

Yoga for anxiety: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Yoga has become a popular approach to improve emotional health. The aim of this review was to systematically assess and meta-analyze the effectiveness and safety of yoga for anxiety. Medline/PubMed, Scopus, the Cochrane Library, PsycINFO, and IndMED were searched through October 2016 for randomized controlled trials (RCTs) of yoga for individuals with anxiety disorders or elevated levels of anxiety. The primary outcomes were anxiety and remission rates, secondary outcomes were depression, quality of life, and safety. Risk of bias was assessed using the Cochrane tool. Eight RCTs with 319 participants (mean age: 30.0-38.5 years) were included. Risk of selection bias was unclear for most RCTs. Meta-analyses revealed evidence for small short-term effects of yoga on anxiety compared to no treatment (standardized mean difference (SMD)=-0.43; 95%confidence interval (CI)=-0.74,-0.11; P=0.008); and large effects compared to active comparators (SMD=-0.86; 95%CI=-1.56,-0.15; P=0.02). Small effects on depression were found compared to no treatment (SMD=-0.35; 95%CI=-0.66,-0.04; P=0.03). Effects were robust against potential methodological bias. No effects were found for patients with DSM-diagnosed anxiety disorders, only for patients diagnosed by other methods and for individuals with elevated levels of anxiety without a formal diagnosis. Only 3 RCTs reported safety-related data but these indicated that yoga was not associated with increased injuries. In conclusion, yoga might be an effective and safe intervention for individuals with elevated levels of anxiety. There was inconclusive evidence for effects of yoga in anxiety disorders. More high quality studies are needed and are warranted given these preliminary findings and plausible mechanisms of action.

Introduction

Anxiety is a normal response to specific situations or events. However, excessive fear or anxiety may be indicative of an anxiety disorder (American Psychiatric Association, 2013). In generalized anxiety disorder, elevated levels of anxiety, which are associated with concerns about health, relationships, work, and financial issues lead to a wide variety of physical symptoms and behavioural changes. Excessive anxiety also has implications for long-term health, with somatic symptoms of anxiety, such as palpitations and irregular heartbeat, associated with an increased risk of cardiovascular disease in women (Nabi et al., 2010). Anxiety disorders are estimated to range in prevalence from 0.9% to 28.3% worldwide (Baxter, Scott, Vos, & Whiteford, 2013), with factors contributing to this variation including demographic factors of gender, age, financial status, and culture, as well as methodological differences such as definitions of anxiety disorders, and measurement or diagnostic tools. In the US, 12 month and lifetime prevalence of GAD have been reported as 2.1% and 4.1% respectively (Grant et al., 2005).

Psychological approaches and medication are the mainstays of treatment for anxiety disorders (Katzman et al., 2014). Guidance on the management of generalised anxiety disorders and panic attacks recommends low-intensity psychological interventions including psychological therapy (such as cognitive behavioral therapy), medication, and self-help (including support groups, and exercise) (National Institute for Health and Care Excellence, 2011). However, many people experiencing high levels of anxiety do not seek a medical opinion, or choose not to accept psychological or pharmaceutical interventions, preferring instead to self-manage their condition (Morgan & Jorm, 2009).

Yoga, a form of mind-body therapy (National Center for Complementary and Integrative Health, 2015), has become a popular approach to achieving and maintaining 'wellness', and is perceived to improve emotional health (Stussman, Black, Barnes, Clarke, & Nahin, 2015). Practice of yoga is increasing, with lifetime and 12-month prevalence of yoga practice in the US being 13.2% and 8.9%, respectively (Cramer et al., 2016). The term 'yoga' in the

Western context is used to describe practices including physical postures (asanas), breath regulation techniques (pranayama), meditation/mindfulness, and relaxation (De Michelis, 2005). Yoga classes may also incorporate discussion of yoga philosophy and lifestyle advice. Yoga classes are increasingly available within the community. A variety of different yoga styles or 'schools' have emerged that put varying focus on physical and mental practices; ranging from pure meditation or breathing practices to quite intense physical activity (De Michelis, 2005; Feuerstein, 1998). Additionally, many people follow their own personal home practice. Results of a 2012 US survey indicated 48.8% of US adults who practiced yoga did not attend formal classes; the remaining individuals attended a mean of 1 class per month (Cramer et al., 2016). Yoga practitioners have reported reduced stress levels and greater relaxation (Stussman et al., 2015), and treating anxiety is one of the main reasons people give for practising mind-body therapies such as yoga (Barnes et al., 2008). Low levels of mindfulness have been found in individuals with GAD and other emotional disorders (Curtiss & Klemanski, 2014), suggesting potential for approaches that increase mindfulness (Vollestad, Nielsen, & Nielsen, 2012). Consequently, there has been research interest in assessing the effects of yoga on anxiety. Previous reviews of the research have been inconclusive. While some reviews now are outdated (Kirkwood, Rampes, Tuffrey, Richardson, & Pilkington, 2005), others have included participants without anxiety and are thus difficult to interpret (Hofmann, Andreoli, Carpenter, & Curtiss, 2016).

The prevalence and burden of anxiety disorders, together with the reported beneficial effects of yoga practice, and increased publication of clinical trials indicate that an updated systematic review is required. The aim of this review was to systematically assess and meta-analyze the effectiveness and safety of yoga in patients with anxiety disorders or related disorders and individuals with elevated levels of anxiety.

Materials and methods

This review was planned and conducted in accordance with PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009) and the recommendations of the Cochrane Collaboration (Higgins & Green, 2008).

Eligibility criteria

Types of studies

Randomized controlled trials (RCTs), cluster-randomized trials, and randomized cross-over studies. All studies from all countries published in any language were eligible. Study quality or risk of bias in the respective study were not a criterion for inclusion.

Types of participants

To be eligible for the review, studies were required to include the following type of participants:

1. Adults with a diagnosis of an anxiety disorder in accordance with the Diagnostic and Statistical Manual, Third Edition (DSM-III or DSM-III-R), Fourth Edition (DSM-IV or DSM-IV-TR) or Fifth Edition (DSM-V) or the International Classification of Disease 10 (ICD-10). It was post hoc decided to exclude studies on adults with a diagnosis of obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), or acute stress disorder because these conditions are no longer classified as anxiety disorders in DSM-V.

