusion criteria. After random allocation, the software produced a unique identification number for each participant.

Both assessors evaluating outcomes and the statistician performing analyses were masked to participant allocation status. Outcome assessors were not involved in any activities that might reveal random allocation of study participants. A formal assessment of the success of masking was not conducted, as there is no methodological consensus of whether such tests are appropriate, reliable and truly informative<sup>16</sup>.

### **Inclusion and exclusion criteria**

Participants were included if they met the following criteria: a) aged 18 years or older; b) able to speak and understand Arabic; c) being under temporary protection according to Law on Foreigners and International Protection; d) experiencing psychological distress, as shown by a score of 3 or more on the 12-item dichotomously-scored General Health Questionnaire<sup>17,18</sup>; e) having completed oral and written informed consent to enter the study.

Exclusion criteria were: a) presence of any mental disorder according to the Mini International Neuropsychiatric Interview (MINI)<sup>19,20</sup>; b) evidence of acute medical conditions contraindicating study participation; c) evidence of imminent suicide risk, or suicide risk scored as “moderate or high” on the MINI; d) signs of impaired decision-making capacity emerging from responses during the clinical interview. Refugees who were excluded because of a diagnosis of a mental disorder and/or imminent suicide risk were referred for treatment to a health professional.

### **Experimental and control intervention**

The Self-Help Plus intervention consists of a pre-recorded audio course, delivered by trained facilitators in a group setting and complemented with an illustrated self-help book adapted for the target cultural group. The intervention is based on acceptance and commitment therapy, a form of cognitive behavioural therapy. It is delivered across five 2-hour sessions. The audio material imparts key information about stress management and guides participants through individual exercises and small group discussions. The self-help book reviews all essential content and concepts.

In this study, a version of the intervention previously adapted for Syrian populations was used. The adaptation followed a WHO protocol and involved adapting the audio recordings to a colloquial form of Arabic widely understood in Syria and culturally adapting the illustrations.

As Self-Help Plus is a pre-recorded intervention, fidelity checking primarily involved ensuring that all of the recordings were played and all activities (e.g., discussions, grounding exercises, stretches) were completed. Fidelity forms were completed after each session by facilitators. Additionally, 20% of all sessions were checked using the same forms by external trained supervisors.

ECAU was provided to participants in both groups, and consisted of routinely delivered social support and/or care. Additionally, participants in the control arm received baseline and follow-up assessments according to the study schedule, information about freely available health and social services, and links to community networks providing support to refugees.

An independent Ethics Advisory Board, consisting of international experts giving advice on any relevant ethical issues, supervised the study.

## Measures

The primary outcome was the presence of current mental disorders at six-month follow-up, ascertained by the MINI<sup>19,20</sup>. The MINI was also administered at baseline before randomization, and at post-intervention. All other assessment instruments measured secondary outcomes at post-intervention and at six-month follow-up.

Psychological distress was measured using the GHQ-12 questionnaire<sup>17,18</sup>, in which items are rated on a four-point Likert scale, giving a maximum total score of 36. PTSD symptoms were assessed by the PTSD Checklist for DSM-5 (PCL-5)<sup>21,22</sup>, a 20-item questionnaire giving a maximum total score of 80. Depression symptoms were measured by the Patient Health Questionnaire, nine-item version (PHQ-9)<sup>23-25</sup>, which gives a maximum total score of 27. Personally identified psychological outcomes were examined using the Psychological Outcome Profiles (PSYCHLOPS)<sup>26,27</sup>, which asks participants to describe two problems from their own perspective and rate their severity on a six-point scale (maximum score: 18).

Functional impairment and subjective well-being were assessed by the WHO Disability Assessment Schedule 2.0 (WHODAS)<sup>28</sup>, and the WHO-5 Well-Being Index (WHO-5)<sup>29,30</sup>, respectively. The WHO-5 contains five questions using a six-point scale (maximum score: 25). For evaluating general health, we administered the European Quality of Life 5-Dimensions 3- Level (EQ-5D-3L) questionnaire, a brief self-report measure consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression)<sup>31-33</sup>.

Traumatic/adverse life events and environmental stressors were explored using the Harvard Trauma Questionnaire (HTQ)-Part A<sup>34,35</sup> and the 17-item Checklist for Post-Migration Living Difficulties (PMLD)<sup>36</sup>. HTQ-Part A asks for lifetime traumatic life events. The

PMLD asks respondents to rate their experience of the problems during the last 12 months on a five-point scale (from “not a problem” to “a very serious problem”).

