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STUDY PROTOCOL

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Self-help plus for refugees and asylum seekers; study protocol for a series of individual participant data meta-analyses

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ABSTRACT

Background: Refugees and asylum seekers face various stressors due to displacement and are especially vulnerable to common mental disorders. To effectively manage psychological distress in this population, innovative interventions are required. The World Health Organization (WHO) Self-Help Plus (SH+) intervention has shown promising outcomes in reducing symptoms of common mental disorders among refugees and asylum seekers. However, individual participant differences in response to SH+ remain largely unknown. The Individual Participant Data (IPD) meta-analysis synthesizes raw datasets of trials to provide cutting-edge evidence of outcomes that cannot be examined by conventional meta-analytic approaches.

Objectives: This protocol outlines the methods of a series of IPD meta-analyses aimed at examining the effects and potential moderators of SH+ in (a) reducing depressive symptoms at post-intervention and (b) preventing the six-month cumulative incidence of mental disorders in refugees and asylum seekers.

Method: RCTs on SH+ have been identified through WHO and all authors have agreed to share the datasets of the trials. The primary outcomes of the IPD meta-analyses are (a) reduction in depressive symptoms at post-intervention, and (b) prevention of six-month cumulative incidence of mental disorders. Secondary outcomes include post-traumatic stress disorder symptoms, well-being, functioning, quality of life, and twelve-month cumulative incidence of mental disorders. One-stage IPD meta-analyses will be performed using mixed-effects linear/logistic regression. Missing data will be handled by multiple imputation.

Conclusions: These results will enrich current knowledge about the response to SH+ and will facilitate its targeted dissemination. The results of these IPD meta-analyses will be published in peer-reviewed journals.

Self-Help Plus para Refugiados y solicitantes de asilo; Protocolo de Estudio para una serie de Meta-análisis de datos de participantes individuales

Antecedentes: Los refugiados y solicitantes de asilo enfrentan numerosos estresores debido al desplazamiento y son especialmente vulnerables a trastornos de salud mental comunes. Para poder manejar efectivamente el malestar psicológico en esta población, se requieren intervenciones innovadoras. La intervención Self- Help Plus (SH+) de la Organización Mundial de la Salud (OMS) ha mostrado resultados prometedores en la reducción de síntomas de trastornos de salud mental comunes entre refugiados y solicitantes de asilo. Sin embargo, las diferencias individuales de los participantes en respuesta a SH+ permanecen mayormente desconocida. El meta-análisis de Datos de Participantes Individuales (IPD) sintetiza bases de datos puros para proveer evidencia de resultados de vanguardia que no puede ser examinada mediante enfoques meta-analíticos convencionales.

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PALABRAS CLAVE
refugiados; solicitantes de asilo; datos de participantes individuales; depresión; trastornos de salud mental comunes

关键词
难民; 寻求庇护者; 个人参与者数据; 抑郁; 常见精神障碍

HIGHLIGHTS

- Refugees and asylum seekers face enormous challenges and, thus, are at risk of mental disorders.
- Low-intensity psychotherapeutic interventions are needed to effectively address symptoms and prevent the full-blown onset of mental disorders in refugees and asylum seekers.

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Objetivos: Este protocolo delinea los métodos de una serie de meta-análisis de IPD enfocados en examinar los efectos y potenciales moderadores de SH+ en (a) reducir síntomas depresivos en la post-intervención y (b) prevenir la incidencia acumulada de trastornos mentales en refugiados y solicitantes de asilo durante seis meses.
Método: Se identificaron RCT sobre SH+ a través de la OMS y todos los autores acordaron compartir la base de datos de sus ensayos. Los resultados primarios de los meta-análisis de IPD son (a) reducción en síntomas depresivos después de la intervención, y (b) prevención de la incidencia acumulada de trastornos mentales en refugiados y solicitantes de asilo durante 6 meses. Entre los resultados secundarios de incluyó síntomas de trastorno de estrés postraumático, bienestar, funcionamiento, calidad de vida e incidencia acumulada de trastornos de salud mental durante 12 meses. Se realizaran meta-análisis de IPD de una etapa usando regresión linear/logística de efectos mixtos. Los datos faltantes se manejaran mediante imputación múltiple.
Conclusiones: Estos resultados enriquecerán el conocimiento actual sobre la respuesta a SH+ y facilitarán su diseminación en su público objetivo. Los resultados de estos meta-análisis de IPD serán publicados en revistas revisadas por pares.

