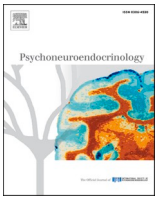
Psychoneuroendocrinology 159 (2024) 106415

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen



Effectiveness of stress management interventions to change cortisol levels: a systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Stress
Mindfulness
Meditation
Talking therapies
Relaxation
HPA axis

ABSTRACT

Stress has a damaging impact on our mental and physical health, and as a result, there is an on-going demand for effective stress management interventions. However, there are no reviews or meta-analyses synthesising the evidence base of randomised controlled trials testing the effectiveness of psychological interventions on changing cortisol levels (the stress hormone) in non-patient groups. Therefore, the primary aim of this systematic review and meta-analysis was to address this gap. Six databases (Medline, PsychInfo, Embase, CINAHL, Cochrane and Web of Science) were searched (1171 studies identified) with 58 studies (combined N = 3508) included in the meta-analysis. The interventions were coded into one of four categories; mind body therapies, mindfulness, relaxation or talking therapies. A random effects meta-analysis on cortisol as measured in blood, saliva or hair found that stress management interventions outperformed pooled control conditions with a medium positive effect size ($g = 0.282$). The studies that utilised cortisol awakening measures ($g = 0.644$) revealed larger effects of stress management interventions than those that measured diurnal cortisol ($g = 0.255$). Mindfulness and meditation ($g = 0.345$) and relaxation ($g = 0.347$) interventions were most effective at changing cortisol levels, while mind body therapies ($g = 0.129$) and talking therapies ($g = 0.107$) were shown to have smaller and non-significant effect sizes. Additionally, studies that utilised an active control group ($g = 0.477$) over passive control group ($g = 0.129$) were found to have stronger effects. Length of the intervention, study quality, risk of bias, age and gender did not influence the effectiveness of interventions and there was no evidence of publication bias. Overall, the current findings confirm that stress management interventions can positively influence cortisol levels. Future research should investigate the longer term implications for health and health outcomes.

1. Introduction

Stress is a profound public health concern and an important mechanism through which the social and physical environment can impact later health outcomes (O'Connor et al., 2021). It is well established that experiencing stressful life events and reporting greater perceived stress over sustained periods of time are associated with poorer mental and physical health (Epel et al., 2018; O'Connor et al., 2021). Additionally, experiencing traumatic life events across one's life have also been consistently found to be associated with poorer health outcomes (Howarth et al., 2020; Liu and Miller, 2014).

A key mechanism regulating how the environment impacts the stress process is the stress hormone – cortisol. Cortisol is a product of the hypothalamic-pituitary adrenal (HPA) axis system which plays an essential role in regulating the body's biological systems - from metabolic to immune systems (Lupien et al., 2009; Sapolsky et al., 2000). The dysregulation of the HPA axis is well documented to have links with negative health outcomes: the chronic over-activation of the HPA axis through experiencing acute stress or stressful life events can lead to allostatic load (McEwen, 1998). Most recently, allostatic *overload* was conceptualised referring to the detrimental impacts of stress on the body's biological systems when stress mediators, such as cortisol, are released to respond to stress in one's environment but their excessive and prolonged use, as well as dysregulation, leads to tissue damage (McEwen and Rasgon, 2018). Collectively, stress, and by part, cortisol, impacts psychological and physical body functioning; subsequently implicated in mental and physical health outcomes, suggesting cortisol regulation plays a key mediating role in the relationship between stress exposure and later negative health outcomes (Adam et al., 2017; Chrousos and Gold, 1992; O'Connor et al., 2021).

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https://doi.org/10.1016/j.psyneuen.2023.106415
Received 21 August 2023; Accepted 9 October 2023
Available online 11 October 2023
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1.1. The stress response and health outcomes

Low and high cortisol responses to stress may be associated with poor health outcomes; research has emerged to suggest that smaller increases, or a blunted cortisol response, to stress may be indicative of current ill-health or future health risks (Lovallo, 2016). Lower cortisol stress reactivity has been shown to be associated with the risk of obesity and with symptoms of depression and anxiety (de Rooij, 2013). In other research it was found that individuals who had previously made a suicide attempt exhibited low levels of cortisol in response to an acute stressor compared to control participants (O'Connor et al., 2017). Moreover, the results of a meta-analysis found evidence of an association between early-life adversity and a blunted cortisol response to social stress (Bunea et al., 2017). Conversely, literature exists whereby heightened cortisol responses are associated with poorer health outcomes. Specifically, in trauma participants, it has been shown that there is an increase in cortisol to a stressor (Heim et al., 2000). Additionally, in another study, an elevated cortisol response to a stressor increased the odds of experiencing hypertension and progression to coronary artery calcification 3 years later (Hamer and Steptoe, 2012). Collectively, evidence points towards both heightened and blunted cortisol responses being associated with poorer health outcomes in the future.

1.2. Cortisol across the day

The cortisol awakening response (CAR) is also implicated in later health status; linked to an array of health outcomes as confirmed in a meta-analysis whereby enhanced CAR is linked to job stress and general life stress. Conversely, reduced CAR has also been found to be associated with fatigue, exhaustion and burnout (Chida and Steptoe, 2009). The natural cortisol fluctuations throughout the day also play an important role in relation to later health. A flatter diurnal slope represented by low morning and high evening levels has also been suggested to be indicative of HPA dysregulation. Flatter diurnal cortisol slopes across the waking day may be one mechanism by which stress influences negative health outcomes (Adam and Kumari, 2009). A number of studies have found that there is an association between a flatter cortisol slope and negative health outcomes such as depression, cardiovascular disease, obesity and suicide attempt (Matthews et al., 2006; O'Connor et al., 2020; Ruttle et al., 2013). This is synthesised in a meta-analysis that found consistent evidence that flatter cortisol slopes were associated with numerous poor health outcomes, from cancer, to depression and even obesity (Adam et al., 2017).

