Psychosocial interventions for post-traumatic stress disorder in refugees and asylum seekers resettled in high-income countries: Systematic review and meta-analysis

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Abstract

Treatment of post-traumatic stress disorder (PTSD) in refugees and asylum seekers resettled in high-income countries presents specific challenges. This systematic review examined the effectiveness of psychosocial interventions for this group. We searched the Cochrane Central Register of randomised trials, CINAHL, EMBASE, PILOTS, PsycINFO, PubMed and Web of Science up to July 2016. Studies included randomised and controlled clinical trials comparing psychosocial interventions with waiting list or treatment as usual in adult refugees and asylum seekers with PTSD resettled in high-income countries. PTSD symptoms post-intervention was the primary outcome. We computed standardized mean differences (SMD) with 95% confidence intervals (CI). This study is registered with PROSPERO: CRD42015027843. Twelve studies were included in the meta-analysis. Psychosocial interventions were effective in decreasing PTSD symptoms relative to control groups (SMD -1.03, 95% CI -1.55 to -0.51; number needed to treat 4.4; I² 86%; 95% CI 77 to 91). Narrative exposure therapy, a manualized short-term variant of cognitive behavioural therapy with a trauma focus, was the best-supported intervention (5 RCTs, 187 participants, SMD -0.78, 95% CI -1.18 to -0.38, I² 37%; 95% CI 0 to 77). Methodological quality of the included studies was limited. Overall, psychosocial interventions for asylum seekers and refugees with PTSD resettled in high-income countries were found to provide significant benefits in reducing PTSD symptoms. Yet, the number of studies is small and their methodological quality limited, so that more rigorous trials should be conducted in the future.

Introduction

Worldwide, around 65 million people are forcibly displaced because of conflict and persecution, including 21.3 million refugees and over 3 million individuals awaiting resolution of their
asylum application. Asylum applications in industrialised countries have significantly increased with 80% of these being lodged in European countries [1]. In 2015, the United Nations High Commissioner for Refugees (UNHCR) reported over one million refugees reaching Europe by sea, and a further 34,000 crossing from Turkey into Bulgaria and Greece by land [2].

Traumatic events, such as torture and war exposure, are disproportionately experienced by refugees and asylum seekers before and during displacement [3,4]. In addition, post-displacement traumatic events important for mental health include resettlement stress [5], and perceived stigma and discrimination [6,7]. In comparison with the general population, refugees and asylum seekers have been shown to experience higher prevalence rates of a range of disorders, including common mental disorders (e.g. depression, anxiety, somatoform disorders), severe mental disorders (e.g. psychosis), substance use disorders, and disorders specifically tied to stress [8–10]. Despite the range of mental disorders of relevance to conflict-affected populations, the best studied mental health outcome in refugees remains post-traumatic stress disorder (PTSD). PTSD is 10 times more likely in refugees and asylum seekers compared to host populations [8–10].

Treatment of PTSD among refugees and asylum seekers resettled in high-income countries presents complex and specific challenges [11]. It can be difficult to distinguish expected temporary distress from PTSD in people who are continuously exposed to various traumatic events. In addition, refugees from various socio-cultural settings may have diverging perspectives on causes and priorities with regard to experienced distress, as compared to the PTSD diagnosis conceptualized in psychiatric classification systems. Trauma experienced by refugees is different in character, severity and duration than that seen in other populations [12–15], leading to the expression of psychopathology with a long-term fluctuating course and a high comorbidity with other disorders, particularly depression [16,17]. In addition, in high-income countries complications with cultural and language barriers, difficulty in developing trust in staff-patient relationships, and increased risk of social marginalisation represent major treatment and social issues [18].

Despite a growing body of literature, including several narrative and systematic reviews that suggested a promising role for some psychosocial interventions [19–25], so far the efficacy of psychosocial interventions on PTSD outcomes in asylum seekers and refugees resettled in high-income countries has never been quantified. Against this background, this study aimed to establish whether the current evidence supports the provision of psychosocial interventions for PTSD in this group. We conducted a systematic review of randomised controlled trials (RCTs) and controlled clinical trials (CCTs) in adult refugees and asylum seekers with PTSD resettled in high income countries.

Materials and methods

The protocol for this review was registered in the International Prospective Register of Systematic Reviews (PROSPERO), registration number: CRD42015027843.

Identification and selection of studies

The following bibliographical databases were searched up to July 2016: Cochrane Central Register of randomised trials (CENTRAL), CINAHL, EMBASE, PILOTS, PsycINFO, PubMed and Web of Science. Terms indicative of PTSD were combined with terms indicative of psychosocial interventions (both MeSH terms and text words). Studies in any language were considered for inclusion. Grey literature was searched using the databases listed in the Cochrane Handbook for Systematic Reviews of Interventions [26]. We also checked the references of narrative
reviews of psychosocial treatment of PTSD in displaced populations. Details of the searches and of the screening process are given in S1 and S2 Tables. The selection process was recorded in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [27].

The inclusion criteria were: (a) RCT or CCT; (b) the effects of a psychosocial intervention were investigated; (c) psychosocial interventions were compared with no psychosocial intervention, a waiting list, treatment as usual, usual care, repeated assessment, or a minimal attention control group akin to psychological placebo; (d) participants were adult (18 years or above) refugees or asylum seekers with PTSD resettled in high-income countries. The terms ‘psychosocial intervention’, ‘asylum seeker’, ‘refugee’ and ‘high-income country’ are defined in S3 Table.