Studies involving participants with comorbid physical or mental disorders were eligible as long as the comorbidity was not the focus of the study, e.g. studies including some patients with anxiety disorders who also had OCD were eligible while studies including only patients with OCD were excluded.

2. Adults with a diagnosis of an anxiety disorder as defined above diagnosed based on any other criteria.

3. Otherwise healthy adults with elevated levels of anxiety at the start of the RCT measured by a validated clinician-based or self-report anxiety symptom questionnaire but without a formal diagnosis of an anxiety disorder.

Differences between the three types of participants were investigated in a subgroup analysis.

Types of interventions

Experimental:

1. Multicomponent yoga interventions, i.e. yoga intervention including both, a) yoga postures (asanas) and/or flowing sequences of yoga postures (vinyasas) and b) breath control (pranayama) and/or meditation and/or deep relaxation (based on yoga theory and/or traditional yoga practices).
2. Posture-based yoga interventions, i.e. yoga intervention including only asanas and/or vinyasas without breath control or meditation.
3. Breathing/meditation-based yoga interventions including pranayama and/or meditation and/or deep-relaxation (based on yoga theory and/or traditional yoga practices) without asanas or vinyasas. Interventions were included only if they were explicitly labelled 'yoga' or 'yogic'.

Differences between the three types of experimental interventions were investigated in a subgroup analysis. No restrictions were made regarding yoga tradition, length, frequency, or duration of the program.

Co-interventions:

Studies allowing individual co-interventions (such as pharmacotherapy) were eligible if all participants in all groups received the same co-interventions.

Control:

Studies comparing yoga to no treatment, usual care, or any active control intervention were eligible. Separate meta-analyses were conducted for different control conditions.

Types of outcome measures

For inclusion in this review, RCTs had to assess at least one primary anxiety outcome:

1. Improvement in the severity of anxiety, measured by validated self-rating scales or clinician-rated scales.
2. Improvement in anxiety measured as the number of patients who reached remission, as measured using validated self-rating scales or clinician-rated scales.

Secondary outcomes included:

1. Improvement in depressive symptoms, measured using validated self-rating scales or clinician-rated scales.
2. Improvement in health-related quality of life, measured by any validated scale
3. Safety of the intervention, assessed as number of participants with adverse events.

Search methods

The following electronic databases were searched from their inception through October 13, 2016: Medline (through PubMed), Scopus, the Cochrane Library, PsycINFO, and IndMED.

The literature search was constructed around search terms for “yoga” and search terms for

“anxiety”. For PubMed, the following search strategy was used: (*"Anxiety"[MeSH] OR "Anxiety Disorders"[MeSH] OR "Stress Disorders, Traumatic"[MeSH] OR anxiety[Title/Abstract] OR phobia[Title/Abstract] OR phobic[Title/Abstract] OR panic[Title/Abstract] OR "stress disorder"[Title/Abstract] OR PTSD[Title/Abstract] OR "obsessive-compulsive disorder"[Title/Abstract] OR OCD[Title/Abstract]*) AND (*"Yoga"[MeSH] OR yoga[Title/Abstract] OR yogic[Title/Abstract] OR asana[Title/Abstract] OR pranayama[Title/Abstract] OR dhyana[Title/Abstract]*). The search strategy was adapted for

each database as necessary. In addition, hand searches were conducted on our own

extensive database (Cramer, Lauche, & Dobos, 2014), reference lists of identified original

articles or reviews, and tables of contents of the International Journal of Yoga Therapy, the Journal of Yoga & Physical Therapy, and the International Scientific Yoga Journal SENSE.

Abstracts identified during the database and hand searches were screened by two review authors (HC, DA) independently, with potentially eligible articles read in full by two review authors (HC, DA) to determine whether they met the eligibility criteria. Disagreements were discussed with a third review author (RL) until consensus was reached. If necessary, additional information was obtained from the study authors.

Data extraction and management

Data on participants (e.g. age, gender, diagnosis), methods (e.g. randomization, allocation concealment), interventions (e.g. yoga style, frequency, and duration), control interventions (e.g. type, frequency, duration), outcomes (e.g. outcome measures, assessment time points), and results were independently extracted by two pairs of review authors (RL, LW; and HC, DA) using an *a priori* data extraction form. Discrepancies were discussed with a third review author (HC; RL) until consensus was reached. If necessary, study authors were contacted for additional information.

Risk of bias in individual studies

Two pairs of review authors (RL, LW; and HC, DA) independently assessed risk of bias on the following domains: selection bias (random sequence generation, allocation concealment), performance bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and other bias using the Cochrane risk of bias tool (Higgins & Green, 2008). All domains were scored as 1) low risk of bias, 2) unclear, or 3) high risk of bias (Higgins & Green, 2008). Discrepancies were discussed with a third review author until consensus was reached.

Data analysis

Effects of yoga compared to different control interventions were analyzed separately, as were short-term, medium-term, and long-term effects. Short-term outcomes were defined as outcome measures taken closest to 12 weeks after randomization, medium-term outcomes as closest to 6 months after randomization, and long-term outcomes as closest to 12 months after randomization.

Assessment of overall effect size

Meta-analyses were conducted using Review Manager 5 software (Version 5.3, The Nordic Cochrane Centre, Copenhagen, Denmark) by a random-effects model if at least two studies assessing this specific outcome were available. For continuous outcomes, standardized mean differences (SMD) with 95% confidence intervals (CI) were calculated as the difference in means between groups divided by the pooled standard deviation (Higgins & Green, 2008). Where no standard deviations were available, they were calculated from standard errors, confidence intervals, or t-values, or attempts were made to obtain the missing data from the trial authors by email. A negative SMD was defined to indicate beneficial effects of yoga compared to the control intervention for all outcomes (e.g. decreased anxiety) except for health-related quality of life where a positive SMD was defined to indicate beneficial effects (e.g. increased well-being). If necessary, scores were inverted by subtracting the mean from the maximum score of the instrument (Higgins & Green, 2008). Cohen's categories were used to evaluate the magnitude of the overall effect size with SMD 0.2 to 0.5 categorized as small; SMD 0.5 to 0.8 as medium, and SMD > 0.8 as large effect sizes (Cohen, 1998).