1.3. Stress management interventions

Therefore, taken together, it is clear that stress can be damaging for our mental and physical health, and as a result, there is an on-going demand for effective stress management interventions. An abundance of stress management interventions exist, however, which type of intervention is most effective? Is there evidence that they can influence cortisol? How do they perform in randomised controlled trials? For example, some of the most increasingly popular intervention approaches are mindfulness based (Khoury et al., 2013). A previous systematic review reported varied success for mindfulness-based interventions on changing cortisol outcomes, finding mindfulness-based interventions had limited effectiveness but that they were more effective when standardised measures of cortisol were assessed such as the CAR and diurnal slope, instead of unstandardised measures such as averages of raw cortisol concentrations (Sanada et al., 2016). A recent meta-analysis found that meditation interventions were effective at lowering cortisol levels but only in highly stress samples that assessed cortisol in blood (Koncz et al., 2021). There is also evidence that psychological interventions can influence cortisol levels in patients with cancer, psychiatric conditions and other health issues (e.g., Antoni et al., 2023, Saban et al., 2022). However, there are no reviews or meta-analyses synthesising the evidence base of randomised controlled trials testing the effectiveness of psychological interventions on changing cortisol levels in non-patient groups.

Therefore, the primary aim of the current systematic review and meta-analysis was to examine the effectiveness of psychological interventions to reduce cortisol levels in healthy adults that used randomised controlled trial designs. The secondary aim was to investigate the heterogeneity of any observed effects in terms of the type of cortisol measurement (in blood, hair or saliva), control group, (active, inactive, waitlist or active/passive) and intervention together with exploring the moderating effects of sample size, study quality and risk of bias.

2. Methods

2.1. Protocol and registration

The inclusion and exclusion criteria, methods for analysis and protocol for the current systematic review and meta-analysis were preregistered on PROSPERO with the following registration number: CRD42019120066. Meta-analyses data are available on the Open Science Framework (https://rb.gy/tkrfp).

2.2. Eligibility criteria

To be included in the review, studies had to have utilised a randomised controlled trial design to investigate the effectiveness of a psychological intervention(s) on cortisol outcomes *and* to have measured cortisol at baseline and post-intervention in order to determine the change in cortisol from pre- to post-intervention. The full study inclusion and exclusion criteria (PICOS) are outlined in Table 1.

2.3. Search

The search was completed across six electronic databases: Medline, PsychInfo, Embase, CINAHL, Cochrane and Web of Science. The key terms such as "cortisol", "stress management intervention" were used.

Table 1
Outline of the study selection criteria.

	Inclusion criteria	Exclusion criteria
Population	Healthy adult subjects (aged > 18 years). Subjects can be stressed or not stressed prior to the study.	Patients with cancer, diseases, obese, pregnancy, psychiatric or other health issues.
Interventions	Any psychological stress-management interventions: including, mindfulness, CBT.	Other pharmacological interventions
Control group	Waitlist control or other intervention	No control group
Outcome	Cortisol level measures in blood, saliva and hair. Cortisol can be measured with and without out an acute stress test.	Heart rate, blood pressure, only stress test assessments.
Studies	RCTs. Published in English language, journal articles, humans, published any year	Non-RCTs, open trials with a pre-post analysis. Published in other languages, reviews, posters, presentations, case reports, dissertations, letters.

Note: RCT = randomised controlled trial, CBT = cognitive behaviour therapy

Table 2
Search strategy for Embase.

1.	"adult" or "adulthood" or "man" or "men" or "women" or "woman" or "young adult" or "worker" or "employee"
2.	"mindfulness" or "mindfulness-based stress reduction" or "MBSR" or "meditation" or "stress management" or "cognitive behavioural stress management" or "CBSM" or "stress management training" or "stress management intervention" or "internet-based CBSM" or "IB-CBSM" or "internet-based stress management intervention" or "internet-based stress management" or "IBSM" or "iSMI" or "stress inoculation training" or "time management training" or "progressive muscle relaxation" or "biofeedback" or "guided imagery"
3.	"cortisol" or "cortisol response" or "cortisol awakening response" or "awakening cortisol response" or "saliva" or "salivary" or "hair cortisol" or "hypothalamic-pituitary-adrenal axis" or "HPA axis" or "salivary free cortisol response" or "diurnal cortisol" or "diurnal"
4.	"random allocation" or "randomised" or "randomized" or "RCT" or "random* trial" or "random* control trial" or "pilot study"
5.	1 AND 2 AND 3 AND 4
6.	Limit 5 limits for abstracts, human, English language, clinical trial (RCT), human age groups (adult 18–64 and 65 +), source types (journal), publication types (article)
7.	Limit 6 dc = 20230317–20230324

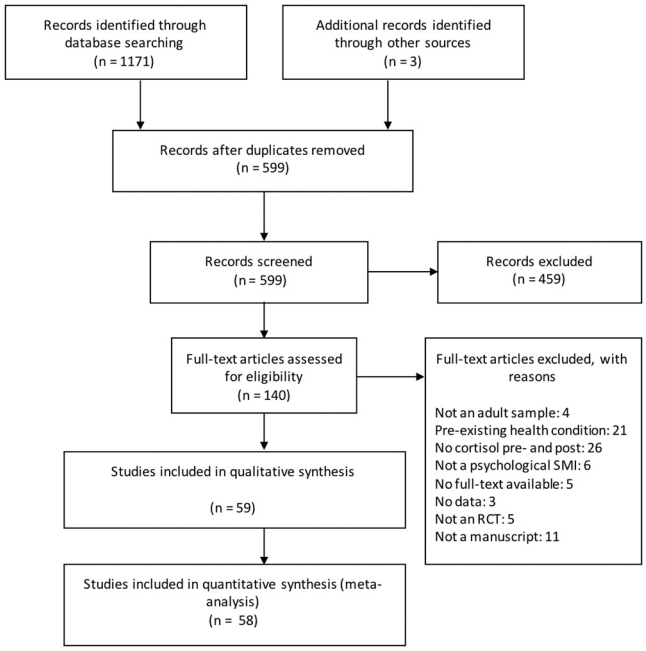

Fig. 1. PRISMA study flow diagram of studies retained in the review. Reasons for exclusion included.

