



## Review article

## A systematic review of yoga for major depressive disorder

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## ABSTRACT

**Background:** The purpose of this review was to investigate the efficacy and safety of yoga interventions in treating patients with major depressive disorder.

**Methods:** MEDLINE, Scopus, and the Cochrane Library were screened through December 2016. Randomized controlled trials (RCTs) comparing yoga to inactive or active comparators in patients with major depressive disorder were eligible. Primary outcomes included remission rates and severity of depression. Anxiety and adverse events were secondary outcomes. Risk of bias was assessed using the Cochrane tool.

**Results:** Seven RCTs with 240 participants were included. Risk of bias was unclear for most RCTs. Compared to aerobic exercise, no short- or medium-term group differences in depression severity was found. Higher short-term depression severity was found for yoga compared to electro-convulsive therapy; remission rates did not differ between groups. No short-term group differences occurred when yoga was compared to antidepressant medication. Conflicting evidence was found when yoga was compared to attention-control interventions, or when yoga as an add-on to antidepressant medication was compared to medication alone. Only two RCTs assessed adverse events and reported that no treatment-related adverse events were reported.

**Limitations:** Few RCTs with low sample size.

**Conclusions:** This review found some evidence for positive effects beyond placebo and comparable effects compared to evidence-based interventions. However, methodological problems and the unclear risk-benefit ratio preclude definitive recommendations for or against yoga as an adjunct treatment for major depressive disorder. Larger and adequately powered RCTs using non-inferiority designs are needed.

## 1. Background

Depression is one of the most prevalent psychiatric disorders as it affects 25% of women and 12% of men during their lifetime and increases the psychological strain for the affected person (Kessler et al., 2003; Moussavi et al., 2007; Rubio et al., 2011). Moreover, depression is characterized by a high comorbidity with several chronic conditions like addictions (Lai et al., 2015), neurodegenerative diseases (Herbert and Lucassen, 2016; Riccelli et al., 2016) or different psychiatric diseases (Azar et al., 2016; Chechko et al., 2016; Chen et al., 2016; Ronconi et al., 2015). Depression is projected as one of the leading causes of disability worldwide (Global Burden of Disease Study Collaborators, 2015).

The most commonly used treatments for depression are pharmacological (antidepressant) therapy, psychotherapy, or a combination of both. Both therapies have been previously shown to be effective for treating depression (Leichsenring et al., 2016). But recent reviews found high dropout rates, low remission rates, and high placebo

responses for these therapies (Mathew and Charney, 2009; Pigott et al., 2010; Rief et al., 2009; Turner et al., 2008); and complementary and alternative therapies can be a promising adjunct in the treatment of depression (Ravindran et al., 2016).

Yoga, a combination of movement, mindfulness and relaxation, is a traditional Indian philosophical and spiritual practice originated around 5000 years ago (Iyengar, 1966). Modern yoga forms based on Hatha yoga, which are commonly used in the western world, are mostly associated with physical postures (asanas), breathing techniques (pranayama), and meditation (dyana) (Yogi Hari, 2006). Yoga has become a popular means to promote physical and mental well-being (Cramer et al., 2016a; Cramer, 2015). The efficacy of yoga in improving comorbid mental symptoms could be shown for different health conditions such as pain (Chang et al., 2016; Kim, 2016), cancer (Sharma et al., 2016b), psychiatric diseases (Cramer et al., 2013b; Hofmann et al., 2016; Pascoe and Bauer, 2015) and other chronic diseases (Desveaux et al., 2015; Schumann et al., 2016). Specifically for depression, a recent review could show that yoga interventions can be

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an effective treatment option (Cramer et al., 2013c). However, this review included a variety of depressive disorders as well as individuals without a formal diagnosis of depression, rendering conclusions on yoga's efficacy in specific disorders difficult.

Due to the complex treatment situation, further information about effectiveness of yoga therapy in treating different levels of depression is needed. The purpose of this review is to investigate the efficacy and safety of yoga interventions in treating patients with major depressive disorder.

## 2. Methods

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009) as well as the recommendations of the Cochrane Collaboration (Higgins and Green, 2008).

### 2.1. Eligibility criteria

#### 2.1.1. Types of studies

Eligible study types included randomized controlled trials (RCTs), cluster-randomized trials and randomized cross-over studies. No language restrictions were applied.