**Outcome measures**

The primary outcome of this review was the mean score post-intervention on the Clinician-Administered PTSD Scale (CAPS) or Harvard Trauma Questionnaire (HTQ) or on any other PTSD rating scale with evidence of adequate validity and reliability. Secondary outcomes were the following: depressive symptoms, as measured by the Hamilton Depression Rating Scale (HDRS), Montgomery-Asberg Depression Rating Scale (MADRS), Clinical Global Impression Rating scale (CGI), or any other depression rating scale with evidence of adequate validity and reliability; PTSD symptoms at follow-up; number of individuals fulfilling PTSD diagnostic criteria at follow-up; number of patients who dropped out during the trial by any cause; and global functioning, as measured by any validated rating scale.

**Data extraction and quality assessment**

Data extraction was performed in agreement with the Cochrane Handbook for Systematic Reviews of Interventions, Chapter 7.19 [26]. Two review authors (MN and FB), independently extracted the data on participant characteristics, intervention details and outcome measures. Disagreements were resolved by discussion and consensus with a third member of the team (CB). For continuous outcomes, the mean scores at end-point or the mean change from baseline to end-point, the standard deviation or standard error of these values, and the number of patients included in these analyses, were extracted. For dichotomous outcomes, the number of individuals fulfilling PTSD diagnostic criteria at the end of the study, the number of patients leaving the study early and the number of patients undergoing the randomisation procedure were recorded. When outcome data were not reported, trial authors were asked to supply the data.

The quality of included studies was assessed using the ‘Risk of bias’ assessment tool developed by the Cochrane Collaboration [26]. This tool assesses possible sources of bias in clinical trials, including the adequate generation of allocation sequence; the concealment of allocation to conditions; the prevention of knowledge of the allocated intervention (blinded outcome assessment); and dealing with incomplete outcome data (this was assessed as positive when intention-to-treat analyses were conducted, meaning that all randomized patients were included in the analyses). Emerging recommendations from the Cochrane Collaboration Non-Randomised Studies Methods Group were followed to rate the quality of clinical trials that did not employ a random allocation procedure. Quality assessment was conducted by two independent review authors (MN and IB), and disagreements were solved through discussion.

**Data synthesis**

Data entry and analysis was performed twice. First, data were entered and analysed with Review Manager (RevMan 5.3), software recommended by the Cochrane Collaboration, and
then independently re-entered into a spreadsheet and analysed within the metan module in STATA 14.1. Statistical outputs were cross-checked for consistency. In accordance with recent efforts towards a data sharing culture [28–29], the spreadsheet with the full dataset is made available as part of this publication.

For continuous outcomes, we pooled the standardised mean differences (SMDs) as different measurement scales were used. A loose intention-to-treat (ITT) analysis was applied, whereby all participants with at least one post-baseline measurement were represented by their last observations carried forward (LOCF) [26]. When only P or standard error values were reported, standard deviations were calculated according to Altman and Bland [30]. If standard deviations could not be calculated, they were imputed using validated methodology [31]. Because some studies had relatively small sample sizes we corrected the effect size for small sample bias, using Hedge’s g [26]. For dichotomous outcomes a Mantel–Haenszel risk ratio was calculated. Continuous and dichotomous outcomes were analysed using a random-effects model, with 95% confidence intervals (CI), as this takes into account any difference between studies even if there is no statistically significant heterogeneity. To provide a measure of clinical significance, the number-needed-to-treat (NNT) was calculated [32].

Studies that compared two or more formats of similar psychosocial interventions were included in meta-analysis by combining group arms into a single group, as recommended in section 16.5 of the Cochrane Handbook [26].

We calculated the $I^2$-statistic, which quantifies the effect of statistical heterogeneity, providing a measure of the degree of inconsistency in the studies’ results in percentages [26]. We calculated 95% CIs around $I^2$, using the non-central chi-squared-based approach within the heterogi module in STATA 14.1.

For PTSD and depressive symptomatology, the following subgroup analyses were performed: type of psychosocial intervention (narrative exposure therapy [NET] vs. cognitive behavioral therapy [CBT] vs. eye movement desensitization and reprocessing [EMDR] vs. trauma-focus psychotherapy [TFP] vs. culture-sensitive oriented peer [CROP] vs. family group intervention [FGI]), study design (RCTs vs. CCT), outcome measure (CAPS or HDRS vs. any other instrument), number of sessions (up to 10; between 11 and 20; more than 20), length of follow-up (up to 4 months; more than 4 months), study country (Germany vs. USA vs. other EU countries), and country of origin (one country vs. two or more countries). As number of sessions and length of follow-up were arbitrarily categorised, we further investigated a potential association between effect size and these continuous variables by means of unrestricted maximum likelihood random effects meta-regression analysis, as implemented in Comprehensive Meta-analysis (CMA) [33].

To investigate the impact of each study on the pooled effect (sensitivity analysis), we consecutively removed each study as a possible outlier to test its impact on the combined effect, as implemented in CMA [34].

Publication bias was tested by visually inspecting the funnel plot on primary outcome measures and by Duval and Tweedie’s trim and fill procedure, which yields an estimate of the effect size after the publication bias has been taken into account (as implemented in CMA). Egger’s test of the intercept was conducted to quantify the bias captured by the asymmetry of the funnel plot and test whether it was significant.

In order to produce a tabular synoptic overview of the main review findings and quality, easily understandable for patients, policy makers, research planners, guideline developers and other stakeholders, data were summarised according to the methodology described by the GRADE working group [35]. We followed the WHO criteria for summarising and aggregating the evidence [36–37].
Results

Characteristics of included studies

The electronic search yielded a total number of 3139 abstracts (after removal of duplicates). After title and abstract screening, 79 full text papers were considered for inclusion, of which 14 studies met the inclusion criteria and were included in the systematic review [38–51] (Fig 1 and S1 Table). References to excluded studies are reported in S4 Table. Of the included studies, two provided no data that could be used in the meta-analysis.

