Risk factors for mental disorder development in asylum seekers and refugees resettled in Western Europe and Turkey: participant-level analysis of two large prevention studies

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Abstract:	Aim: This study investigated the risk factors for mental disorder development in a large group of asylum seekers and refugees resettled in high- and middle-income settings. Methods: Participant-level data from two randomized prevention studies involving asylum seekers and refugees resettled in Western European countries and in Turkey were pooled. The two studies randomized participants with psychological distress, but without a diagnosis of mental disorder, to the Self-Help Plus psychological intervention or

	enhanced care as usual. At baseline, exposure to potentially traumatic events was measured using the Harvard Trauma Questionnaire-part I, while psychological distress and depressive symptoms were assessed with the General Health Questionnaire and the Patient Health Questionnaire. After three and six months of follow-up, the proportion of participants who developed a mental disorder was calculated using the Mini International Neuropsychiatric Interview. Results: A total of 1,101 participants were included in the analysis. At three- and six-month follow-up the observed frequency of mental disorders was 13.51% (115/851) and 24.30% (207/852), respectively, while the frequency estimates after missing data imputation were 13.95% and 23.78%, respectively. After controlling for confounders, logistic regression analysis showed that participants with a lower education level ($p = 0.034$), a shorter duration of journey ($p = 0.057$), and arriving from countries with war-related contexts ($p = 0.017$), were more at risk of developing mental disorders. Psychological distress ($p = 0.004$), depression ($p = 0.001$), and exposure to potentially traumatic events ($p = 0.020$) were predictors of mental disorder development. Conclusions: This study identified several risk factors for the development of mental disorders in asylum seekers and refugees, some of which may be the target of risk reduction policies. The identification of asylum seekers and refugees at increased risk of mental disorders should guide the implementation of focused preventative psychological interventions

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Risk factors for mental disorder development in asylum seekers and refugees resettled in Western Europe and Turkey: participant-level analysis of two large prevention studies

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Abstract

Background: In asylum seekers and refugees, the frequency of mental disorders, such as depression, anxiety, and post-traumatic stress disorder, is higher than the general population, but there is a lack of data on risk factors for the development of mental disorders in this population.

Aim: This study investigated the risk factors for mental disorder development in a large group of asylum seekers and refugees resettled in high- and middle-income settings.

Methods: Participant-level data from two randomized prevention studies involving asylum seekers and refugees resettled in Western European countries and in Turkey were pooled. The two studies randomized participants with psychological distress, but without a diagnosis of mental disorder, to the Self-Help Plus psychological intervention or enhanced care as usual. At baseline, exposure to potentially traumatic events was measured using the Harvard Trauma Questionnaire-part I, while psychological distress and depressive symptoms were assessed with the General Health Questionnaire and the Patient Health Questionnaire. After three and six months of follow-up, the proportion of participants who developed a mental disorder was calculated using the Mini International Neuropsychiatric Interview.

Results: A total of 1,101 participants were included in the analysis. At three- and six-month follow-up the observed frequency of mental disorders was 13.51% (115/851) and 24.30% (207/852), respectively, while the frequency estimates after missing data imputation were 13.95% and 23.78%, respectively. After controlling for confounders, logistic regression analysis showed that participants with a lower education level ($p = 0.034$), a shorter duration of journey ($p = 0.057$), and arriving from countries with war-related contexts ($p = 0.017$), were more at risk of developing mental disorders. Psychological distress ($p = 0.004$), depression ($p = 0.001$), and

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exposure to potentially traumatic events (p = 0.020) were predictors of mental disorder development.

Conclusions: This study identified several risk factors for the development of mental disorders in asylum seekers and refugees, some of which may be the target of risk reduction policies. The identification of asylum seekers and refugees at increased risk of mental disorders should guide the implementation of focused preventative psychological interventions.

Key-words: asylum seekers, refugees, migrants, mental health, mental disorders, high-income countries, low-income countries

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Introduction

According to the last United Nations Refugee Agency data, despite COVID-related movement restrictions, at the end of 2020 more than 82 million people were forcibly displaced as a result of persecution, conflict, violence, and other human rights violations (UNHCR, 2022). Of these, more than 30 million were asylum seekers or refugees. While Turkey continued to host the largest number of refugees, most of whom were Syrian refugees, 10% of all the world's refugees were resettled in Europe at the end of 2020 (UNHCR, 2022). These numbers are expected to further increase, as recent estimates have suggested that over 6.5 million refugees from Ukraine have crossed to Poland, Hungary, Romania, Moldova and other countries (UNHCR, 2022).

Despite heterogeneity between the studies and the populations of refugees and asylum seekers assessed (Giacco, 2019), a large body of evidence consistently showed that the frequency of mental disorders in refugees and asylum seekers is increased as compared with the general population. Existing World Health Organization (WHO) estimates suggest a prevalence of 13.0% for mild forms of depression, anxiety, and post-traumatic stress disorder (PTSD), and 4.0% for moderate forms (Charlson *et al.*, 2019). Other reviews of prevalence studies found adult refugee and asylum seekers have high and persistent rates of depression and PTSD, while the prevalence of anxiety disorders and psychosis are more comparable to findings from general populations (Blackmore *et al.*, 2020, Henkelmann *et al.*, 2020).

The increased frequency of mental disorders in refugees and asylum seekers may be related to the refugee experience, which is characterized by loss of homes, hopes, possessions, and disruption of personal, family, and professional life projects. In addition, a wide range of physical, psychological, and psychosocial problems associated with adversities may occur, such as bombings, threats, captivity, torture, injury, witnessing death or injury of loved ones, discrimination, economic stress, and uncertainty about the future (Priebe *et al.*, 2016).

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Interestingly, while these factors have been studied as determinants of poor mental health outcomes, or as determinants of psychological distress (Jannesari *et al.*, 2020), to our knowledge they have never been investigated in this population as risk factors for the development of mental disorders considered as full-blown diagnostic entities (Gleeson *et al.*, 2020, Hajak *et al.*, 2021). Knowledge of determinants of the development of mental disorders is particularly important to implement policies aiming at decreasing exposure to such determinants, to improve identification of refugees and asylum seekers at increased risk of developing mental disorders, and to plan the provision of psychological interventions to individuals and communities at risk.

Aiming to test the effect of Self Help Plus (SH+), a low intensity, group-based, self-help psychological intervention recently developed by the WHO (Epping-Jordan *et al.*, 2016, World Health Organization, 2021a), in reducing the frequency of mental disorders, we conducted two large randomized prevention trials in asylum seekers and refugees, one in western Europe and another in Turkey (Purgato *et al.*, 2019). The studies followed the same research protocol and were conducted in parallel (Acarturk *et al.*, 2022, Purgato *et al.*, 2021). Both the Western European and Turkey studies showed evidence of an effect of SH+ in preventing the onset of mental disorders, but differences were observed between the studies. The effect was much more pronounced for the Turkey study where efficacy (i.e. reducing the frequency of any mental disorder) was observed at 6 months, compared to the Western European study where a preventative effect was only found post-intervention and not after six months (Acarturk *et al.*, 2022, Purgato *et al.*, 2021). As these are the only two studies that enrolled asylum seekers and refugees without any mental disorders at baseline, and that assessed the frequency of mental disorders at follow-up as primary outcome (Papola *et al.*, 2020), they offered a unique opportunity to prospectively investigate the risk factors for the onset of mental disorders in a large group of asylum seekers and refugees.

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Methods

Participants and measures

Participant-level data from two randomized prevention trials involving asylum seekers and refugees resettled in Western European countries (Austria, Finland, Germany, Italy, and UK) and in Turkey were pooled (Acarturk *et al.*, 2022, Purgato *et al.*, 2021). In both studies, participants were randomly assigned to the SH+ psychological intervention, consisting of SH+ combined with enhanced care as usual (ECAU), or to ECAU only. The two studies were conducted in parallel following the same study design (Purgato *et al.*, 2019). The protocol of the present study was registered within the Open Science Framework (https://osf.io/37h5n).

In both studies, participants were included if they met the following criteria: a) aged 18 years or older; b) able to speak and understand Arabic, Dari, English, or Urdu; c) being under temporary protection with a refugee or asylum seeker status; d) experiencing psychological distress, as shown by a score of 3 or more on the 12-item dichotomously-scored General Health Questionnaire (el-Rufaie and Daradkeh, 1996, Goldberg *et al.*, 1998, Kilic *et al.*, 1997); 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 (M.I.N.I.), a brief structured diagnostic interview for the major psychiatric disorders in DSM-III-R, DSM-IV and DSM-5 and ICD-10. (Kadri *et al.*, 2005, Sheehan *et al.*, 1998); 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 M.I.N.I.; d) signs of impaired decision-making capacity emerging from responses during the clinical interview.

The M.I.N.I. was administered before random allocation, in order to exclude participants with a mental disorder, and at three and six months of follow-up, in order to calculate the proportion

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of participants who developed a mental disorder. Exposure to potentially traumatic events was measured at baseline using the Harvard Trauma Questionnaire-part I (HTQ) (Mollica *et al.*, 1992). The HTQ-part I covers a variety of trauma events that may affect refugee mental health, and the scoring represents the number of different types of traumatic events experienced by the participants (higher score is associated with high number of traumatic events). In addition to using the HTQ total score, we identified subtypes of traumatic events performing a Principal Components analysis (PCA).