Table 2 provides an example of the search strategy used in Embase. The search was regularly updated to ensure all relevant articles were included. The date of the last search was 06/04/23. Additionally, Google Scholar was used to thoroughly search through all studies citing the included studies.

Fig. 1 shows the selection of studies throughout the meta-analysis.

2.4. Study Selection

A total of 1171 studies were identified during the searches and 3 additional papers through Google Scholar. Title and abstract screening were completed for eligibility by OR and a 20% overlap completed by SW. Duplicates were detected and removed through Endnote library. Full text screening was done by OR and 20% overlap completed by SW. Any disagreements were resolved by consensus and if an agreement could not be reached, a third researcher was required (DO'C). The inter-rater reliability on study selection was calculated to indicate a high level of agreement (K = 0.76, $p < .001$).

2.5. Data collection process and coding procedure

A data extraction table was used for extracting key information from the studies, this was based upon the Cochrane collaborative data collection template form (Cochrane Training, 2014). Additional components were added to the table, taken from O'Connor et al. (2016), to ensure data was extracted specific to cortisol measurement. In any instance of study information for data extraction not being clear, study authors were contacted to ask for more detail.

In instances when the mean age was not available in a study paper, the mean age was calculated from the age range information (e.g., Christopher et al., 2018; MacLean et al., 1997; Tsiouli et al., 2014). For some studies, overall mean age was calculated through taking the average of the intervention and control groups (Bottaccioli et al., 2020; Danucalov et al., 2013; Feicht et al., 2013; MacDonald and Minahan, 2018).

For some included studies, the standard error (SE) was presented. The standard deviation was calculated from SE and sample size using the following formula (SE x $\sqrt{N}$; Cochrane, 2014). This formula was utilised for the following papers: Domes et al. (2019), Fan et al. (2014), MacLean et al. (1997), Nyklíček et al. (2013) and Rosenkranz et al. (2013). Although for Rosenkranz et al. (2013) the average SE was first calculated across the 5 measures. In one included study the 95% confidence intervals were presented (e.g., Laudenslager 2015). Therefore the SD was calculated using the following formula: SD = $\sqrt{N}$ x (upper limit – lower limit) / 3.92.

The current meta-analysis prioritised diurnal measures of cortisol over single measures. If the diurnal mean was possible to be calculated from the data included in a study, this was done using the following formula: sum of the mean at each time point/number of time points. for the following studies: Fotiou et al. (2016); Oken et al. (2010); Rosenkranz et al. (2013). To calculate the standard deviation when the diurnal mean was produced, this was done using the following formula: SQRT((sum of the SD at each time point^2 + b + c)/k). As one study, Rosenkranz et al. (2013), provided SEM so this was converted to SD first then the above formula was used to produce the SD in relation to the diurnal mean calculation.

For studies whereby the sample was not clear if N represented participants who completed both baseline and post-intervention, the author was contacted in the first instance. If we could not obtain additional information, the smaller of the two sample sizes was chosen to avoid overestimation of the effect size. For instance, Fendel et al. (2021) we took the T2 sample size as the intervention/control group size. For Jensen et al. (2012), for the mindfulness group, n = 14 was taken. Finally, Jensen et al. (2015) was contacted and responded regarding cortisol sample (n = 47).

In the current meta-analysis, there were three crossover trials. In these instances, we inflated the sample size – for instance, in Benvenutti et al. (2017) they had a sample size of 24 who all completed the intervention and control conditions - therefore we inflated the total sample size to 48.

In cases of studies that had multiple active or passive control groups, we included both groups and divided the intervention sample size by the number of control groups to prevent inflation of the effect size and allow comparison against a variety of controls. The meta-analytic software used to conduct the analysis, Comprehensive Meta-Analysis (CMA), takes the average of the effect sizes in one study as these are not independent from each other before calculating a grand average.

When studies had more than one intervention group, the main psychological intervention was used in the meta-analysis and we treated the remaining intervention as a control condition because we were exploring determinants of effectiveness (*as per* Michie et al. (2009). This was the case for both studies by Bowden et al. (2012) and Brinkmann et al. (2020) who had two intervention groups; Bowden et al. (2012) compared brain wave vibration and mindfulness compared to yoga. The

meta-analysis compared mindfulness to two comparison groups – brain wave vibration and yoga. Whereas Brinkmann et al. (2020) investigated the effects of biofeedback and mindfulness compared to waitlist controls. The current meta-analysis considered mindfulness as the intervention only.

2.6. Risk of bias and study quality

The Cochrane Collaborations tool for assessing risk of bias in RCTs was used (RoB2; (Sterne et al., 2019a). The first reviewer covered all studies, whilst the second reviewer (AP) reviewed 50% of the studies. Kappa coefficients were calculated for the all items in the RoB2 and indicated a moderate level of agreement ($K = 0.60$ $p < .001$). Following the assessment, the discrepancies lay in cortisol assessment criteria and these were resolved through discussion.

Since there is no validated rating scale available assessing the consideration of confounding influences during measurement of cortisol concentrations, we utilised a cortisol quality index from the existing literature (Laufer et al., 2018). This scale consists of several items which influence the measurement, and accuracy, of cortisol measurement dependent on whether it is measured in saliva or blood. We applied the scale to also consider hair cortisol in this instance. Items can be allocated to one of four categories: report of sampling design; reported strategies enhancing accuracy of sampling; consideration of confounders on the particular sampling day ("state covariates"; Stalder et al., 2016), consideration of confounders with regard to sociodemographic and health variables ("trait covariates"; Stalder et al., 2016). Items include whether cortisol was measured over consecutive days, if authors considered time of awakening and even the use of oral contraception in female samples. For each item, it is rated as either '0 – not considered', '1 – considered' or N/A as not all items are applicable to the study, depending on how cortisol was measured. The term 'considered' was indicated if the study addressed the potential confounder in one of the following: sampling instructions, a covariate in the analyses, reported in the descriptive statistics or included in the exclusion criteria of the study sample. The sum scores for each of the four categories were calculated and divided by the maximum score the study could achieve in that category, based on the modality of cortisol. This created a percentage used to rate consideration as good consideration (100–66.1%), moderate consideration (66–33.1%) or low consideration (33–0%).