For dichotomous outcomes, odds ratios (RR) with 95% CI were calculated by dividing the odds of an adverse event in the intervention group (i.e. the number of participants with the respective type of adverse event divided by the number of participants without the respective type of adverse event) by the odds of an adverse event in the control group (Higgins & Green, 2008). Where studies reported zero events in one or both intervention groups, a value of 0.5 was added to all cells of the respective study.

Assessment of heterogeneity

Statistical heterogeneity between studies was analyzed using the I^2 statistic, a measure of how much variance between studies can be attributed to differences between studies rather than chance. The magnitude of heterogeneity was categorized as 1) $I^2 = 0-24\%$: low heterogeneity; $I^2 = 25-49\%$: moderate heterogeneity; $I^2 = 50-74\%$: substantial heterogeneity; and $I^2 = 75-100\%$: considerable heterogeneity (Higgins & Green, 2008). The Chi^2 test was used to assess whether differences in results were compatible with chance alone. Given the low power of this test when only few studies or studies with low sample size are included in a meta-analysis, a P-value ≤ 0.10 was considered to indicate significant heterogeneity (Higgins & Green, 2008).

Subgroup and sensitivity analyses

Four subgroup analyses were conducted:

- 1) Type of participants (patients with anxiety disorders diagnosed according to DSM III, DSM IV, DSM V or ICD-10; patients with anxiety disorders diagnosed according to any other criterion; individuals with elevated levels of anxiety but without a formal diagnosis of an anxiety disorder);
- 2) Type of yoga intervention (multicomponent; posture-based; breathing/meditation-based);
- 3) Country of origin (India; other countries);
- 4) Gender (mixed; female only; male only).

To test the robustness of significant results, sensitivity analyses were conducted for studies with low risk of bias on the following domains: selection bias (random sequence generation and allocation concealment), detection bias (blinding of outcome assessment), and attrition bias (incomplete outcome data). If statistical heterogeneity was present in the respective meta-analysis, subgroup and sensitivity analyses were also used to explore possible reasons for heterogeneity.

Risk of bias across studies

If at least 10 studies were included in a meta-analysis, assessment of risk of publication bias was originally planned using funnel plots generated by the Cochrane Review Manager 5 software (Higgins & Green, 2008). As less than 10 studies were included in each analysis, this was not possible.

Results

Literature search

The results of the literature search and screening process are summarized in Figure 1. The literature search returned 1993 records. Of 1188 non-duplicate records, 1161 were excluded because they were not randomized, did not include patients with anxiety, did not include relevant outcomes and/or did not include yoga interventions. Twenty-seven full-text articles were assessed, and 5 were excluded because they were not randomized (Clark et al., 2014; Sharma, Azmi, & Settiwar, 1991; Telles, Gaur, & Balkrishna, 2009; Tolbaños Roche, Miró Barrachina, & Ibáñez Fernández, 2016; Valentine, Meyer-Dinkgräfe, Acs, & Wasley, 2006). For two further articles it was unclear whether they were randomized or not (Kozasa et al., 2008; Vahia, Doongaji, Jeste, Ravindranath, et al., 1973); the authors of one article clarified that the trial was not randomized (Kozasa et al., 2008); both articles were excluded. Eleven further articles were excluded because they did not include relevant participants (i.e. those participants that were defined in our inclusion criteria) (Javnbakht, Hejazi Kenari, & Ghasemi, 2009; Khalsa, Shorter, Cope, Wyshak, & Sklar, 2009; Nemati & Habibi, 2012; Shankarapillai, Nair, & George, 2012; Sureka et al., 2014) or did not assess one of the pre-specified primary outcomes (severity of anxiety or remission rates) (Carter et al., 2013; Quinones, Maquet, Velez, & Lopez, 2015; S. Reddy, Dick, Gerber, & Mitchell, 2014; Rhodes, Spinazzola, & Van Der Kolk, 2016; Shannahoff-Khalsa et al., 1999; van der Kolk et al., 2014); one further article was published as a conference abstract only and did not provide enough information to be

eligible (Annapoorna, Latha, Bhat, & Bhandary, 2011). For two articles it was unclear whether all participants actually had elevated levels of anxiety; the authors of one study clarified that this was the case (Davis, Goodman, Leiferman, Taylor, & Dimidjian, 2015), those of the other article provided a subgroup analysis for participants with elevated levels of anxiety (de Manincor et al., 2016). Both articles were thus included. Eight articles were included in the qualitative synthesis (Broota & Sanghvi, 1994; Davis et al., 2015; de Manincor et al., 2016; Gupta & Mamidi, 2013; Norton & Johnson, 1983; Parthasarathy, Jaiganesh, & Duraisamy, 2014; Sahasi, Chawla, Dhar, & Katiyar, 1991; Vahia, Doongaji, Jeste, Kapoor, et al., 1973). Two articles did not provide the necessary raw data for meta-analysis (Broota & Sanghvi, 1994; Norton & Johnson, 1983); as these data could not be obtained from the study authors, both articles were excluded from the meta-analysis (Figure 1).

Study characteristics

Characteristics of the sample, interventions, outcome assessment, and results are shown in Table 1. Of the 8 included RCTs, one originated from the US (Davis et al., 2015), one from Canada (Norton & Johnson, 1983), five from India (Broota & Sanghvi, 1994; Gupta & Mamidi, 2013; Parthasarathy et al., 2014; Sahasi et al., 1991; Vahia, Doongaji, Jeste, Kapoor, et al., 1973), and one from Australia (de Manincor et al., 2016). Five RCTs included patients with a diagnosis of anxiety disorder of any kind (Parthasarathy et al., 2014), generalized anxiety disorder (Gupta & Mamidi, 2013), snake phobia (Norton & Johnson, 1983), or obsolete diagnoses such as anxiety neurosis (Sahasi et al., 1991) and psychoneurosis (Vahia, Doongaji, Jeste, Kapoor, et al., 1973). Diagnoses were based on DSM-III or DSM-IV-TR in one RCT each. In two studies, the authors did not state how the patients were diagnosed; and one study defined snake phobia as a value on a questionnaire beyond a predefined cut-off. Three RCTs included participants with unspecific (Davis et al., 2015; de Manincor et al., 2016) or specific (examination-related) (Broota & Sanghvi, 1994) anxiety but without a formal diagnosis of an anxiety disorder. A total of 319 participants were included in the 8 RCTs; sample size ranged from 12 to 78 (median: 41). Participants' mean

age ranged from 30.0 to 38.5 years (median 36.3 years). Between 26.8-100.0% (median 73.7%) of participants in each study were female; between 0.0-78.0% (median 78.0%) were Caucasian (where reported).