Assessments were conducted as face-to-face interviews or remotely by telephone or secure online audio/video communication (for reasons of feasibility, including physical distancing requirements related to the COVID-19 pandemic). Adverse events reported spontaneously by the participants or observed by the research staff were recorded, reviewed by the Ethics Advisory Board in regular meetings, and reported to the WHO Ethics Review Committee.

## **Statistical analysis**

We expected a frequency of mental disorders of 25% at six months in this population group<sup>14</sup>. We hypothesized that Self-Help Plus would show a clinically significant advantage by producing a between-groups absolute difference of 10%<sup>14</sup>. With these figures, to achieve at least 80% power for a 0.05 level of significance in a chi-square test, a sample size of 500 participants (250 per group) was needed. Assuming that a proportion of refugees might be lost at study endpoint (due to the specific characteristics of this population), a final sample size of 600 participants (300 per group) was planned.

Descriptive statistics were calculated on sociodemographic, pre-migration, migration and post-migration variables at baseline. Balance between treatment groups was checked calculating standardized mean differences (SMDs). SMD values of 0.1 and –0.1 were used as thresholds for imbalance<sup>37</sup>.

We followed an intent-to-treat approach for analysis of primary and secondary outcomes. The intent-to-treat population consisted of all randomized participants who completed baseline assessment, irrespective of the number of Self-Help Plus sessions received. To check the robustness of results, the primary outcome was also analyzed using a per-protocol approach, including only participants who completed at least three Self-Help Plus sessions.

The primary outcome was compared between the two groups using Cramer's V, together with a risk ratio (RR) and its 95% confidence interval (95% CI). A multivariate secondary analysis was performed through a Poisson regression model, with a robust error variance, to estimate RRs directly, and to explore the potential confounding effect of prognostic factors controlling for variables showing imbalance at baseline.

For each secondary outcome, a mixed analysis of covariance (ANCOVA) controlling for baseline scores, with robust standard errors and distinct variances for post-intervention and six-month follow-up, was performed. In addition to mixed models, a last observation carried



forward (LOCF) approach was also used to account for missing observations at six months. Standardized coefficients were estimated with the Stata "stdBeta" command.

For each questionnaire, in case of missing items, we used the corrected item mean substitution method (i.e., the item mean across participants weighted by the subject's mean of completed items)<sup>38</sup>, using information from subjects belonging to the same treatment arm for the same follow-up time, through the Stata "hotvalue" command. The substitution was only performed if resulting in admissible values, and only for observations having less than 50% of missing items. As a sensitivity analysis, we re-ran our models without any data imputation.

The hypothesis that the experimental intervention had no effect on GHQ-12, PCL-5, PHQ-9, PSYCHLOPS, WHODAS 2.0, WHO-5 and EQ-5D-3L scores was tested by performing seemingly unrelated regression (SUR)<sup>39</sup>, in its modification to allow for unbalanced data through the Stata "suregub" command. SUR was performed for each time point, controlling for baseline values.

Possible interactions between treatment and specific variables (gender, age, years of education, length of stay in the hosting country) were evaluated. In particular, in the case of continuous outcomes, SUR for unbalanced data on all outcomes was performed, with their value at baseline, treatment status, all potential moderators, and their interactions with treatment status, as predictors. A global test on all interaction terms was implemented and, in case of significance, the same test was performed for each scale. Finally, for scales meeting the statistical significance threshold, single regressions were conducted.

As for binary outcomes, to avoid the issue of poor performance of the model in case of solutions near the boundary<sup>40</sup>, Poisson regression models were performed with robust standard errors, setting as regressors the variable "intervention allocation", each variable separately, and their interaction with treatment. The Bonferroni correction was used to take into account multiple testing.

Multivariate analyses were performed for each secondary outcome to take confounding factors into account, again including the baseline value as a covariate. Finally, lost-to-follow-up was compared between the two groups using a chi-square or a Fisher exact test, as appropriate. All analyses were performed using Stata/SE, Release 15.1<sup>41</sup>.

## RESULTS

After screening 1,186 potentially eligible participants, 544 were excluded. A total of 123 were excluded because their level of distress was below the established cut-off, 282 because

of a positive MINI, and 139 for other reasons (e.g., mental health was not a priority for them or they were not available to receive the intervention) (see Figure 1). This left 642 individuals who met the inclusion criteria, consented to be randomized, and were randomly allocated to either Self-Help Plus (N=322) or ECAU (N=320).