Mental health symptoms were measured using the following validated instruments. The GHQ-12 questionnaire was used to measure psychological distress (el-Rufaie and Daradkeh, 1996, Goldberg *et al.*, 1998, Kilic *et al.*, 1997), while PTSD was assessed with the PTSD Checklist for DSM-5 (PCL-5), a 20-item questionnaire that measures overall PTSD symptoms (score zero to 80) and symptoms by cluster (intrusions, avoidance, negative changes in thoughts and mood, and changes in arousal), with higher scores indicating higher levels of PTSD symptoms (Blanchard *et al.*, 1996). Levels of self-reported depression symptoms were measured with the Patient Health Questionnaire, nine-item version (PHQ-9) which has a four-point scale (score 0 to 27) (Kroenke *et al.*, 2001). All measures were collected at baseline before random allocation, and after three and six months of follow-up. Assessors were trained in the administration of rating scales, instructed on how to perform follow-up assessments while preserving effective masking, and assisted by cultural mediators when needed.

Interventions

The SH+ intervention was developed by the WHO, as described elsewhere (Acarturk *et al.*, 2022, Purgato *et al.*, 2021), and is now publicly available (World Health Organization, 2021a). SH+ consists of a pre-recorded audio course complemented with an illustrated self-help book. The book has been recently updated and published by WHO as Doing What Matters in Times of

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Stress (World Health Organization, 2021b). All SH+ materials were adapted for the cultural groups included in the studies. The SH+ pre-recorded audio material was delivered across five 2-hour sessions to groups of up to 30 people. The audio material imparts key information about stress management and guides participants through individual exercises and small group discussions. To augment the audio recordings, an illustrated self-help book reviews all essential content and concepts. The SH+ intervention was fully delivered in the language of participants by trained facilitators with a migration background, who were native speakers of the target languages. ECAU, provided both to the experimental and control group, consisted of routinely delivered social support and/or care according to local regulations. Participants in the ECAU arm received the same baseline and follow-up assessments of the intervention arm, according to the study schedule (around three and six months after randomization), information about freely available health and social services, and links to community networks providing support to refugees and asylum seekers.

Statistical analysis

Descriptive statistics (mean and SD for continuous variables and absolute numbers and percentages for dichotomous variables) were computed on sociodemographic, premigration, migration and postmigration variables at baseline, and for clinical variables.

Participants who met criteria for any mental disorder on the M.I.N.I. at three or six-month follow-up were considered cases with a mental disorder. Multiple imputation was adopted to address the issue of missing data in all the variables included in the model. In particular, in case of missing data at the M.I.N.I. in one timepoint, imputation was performed on single M.I.N.I. values at three and six months. In case of missing values on continuous clinical measures, the imputation was performed on single item scales. Specifically, imputation followed the approach reported by Plumpton and colleagues (Plumpton *et al.*, 2016), that is we used scale totals within

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prediction equations and, for imputations of responses to individual scale items, we additionally included the responses to the other scale items, using the "ice" Stata routine (Royston, 2005, Sterne *et al.*, 2009), and considering single-item scores as ordered categorical variables. M.I.N.I. values at the two time-points were used in the prediction equations of regression predictors, and upper and lower bounds were set for continuous variables with missing values as appropriate. The number of imputed samples was determined by following the rule of thumb suggested by White and colleagues, i.e.: "at least equal to the percentage of incomplete cases" (White *et al.*, 2011). We rounded such number to the nearest multiple of 10 above.

In order to identify subtypes of traumatic events, we performed a PCA on tetrachoric correlations of HTQ items, with Quartimin oblique rotation to allow for between-factor non-null correlations (Tabachnick, 2007), and summing items with loadings above 0.40 on the same factor to create scores for the regression model (Stevens, 2002). The number of factors was determined by adopting Kaiser's rule (Kaiser, 1960), i.e. using the cut-off scores of 1 for the eigenvalues.

In order to investigate predictors of the development of mental disorders, unadjusted and adjusted logistic regression analyses were performed, using the frequency of participants with a mental disorder in at least one timepoint as binary dependent variable. The following independent variables were inserted into the model: age (years), gender (men, women), education (years), unemployment (yes/no), country of origin (Syria, Iraq, Nigeria, other countries), length of journey (below one month, between one and three months, above three months), study (Western Europe versus Turkey), length of stay in the resettlement country (months), HTQ (total score at baseline), GHQ-12 (total score at baseline), PCL-5 (total score at baseline), PHQ-9 (total score at baseline), number of SH+ sessions received (zero to five). Considering that PTSD and depression are known to be interrelated experiences following

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trauma (Rytwinski *et al.*, 2013), and considering that the PCL-5 largely overlaps with the HTQ (Patel *et al.*, 2022), and that a substantial overlap exists between the PCL-5 and the PHQ-9 (Dabrowski CL, 2020), we excluded the PCL-5 from the final model, but it was included (total score at baseline) in the imputation model.

In order to check the robustness of the analysis, we re-ran the model after excluding the arm receiving SH+. As a further sensitivity analysis, in order to estimate within-centre effects, we performed a model including a fixed effect for recruiting centre. As a subgroup analysis, we re-ran the logistic regression analysis separately for each study sample (western Europe versus Turkey). All analyses were performed using Stata 17 (Statacorp, 2017).

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Results

Participants

The two prevention trials randomized a total of 1,101 participants. After six months, 249 participants (22.6%) were not available for follow-up assessments, for the reasons reported in Figure 1. Participant characteristics at baseline are presented in Table 1. Almost half were female, with a mean age of 32 (SD 9.521) years, and a mean education of 10 years (SD 4.424). Slightly less than 40% was unemployed. The migration journey lasted more than three months in around one third of participants, in another one third it lasted between one and three months, while in the remaining 40% the host country was reached in less than one month. On average, the mean length of stay in the resettlement country was slightly more than three years. Most of the participants were from Syria, Nigeria and Iraq (Table 1). Participants attended a mean number of 1.4 (SD 2.015) SH+ sessions. The mean (SD) baseline scores on the measures of interest are reported in Table 1.

Frequency and determinants of mental disorders

At three- and six-month follow-up the observed frequency of mental disorders, as measured with the M.I.N.I., was 13.51% (115/851) and 24.30% (207/852), respectively, while the frequency estimates after missing data imputation were 13.95% and 23.78%, respectively. The majority of detected mental disorders were major depressive disorders (9.5% and 20.3% after three and six months), PTSD (3.2% and 6.7%), and anxiety disorders (2.1% and 4.1%) (Figure 1).

The PCA model found a 3-factor solution where the set of items was exhaustive and mutually exclusive, with the HTQ items grouped as follows: factor 1 - lack of basic needs: lack of food or water, ill health without access to medical care, lack of shelter; factor 2 - violence and abuse: imprisonment, serious injury, brain washing, rape or sexual abuse, forced isolation from others, forced separation from family members, torture, other (e.g. domestic violence;) factor 3 - being close to death: combat situation, being close to death, murder of family or friend, unnatural death of family or friend, murder of stranger(s), lost or kidnapped. The factor loadings of the PCA-model with Quartimin oblique rotation are reported in the Supplemental Materials.

The results of unadjusted and adjusted logistic regression analyses investigating factors associated with the development of mental disorders are presented in Table 2. Participants with lower education level ($p = 0.034$), a shorter duration of journey ($p = 0.057$), and arriving from countries with war-related contexts (Iraq, Syria) ($p = 0.017$), were those more at risk of developing mental disorders. In terms of mental health symptoms and exposure to traumatic events, psychological distress ($p = 0.004$), depressive symptoms ($p = 0.001$), and HTQ total score ($p = 0.020$) at baseline were predictors of mental disorder development, as was the HTQ factor violence and abuse (imprisonment, serious injury, brain washing, rape or sexual abuse, forced isolation from others, forced separation from family members, torture, domestic violence) ($p =$

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0.008). In terms of post-migration factors, the number of SH+ sessions ($p < 0.001$) was inversely associated with the risk of developing mental disorders (Table 2).

Secondary logistic regression analyses including only the ECAU arms of the two studies, and analysing the two studies separately, confirmed the role of mental health symptoms and exposure to traumatic events as risk factors for mental disorders (Supplemental Materials). However, due to lower statistical power, some factors lost significance despite a similar or even higher estimated effect, as for example the HTQ in the model restricted to the western European study, or years of education and travel duration in the model restricted to the ECAU sample, and GHQ-12 in the model restricted to the study conducted in Turkey (Supplemental Materials).

Consistently with the results of the two studies, the number of SH+ sessions was inversely associated with the frequency of mental disorders only in the study conducted in Turkey Supplemental Materials). The inclusion of recruiting centres as predictor variables revealed that, in comparison with participants recruited in Istanbul, participants recruited in Vienna were less likely to develop a mental disorder (Supplemental Materials).

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Discussion

To the best of our knowledge, this is the first prospective study that examined risk factors for the onset of mental disorders among asylum seekers and refugees without a mental disorder at baseline. We showed the significant influence of socio-demographic, clinical, and contextual factors, including potentially traumatic events, on the development of mental disorders in asylum seekers and refugees resettled in Western European countries and in Turkey.

Overall, one in four refugees and asylum seekers developed a diagnosable mental disorder over a period of six months. Interestingly, the most frequently reported diagnostic group was

depression, followed by PTSD and anxiety disorders. These figures, derived from two intervention studies, cannot be compared with those from epidemiological studies, which generally show similar frequencies for depression and PTSD, or slightly higher frequencies for depression, depending on the population surveyed and the study setting (Blackmore *et al.*, 2020, Charlson *et al.*, 2019, Henkelmann *et al.*, 2020, Hoell *et al.*, 2021). In migrants exposed to armed conflict, by contrast, the frequency of PTSD was found to be higher than depression (31% vs 25%) (Mesa-Vieira *et al.*, 2022).