2.7. Data extraction plan

The following data was extracted from each study: number of participants analysed with cortisol, the number of participants in the intervention and control group(s), the mean age of the entire sample and separate intervention/control groups (if available). The percentage of females in the study, the included control conditions (active, inactive, waitlist), pooled control conditions (active/passive), type of intervention, broad intervention category, length of intervention in absolute minutes (if available), an interpretation of length of intervention (as short (0 – 250 minutes), medium (251 – 800 minutes), long >801 minutes), type of cortisol sampling (blood/saliva/hair), categorisation of cortisol measurement (awakening/diurnal), number of days cortisol was measured on, number of times per day cortisol measured, timing of cortisol measurement (AM/PM/AM – PM), study quality (as described above) and whether the sample was stressed or non-stressed.

2.8. Meta-analytic procedure

All analyses were conducted using the Comprehensive Meta-Analysis 4.0 (CMA) software (Borenstein, 2022). The aim of the meta-analysis was to determine the effectiveness of stress management interventions on the change in cortisol levels from pre-intervention to post-intervention; meaning the dependent variable was the standardised mean difference change in cortisol from pre- to post-intervention between the intervention and comparator group. By utilising the standardised mean difference it permitted us to summarise evidence when studies used a variety of sampling strategies; from single measure, cortisol awakening response to diurnal cortisol. Following the procedure of Koncz et al. (2021) we devised a hierarchy of cortisol reporting, should different indices be available in a study; selecting the AUCg measure first, followed by the mean of multiple measures then choosing a single measurement. Additionally, if a study reported more than one control condition we included both contrasts (for instance, Errazuriz et al., 2022 utilised an active and waitlist control group). CMA software takes an average of multiple effects sizes in one study, as these are not independent of one another, before calculating a grand average. The current meta-analysis utilised the random effects model and Hedges *g* as a measure of effect size; the magnitude of the effect is interpreted using the following parameters where a low effect size is approximately 0.20, medium is 0.50 and large is 0.80 (Cohen, 2013).

When considering the direction of effect, a positive effect size indicates favouring the intervention condition, shown by a larger decrease, or a smaller increase, in change in cortisol levels from pre- to post-test. As the included studies employed varied in the samples, interventions, control conditions and cortisol sampling approaches, average effect sizes and corresponding 95% confidence intervals were calculated based on the random-effects model, which accounts for between-study variances (Borenstein et al., 2009).

Funnel plots were inspected to determine the degree of publication bias whereby we can visually plot how the inherent difficulties of publishing non-significant results can lead to an overrepresentation of significant findings in the literature. We also utilised Egger's regression coefficient to identify publication bias (Egger et al., 1997) and Duval and Tweedie's trim and fill analysis to understand the number of missing studies to the left and the right of the mean (Duval and Tweedie, 2000).

Lastly, sensitivity analyses were also performed by removing each study from the analyses one at a time. Further subgroup analyses investigated the effectiveness of types of intervention relative to control conditions (active, inactive and waitlist controls, as well as broader active/passive control groups), types of cortisol sampling (blood, saliva, hair), intervention group (mindfulness, relaxation, mind body therapy and talking therapy; see below), length of intervention (short, medium and long), study quality (low, average and high), stress risk (low risk, high risk), risk of bias (low, some concerns, high) and cortisol measurement (awakening, diurnal). Meta-regressions were also conducted to identify moderating variables (time elapsed between the end of the intervention and post-intervention cortisol measure and sample demographics)).

3. Results

3.1. Study characteristics

Of the 59 studies, 56 were RCTs and 3 were crossover trials (Benvenutti et al., 2017; Bittman et al., 2001; Lai and Li, 2011). 57 studies provided a baseline and post-intervention measure, 2 studies provided the pre-post intervention change in cortisol. In total, there were 3508 participants who were included in the meta-analysis, with the individual study sample size ranging from 12 to 154. There were 1648 participants allocated to the intervention condition and 1860 allocated to the control condition. Collectively, there was a mean age of 35.84 years and the proportion of included females was 64.84%. The average intervention length was 19 hours in length across the studies but this ranged from 20 minutes to 4560 minutes (see Supplementary Table 1 for study characteristics). A total of 15 studies included samples with individuals considered to be at a stress risk; including samples of caregivers, healthcare workers and individuals who reported prolonged stress. The remaining 44 studies were considered to have samples with no stress risk. For the type of cortisol measured, 13 were in blood, 43 were in saliva and 3 were in hair. We also characterised the cortisol measurements in

relation to the time the cortisol measurement was taken; in the morning only (AM), in the afternoon/evening only (PM) or taken both in the morning and the afternoon (AM and PM). Moreover, we characterised the cortisol measurements as awakening or diurnal cortisol.

We conceptualised the control comparison groups as active, inactive or passive. We also followed previous meta-analyses (e.g. Koncz et al., 2021) to look at whether collapsing the inactive and waitlist groups into a larger, passive control group made a difference to understanding subgroup differences in explaining the heterogeneity of our results.

When considering the risk of bias, a large proportion of the included studies were categorised as 'some concerns', with six studies being 'high risk'. As seen in Fig. 4 below, the greatest risk of bias stemmed from the category 'missing outcome data'; often due to participants dropping out of the study. There was also a greater risk derived from lack of detail in relation to the method of cortisol sampling and failure to conduct sensitivity analyses in the included studies to understand if the findings were biased by missing data. Additionally, there was a lack of clarity regarding the category 'selection of the reported result' where despite a standardised cortisol collection procedure being implemented, the study did not make clear whether the study personnel were aware of group allocation.

