Short title: Interventions in survivors of mass violence

Meta-analysis of interventions for post-traumatic stress disorder and depression in adult survivors of mass violence in low- and middle-income countries

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CONFLICT OF INTEREST

The authors report no conflicts of interest. This meta-analysis was supported by a fellowship from the Netherlands Institute for Advanced Study (NIAS) given to N.M. The NIAS had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication.

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1002/da.22618](https://doi.org/10.1002/da.22618).

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Abstract

Background: Most survivors of mass violence live in low- and middle-income countries (LMICs). We conducted a meta-analysis of randomized controlled psychotherapy trials for adult post-traumatic stress disorder (PTSD) and/or depression in LMICs. **Methods:** We included eighteen clinical trials (3058 participants), in which 25 and 18 treatment arms measured symptoms of PTSD and depression, respectively. **Results:** Active treatments for PTSD yielded a large aggregated pre-post effect size ($g = 1.29$; 95% CI = [0.99; 1.59]) and a small to medium effect size at post-treatment when compared to control conditions ($g = 0.39$; 95% CI = [0.24; 0.55]). Effect sizes were similar for pre-treatment vs follow-up ($g = 1.75$; 95% CI = [1.17; 2.32]) and in comparison to waitlist at follow-up ($g = 0.93$; 95% CI = [0.56; 1.31]). Active treatments for depression produced large pre-post ($g = 1.28$; 95% CI = [0.96; 1.61]) and controlled effect sizes (post-treatment, comparison to control conditions, $g = 0.86$; 95% CI = [0.54; 1.18]). **Conclusions:** Our findings suggest that psychological interventions can effectively reduce symptoms of PTSD and depression in LMICs. Future research needs to focus on cost-effective interventions that are likely to be disseminated to the large numbers of war survivors in LMICs.

Keywords: PTSD, depression, clinical trials, treatment, meta-analysis

Most research on the effect of war-related traumatic experiences on mental health as well as potential efficacy of treatment has been conducted with war combat veterans and refugees living in Western countries. However, civilian war survivors make up the absolute majority of war casualties

(Bartov, 2000) and the overwhelming majority of civilian war survivors live in low- and middle-income countries (LMICs). Furthermore, current open conflicts (Pettersson & Wallensteen, 2015) are leading to a continuously increasing number of individuals affected by mass violence. Epidemiological studies have documented high prevalence of post-traumatic stress disorder (PTSD) and depression in war-affected communities (de Jong et al., 2001; Priebe et al., 2010; Steel et al., 2009). Both PTSD and depression can become chronic if untreated and contribute significantly to the global burden of disease (Kessler, 2012; Morina, Wicherts, Lobbrecht, & Priebe, 2014; Sabes-Figuera et al., 2012).

Research in Western countries suggests that psychological interventions can successfully be used to treat PTSD and associated symptoms (Bisson, Roberts, Andrew, Cooper, & Lewis, 2013; Ehrling et al., 2014). Yet, significant challenges hinder implementing evidence-based interventions in LMICs. These include insufficient mental health services, barriers in adapting established interventions to the needs of LMICs contexts, and inadequately qualified practitioners to deliver interventions (Morina, Rushiti, Salihu, & Ford, 2010). To date, several controlled trials of psychological interventions for PTSD and associated symptoms (mostly depression) have been carried out in LMICs. There is an urgent need to consider the aggregated results of these various trials by conducting a meta-analytic review of the efficacy of these interventions. Tol et al. (2011) conducted a meta-analysis of psychosocial support for survivors of natural disasters, technological disasters, or armed conflicts in LMICs. The seven randomized controlled trials (RCTs) with adult participants included in this meta-analysis produced an aggregated effect size of 0,38 as compared to control conditions. There are several factors, however, that limit the generalizability of these findings to war survivors in LMIC. First, two of the included clinical trials were conducted with earthquake survivors rather than survivors of mass violence. Furthermore, one of the trials with war survivors (Dybdahl, 2001) had examined the efficacy of a psychosocial intervention program for

patients in an ongoing medical care program, which makes conclusions about the sole efficacy of the psychosocial intervention rather difficult. Overall, Tol et al. concluded that a number of the included trials had serious limitations in study design. More recently, Weiss et al. (2016) published a review of the literature on clinical trials with survivors of torture and other systematic violence. Based on this review that included trials with different study designs, cognitive behavior interventions produce the highest treatment outcome among individuals with PTSD and/or depression. Furthermore, the authors concluded that the quality of reporting of RCTs was generally good, whereas publications on other forms of clinical trials showed poor quality of documentation. Weiss et al., however, did not apply meta-analytic means to measure the efficacy of interventions and did not specifically focus on LMICs. There is a need for an updated systematic review of the efficacy of these interventions to determine their actual treatment efficacy. The current meta-analysis will include several randomized controlled trials on the efficacy of psychological interventions for adult survivors of war that have been published in the interim. We surveyed the published literature on psychological interventions for adults in LMICs and assessed the extent through meta-analysis of the effects of psychological interventions on PTSD and depression symptoms. On the basis that comparable psychological interventions have achieved moderate-strong effects in developed contexts, we expected that psychological interventions would achieve medium to large effect sizes for PTSD and depression symptom severity in LMICs as well.