Fig 1. PRISMA flow-chart diagram.
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Of the 14 included studies, 12 were RCTs [38,39,41–43,45–51], and two were CCTs [40,44]. Nine studies had a waiting list control condition, while five compared a psychosocial intervention with treatment as usual (Table 1). The mean study sample size was 63 participants (range 10 to 197), and the mean length of follow-up was five months (range 2 to 12) (Table 1). Nine studies were conducted in Europe and five in the United States of America. Study participants were from a single country in seven studies, while a mix of participants from more than one country was included in the remaining studies. No studies were carried out within newly arrived asylum seekers; time since resettlement ranged from 2 to 16 years.

Interventions were all psychological: NET, a manualized short-term variant of CBT with a trauma focus (five RCTs), other types of CBT (five RCTs), TFP (two CCTs), CROP (one RCT), and FGI (one RCT) (Table 1). Four studies assessed group interventions [40,48,49,51], of which two were included in the analysis [40,49]. Study participants were exposed to an average number of 17 face-to-face sessions (range 3 to 25) of psychosocial interventions. The main characteristics of these interventions are described in S5 Table.

The quality of the studies varied (Fig 2 and S6 Table). No study met all seven quality criteria. Four of five studies on NET included authors who developed the NET manual. Using the GRADE framework, the quality of evidence ranged between low and very low (S7 Table).
The meta-analysis of the primary outcome (12 studies, 543 patients) showed that psychosocial interventions were effective in decreasing PTSD symptoms relative to inactive controls (SMD -1.03, 95% CI -1.55 to -0.51) (Fig 2). The magnitude of effect corresponds to a NNT of 4.4. Heterogeneity was high ($I^2 = 86%; 95% CI 77 to 91$). Visual inspection of the funnel plot and Egger’s test ($p = 0.04$) suggested the possibility of publication bias (S1 Fig). Removing each of the studies as a possible outlier, including one RCT that was retracted for administrative but not scientific abnormalities (S6 Table), resulted in no change in the overall estimate (S2 Fig).

The meta-analysis of depressive outcomes (eight studies, 378 patients) showed that psychosocial interventions were effective in decreasing depression relative to inactive controls (SMD -1.10, 95% CI -1.67 to -0.54) (Fig 3). The magnitude of effect corresponds to a NNT of 3.1. Heterogeneity was high ($I^2 = 81%; 95% CI 64 to 90$). Very few studies contributed to the analyses of the other secondary outcomes. In terms of PTSD symptoms at follow-up, psychosocial interventions were not more effective than control groups, although a wide CI around the overall point estimate leaves the possibility of clinically relevant differences (SMD 0.01, 95% CI -1.26 to 1.28). Psychosocial interventions showed a positive effect in terms of participants still fulfilling PTSD criteria at follow-up (three studies, 158 participants, RR 0.39, 95% CI 0.19 to 0.83, $I^2 = 84%; 95% CI 52 to 95, NNT = 2$), while in terms of dropout rate no differences were observed (S3 Fig). For the secondary outcome global functioning we found no data suitable for meta-analysis.

In terms of type of psychosocial intervention, subgroup analyses of PTSD outcomes showed that NET was effective in decreasing PTSD symptoms relative to inactive controls (five RCTs, 187 participants, SMD -0.78, 95% CI -1.18 to -0.38, $I^2 = 37%; 95% CI 0 to 77$). The magnitude of effect corresponds to a NNT of 4.4. Heterogeneity was high ($I^2 = 86%; 95% CI 77 to 91$). Visual inspection of the funnel plot and Egger’s test ($p = 0.04$) suggested the possibility of publication bias (S1 Fig). Removing each of the studies as a possible outlier, including one RCT that was retracted for administrative but not scientific abnormalities (S6 Table), resulted in no change in the overall estimate (S2 Fig).
of the effect corresponds to a NNT of 6.7 participants (Table 2). Other types of CBT taken together failed to show a significant effect, although the confidence interval around the point estimate did not exclude the possibility of a clinically relevant benefit (Table 2). The magnitude of effect of TFSuppP was substantial, but supported by two CCTs only. CROP was studied in one RCT only and no studies on EMDR were found (Table 2) (S4 Fig).

The magnitude of effect was higher in CCTs compared to RCTs, and in studies with more sessions and lasting more than four months (Table 2). Using meta-regression analyses to further investigate the association between number of sessions and effect size (p = 0.44), and between length of follow-up and effect size (p = 0.08), a similar trend was observed (S5 and S6 Figs).

Other subgroup analyses of PTSD outcomes showed no difference between the SMDs in terms of study quality, use of CAPS versus other outcome measures, country where the study was carried out, or ethnicity (Table 2).

Subgroup analyses of depression outcomes (S7 Fig) showed that NET was effective in decreasing depressive symptoms relative to control groups (three RCTs, 116 participants, SMD -0.86, 95% CI -1.65 to -0.06, I² = 70%; 95% CI 0 to 91). The magnitude of effect corresponds to a NNT of 4.3 participants (Table 3). Other types of CBT taken together failed to show a significant effect, although the confidence interval around the point estimate did not exclude the possibility of a clinically relevant benefit (Table 3). The effect of TFP and CROP on depressive symptoms was significant, but supported by one small study only. No studies on EMDR were found (Table 3).

Other subgroup analyses of depression outcomes showed no difference between the SMDs in terms of study design, quality, use of HDRS versus other outcome measures, number of sessions, length of follow-up, country where the study was carried out, and ethnicity (Table 3).