As the outcome of interest was cortisol, as measured in either saliva, blood or hair, it was essential to recognise the variability of the quality of cortisol measurement across studies and its potential impact on determining the effectiveness of interventions in the changes in cortisol. The current meta-analysis utilised the cortisol quality tool as devised by (Laufer et al., 2018), we adapted this measure to additionally be used for hair cortisol; previously this tool was used in saliva and blood only. The cortisol quality measure uncovered patterns in the cortisol sampling that may confound effectiveness of the interventions utilised. Notably the lack of reporting of state confounders that could influence cortisol measurement, such as time of day the measurement was taken, consideration of medication or menstrual phase in female samples were the most frequent indicators of poorer cortisol sampling. See Supplementary Table 1 for a summary of the study characteristics.

3.2. Categorising the interventions

There was a great variety of interventions included in the meta-analysis. For the purpose of analyses, and to improve understanding of differential effectiveness of different broad types of interventions, we summarised the underlying concepts of the interventions and this allowed us to categorise each intervention into one of four broad categories to allow meaningful comparison of key intervention components (see Fig. 2).

We conceptualised four categories of intervention: 1) *mindfulness and meditation*, incorporating any mindfulness meditation, mindfulness based therapy, including mindfulness based stress reduction and mindfulness based cognitive therapy where the central core of the intervention is to gain a greater awareness of one's physical, mental and emotional condition; 2) *talking therapies* included psychological interventions involving talking one-to-one, in a group, online, over the phone or with friends, family or co-workers, an example of talking therapy being cognitive behavioural therapy; 3) *relaxation*, included any intervention specifying muscle relaxation, biofeedback assisted relaxation and breathing exercises; 4) *mind body training*, incorporated yoga and biofeedback where there was an awareness of bodily movement to influence mental state.

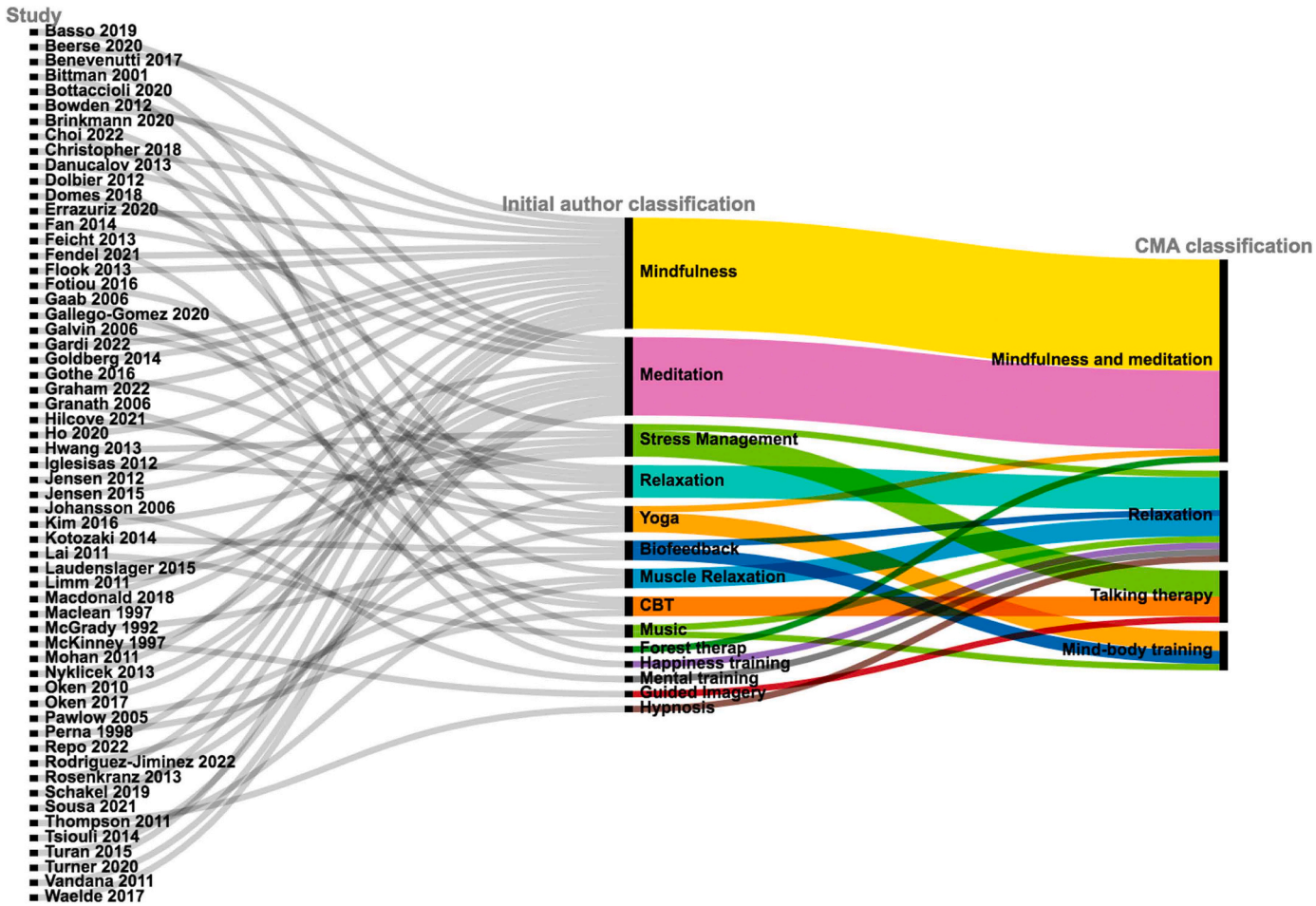

Fig. 2. An alluvial diagram mapping the categorisation of study interventions.

3.3. Grand meta-analysis

This analysis is based on 58 studies that investigated the effect of stress management interventions on cortisol (as measured in blood, hair or saliva). The meta-analysis excluded one study, Danucalov et al. (2013), due to being identified as an outlier with inflated effect sizes. The grand meta-analysis found that stress management interventions led to a small-to-medium, and heterogeneous, positive effect on cortisol levels ($g = 0.282$, 95% CI = 0.166, 0.398, Z = 4.749, $p < 0.001$; $I^2 = 60.3\%$, $Q_{(57)} = 143.603$, $p < 0.001$) reflecting a favourable outcome for the psychological intervention compared to the control condition. See Supplementary Fig. 1 for the high resolution plot of effect sizes.