Method

Following the recommendations by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) group (Moher, Liberati, Tetzlaff, Altman, & PRISMA Grp, 2009), we defined the main structured research question describing the Population, Intervention, Comparison, Outcome, and Study design (PICOS) as “In adults with PTSD and/or depression (P), does psychological

treatment (I), compared to control conditions (C), improve PTSD and/or depression symptoms (O) in randomized controlled trials (S)?”.

Literature Search Strategy

Studies meeting the following inclusion criteria were selected for the meta-analysis: 1) the study was conducted in a LMIC with survivors of mass violence older than 17 years who sought treatment for PTSD and/or depression complaints, 2) participants were randomly assigned to treatment conditions, 3) at least 10 participants completed an active psychological treatment with the aim of reducing PTSD or depression, or both. No restrictions were made regarding intervention format, publication type, or publication language. If studies did not provide sufficient data for performing the meta-analysis, the authors were contacted by e-mail to retrieve these data. After two contact-attempts, the publications were excluded if the authors did not respond with sufficient data to perform the meta-analysis.

We searched the following databases: PsycINFO, MEDLINE, and PILOTS up to November 1 2016. The following search terms in keywords, titles, and abstracts were used: *posttraumatic stress or PTSD or PTSS or depress* or MDD AND genocide or war* or prisoners of war or mass violence or mass conflict* or post-conflict* or political conflict* or armed conflict* or ethnic cleansing or terrorism or torture or persecution or civilian* AND treatment* or intervention* or therapy or psychotherapy or exposure or trial*. To retrieve additional publications, reference lists of identified publications and systematic reviews were examined.

Coding of Studies

The publications were coded by the first and the second authors. From each publication, the following study, intervention and participant characteristics were coded and extracted: main

treatment target (PTSD or depression or both), number of participants, comparison group(s), type of outcome measure used (i.e., self-report measurement or structured interview), intervention format (i.e., individual or group), type of intervention, number of sessions, country, and gender. If reported, scores of general function impairment were also coded and extracted. The pre-, post-, and follow-up assessment mean and standard deviation scores and/or mean and standard deviation change scores for each outcome measure also were recorded. If mean age or gender-proportions were not reported separately for each condition, the reported average data was used for all conditions.

Quality Assessment

Two raters independently rated the quality of the included trials by using the Cochrane Collaboration's tool for assessing risk of bias. Specifically, we evaluated 1) selection bias (random sequence generation and allocation concealment), 2) detection bias, 3) attrition bias, 4) reporting bias, and 5) other sources of bias (Higgins, Altman, & Sterne, 2011). We classified risk of bias in each domain as low, high, or unclear.

Coding of treatment characteristics.

Treatment characteristics were first coded as either *active treatment* or *control group*. Second, active treatments were subdivided into *trauma-focused cognitive-behavior therapy* (CBT; treatments focusing on the memory of the trauma and/or its meaning; see also Bisson et al., 2013), or other active conditions. The other conditions were: *interpersonal psychotherapy*, *eye movement desensitization and reprocessing*, *behavioral activation treatment for depression*, *multidisciplinary treatment* (treatments including intervention techniques from different therapeutic approaches), *common elements treatment approach*, *dialogical exposure*, and *thought field therapy*. Control conditions were subdivided into *supportive counseling*, *psychoeducation*, or *waitlist/non-active*

control. Third, all active treatments were divided based on whether they were delivered as individual or group treatment.

Statistical Analysis

Given the limited number of trials meeting our criteria and accordingly the limited number of controlled trials, we found it informative to first compute within group effect sizes for the impact of treatment on PTSD symptomatology (i.e., change from pre- to post-treatment and follow-up, respectively). However, as uncontrolled effect sizes do not account for the impact of time on symptoms, we view controlled effect sizes as more reliable when it comes to assessing treatment efficacy. We used data resulting from intent-to-treat (ITT) samples when available (14 publications in total) and data from completer samples if ITT samples were not provided (four publications in total). For uncontrolled effect sizes, the post-treatment or follow-up mean was subtracted from the pre-treatment mean and for controlled effect sizes the control group mean was subtracted from the treatment group mean at post-treatment or follow-up, respectively, and divided by the pooled standard deviation. Subsequently, to obtain the effect size Hedges's g the outcome was multiplied by a sample size correction factor $J = 1 - (3/(4df - 1))$ (Lipsey & Wilson, 2001). Subgroup analyses were conducted if a specific group of interventions consisted of four or more trials. Analyses were completed with comprehensive meta-analysis (CMA; version 3, Borenstein, Hedges, Higgins, & Rothstein, 2009). Furthermore, we used random effects model to calculate effect sizes given the heterogeneity of the studies (Field & Gillett, 2010). Effect sizes g may be conservatively interpreted with Cohen's convention of small (0.2), medium (0.5) and large (0.8) effects (Cohen, 1988). As a test of homogeneity of effect sizes, we calculated the Q-statistic and the I^2 -statistic that is an indicator of heterogeneity in percentages, with higher percentages indicating high heterogeneity.