#### 2.1.2. Types of participants

Studies that included participants with a DSM-IV or DSM-V diagnosis of major depressive disorder were eligible. It was post-hoc decided to also include studies in which the majority of participants ( $\geq 75\%$ ) were diagnosed with major depressive disorder and the remaining participants with other depressive disorders.

#### 2.1.3. Types of interventions

Studies were eligible if they compared yoga with no specific treatment, pharmacological or non-pharmacological interventions. No restrictions were made regarding yoga tradition, length, frequency, or duration of the program. Co-interventions were allowed as long as participants in all intervention groups received the same co-interventions. Head-to-head comparisons of different types of yoga without a non-yoga control group were excluded.

#### 2.1.4. Types of outcome measures

To be eligible, studies had to assess at least one of the main outcome measures:

1. Remission rates, i.e. the number of participants who obtained remission
2. Severity of depression measured by self-rating scales or by clinician-rated scales

Secondary outcome measures included:

1. Severity of anxiety measured by self-rating scales or by clinician-rated scales
2. Serious adverse events (including suicide and suicide attempts)
3. Non-serious adverse events

Adverse events resulting in 1) death, 2) life-threatening situations, 3) hospitalization, 4) disability or permanent damage, 5) congenital anomaly/birth defect, or 6) the need for medical or surgical intervention to prevent outcomes 1–5 were defined as serious. All other adverse events were regarded as non-serious (Food and Administration, 2016).

### 2.2. Search methods

Medline/PubMed, Scopus, and the Cochrane Central Register of Controlled Trials (Central) were searched from their inception through

December 06, 2016. The literature search was constructed around search terms for “yoga” and search terms for “major depressive disorders”. The complete search strategy for PubMed/Medline was (“Depression”[Mesh] OR “Depressive Disorder”[Mesh] OR depression[Title/Abstract] OR depressive[Title/Abstract]) AND (“Yoga”[Mesh] OR yoga[Title/Abstract] OR yogic[Title/Abstract]). The search strategy was adapted for each database as necessary.

In addition, our own extensive database (Cramer et al., 2014), reference lists of identified original articles or reviews and the tables of contents of the International Journal of Yoga Therapy, the Journal of Yoga & Physical Therapy, and the International Scientific Yoga Journal SENSE were searched manually.

Two review authors independently screened abstracts identified during literature search were screened and read potentially eligible articles in full to determine whether they met the eligibility criteria.

### 2.3. Data extraction and management

Two review authors independently extracted data on participants (e.g. diagnostic criteria, age, gender, race), interventions (e.g. yoga type, components, duration), control interventions (e.g. type, duration), outcomes (e.g. outcome measures, assessment time points), and results using an a priori developed data extraction form. Discrepancies were discussed with a third review author until consensus was reached.

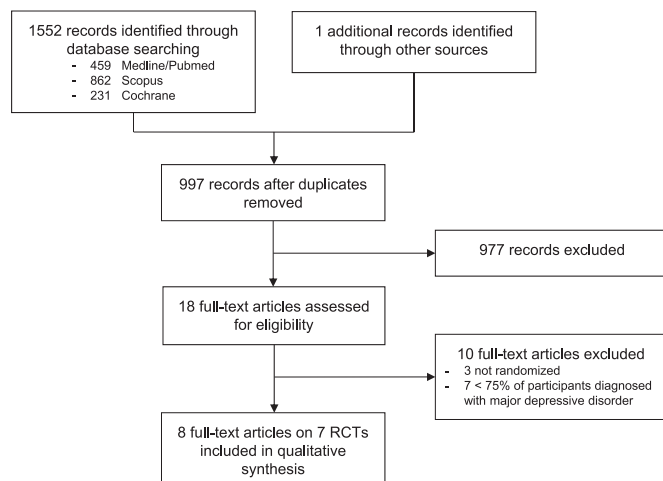
### 2.4. Risk of bias in individual studies

Two review authors 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 and Green, 2008). All domains were scored as 1) low risk of bias, 2) unclear, or 3) high risk of bias. Discrepancies were discussed with a third review author until consensus was reached.