3.4. Publication bias and sensitivity analysis

Egger's regression coefficient did not indicate presence of publication bias when all studies were considered together (*see* Fig. 3; *intercept* = 1.284, *df* = 56, $p = .082$). Duval and Tweedie's trim and fill analyses indicated there were no missing studies either side of the mean. Sensitivity analyses were performed to determine the impact of removing each study from the analyses, one at a time. These analyses did not detect any studies that had a significant independent impact on the overall effect size at post-intervention (effect sizes (*hedges g*) ranged from 0.250 to 0.298).

3.5. Subgroup analyses

3.5.1. Cortisol measurement type

To compare the effectiveness of the interventions in studies utilising different cortisol outcomes, as measured in blood, hair or saliva, a subgroup analysis was conducted. As outlined earlier, there were only 3 studies utilising hair cortisol, therefore, this category was omitted from the analysis as there were too few studies to have adequate power to conduct the analysis. There was a main effect of the interventions, when compared to controls, in blood ($g = 0.331$, $SE = 0.136$, $p = .015$) and saliva ($g = 0.284$, $SE = 0.074$, $p < .001$). However, there was no evidence that the effect sizes varied as a function of cortisol outcome measure ($Q = 0.093$, $p = .761$).

3.5.2. Types of intervention

We explored whether the type of intervention impacted the effectiveness of stress management interventions (see Supplementary Table 2). The interventions were grouped into one of four categories; mind body therapies, mindfulness, relaxation or talking therapies. The subgroup analysis revealed the largest, significant effect sizes for mindfulness ($g = 0.345$, $SE = 0.085$, $p < .001$) and relaxation ($g = 0.347$, $SE = 0.125$, $p = .005$). We observed much smaller, non-significant, effect sizes for mind body therapies ($g = 0.129$, $SE = 0.187$, $p = .492$) and talking therapies ($g = 0.107$, $SE = 0.162$, $p = .510$). Overall, there was no evidence that the effect sizes varied as a function of the type of intervention received ($Q = 2.643$, $p = .450$).

3.5.3. Comparison group

In this subgroup analysis we only included studies with *one* control group; for instance, a study that had two control groups would be excluded (e.g. Errazuriz et al., 2022). In studies where the intervention group was compared against an active control group, we observed a large, significant, effect size ($g = 0.477$, $SE = 0.109$, $p < .001$). In studies where the intervention was compared against a passive control group there was a much smaller, non-significant, effect observed ($g = 0.129$, $SE = 0.076$, $p = .093$). Additionally, the effect sizes varied as a function of the type of comparison group the intervention was compared against and was significantly different across conditions. The analyses indicated that when the stress management interventions were compared against an active control group the effect sizes were much larger and significantly different than when compared to a passive control group ($Q = 6.967$, $p = .009$). The same pattern emerged when the comparison groups were classified into active, inactive and waitlist categories (for main effects of each control group, see Supplementary material Table 2).

3.5.4. Awakening or diurnal

Next, analyses were conducted to explore whether the effectiveness of interventions on cortisol varied based on the *type* of cortisol measure – awakening or diurnal cortisol. The analyses found a large, significant effect when studies utilised awakening measures of cortisol ($g = 0.644$, $SE = 0.153$, $p < .001$), and smaller, but also significant, effects when using diurnal measures of cortisol ($g = 0.225$, $SE = 0.063$, $p < .001$). Moreover, the magnitude of effect was significantly different in studies that assessed the awakening response compared to diurnal levels, indicating that the interventions were more effective at changing cortisol in the morning awakening measures compared to diurnal cortisol measures ($Q = 6.37$, $p = .012$).

3.5.5. Length of intervention

One study was excluded from this subgroup analysis as it did not provide detail on the length of the intervention (Johansson and Uneståhl, 2006). When considering the length of intervention, categorised as short, medium or long in length, there was a significant effect for long interventions (more than 801 min; $g = 0.348$, $SE = 0.093$, $p < .001$) as

Fig. 3. Funnel plot based on Hedge's g, 95% CI's for cortisol.

well as for short interventions (less than 250 min; g = 0.306, SE = 0.084, p < .001). However, no significant effect was found for medium length interventions (251 – 800 min; $g = 0.150$, $SE = 0.147$, $p = .308$). Overall, there was no significant difference on the effectiveness of the intervention based on the length of the intervention (Q = 1.299, $p = .522$).

3.5.6. Study quality

We conducted subgroup analysis to determine the effect of study quality on the effectiveness of interventions on change in cortisol. For studies with moderate study quality we observed significant effects ($g = 0.346$, $SE = 0.080$, $p < .001$). However, high study quality was not significant ($g = 0.212$, $SE = 0.130$, $p = .103$) and low study quality had the smallest effect size but also non-significant ($g = 0.195$, $SE = 0.144$, $p = 0.178$). Overall, we found no difference in effect sizes based on study quality (Q = 1.272, $p = 0.529$).

3.5.7. Risk of bias

We explored the impact of risk of bias on the observed effect sizes. For studies with 'low risk' of bias, we observed significant effect sizes ($g = 0.295$, $SE = 0.100$, $p = .003$) and studies categorised as 'some risk of bias' observed a similar effect size ($g = 0.303$, $SE = 0.087$, $p < .001$). However, for studies with high risk of bias there were smaller, non-significant effects ($g = 0.207$, $SE = 0.186$, $p = .267$). Overall there were no significant differences in effect sizes according to the risk of bias categorisation (Q = 0.224, $p = 0.894$). A summary of the evaluation of the risk of bias across studies can be seen in Fig. 4.

3.5.8. Stress risk

When considering the stress risk of the participants in the included studies, we explored whether having a 'stress risk' sample influenced the effectiveness of the interventions on change in cortisol. We found that the interventions were effective in non-stressed samples, shown by a medium sized significant effect ($g = 0.351$, $SE = 0.075$, $p < .001$). However, in samples experiencing stress, the interventions were much less effective and this was shown by a smaller, non-significant effect size ($g = 0.135$, $SE = 0.098$, $p = .169$). Overall, there was no significant differences of the stress risk of the sample on the effectiveness of the intervention on cortisol (Q = 3.078, $p = .079$).