We evaluated the risk of publication bias by examining the relation between effect- and sample size with relatively higher effect sizes of smaller studies being an indicator for publication bias. We assessed this for the primary outcome measures through visual inspection of the funnel plot and the calculation of the likely number of missing studies using the trim-and fill procedure (Duval & Tweedie, 2000). This procedure yields an estimate of the effect size after publication bias has been taken into account (as implemented in CMA) by calculating adjusted values of the mean pooled effect size and 95%-confidence interval. In this procedure, we used the random effects model too. We examined publication bias only if an analysis consisted of ten or more trials as suggested by Sterne et al. (2011).

Results

Study characteristics

A total of 18 clinical trials met our criteria and could be included into the meta-analysis (see Fig. 1 and Table 1). All publications were published in peer-reviewed journals. Seventeen of the trials assessed PTSD and 13 trials assessed depression. Of the 12 trials assessing symptoms of both PTSD and depression, seven trials had focused on both PTSD and depression (Acarturk et al., 2016; Acarturk et al., 2015; J. Bass et al., 2016; J. K. Bass et al., 2013; Bolton, Lee et al., 2014; Meffert et al., 2014; Weiss et al., 2015), four reported treatment of PTSD as the major focus and additionally measured the efficacy of the intervention for depression among individuals with PTSD (Bryant et al., 2011; Connolly & Sakai, 2011; Hagl, Powell, Rosner, & Butollo, 2015; Knaevelsrud, Brand, Lange, Ruwaard, & Wagner, 2015), and one reported treatment of depression as the main focus and assessed symptoms of PTSD as secondary outcome (Bolton, Bass et al., 2014). Five trials assessed PTSD only (Igreja, Kleijn, Schreuder, Van Dijk, & Verschuur, 2004; Jacob, Neuner, Maedl, Schaal, &

Elbert, 2014; Neuner et al., 2008; Neuner, Schauer, Klaschik, Karunakara, & Elbert, 2004; Yeomans, Forman, Herbert, & Yuen, 2010), whereas one trial assessed depression only (Bolton et al., 2003).

In total, 2124 treated participants and 934 participants in the wait-list condition were included in the analyses. In the 18 trials, 25 and 18 treatment arms measured symptoms of PTSD and depression, respectively. Furthermore, active treatments were compared to waitlist groups 15 and 12 times regarding PTSD and depression symptoms, respectively. The number of participants per condition varied from 11 to 248, with a mean of 78.67 ($SD = 61.92$). The mean age of participants was 36.71 years ($SD = 10.76$), and 84.03% of them were female.

Both structured clinical interviews and self-reports were used as primary outcome measures. With regard to the 17 trials assessing PTSD, structured clinical interviews were used in two trials only and self-reports in the remaining trials. However, self-reports were administered thirteen times as interviews rather than completed by the participants themselves. For the assessment of depression, only self-reports were used, administered as interviews in nine trials and filled out by the participant in three trials (see Table 1).

In total, nine and three of the publications reported how many participants fulfilled diagnostic criteria for PTSD and depression at pre-assessment, respectively. With regard to PTSD, six trials reported that all participants had PTSD at pre-assessment and three studies reported prevalence of PTSD between 60 and 94% (see Table 1). With regard to depression, the reported prevalence among the three studies in question ranged between 71 and 98%.

The number of sessions ranged from one to 16 ($M = 9.74$, $SD = 7.55$). In one trial, however, three full-day workshops were offered, with a one-day follow-up workshop offered one month later (Yeomans et al., 2010). Most of the studies applied an individual intervention setting rather than a group intervention setting ($k = 14$ and four, respectively).

Follow-up assessments ranged from 1 to 24 months. Given the limited number of included trials, all follow-up assessments regardless of the time of assessment were entered as one group in the meta-analysis. Seventeen publications reported on the number of clients dropping out of treatment. Drop-out percentages ranged from 0 (Bryant et al., 2011) to 40.5% (Knaevelsrud et al., 2015) and had an average of 11.5%. Twelve publications reported the amount of training in days given to individuals who conducted the treatment that ranged from one (Yeomans et al., 2010) to 30 days of training (Neuner et al., 2008) and had an average of nine days. In one additional publication it was reported that therapists participated in six therapy demonstration sessions with a client suffering from PTSD (Jacob et al., 2014).