## 3. Results

### 3.1. Literature search

Nine hundred ninety-seven non-duplicate records were retrieved by literature search; 979 of which were excluded because they were not randomized, did not include participants with major depression and/or did not include yoga as an intervention. Eighteen full-texts were assessed for eligibility (Butler et al., 2008; Field et al., 2013a, 2013b, 2012; Gangadhar et al., 2013; Janakiramaiah et al., 2000; Kinser et al., 2013, 2014; Lavretsky et al., 2013; Naveen et al., 2013, 2016; Rohini et al., 2000; Sarubin et al., 2014; Schuver and Lewis, 2016; Sharma et al., 2016a, 2005; Thirthalli et al., 2013; Uebelacker et al., 2016); and 9 articles were excluded because they were either not randomized (Naveen et al., 2013, 2016; Thirthalli et al., 2013), no non-yoga control group was used (Rohini et al., 2000), the included participants were not diagnosed with a depressive disorder (Lavretsky et al., 2013), they were diagnosed with a depressive disorder but less than 75% with major depressive disorder (Butler et al., 2008), or it was unclear with what depressive disorder the participants were diagnosed (Field et al., 2013a, 2013b, 2012). One additional full-text was excluded because it was originally planned as an RCT but later changed to a non-randomized controlled study design and only a minority of participants actually were randomized (Gangadhar et al., 2013). Eight articles reporting seven RCTs on yoga for participants with major depressive disorder, encompassing 240 participants, were finally included in the analysis (Fig. 1) (Janakiramaiah et al., 2000; Kinser et al., 2013, 2014; Sarubin et al., 2014; Schuver and Lewis, 2016; Sharma et al., 2016a, 2005; Uebelacker et al., 2016).



**Fig. 1.** Flowchart of the results of the literature search.

### 3.2. Characteristics of the included studies

The characteristics of the included studies are shown in Table 1.

### 3.3. Setting and participant characteristics

Seven RCTs with a total of 240 participants were included. Sample size ranged from 20 to 53 with a median size of 30 participants. Two RCTs originated from India (Janakiramaiah et al., 2000; Sharma et al., 2005), four from the USA (Kinser et al., 2013, 2014; Schuver and Lewis, 2016; Sharma et al., 2016a; Uebelacker et al., 2016), and one from Germany (Sarubin et al., 2014). Participants were recruited from psychiatric inpatient (Sharma et al., 2005), psychiatric (Janakiramaiah et al., 2000; Sharma et al., 2016a), gynecological (Uebelacker et al., 2016), or other outpatient services (Kinser et al., 2013, 2014), and through online advertisements (Schuver and Lewis, 2016). One RCT did not report methods of recruitment (Sarubin et al., 2014). All seven RCTs used DSM-IV diagnostic criteria; all but two included exclusively patients with major depressive disorder; and patients in all RCTs were in a current major depressive episode. Participants' mean age ranged from 28.4 years to 43.4 years with a median age of 38.7 years. Between 28.3% and 100.0% (median: 72%) of participants in each study were female. Only three studies reported on ethnicity; between 63% and 100% (median: 93.5%) were of Caucasian ethnicity (Kinser et al., 2013, 2014; Schuver and Lewis, 2016; Uebelacker et al., 2016).

### 3.4. Intervention characteristics

Five RCTs used yoga interventions which included yoga postures, breathing exercises, meditation, and relaxation (Kinser et al., 2013, 2014; Sarubin et al., 2014; Schuver and Lewis, 2016; Sharma et al., 2016a; Uebelacker et al., 2016). Two of those RCTs utilized Hatha yoga without specifying a yoga style (Kinser et al., 2013, 2014; Sarubin et al., 2014), one used mindfulness-yoga, i.e. combined the DVD-delivered LifeForce yoga program with telephone counseling based on the Mindfulness-Based Stress Reduction program (Schuver and Lewis, 2016), one used a prenatal yoga program (Uebelacker et al., 2016) and one used Sudarshan Kriya Yoga breathing exercises combined with yoga postures and meditation (Sharma et al., 2016a). The other two RCTs used yoga interventions without physical postures that encompassed meditation either alone, i.e. Sahaj yoga meditation (Sharma et al., 2005), or in combination with breathing exercises, i.e. Sudarshan Kriya Yoga (Janakiramaiah et al., 2000). The yoga intervention was delivered by yoga teachers (Janakiramaiah et al., 2000; Kinser et al., 2013, 2014; Sharma et al., 2005; Uebelacker et al., 2016), physical therapists (Sarubin et al., 2014) or unsupervised using a DVD with

discussion of the yoga experience during weekly telephone counseling (counselors' qualification not reported) (Schuver and Lewis, 2016). Interventions were delivered in group setting except for one RCT using unsupervised yoga (Schuver and Lewis, 2016); for three further RCTs it was unclear whether group settings or individual interventions were used (Janakiramaiah et al., 2000; Sarubin et al., 2014; Sharma, 2005). The interventions were delivered for 5–12 weeks (median: 8 weeks); frequency ranged from 1 to 6 sessions per week with a median of 2 session per week; and the sessions' duration ranged from 30 to 210 min (median 75 min) per session. Overall, between 120 and 1890 min of contact time with the therapist were offered (median 675 min).