3.6. Meta-regressions

3.6.1. Time elapsed between end of intervention and cortisol measurement

This analysis was conducted on the 45 studies which provided detail on the time elapsed between the end of the intervention and post-intervention cortisol measure. There were no significant relationships between the time elapsed after the intervention and post-intervention measure ($B = -0.0002$, $SE = 0.001$, *95% CI* [−0.002, 0.001], $p = .734$).

3.6.2. Demographics

When considering whether the total number of participants included in the study influenced the observed effect sizes, there was no significant effect of total sample size on the observed effect ($B = -0.002$, $SE = 0.002$, $p = .273$). Second, when considering the demographics of the samples, the meta-regressions were conducted on the 28 studies which reported the demographics for the participants providing cortisol samples, as opposed to the total study sample. There was no significant effect of age ($B = 0.012$, $SE = 0.074$, 95% CI −0.0025, 0.0264]. $p = .1048$) or gender ($B = .0002$, $SE = 0.0029$, $p = .955$) on the effect sizes of the observed studies.

4. Discussion

The current systematic review and meta-analysis explored the effectiveness of stress management interventions in changing cortisol levels and considered moderators influencing the effectiveness of the interventions. There was clear evidence that stress management interventions had a positive effect in improving cortisol levels from pre- to post-intervention. The review was comprehensive; considering healthy individuals with no reported pre-existing health conditions, yet inclusive of samples that may experience periods of short- or long-term stress where it is imperative to have effective stress management interventions. Previous reviews of the effectiveness of stress management interventions on cortisol levels have focussed on a singular form of intervention, such as meditation (Koncz et al., 2021). However, a plethora of stress management interventions exist and the effects of these interventions could vary. In the current review and meta-analysis we considered the array of interventions available to reflect the heterogeneity of stress management interventions, aiming to provide a more comprehensive overview of the effects of stress management interventions on cortisol levels.

The current meta-analysis acknowledges potential moderating variables influencing the effectiveness of stress management interventions, such as: cortisol sampling strategies (diurnal, awakening), cortisol outcomes (blood, hair, saliva), control conditions (active, passive), quality of cortisol measurement, risk of bias within studies and sample demographics. Specifically we found that mindfulness and relaxation interventions appeared most effective at changing cortisol levels. We also found interventions that compared against an active control group, rather than a passive control group, were also more effective at reducing cortisol levels. This is consistent with previous literature whereby mindfulness-based interventions were slightly superior to other active controls in adults when analysing a variety of health outcomes, including stress (Goldberg et al., 2022). Additionally, studies that measured awakening cortisol revealed greater effectiveness of interventions in changing cortisol levels than those measuring diurnal cortisol. However, the type of intervention, length of the intervention, study quality, and risk of bias did not appear to influence the

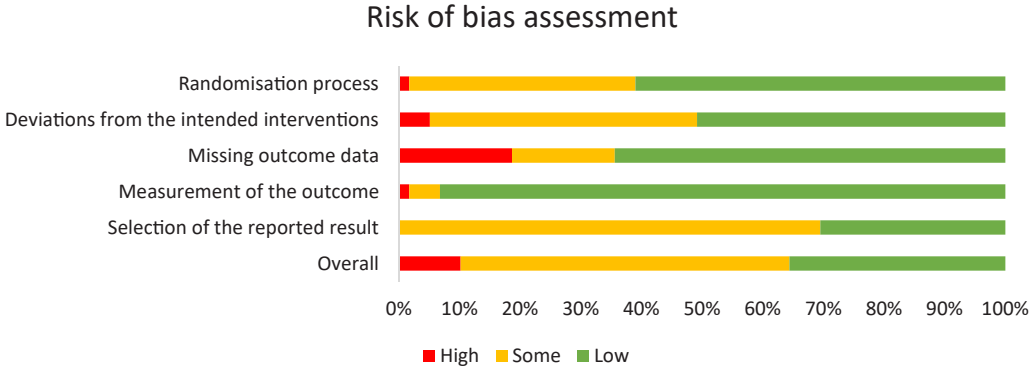

Fig. 4. A summary of risk of bias across studies.

effectiveness of interventions. The findings emphasise the need to recognise the diversity of interventions, and cortisol measurement, especially when interpreting the disparate findings observed in previous literature regarding the success of stress management interventions.

To our knowledge, this is the first meta-analysis to compare the effectiveness of different types of interventions for cortisol changes from pre- to post-intervention in a single statistical model. It is apparent from our analysis that there is no clear indication of one intervention being *more* effective than another intervention when directly compared, per se. However, we can conclude that mindfulness and meditation and relaxation were the only statistically significant effective interventions and yielded the largest effect sizes. It is worth noting that mindfulness, meditation and relaxation studies also represent the largest study groups and generally were longer interventions, therefore, we cannot rule out the possibility that as the number of studies increase, that these conclusions may need to change. Nevertheless, the question remains as to what is the underlying driver of these differential findings? Is it the intervention content, length, delivery, or sample size that is driving the observed effects. The current findings provide further evidence for the effectiveness of mindfulness and meditation-based interventions. For example, a recent meta-analysis found that mindfulness-based interventions had beneficial effects on cortisol in healthy adults but also recognised the heterogeneity in delivery of studies and what is the true driver of the effect (Sanada et al., 2016). These congruent findings open opportunities to understand the extent to which third wave interventions that include mindfulness, such as Acceptance Commitment Therapy, could influence cortisol levels (Prudenzi et al., 2021). Further research is needed to understand the nuanced effects of different interventions.