难民和寻求庇护者自助服务:一系列个人参与者数据元分析的研究方案
背景: 由于移居, 难民和寻求庇护者面临各种应激源, 尤其对常见精神障碍易感。为了有效管理该人群的心理困扰, 需要采取创新的干预措施。世界卫生组织 (WHO) 自助服务 (SH +) 干预在减轻难民和寻求庇护者的常见精神障碍症状方面表现出有前景的结果。但是, 个体参与者对SH +的反应差异仍不清楚。个人参与者数据 (IPD) 元分析综合了试验的原始数据集, 以提供常规元分析方法无法考查的结果的前沿证据。
目标: 本方案概述了一系列IPD元分析的方法, 旨在考查难民和寻求庇护者中SH +在 (a) 干预后减轻抑郁症状和 (b) 预防六个月的精神障碍累积发病率中的作用和潜在调节因素。
方法: 已通过WHO确定了关于SH +的RCT, 所有作者均同意共享试验数据集。IPD元分析的主要结果是 (a) 干预后抑郁症状的减轻, 以及 (b) 预防六个月的精神障碍累积发病率。次要结果包括创伤后应激障碍症状, 幸福感, 功能, 生活质量以及十二个月的精神疾病累积发病率。一阶段IPD元分析将使用混合效应线性/逻辑回归。缺失数据将通过多重插补处理。
结论: 这些结果将丰富关于SH +反应的现有知识, 并有助于其针对性传播。这些IPD元分析的结果将发表在同行评审期刊上。

1. Introduction

The past decade has seen a significant increase in the number of people who were forced to seek refugee status due to ongoing war, conflict or persecution in Syria, Iraq, Afghanistan, and South Soudan, among other countries (UNHCR, 2020, 2017a, 2017b). Destinations for the displaced individuals include Western European countries, such as Germany, Sweden, Finland and Austria (UNHCR, 2020), while Turkey is the country hosting most forcibly displaced individuals worldwide (roughly 3.6 million) (UNHCR, 2020). This forceful displacement involves enormous mental and physical challenges to individuals and communities, including poverty, loss of livelihoods, violence, separation from family, discrimination, and resettlement issues (Fazel, Wheeler, & Danesh, 2005; Steel et al., 2009). Although many refugees and asylum seekers exhibit resilience and fortitude in the face of these difficulties, common mental disorders, like depression, are particularly prevalent in this population as a result of stressful experiences before, during, and after displacement (Blackmore et al., 2020; Charlson et al., 2019; Fazel et al., 2005; Steel et al., 2009). More specifically, according to a recent meta-analysis, depression is among the most common and persistent disorders in refugees and asylum seekers (31.5%) (Blackmore et al., 2020). Symptoms of depression may impair overall psychological functioning, wellbeing and overall quality of life, contribute to somatic health problems and somatization, and may lead to reduced possibilities to adjust to the new country (McGrath et al., 2020; Schick et al., 2016; Sijbrandij, 2018). Feasible and (cost-) effective interventions are warranted to manage symptoms of depression, reduce the probability of a full-blown onset of mental disorders, and improve quality of life in refugees and asylum-seekers Nevertheless, timely provision of psychological interventions is often hampered by language barriers and limited access to the mental healthcare facilities in the host countries.

In this context, the World Health Organization (WHO) has developed a stress management programme aimed at overcoming access-to-treatment barriers, reducing stress and improving overall functioning, named Self-Help Plus (SH+). SH+ can be implemented in a group format, facilitated by a non-specialist peer-facilitator, using pre-recorded audios to deliver content. An illustrated stress management guide called 'Doing What Matters in Times of Stress' and accompanying audio exercises support practise outside of sessions. Such a task-sharing approach offers key-benefits by empowering community members. This intervention is based on acceptance and commitment therapy (ACT), a form of cognitive behavioural therapy that incorporates mindfulness and other acceptance-based practices to help people

adaptively cope with distress and commit to actions that are aligned with their values (Epping-Jordan et al., 2016). Although ACT does not directly focus on symptom reduction, mounting research suggests that it is an effective treatment approach for common mental disorders like depression (Bai, Luo, Zhang, Wu, & Chi, 2020; French, Golijani-Moghaddam, & Schröder, 2017)

Thus far, SH+ has been shown to be feasible and acceptable when tested in pilot studies including refugees and people affected by war (Purgato et al., 2019; Tol et al., 2018, 2018). Following these positive preliminary findings, SH+ was tested with South Sudanese female refugees in Uganda in a cluster randomized controlled trial (cRCT) (Tol et al., 2020). Results indicated strong improvements in psychological distress in favour of SH+ compared to the control condition (i.e. enhanced treatment-as-usual) at post-intervention. Furthermore, SH+ resulted in improved personally identified problems, symptoms of depression, symptoms of post-traumatic stress disorder (PTSD), feelings of anger, overall functioning, social interactions, and well-being. Currently, the (cost-) effectiveness of SH+ in preventing mental disorders among forcibly displaced individuals in Western Europe and Turkey is being examined by two multicentre parallel-group RCTs. The first RCT is conducted in Italy, Austria, Finland, Germany, and the UK and the second in Turkey (Purgato et al., 2019). Both RCTs aim to inform the wide implementation of SH+ in the given population (Purgato et al., 2019).