Discussion

Considering that since 2008 a total of nearly 1.1 million asylum seekers have been granted a refugee status in Europe, this review may be relevant for the care of nearly 100,000 people with
PTSD recently resettled in Europe alone [2]. With respect to PTSD symptoms, the findings suggest that between four and five refugees and asylum seekers with PTSD need to be treated in order for one to benefit. A slightly higher magnitude of effect was observed on depressive outcomes. However, the limited study quality casts uncertainty about these effects. Seven of the 12 studies included in the primary outcome analysis were at high risk of bias in two or

| Table 2. Standardized effect sizes of psychosocial interventions for PTSD in refugees and asylum seekers displaced in high-income countries: subgroup analyses of PTSD outcomes. |
|---------------------------------|---------|---------|---------|---------|---|---|---|---|
| Meta-analysis                   | Studies (N) | Patients (N) | SMD | 95% CI | $I^2$ a) | 95% CI b) | $P$ c) | NNT |
| Overall PTSD outcomes           | 12 | 543 | -1.03 | -1.55 to -0.51 | 86 | 77 to 91 | 0.00 | 4.4 |
| Subgroup analyses               |         |         |       |        |     |        |     |    |
| Intervention                    |         |         |       |        |     |        |     |    |
| NET                             | 5 | 187 | -0.78 | -1.18 to -0.38 | 37 | 0 to 77 | 18 | 6.7 |
| CBT                             | 4 | 182 | -0.97 | -2.20 to 0.26 | 91 | 79 to 96 | 1.8 | 2.1 |
| EMDR                            | 0 |     |       |        |     |        |     |    |
| TFP                             | 2 | 146 | -1.92 | -3.05 to -0.80 | 85 | NA | 0.07 | 2.1 |
| CROP                            | 1 | 28 | -0.41 | -1.17 to 0.34 | NA | NA | 0.98 | 4.3 |
| Study design                    |         |         |       |        |     |        |     |    |
| RCT                             | 10 | 397 | -0.81 | -1.28 to -0.33 | 78 | 60 to 88 | 0.05 | 6.3 |
| CCT                             | 2 | 146 | -1.92 | -3.05 to -0.80 | 85 | NA | 0.98 | 2.1 |
| Study quality                   |         |         |       |        |     |        |     |    |
| Low RoB                         | 5 | 223 | -1.04 | -1.95 to -0.13 | 88 | 75 to 94 | 0.05 | 4.3 |
| High RoB                        | 7 | 320 | -1.03 | -1.69 to -0.37 | 84 | 69 to 92 | 0.98 | 4.4 |
| Rating scale                    |         |         |       |        |     |        |     |    |
| CAPS                            | 4 | 153 | -1.28 | -1.99 to -0.56 | 72 | 21 to 90 | 47 | 3.2 |
| Others                          | 8 | 390 | -0.90 | -1.60 to -0.21 | 89 | 80 to 94 | 0.05 | 5.0 |
| No of sessions                  |         |         |       |        |     |        |     |    |
| Up to 10                        | 4 | 164 | -0.54 | -0.93 to -0.16 | 28 | 0 to 73 | 0.05 | 11.3 |
| 11–20                           | 6 | 233 | -1.08 | -1.93 to -0.22 | 87 | 73 to 93 | 0.05 | 4.1 |
| More than 20                    | 2 | 146 | -1.92 | -3.05 to -0.80 | 85 | NA | 0.05 | 2.1 |
| Length of FU                    |         |         |       |        |     |        |     |    |
| Up to 4 months                  | 6 | 188 | -0.86 | -1.52 to -0.20 | 76 | 46 to 89 | 55 | 5.8 |
| More than 4 months              | 6 | 355 | -1.18 | -2.02 to -0.35 | 91 | 83 to 95 | 55 | 3.6 |
| Country                         |         |         |       |        |     |        |     |    |
| Germany                         | 5 | 177 | -1.22 | -2.11 to -0.32 | 85 | 66 to 93 | 41 | 3.4 |
| USA                             | 3 | 96 | -1.46 | -2.91 to -0.01 | 87 | 64 to 96 | 23 | 2.6 |
| Other EU countries              | 4 | 270 | -0.58 | -1.30 to 0.13 | 85 | 64 to 94 | 41 | 7.5 |
| Ethnicity                       |         |         |       |        |     |        |     |    |
| One country                     | 5 | 188 | -1.46 | -2.50 to -0.42 | 89 | 76 to 95 | 23 | 2.6 |
| Two or more                     | 7 | 355 | -0.74 | -1.27 to -0.21 | 79 | 57 to 90 | 23 | 6.3 |

Abbreviations: PTSD: Posttraumatic stress disorder; NET: Narrative exposure therapy; CBT: Cognitive behavioural therapy; EMDR: Eye movement desensitization and reprocessing; TFP: Trauma focused psychotherapy; CROP: Culture-Sensitive Oriented Peer; RCT: Randomized clinical trial; CCT: Controlled clinical trial; RoB: Risk of bias; CAPS: Clinician-administered PTSD scale; FU: Follow-up; SMD: Standardized mean difference; CI: Confidence interval; NNT: number-needed-to-be-treated.

a) Calculated when at least two studies contributed to the analysis.

b) Calculated when at least three studies (two degrees of freedom) contributed to the analysis.

c) The p-value in this column indicates whether the effect sizes of subgroups differ significantly from each other in the subgroup analyses.

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more items of the Cochrane risk of bias tool, with no studies being free from bias in all quality items. In particular, in four studies blinding of outcome assessment was not mentioned.

