Yoga for Anxiety: 
A systematic review and meta-analysis of randomized controlled trials

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• Methodology
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Introduction to systematic review

• Systematic review
  – Literature review that uses systematic methods to collect secondary data, critically appraise research studies, and synthesize findings qualitatively or quantitatively.
  – Aims to provide a complete, exhaustive summary of current literature relevant to a research question.
Introduction to meta-analysis

• Meta-analysis
  – Term “Meta-analysis” was coined in 1976 by the statistician ‘Gene V, Glass.
  – Analysis of analyses.
  – A statistical analysis that combines the results of multiple scientific studies.
  – Performed when there are multiple scientific studies addressing the same question.
Risk of Bias

Domains to address

• Random sequence generation
• Allocation concealment
• Blinding of participants and personnel
• Blinding of outcome assessments
• Incomplete outcome data
• Selective reporting
• Other bias
Sources of bias

- Random sequence generation
- Allocation concealment

Target population

Allocation

Intervention group

Control group

Outcome assessment

Publication of study outcomes
Random sequence generation

- Occurs at the start of the study.
- Determines a random order of assigning people into intervention and control group.
- Commonly used are random number table, computer random number generator and so on.
Allocation concealment

- Occurs at the start of the trial during allocation of participants.
- When a person is recruited to the study, no one can predict which group they will be allocated to.
- Ensures the strict implementation of the random sequence.
  - Prevents changing the order.
  - Prevents selecting who to recruit.
- Commonly used: sequentially numbered, sealed, opaque envelopes.
Sources of bias

Target Population

Allocation

Intervention group

Control group

Outcome assessment

Publication of study outcomes

Blinding of participants, personnel

Selection

Performance

Detection

Attrition

Reporting
Blinding of participants and personnel

• Avoids performance bias.
• Different treatment of the intervention groups.
• Different participant expectations
• Leads to changes in the actual outcomes.
Sources of bias

- Target Population
  - Allocation
    - Intervention group
    - Control group
  - Outcome assessment
  - Publication of study outcomes
- Selection
- Performance
- Detection: Blinding of outcome assessment
- Attrition
- Reporting
Blinding of outcome assessment

- Avoids detection bias
- Measurement of outcomes affected by knowledge of the intervention received.
- May be feasible even where blinding of participants and care providers is not.
- Its low risk, when no blinding, but measurements unlikely to be influenced.
- High risk when no blinding and measurements likely to be influenced.
Sources of bias

- Selection
- Performance
- Detection
- Attrition

Target Population
  - Allocation
    - Intervention group
    - Control group

Outcome assessment
- Publication of study outcomes

Incomplete outcome data
Incomplete outcome data

- When complete outcome data for all the participants is not available for your review.
  - Attrition - Loss to follow up, withdrawals, other missing data.
  - Exclusions - some available data not included in report.
- Can lead to attrition bias
- Intent to treat analysis: Regardless of what happened during the study.
Sources of bias

- Selection
- Performance
- Detection
- Attrition

Target Population

Allocation

Intervention group
Control group

Outcome assessment

Publication of study outcomes

Selective reporting
Selective reporting

- Can lead to reporting bias
- Statistically significant results more likely to be reported.
- As planned
- In detail
- Low risk: Protocol is available and all pre-specified outcomes of interest to the review reported in the pre-specified way.
- Unclear: Most studies judge in this category.
- High risk: outcomes not reported (or incomplete) as pre-specified or expected.
Aims and Objectives

Aim of the study:

• To systematically assess and meta-analyze the effectiveness and safety of yoga for anxiety.
Materials and Methods

• Type of Studies: RCT (8 nos)
• N= 319 (mean age: 30.0 to 38.5yrs)
• Nature of studies: Yoga for Individuals with anxiety disorders or elevated levels of anxiety.
• Period of search: Till October 2016
• Search engines: Medline/PubMed, Scopus, Cochrane Library, PsychINFO, IndMED

Key words: Anxiety, anxiety disorders, meta-analysis, yoga.
Inclusion criteria for studies

• Trials
  – Randomized controlled trials
  – Cluster-randomized trials
  – Randomized cross over

• From all countries

• In all languages
Type of participants

• Diagnostic criteria
  – Adults with a diagnosis of an anxiety disorder in accordance with DSM-III or DSM-III-R, DSM-IV or DSM-IV-TR or DSM-V or ICD-10
  – Adults with a diagnosis of an anxiety disorder based on any other criteria
  – 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.
Type of Intervention

• Multicomponent yoga interventions, i.e. yoga intervention including both,
  – Yoga postures (asanas) and/or flowing sequences of yoga postures (vinyasas) and
  – Breath control (pranayama) and/or meditation and/or deep relaxation (based on yoga theory and/or traditional yoga practices).