One RCT used meditation only (Norton & Johnson, 1983); the other RCTs used multicomponent yoga interventions, including breathing techniques and/or meditation in addition to physical postures. The intervention in one study was conducted in individual consultations (de Manincor et al., 2016); the remaining studies used group classes or did not report whether the intervention was conducted in group classes or individually. Yoga was compared to no specific treatment in three RCTs (Davis et al., 2015; de Manincor et al., 2016; Parthasarathy et al., 2014) and to active comparators, mainly relaxation, in five RCTs (Broota & Sanghvi, 1994; Gupta & Mamidi, 2013; Norton & Johnson, 1983; Sahasi et al., 1991; Vahia, Doongaji, Jeste, Kapoor, et al., 1973).

All RCTs assessed anxiety severity. Three also assessed remission rates (de Manincor et al., 2016; Gupta & Mamidi, 2013; Sahasi et al., 1991), two assessed depression severity (Davis et al., 2015; de Manincor et al., 2016), and one assessed quality of life (de Manincor et al., 2016). Only three RCTs reported safety-related data (Davis et al., 2015; de Manincor et al., 2016; Gupta & Mamidi, 2013).

Risk of bias in individual studies

Risk of selection bias was unclear for most RCTs, only two studies reported adequate random sequence generation (Davis et al., 2015; de Manincor et al., 2016), and only one reported adequate allocation concealment (de Manincor et al., 2016). The remaining studies used inadequate methods or did not report methods. No study reported adequate blinding of participants and personnel, and only one RCT reported that outcome assessors were blinded (Vahia, Doongaji, Jeste, Kapoor, et al., 1973). Risk of attrition bias was low in four RCTs (Davis et al., 2015; de Manincor et al., 2016; Gupta & Mamidi, 2013; Parthasarathy et al., 2014), and high or unclear in the remaining studies (figure 2).

Assessment of overall effect

Primary outcomes

Meta-analyses revealed evidence for small short-term effects of yoga on anxiety compared to no treatment (SMD=-0.43; 95% CI=-0.74 to -0.11; P=0.008; Figure 3); and large effects compared to active comparators (SMD=-0.86; 95% CI=-1.56 to -0.15; P=0.02; Figure 3). The single study that compared remission rates between yoga and no treatment found no group differences (de Manincor et al., 2016). Likewise, no group differences in remission rates between yoga and active comparators were found in the meta-analysis (2 RCTs; OR=1.89; 95% CI=0.15 to 24.20; p=0.62; I²=0%).

Secondary outcomes

Evidence for small short-term effects of yoga compared to no treatment was found for depression (SMD=-0.35; 95% CI -0.66 to -0.04; P=0.03; figure 4). Quality of life was assessed in one RCT that found positive effects of yoga compared to no treatment on mental but not on physical quality of life (de Manincor et al., 2016). Only three RCTs reported safety-related data. Two RCTs reported that no adverse events and/or adverse effects (de Manincor et al., 2016; Gupta & Mamidi, 2013) occurred. An RCT on pregnant women with elevated levels of anxiety reported that rates of pregnancy-related adverse events were equal to or lower than the national prevalence rate for such events without specifying rates (Davis et al., 2015).

Subgroup analyses and sensitivity analyses

Results were comparable to the overall sample when only individuals with elevated levels of anxiety but without a formal diagnosis of an anxiety disorder were included. The same was true for patients that were described to have an anxiety disorder but where the authors did not state how this disorder was diagnosed, and for patients that were diagnosed by questionnaires rather than using adequate diagnostic criteria. No effects were found in studies on patients with anxiety disorders diagnosed according to DSM III or DSM IV TR

(Table 2). Results did not change substantially when only RCTs with multicomponent yoga interventions were included in the meta-analysis (Table 2). No subgroup analyses for posture-based or breathing/meditation-based yoga interventions could be performed because insufficient studies using these interventions were available for each analysis. Regarding country of origin, RCTs conducted in India revealed large positive effects of yoga compared to active comparators on anxiety, while RCTs from Western countries found small positive effects of yoga compared to no treatment on anxiety and depression (Table 2). Studies including both male and female participants found small effects on anxiety and depression for yoga compared to no treatment. Small effects on anxiety also were found in studies including only female participants when comparing yoga to no treatment (Table 2). No studies including only male participants were included.

The effects of yoga compared to no treatment on anxiety and depression did not change substantially when only RCTs with low risk of selection, detection, or attrition bias were assessed.

Discussion

Summary of results

This systematic review and meta-analysis found that yoga might be beneficial in the short-term for improving intensity of anxiety when compared to untreated controls or active comparators. However, no effects were found when only patients with DSM-diagnosed anxiety disorder were included in the analyses. Overall, the application of yoga was not associated with increased injuries or increased anxiety symptoms, with the caveat that only 3 RCTs reported safety-related data.

Comparison to prior reviews

Only few systematic reviews have examined the evidence on yoga for anxiety disorders. One review conducted in 2005 (Kirkwood et al., 2005) searched for uncontrolled, controlled, and

randomized controlled trials, and included 8 studies. Their review found poor reporting of study methodology with high potential risk of bias and, based on their results, concluded that while all studies actually reported benefits following participation in yoga interventions, evidence was encouraging at best. Furthermore, while encouraging results for OCD were found, OCD is no longer considered an anxiety disorder and results were based on changes in an OCD-specific outcome rather than anxiety levels per se. In 2009, de Silva and colleagues conducted a systematic review on the effects of yoga for mood and anxiety disorders (da Silva, Ravindran, & Ravindran, 2009). The review included 13 mainly non-randomized studies, on participants with a variety of anxiety disorders. The authors concluded that the evidence of yoga for anxiety disorders must be considered preliminary.