Two RCT used an inactive control group that did not receive any specific intervention besides standard care (see below) (Sarubin et al., 2014; Sharma et al., 2016a); the remaining five RCTs used active control groups. Control interventions consisted of an attention-control intervention of the same time and therapists' attention but without the assumed therapeutic component (Kinser et al., 2013, 2014; Sharma et al., 2005; Uebelacker et al., 2016), a home-based walking intervention with additional telephone counseling of the same intensity as the yoga intervention (Schuver and Lewis, 2016), electro-convulsive therapy three times per week over a period of 4 weeks (Janakiramaiah et al., 2000), and the tricyclic antidepressant Imipramin once daily 150 mg over a period of 4 weeks (Janakiramaiah et al., 2000).

One RCT precluded any additional antidepressant medication (a tricyclic antidepressant was used as a control intervention) (Janakiramaiah et al., 2000); four RCTs allowed individual antidepressant medication (Kinser et al., 2013, 2014; Schuver and Lewis, 2016; Sharma et al., 2005; Uebelacker et al., 2016). Participants in one RCT were treated with either atypical antipsychotic drugs with antidepressant properties or SSRIs in addition to the allocated study treatment (Sarubin et al., 2014), participants in another RCT were on a stable dose of any antidepressant medication in addition to the allocated study treatment (Sharma et al., 2016a).

### 3.5. Outcome measures

Outcomes were assessed immediately after the end of the intervention in all RCTs. One RCT additionally assessed outcomes at one-month follow-up (Schuver and Lewis, 2016), and one assessed outcomes at one-year follow-up (Kinser et al., 2013, 2014). All RCTs assessed severity of depression using clinician-assessed instruments such as the Hamilton Rating Scale for Depression (Janakiramaiah et al., 2000; Sarubin et al., 2014; Sharma et al., 2016a, 2005), or the Quick Inventory of Depressive Symptoms-Clinician Rating (Uebelacker et al., 2016), or patient-reported measures such as the Beck Depression Inventory (Janakiramaiah et al., 2000; Schuver and Lewis, 2016; Sharma et al., 2016a), the Edinburgh Postnatal Depression Scale (Uebelacker et al., 2016), or the Patient Health Questionnaire (Kinser et al., 2013, 2014). Three RCTs assessed remission rates defined as the number of participants with a depression severity below a specific threshold (Janakiramaiah et al., 2000; Sharma et al., 2016a, 2005). Two further RCTs assessed responder rates defined as the number of participants with a reduction of depression severity of more than 50% (Sarubin et al., 2014; Sharma et al., 2016a). Two RCTs assessed severity of comorbid anxiety using the physician-assessed Hamilton Rating Scale for Anxiety (Sharma et al., 2005) or the Beck Anxiety Inventory (Sharma et al., 2016a). None of the included RCTs assessed the total frequency of serious adverse events or non-serious adverse events but two RCTs assessed treatment-related adverse events (Sharma et al., 2016a; Uebelacker et al., 2016).

### 3.6. Risk of bias in individual studies

Risk of bias in individual studies is shown in Table 2. Risk of selection bias generally was unclear; only three RCTs reported ade-