Contrary to expectations, the results of this meta-analysis suggest that stress management interventions were more effective when compared to active controls, as opposed to passive controls. There are several possible explanations for this pattern of results. One possibility is that the studies with active control conditions were of higher quality and this was reflected in enhanced intervention delivery and fidelity leading to improved outcomes. Of course, the converse may also be true, the studies with passive control conditions may have had inferior intervention delivery and fidelity. This finding is somewhat surprising when considering previous meta-analyses found studies with inactive controls had larger effect sizes than active (Witarto et al., 2022) and larger magnitude of effects specific to mindfulness interventions were when compared to passive controls, with smaller, yet still significant effects when compared to some active controls (Goldberg et al., 2022). Nonetheless, it is noteworthy that only with an appropriate active control group can we attribute differential improvements to the potency of the stress management intervention and it is a more rigorous test of intervention efficacy as to whether these interventions should be considered for stress reduction. For example, if an active control group receives an evidence-based intervention, then we can be more confident that the change in cortisol levels seen in the stress management intervention group is due to the specific components of that intervention, rather than simply the fact that participants were receiving any intervention at all. Additionally, unless the design of the study is a double-blind design, the true effectiveness of an intervention cannot be concluded (Boot et al., 2013). Future research should use appropriate active control groups and double-blind designs to more accurately assess the effectiveness of stress management interventions.

The meta-analysis also found interventions to be *more* effective in “no stress” risk samples than in “stress risk” samples; contrary to previous research only yielding significant effects for stress risk samples, with no significant effects in non-stressed samples, when considering blood cortisol (Koncz et al., 2021). However, the lack of statistical power in previous research meant that direct comparisons between stressed and non-stressed groups could not be conducted. The current study was able to conduct analyses to directly compare stress and no stress risk groups, finding no statistically significant differences in intervention effectiveness depending on whether participants were at stress risk or not. It is also important to recognise that the "stress risk” grouping in the Koncz et al. (2021) review differed slightly from the stress risk samples in the current meta-analysis. For example, the stress risk groups in previous research included low-income family members, dementia caregivers, cancer survivors or cancer patients, while the stressed samples in the current meta-analysis were comprised of caregivers, healthcare workers, and people who reported prolonged stress. The key difference being the current meta-analysis did not include anyone with a diagnosed somatic or mental illness. These differential findings are difficult to reconcile and highlight the need for more careful consideration of how samples are classified as stress risk versus no stress as this may not be a useful arbitrary distinction. It is likely there is a large amount of variability within and across groupings and samples. Future research ought to consider this issue further.

The current meta-analysis also found stronger evidence for intervention effectiveness when studies utilised the cortisol awakening response compared to a diurnal cortisol measure. The smaller effects for diurnal cortisol measures highlight potential divergence in the sensitivity of different diurnal cortisol indices to training effects. The diurnal cortisol measures were still significantly influenced by interventions, although the effects being smaller could be due to one of many factors such as the varied and inconsistent quantification of diurnal cortisol utilised, differences in the number and timing of daily samples across the day as well as variation in daily lifestyle factors. Whereas cortisol levels measured after awakening may be less confounded by the diverse influences of the day (e.g., food intake, exercise), and thus are less ‘noisy’ measures (Engert et al., 2023). It could be said that if studies were better controlled and quality checked, different effects may emerge. Although, when conducting further analysis we did not find any significant difference in intervention effectiveness based on study quality, nor a relationship between study quality and type of cortisol measurement.

Two quality assessment tools were used, the RoB2 and a cortisol quality assessment tool (Laufer et al., 2018; Sterne et al., 2019). Determining the quality of the cortisol measurements in the included studies was imperative to consider because the methods of cortisol collection are likely to impact study findings of intervention effectiveness (Adam et al., 2017). It is apparent from the study quality assessments that studies lack true consideration of state covariates such as time of day, psychotropic medication, oral contraceptives and somatic disease and there is room for improvement in this area especially considering these factors greatly influence cortisol measurement (Stalder et al., 2016). We found studies with the poorest study quality, and greatest risk of bias, to have the smallest effect sizes and these main effects were not significant suggesting that poorer controlled studies fail to determine the true effectiveness of stress management interventions. However, there were no significant differences between categories of study quality or risk of bias groups; this could be attributed partially to the heterogeneity of the sampling procedures across the included studies. Nevertheless, the current findings highlight the importance for researchers in this area to ensure that their intervention studies are designed to be of the highest quality in order to robustly and accurately test the effectiveness of their interventions.

There are inevitable shortcomings to any research including the current meta-analysis. First, due to the heterogeneity of the included participant samples, psychological interventions and cortisol measurement procedures; there was a great variety in frequency, timings, procedures and measures of cortisol which may have caused further confounding of the true effectiveness of the included interventions. Second, we recognise the small number of hair cortisol studies available in the current meta-analysis which prevented us from comparing effectiveness of the interventions against studies that utilised blood and saliva samples. The studies utilising hair cortisol are more recent publications, possibly represent better controlled studies and it is hoped that further research continues to utilise this measurement parameter in the future. Third, when categorising the stress management interventions it

is inevitably vulnerable to a degree of subjectivity therefore it may be that others may consider the interventions to reflect different intervention mechanisms. However, we ensured a second screener independently categorised a proportion of the interventions and reached consensus with the first reviewer prior to categorisation. Lastly, the scope of the review focussed exclusively on healthy participants which limits our conclusions to a degree. Future research is needed to confirm these findings and to identify the most effective interventions for reducing cortisol levels stratified by different populations.

Overall, the current systematic review and meta-analysis found a positive effect of stress management interventions on cortisol, with robust conclusions for blood and saliva cortisol. Interventions were more effective when compared to active control groups than passive control groups and more effective at changing the cortisol awakening response measures compared to diurnal cortisol measures. There was no significant difference in the effectiveness of interventions based on the type of cortisol measurement (blood, saliva, or hair) nor for the length of the intervention. Mindfulness and meditation and relaxation interventions were found to be most effective yielding the largest effect sizes, while mind body therapies and talking therapies were shown to have smaller and non-significant effect sizes. The current findings confirm that stress management interventions can positively influence cortisol levels. Future research should investigate the longer term implications for health and health outcomes.

Declaration of Competing Interest

The authors have no declaration of interests to declare.

Acknowledgements

Research completed as partial fulfilment of first authors PhD funded by the Economic and Social Research Council (Grant number: ES/P000745/1).

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2023.106415.

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