The finding that educational level is inversely associated with the development of mental disorders expands previous data collected in the general population showing that higher educational level seems to have a protective effect against anxiety and depression symptoms, and against common mental disorders in general (Araya *et al.*, 2003, Bjelland *et al.*, 2008). In the general population, poor education has been suggested to be a marker of lack of opportunities and resources, including material and psychological resources, and a marker of childhood adversity (Araya *et al.*, 2003). In asylum seekers and refugees, these factors may directly contribute to the emergence of mental disorders, or may interfere with the coping skills required to deal with all the adversities associated with the migration and resettlement process, which, in turn, may increase the risk of developing mental disorders (Kirmayer *et al.*, 2011).

Consistently with an extensive literature showing that exposure to potentially traumatic events represents a risk factor for poor mental health and well-being (Gleeson *et al.*, 2020, Hajak *et al.*, 2021, Priebe *et al.*, 2016), the present study adds that exposure to potentially traumatic events is also a risk factor for the development of mental disorders considered as full-blown diagnostic entities. The finding that being displaced from countries with war-related contexts emerged as an additional risk factor for mental disorders further corroborates this association. War-related contexts imply exposure to multiple and serious traumatic events, and the exposure to combat

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situations creates the risk of witnessing violence and/or death and experiencing physical and psychological violence (Crepet *et al.*, 2017). Extensive literature shows that these situations are associated with poor mental health outcomes, including PTSD, depression, anxiety, and somatization symptoms (Jongedijk *et al.*, 2020, Knipscheer *et al.*, 2015, Nickerson *et al.*, 2021).

The present study has limitations and strengths. A first limitation is that the population enrolled in the two trials cannot be considered representative of the general population of asylum seekers and refugees, as we selected participants scoring above a threshold of psychological distress, and we excluded those at suicide risk. During the studies, in addition, around half of the participants was exposed to a psychological intervention aimed at preventing the development of mental disorders. For these reasons, the overall frequency estimate of mental disorders cannot apply to the general population of asylum seekers and refugees resettled in Western European countries or in Turkey. A second issue is that we did not calculate a true incidence of mental disorders, but only frequency figures at two time points with a structured diagnostic interview that might overestimate the true frequency of some mental disorders, such as depression (Wu *et al.*, 2020). Third, the SARS-CoV2 pandemic impacted the study procedures, because in all the recruiting sites follow-up assessments were conducted using online tools instead of face-to-face meetings. Although assessors were trained in the administration of rating scales, instructed on how to perform online follow-up assessments, and assisted by cultural mediators when needed, it is unknown whether this may have impacted the responses of participants to the instruments. Related to this, 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 (Acarturk *et al.*, 2021) we acknowledge that formal studies on use of these tools in refugee groups are lacking. Fourth, despite a growing body of literature showed that the duration of the asylum procedure is an important risk factor for mental health

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conditions (Laban et al. 2004; Winkler et al. 2019), we acknowledge that this information was not collected. However, months in host country, which may be considered a proxy of length of asylum procedure, was included in the model but did not emerge as a significant factor.

Despite these limitations, there are strengths that should be emphasised. The main strength is the exclusion of participants with a mental disorder at baseline, and the choice of a dependent variable that is fully consistent with a preventative design, namely the frequency of mental disorders at follow-up, assessed with validated measures. This design allowed to prospectively investigate the determinants of mental disorders rather than of poor mental health, as previous studies have done in populations who might already be with mental disorders at baseline (Priebe *et al.*, 2016). Another strength is a sample size of over a thousand of asylum seekers and refugees, resettled in a variety of western European sites and in Turkey. This aspect is of relevance not only in terms of statistical power, but also in terms of generalisability and applicability of study findings to different types of reception settings in high-income and middle-income countries. Lastly, despite an attrition rate of around 20%, a follow-up assessment of six months is noteworthy in such a difficult-to-follow population, who is often moved from one reception site to another, and may not perceive mental health as a priority, having a number of other challenging concerns such as housing, unstable working conditions, management of visa issues, safety of family members, fear of being returned to home country, plans to move to another country or to another location.

The present study has important practical implications. The finding of a positive relationship between exposure to potentially traumatic events and risk of mental disorder development suggests a pressing need of developing policies aiming to decrease exposure to such traumatic experiences after resettlement. Host countries may have opportunities to decrease exposure to situations such as material and economic hardship that could affect integrity, independence,

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dignity and well-being (financial strain), social hardship due to loss of status (social strain), feelings of inadequacy in relation with specific skills needed in the host-country to successfully function in daily life (competency strain), experiences of unfair treatment on the basis of prejudice (perceived discrimination). This ambitious goal may be achieved by implementing reception conditions that optimize internationally recognized minimal quality standards. For example, standards for the reception of applicants for international protection have been established by Directive 2013/33/EU of the European Parliament. The Directive clearly reports that national authorities should ensure that reception modalities are specifically designed to meet the needs of persons requiring international protection, including legal assistance, document provision, material support, links with local communities, freedom of movement, information about labor market access, vocational training, social support. Health care, including mental health care, is also mentioned as a key intervention where needed. It would be important to ensure that efforts to support forcibly displaced people are coordinated across the different layers of the social environments in which they are hosted, i.e. at the level of the individual, their family, the community, and the institutions that have governance responsibility for their care and support (White and Van der Boor, 2021).

In addition to implications in terms of risk reduction policies, the present study has implications in terms of provision of psychological interventions aimed at preventing the development of mental disorders (Miller *et al.*, 2021). As the implementation of preventative psychological interventions to the whole population of asylum seekers and refugees may not be sustainable by host countries, national authorities may consider to offer psychological interventions to at-risk populations. The finding that persons with lower education level, a shorter duration of journey, arriving from countries with war-related contexts (Iraq, Syria), and with high level of psychological distress and depressive symptoms, are those more at risk of developing mental disorders, appears to identify a target population for focused psychological prevention

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interventions. The WHO has recently developed a number of low-intensity psychological interventions that may be scaled up as public health strategies to address mental disorders and psychological distress in refugee populations exposed to ongoing adversities (World Health Organization, 2017). In addition to WHO interventions, other psychological treatments have been shown to be effective in alleviating psychological symptoms in asylum seekers and refugees (Turrini *et al.*, 2021, Uphoff *et al.*, 2020), but a preventative effect has been investigated for SH+ only. The present results, by showing an inverse association between number of SH+ sessions and risk of developing a mental disorder, further corroborate the value of SH+ as a prevention intervention. The finding that trauma exposure stands out as a predictor for development of mental disorders would additionally suggest that interventions may need to include a focus on traumatic memories and experiences, in addition to being focused on low mood.

In parallel with the provision of psychological interventions to at-risk populations, national authorities should ensure regular access to such interventions supporting at risk populations to engage through reducing barriers that might prevent or limit access or use (Fuhr *et al.*, 2019). This can be achieved by optimizing access (e.g. accessible services and supports) to a range of interventions depending on need (e.g. stepped care), and by using different delivery mechanisms (e.g. digital or peer delivered support).

As the number of persons in need of protection is likely to substantially increase globally, driven by long-lasting wars as well as by new conflicts such as the Russo-Ukrainian war which broke out recently (Barbui *et al.*, 2022, Pandi-Perumal *et al.*, 2022), national authorities are urged to develop reception and resettlement programs meeting the needs of this vulnerable group. These programs should be designed and implemented attempting to decrease the risk of post-migration stressors that may contribute to worsening the mental health of a population already

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exposed to potentially traumatic experiences before and during the migration process. Evidence-based focused psychological support should be an important program component to be delivered to asylum seekers and refugees at-risk of developing a mental disorder.

Contributors CB, MP, and FT conceived the study. FT statistically analysed the data. CB, GO and FT accessed and verified the data. CB wrote the first draft of the manuscript with input from FT and MP. All authors contributed to the conception and design of the study, data interpretation and manuscript revision. All authors read and approved the submitted manuscript and had final responsibility for the decision to submit for publication. CB was the overall guarantor of the content.

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Competing interests None declared.

Ethics approval This was a secondary analysis of deidentified participant data. The initial study was approved by the WHO Research Ethics Review Committee, and from the Ethics Committees of all participating sites. Before participation, a written informed consent was obtained from each participant, allowing investigators to use anonymised data for future analysis. Participants gave informed consent to participate in the study before taking part.

Data availability statement Data collected in the RE-DEFINE study are stored in the online repository EUDAT B2SHARE (study in Western Europe: https://b2share.eudat.eu/records/fa7264d624364683830ff37acee01c04; study in Turkey: http://doi.org/10.23728/b2share.8ac4f28d2415413e89de7847c05471fc.). The reuse of data will be offered only upon motivated request, which will undergo the scrutiny of the RE-DEFINE General Assembly.