Five out of the eight studies on which the present review was based have been published in the past five years, leading to a substantial increase in the overall evidence. Despite the large number of new trials included in this review, the evidence must still be considered insufficient. Yoga appears to be beneficial over no-treatment controls based on the intensity of anxiety, but there are several limitations to this review including the variety of diagnoses included, the heterogeneity of interventions, and the potential bias in the included trials. As such, no effect in yoga compared to untreated control groups or those treated with other interventions was found in the present review when only studies that applied DSM anxiety disorder diagnosis were included. Thus the conclusion of this review can still only be considered preliminary, and further trials are required for conclusive recommendation.

While there remains a need for further high quality, methodologically robust RCTs in order to examine the effects of yoga on anxiety disorders, the rationale for yoga interventions with a physical component to treat such disorders is plausible. Exercise interventions, for example, have been shown to introduce multiple physiological adaptations in the human body leading to improvements in anxiety and depression. Experimental studies revealed that exercise induces alterations in the serotonergic and noradrenergic system, which are both targeted by pharmacotherapy of mood disorders (DeBoer, Powers, Utschig, Otto, & Smits, 2012). The

exercise-induced release of endogenous opioids may be linked to the reduction in pain (Kosek & Lundberg, 2003) and the induction of heightened mood (Dishman & O'Connor, 2009) as shown by systematic reviews on yoga (Cramer, Lauche, Haller, & Dobos, 2013; Cramer, Lauche, Langhorst, & Dobos, 2013). Exercise, as well as meditation, also influences the hypothalamic-pituitary-adrenal responsiveness, and leads to adaptations in endocrine secretion of substances such as cortisol and adrenocorticotrophic hormones (Anderson & Shivakumar, 2013; Infante et al., 1998; MacLean et al., 1997).

Yoga has further been found to increase thalamic GABA (γ -Aminobutyric acid) levels (Streeter et al., 2007; Streeter et al., 2010), and as pharmacologic agents for anxiety (and mood disorders) act via increase of GABA levels, it is plausible that the increase in GABA after yoga may be part of its mode of action to improve anxiety. Pranayama, or breath control, is also thought to recalibrate the sympathetic nervous system, through inducing a shift towards a dominance of the parasympathetic nervous system activity via vagal stimulation (Brown & Gerbarg, 2005a, 2005b). This is in line with experimental research findings that have found associations between anxiety and sympathetic activation, vagal deactivation, an increase in breathing frequency, and a decrease in the depth of breathing (Kreibig, 2010). It is furthermore supported by studies showing high prevalence of anxiety and depression in patients with breathing disorders (Kunik et al., 2005). Indeed, breathing retraining has been an essential part of many cognitive behavior therapy approaches for panic disorders (Hazlett-Stevens & Craske, 2009; Schmidt et al., 2000). Those findings are supplemented by qualitative studies and case reports reporting increased self-efficacy and coping abilities after yoga classes (Cramer, Lauche, Haller, Langhorst, et al., 2013; Evans et al., 2011; Williams-Orlando, 2013).

Limitations

This systematic review has several limitations. Firstly, the paucity of trials in general, and the paucity of trials for specific anxiety disorders in particular, rendered in-depth meta-analyses impossible. Where there was more than one trial for one condition, trials were still

heterogeneous regarding sample or intervention characteristics. Secondly, many of the included trials did not use standardized formal diagnostic criteria, such as the DSM. While diagnostic criteria change over time, the use of such criteria may have more accurately described the participant populations involved in the trials. Third, very few trials included in this review had a low risk of bias regarding random sequence generation, allocation concealment, or blinding. While the latter may be implausible due to the nature of yoga interventions, there are possibilities for reducing the potential risk of bias; for example, by selecting adequate control groups, and examining patients' expectations prior to the trial. Authors of prospective research would further improve the reporting of yoga trials by adhering to standard reporting guidelines (e.g. CONSORT). Lastly, the large effects of yoga compared to active comparators were mainly driven by one of the three included studies while the other two studies had more moderate effects.

The findings of this meta-analysis indicate that yoga might be an effective and safe intervention for individuals with elevated levels of anxiety. While this systematic review found there was no conclusive evidence for the effective use of yoga in anxiety disorders, yoga may, however, be considered a safe (Cramer et al., 2015; M. S. Reddy & Vijay, 2016), ancillary intervention for patients unwilling to commit to other forms of exercise. More high quality studies are needed and are warranted given these preliminary findings and plausible mechanisms of action.

Tables

Table 1: Characteristics of included studies

Reference	Setting	Sample	Duration	Intervention	Control Intervention(s)	Outcomes	Results
						1) Anxiety 2) Remission 3) Depression 4) Quality of life 5) Safety	1) Anxiety 2) Remission 3) Depression 4) Quality of life 5) Safety
Broota & Sanghvi, 1994 (41)	Origin: India Recruited from: University	Sample size: 30 Mean Age: not reported Gender: not reported Ethnicity: not reported Diagnosis: History of examination anxiety, and high level of anxiety on STAI	Intervention duration: 3 days Outcome assessment: 3 days	Broota Relaxation Technique (postures, breathing techniques, relaxation) Unspecified individual or group classes: 1x20 minutes/day for 3 days	1) Progressive muscle relaxation Group classes: 1x20 minutes/day for 3 days 2) Social interaction Individual phone conversations: 1x20 minutes/day for 3 days	1) Symptom Checklist (not validated); ladder scale (not validated) 2) Not assessed 3) Not assessed 4) Not assessed 5) Not reported	1) Significant group differences favoring yoga on symptom checklist but not on ladder scale
Davis et al, 2015 (39)	Origin: USA Recruited from: Health care providers and advertisement	Sample size: 46 Mean Age: 30 years Gender: 100% female Ethnicity: 78% White Diagnosis: Pregnant	Intervention duration: 8 weeks Outcome assessment: Up to 8 weeks	Ashtanga Vinyasa Yoga (postures, breathing techniques, relaxation) Group classes: 1x20 minutes/week for 8	Treatment-as-usual	1) STAI; PANAS-N 2) Not assessed 3) EPDS 4) Not assessed 5) Adverse events	1) Significant group differences favoring yoga on PANAS-N but not on STAI 3) No significant group difference 5) Rates of adverse events