At six-month follow-up (primary outcome), we could not assess 95 individuals (14.8%). They were lost to follow-up because they refused to participate (N=46) or because they were not reachable and/or moved to other locations (N=49). The distribution of participants lost to follow-up was similar between the study groups (15.53% vs. 14.06%, Cramer's  $V=0.021$ ,  $p=0.601$ ;  $RR=1.104$ , 95% CI: 0.761-1.602).

The main sociodemographic characteristics of the included participants are shown in Table 1. Their mean age was  $31.5 \pm 9.0$  years; 62.9% of them were women. For 61.8% of them, primary school was the highest level of education, while 14.5% received academic education. Almost all participants came from Syria (628 of 642, 97.8%). The remaining 14 participants came from Iraq (N=11), Yemen (N=1), or occupied Palestinian territory (N=1). One additional participant did not consent to reveal this information. The mean age at departure was  $27.1 \pm 10.1$  years. A minority of participants (5.2%) experienced detention during their transition to Turkey.

Assessment of 20% of Self-Help Plus sessions showed that all the components of the intervention were delivered in line with the manual. No adverse events related to the study participation were reported. In addition to Self-Help Plus sessions or ECAU, participants received minimal health care during the study period, which did not differ between the two groups (see supplementary information).

Differences between study conditions on primary and secondary outcome measures are reported in Table 2. Analysis of the primary outcome revealed that Self-Help Plus arm participants were significantly less likely to meet criteria for a mental disorder at six-month follow-up (59/272, 21.69%) compared to ECAU participants (112/275, 40.73%) (Cramer's  $V=0.205$ ,  $p<0.001$ ,  $RR=0.533$ , 95% CI: 0.408-0.696). The mental disorders at follow-up were major depressive disorder (51/272 participants in the Self-Help Plus group and 94/275 participants in the ECAU group), PTSD (16/272 vs. 35/275), anxiety disorders (10/272 vs. 20/275), obsessive-compulsive disorder (three participants in the Self-Help Plus group) and bipolar disorder with psychotic features (one participant in the ECAU group). By contrast, at post-intervention, the frequency of any mental disorders was similar in the two groups ( $p=0.784$ ) (see Table 2).

Compared with ECAU, Self-Help Plus was also associated with improvements at six-months for the secondary outcomes of depression symptoms ( $p<0.001$ ), personally identified psychological outcomes ( $p=0.036$ ), and quality of life ( $p=0.001$ ). Psychological distress as

measured with the GHQ-12 showed a significant improvement in favor of the Self-Help Plus group at post-intervention only ( $p=0.028$ ) (Table 2). These results were confirmed by global statistical significance of the intervention on all secondary outcomes by performing SUR ( $p=0.005$  at post-intervention,  $p<0.001$  at 6 months).

The intent-to-treat analysis results were confirmed by the per-protocol analysis. Self-Help Plus arm participants were significantly less likely to meet criteria for a mental disorder at six-month follow-up (47/218, 21.56%) compared to ECAU participants (112/275, 40.73%) (Cramer's  $V=0.204$ ,  $p<0.001$ ,  $RR=0.529$ , 95% CI: 0.396-0.708) (see supplementary information for other results).

Results of secondary analyses of continuous outcomes conducted without any imputations of missing values were comparable to those of our main analyses. Secondary analyses accounting for baseline imbalance between groups did not identify relevant differences with respect to our main analyses on both primary and secondary outcomes (see supplementary information).

We investigated possible heterogeneity of the effect of treatment on outcomes by testing for interactions between intervention allocation and potential moderators. None of the interactions reached the statistical significance threshold for binary outcomes after applying the Bonferroni correction. By performing SUR on post-intervention secondary outcomes, a global test on all interactions of the variable "intervention allocation", with center and the potential moderators on all regressions, was not significant ( $p=0.292$ ). Similarly, none of the interactions for continuous outcomes reached the significance threshold at 6 months ( $p>0.05$  in all cases).

## DISCUSSION

To the best of our knowledge, this is the first prevention RCT conducted among refugees experiencing psychological distress but without a mental disorder<sup>7</sup>. We found that the likelihood of having a mental disorder at six-month follow-up was approximately half for Self-Help Plus vs. ECAU participants, and that such risk reduction appeared to be consistent across the most common diagnoses, i.e. depression, PTSD and anxiety disorders. Consistent with this, Self-Help Plus participants also showed improvements in depression symptoms, personally identified psychological outcomes, and quality of life at six-month follow-up. We did not detect significant differences between the Self-Help Plus and control groups on any outcome measure immediately post-intervention, with the exception of psychological distress.