While the evidence-base around the effectiveness of SH+ is growing, it remains unclear how individuals may respond differently to this intervention. Individuals differ in various ways, including epidemiological characteristics, background and living circumstances, life events they might have experienced, and type and severity of symptomatology. Such individual differences may result in differential responses to the intervention. Some people may benefit more, whereas others may benefit less from the SH+ intervention or even deteriorate. Understanding who is more likely to benefit from SH+ will substantially aid its targeted dissemination and implementation. Nevertheless, trials and conventional meta-analytic approaches are limited in their capacity to examine individual participant differences to intervention response. To achieve this goal, novel analytic strategies are required. The individual participant data (IPD) meta-analytic approach synthesizes raw datasets from clinical trials. In this way, sufficient statistical power is achieved to examine a range of moderators of intervention outcomes. Also IPD meta-analyses improve the precision of the overall estimates of the treatment effect (Bower et al., 2013).

In this study, we aim to conduct a series of IPD meta-analyses to synthesize available data from RCTs examining the effects of SH+ in refugees and asylum seekers. More specifically, we aim to examine:

(1) The effectiveness of SH+ compared to Enhanced Intervention-as-Usual (ETAU) in reducing depressive symptoms among refugees and asylum seekers. Secondary outcomes are reduction in post-traumatic stress and improvements in well-being, psychosocial functioning and quality of life.
(2) The effectiveness of SH+ compared to Enhanced Intervention-as-Usual (ETAU) to prevent the six-month cumulative incidence of any mental disorder among refugees and asylum seekers. Secondary outcomes are prevention of twelve-month cumulative incidence of any mental disorders.
(3) The moderating effects of participants' sociodemographic, migratory, and clinical characteristics to the differential effectiveness of SH+ relative to ETAU among refugees and asylum seekers.

2. Methods

The protocol registration is available in Open Science Framework (https://osf.io/jg4hs)

2.1. Identification of eligible studies

We will exclusively focus on examining the effectiveness of the SH+ intervention. The complete SH+ package will be made publicly available by WHO in 2021, and until that time all studies on SH+ need to be approved by the WHO. Thus, for the present study, a systematic literature search is not needed as WHO confirmed the existence of three RCTs on SH+ (Purgato et al., 2019; Tol et al., 2020), which are all on refugees and asylum seekers. The RCTs were conducted in Uganda, Turkey, and one RCT was conducted across five Western European countries (Italy, Germany, Finland, Austria, UK).

In this study, we will focus on examining moderators of the effects of SH+ as compared to ETAU. Thus, uncontrolled pilot trials will be excluded from our IPD meta-analyses.

2.2. Participants and procedure

In the identified RCTs, participants were refugees and asylum-seekers (≥ 18 years of age) with elevated psychological distress levels based on cut-off scores in self-report outcome measures [a score of ≥ 3 at the 12-item General Health Questionnaire – GHQ-12 for the RCTs in Turkey and Europe (Purgato et al., 2019) and a score of ≥ 5 on the Kessler-6 (K-6) in Uganda (Tol et al., 2020)]. 'Refugees and asylum seekers' were

individuals who (a) have been recognized as having a refugee status under the 1951 United Nations convention (United Nations General Assembly resolution, 1950), (b) sought international protection but whose application for refugee status had not yet been concluded (United Nations General Assembly resolution, 1950), or (c) were under temporary protection.

The RCTs in Turkey and Western Europe included both genders, whereas the RCT in Uganda included only females. The RCTs in Turkey and Western Europe excluded individuals meeting criteria for a DSM-5 diagnosis of mental disorder using the MINI Neuropsychiatric Interview and individuals suffering from an acute medical condition (Sheehan et al., 2010). Further, imminent risk of suicide was an exclusion criterion in all three RCTs.

In terms of study procedures, the RCTs in Western Europe and Turkey used individual randomization, whereas the study in Uganda used cluster randomization, in which 14 villages were randomized in either the intervention or the control groups to avoid contamination of the intervention materials within villages (Tol et al., 2020).

2.3. Intervention

The SH+ intervention has been developed by WHO and is designed to help individuals cope with stress and manage adversity. SH+ comprises of five weekly sessions, lasting approximately two hours. It is designed to be delivered in groups of up to 40 people and delivers content on: building awareness and grounding during stressful situations (session 1); noticing and naming difficult thoughts and feelings (session 2); identifying and acting on values (session 3), being kind (compassion) towards self and others (session 4); accepting and living with difficult thoughts and feelings (session 5). Each session provides information and experiential practise on the core concept of that session, with additional time to review and practise previous content. Techniques throughout the course have a number of similar features so each concept builds on the last (Purgato et al., 2019; Tol et al., 2020).