**Table 1**  
Characteristics of the included studies.

| Reference                  | Participants   | Co-interventions                                       | Intervention groups  | Assessment time points                               | Outcome measures  | Results  |
|----------------------------|--|--|--|--|---|--|
| Janakiramaiah et al., 2000 | 45 participants DSM-IV diagnosis<br>100.0% MDD Mean age 38.7 years<br>44.4% female Ethnicity not reported      | None   | <ul style="list-style-type: none"> <li>● <b>Sudarshan Kriya Yoga</b> (breathing exercises, meditation): 4 weeks, 6×45 min/week</li> <li>● <b>Electro-convulsive therapy</b>: 4 weeks, 3x/week</li> <li>● <b>Imipramin</b>: 4 weeks, 1×150 mg/day</li> <li>● <b>Hatha yoga</b> (postures, breathing exercises, meditation): 8 weeks, 1×75 min/week</li> <li>● <b>Attention-control group</b>: 8 weeks, 1×75 min/week</li> </ul>   | 4 weeks  | <ul style="list-style-type: none"> <li>● <b>Remission rates</b> assessed as HAM-D &lt; 8</li> <li>● <b>Depression severity</b> assessed on HAM-D and BDI</li> </ul>   | Significant short-term group differences favoring electro-convulsive therapy over yoga regarding remission rates. No further group differences.          |
| Kinser et al., 2013, 2014  | 27 participants 81.5% MDD Mean age 43.4 years 100.0% female 63.0% Caucasians                                   | Antidepressant medication allowed                      | <ul style="list-style-type: none"> <li>● <b>Hatha yoga</b> (postures, breathing exercises, meditation): 5 weeks, 1×60 min/week</li> <li>● <b>No specific intervention</b>: 5 weeks</li> <li>● <b>Lifeforce yoga program</b> (postures, breathing exercises, meditation): 12 weeks home-practice</li> <li>● <b>Walking</b>: 12 weeks home-practice</li> <li>● <b>Sahaj yoga meditation</b>: 8 weeks, 3×30 min/week</li> <li>● <b>Sitting quietly</b>: 8 weeks, 3×30 min/week</li> </ul> | 2 weeks<br>4 weeks<br>6 weeks<br>6 weeks<br>52 weeks | <ul style="list-style-type: none"> <li>● <b>Depression severity</b> assessed on PHQ-9</li> <li>● <b>Anxiety</b> assessed on STAI</li> </ul>   | No significant short-term group differences. Significant long-term group differences favoring yoga over attention-control regarding depression severity. |
| Sarubin et al., 2014       | 53 participants DSM-IV diagnosis 100.0% MDD Mean age 40.3 years 28.3% female Ethnicity not reported            | Quetiapine fumarate extended release or escitalopram   | <ul style="list-style-type: none"> <li>● <b>Hatha yoga</b> (postures, breathing exercises, meditation): 5 weeks, 1×60 min/week</li> <li>● <b>No specific intervention</b>: 5 weeks</li> <li>● <b>Lifeforce yoga program</b> (postures, breathing exercises, meditation): 12 weeks home-practice</li> <li>● <b>Walking</b>: 12 weeks home-practice</li> <li>● <b>Sahaj yoga meditation</b>: 8 weeks, 3×30 min/week</li> <li>● <b>Sitting quietly</b>: 8 weeks, 3×30 min/week</li> </ul> | 5 weeks  | <ul style="list-style-type: none"> <li>● <b>Depression severity</b> assessed on HAM-D</li> </ul>  | No significant short-term group differences.   |
| Schuer and Lewis, 2016     | 40 participants DSM-IV diagnosis 100.0% MDD Mean age 42.7 years 100.0% female 95% non-Hispanic                 | Antidepressant medication and/or psychotherapy allowed | <ul style="list-style-type: none"> <li>● <b>No specific intervention</b>: 5 weeks</li> <li>● <b>Lifeforce yoga program</b> (postures, breathing exercises, meditation): 12 weeks home-practice</li> <li>● <b>Walking</b>: 12 weeks home-practice</li> <li>● <b>Sahaj yoga meditation</b>: 8 weeks, 3×30 min/week</li> <li>● <b>Sitting quietly</b>: 8 weeks, 3×30 min/week</li> </ul>  | 12 weeks, 16 weeks                                   | <ul style="list-style-type: none"> <li>● <b>Depression severity</b> assessed on BDI</li> </ul>  | No significant short-term or medium-term group differences.  |
| Sharma et al., 2005        | 30 participants DSM-IV diagnosis 100.0% MDD Mean age 31.8 years 36.7% female Ethnicity not reported            | Antidepressant medication allowed                      | <ul style="list-style-type: none"> <li>● <b>Sudarshan Kriya Yoga</b> (breathing exercises, meditation): 1 week, 6×210 min/week, then 7 weeks, 1×90 min/week</li> <li>● <b>No specific intervention</b>: 8 weeks</li> </ul>   | 4 weeks<br>8 weeks                                   | <ul style="list-style-type: none"> <li>● <b>Remission rates</b> assessed as HAM-D &lt; 8</li> <li>● <b>Depression severity</b> assessed on HAM-D</li> <li>● <b>Anxiety</b> assessed on HAM-A</li> <li>● <b>Remission rates</b> assessed as HAM-D &lt; 8 and &gt; 50% reduction on HAM-D</li> <li>● <b>Depression severity</b> assessed on HAM-D and BDI</li> <li>● <b>Anxiety</b> assessed on BAI</li> <li>● <b>Safety</b> assessed as number of treatment-emergent adverse events</li> </ul> | Significant short-term group differences favoring yoga over control group regarding remission rates, depression severity and anxiety.                    |
| Sharma et al. 2016a        | 25 participants DSM-IV-TTR diagnosis 100.0% MDD Mean age 37.2 years 72.0% female 92.0% Caucasians              | Stable dose of antidepressant medication               | <ul style="list-style-type: none"> <li>● <b>Sudarshan Kriya Yoga</b> (breathing exercises, meditation): 1 week, 6×210 min/week, then 7 weeks, 1×90 min/week</li> <li>● <b>No specific intervention</b>: 8 weeks</li> </ul>   | 4 weeks<br>8 weeks                                   | <ul style="list-style-type: none"> <li>● <b>Remission rates</b> assessed as HAM-D &lt; 8 and &gt; 50% reduction on HAM-D</li> <li>● <b>Depression severity</b> assessed on HAM-D and BDI</li> <li>● <b>Anxiety</b> assessed on BAI</li> <li>● <b>Safety</b> assessed as number of treatment-emergent adverse events</li> </ul>  | Significant short-term group differences favoring yoga over control group regarding depression severity and anxiety but not regarding remission rates.   |
| Uebelacker et al., 2016    | 20 participants (pregnant women) DSM-IV diagnosis 75.0% MDD Mean age 28.4 years 100.0% female 95.0% Caucasians | Antidepressant medication allowed                      | <ul style="list-style-type: none"> <li>● <b>Prenatal yoga program</b> (postures, breathing exercises, meditation): 9 weeks, 1×75 min/week</li> <li>● <b>Mom-baby wellness workshop</b>: 9 weeks, 1×75 min/week</li> </ul>  | 3 weeks<br>6 weeks<br>9 weeks                        | <ul style="list-style-type: none"> <li>● <b>Depression severity</b> assessed on QIDS and EPDS</li> <li>● <b>Safety</b> assessed as number of adverse events due to yoga</li> </ul>  | No significant short-term group differences.   |