Four out of ten participants in the control group developed a mental disorder. This very high frequency may be explained by events occurring during the study. First, before completion of six-month assessments, in October-November 2019, Operation Peace Spring was launched in northern Syria at the border with Mardin, a Turkish area where most study participants lived. The aim was to create a safe zone where Syrian refugees could be resettled<sup>42</sup>. However, this event caused fears of deportation, and this stressor may have increased the risk for mental disorders. Second, many six-month follow-up assessments were completed during the first lockdown period to control COVID-19 pandemic in 2020, which led to the cutting off of core services and income generating activities for refugees, causing severe economic hardships and adversity<sup>43</sup>.

Though there is limited information on the psychological effects of COVID-19 pandemic among refugees in Turkey, a prospective study with displaced populations in Iraq indicated a substantial increase in their depression, anxiety and PTSD during the pandemic<sup>44</sup>. Refugees settled in countries where existing services have not been well-established are even more vulnerable to financial and psychosocial problems when new crises arise. Within this context, the Self-Help Plus intervention may have been particularly beneficial in tackling severe and ongoing stress and adversities.

The positive impact of Self-Help Plus at six-month follow-up is in line with previous studies indicating an incubation effect in acceptance and commitment therapy trials<sup>45,46</sup>. However, a RCT among asylum seekers and refugees resettled in Western European countries, conducted following a similar protocol on a smaller sample of participants, did not report this pattern of findings, possibly because it did not reach the target sample size<sup>47</sup>. In addition, participants in the Western European trial might have faced different stressors as compared with the present sample, which was exposed to severe and persistent stress throughout the follow-up period.

The results of the present study consolidate recent research evidence showing that prevention programmes can be effective in reducing mental health problems. For example, a recent meta-analysis of 50 prevention trials indicated that psychological interventions can reduce the incidence of depressive episodes by 19%<sup>48</sup>.

This study has some limitations. First, as for most RCTs of psychological interventions, a double-blind design was not feasible. However, outcome assessors were masked, and they were not involved in any trial phase that might reveal random allocation. In addition, both participants and assessors were instructed not to mention any interventions received during the study. Second, we had to switch from face-to-face to remote (online or telephone) assessments due to the COVID-19 pandemic during follow-up. It is unclear if this change, which equally applied to both study arms, might have affected the participants' responses.

Even though several studies documented that a careful and culturally appropriate use of available instruments is feasible and allows a standardization of the screening process and a systematic recognition of psychological distress and psychiatric diagnoses<sup>6</sup>, formal studies on online or telephone use of these tools in refugee groups are lacking. Third, at baseline we did not assess the history of any previous mental disorder. Consequently, mental disorders at follow-up could include both new cases and recurrences of previous mental disorders.

Considering the size of the effect observed in the present study, and that Self-Help Plus can be provided by briefly trained peer non-specialist facilitators in large groups of up to 30 participants at a time, we suggest that it could be offered to forced migrants to support and improve their functioning, and to decrease the pressure on mental health services. Moreover, the use of an illustrated guide and audio recording for delivery decreases the need for extensive training and supervision of facilitators, while increasing intervention fidelity.

In the light of these advantages, Self-Help Plus could be scaled up as a public health strategy to prevent mental disorders in refugee populations exposed to ongoing adversities. Since the intervention does not address the determinants of the refugees' mental health problems, it should be applied in tandem with strong advocacy for protection of those who face adversity, and for services that address their social, physical and broad mental health needs.