Treatment Effects on PTSD Symptomatology

Pre-post effect sizes. Across all active interventions ($k = 16$), a large pre-post effect size was found, $g = 1.29$; 95% CI = [0.99; 1.59], see Fig. 2 for a forest plot. Change from pre-treatment to follow-up resulted in a large effect size across active treatments, $g = 1.75$, 95% CI = [1.17; 2.32], $k = 14$.

Controlled effect sizes. The average between-group effect size comparing active treatments versus control conditions at post-treatment ($k = 15$) was small to medium, $g = 0.39$; 95% CI = [0.249; 0.55], see Fig. 3 for a forest plot. The comparison between active conditions with waitlist only ($k = 10$) produced a small to medium effect size, $g = 0.37$; 95% CI = [0.18; 0.57]. The average between-group effect size comparing active treatments versus control conditions at follow-up was large, $g = 0.93$; 95% CI = [0.56; 1.31], $k = 10$.

Treatment Effects on Depressive Symptomatology

Pre-post effect sizes. Across all interventions ($k = 11$), a large pre-post effect size was found, $g = 1.28$; 95% CI = [0.96; 1.61], see Fig. 2 for a forest plot. Uncontrolled effect sizes for changes in depression from pre-treatment to follow-up showed a large pre-follow-up-effect size, $g = 1.56$, 95% CI = [0.94; 2.18], $k = 8$.

Controlled effect sizes. The aggregated between-group effect size comparing active treatments versus control conditions at post-treatment ($k = 11$) was large, $g = 0.86$; 95% CI = [0.54; 1.18], see Fig. 3 for a forest plot. The comparison between active conditions with waitlist only ($k = 8$) produced a large effect size, $g = 0.86$; 95% CI = [0.46; 1.25]. The average between-group effect size comparing active treatments versus control conditions at follow-up was medium to large, $g = 0.90$; 95% CI = [0.49; 1.33], $k = 5$.

Heterogeneity. Heterogeneity was large for within-group effect sizes (PTSD: $I^2 = 92.03$; $Q = 188.36$, $df = 15$, $p < .001$; depression: $I^2 = 90.74$; $Q = 108.03$, $df = 10$, $p < .001$). Heterogeneity was further significant for between-group effect sizes for PTSD ($I^2 = 44.31$; $Q = 24.14$, $df = 14$, $p = .03$) and depression ($I^2 = 85.50$; $Q = 68.98$, $df = 10$, $p < .001$). Accordingly, the results indicate substantial heterogeneity in effect sizes between studies. Table 2 shows the average effect sizes for the different groups of treatment included.

Effect of Treatments on Associated Symptomatology

Six publications reported the effect of treatment on functional impairment. Across all interventions, large pre-post and pre-follow-up effect sizes were found, $g = 0.73$; 95% CI = [0.52; 0.98] and $g = 0.91$; 95% CI = [0.71; 1.11]. The aggregated between-group effect size comparing active treatments versus control conditions at post-treatment ($k = 4$) was medium, $g = 0.59$; 95% CI = [0.24; 0.93]. Three publications only reported on the effect of treatment on functional impairment at follow-up.

Publication Bias

The inspection of the funnel plot depicting the uncontrolled effect sizes (pre- vs. post-treatment) for both PTSD and depression suggested the presence of asymmetry as the direction of the effect of the smaller trials was toward the right. This indicates that nonsignificant trials might not have been published. Duval and Tweedie's (2000) trim-and-fill procedure identified three and five studies to be missing regarding the uncontrolled effect sizes for PTSD and depression, respectively. The produced imputed point estimates resulting from the analysis was 1.08 95% CI = [0.77; 1.39] and 0.85 95% CI = [0.49; 1.22], respectively. With regard to controlled effect sizes (active treatments vs. control conditions) at post-treatment, the inspection of the funnel plots did not suggest the presence of asymmetry for neither PTSD nor depression. This was supported by Duval and Tweedie's trim-and-fill procedure that suggested that no studies were missing.

Risk of Bias in included trials

The Intraclass Correlation Coefficient (ICC) of the total score for all studies combined was 0.81, 95% CI [0.72, 0.87], indicating good inter-rater reliability. The majority of the trials were rated as having low risk of bias in the domains other sources of bias (k = 16), attrition bias (k = 14), random sequence generation (k = 13), and detection bias (k = 12). The number of trials rated as having high or unknown risk in the specific domains were as follows: random sequence generation (k = five trials), allocation concealment (k = eleven trials), detection bias (k = six trials), attrition bias (k = four trials), reporting bias (k = nine trials). Altogether, the risk of bias was rated as low in 49% of cases. The trials did not differ substantially on risk of bias and therefore this variable was not included in sub-analyses.