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Table 1. Participants characteristics at baseline

Means	M (SD)
Age (years)	31.797 (9.521)
Years of education	9.556 (4.424)
Months in host country	40.636 (32.599)
Host country GDP in thousand dollars (2019)	
Austria	58,091.3
Finland	50,321.6
Germany	55 652.9
Italy	44,334.2
Turkey	27,144.2
UK	49,070.3
Number of SH+ sessions	1.434 (2.015)
GHQ	5.737 (2.230)
PHQ-9	7.232 (5.230)
HTQ Total score	5.795 (4.349)
HTQ Lack of basic needs	1.277 (1.210)
HTQ Violence and abuse	1.753 (2.085)
HTQ Being close to death	2.766 (1.947)
Frequencies	**n/N (%)**
Gender (Female)	538/1,101 (48.86%)
Unemployed	418/1,099 (38.03%)
Country of origin	
Nigeria	114/1,100 (10.36%)
Syria	758/1,100 (68.91%)
Iraq	94/1,100 (8.55%)
Other	134/1,100 (12.18%)
Travel duration	
Less than one month	277 (40.44%)
One to three months	203 (29.64%)
More than three months	205 (29.93%)
Study	
Western Europe	459 (41.69%)
Turkey	642 (58.31%)

M: mean; SD: standard deviation; SH+: Self-Help Plus; GDP: Gross Domestic Product; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

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Table 2. Determinants of mental disorder development: logistic regression analyses

	Unadjusted regressions		Adjusted regressions			
			With HTQ total score		With HTQ factors	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Age in years	1.001 (0.986; 1.015)	0.920	0.996 (0.980; 1.013)	0.672	0.998 (0.981; 1.015)	0.830
Female gender	1.318 (0.987; 1.759)	0.061	0.962 (0.680; 1.360)	0.825	0.977 (0.689; 1.385)	0.896
Years of education	0.972 (0.941; 1.004)	0.088	**0.959 (0.923; 0.997)**	**0.034**	**0.959 (0.922; 0.996)**	**0.032**
Unemployed	0.938 (0.702; 1.253)	0.664	1.171 (0.832; 1.647)	0.365	1.180 (0.836; 1.664)	0.347
Country of origin: Syria Iraq Nigeria Other	 Reference category 1.180 (0.710; 1.960) **0.209 (0.101; 0.432)** **0.403 (0.240; 0.674)**	**<0.001**	 Reference category 1.592 (0.807; 3.142) **0.376 (0.142; 0.997)** 0.577 (0.273; 1.222)	**0.017**	 Reference category 1.672 (0.840; 3.325) **0.318 (0.118; 0.861)** 0.519 (0.241; 1.114)	**0.006**
Travel duration (months) Less than one month One to three months More than three months	 Reference category **0.616 (0.398; 0.952)** **0.312 (0.198; 0.494)**	**<0.001**	 Reference category 0.653 (0.414; 1.028) **0.512 (0.267; 0.983)**	0.057	 Reference category 0.658 (0.417; 1.041) **0.502 (0.260; 0.969)**	0.057
Months in host country	1.002 (0.997; 1.007)	0.503	1.000 (0.994; 1.006)	0.943	1.000 (0.994; 1.006)	0.973
Turkish trial	**2.058 (1.513; 2.800)**	**<0.001**	1.795 (0.997,3.235)	0.051	1.802 (0.998; 3.253)	0.051
Number of SH+ sessions	**0.888 (0.827; 0.953)**	**0.001**	**0.853 (0.788; 0.923)**	**<0.001**	**0.850 (0.785; 0.921)**	**<0.001**

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GHQ-12	**1.188 (1.114; 1.268)**	**<0.001**	**1.117 (1.036; 1.204)**	**0.004**	**1.119 (1.038; 1.206)**	**0.003**
PHQ-9	**1.071 (1.042; 1.100)**	**<0.001**	**1.061 (1.026; 1.097)**	**0.001**	**1.061 (1.026; 1.097)**	**0.001**
HTQ Total score	1.002 (0.970; 1.036)	0.883	**1.051 (1.008; 1.096)**	**0.020**	-	-
HTQ Factor 1 - Lack of basic needs	0.999 (0.890; 1.122)	0.988	-	-	1.007 (0.863; 1.176)	0.928
HTQ Factor 2 - Violence and abuse	0.995 (0.929; 1.066)	0.894	-	-	**1.163 (1.041; 1.299)**	**0.008**
HTQ Factor 3 - Being close to death	1.018 (0.947; 1.095)	0.769	-	-	0.978 (0.888; 1.077)	0.650

CI: Confidence Interval; SH+: Self-Help Plus; GDP: Gross Domestic Product; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

For Peer Review

Risk factors for mental disorder development in asylum seekers and refugees resettled in Western Europe and Turkey: participant-level analysis of two large prevention studies

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Abstract

Background: In asylum seekers and refugees, the frequency of mental disorders, such as depression, anxiety, and post-traumatic stress disorder, is higher than the general population, but there is a lack of data on risk factors for the development of mental disorders in this population.

Aim: This study investigated the risk factors for mental disorder development in a large group of asylum seekers and refugees resettled in high- and middle-income settings.

Methods: Participant-level data from two randomized prevention studies involving asylum seekers and refugees resettled in Western European countries and in Turkey were pooled. The two studies randomized participants with psychological distress, but without a diagnosis of mental disorder, to the Self-Help Plus psychological intervention or enhanced care as usual. At baseline, exposure to potentially traumatic events was measured using the Harvard Trauma Questionnaire-part I, while psychological distress and depressive symptoms were assessed with the General Health Questionnaire and the Patient Health Questionnaire. After three and six months of follow-up, the proportion of participants who developed a mental disorder was calculated using the Mini International Neuropsychiatric Interview.

Results: A total of 1,101 participants were included in the analysis. At three- and six-month follow-up the observed frequency of mental disorders was 13.51% (115/851) and 24.30% (207/852), respectively, while the frequency estimates after missing data imputation were 13.95% and 23.78%, respectively. After controlling for confounders, logistic regression analysis showed that participants with a lower education level ($p = 0.034$), a shorter duration of journey ($p = 0.057$), and arriving from countries with war-related contexts ($p = 0.017$), were more at risk of developing mental disorders. Psychological distress ($p = 0.004$), depression ($p = 0.001$), and

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exposure to potentially traumatic events (p = 0.020) were predictors of mental disorder development.

Conclusions: This study identified several risk factors for the development of mental disorders in asylum seekers and refugees, some of which may be the target of risk reduction policies. The identification of asylum seekers and refugees at increased risk of mental disorders should guide the implementation of focused preventative psychological interventions.

Key-words: asylum seekers, refugees, migrants, mental health, mental disorders, high-income countries, low-income countries

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Introduction

According to the last United Nations Refugee Agency data, despite COVID-related movement restrictions, at the end of 2020 more than 82 million people were forcibly displaced as a result of persecution, conflict, violence, and other human rights violations (UNHCR, 2022). Of these, more than 30 million were asylum seekers or refugees. While Turkey continued to host the largest number of refugees, most of whom were Syrian refugees, 10% of all the world's refugees were resettled in Europe at the end of 2020 (UNHCR, 2022). These numbers are expected to further increase, as recent estimates have suggested that over 6.5 million refugees from Ukraine have crossed to Poland, Hungary, Romania, Moldova and other countries (UNHCR, 2022).

Despite heterogeneity between the studies and the populations of refugees and asylum seekers assessed (Giacco, 2019), a large body of evidence consistently showed that the frequency of mental disorders in refugees and asylum seekers is increased as compared with the general population. Existing World Health Organization (WHO) estimates suggest a prevalence of 13.0% for mild forms of depression, anxiety, and post-traumatic stress disorder (PTSD), and 4.0% for moderate forms (Charlson *et al.*, 2019). Other reviews of prevalence studies found adult refugee and asylum seekers have high and persistent rates of depression and PTSD, while the prevalence of anxiety disorders and psychosis are more comparable to findings from general populations (Blackmore *et al.*, 2020, Henkelmann *et al.*, 2020).

The increased frequency of mental disorders in refugees and asylum seekers may be related to the refugee experience, which is characterized by loss of homes, hopes, possessions, and disruption of personal, family, and professional life projects. In addition, a wide range of physical, psychological, and psychosocial problems associated with adversities may occur, such as bombings, threats, captivity, torture, injury, witnessing death or injury of loved ones, discrimination, economic stress, and uncertainty about the future (Priebe *et al.*, 2016).

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Interestingly, while these factors have been studied as determinants of poor mental health outcomes, or as determinants of psychological distress (Jannesari *et al.*, 2020), to our knowledge they have never been investigated in this population as risk factors for the development of mental disorders considered as full-blown diagnostic entities (Gleeson *et al.*, 2020, Hajak *et al.*, 2021). Knowledge of determinants of the development of mental disorders is particularly important to implement policies aiming at decreasing exposure to such determinants, to improve identification of refugees and asylum seekers at increased risk of developing mental disorders, and to plan the provision of psychological interventions to individuals and communities at risk.

Aiming to test the effect of Self Help Plus (SH+), a low intensity, group-based, self-help psychological intervention recently developed by the WHO (Epping-Jordan *et al.*, 2016, World Health Organization, 2021a), in reducing the frequency of mental disorders, we conducted two large randomized prevention trials in asylum seekers and refugees, one in western Europe and another in Turkey (Purgato *et al.*, 2019). The studies followed the same research protocol and were conducted in parallel (Acarturk *et al.*, 2022, Purgato *et al.*, 2021). Both the Western European and Turkey studies showed evidence of an effect of SH+ in preventing the onset of mental disorders, but differences were observed between the studies. The effect was much more pronounced for the Turkey study where efficacy (i.e. reducing the frequency of any mental disorder) was observed at 6 months, compared to the Western European study where a preventative effect was only found post-intervention and not after six months (Acarturk *et al.*, 2022, Purgato *et al.*, 2021). As these are the only two studies that enrolled asylum seekers and refugees without any mental disorders at baseline, and that assessed the frequency of mental disorders at follow-up as primary outcome (Papola *et al.*, 2020), they offered a unique opportunity to prospectively investigate the risk factors for the onset of mental disorders in a large group of asylum seekers and refugees.