Abbreviations: BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; EPDS: Edinburgh Postnatal Depression Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Rating Scale for Depression; MDD: Major Depressive Disorder; PHQ-9: Patient Health Questionnaire; QIDS: Quick Inventory of Depressive Symptom-Clinician Rating; STAI: State-Trait Anxiety Inventory.



**Table 2**  
Risk of bias assessment of the included studies.

|                            |   | Bias                                    |   |   |  |                                      |            |  |
|----------------------------|---|---|---|---|--|--------------------------------------|------------|--|
| Author, year               | 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 |  |
| Janakiramaiah et al., 2000 | Unclear                                     | Unclear                                 | Unclear   | Unclear   | Low risk                                 | Low risk                             | Low risk   |  |
| Kinser et al., 2013, 2014  | Low risk                                    | Unclear                                 | Unclear   | Unclear   | High risk                                | Unclear                              | Low risk   |  |
| Sarubin et al., 2014       | Unclear                                     | Unclear                                 | Unclear   | Unclear   | Unclear                                  | Low risk                             | Unclear    |  |
| Schuver and Lewis, 2016    | Low risk                                    | Unclear                                 | High risk   | Low risk  | Low risk                                 | Low risk                             | Low risk   |  |
| Sharma et al., 2005        | Unclear                                     | Unclear                                 | Unclear   | Unclear   | Unclear                                  | High risk                            | Unclear    |  |
| Sharma et al., 2016a       | Low risk                                    | Unclear                                 | High risk   | Low risk  | Low risk                                 | High risk                            | Low risk   |  |
| Uebelacker et al., 2016    | Unclear                                     | Unclear                                 | High risk   | Unclear   | Low risk                                 | Low risk                             | Low risk   |  |

quate methods of random sequence generation (Kinser et al., 2013, 2014; Schuver and Lewis, 2016; Sharma et al., 2016a); and no RCT reported on allocation concealment. Only three RCTs reported on blinding and two reported adequate blinding of outcome assessment but all reported lack of blinding of study participants (Kinser et al., 2013, 2014; Schuver and Lewis, 2016; Sharma et al., 2016a). Only one RCT used an intention-to-treat analysis (Sharma et al., 2016a), but two further RCTs had a low attrition rate (Janakiramaiah et al., 2000; Schuver and Lewis, 2016). Risk of reporting bias and other bias were low in all but three RCTs (Kinser et al., 2013, 2014; Sharma et al., 2016a, 2005).