The five sessions of SH+ are administered in a group setting by trained facilitators using a pre-recorded audio recording. This delivery mode potentially reduces the time needed to train facilitators to deliver the content verbally. Instead, facilitators focus on managing the group and ensuring safety, as well as providing encouragement to practise the exercises contained in the audio recordings and answering additional questions that may arise. The audio provides psychoeducation about stress as well as instructions for experiential exercises. Moreover, SH+ is transdiagnostic (targets psychological distress broadly, including symptoms of various psychological conditions like posttraumatic stress disorder, depression, anxiety in people with or without diagnosed mental disorders), easily adaptable to different cultures and languages (it has been used for research studies in English, Arabic, Dari, Urdu and Juba Arabic), and suitable for individuals with or without mental health problems. Depending on the cultural norms, SH+ can be delivered in groups with mixed or single-gender representation (Purgato et al., 2019; Tol et al., 2020).

SH+ is delivered by non-specialist facilitators trained in a task-sharing approach (Fulton et al., 2011). In the studies, non-specialist facilitators had experience as volunteers, community workers or similar profiles and worked in healthcare or related settings. It should be noted that many of the volunteers had a lived experience of being forcibly displaced and were drawn from the communities to which they delivered the intervention to. They received 4–5 days training and supervision on SH+ from local supervisors who had received training in SH+ from WHO (Purgato et al., 2019; Tol et al., 2020).

2.4. Comparison

The identified studies compared SH+ to ETAU. In this control condition, participants received routine social support or healthcare support and treatment according to the local regulations and practices. Moreover, participants in ETAU received information about all freely available social and mental healthcare services for refugees and asylum-seekers individuals in the community.

2.5. Outcomes

In the planned IPD meta-analyses, we will have the following primary outcomes: (a) post-intervention depression symptom severity on PHQ-9 (Kroenke, Spitzer, & Williams, 2001) and (b) prevention of six-month cumulative incidence of any mental disorder based on a clinical interview. Secondary outcomes include reduction in post-traumatic stress symptoms on The Post-Traumatic Checklist-6 (Lang & Stein, 2005; Weathers et al., 2013) and improvements in quality of life on WHODAS (Üstün, Kostanjsek, Chatterji, & Rehm, 2010) version 2, and functioning on PSYCHLOPS (Ashworth, Kordowicz, & Schofield, 2012), and well-being on WHO-5 (Bech, 2004). Moreover, we will examine effects of SH+ on prevention of the 12-month new incidence rates of any mental disorder based on a clinical diagnostic interview.

2.6. Study-level variables

We will extract study-level data from the published reports of the trials including time of post-intervention assessment, country where the study was conducted, and type of randomization (cluster vs. individual randomiza tion), target group (e.g. South Sudanese female refugees),

and data related to the risk of bias assessment as described below (see section Risk of Bias assessment). One reviewer will extract the data from the published/under review reports and a second reviewer will check the extracted data for accuracy. In case, the reports of trials have not yet been published, the primary investigators will be asked to provide all the necessary information.

2.7. Individual-level variables

We will examine the role of a range of variables in moderating the effects of SH+ on the effects of the intervention. Moderator variables examine differential intervention effects on response (who benefits more or less from SH+ to ETAU). The variables will be chosen based on their availability in the included studies. We will gather and synthesize all socio-demographic (e.g. age, gender, educational and marital status, etc.), clinical characteristics (e.g. levels of distress, previous psychological conditions, symptoms of depression, the exposure and type of traumatic events, the overall quality of life, functioning and wellbeing, etc.) and migration variables (time since resettlement, migration route, length of migration process, etc.) A full list of possible moderators is presented in Table 1.

2.8. IPD collection and aggregation

The research groups that have conducted the identified RCTs have agreed to contribute data to these IPD meta-analyses. The transfer of de-identified primary datasets will be done using secure password protected data links. Further, the data will be safely stored in a secure cloud service (Surfdrive) developed for the Dutch education and research community, which can only be accessed by the members of the IPD meta-analysis research team. Transferring, storing, and handling of data will follow the EU General Data Protection Regulations (GDPR).

After gathering all primary datasets of the eligible RCTs, the data will be checked against the published reports of the trials to ensure the accuracy of the dataset. More specifically, we will check the frequencies of socio-demographic variables (e.g. age, gender, education, marital status, etc.) as well as the mean scores of continuous scales. In case inconsistencies are found (e.g. extreme values or discrepancies between the trial report and the data), these will be discussed and clarified with the authors of the primary studies. After checking each dataset, we will merge the data into the IPD meta-analytic dataset.