Methods

Participants and measures

Participant-level data from two randomized prevention trials involving asylum seekers and refugees resettled in Western European countries (Austria, Finland, Germany, Italy, and UK) and in Turkey were pooled (Acarturk *et al.*, 2022, Purgato *et al.*, 2021). In both studies, participants were randomly assigned to the SH+ psychological intervention, consisting of SH+ combined with enhanced care as usual (ECAU), or to ECAU only. The two studies were conducted in parallel following the same study design (Purgato *et al.*, 2019). The protocol of the present study was registered within the Open Science Framework (https://osf.io/37h5n).

In both studies, participants were included if they met the following criteria: a) aged 18 years or older; b) able to speak and understand Arabic, Dari, English, or Urdu; c) being under temporary protection with a refugee or asylum seeker status; d) experiencing psychological distress, as shown by a score of 3 or more on the 12-item dichotomously-scored General Health Questionnaire (el-Rufaie and Daradkeh, 1996, Goldberg *et al.*, 1998, Kilic *et al.*, 1997); 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 (M.I.N.I.), a brief structured diagnostic interview for the major psychiatric disorders in DSM-III-R, DSM-IV and DSM-5 and ICD-10. (Kadri *et al.*, 2005, Sheehan *et al.*, 1998); 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 M.I.N.I.; d) signs of impaired decision-making capacity emerging from responses during the clinical interview.

The M.I.N.I. was administered before random allocation, in order to exclude participants with a mental disorder, and at three and six months of follow-up, in order to calculate the proportion

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of participants who developed a mental disorder. Exposure to potentially traumatic events was measured at baseline using the Harvard Trauma Questionnaire-part I (HTQ) (Mollica *et al.*, 1992). The HTQ-part I covers a variety of trauma events that may affect refugee mental health, and the scoring represents the number of different types of traumatic events experienced by the participants (higher score is associated with high number of traumatic events). In addition to using the HTQ total score, we identified subtypes of traumatic events performing a Principal Components analysis (PCA).

Mental health symptoms were measured using the following validated instruments. The GHQ-12 questionnaire was used to measure psychological distress (el-Rufaie and Daradkeh, 1996, Goldberg *et al.*, 1998, Kilic *et al.*, 1997), while PTSD was assessed with the PTSD Checklist for DSM-5 (PCL-5), a 20-item questionnaire that measures overall PTSD symptoms (score zero to 80) and symptoms by cluster (intrusions, avoidance, negative changes in thoughts and mood, and changes in arousal), with higher scores indicating higher levels of PTSD symptoms (Blanchard *et al.*, 1996). Levels of self-reported depression symptoms were measured with the Patient Health Questionnaire, nine-item version (PHQ-9) which has a four-point scale (score 0 to 27) (Kroenke *et al.*, 2001). All measures were collected at baseline before random allocation, and after three and six months of follow-up. Assessors were trained in the administration of rating scales, instructed on how to perform follow-up assessments while preserving effective masking, and assisted by cultural mediators when needed.

Interventions

The SH+ intervention was developed by the WHO, as described elsewhere (Acarturk *et al.*, 2022, Purgato *et al.*, 2021), and is now publicly available (World Health Organization, 2021a). SH+ consists of a pre-recorded audio course complemented with an illustrated self-help book. The book has been recently updated and published by WHO as Doing What Matters in Times of

Stress (World Health Organization, 2021b). All SH+ materials were adapted for the cultural groups included in the studies. The SH+ pre-recorded audio material was delivered across five 2-hour sessions to groups of up to 30 people. The audio material imparts key information about stress management and guides participants through individual exercises and small group discussions. To augment the audio recordings, an illustrated self-help book reviews all essential content and concepts. The SH+ intervention was fully delivered in the language of participants by trained facilitators with a migration background, who were native speakers of the target languages. ECAU, provided both to the experimental and control group, consisted of routinely delivered social support and/or care according to local regulations. Participants in the ECAU arm received the same baseline and follow-up assessments of the intervention arm, according to the study schedule (around three and six months after randomization), information about freely available health and social services, and links to community networks providing support to refugees and asylum seekers.

Statistical analysis

Descriptive statistics (mean and SD for continuous variables and absolute numbers and percentages for dichotomous variables) were computed on sociodemographic, premigration, migration and postmigration variables at baseline, and for clinical variables.

Participants who met criteria for any mental disorder on the M.I.N.I. at three or six-month follow-up were considered cases with a mental disorder. Multiple imputation was adopted to address the issue of missing data in all the variables included in the model. In particular, in case of missing data at the M.I.N.I. in one timepoint, imputation was performed on single M.I.N.I. values at three and six months. In case of missing values on continuous clinical measures, the imputation was performed on single item scales. Specifically, imputation followed the approach reported by Plumpton and colleagues (Plumpton *et al.*, 2016), that is we used scale totals within

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prediction equations and, for imputations of responses to individual scale items, we additionally included the responses to the other scale items, using the "ice" Stata routine (Royston, 2005, Sterne *et al.*, 2009), and considering single-item scores as ordered categorical variables. M.I.N.I. values at the two time-points were used in the prediction equations of regression predictors, and upper and lower bounds were set for continuous variables with missing values as appropriate. The number of imputed samples was determined by following the rule of thumb suggested by White and colleagues, i.e.: "at least equal to the percentage of incomplete cases" (White *et al.*, 2011). We rounded such number to the nearest multiple of 10 above.

In order to identify subtypes of traumatic events, we performed a PCA on tetrachoric correlations of HTQ items, with Quartimin oblique rotation to allow for between-factor non-null correlations (Tabachnick, 2007), and summing items with loadings above 0.40 on the same factor to create scores for the regression model (Stevens, 2002). The number of factors was determined by adopting Kaiser's rule (Kaiser, 1960), i.e. using the cut-off scores of 1 for the eigenvalues.

In order to investigate predictors of the development of mental disorders, unadjusted and adjusted logistic regression analyses were performed, using the frequency of participants with a mental disorder in at least one timepoint as binary dependent variable. The following independent variables were inserted into the model: age (years), gender (men, women), education (years), unemployment (yes/no), country of origin (Syria, Iraq, Nigeria, other countries), length of journey (below one month, between one and three months, above three months), study (Western Europe versus Turkey), length of stay in the resettlement country (months), HTQ (total score at baseline), GHQ-12 (total score at baseline), PCL-5 (total score at baseline), PHQ-9 (total score at baseline), number of SH+ sessions received (zero to five). Considering that PTSD and depression are known to be interrelated experiences following

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trauma (Rytwinski *et al.*, 2013), and considering that the PCL-5 largely overlaps with the HTQ (Patel *et al.*, 2022), and that a substantial overlap exists between the PCL-5 and the PHQ-9 (Dabrowski CL, 2020), we excluded the PCL-5 from the final model, but it was included (total score at baseline) in the imputation model.

In order to check the robustness of the analysis, we re-ran the model after excluding the arm receiving SH+. As a further sensitivity analysis, in order to estimate within-centre effects, we performed a model including a fixed effect for recruiting centre. As a subgroup analysis, we re-ran the logistic regression analysis separately for each study sample (western Europe versus Turkey). All analyses were performed using Stata 17 (Statacorp, 2017).

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Results

Participants

The two prevention trials randomized a total of 1,101 participants. After six months, 249 participants (22.6%) were not available for follow-up assessments, for the reasons reported in Figure 1. Participant characteristics at baseline are presented in Table 1. Almost half were female, with a mean age of 32 (SD 9.521) years, and a mean education of 10 years (SD 4.424). Slightly less than 40% was unemployed. The migration journey lasted more than three months in around one third of participants, in another one third it lasted between one and three months, while in the remaining 40% the host country was reached in less than one month. On average, the mean length of stay in the resettlement country was slightly more than three years. Most of the participants were from Syria, Nigeria and Iraq (Table 1). Participants attended a mean number of 1.4 (SD 2.015) SH+ sessions. The mean (SD) baseline scores on the measures of interest are reported in Table 1.

Frequency and determinants of mental disorders

At three- and six-month follow-up the observed frequency of mental disorders, as measured with the M.I.N.I., was 13.51% (115/851) and 24.30% (207/852), respectively, while the frequency estimates after missing data imputation were 13.95% and 23.78%, respectively. The majority of detected mental disorders were major depressive disorders (9.5% and 20.3% after three and six months), PTSD (3.2% and 6.7%), and anxiety disorders (2.1% and 4.1%) (Figure 1).

The PCA model found a 3-factor solution where the set of items was exhaustive and mutually exclusive, with the HTQ items grouped as follows: factor 1 - lack of basic needs: lack of food or water, ill health without access to medical care, lack of shelter; factor 2 - violence and abuse: imprisonment, serious injury, brain washing, rape or sexual abuse, forced isolation from others, forced separation from family members, torture, other (e.g. domestic violence;) factor 3 - being close to death: combat situation, being close to death, murder of family or friend, unnatural death of family or friend, murder of stranger(s), lost or kidnapped. The factor loadings of the PCA-model with Quartimin oblique rotation are reported in the Supplemental Materials.