Discussion

The results of this meta-analysis indicate that psychological interventions can effectively reduce symptoms of PTSD and depression among survivors of war in LMICs. The efficacy of treatments was observed in both controlled effect sizes as well as pre-post effect sizes. Yet, controlled effect sizes for PTSD (i.e., when active treatment conditions were compared to control conditions) produced small to medium effect sizes only.

Given the urgent public health issues raised by escalating levels of violence and civil conflict in LMICs, it is essential for government and non-government agencies to have the most reliable evidence to shape policy and practice. The most important lesson to emerge from this analysis is that evidence-based psychological treatments resulted in moderate to large effect sizes. Within analyses revealed that the effect sizes for both PTSD and depression were higher than 1.25 at post-treatment as well as at follow-up. This means that about 90% of patients at post-treatment or at follow-up had less symptoms of PTSD and depression than the mean of the group at pre-treatment. The comparison of active treatments to passive treatments at post assessment revealed that the PTSD and depression scores of the average person in the experimental group were lower than the scores of 66% and 80% of the control group, respectively. With regards to functional impairment, more than 70% of patients in the active treatment group reported lower functional impairment at post-assessment than the average patient in the control group. This suggests that those treatments that have been shown to work effectively in developed countries also demonstrate efficacy when applied to treating the mental health needs in LMICs. Interestingly, similar results were also reported in a recently published meta-analysis on the efficacy of psychological interventions for PTSD and depression in children and adolescents who had survived mass violence in LMICs (Morina, Malek, Nickerson, and Bryant, in press).

It is commonly proposed that the treatment of choice in developed countries for individuals affected by trauma is trauma-focused psychotherapy, which typically involves strategies that address memories of the traumatic experience (Ehlers et al., 2010). In our meta-analysis, CBT treatments that focused on the trauma produced a large pre-post effect size. Yet, the other interventions produced similar results and the number of trials was rather too small to allow meta-analytic conclusions about the efficacy of trauma-focused CBT interventions relative to other forms of interventions. This topic is frequently debated in global mental health: should treatment focus on past traumatic experiences or address more immediate problems of current adversity, which is commonly experienced in LMICs (Hubbard & Pearson, 2004). It is proposed that mass violence does not simply result in psychopathology emanating from the stress of war-related stressors but is also strongly affected by the subsequent social upheaval, poverty, marginalization, lack of infrastructure, and overcrowding (Miller & Rasmussen, 2010). Supporting this view is much evidence that ongoing stressors have a significant impact on the mental health of survivors of war and conflict (de Jong et al., 2001; Lev-Wiesel, Al-Krenawi, & Sehwal, 2007; Miller, Omidian, Rasmussen, Yaqubi, & Daudzai, 2008; Rasmussen et al., 2010). On the basis of the currently reviewed studies, there is indication that both approaches may effectively reduce PTSD symptoms. Yet, more research is needed to draw more reliable conclusions.

Notably the effect sizes for depression in this meta-analysis were large, both at posttreatment and follow-up. This is somewhat surprising because a significant proportion of the trials were specifically designed to address PTSD rather than depression. There is considerable evidence that psychological interventions that are trauma-focused do have marked secondary effects on depression (Bryant et al., 2008; Ehlers et al., 2014). This is an important benefit of psychological treatments in LMICS affected by mass violence because depression represents a very common condition in these settings and contributes markedly to burden of disease (Morina et al., 2013; Patel, 2007).

Controlled effect-sizes from the included trials in this meta-analysis resulted mainly from comparing active treatments to waitlist groups. The importance of wait list conditions is usually dismissed because they are often regarded as a null intervention that serves as a low reference against which the active treatments can be compared. Put another way, there is convergent opinion that measuring an active treatment against a wait list may inflate the effect size of the active treatment (Cunningham, Kypri, & McCambridge, 2013; Mohr et al., 2009). Despite this opinion, it is worth noting that previous reviews of treatments of different conditions have reported reductions in distress after being placed on a wait list (Deville & McFarlane, 2009; Hesser, Weise, Rief, & Andersson, 2011). The exact mechanism for this improvement is not well specified, although there is evidence that receiving assessments can bring about considerable therapeutic change to people (Poston & Hanson, 2010). In any case, one interpretation of this finding is that assessing war survivors in LMICs may be a cost-effective way of achieving some level of symptom reduction.

Although the conclusion for this study can be construed positively insofar as psychological treatments are moderately effective, we note some serious limitations to the treatments that have been subjected to controlled evaluation. First, only five studies required PTSD diagnosis as an entry criterion for all participants, and so it is difficult to ascertain the level of PTSD severity that the trials targeted. Second, four out of 14 trials reported treatment completer data and the remainder reported intent-to-treat analyses; this heterogeneity in handling missing values raises difficulties in interpretation of results for a meta-analysis. Third, only two of the studies used a structured clinical interview, and of the 16 others that used self-report measures of PTSD twelve of them administered these as interviews; this variability in assessment by interview and self-report potentially raises more heterogeneity in response as a result of measurement artifact.