### 3.7. Outcomes

#### 3.7.1. Yoga vs. attention control

Compared to an attention-control intervention, positive short-term effects of yoga on physician-assessed severity of depression and anxiety were found in one of three RCTs. Further group differences occurred in this RCT regarding remission rates with 47% of participants in the yoga group being in remission after 8 weeks of intervention compared to 13% in the attention-control group (Sharma et al., 2005). Another RCT found positive long-term effects of yoga on patient-reported severity of depression but only 7 and 2 participants were included in the yoga and control group, respectively, for this analysis (Kinser et al., 2013, 2014). Risk of selection and detection bias was mixed.

#### 3.7.2. Yoga vs. exercise

When yoga was compared to an intensity- and attention-matched walking intervention, no groups differences in severity of depression was found at the end of the 12-week intervention period or at one-month follow-up (Schuver and Lewis, 2016). Risk of selection bias was mixed, however risk of detection bias was low.

#### 3.7.3. Yoga vs. electro-convulsive therapy

After four weeks of treatment, significantly higher severity of depression was found for participants in the yoga group compared to participants receiving electro-convulsive therapy. Remission rates did not differ significantly between groups although 93% of participants receiving electro-convulsive therapy remitted compared to 67% of participants in the yoga group (Janakiramaiah et al., 2000). Risk of selection and detection bias were unclear.

#### 3.7.4. Yoga vs. medication

Comparing yoga to antidepressant medication, no group difference in depression severity was found. After 4 weeks of intervention, 67% of participants in the yoga group were in remission compared to 73% in the medication group (Janakiramaiah et al., 2000). Risk of selection and detection bias were unclear.

When yoga as an add-on to antidepressant medication was compared to medication alone, one of two RCTs found positive effects of yoga on depression severity (Sharma et al., 2016a), while the other found no group difference (Sarubin et al., 2014). Responder rates did not differ between groups in both studies. One RCT reported 59% responders in the yoga group and 58% responders in the control group (Sarubin et al., 2014), the second RCT found 8.3% and 46.2% responders in the yoga and control group, respectively, and 8.3% and 30.8% remitters, respectively (Sharma et al., 2016a). None of these group differences was significant. One RCT assessed safety-related data and reported that no treatment-emergent adverse events were reported. Risk of selection and detection bias was unclear in one of the RCTs (Sarubin et al., 2014); risk of selection bias was mixed and risk of selection bias was low in the other one (Sharma et al., 2016a).

## 4. Discussion

### 4.1. Summary of evidence

In this systematic review of seven RCTs, comparable effects were found for yoga compared to exercise and medication. Electro-convulsive therapy induced stronger antidepressant effects than yoga. Conflicting evidence was found when yoga was compared to attention-control interventions or when yoga was used as an add-on to antidepressant medication was compared to medication alone. The safety of the intervention remained largely unclear.

### 4.2. Agreements with prior systematic reviews

To the best of our knowledge, this is the first systematic review specifically investigating yoga practice in patients diagnosed with major depressive disorder. However, the findings are partly in line with prior systematic reviews on yoga across the depression spectrum (Cramer et al., 2013c; Pilkington et al., 2005). In an early review, Pilkington et al. concluded that yoga might have potential beneficial effects for patients with depressive disorders (Pilkington et al., 2005). In line with the current review, the authors saw their conclusions limited by the high risk of bias and the lack of safety data in the included trials. A further review concluded that yoga as a treatment for depression is based on plausible mechanisms and can augment current depression treatment strategies (Uebelacker et al., 2010). A more recent review and meta-analysis found positive effects of yoga for depressive disorders but only when compared to relaxation but not when compared to usual care (Cramer et al., 2013c). In contrast to the current review, yoga was superior to aerobic exercise; however this finding was limited to individuals with elevated levels of depression without a formal psychiatric diagnosis. Again, high risk of bias and lack of safety data limited the expressiveness of the findings. It should be noted, that the prior reviews included only one (Pilkington et al., 2005) or two (Cramer et al., 2013c) of the RCT that were included in the current review. Finally, a recent overview of systematic reviews focusing on mental health professionals concluded that there is growing evidence supporting the use of yoga for the management of depression but that further high-quality research is needed (Butterfield et al., 2017).