The results of unadjusted and adjusted logistic regression analyses investigating factors associated with the development of mental disorders are presented in Table 2. Participants with lower education level ($p = 0.034$), a shorter duration of journey ($p = 0.057$), and arriving from countries with war-related contexts (Iraq, Syria) ($p = 0.017$), were those more at risk of developing mental disorders. In terms of mental health symptoms and exposure to traumatic events, psychological distress ($p = 0.004$), depressive symptoms ($p = 0.001$), and HTQ total score ($p = 0.020$) at baseline were predictors of mental disorder development, as was the HTQ factor violence and abuse (imprisonment, serious injury, brain washing, rape or sexual abuse, forced isolation from others, forced separation from family members, torture, domestic violence) ($p =$

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0.008). In terms of post-migration factors, the number of SH+ sessions ($p < 0.001$) was inversely associated with the risk of developing mental disorders (Table 2).

Secondary logistic regression analyses including only the ECAU arms of the two studies, and analysing the two studies separately, confirmed the role of mental health symptoms and exposure to traumatic events as risk factors for mental disorders (Supplemental Materials). However, due to lower statistical power, some factors lost significance despite a similar or even higher estimated effect, as for example the HTQ in the model restricted to the western European study, or years of education and travel duration in the model restricted to the ECAU sample, and GHQ-12 in the model restricted to the study conducted in Turkey (Supplemental Materials).

Consistently with the results of the two studies, the number of SH+ sessions was inversely associated with the frequency of mental disorders only in the study conducted in Turkey Supplemental Materials). The inclusion of recruiting centres as predictor variables revealed that, in comparison with participants recruited in Istanbul, participants recruited in Vienna were less likely to develop a mental disorder (Supplemental Materials).

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Discussion

To the best of our knowledge, this is the first prospective study that examined risk factors for the onset of mental disorders among asylum seekers and refugees without a mental disorder at baseline. We showed the significant influence of socio-demographic, clinical, and contextual factors, including potentially traumatic events, on the development of mental disorders in asylum seekers and refugees resettled in Western European countries and in Turkey.

Overall, one in four refugees and asylum seekers developed a diagnosable mental disorder over a period of six months. Interestingly, the most frequently reported diagnostic group was

depression, followed by PTSD and anxiety disorders. These figures, derived from two intervention studies, cannot be compared with those from epidemiological studies, which generally show similar frequencies for depression and PTSD, or slightly higher frequencies for depression, depending on the population surveyed and the study setting (Blackmore *et al.*, 2020, Charlson *et al.*, 2019, Henkelmann *et al.*, 2020, Hoell *et al.*, 2021). In migrants exposed to armed conflict, by contrast, the frequency of PTSD was found to be higher than depression (31% vs 25%) (Mesa-Vieira *et al.*, 2022).

The finding that educational level is inversely associated with the development of mental disorders expands previous data collected in the general population showing that higher educational level seems to have a protective effect against anxiety and depression symptoms, and against common mental disorders in general (Araya *et al.*, 2003, Bjelland *et al.*, 2008). In the general population, poor education has been suggested to be a marker of lack of opportunities and resources, including material and psychological resources, and a marker of childhood adversity (Araya *et al.*, 2003). In asylum seekers and refugees, these factors may directly contribute to the emergence of mental disorders, or may interfere with the coping skills required to deal with all the adversities associated with the migration and resettlement process, which, in turn, may increase the risk of developing mental disorders (Kirmayer *et al.*, 2011).

Consistently with an extensive literature showing that exposure to potentially traumatic events represents a risk factor for poor mental health and well-being (Gleeson *et al.*, 2020, Hajak *et al.*, 2021, Priebe *et al.*, 2016), the present study adds that exposure to potentially traumatic events is also a risk factor for the development of mental disorders considered as full-blown diagnostic entities. The finding that being displaced from countries with war-related contexts emerged as an additional risk factor for mental disorders further corroborates this association. War-related contexts imply exposure to multiple and serious traumatic events, and the exposure to combat

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situations creates the risk of witnessing violence and/or death and experiencing physical and psychological violence (Crepet *et al.*, 2017). Extensive literature shows that these situations are associated with poor mental health outcomes, including PTSD, depression, anxiety, and somatization symptoms (Jongedijk *et al.*, 2020, Knipscheer *et al.*, 2015, Nickerson *et al.*, 2021).

The present study has limitations and strengths. A first limitation is that the population enrolled in the two trials cannot be considered representative of the general population of asylum seekers and refugees, as we selected participants scoring above a threshold of psychological distress, and we excluded those at suicide risk. During the studies, in addition, around half of the participants was exposed to a psychological intervention aimed at preventing the development of mental disorders. For these reasons, the overall frequency estimate of mental disorders cannot apply to the general population of asylum seekers and refugees resettled in Western European countries or in Turkey. A second issue is that we did not calculate a true incidence of mental disorders, but only frequency figures at two time points with a structured diagnostic interview that might overestimate the true frequency of some mental disorders, such as depression (Wu *et al.*, 2020). Third, the SARS-CoV2 pandemic impacted the study procedures, because in all the recruiting sites follow-up assessments were conducted using online tools instead of face-to-face meetings. Although assessors were trained in the administration of rating scales, instructed on how to perform online follow-up assessments, and assisted by cultural mediators when needed, it is unknown whether this may have impacted the responses of participants to the instruments. Related to this, 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 (Acarturk *et al.*, 2021) we acknowledge that formal studies on use of these tools in refugee groups are lacking. Fourth, despite a growing body of literature showed that the duration of the asylum procedure is an important risk factor for mental health

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conditions (Laban et al. 2004; Winkler et al. 2019), we acknowledge that this information was not collected. However, months in host country, which may be considered a proxy of length of asylum procedure, was included in the model but did not emerge as a significant factor.

Despite these limitations, there are strengths that should be emphasised. The main strength is the exclusion of participants with a mental disorder at baseline, and the choice of a dependent variable that is fully consistent with a preventative design, namely the frequency of mental disorders at follow-up, assessed with validated measures. This design allowed to prospectively investigate the determinants of mental disorders rather than of poor mental health, as previous studies have done in populations who might already be with mental disorders at baseline (Priebe *et al.*, 2016). Another strength is a sample size of over a thousand of asylum seekers and refugees, resettled in a variety of western European sites and in Turkey. This aspect is of relevance not only in terms of statistical power, but also in terms of generalisability and applicability of study findings to different types of reception settings in high-income and middle-income countries. Lastly, despite an attrition rate of around 20%, a follow-up assessment of six months is noteworthy in such a difficult-to-follow population, who is often moved from one reception site to another, and may not perceive mental health as a priority, having a number of other challenging concerns such as housing, unstable working conditions, management of visa issues, safety of family members, fear of being returned to home country, plans to move to another country or to another location.

The present study has important practical implications. The finding of a positive relationship between exposure to potentially traumatic events and risk of mental disorder development suggests a pressing need of developing policies aiming to decrease exposure to such traumatic experiences after resettlement. Host countries may have opportunities to decrease exposure to situations such as material and economic hardship that could affect integrity, independence,

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dignity and well-being (financial strain), social hardship due to loss of status (social strain), feelings of inadequacy in relation with specific skills needed in the host-country to successfully function in daily life (competency strain), experiences of unfair treatment on the basis of prejudice (perceived discrimination). This ambitious goal may be achieved by implementing reception conditions that optimize internationally recognized minimal quality standards. For example, standards for the reception of applicants for international protection have been established by Directive 2013/33/EU of the European Parliament. The Directive clearly reports that national authorities should ensure that reception modalities are specifically designed to meet the needs of persons requiring international protection, including legal assistance, document provision, material support, links with local communities, freedom of movement, information about labor market access, vocational training, social support. Health care, including mental health care, is also mentioned as a key intervention where needed. It would be important to ensure that efforts to support forcibly displaced people are coordinated across the different layers of the social environments in which they are hosted, i.e. at the level of the individual, their family, the community, and the institutions that have governance responsibility for their care and support (White and Van der Boor, 2021).

In addition to implications in terms of risk reduction policies, the present study has implications in terms of provision of psychological interventions aimed at preventing the development of mental disorders (Miller *et al.*, 2021). As the implementation of preventative psychological interventions to the whole population of asylum seekers and refugees may not be sustainable by host countries, national authorities may consider to offer psychological interventions to at-risk populations. The finding that persons with lower education level, a shorter duration of journey, arriving from countries with war-related contexts (Iraq, Syria), and with high level of psychological distress and depressive symptoms, are those more at risk of developing mental disorders, appears to identify a target population for focused psychological prevention

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interventions. The WHO has recently developed a number of low-intensity psychological interventions that may be scaled up as public health strategies to address mental disorders and psychological distress in refugee populations exposed to ongoing adversities (World Health Organization, 2017). In addition to WHO interventions, other psychological treatments have been shown to be effective in alleviating psychological symptoms in asylum seekers and refugees (Turrini *et al.*, 2021, Uphoff *et al.*, 2020), but a preventative effect has been investigated for SH+ only. The present results, by showing an inverse association between number of SH+ sessions and risk of developing a mental disorder, further corroborate the value of SH+ as a prevention intervention. The finding that trauma exposure stands out as a predictor for development of mental disorders would additionally suggest that interventions may need to include a focus on traumatic memories and experiences, in addition to being focused on low mood.

In parallel with the provision of psychological interventions to at-risk populations, national authorities should ensure regular access to such interventions supporting at risk populations to engage through reducing barriers that might prevent or limit access or use (Fuhr *et al.*, 2019). This can be achieved by optimizing access (e.g. accessible services and supports) to a range of interventions depending on need (e.g. stepped care), and by using different delivery mechanisms (e.g. digital or peer delivered support).