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## REFERENCES

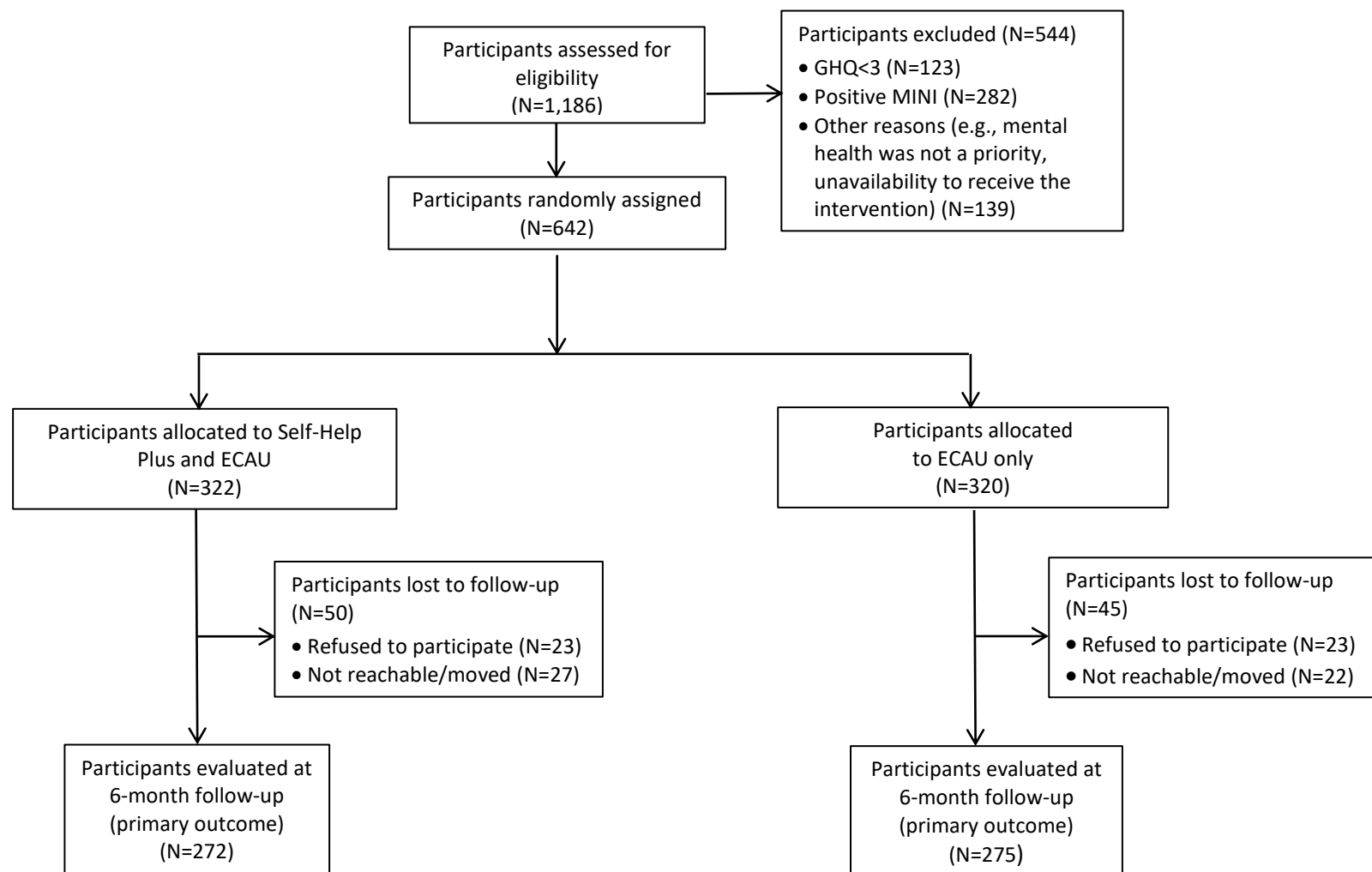
1. United Nations High Commissioner for Refugees. Forced displacement passes 80 million by mid-2020 as COVID-19 tests refugee protection globally. <https://www.unhcr.org>.
2. Inter-Agency Standing Committee. IASC guidelines on mental health and psychosocial support in emergency settings. Geneva: Inter-Agency Standing Committee, 2007.