2.9. Risk of bias assessment

Two reviewers will examine independently the risk of bias for the primary outcomes in the three included studies using the criteria of the Cochrane Collaboration risk of bias assessment (RoB) tool 2.0 (Sterne, Savović, & Page et al., 2019). This tool examines bias arising from randomization, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of reported results. Given that the present study is an IPD meta-analysis, we will not evaluate bias related to missing outcome data and selection of reported results. We will exclude these domains of bias from the RoB assessment because we will have access to the primary full datasets of the trials. The RoB will be evaluated based on the information provided in the published reports of the papers. However, if there are unclear items, the primary authors of the trials will be asked. We will evaluate each item of the RoB assessment tool 2.0 as at low or high risk of bias (Sterne et al., 2019).

2.10. The IPD meta-analysis

All analyses will be conducted in STATA (version 16.0). The analysis will be conducted according to the intention-to-treat principle (all randomized participants will be included in the analyses). We will use multiple imputation to handle incomplete outcome data at the post-intervention assessment. Missing values will be estimated under the missing-at-random assumption (20 imputations). To estimate the missing values, complete baseline variables will be used (e.g. distress levels at baseline, age, gender, etc.). We will also conduct a sensitivity analysis using complete cases only to test the difference between imputed and complete values.

To calculate the effectiveness of SH+ in reducing depressive symptoms, we will merge the IPD from all available studies using the 'one-stage IPD meta-analytic' approach, which combines all the IPD from all the studies to perform a single analysis. The 'one-stage IPD meta-analysis' will result in a 'mega-trial analysis' in which data will be analysed as if they belonged to a single trial with participants nested within studies. This approach allows for a more sophisticated modelling of the moderators and thus it is preferred over the two-stage IPD approach (Debray et al., 2018; Stewart et al., 2015).

To examine the effects of SH+ on reduction in depressive symptoms at post-intervention, we will perform a mixed effect linear regression with random intercept model with each trial having a random effect and a fixed effect for the intervention and the severity of depression symptoms. The severity of depressive symptoms at the post-intervention will be used as the dependent variable, while the condition will be the independent variable while adjusting for baseline depression symptom severity. The post-intervention depression scores on PHQ-9 will be used as the dependent variable and trial arm condition (SH+ vs ETAU) as the independent variable, while controlling for baseline depressive symptom severity.

Table 1. List of possible moderators.

Moderators	Explanation & possible categories
Gender	Male vs Female
Age	Continuous (in years)
Country	e.g. Syria, Iraq, Nigeria
Relationship Status	Not in a relationship vs In a relationship
Educational Level	Illiterate vs Primary school/junior high school vs High school vs University degree and above
Years of education	Continuous (in years)
Employment	Employed vs Other
Number of relatives	1–3 relatives 4–6 relatives > 6 relatives
Number of children	1–2 children 3–4 children > 4 children
Religion	Muslim vs Other
Family's agreement for departure	Yes/No
Route of migration	Eastern Mediterranean route vs African Mediterranean route vs Other route
Host county is the final destination	Yes/No
Detention	Yes/No
Travelled with company	with friends/relatives vs with other migrants vs With others vs
Relatives in the country of origins	Yes/No
Legal Status	Humanitarian protection vs Subsidiary protection vs Political asylum vs Other legal status
Length of stay in host country	Continuous (in months)
Living situation	Living situation vs Living with a partner/children vs Living with parents vs Living with others
Accommodation	Refugee reception centre vs Rented apartment
Distress levels at BL	Continuous (standardized)
Length of stay	Continuous (in months)
Post-traumatic symptoms at BL	Continuous (PCL-C)
Depressive symptoms at BL	Continuous (PHQ-9)
Traumatic experiences	Either continuous (HTQ), or
• Lack of food or water	Yes/No
• No Medical Access	Yes/No
• Lack of Shelter	Yes/No
• Imprisonment	Yes/No
• Serious Injury	Yes/No
• Combat	Yes/No
• Rape or Sexual Abuse	Yes/No
• Close to death	Yes/No
• Murder	Yes/No
• Abduction	Yes/No
• Torture	Yes/No
Wellbeing	Continuous (WHO-5)
Functioning	Continuous (PSYCHLOPS)
Quality of Life	Continuous (WHODAS)

Abbreviations: HTQ: Harvard Trauma Questionnaire; PCL-C: Post-traumatic checklist; PHQ-9: Patient Health Questionnaire – 9 items; PSYCHLOPS: Psychological Outcomes Profiles; WHO-5: The World Health Organization – Five Well-Being Index; WHODAS: The World Health Organization Disability Assessment Schedule.

These moderators have been chosen based on the availability across the eligible studies. Possible use of these moderators in the series of IPDMAs depends on whether the analyses will focus on the 3 or the 2 eligible studies.

To examine the effects of SH+ in preventing the six-month cumulative incidence of any mental disorder, we will focus only the trials including six-month clinical interviews and excluded individuals who met criteria for any mental disorder at the baseline (Purgato et al., 2019; Tol et al., 2020). We will perform a mixed effect logistic regression with random intercept model with each trial having a random effect and a fixed effect for the intervention and the severity of depression symptoms. Six-month cumulative incidence (yes/no) will be used as the dependent variable, while the condition will be the independent variable. In a similar manner, in secondary analyses, we will test the effects of SH+ in reducing the 12-month cumulative incidence of any mental disorder.