As the number of persons in need of protection is likely to substantially increase globally, driven by long-lasting wars as well as by new conflicts such as the Russo-Ukrainian war which broke out recently (Barbui *et al.*, 2022, Pandi-Perumal *et al.*, 2022), national authorities are urged to develop reception and resettlement programs meeting the needs of this vulnerable group. These programs should be designed and implemented attempting to decrease the risk of post-migration stressors that may contribute to worsening the mental health of a population already

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exposed to potentially traumatic experiences before and during the migration process. Evidence-based focused psychological support should be an important program component to be delivered to asylum seekers and refugees at-risk of developing a mental disorder.

Contributors CB, MP, and FT conceived the study. FT statistically analysed the data. CB, GO and FT accessed and verified the data. CB wrote the first draft of the manuscript with input from FT and MP. All authors contributed to the conception and design of the study, data interpretation and manuscript revision. All authors read and approved the submitted manuscript and had final responsibility for the decision to submit for publication. CB was the overall guarantor of the content.

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Competing interests None declared.

Ethics approval This was a secondary analysis of deidentified participant data. The initial study was approved by the WHO Research Ethics Review Committee, and from the Ethics Committees of all participating sites. Before participation, a written informed consent was obtained from each participant, allowing investigators to use anonymised data for future analysis. Participants gave informed consent to participate in the study before taking part.

Data availability statement Data collected in the RE-DEFINE study are stored in the online repository EUDAT B2SHARE (study in Western Europe: https://b2share.eudat.eu/records/fa7264d624364683830ff37acee01c04; study in Turkey: http://doi.org/10.23728/b2share.8ac4f28d2415413e89de7847c05471fc.). The reuse of data will be offered only upon motivated request, which will undergo the scrutiny of the RE-DEFINE General Assembly.

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Table 1. Participants characteristics at baseline

Means	M (SD)
Age (years)	31.797 (9.521)
Years of education	9.556 (4.424)
Months in host country	40.636 (32.599)
Host country GDP in thousand dollars (2019)	
Austria	58,091.3
Finland	50,321.6
Germany	55 652.9
Italy	44,334.2
Turkey	27,144.2
UK	49,070.3
Number of SH+ sessions	1.434 (2.015)
GHQ	5.737 (2.230)
PHQ-9	7.232 (5.230)
HTQ Total score	5.795 (4.349)
HTQ Lack of basic needs	1.277 (1.210)
HTQ Violence and abuse	1.753 (2.085)
HTQ Being close to death	2.766 (1.947)
Frequencies	**n/N (%)**
Gender (Female)	538/1,101 (48.86%)
Unemployed	418/1,099 (38.03%)
Country of origin	
Nigeria	114/1,100 (10.36%)
Syria	758/1,100 (68.91%)
Iraq	94/1,100 (8.55%)
Other	134/1,100 (12.18%)
Travel duration	
Less than one month	277 (40.44%)
One to three months	203 (29.64%)
More than three months	205 (29.93%)
Study	
Western Europe	459 (41.69%)
Turkey	642 (58.31%)

M: mean; SD: standard deviation; SH+: Self-Help Plus; GDP: Gross Domestic Product; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

For Peer Review

Table 2. Determinants of mental disorder development: logistic regression analyses

	Unadjusted regressions		Adjusted regressions			
			With HTQ total score		With HTQ factors	
	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value	Odds Ratio (95% CI)	P-value
Age in years	1.001 (0.986; 1.015)	0.920	0.996 (0.980; 1.013)	0.672	0.998 (0.981; 1.015)	0.830
Female gender	1.318 (0.987; 1.759)	0.061	0.962 (0.680; 1.360)	0.825	0.977 (0.689; 1.385)	0.896
Years of education	0.972 (0.941; 1.004)	0.088	**0.959 (0.923; 0.997)**	**0.034**	**0.959 (0.922; 0.996)**	**0.032**
Unemployed	0.938 (0.702; 1.253)	0.664	1.171 (0.832; 1.647)	0.365	1.180 (0.836; 1.664)	0.347
Country of origin: Syria Iraq Nigeria Other	Reference category 1.180 (0.710; 1.960) **0.209 (0.101; 0.432)** **0.403 (0.240; 0.674)**	**<0.001**	Reference category 1.592 (0.807; 3.142) **0.376 (0.142; 0.997)** 0.577 (0.273; 1.222)	**0.017**	Reference category 1.672 (0.840; 3.325) **0.318 (0.118; 0.861)** 0.519 (0.241; 1.114)	**0.006**
Travel duration (months) Less than one month One to three months More than three months	Reference category **0.616 (0.398; 0.952)** **0.312 (0.198; 0.494)**	**<0.001**	Reference category 0.653 (0.414; 1.028) **0.512 (0.267; 0.983)**	0.057	Reference category 0.658 (0.417; 1.041) **0.502 (0.260; 0.969)**	0.057
Months in host country	1.002 (0.997; 1.007)	0.503	1.000 (0.994; 1.006)	0.943	1.000 (0.994; 1.006)	0.973
Turkish trial	**2.058 (1.513; 2.800)**	**<0.001**	1.795 (0.997,3.235)	0.051	1.802 (0.998; 3.253)	0.051
Number of SH+ sessions	**0.888 (0.827; 0.953)**	**0.001**	**0.853 (0.788; 0.923)**	**<0.001**	**0.850 (0.785; 0.921)**	**<0.001**

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GHQ-12	**1.188 (1.114; 1.268)**	**<0.001**	**1.117 (1.036; 1.204)**	**0.004**	**1.119 (1.038; 1.206)**	**0.003**
PHQ-9	**1.071 (1.042; 1.100)**	**<0.001**	**1.061 (1.026; 1.097)**	**0.001**	**1.061 (1.026; 1.097)**	**0.001**
HTQ Total score	1.002 (0.970; 1.036)	0.883	**1.051 (1.008; 1.096)**	**0.020**	-	-
HTQ Factor 1 - Lack of basic needs	0.999 (0.890; 1.122)	0.988	-	-	1.007 (0.863; 1.176)	0.928
HTQ Factor 2 - Violence and abuse	0.995 (0.929; 1.066)	0.894	-	-	**1.163 (1.041; 1.299)**	**0.008**
HTQ Factor 3 - Being close to death	1.018 (0.947; 1.095)	0.769	-	-	0.978 (0.888; 1.077)	0.650

CI: Confidence Interval; SH+: Self-Help Plus; GDP: Gross Domestic Product; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