3. World Health Organization. Interim guidance for refugee and migrant health in relation to COVID-19 in the WHO European Region. Copenhagen: World Health Organization Regional Office for Europe, 2020.
4. Hou WK, Liu H, Liang L et al. Everyday life experiences and mental health among conflict-affected forced migrants: a meta-analysis. *J Affect Disord* 2020;264:50-68.
5. Charlson F, van Ommeren M, Flaxman A et al. New WHO prevalence estimates of mental disorders in conflict settings: a systematic review and meta-analysis. *Lancet* 2019;394:240-8.
6. Acarturk C, McGrath M, Roberts B et al. Prevalence and predictors of common mental disorders among Syrian refugees in Istanbul, Turkey: a cross-sectional study. *Soc Psychiatry Psychiatr Epidemiol* 2021;56:475-84.
7. Papola D, Purgato M, Gastaldon C et al. Psychological and social interventions for the prevention of mental disorders in people living in low- and middle-income countries affected by humanitarian crises. *Cochrane Database Syst Rev* 2020;9:CD012417.
8. Dawson KS, Bryant RA, Harper M et al. Problem Management Plus (PM+): a WHO transdiagnostic psychological intervention for common mental health problems. *World Psychiatry* 2015;14:354-7.
9. Epping-Jordan JE, Harris R, Brown FL et al. Self-Help Plus (SH+): a new WHO stress management package. *World Psychiatry* 2016;15:295-6.
10. Tol WA, Leku MR, Lakin DP et al. Guided self-help to reduce psychological distress in South Sudanese female refugees in Uganda: a cluster randomised trial. *Lancet Glob Health* 2020;8:e254-63.
11. Rahman A, Khan MN, Hamdani SU et al. Effectiveness of a brief group psychological intervention for women in a post-conflict setting in Pakistan: a single-blind, cluster, randomised controlled trial. *Lancet* 2019;393:1733-44.
12. Rahman A, Hamdani SU, Awan NR et al. Effect of a multicomponent behavioral intervention in adults impaired by psychological distress in a conflict-affected area of Pakistan: a randomized clinical trial. *JAMA* 2016;316:2609-17.
13. Bryant RA, Schafer A, Dawson KS et al. Effectiveness of a brief behavioural intervention on psychological distress among women with a history of gender-based violence in urban Kenya: a randomised clinical trial. *PLoS Med* 2017;14:e1002371.
14. Purgato M, Carswell K, Acarturk C et al. Effectiveness and cost-effectiveness of Self-Help Plus (SH+) for preventing mental disorders in refugees and asylum seekers in Europe and Turkey: study protocols for two randomised controlled trials. *BMJ Open* 2019;9:e030259.
15. Castor EDC. Castor electronic data capture. <https://www.castoredc.com>.
16. Hrobjartsson A, Forfang E, Haahr MT et al. Blinded trials taken to the test: an analysis of randomized clinical trials that report tests for the success of blinding. *Int J Epidemiol* 2007;36:654-63.
17. Kilic C, Rezaki M, Rezaki B et al. General Health Questionnaire (GHQ12 & GHQ28): psychometric properties and factor structure of the scales in a Turkish primary care sample. *Soc Psychiatry Psychiatr Epidemiol* 1997;32:327-31.

18. el-Rufaie OF, Daradkeh TK. Validation of the Arabic versions of the thirty- and twelve-item General Health Questionnaires in primary care patients. *Br J Psychiatry* 1996;169:662-4.
19. Kadri N, Agoub M, El Gnaoui S et al. Moroccan colloquial Arabic version of the Mini International Neuropsychiatric Interview (MINI): qualitative and quantitative validation. *Eur Psychiatry* 2005;20:193-5.
20. Sheehan DV, Lecrubier Y, Sheehan KH et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59(Suppl. 20):22-33.
21. Ibrahim H, Ertl V, Catani C et al. The validity of Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5) as screening instrument with Kurdish and Arab displaced populations living in the Kurdistan region of Iraq. *BMC Psychiatry* 2018;18:259.
22. Weathers F, Litz B, Keane T et al. The PTSD Checklist for DSM-5 (PCL-5). <https://www.ptsd.va.gov>.
23. AlHadi AN, AlAteeq DA, Al-Sharif E et al. An Arabic translation, reliability, and validation of Patient Health Questionnaire in a Saudi sample. *Ann Gen Psychiatry* 2017;16:32.
24. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606-13.
25. Sawaya H, Atoui M, Hamadeh A et al. Adaptation and initial validation of the Patient Health Questionnaire - 9 (PHQ-9) and the Generalized Anxiety Disorder - 7 Questionnaire (GAD-7) in an Arabic speaking Lebanese psychiatric outpatient sample. *Psychiatry Res* 2016;239:245-52.
26. PSYCHLOPS. Psychological outcome profiles. <http://www.psychlops.org.uk>.
27. Ashworth M, Shepherd M, Christey J. A client-generated psychometric instrument: the development of 'PSYCHLOPS'. *Couns Psychother Res* 2004;4:27-31.
28. Ustun T. Measuring health and disability: manual for WHO Disability Assessment Schedule WHODAS 2.0, 2010. <https://apps.who.int>.
29. Sibai AM, Chaaya M, Tohme RA et al. Validation of the Arabic version of the 5-item WHO Well Being Index in elderly population. *Int J Geriatr Psychiatry* 2009;24:106-7.
30. Heun R, Burkart M, Maier W et al. Internal and external validity of the WHO Well-Being Scale in the elderly general population. *Acta Psychiatr Scand* 1999;99:171-8.
31. Bekairy AM, Bustami RT, Almotairi M et al. Validity and reliability of the Arabic version of the EuroQOL (EQ-5D). A study from Saudi Arabia. *Int J Health Sci* 2018;12:16-20.
32. EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
33. Aburuz S, Bulatova N, Twalbeh M et al. The validity and reliability of the Arabic version of the EQ-5D: a study from Jordan. *Ann Saudi Med* 2009;29:304-8.
34. Vindbjerg E, Carlsson J, Mortensen EL et al. The latent structure of post-traumatic stress disorder among Arabic-speaking refugees receiving psychiatric treatment in Denmark. *BMC Psychiatry* 2016;16:309.