We also note some limitations with our meta-analysis. Although the analysis is based on a systematic review of all published studies of psychological treatments of adults affected by mass violence, the actual number of studies is relatively small. One consequence of this is that it is difficult to conduct sub-analyses of different groups because there are insufficient numbers of studies representative of these subgroups. We also note the range of measures employed across a large number of LMICs. There has been much debate over the years concerning the difficulties in presuming that psychological measures maintain consistent validity in different cultural contexts (Kohrt et al., 2014). A meta-analysis cannot accommodate the cultural variability of measurement tools since it reduces each result to an effect size, however we do note the limited cross-cultural validity of certain measures of PTSD. Finally, we recognize that the focus in this analysis on PTSD ignores other important constructs in post-conflict settings. We were able to locate only four measures of functioning and a higher number of trials assessing this variable would be another important indicator of the success of psychological interventions.

Although this meta-analysis indicates that evidence-based interventions with proven efficacy in developed countries are also able to be efficacious in LMICs, there is a need for caution when considering the capacity of these interventions to be implemented in such settings. Across the studies reported in this analysis, the mean number of treatment sessions prescribed by the treatment protocols was 10 sessions. This is a critical issue because many evidence-based interventions require a substantive commitment to attend the treatment program. This can be a significant barrier in LMICs because of difficulties for transportation to the site of intervention, civil conflict disrupting treatment access, or priority being given to more immediate needs (e.g. working to assist family income, Dawson et al., 2015). Second, many of the studies required considerable training of the providers of the treatment, as well as sustained supervision, in order to ensure that the intervention was delivered adequately (Neuner et al., 2008). Most settings affected by trauma

are not adequately resourced by mental health services (Saxena, Thornicroft, Knapp, & Whiteford, 2007), and so there is increasing recognition that interventions need to be both efficacious and also capable of being scaled up to the point that they can be readily implemented in poorly resourced settings (Patel et al., 2013). That is, a limitation of many of the efficacious treatments observed in this meta-analysis is that they require intensive training, sustained supervision, and lengthy duration of treatment to enable the intervention to be adequately delivered (Tol, Patel et al., 2011). A major challenge for global mental health is to develop more low intensity interventions that can still achieve reasonable effect sizes but simultaneously provide cost-effective solutions to LMICs. To this end, it is noteworthy that there is an increasing evidence-base of collaborative care models evaluated in developed countries, which aim to enhance the reach of efficacious treatments within primary care to optimize the number of patients who can benefit from interventions (Roy-Byrne et al., 2010). Much work has also been conducted in LMICs to evaluate affordable interventions that can be delivered by local providers within primary care settings in ways that are amenable to implementation within health structures so they can develop the long-term and sustainable capacity to disseminate the interventions and to promote optimal reach to large numbers of those in need (Patel et al., 2010; Rahman et al., 2016); for a review see (Singla et al., 2017). These factors highlight that whereas the meta-analytic approach undertaken with the studies reviewed here reflect the efficacy of outcomes in controlled trials, the findings do not portray the extent to which these interventions can impact mental health at a population level. In this context, it is worth noting that one comparison of a controlled intervention of PTSD versus a collaborative care approach embedded in a primary care setting found that whereas the collaborative care approach had a smaller clinical effect size, it nevertheless reached many more patients who could benefit from intervention (Zatzick, 2012).

In conclusion, the current findings indicate that treatments that have been shown to work effectively in developed countries can be effective in treating the mental health needs in LMICs. However, we were able to find only eighteen randomized clinical trials conducted among survivors of mass violence in LMICs and this demonstrates that treatment outcome research among this population is lagging behind the general treatment research in developed countries. Furthermore, more research needs to evaluate interventions aimed at enhancing the number of survivors of mass violence who could benefit from mental health services.

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Table 1. Overview of included trials

Study and type of treatment	N pre-post analyses	Treatment focus	Primary outcome	Modality	Months follow-up	Female (%)	Analysis	Diagnosis (%) PTSD Depression	Country	
Acarturk et al., 2016	49	PTSD & depression	HTQ & BDI-II	Individual	1	39	ITT	49	n.r	Turkey (Syrian refugees)
EMDR (7 sessions)	49	n				34		49	.	
WL										
Acarturk et al., 2015	15	PTSD & depression	IES-R & BDI-II	Individual	1	11	ITT	n.r	n.r	Turkey (Syrian refugees)
EMDR (7 sessions)	14	n				11		.	.	
WL										
Bass et al., 2013	157	PTSD & depression	PCL-C & HSCL-25	Group	6	100	ITT	60	71	Congo
TFCBT (12 sessions)	248	n		Individual		100		83	83	
SC (5										