		women up to 28 weeks gestation with elevated anxiety (STAI)		weeks			equal to or lower than national prevalence rates
de Manicor et al, 2016 (40)	Origin: Australia Recruited from: Health service providers and advertisement	Sample size: 78 Mean Age: 38.5 years Gender: 74,4% female Ethnicity: not reported Diagnosis: At least mild anxiety based on the DASS-21	Intervention duration: 6 weeks Outcome assessment: 6 and 12 weeks	Individualized yoga (postures, breathing techniques, meditation, relaxation) One-to-one consultations (4 x 1 hour each, over 6 weeks) and individualized home practice: approx. average 30 minutes x 5 days/week for 6 weeks	Waitlist control	1) DASS-21 2) Not assessed 3) DASS-21; K10 4) SF-12 5) Adverse effects	1) Significant group differences favoring yoga 3) Significant group differences favoring yoga 4) Significant group differences favoring yoga 5) No yoga-related adverse effects
Gupta & Mamidi, 2013 (42)	Origin: India Recruited from: Outpatient center	Sample size: 12 Mean Age: 36.25 years Gender: 50% female Ethnicity: NR Diagnosis: GAD based on DSM-IV TR	Intervention duration: 3 weeks Outcome assessment: 3 weeks	Yoga (postures, breathing techniques, prayer) Unspecified individual or group classes: 7x60 minutes/week for 3 weeks	Naturopathy (Massage, acupuncture, breathing techniques) Individual treatments 7x60 minutes/week for 3 weeks	1) HARS 2) Number of "cured" patients 3) Not assessed 4) Not assessed 5) Adverse events and adverse effects	1) Significant group differences favoring yoga 2) no patient "cured" in either group 5) no adverse events or adverse effects
Norton et al., 1983 (45)	Origin: Canada Recruited from: University	Sample size: 40 Mean Age: not reported Gender: 73% female	Intervention duration: 3 weeks Outcome assessment:	Agni Yoga (meditation) Group classes: 4x45 minutes within 3 weeks, and	Progressive relaxation Group classes: 4x45 minutes	1) Approach score; fear thermometer; SNAQ 2) Not assessed	1) No significant group differences

		<p>Ethnicity: not reported</p> <p>Diagnosis: Moderate to very fearful snake anxiety (SNAQ)</p>	3 weeks	encouraged (with alternate days phone contact) to do daily home practice throughout the 3 weeks.	within 3 weeks. Home practice not specified.	<p>3) Not assessed</p> <p>4) Not assessed</p> <p>5) Not reported</p>	
Parthasarathy et al., 2014 (46)	<p>Origin: India</p> <p>Recruited from: Tertiary care center</p>	<p>Sample size: 45</p> <p>Mean Age: not reported</p> <p>Gender: 100% female</p> <p>Ethnicity: not reported</p> <p>Diagnosis: Anxiety disorder (diagnostic criteria not reported)</p>	<p>Intervention duration: 8 weeks</p> <p>Outcome assessment: 8 weeks</p>	<p>1) Yoga (postures, breathing techniques, relaxation)</p> <p>Group classes: 7x45 minutes/week for 8 weeks</p> <p>2) Integrated Yoga module (postures, breathing techniques, relaxation)</p> <p>Group classes: 7x45 minutes/week for 8 weeks</p>	No treatment	<p>1) TMAS</p> <p>2) Not assessed</p> <p>3) Not assessed</p> <p>4) Not assessed</p> <p>5) Not reported</p>	1) Significant group differences favoring yoga
Sahasi et al., 2014 (48)	<p>Origin: India</p> <p>Recruited from: Psychiatry department</p>	<p>Sample size: 40</p> <p>Mean Age: not reported</p> <p>Gender: 26.8% female</p> <p>Ethnicity: not reported</p> <p>Diagnosis: Anxiety neurosis based on DSM-III</p>	<p>Intervention duration: not reported</p> <p>Outcome assessment: 1 week, 12 weeks</p>	<p>Yoga (postures, relaxation)</p> <p>frequency, length, duration not reported</p> <p>Unspecified individual or group classes. Participants asked to practice at home.</p>	<p>Progressive muscle relaxation</p> <p>frequency, length, duration not reported</p>	<p>1) STAI; IPAT anxiety scale</p> <p>2) Number of patients with complete recovery</p> <p>3) Not assessed</p> <p>4) Not assessed</p> <p>5) Not reported</p>	<p>1) No group comparison reported</p> <p>2) 1 and 0 patients completely recovered in yoga and control group, respectively</p>

<p>Vahia et al., 1973 (26)</p>	<p>Origin: India Recruited from: Outpatient center</p>	<p>Sample size: 27 Mean Age: not reported Gender: not reported Ethnicity: 0% Caucasians Diagnosis: Psychoneurosis (diagnostic criteria not reported)</p>	<p>Intervention duration: 4 weeks Outcomes: 4 weeks</p>	<p>Psychophysiological therapy based on the concepts of Patanjali (postures, breathing techniques, relaxation) Unspecified individual or group classes. 7x60 minutes/week for 4 week</p>	<p>Pseudo-treatment (postures, breathing, relaxation) 7x60 minutes/week for 4 week</p>	<p>1) TMAS 2) Not assessed 3) Not assessed 4) Not assessed 5) Not reported</p>	<p>1) Significant group differences favoring yoga</p>
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Abbreviations: BAI, Beck Anxiety Inventory; BRS, Behavioral Self-Rating Scale; CSTAQ, Cognitive-Somatic Trait Anxiety Questionnaire; DASS-21, Depression Anxiety and Stress Scale - 21 item; DSM-III, Diagnostic and Statistical Manual of Mental Disorders Version III; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders Version IV Text Revision; EPDS, Edinburgh Postnatal Depression Scale; GAD, Generalized Anxiety Disorder; HARS, Hamilton Anxiety Rating Scale; IPAT, Institute for Personality & Ability Testing; K10, Kessler Psychological Distress Scale; MASQ, Mood and Anxiety Symptoms Questionnaire; OCD, Obsessive Compulsive Disorder; PANAS-N, Positive and Negative Affect Schedule - Negative Subscale; PASS, Performance Anxiety Self Statement; PTSD, Posttraumatic Stress Disorder; STAI, State Trait Anxiety Inventory; SF-12, Short-Form Health Survey; SNAQ, Snake Attitude Questionnaire; TMAS, Taylor's Manifest Anxiety Scale

Table 2: Effect sizes of a) different participant samples b) different yoga interventions, c) different countries of origin, and d) different genders.