35. Mollica RF, Caspi-Yavin Y, Bollini P et al. The Harvard Trauma Questionnaire. Validating a cross-cultural instrument for measuring torture, trauma, and posttraumatic stress disorder in Indochinese refugees. *J Nerv Ment Dis* 1992;180:111-6.
36. Riley A, Varner A, Ventevogel P et al. Daily stressors, trauma exposure, and mental health among stateless Rohingya refugees in Bangladesh. *Transcult Psychiatry* 2017;54:304-31.
37. Normand ST, Landrum MB, Guadagnoli E et al. Validating recommendations for coronary angiography following acute myocardial infarction in the elderly: a matched analysis using propensity scores. *J Clin Epidemiol* 2001;54:387-98.
38. Huisman M. Item nonresponse: occurrence, causes, and imputation of missing answers to test item. Groningen: University of Groningen, 1999.
39. Zellner A. An efficient method of estimating seemingly unrelated regressions and tests for aggregation bias. *J Am Stat Assoc* 1962;46:348-68.
40. Chu C, Blizzard L, Stankovich J et al. Be wary of using Poisson regression to estimate risk and relative risk. *Biostat Biometrics Open Access J* 2018;4:1-3.
41. StataCorp. Stata Statistical Software: Release 15. College Station: StataCorp, 2017.
42. United Nations. Turkey's military operation has displaced thousands of civilians, worsened Syria's dire humanitarian crisis, top official warns Security Council. <https://www.un.org>.
43. ReliefWeb. Impact of the COVID-19 outbreak on Syrian refugees in Turkey: results from rapid needs assessment conducted in Istanbul, Izmir, Manisa, Gaziantep, Kilis and Reyhanli. <https://reliefweb.int>.
44. Kizilhan JI, Noll-Hussong M. Psychological impact of COVID-19 in a refugee camp in Iraq. *Psychiatry Clin Neurosci* 2020;74:659-60.
45. González-Menéndez A, Fernández P, Rodríguez F et al. Long-term outcomes of Acceptance and Commitment Therapy in drug-dependent female inmates: a randomized controlled trial. *Int J Clin Health Psychol* 2014;14:18-27.
46. Clarke S, Taylor G, Lancaster J et al. Acceptance and commitment therapy-based self-management versus psychoeducation training for staff caring for clients with a personality disorder: a randomized controlled trial. *J Pers Disord* 2015;29:163-76.
47. Purgato M, Carswell K, Tedeschi F et al. Effectiveness of Self-Help Plus in preventing mental disorders in refugees and asylum seekers in Western Europe: a multinational randomized controlled trial. *Psychother Psychosom* (in press).
48. Cuijpers P, Pineda BS, Quero S et al. Psychological interventions to prevent the onset of depressive disorders: a meta-analysis of randomized controlled trials. *Clin Psychol Rev* 2021;83:101955.





**Figure 1** CONSORT flow diagram. ECAU – Enhanced Care As Usual, GHQ – General Health Questionnaire, MINI – Mini International Neuropsychiatric Interview

**Table 1** Sociodemographic characteristics of Syrian refugees randomly allocated to the Self-Help Plus (SH+) and the Enhanced Care As Usual (ECAU) groups

	SH+	ECAU	Difference (standard error)	SMD
Age (years, mean±SD)	31.22±8.89	31.73±9.16	−0.508 (0.712)	−0.040
Gender (% females)	63.98	61.87	0.021 (0.038)	0.031
Education (years, mean±SD)	8.94±3.72	9.12±3.73	−0.173 (0.300)	−0.033
Type of education (%)				
Illiterate	5.28	2.50	0.028 (0.015)	0.102
Primary school	62.73	60.94	0.018 (0.038)	0.026
High school	16.46	20.00	−0.035 (0.030)	−0.065
University	14.60	14.38	0.002 (0.028)	0.004
Not reported	0.93	2.19	−0.013 (0.010)	−0.072
N. relatives (mean±SD)	5.04±3.71	4.87±2.27	0.168 (0.250)	0.039
N. children (mean±SD)	2.73±1.89	2.73±1.92	0.002 (0.157)	0.001
Age at departure (years, mean±SD)	26.91±11.13	27.20±8.96	1.071 (0.944)	−0.021
Detention during transition (%)	5.00	5.37	−0.004 (0.018)	−0.012
Months of detention (mean±SD)	10.89±23.00	8.27±19.33	−2.620 (9.051)	0.087
Total HTQ score (mean±SD)	4.35±4.00	4.12±3.56	0.229 (0.299)	0.043