Findings from this review add to the existing literature on the effectiveness of psychosocial interventions in individuals with PTSD who were selected for being forcibly displaced because of conflict and persecution. Crumlish and colleagues, who conducted a qualitative review of randomised controlled trials of treatments of PTSD among refugees and asylum seekers,

**Table 3. Standardized effect sizes of psychosocial interventions for PTSD in refugees and asylum seekers displaced in high-income countries: subgroup analyses of depressive outcomes.**

| Meta-analysis                      | Studies (N) | Patients (N) | SMD   | 95% CI     | I² a) | 95% CI b) | P c) | NNT |
|-----------------------------------|-------------|--------------|-------|------------|-------|-----------|------|-----|
| Overall depressive outcomes       | All studies | 8            | 378   | -1.10      | -1.67 to -0.54 | 81 | 64 to 90 | .00  | 3.1 |
| Subgroup analyses                 | Intervention|              |       |            |       |           |      |     |
| NET                               | 3           | 116          | -0.86 | -1.65 to -0.06 | 70 | 0 to 91 | 4.3  |     |
| CBT                               | 3           | 152          | -1.54 | -3.38 to 0.29 | 93 | 83 to 97 |      |     |
| EMDR                              | 0           |              |       |            |       |           |      |     |
| TFP                               | 1           | 82           | -1.04 | -1.59 to -0.50 | NA | NA       | 3.3  |     |
| CROP                              | 1           | 28           | -0.95 | -1.75 to -0.16 | NA | NA       | 3.7  |     |
| Study design                      |             |              |       |            |       |           | -84  |     |
| RCT                               | 7           | 296          | -1.13 | -1.81 to -0.46 | 83 | 67 to 92 | 3.0  |     |
| CCT                               | 1           | 82           | -1.04 | -1.59 to -0.50 | NA | NA       | 3.3  |     |
| Study quality                     |             |              |       |            |       |           | -45  |     |
| Low RoB                           | 4           | 193          | -1.34 | -2.49 to -0.19 | 90 | 78 to 96 | 2.4  |     |
| High RoB                          | 4           | 185          | -0.86 | -1.38 to -0.33 | 53 | 0 to 84 | 4.3  |     |
| Rating scale                      |             |              |       |            |       |           | -42  |     |
| HDRS                              | 3           | 153          | -0.82 | -1.67 to 0.03 | 77 | 27 to 93 |      |     |
| Others                            | 5           | 225          | -1.29 | -2.09 to -0.49 | 82 | 60 to 92 | 2.7  |     |
| No of sessions                    |             |              |       |            |       |           | -06  |     |
| Up to 10                          | 1           | 63           | -0.30 | -0.82 to 0.22 | NA | NA       |      |     |
| 11–20                             | 6           | 233          | -1.32 | -2.15 to -0.49 | 85 | 69 to 93 | 2.4  |     |
| More than 20                      | 1           | 82           | -1.04 | -1.59 to -0.50 | NA | NA       | 3.3  |     |
| Length of FU                      |             |              |       |            |       |           | -63  |     |
| Up to 4 months                    | 5           | 177          | -1.24 | -2.09 to -0.38 | 83 | 61 to 92 | 2.6  |     |
| More than 4 months                | 3           | 201          | -0.94 | -1.81 to -0.06 | 83 | 49 to 94 | 3.8  |     |
| Country                           |             |              |       |            |       |           | -49  |     |
| Germany                           | 2           | 53           | -1.26 | -2.44 to -0.08 | 68 | NA       | 2.6  |     |
| USA                               | 3           | 115          | -1.58 | -3.31 to 0.14 | 91 | 77 to 97 | 1.9  |     |
| Other EU countries                | 3           | 210          | -0.68 | -1.30 to -0.07 | 72 | 6 to 92 | 4.9  |     |
| Ethnicity                         |             |              |       |            |       |           | -42  |     |
| One country                       | 4           | 143          | -1.40 | -2.55 to -0.25 | 87 | 68 to 95 | 2.2  |     |
| Two or more                       | 4           | 235          | -0.85 | -1.48 to -0.22 | 75 | 31 to 91 | 4.9  |     |

Abbreviations: PTSD: Posttraumatic stress disorder; NET: Narrative exposure therapy; CBT: Cognitive behavioural therapy; EMDR: Eye movement desensitization and reprocessing; TFP: Trauma focused psychotherapy; CROP: Culture-Sensitive Oriented Peer; RCT: Randomized clinical trial; CCT: Controlled clinical trial; RoB: Risk of bias; HDRS: Hamilton depression rating scale; FU: Follow-up; SMD: Standardized mean difference; CI: Confidence interval; NNT: number-needed-to-be-treated.

a) Calculated when at least two studies contributed to the analysis.

b) Calculated when at least three studies (two degrees of freedom) contributed to the analysis.

c) The p-value in this column indicates whether the effect sizes of subgroups differ significantly from each other in the subgroup analyses.

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irrespective of the country in which they resettled, suggested that NET, a manualized short-term variant of trauma-focused cognitive behavioural therapy, was the best-supported modality [19]. A similar conclusion was reached by Gwozdiewycz and Mehl-Madrona, who considered seven studies related to narrative exposure methods for treating trauma in refugees, irrespective of the setting of care [20]. For torture survivors, a population with some commonalities with refugee survivors, a Cochrane review showed that NET and other forms of CBT were found to provide moderate benefits in reducing distress and PTSD symptoms over the medium term, although evidence was of very low quality [21]. Our findings provide further empirical evidence that psychosocial interventions that are effective for PTSD in the general population may not completely overlap with those that are appropriate for PTSD in asylum seekers and refugees in high-income settings. In the general population of adults with PTSD existing guidelines suggest CBT with a trauma focus, EMDR, or stress management [22,23]. By contrast, this systematic review found that some evidence existed in support of NET, that TFP was supported by two heterogeneous studies, and that for other types of CBT taken together the evidence was inconclusive. No studies were found for EMDR. It should be considered, however, that NET is a variant of trauma-focused CBT, and that interventions based on CBT included in this review might have a trauma-focused component; therefore, there might be a varying degree of overlap in content between NET and CBT as provided in the included studies. Indirectly, this is also supported by very similar overall effect size estimates for NET and CBT studies.