• Posture-based yoga interventions, i.e. yoga intervention including only asanas and/or vinyasas without breath control or meditation.
Type of Intervention

• 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’.
Type of Intervention

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

• **Primary**: Anxiety and Remission rates

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

- **Secondary**: Depression, QoL and safety.

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

- Electronic databases
  - through October 13, 2016
- Medline (through PubMed), Scopus, the Cochrane Library, PsycINFO, and IndMED.
- Search terms for “yoga” and search terms for “anxiety.”
- Hand searches were conducted on our own extensive database (Cramer, Lauche, & Dobos, 2014),
- Reference lists of identified original articles or reviews,
Search Methods

• For PubMed, the following search strategy was used:
  – 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])
Screening

• Abstracts identified during the database and hand searches were screened by two review authors independently, with potentially eligible articles read in full by two review authors to determine whether they met the eligibility criteria.

• Disagreements were discussed with a third review author (RL) until consensus was reached.

• 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),
  – Results

• Independently extracted by two pairs of review authors using an *a priori* data extraction form
• Discrepancies were discussed with a third review author until consensus was reached.
• If necessary, study authors were contacted for additional information.
Risk of bias

• Two pairs of review authors (RL, LW or 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.

• All domains were scored as
  – Low risk of bias,
  – Unclear, or
  – High risk of bias.

• 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 short-, medium-, 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.
  - 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) using random-effects model.

• For continuous outcomes
  – SMD with 95% confidence intervals (CI) were calculated as the difference in means between groups divided by the pooled standard deviation.

• Where no standard deviations were available, they were calculated from standard errors, CI, or t values,

• Attempts were made to obtain the missing data from authors by email.
Assessment of overall effect size

• 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.

• A positive SMD was defined to indicate beneficial effects (e.g. increased well-being).

• Cohen's categories were used to evaluate the magnitude of the overall effect size with SMD: 0.2–0.5 categorized as small; 0.5–0.8 as medium, and > 0.8 as large-effect sizes.
Assessment of overall effect size

• For dichotomous outcomes
  – Odds ratios 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.

• 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
  - $I^2 = 0–24\%$, low heterogeneity;
  - $I^2 = 25–49\%$, moderate heterogeneity;
  - $I^2 = 50–74\%$, substantial heterogeneity;
  - $I^2 = 75–100\%$, considerable heterogeneity
- The $\chi^2$ test was used to assess whether differences in results were compatible with chance alone.
Subgroup and sensitivity analyses

Four subgroup analyses were conducted

- 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).

- Type of yoga intervention (multicomponent; posture-based; breathing-meditation-based).

- Country of origin (India; other countries).

- Gender (mixed; female only; male only).
Sensitivity Analyses

• 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),
  – 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.

- As less than 10 studies were included in each analysis, this was not possible.
Results
Flow chart of the results of the literature search

1993 records identified through database searching
- 526 MEDLINE/PubMed
- 251 Cochrane Library
- 854 Scopus
- 322 PsycINFO
- 40 IndMED

2 additional records identified through other sources

1188 records after duplicates removed

1161 records excluded

35 full-text articles assessed for eligibility

19 full-text articles excluded
- 6 not randomized
- 1 allocation unclear
- 5 not on anxiety
- 6 no relevant outcomes
- 1 no full-text

8 studies included in qualitative synthesis

2 full-text articles excluded
- 2 insufficient raw data

6 studies included in quantitative synthesis (meta-analysis)
Results

- A total of 319 participants were included in the eight 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).
- All RCTs assessed anxiety severity.
- Three also assessed remission rates.
- Two assessed depression severity.
- One assessed quality of life.
- Only three RCTs reported safety-related data.
<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis 2015</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>de Manincor 2016</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Gupta 2013</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Parthasarathy 2014</td>
<td>?</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Results

• 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; \(P = .008\)), and
  – Large effects compared to active comparators (SMD=−0.86; 95% CI=−1.56, −0.15; \(P = .02\)).
  – Small effects on depression were found compared to no treatment (SMD=−0.35; 95% CI=−0.66, −0.04; \(P = .03\)).
• Effects were robust against potential methodological bias.
• No effects were found for patients with anxiety disorders diagnosed by Diagnostic and Statistical Manual criteria, only for patients diagnosed by other methods, and for individuals with elevated levels of anxiety without a formal diagnosis.
• Only three RCTs reported safety-related data but these indicated that yoga was not associated with increased injuries.
Forest plot of yoga versus no treatment or active comparators for Anxiety severity