We will calculate the standardized β coefficient for the examined comparisons. This estimate indicates how many SDs the dependent variable (depression, well-being, quality of life, and functioning) changes per SD increase in the predictor variable. Thus, the higher the β is the greater the effect of the predictor variable on the dependent variable, although there is no association among the variables if the β is 0.

To ensure robustness of our findings, the analysis of the main outcomes will be repeated using a 'two-stage IPD meta-analytic approach', in which we will analyse the IPD separately in each study and then combining the estimates to calculate the pooled effect sizes (Cohen's d) (Cohen, 2013) for all outcomes using the random-effects model.

2.11. Participant- and study-level moderators

We will test whether socio-demographic, clinical variables and migration variables moderate the effects of SH + at the post-intervention assessment. To examine the effects of potential moderators, we will add the interaction between each moderator variable and SH+ effect on depressive symptoms into the mixed-effects linear/logistic regression model. Each potential moderator variable will be added into separate bivariate models.

2.12. Heterogeneity

Statistical heterogeneity will be assessed with I^2, with 0% indicating no heterogeneity, 25% low heterogeneity, 50% moderate heterogeneity and 75% as being high heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). We will also calculate the 95% Confidence Intervals (CI) around I^2 square to give the full magnitude of heterogeneity (Ioannidis & Trikalinos, 2007). The 95% CI will be calculated using the non-central chi-squared-based approach (Orsini, Bottai, Higgins, & Buchan, 2006).

2.13. Publication bias

The present IPD meta-analysis focuses on SH+ and intervention developed by WHO. Therefore, we have access to all datasets using this intervention up to date,

which means that publication bias is not applicable to the present work.

3. Discussion

SH+ has shown promise in the prevention and treatment of common mental disorders among refugees and asylum seekers. In the present paper, we have described the procedures of a series of IPD meta-analyses aimed at examining the effects as well as individual participant differences in response to SH+ as compared to ETAU.

3.1. Strengths and limitations

RCTs and study-level meta-analyses often lack the power to identify statistically significant moderators of intervention response. The IPD meta-analytic approach offers key benefits to conventional methods as it allows us to examine outcomes that have not been reported by primary studies. Further, this methodology maximizes the statistical power and precision in the estimates and enables testing of moderators at a meta-analytic level (Bower et al., 2013).

Nevertheless, we should anticipate several limitations. First, there is a chance that clinically important moderator variables might not be available across all eligible studies, meaning that the number of observations might be small for specific variables. Thus, the overall statistical power of our analysis might be reduced. Also, clinical heterogeneity should be expected. For instance, we expect variability across participants due to factors such as legal status (e.g. refugees or asylum seekers), country of origin and living situation as they are not a homogenous target group. Moreover, SH+ was delivered in different settings across countries, ranging from refugee camps to healthcare or community facilities, and this might impact the intervention's effect. Finally, the identified studies differ in terms of depression severity. For instance, Tol et al. (2020) included a proportion of participants with likely mental disorders at entry into the trial, while this was an exclusion criterion in the other two eligible studies. To address this possible limitation, in our analyses, we will adjust for different levels of depression severity at baseline to improve the precision of our estimates and the interpretation of our findings.

Despite the potential limitations, synthesizing all available evidence of the WHO SH+ is needed for several reasons. First, to our knowledge, this would be the first IPD meta-analytic effort to examine moderators of a guided self-help intervention delivered by non-specialist facilitators. Given the novelty of the examined intervention in this context, pooling the data of all existing trials is needed to guide future studies in this field. It should be noted that although the number of eligible trials is small ($n = 3$), the number of total participants is large ($n = 1795$), thereby justifying the use of the IPD meta-analytic methodology. Second, WHO intends to make the SH+ intervention publicly available in 2021 for use. This low-intensity intervention delivered by non-specialists has the potential to bridge the gap between intervention supply and demand in the particularly vulnerable population of refugees and asylum seekers. Knowing who is more likely to respond to SH+ will ensure its most efficient dissemination and implementation providing timely access to effective care for psychological distress. Finally, the IPDMAs will importantly contribute to the knowledge base concerning the effects of preventive interventions for adversity-affected populations such as refugees and asylum seekers."

Acknowledgments

The authors alone are responsible for the views expressed in this article, and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

Author contributions

EK and MS drafted the study protocol. All the authors provided input into the study design and helped in the protocol writing. MP, CA, DL, DB, EP, EU, JW, JA, MV, MK, MP, MR, MA, RC, RW, SA-H, TL, TK, WAT, and CB contributed to the original data acquisition. FT helped with data synthesis and administration for the IPDMA. CB and PC supervised the overall conduct of the study. All the authors read and approved the final protocol. EK is the guarantor of the review.