sessions)										
Bass et al., 2016** MDT (12) WL	159 50	Depression & PTSD	HSCL-25 & HTQ	Individual Individual	n.a.	54 15	ITT	n.r .	n.r .	Iraq
Bolton et al., 2014 BATD (12 sessions) TFCBT (12 sessions) WL	114 101 66	Depression*	HSCL-25 & HTQ	Individual Individual Individual	n.a.	65 59 39	ITT	n.r . .	n.r . .	Iraq
Bolton et al., 2014** CETA (13 sessions) WL	182 165	Depression & PTSD	HSCL-25 & HTQ	Individual Individual	1	111 106	ITT	n.r . .	n.r . .	Thailand (Burmese refugees)
Bolton et al., 2003 IPT (16 sessions) WL	107 117	Depression only	HSCL-25	Group	n.a.	50 53	ITT	n.a .	86 94	Uganda
Bryant et al., 2011 TFCBT (8 sessions) SC (8 sessions)	16 12	PTSD*	PSS-I & BDI-II	Individual Individual	3	100 85	ITT	10 0 10 0	n.r .	Thailand
Connolly & Sakai, 2011 TFT (1 session)	50 49	PTSD*	MPSS & TSI	Individual	24	80 84	Completer	72 66	n.r .	Rwanda

WL										
Hagl et al, 2015 DE (7 sessions) SC (7 sessions)	55 57	PTSD*	IES & GHQ-28	Group Group	12	100 100	Completer	n.r .	n.r .	Bosnia
Igreja et al., 2004 TFCBT (1 session) WL	63 68	PTSD only	SIFP	Individual	n.a.	41 46	Completer	10 0 10 0	n.a .	Mozambique
Jacob et al., 2014*** TFCBT (8 sessions) WL	37 36	PTSD only	CAPS	Individual	12	100 100	ITT	10 0 10 0	n.a .	Rwanda
Knaevelsrud et al., 2015 TFCBT (10 sessions) WL	79 80	PTSD*	PDS & HSCL-25	Individual	3	60 55	ITT	94 94	96 98	Iraq
Meffert et al., 2014 IPT (6 sessions) WL	11 8	PTSD & depression	HTQ & BDI-II	Individual	n.a.	83 78	ITT	n.r .	n.r .	Egypt (Sudanese refugees)
Neuner et al., 2004 TFCBT (4 sessions) SC (4 sessions)	15 13 13	PTSD only	PDS	Individual Individual Individual	12	53 57 75	ITT	10 0 10 0 10	n.a .	Uganda (Sudanese refugees)

PE (1 session)										
Neuner et al., 2008	111	PTSD only	PDS	Individual	6	51	ITT	10	n.a	Uganda (Rwandan & Somalian refugees)
TFCBT (6 sessions)	111			al		43		0	.	
MDT (6 sessions)	55			Individual		49		10		
WL								0		
Weiss et al., 2015**	154	PTSD & depressio	HTQ & HSCL-25	Individual	4	42	ITT	n.r	n.r	Iraq
TFCBT (12 sessions)	99	n		Individual		32		.	.	
CETA (12 sessions)	114			Individual		38				
WL										
Yeomans et al., 2010	38	PTSD only	HTQ	Group	n.a.	44	Completer	n.r	n.a	Burundi
MDT (3-day-workshop)	37			Group		44		.	.	
MDT without PE (3-day-workshop)	38					44				
WL										

Note: * = depression was not reported as being main treatment target; ** = the publication reported pre and follow-up data only (i.e., no post-treatment data); *** = the publication reported pre and follow-up data only (i.e., no post-treatment data) and the follow-up assessment took place at different time periods for the experimental and wait-list conditions, respectively. Therefore, the trial was not included into the controlled effect size calculation; BATD = Behavioral Activation Treatment for Depression; BDI-II = Beck Depression Inventory – II; CAPS = Clinician Administered PTSD Scale; DE = Dialogical Exposure; CETA = Common Elements Treatment Approach; HSCL-25 = Hopkins Symptom Checklist – 25; HTQ = Harvard Trauma Questionnaire; IES = Impact of Event Scale; IES-R = IES-Revised; EMDR = Eye Movement Desensitization and Reprocessing; IPT =

Interpersonal Psychotherapy; ITT = Intent to treat; GHQ-28 = General Health Questionnaire; MDT = Multidisciplinary Treatment; MPSS = Modified PTSD Symptom Scale; n.a. = not applicable; n.r. = not reported; PCL-C = PTSD Checklist – civilian version; PE = Psycho-Education; PDS = Posttraumatic Stress Diagnostic Scale; PSS-I = PTSD Symptom Scale – Interview; SC = Supportive Counseling; SIFP = Self-Inventory for PTSD; TFCBT = trauma-focused cognitive-behavior therapy; TFT = Thought Field Therapy; TSI = Trauma Symptom Inventory; WL = Wait List.