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Yoga</th>
<th>Control</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>1.1.1 Yoga vs. no treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davis 2015</td>
<td>34.8</td>
<td>10.68</td>
<td>20</td>
</tr>
<tr>
<td>de Manincor 2016</td>
<td>10.83</td>
<td>7.02</td>
<td>36</td>
</tr>
<tr>
<td>Parthasarathy 2014</td>
<td>16.43</td>
<td>6.9</td>
<td>30</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>86</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 2.63 (P = 0.008)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Yoga</th>
<th>Control</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>1.1.4 Yoga vs. active comparator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gupta 2013</td>
<td>-16.83</td>
<td>9.66</td>
<td>6</td>
</tr>
<tr>
<td>Sahasi 1991</td>
<td>-10.2</td>
<td>8.81</td>
<td>20</td>
</tr>
<tr>
<td>Vahia 1973</td>
<td>18.87</td>
<td>6.9</td>
<td>15</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.19; Chi² = 3.96, df = 2 (P = 0.14); I² = 50%
Test for overall effect: Z = 2.39 (P = 0.02)

Test for subgroup differences: Chi² = 1.20, df = 1 (P = 0.27). I² = 16.8%
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, −0.04; $P = .03$);
- 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.
- Only three RCTs reported safety-related data. Two RCTs reported that no adverse events and/or adverse effects 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.
Effects of yoga versus no treatment on depression severity

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Yoga Mean</th>
<th>Yoga SD</th>
<th>Yoga Total</th>
<th>Control Mean</th>
<th>Control SD</th>
<th>Control Total</th>
<th>Weight %</th>
<th>Std. Mean Difference</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.3.1 Yoga vs. no treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davis 2015</td>
<td>6.35</td>
<td>3.99</td>
<td>20</td>
<td>7.32</td>
<td>5.06</td>
<td>19</td>
<td>34.0%</td>
<td>-0.21 [-0.84, 0.42]</td>
<td></td>
</tr>
<tr>
<td>de Manincor 2016</td>
<td>11.5</td>
<td>9.29</td>
<td>36</td>
<td>16.52</td>
<td>10.94</td>
<td>42</td>
<td>66.0%</td>
<td>-0.49 [-0.94, -0.03]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td>56</td>
<td>61</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>-0.39 [-0.76, -0.03]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.49, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 2.09 (P = 0.04)

Test for subgroup differences: Not applicable
Subgroup analyses and sensitivity analyses

• Results were comparable to the overall sample

 Individuals with elevated levels of anxiety but without a formal diagnosis of an anxiety disorder.

 Patients that were described to have an anxiety disorder but where the authors did not state how this disorder was diagnosed,

 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
Results

• Results did not change substantially when only RCTs with multicomponent yoga interventions were included in the meta-analysis.

• 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, whereas RCTs from Western countries found small positive effects of yoga compared to no treatment on anxiety and depression.
Results

• Studies including both male and female participants found small effects on anxiety and depression for yoga compared to no treatment.

• Small effects on anxiety were also found in studies including only female participants when comparing yoga to no treatment.

• 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

• 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.

• No effects were found when only patients with DSM-diagnosed anxiety disorder were included in the analyses.

• The application of yoga was not associated with increased injuries or increased anxiety symptoms, with the caveat that only three RCTs reported safety-related data.
Comparison to prior reviews

- Outdated reviews
- Insufficient trials
- Heterogeneity of trials
- Rationale for yoga interventions with a physical component
- To treat such disorders is plausible
- Variety of diagnosis
- Potential bias in the trials
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, methodologically robust studies are needed and are warranted given these preliminary findings and plausible mechanisms of action.
Limitations of the study

• Insufficient amount of trials in general.

• Insufficient quantity of trials for specific anxiety disorders in particular rendered in dept meta-analysis impossible.

• Heterogeneous trials regarding sample or intervention characteristics.

• 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.

• **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 eg: by selecting adequate control groups, and examining patients’ expectations prior to the trial.
Implications of the study

• Report the yoga trials by adhering to standard reporting guidelines (eg: CONSORT)

• To follow standardized diagnostic criteria such as DSM /ICD.

• To follow the PRISMA or Cochrane guidelines for systematic review and met-analysis.

• To use a validated generic yoga interventions.
References


Acknowledgement

- Dr. Vinod Kumar
- Dr. Ramajayam G
THANK YOU :}

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