For Peer Review

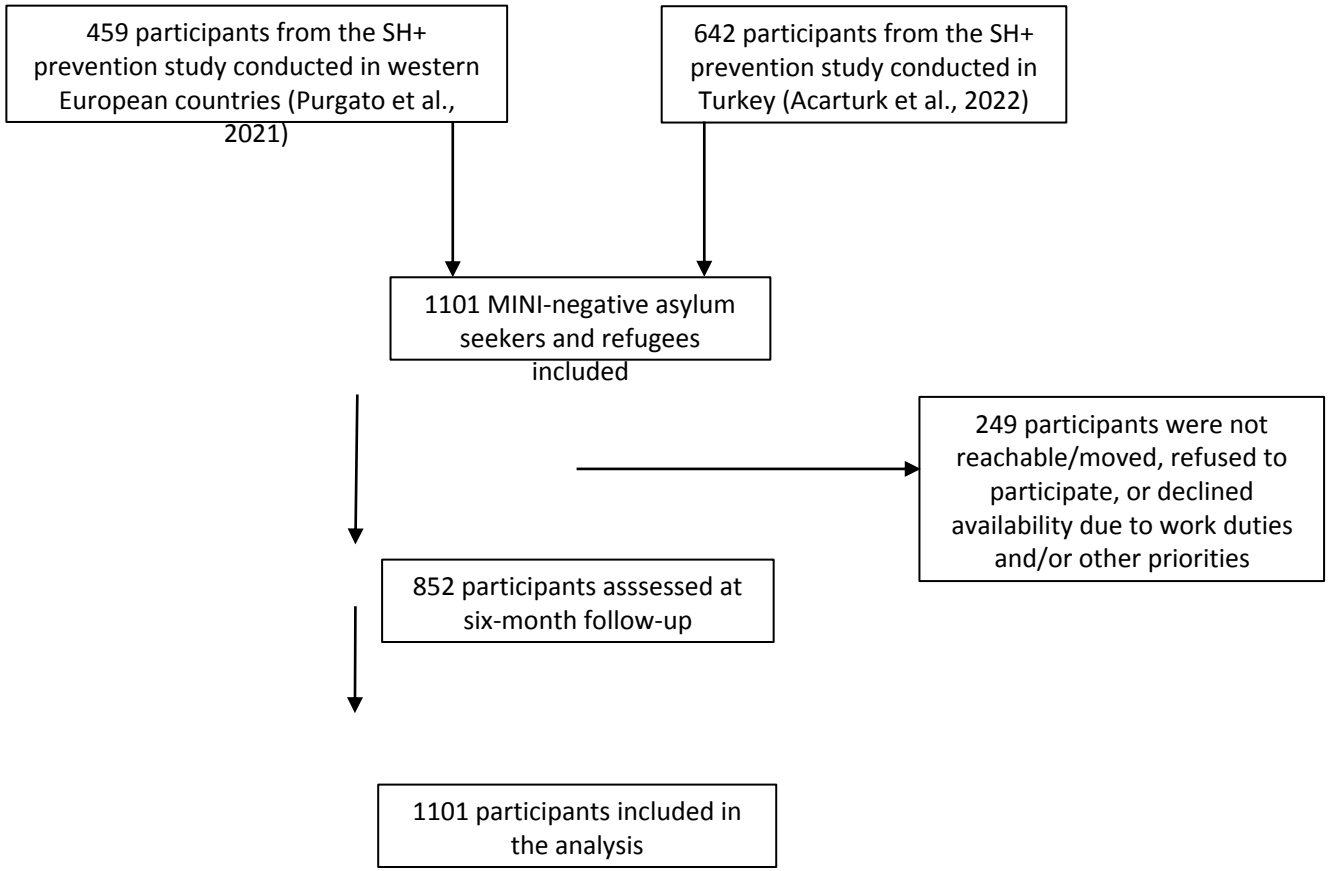


Figure 1. Flow-diagram of participant enrolment and follow-up

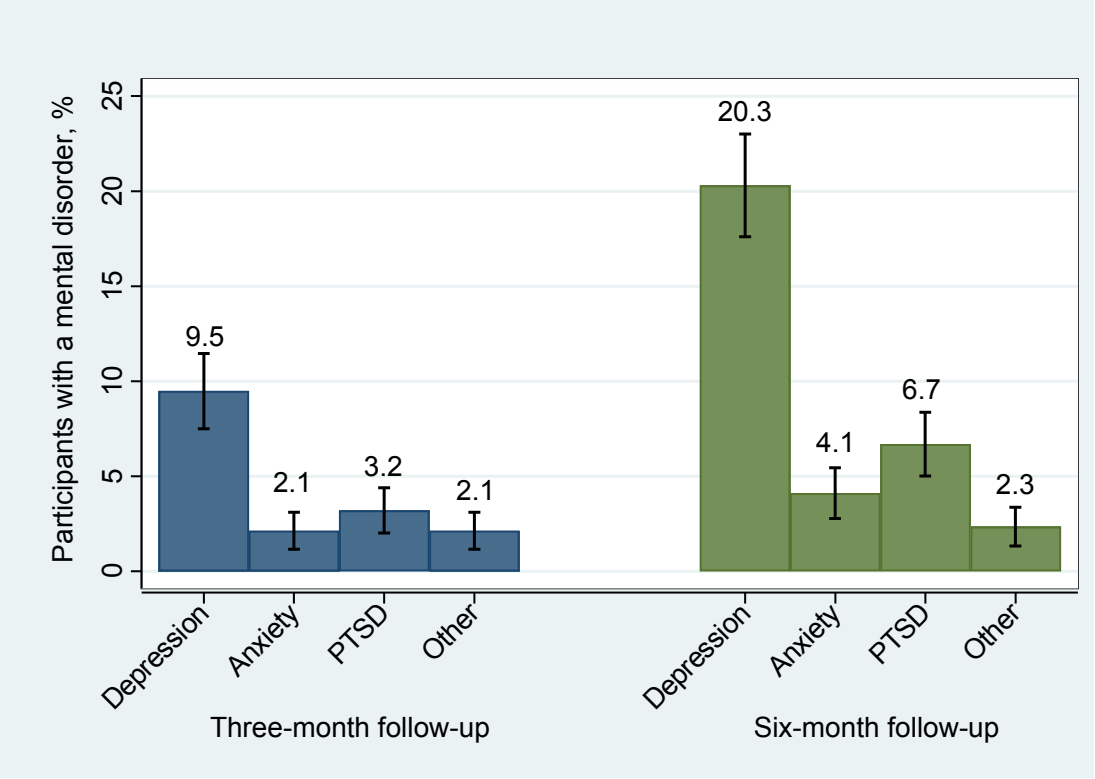


Figure 2. Frequency of mental disorders, as measured with the M.I.N.I., after three and six months of follow-up

Risk factors for mental disorder development in asylum seekers and refugees resettled in Western Europe and Turkey: participant-level analysis of two large prevention trials

Supplemental Materials

For Peer Review

Factor loadings from principal component analysis of HTQ items

	Factor 1	Factor 2	Factor 3
Lack of food or water	-0.031	-0.031	**0.952**
Ill health w/o access to medical care	0.057	0.037	**0.841**
Lack of shelter	0.155	0.079	**0.745**
Imprisonment	**0.593**	0.205	0.144
Serious injury	**0.475**	0.249	0.267
Combat situation	-0.374	**0.590**	0.315
Brain washing	**0.673**	-0.151	0.206
Rape or sexual abuse	**0.871**	0.018	-0.114
Forced isolation from others	**0.706**	0.085	0.180
Being close to death	0.297	**0.460**	0.276
Forced separation from family	**0.547**	0.304	0.095
Murder of family or friends	0.066	**0.779**	0.058
Unnatural death of family or friends	0.053	**0.806**	0.082
Murder of stranger(s)	-0.028	**0.906**	-0.039
Lost or kidnapped	0.372	**0.657**	-0.061
Torture	**0.671**	0.366	0.040
Other (e.g. domestic violence)	**0.659**	-0.260	0.266

HTQ: Harvard Trauma Questionnaire

Factor loadings above 0.4 marked in bold

For Peer Review

Secondary analysis: logistic regression including only the enhanced care as usual (ECAU) arm

	Odds Ratio	95% CI	P-value
Age in years	0.998	0.975; 1.021	0.849
Female gender	0.935	0.595; 1.469	0.755
Unemployed	1.101	0.694; 1.747	0.611
Years of education	0.962	0.915; 1.011	0.126
Months in host country	0.996	0.985; 1.008	0.608
Turkish trial	1.912	0.876; 4.173	0.081
Country of origin: Syria Iraq Nigeria Other	 Reference cat. 1.225 0.412 0.691	 0.501; 2.998 0.118; 1.440 0.263; 1.821	0.415
Travel duration (months) Less than one month One to three months More than three months	 Reference cat. 0.611 0.412	 0.323; 1.156 0.161; 1.054	0.071
GHQ-12	1.131	1.024; 1.249	**0.018**
PHQ-9	1.048	1.001; 1.097	**0.045**
HTQ Total score	1.067	1.002; 1.136	**0.037**

CI: Confidence Interval; GDP: GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

Significant values marked in bold

For Peer Review

Secondary analysis: logistic regression including only the study conducted in Western Europe

	Odds Ratio	95% CI	P-value
Age in years	0.979	0.949; 1.009	0.172
Female gender	1.093	0.555; 2.154	0.796
Unemployed	1.448	0.748; 2.804	0.271
Years of education	0.986	0.927; 1.048	0.646
Number of SH+ sessions	0.903	0.776; 1.052	0.190
Months in host country	0.996	0.979; 1.014	0.669
Country of origin: Syria Iraq Nigeria Other	 Reference cat. 1.571 0.204 0.388	 0.675; 3.652 0.065; 0.640 0.151; 0.999	**0.004**
Travel duration (months) Less than one month One to three months More than three months	 Reference cat. 0.990 0.668	 0.431; 2.276 0.245; 1.822	0.589
GHQ-12	1.114	0.972; 1.276	0.120
PHQ-9	1.088	1.026; 1.154	**0.005**
HTQ Total score	1.091	1.007; 1.183	**0.034**

CI: Confidence Interval; SH+: Self-Help Plus; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

Significant values marked in bold

For Peer Review

Secondary analysis: logistic regression including only the study conducted in Turkey

	Odds Ratio	95% CI	P-value
Age in years	1.005	0.984; 1.026	0.647
Female gender	0.942	0.618; 1.437	0.782
Unemployed	1.087	0.713; 1.657	0.698
Years of education	0.935	0.887; 0.986	**0.014**
Number of SH+ sessions	0.821	0.745; 0.905	**<0.001**
Months in host country	1.003	0.996; 1.010	0.474
Country of origin: Syria	0.225	0.061; 0.826	**0.025**
Travel duration (months) Less than one month One to three months More than three months	 Reference cat. 0.577 0.661	 0.308; 1.1080 0.112; 3.899	0.160
GHQ-12	1.092	0.995; 1.198	0.065
PHQ-9	1.052	1.006; 1.101	**0.028**
HTQ Total score	1.056	1.001; 1.114	**0.045**

CI: Confidence Interval; SH+: Self-Help Plus; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

For Peer Review

Secondary analysis: logistic regression including recruiting centres as independent variable

	Odds Ratio	95% CI	P-value
Age in years	0.997	0.980; 1.014	0.739
Female gender	0.967	0.683; 1.369	0.850
Unemployed	1.117	0.790; 1.578	0.532
Years of education	0.951	0.914; 0.990	**0.015**
Number of SH+ sessions	0.851	0.786; 0.922	**<0.001**
Months in host country	1.001	0.995; 1.007	0.856
Country of origin:			
Syria	Reference cat.		
Iraq	1.782	0.800; 3.969	0.090
Nigeria	0.388	0.080; 1.872	
Other	1.181	0.354; 3.934	
Travel duration (months)			
Less than one month	Reference cat.		**0.039**
One to three months	0.672	0.420; 1.076	
More than three months	0.445	0.226; 0.874	
Recruitment centre			
Istanbul	Reference cat.		
Wien	0.093	0.017; 0.512	
Liverpool	0.399	0.156; 1.022	**0.030**
Turku	0.469	0.200; 1.100	
Ulm	0.880	0.355; 2.179	
Verona	0.602	0.137; 2.646	
York	0.720	0.270; 1.915	
GHQ-12	1.108	1.026; 1.195	**0.009**
PHQ-9	1.064	1.029; 1.101	**<0.001**
HTQ Total score	1.047	1.003; 1.093	**0.035**

CI: Confidence Interval; SH+: Self-Help Plus; GHQ: General Health Questionnaire; PHQ: Patient Health Questionnaire; HTQ: Harvard Trauma Questionnaire

Significant values marked in bold

For Peer Review