Data availability statement

A data-access request should be addressed to prof. Dr. Corrado Barbui. Data can be shared upon the approval of the RE-DEFINE consortium.

Disclosure statement

Dr. Ross White acted as a consultant reviewer to the WHO in the development of the SH+ intervention, and I am an author on the papers reporting on the RCTs in the EU and Uganda.

Ethics and dissemination

Ethical approval is not required for this study because we will perform secondary analyses of de-identified data. These results will enrich current knowledge about the response to SH+ and will facilitate its targeted dissemination. The results of these IPD meta-analyses will be published in peer-reviewed journals.

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References

Ashworth, M., Kordowicz, M., & Schofield, P. (2012). *Le PSYCHLOPS (Psychological Outcome Profiles)*, *10 outils*, 38.

Bai, Z., Luo, S., Zhang, L., Wu, S., & Chi, I. (2020). Acceptance and commitment therapy (ACT) to reduce depression: A systematic review and meta-analysis. *Journal of Affective Disorders*, *260*, 728–737. doi:10.1016/j.jad.2019.09.040

Bech, P. (2004). Measuring the dimension of psychological general well-being by the WHO-5. *Quality of Life Newsletter*, 15–16.

Blackmore, R., Boyle, J. A., Fazel, M., Ranasinha, S., Gray, K. M., Fitzgerald, G., … Spiegel, P. (2020). The prevalence of mental illness in refugees and asylum seekers: A systematic review and meta-analysis. *PLoS Medicine*, *17*(9), e1003337. doi:10.1371/journal.pmed.1003337

Bower, P., Kontopantelis, E., Sutton, A., Kendrick, T., Richards, D. A., Gilbody, S., … Liu, E. T. H. (2013). Influence of initial severity of depression on effectiveness of low intensity interventions: Meta-analysis of individual patient data. *BMJ*, *346*, f540. doi:10.1136/bmj.f540

Charlson, F., Van Ommeren, M., Flaxman, A., Cornett, J., Whiteford, H., & Saxena, S. (2019). New WHO prevalence estimates of mental disorders in conflict settings: A systematic review and meta-analysis. *The Lancet*, *394* (10194), 240–248. doi:10.1016/S0140-6736(19)30934-1

Cohen, J. (2013). *Statistical power analysis for the behavioral sciences*. London, UK: Academic press.

Debray, T. P., Schuit, E., Efthimiou, O., Reitsma, J. B., Ioannidis, J. P., Salanti, G., & Moons, K. G. (2018). An overview of methods for network meta-analysis using individual participant data: When do benefits arise? *Statistical Methods in Medical Research*, *27*(5), 1351–1364. doi:10.1177/0962280216660741

Epping-Jordan, J. E., Harris, R., Brown, F. L., Carswell, K., Foley, C., García-Moreno, C., … Van Ommeren, M. (2016). Self-Help Plus (SH+): A new WHO stress management package. *World Psychiatry*, *15*(3), 295. doi:10.1002/wps.20355

Fazel, M., Wheeler, J., & Danesh, J. (2005). Prevalence of serious mental disorder in 7000 refugees resettled in western countries: A systematic review. *Lancet*, *365* (9467), 1309–1314. doi:10.1016/S0140-6736(05)61027-6

French, K., Golijani-Moghaddam, N., & Schröder, T. (2017). What is the evidence for the efficacy of self-help acceptance and commitment therapy? A systematic review and meta-analysis. *Journal of Contextual Behavioral Science*, *6* (4), 360–374. doi:10.1016/j.jcbs.2017.08.002

Fulton, B. D., Scheffler, R. M., Sparkes, S. P., Auh, E. Y., Vujicic, M., & Soucat, A. (2011). Health workforce skill mix and task shifting in low income countries: A review of recent evidence. *Human Resources for Health*, *9*(1), 1. doi:10.1186/1478-4491-9-1

Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *Bmj*, *327*(7414), 557–560. doi:10.1136/bmj.327.7414.557

Ioannidis, J. P., & Trikalinos, T. A. (2007). An exploratory test for an excess of significant findings. *Clinical Trials*, *4* (3), 245–253. doi:10.1177/1740774507079441

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, *16*(9), 606–613. doi:10.1046/j.1525-1497.2001.016009606.x

Lang, A. J., & Stein, M. B. (2005). An abbreviated PTSD checklist for use as a screening instrument in primary care. *Behaviour Research and Therapy*, *43*(5), 585–594. doi:10.1016/j.brat.2004.04.005

McGrath, M., Acarturk, C., Roberts, B., Ilkkursun, Z., Sondorp, E., Sijbrandij, M., … Fuhr, D. C. (2020). Somatic distress among Syrian refugees in Istanbul, Turkey: A cross-sectional study. *Journal of Psychosomatic Research*, *132*, 109993. doi:10.1016/j.jpsychores.2020.109993