Outcome**	No. of studies	No. of patients (yoga)	No. of patients (control)	Standardized mean difference (95% confidence interval)**	P (overall effect)	Heterogeneity I ² ; Chi ² ;P
A) Participant sample						
Anxiety disorder DSM or ICD						
Anxiety						
Yoga vs. active comparator	2	26	26	-0.52 (-1.08, 0.03)	0.06	0%; 0.02; 0.88
Remission rates**						
Yoga vs. active comparator	2	26	24	1.89 (0.15, 24.20)	0.69	0%; 0.15; 0.69
Anxiety disorder other diagnoses						
Anxiety						
Yoga vs. no treatment	1	30	15	-0.37 (-1.00, 0.20)	0.24	-
Yoga vs. active comparator	1	15	12	-1.58 (-2.47, -0.69)	<0.001	-
Elevated levels of anxiety						
Anxiety						
Yoga vs. no treatment	2	56	61	-0.44 (-0.81, -0.08)	0.02	0%; 0.23; 0.63
Depression						
Yoga vs. no treatment	2	56	61	-0.39 (-0.76, -0.03)	0.04	0%; 0.49; 0.48
B) Yoga intervention						
Multicomponent yoga interventions						
Anxiety						
Yoga vs. no treatment	3	86	76	-0.43 (-0.748, -0.11)	<0.001	0%; 0.27; 0.87
Yoga vs. active comparator	3	41	38	-0.86 (-1.56, -0.15)	0.02	50%; 3.96; 0.14
Remission rates**						
Yoga vs. active comparator	2	26	24	1.89 (0.15, 24.20)	0.69	0%; 0.15; 0.69
Depression						
Yoga vs. no treatment	2	56	61	-0.39 (-0.76, -0.03)	0.04	0%; 0.49; 0.48
C) Country of origin						
India						
Anxiety						
Yoga vs. no treatment	1	30	15	-0.37 (-1.00, 0.20)	0.24	-
Yoga vs. active comparator	3	41	38	-0.86 (-1.56, -0.15)	0.02	50%; 3.96; 0.14
Remission rates**						
Yoga vs. active comparator	2	26	24	1.89 (0.15, 24.20)	0.69	0%; 0.15; 0.69
Others						
Anxiety						
Yoga vs. no treatment	2	56	61	-0.44 (-0.81, -0.08)	0.02	0%; 0.23; 0.63

Depression						
Yoga vs. no treatment	2	56	61	-0.39 (-0.76, -0.03)	0.04	0%; 0.49; 0.48
C) Gender						
Mixed						
Anxiety						
Yoga vs. no treatment	1	36	42	-0.51 (-0.96, -0.06)	0.03	-
Yoga vs. active comparator	2	26	26	-0.52 (-1.08; 0.03)	0.06	0%; 0.02; 0.88
Remission rates**						
Yoga vs. active comparator	2	26	24	1.89 (0.15, 24.20)	0.69	0%; 0.15; 0.69
Depression						
Yoga vs. no treatment	1	36	41	-0.49 (-0.94; -0.03)	0.03	-
Female only						
Anxiety						
Yoga vs. no treatment	2	66	57	-0.46 (-0.83; -0.10)	0.01	0%; 0.12; 0.73
Depression						
Yoga vs. no treatment	1	20	19	-0.21 (-0.84; 0.42)	0.52	-

*Outcomes are only shown if sufficient data for meta-analysis were available.

**Remission rates were analyzed using odds ratios (95% confidence intervals)

2

Figure captions

Figure 1: Flow chart of the results of the literature search.