The review has some limitations. A limited number of studies were included, with a relatively low total number of patients contributing to the primary analysis. It should be acknowledged, however, that conducting research with refugees and asylum seekers is challenging, as potential participants may have limited command of the language of the host country, which complicates psychological treatments and obtaining informed consent for participating in research. Moreover, potential participants may not fully understand the health care system, the rules governing research and the reasons for being offered both a psychosocial intervention and participation in a research trial. It would have been possible to follow a narrative rather than quantitative description of the evidence base, but we argue that the pooling process had several merits, including the possibility of detecting and quantifying between-study heterogeneity, which was then further investigated by means of subgroup analyses, and that of increasing the power of some comparisons. Another limitation is that the included studies differed with respect to country of origin, time since resettlement, year and country of study publication, outcome measures, content and modalities of delivering psychosocial interventions. This may explain statistical heterogeneity when all studies were pooled together. However, heterogeneity was decreased in some subgroup analyses. For example, the effectiveness of NET was supported by five RCTs showing a relatively large effect with reasonably low heterogeneity. In addition, we were not able to conduct subgroup analyses to investigate the role of some clinically important variables, such as the time since resettlement, as this information was not systematically reported, and the modality of delivering the intervention (individual versus group), as only one study on CROP and one on TFP used a group treatment format. We also cannot rule out the possibility that publication bias might have inflated the overall magnitude of treatment effect.

In terms of implications for practice and research, this review summarises the effectiveness of psychosocial interventions for PTSD in refugees in the context of high-income countries, and therefore provides an evidence base to inform decisions in clinical practice and in policy making. Overall, the review may be used to underpin calls for the provision of psychosocial treatments for refugees with PTSD, particularly CBT treatments with a trauma focus. This is also the case for refugees with PTSD and comorbid disorders, which is frequently reported. Yet, the provision of psychosocial interventions requires resources for the organisation of
treatments, while refugees are in challenging contexts, as well as the staff time needed for the treatment sessions, training and supervision. Whether the expected benefits of psychosocial interventions outweigh the associated costs may depend on context factors and local standards of routine mental health care for refugees and asylum seekers. Furthermore, there is consensus amongst humanitarian agencies that specialized treatments for conflict-affected populations need to be integrated in a multi-layered and multi-sectoral system of care, which caters for the diverse mental health needs of refugees—including but not limited to PTSD [52–56].

The current evidence base needs to be expanded with more rigorous trials focusing on a wider range of mental health disorders. New studies will be essential to address several clinical aspects that have not yet been investigated. This includes longer-term studies to establish whether benefits are maintained over the time or even only materialise after some time, and comparative studies to test whether the effectiveness of psychosocial treatments differs between different groups, as treating newly arrived refugees might be different from treating already resettled people. Future research should also explore how interventions might be adapted based on refugees’ understanding of traumatic experiences and psychosocial distress. Finally, head-to-head studies may assess the comparative cost-effectiveness of different psychosocial interventions.

Supporting information

S1 Table. PRISMA checklist.
(DOCX)

S2 Table. Search strategy.
(DOCX)

S3 Table. Definitions.
(DOCX)

S4 Table. References to excluded studies with reasons.
(DOCX)

S5 Table. Description of psychosocial interventions.
(DOCX)

S6 Table. Risk of bias: review authors’ judgements about each risk of bias item for each included study.
(DOCX)

S7 Table. GRADE summary of findings table.
(DOCX)

S1 Fig. Publication bias.
(DOCX)

S2 Fig. Impact of each study on the pooled effect (sensitivity analysis): consecutively removal of each study as a possible outlier to test what the impact is on the combined effect.
(DOCX)

S3 Fig. Forest plot of secondary outcomes not reported in the main report.
(DOCX)

S4 Fig. Forest plot of subgroup analysis–PTSD symptoms.
(DOCX)
S5 Fig. Unrestricted maximum likelihood random effects meta-regression analysis investigating the association between number of sessions and effect size (Hedges’s g).

(DOCX)

S6 Fig. Unrestricted maximum likelihood random effects meta-regression analysis investigating the association between length of follow-up and effect size (Hedges’s g).

(DOCX)

S7 Fig. Forest plot of subgroup analysis–Depressive symptoms.

(DOCX)

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References
1. UNHCR. Global trends. Forced displacement in 2015. Geneva: United Nations High Commissioners for Refugees; 2016.
2. Eurostat Press Office. EU Member States granted protection to more than 330 000 asylum seekers in 2015. Available from: http://ec.europa.eu/eurostat/documents/2995521/7233417/3-20042016-AP-EN.pdf/34c4f5af-eb93-4ecd-984c-577a5271c8c5
3. Hargreaves S. A body of evidence: torture among asylum seekers to the West. Lancet 2002; 359: 793–4. doi: 10.1016/S0140-6736(02)07889-1 PMID: 11888611
4. Hollifield M, Warner TD, Lian N, Krakow B, Jenkins JH, Kesler J, et al. Measuring trauma and health status in refugees: a critical review. JAMA 2002; 288: 611–21. PMID: 12150673
5. Ke Miller, Kulkarni M, Kushner H. Beyond trauma-focused psychiatric epidemiology: bridging research and practice with war-affected populations. Am J Orthopsychiatry 2006; 76: 409–22. doi: 10.1037/0002-9432.76.4.409 PMID: 17209709
6. Ellis BH, Macdonald HZ, Klunk-Gillis J, Lincoln A, Struinin L, Cabral HJ. Discrimination and mental health among Somali refugee adolescents: the role of acculturation and gender. Am J Orthopsychiatry 2010; 80: 564–75. doi: 10.1111/j.1939-0025.2010.01061.x PMID: 20950297
7. Ellis BH, Macdonald HZ, Lincoln AK, Cabral HJ. Mental health of Somali adolescent refugees: the role of trauma, stress, and perceived discrimination. J Consult Clin Psychol 2008; 76: 184–93. doi: 10.1037/0022-006X.76.2.184 PMID: 18377116
8. Fazel M, Wheeler J, Danesh J. Prevalence of serious mental disorder in 7000 refugees resettled in western countries: a systematic review. Lancet 2005; 365: 1309–14. doi: 10.1016/S0140-6736(05)61027-6 PMID: 15823380
9. Bogic M, Njoku A, Priebe S. Long-term mental health of war-refugees: a systematic literature review. BMC Int Health Hum Rights 2015; 15: 29. doi: 10.1186/s12914-015-0064-9 PMID: 26510473