SMD – standardized mean difference, HTQ – Harvard Trauma Questionnaire

**Table 2** Summary statistics of results for primary and secondary outcomes at each time point

Frequency of mental disorders	SH+	ECAU	Cramer's V	p	RR (95% CI)
Baseline	0/322 (0%)	0/320 (0%)			
Post-intervention	30/237 (12.66%)	36/267 (13.48%)	0.012	0.784	0.939 (0.598-1.475)
6 months (primary outcome)	59/272 (21.69%)	112/275 (40.73%)	0.205	<0.001	0.533 (0.408-0.696)
Secondary outcomes			Coefficient	p	Standardized coefficient (SE)
GHQ-12 score (0-36), mean±SD					
Baseline (N=642)	17.363±4.519	16.776±4.299			
Post-intervention (N=503)	12.657±4.947	13.491±5.101	-0.974	0.028	-0.096 (0.044)
Six months LOCF (N=574)	13.269±4.825	13.768±4.548	-0.578	0.139	-0.062 (0.042)
PCL-5 score (0-80), mean±SD					
Baseline (N=640)	20.724±14.904	20.138±14.278			
Post-intervention (N=504)	16.824±12.831	14.814±14.597	1.754	0.134	0.063 (0.042)
Six months LOCF (N=574)	13.991±11.454	15.085±12.855	-1.278	0.195	-0.052 (0.040)
PHQ-9 score (0-27), mean±SD					
Baseline (N=642)	6.449±4.696	6.299±4.725			
Post-intervention (N=503)	5.241±4.905	5.324±5.124	-0.196	0.648	-0.020 (0.043)
Six months LOCF (N=522)	4.928±5.048	6.694±5.455	-1.842	<0.001	-0.172 (0.040)
WHO-5 (0-100), mean±SD					
Baseline (N=642)	42.458±4.418	43.591±23.766			
Post-intervention (N=504)	50.903±24.599	48.494±23.520	2.743	0.196	0.057 (0.044)
Six months LOCF (N=574)	52.143±21.709	49.320±22.670	3.154	0.085	0.071 (0.041)
WHODAS (12-60), mean±SD					
Baseline (N=638)	18.418±7.282	17.924±7.089			
Post-intervention (N=501)	15.380±4.705	15.561±6.477	-0.205	0.665	-0.018 (0.041)
Six months LOCF (N=570)	14.804±4.787	14.269±4.261	0.488	0.190	0.054 (0.041)

PSYCHLOPS score (0-20), mean±SD					
Baseline (N=488)	9.422±5.592	8.911±5.269			
Post-intervention (N=388)	6.230±5.727	6.890±5.640	-1.071	0.104	-0.091 (0.056)
Six months LOCF (N=543)	4.852±5.375	6.168±6.499	-1.215	0.036	-0.100 (0.047)
PMLD score (0-68), mean±SD					
Baseline (not measured)	-	-	-	-	-
Post-intervention (N=501)	16.569±11.022	18.864±12.689			
Six months (N=524)	13.422±10.451	12.322±11.536	1.824	0.075	0.080 (0.045)
EQ-5D-3L score, mean±SD					
Baseline (N=627)	0.718±0.275	0.720±0.282			
Post-intervention (not measured)	-	-	-	-	-
Six months (N=513)	0.857±0.218	0.799±0.250	0.067	0.001	0.147 (0.044)

SH+ – Self-Help Plus, ECAU – Enhanced Care As Usual, RR – risk ratio, SE – standard error, LOCF – last observation carried forward, GHQ-12 – General Health Questionnaire, 12-item version, PCL-5 – PTSD Checklist for DSM-5, PHQ-9 – Patient Health Questionnaire, 9-item version, WHO-5 – WHO-5 Well-Being Index, WHODAS – WHO Disability Assessment Schedule 2.0, PSYCHLOPS – Psychological Outcome Profiles, PMLD – Checklist for Post-Migration Living Difficulties, EQ-5D-3L – European Quality of Life 5-Dimensions 3-Level