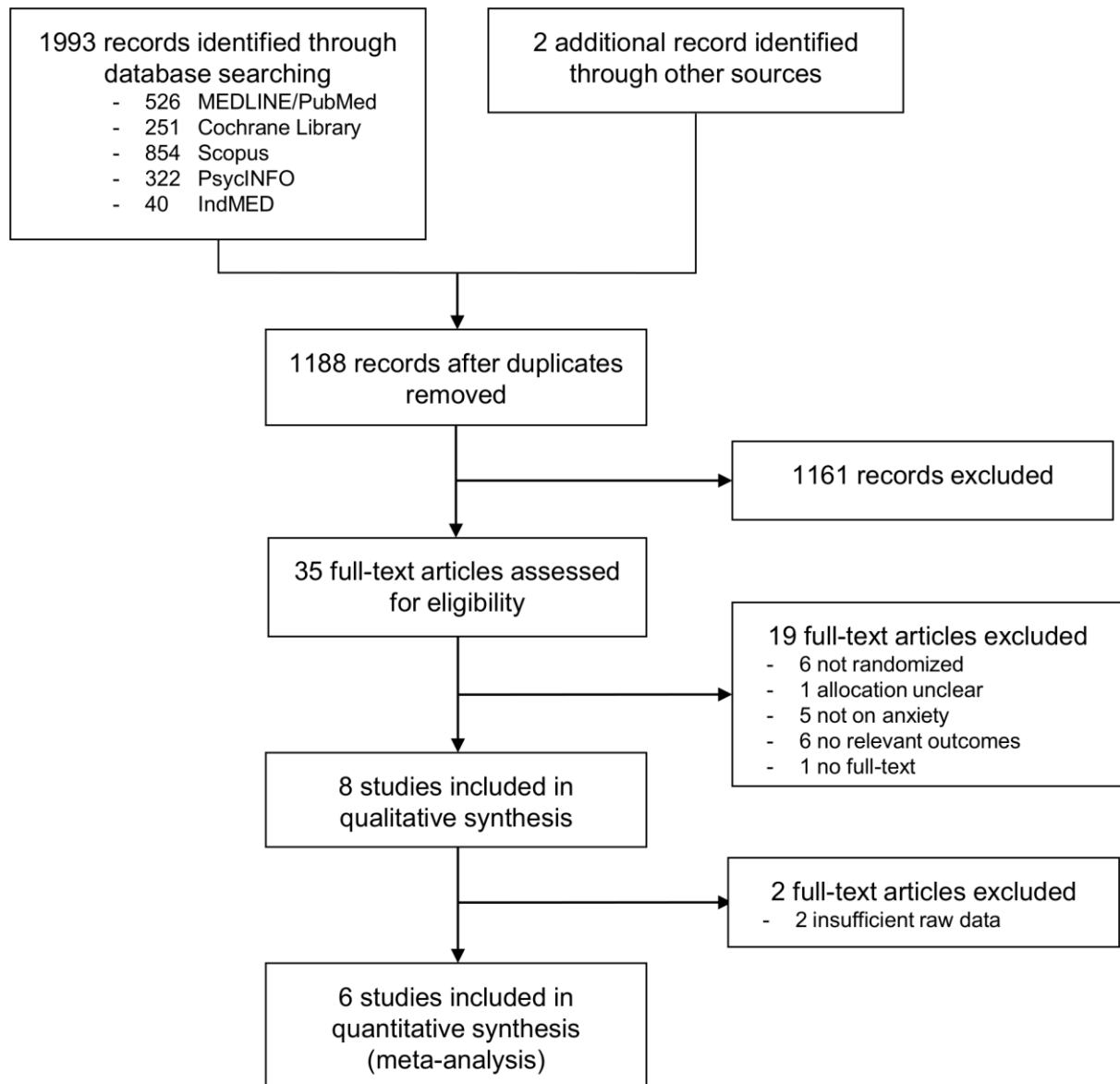


Figure 2: Risk of bias in individual studies. +, low risk of bias; ?, unclear risk of bias; - high risk of bias.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Broota 1994	?	?	?	?	-	-	-
Davis 2015	+	?	?	?	+	+	?
de Manincor 2016	+	+	?	-	+	+	+
Gupta 2013	-	-	?	?	+	+	+
Norton 1983	?	?	?	?	?	?	-
Parthasarathy 2014	?	+	?	?	?	+	+
Sahasi 1991	?	?	?	?	+	-	+
Vahia 1973	?	?	?	+	-	-	-

Figure 3: Forest plot of yoga versus no treatment or active comparators for anxiety severity. CI - confidence interval; IV - inverse variance; SD - standard deviation

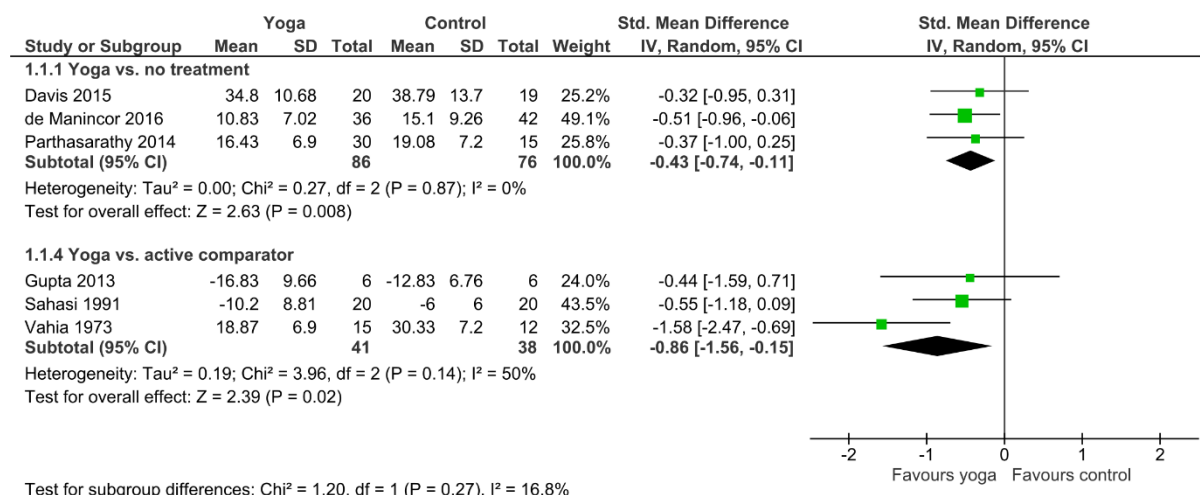
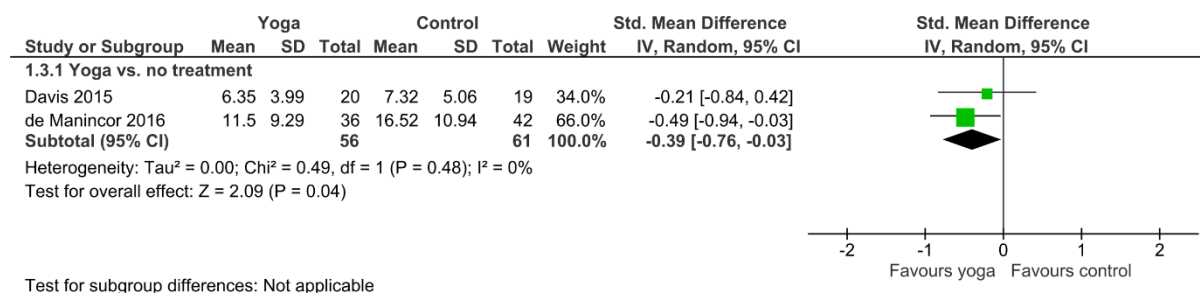


Figure 4: Effects of yoga versus no treatment on depression severity. CI - confidence interval; IV - inverse variance; SD - standard deviation



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