### 4.3. External and internal validity

The RCTs included patients from North America, Europe and Asia. All patients were diagnosed by DSM-IV criteria. Given that the removal of the bereavement exclusion was the main change for a diagnosis of major depressive disorder from DSM-IV to DSM-V, all patients in all included studies would most likely still be diagnosed with the same disorder (American Psychiatric Association, 2013). The findings of the included RCTs can however not be applied to patients suffering from depressive symptoms lasting less than two months following the death of a loved one. The applicability of the findings is further limited by the low number of included RCTs and their unclear to high risk of bias.

### 4.4. Strengths and weaknesses

Strengths of this review include the comprehensive literature search and the assessment of applicability of the results (Gartlehner, 2008). The primary limitation of this review is the deficiency of eligible studies, resulting in a rather low overall sample size. Specifically, most comparisons (yoga vs. exercise, electro-convulsive therapy, or medication) were based on only one RCT each. The applicability of the findings was limited and safety was not adequately reported in any RCT. Due to the low number of eligible trials and their heterogeneity regarding participants, interventions, and control groups, no meta-analysis could be performed.

### 4.5. Implications for further research

More RCTs on yoga specifically for major depressive disorders are needed to conclusively judge its potential in this population. Authors of prospect research should improve the reporting of yoga trials and adhere to standard reporting guidelines (e.g. CONSORT) (Schulz et al., 2010). Further RCTs should ensure rigorous methodology including a-priori sample size calculations to prevent negative results due to lack of power. They should further apply adequate methods of randomization, allocation concealment, intention-to-treat analysis, and blinding of at least outcome assessors (Schulz et al., 2010).

Yoga RCTs should also improve reporting of safety. While no evidence for serious yoga-associated adverse events or an accumulation of adverse events has been found in yoga RCTs reporting on safety (Cramer et al., 2015), there clearly is a lack of sufficient reporting of yoga-associated adverse events. Yoga has also been occasionally associated with serious adverse events, and patients with psychiatric disorders might be particularly prone to symptom aggravation due to yoga practice (Cramer et al., 2013a). About five percent of yoga practitioners diagnosed with bipolar disorder have e.g. reported yoga-associated aggravations of their depressive symptoms (Uebelacker et al., 2014). This should be closely monitored in future RCTs.

While this review found comparable effects of yoga compared to other evidence-based interventions (Gelenberg et al., 2010), this finding might mainly reflect a lack of power due to the small number of eligible RCTs and their relatively low sample size; none of the RCTs comparing yoga to an active intervention included more than 20 patients per study arm. Larger and adequately powered RCTs using non-inferiority designs are needed before the comparative effectiveness of yoga compared to exercise and medication can be conclusively judged.

Likewise, the conflicting evidence found for yoga compared to attention-control interventions or as an add-on to antidepressant medication might be explained by the very low sample size in the included RCTs, resulting in a too low power to detect positive effects. E.g., Uebelacker et al., 2016 would have need to include a total of 146 patients in their analysis to be able to detect the group differences found in their study with a power of 80%. Larger adequately powered studies are needed to assess whether yoga actually can reduce depression severity and/or increase remission rates in a clinically relevant way.

In this review, electro-convulsive therapy was more effective than yoga in treating depression. Electro-convulsive therapy has been shown to be highly effective for treating major depression but to be far less tolerated than other interventions (Chen et al., 2017). On the other hand, yoga has been shown to be very well tolerated by most participants (Cramer et al., 2016b). Given the very short-term intervention period in the included RCT (Janakiramaiah, 2000), the comparative long-term effectiveness and tolerability of yoga and electroconvulsive therapy needs to be investigated in future trials.

### 4.6. Implications for clinical practice

While this review found some evidence for positive effects beyond placebo and comparable effects compared to other evidence-based interventions (Gelenberg et al., 2010), the latter might mainly reflect a statistical artifact. Although prior systematic reviews suggest that yoga can be used as an adjunct intervention for otherwise healthy individuals with depressive symptoms (Cramer et al., 2013), its use in major depressive disorder is less clear. Given the small number of included patients, unclear methodology and – most importantly – the unclear risk-benefit ratio of the intervention, no recommendation for or against yoga as an alternative or adjunct treatment for major depressive disorder can be made. The value of adding yoga to a treatment plan for patients with major depressive disorders needs to be evaluated on an individual basis.

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