10. Slew a-Younan S, Uribe Guajardo MG, Heriaseanu A, Hasan T. A Systematic Review of Post-traumatic Stress Disorder and Depression Amongst Iraqi Refugees Located in Western Countries. J Immigr Minor Health 2015; 17: 1231–9. doi: 10.1007/s10903-014-0046-3 PMID: 24899586

11. Yaser A, Slew a-Younan S, Smith CA, Olson RE, Guajardo MG, Mond J. Beliefs and knowledge about post-traumatic stress disorder amongst resettled Afghan refugees in Australia. Int J Ment Health Syst 2016; 10: 31. doi: 10.1186/s13033-016-0065-7 PMID: 27073412

12. Robertson CL, Savik K, Mathiasson-Moore M, Mohammed A, Hoffman S. Modeling Psychological Functioning in Refugees. J Am Psychiatr Nurses Assoc 2016; in press.

13. Schick M, Zunwald A, Knopfl B, Nickerson A, Bryant RA, Schnyder U, et al. Challenging future, challenging past: the relationship of social integration and psychological impairment in traumatized refugees. Eur J Psychotraumatol 2016; 7: 28057. doi: 10.3402/ejpt.v7.28057 PMID: 26886484

14. Uribe Guajardo MG, Slew a-Younan S, Smith M, Eagar S, Stone G. Psychological distress is influenced by length of stay in resettled Iraqi refugees in Australia. Int J Ment Health Syst 2016; 10: 4. doi: 10.1186/s13033-016-0036-z PMID: 26793271

15. Ullmann E, Barthel A, Tache S, Bornstein A, Licinio J, Bornstein SR. Emotional and psychological trauma in refugees arriving in Germany in 2015. Mol Psychiatry 2015; 20: 1483–4. doi: 10.1038/mp.2015.164 PMID: 26527128

16. Priebe S, Gavrilovic J, Bremner S, Ajdukovic D, Franciskovic T, Neri G, et al. Course of post-traumatic stress disorder following war in the Balkans: 1-year follow-up study. Psychol Med 2013; 43: 1837–47. doi: 10.1017/S0033291712002681 PMID: 23190477

17. Priebe S, Jankovic Gj, Bremner S, Ajdukovic D, Franciskovic T, Galeazzi GM, et al. Psychological symptoms as long-term consequences of war experiences. Psychopathology 2013; 46: 45–54. doi: 10.1159/000338640 PMID: 22890384

18. Sandhu S, Bjerre NV, Dauvrin M, Dias S, Gaddini A, Greacen T, et al. Experiences with treating immigrants: a qualitative study in mental health services across 16 European countries. Soc Psychiatry Psychiatr Epidemiol 2013; 48: 105–16. doi: 10.1007/s00127-012-0528-3 PMID: 22714866

19. Crumlish N, O’rourke K. A systematic review of treatments for post-traumatic stress disorder among refugees and asylum-seekers. J Nerv Ment Dis 2010; 198: 237–51. doi: 10.1097/NMD.0b013e3181d61258 PMID: 20386252

20. Lambert JE, Alhassoon OM. Trauma-focused therapy for refugees: A critical review of psychological health and well-being of torture survivors. Cochrane Database Syst Rev 2014; 11: CD009317.

21. Higgins JP, Green S. Cochrane Handbook for systematic reviews of interventions Version 5.1.0. The Cochrane Collaboration. Available from www.cochrane-handbook.org

22. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009; 339: b2535. doi: 10.1136/bmj.b2535 PMID: 19622551

23. Barbui C. Sharing all types of clinical data and harmonizing journal standards. BMC Med 2016; 14: 63. doi: 10.1186/s12916-016-0612-8 PMID: 27038634

24. Barbui C, Gureje O, Puschner B, Patten S, Thornicroft G. Implementing a data sharing culture. Epilemiol Psychiatr Sci 2016; in press.

25. Nickerson A, Bryant RA, Silove D, Steel Z. A critical review of psychological treatments of posttraumatic stress disorder in refugees. Mental Health Review J 2017; 22: 6–23. doi: 10.1002/mhj.1245 PMID: 28004106
33. Ostuzzi G, Benda L, Costa E, Barbui C. Efficacy and acceptability of antidepressants on the continuum of depressive experiences in patients with cancer: Systematic review and meta-analysis. Cancer Treat Rev 2015; 41: 714–24. doi: 10.1016/j.ctrv.2015.06.003 PMID: 26118318

34. Sijbrandij M, Kleiboer A, Bisson JI, Barbui C, Cuijpers P. Pharmacological prevention of post-traumatic stress disorder and acute stress disorder: a systematic review and meta-analysis. Lancet Psychiatry 2015; 2: 413–21. doi: 10.1016/S2215-0366(14)00121-7 PMID: 26360285

35. Guyat G, Ooxman Ad, Aki Ea, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction- GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011; 64: 383–94. doi: 10.1016/j.jclinepi.2010.04.026 PMID: 21195583

36. Barbui C, Dua T, Van Ommeren M, Yasamy M, Fleischmann A, Clark N, et al. Challenges in Developing Evidence-Based Recommendations Using the GRADE Approach: The Case of Mental, Neurological, and Substance Use Disorders. Plos Med 2010; 7(8): e1000322. doi: 10.1371/journal.pmed.1000322 PMID: 20824176