Table 2. Subgroup analyses (*Hedges's g*)

Within-Group Effect Sizes Pre vs. Post Pre vs. FU									
PTSD	<i>k</i>	<i>M</i>	<i>SE</i>	<i>95% CI</i>		<i>k</i>	<i>M</i>	<i>SE</i>	<i>95% CI</i>
active interv.*	16	1.29	0.15	[0.99; 1.60]		14	1.75	0.29	[1.17; 2.32]
TFCBT	7	1.29	0.19	[0.91; 1.67]		7	1.56	0.40	[0.78; 2.34]
other**	7	1.58	0.30	[1.00; 2.16]		4	1.95	0.48	[1.00; 2.90]
Depression									
active interv.*	11	1.28	0.17	[0.96; 1.61]		8	1.56	0.32	[0.94; 2.18]
TFCBT	4	1.35	0.31	[0.74; 1.97]		4	1.60	0.48	[0.67; 2.53]
other**	7	1.25	0.21	[0.83; 1.67]		4	1.51	0.50	[0.52; 2.51]
Between-Group Effect Sizes Pre vs. Post Pre vs. FU									
PTSD	<i>k</i>	<i>M</i>	<i>SE</i>	<i>95% CI</i>		<i>k</i>	<i>M</i>	<i>SE</i>	<i>95% CI</i>
active interv.* vs WL	10	0.37	0.10	[0.18; 0.57]		6	1.03	0.25	[0.53; 1.52]
TFCBT vs WL	<i>n.a.</i>					<i>n.a.</i>			
other** vs WL	8	0.44	0.13	[0.19; 0.68]		4	1.30	0.37	[0.57; 2.03]
						<i>n.a.</i>			
Depression									

Within-Group Effect Sizes Pre vs. Post Pre vs. FU									
PTSD	<i>k</i>	<i>M</i>	<i>SE</i>	<i>95% CI</i>		<i>k</i>	<i>M</i>	<i>SE</i>	<i>95% CI</i>
active interv.* vs WL	8	0.86	0.20	[0.46; 1.25]		4	1.00	0.24	[0.53; 1.46]
TFCBT vs WL	<i>n.a.</i>					<i>n.a.</i>			
other** vs WL	7	0.95	0.21	[0.53; 1.36]		<i>n.a.</i>			

Note: * All active interventions excluding supportive counseling and psychoeducation; ** Included Behavioral Activation Treatment for Depression, Common Elements Treatment Approach, Dialogical Exposure, Eye Movement Desensitization and Reprocessing; Interpersonal Psychotherapy, Multidisciplinary Treatment, and Thought Field Therapy; TFCBT = trauma focused Cognitive Behavior Therapy; WL = waitlist; *k* = number of treatment arms; *n.a.* = number of trials too small ($k < 4$) to conduct analysis.

Figure legends:

Fig. 1. Flow diagram of study selection process

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Fig. 2. Uncontrolled effect size estimates (pre-vs. post-assessment) for the efficacy of active treatments on depression and PTSD

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Note: BATD = Behavioral Activation Treatment for Depression; CETA = Common Elements Treatment Approach; DE = Dialogical Exposure; EMDR = Eye Movement Desensitization and Reprocessing; IPT = Interpersonal Psychotherapy; MDT = Multidisciplinary Treatment; MDTno/wPE = MDT without/with Psychoeducation; PTSD = Post-traumatic Stress Disorder; TFCBT = trauma-focused cognitive-behavior therapy; TFT = Thought Field Therapy.

Fig. 3. Forest plot of effect sizes comparing active treatments to control conditions on depression and PTSD at post-treatment

Fig. 3. Forest plot of effect sizes comparing active treatments to control conditions on depression and PTSD at post-treatment.
 Note: BATD = Behavioral Activation Treatment for Depression; CETA = Common Elements Treatment Approach; DE = Dialogical Exposure; EMDR = Eye Movement Desensitization and Reprocessing; IPT = Interpersonal Psychotherapy; MDT = Multidisciplinary Treatment; MDTw/wPE = MDT without/with Psychoeducation; PTSD = Post-traumatic Stress Disorder; TFCBT = trauma-focused cognitive-behavior therapy; TFT = Thought Field Therapy.

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Title:

Meta-analysis of interventions for posttraumatic stress disorder and depression in adult survivors of mass violence in low- and middle-income countries

Date:

2017-08-01

Citation:

Morina, N., Malek, M., Nickerson, A. & Bryant, R. A. (2017). Meta-analysis of interventions for posttraumatic stress disorder and depression in adult survivors of mass violence in low- and middle-income countries. *DEPRESSION AND ANXIETY*, 34 (8), pp.679-691. <https://doi.org/10.1002/da.22618>.

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