Orsini, N., Bottai, M., Higgins, J., & Buchan, I. (2006). *Heterogi: Stata module to quantify heterogeneity in a meta-analysis*. https://econpapers.repec.org/software/bocbocode/s449201.htm

Purgato, M., Carswell, K., Acarturk, C., Au, T., Akbai, S., Anttila, M., … Van Ommeren, M. (2019). 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*, *9*(5), e030259. doi:10.1136/bmjopen-2019-030259

Schick, M., Zumwald, A., Knopfli, B., Nickerson, A., Bryant, R. A., Schnyder, U., … Morina, N. (2016). Challenging future, challenging past: The relationship of social integration and psychological impairment in traumatized refugees. *European Journal of Psychotraumatology*, *7*, 28057. doi:10.3402/ejpt.v7.28057

Sheehan, D. V., Sheehan, K. H., Shytle, R. D., Janavs, J., Bannon, Y., Rogers, J. E., … Wilkinson, B. (2010). Reliability and validity of the mini international neuropsychiatric interview for children and adolescents (MINI-KID). *The Journal of Clinical Psychiatry*, *71*(3), 313–326. doi:10.4088/JCP.09m05305whi

Sijbrandij, M. (2018). Expanding the evidence: Key priorities for research on mental health interventions for refugees in high-income countries. *Epidemiology and Psychiatric Sciences*, *27*(2), 105–108. doi:10.1017/S2045796017000713

Steel, Z., Chey, T., Silove, D., Marnane, C., Bryant, R. A., & Van Ommeren, M. (2009). Association of torture and other potentially traumatic events with mental health outcomes among populations exposed to mass conflict and displacement: A systematic review and meta-analysis. *JAMA*, *302*(5), 537–549. doi:10.1001/jama.2009.1132

Sterne, J. A., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H-Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Juni, P., Kirkham, J. J., Lasserson, T., Li, T., ... Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ*, 366, l4898. https://doi.org/10.1136/bmj.l4898

Stewart, L. A., Clarke, M., Rovers, M., Riley, R. D., Simmonds, M., Stewart, G., & Tierney, J. F. (2015). Preferred reporting items for a systematic review and meta-analysis of individual participant data: The PRISMA-IPD statement. *Jama*, *313*(16), 1657–1665. doi:10.1001/jama.2015.3656

Tol, W. A., Augustinavicius, J., Carswell, K., Brown, F. L., Adaku, A., Leku, M. R., ... Van Ommeren, M. (2018). Translation, adaptation, and pilot of a guided self-help intervention to reduce psychological distress in South Sudanese refugees in Uganda. *Global Mental Health*, *5*, e25. doi:10.1017/gmh.2018.14

Tol, W. A., Augustinavicius, J., Carswell, K., Leku, M. R., Adaku, A., Brown, F. L., ... Van Ommeren, M. (2018). Feasibility of a guided self-help intervention to reduce psychological distress in South Sudanese refugee women in Uganda. *World Psychiatry*, *17*(2), 234. doi:10.1002/wps.20537

Tol, W. A., Leku, M. R., Lakin, D. P., Carswell, K., Augustinavicius, J., Adaku, A., ... Van Ommeren, M. (2020). Guided self-help to reduce psychological distress in South Sudanese female refugees in Uganda: A cluster randomised trial. *The Lancet Global Health*, *8*(2), e254–e63. doi:10.1016/S2214-109X(19)30504-2

UNHCR. (2017a). *Global trends. Forced displacement in 2016*. Geneva. https://www.unhcr.org/globaltrends2016/#:~:text=and%20location%20data-,TRENDS%20AT%20A%20GLANCE,remained%20at%20a%20record%20high

UNHCR. (2017b). The UN Refugee Agency. Retrieved from https://www.unhcr.org/globaltrends

UNHCR. (2020). *Global trends. Forced displacement in 2019*. Geneva. https://www.unhcr.org/unhcr-global-trends-2019-media.html?gclid=CjwKCAjwwqaGBhBKEiwAMk-FtOiGwWWdhbB_uo3e6LuIjwZ9aL91aWaa2eQAL_TU9PV_GYksamvcLhoCgEQQAvD_BwE&gclsrc=aw.ds

United Nations General Assembly resolution. (1950, December). 429(V) of 14. Retrieved from http://www.unhcr.org/refworld/docid/3b00f08a27.html

Üstün, T. B., Kostanjsek, N., Chatterji, S., & Rehm, J. (2010). *Measuring health and disability: Manual for WHO disability assessment schedule WHODAS 2.0*. Geneva: World Health Organization.

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., & Schnurr, P. P. (2013). The PTSD checklist for DSM-5 (PCL-5). *Scale Available from the National Center for PTSD at Www PTSD Va Gov*, *10*, 10