37. Barbui C, Dua T, Harper M, Tablante EC, Thornicroft G, Saxena S. Using GRADE to update WHO recommendations for MNS. Lancet Psychiatry 2015; 2: 1054–6. doi: 10.1016/S2215-0366(15)00456-3 PMID: 26613845

38. Adenauer H, Catani C, Gola H, Keil J, Ruf M, Schaue r M, et al. Narrative exposure therapy for PTSD increases top-down processing of aversive stimuli—evidence from a randomized controlled treatment trial. BMC Neurosci 2011; 12: 127. doi: 10.1186/1471-2202-12-127 PMID: 2218346

39. Buhmann CB, Nordentoft M, Ekstroem M, Carlsson J, Mortensen EL. The effect of flexible cognitive-behavioural therapy and medical treatment, including antidepressants on post-traumatic stress disorder and depression in traumatised refugees: pragmatic randomised controlled clinical trial. Br J Psychiatry 2016; 208: 252–9. doi: 10.1192/bjp.bp.115.150961 PMID: 26541687

40. Drožđek B, Bolwek N. Evaluation of group therapy with traumatized asylum seekers and refugees—the Den Bosch Model. Traumatology 2010; 16: 117–27.

41. Hijazi AM, Lumley MA, Ziaddi MS, Haddad L, Rapport LJ, Arnetz BB. Brief narrative exposure therapy for posttraumatic stress in Iraqi refugees: a preliminary randomized clinical study. J Trauma Stress 2014; 27: 314–22. doi: 10.1002/jts.21922 PMID: 24866253

42. Hinton DE, Chhean D, Pich V, Safren SA, Hofmann SG, Pollack MH. A randomized controlled trial of cognitive-behavior therapy for Cambodian refugees with treatment-resistant PTSD and panic attacks: a cross-over design. J Trauma Stress 2005; 18: 617–29. doi: 10.1023/B:JOTS.0000048956.03529.fa PMID: 15633922

43. Hinton DE, Pham T, Tran M, Safren SA, Otto MW, Pollack MH. CBT for Vietnamese refugees with treatment-resistant PTSD and panic attacks: a pilot study. J Trauma Stress 2004; 17: 429–33. doi: 10.1023/B: JOTS.0000048956.03529.fa PMID: 15633922

44. Kruse J, Joksimovic L, Cavka M, Woller W, Schmitz N. Effects of trauma-focused psychotherapy upon war refugees. J Trauma Stress 2009; 22: 585–92. doi: 10.1002/jts.20477 PMID: 19960519

45. Liedl A, Muller J, Morina N, Karl A, Denke C, Knaevelsrud C. Physical activity within a CBT intervention improves coping with pain in traumatized refugees: results of a randomized controlled design. Pain Med 2011; 12: 234–45. doi: 10.1111/j.1526-4637.2010.01040.x PMID: 21223501

46. Morath J, Gola H, Sommersho f A, Hamuni G, Kolassa S, Catani C, et al. The effect of trauma-focused therapy on the altered T cell distribution in individuals with PTSD: evidence from a randomized controlled trial. J Psychiatr Res 2014; 54: 1–10. doi: 10.1016/j.jpsychires.2014.03.016 PMID: 24726027

47. Neuner F, Kurreck S, Ruf M, Odenwald M, Elbert T, Schauer M. Can asylum-seekers with posttraumatic stress disorder be successfully treated? A randomized controlled pilot study. Cogn Behav Ther 2010; 39: 81–91. doi: 10.1080/16506070903121042 PMID: 19816834

48. Otto MW, Hinton D, Korbly NB, Chea A, Ba P, Gershuny BS, et al. Treatment of pharmaco therapy-refractory posttraumatic stress disorder among Cambodian refugees: a pilot study of combination treatment with cognitive-behavior therapy vs sertraline alone. Behav Res Ther 2003; 41: 1271–6. PMID: 14527527

49. Renner W, B-He, Peltzer K. Culture-Sensitive and Resource Oriented Peer (CROP) - Groups as a community based intervention for trauma survivors: A randomized controlled pilot study with refugees and asylum seekers from Chechnya. Australasian Journal of Disaster and Trauma Studies 2011; 1: 1–13.

50. Stenmark H, Catani C, Neuner F, Elbert T, Holen A. Treating PTSD in refugees and asylum seekers within the general health care system. A randomized controlled multicenter study. Behav Res Ther 2013; 51: 641–7. doi: 10.1016/j.brat.2013.07.002 PMID: 23916633

51. Weine S, Kulauzovic Y, Klebic A, Besic S, Mujagic A, Muzurovic, et al. Evaluating a multiple-family group access intervention for refugees with PTSD. J Marital Fam Ther 2008; 34: 149–64. doi: 10.1111/ j.1752-0606.2008.00061.x PMID: 18412823
52. Inter-Agency Standing Committee (IASC): IASC Guidelines on Mental Health and Psychosocial Support in Emergency Settings. Geneva, IASC 2007.

53. Tol WA, Purgato M, Bass JK, Galappatti A, Eaton W. Mental health and psychosocial support in humanitarian settings: a public mental health perspective. Epidemiol Psychiatr Sci 2015; 24: 484–94. doi: 10.1017/S2045796015000827 PMID: 26399635

54. Szabo CP. A public mental health approach in humanitarian settings is worthy of consideration, with evidence. Epidemiol Psychiatr Sci 2015; 24: 498–9. doi: 10.1017/S2045796015000839 PMID: 26427932

55. Raphael B. Disaster, hope, help, reality. Epidemiol Psychiatr Sci 2015; 24: 500–2. doi: 10.1017/S204579601500075X PMID: 26349932

56. Wessells M. A reflection on the strengths and limits of a public health approach to mental health in humanitarian settings. Epidemiol Psychiatr Sci 2015; 24: 495–7. doi: 10.1017/S204579601500058X PMID: 26349769