



# Effects of Yoga-Based Interventions on Rheumatoid Arthritis Outcomes: Systematic Review and Meta-Analysis

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## Abstract

**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease significantly impacting patients' quality of life and functional capacity. While conventional disease-modifying anti-rheumatic drugs (DMARDs) remain the cornerstone of treatment, complementary interventions like yoga have gained attention for their potential therapeutic benefits.

**Objective:** To systematically review and analyze the effects of yoga-based interventions on clinical, immunological, and molecular outcomes in patients with rheumatoid arthritis.

**Methods:** A comprehensive search was conducted following PRISMA 2020 guidelines. Four randomized controlled trials (RCTs) involving 331 participants with rheumatoid arthritis were included. Studies evaluated yoga interventions ranging from 8 to 12 weeks compared to usual care or educational control groups. Primary outcomes included disease activity scores (DAS28-ESR), health-related quality of life measures, and various biomarkers. Data synthesis was performed using standardized mean differences with 95% confidence intervals.

**Results:** Meta-analysis revealed significant improvements in disease activity (pooled SMD: -0.52, 95% CI: -0.78 to -0.26,  $p < 0.001$ ) and fatigue scores (SMD: -0.48, 95% CI: -0.72 to -0.24,  $p < 0.001$ ). Yoga interventions demonstrated beneficial effects on inflammatory markers, including IL-6, IL-17, and TNF- $\alpha$ , while enhancing anti-inflammatory cytokines like TGF- $\beta$  and IL-10. Molecular analyses revealed improved mitochondrial function, normalized T cell populations, and favorable gene expression patterns.

**Conclusions:** Yoga-based interventions show promise as adjunctive therapy for rheumatoid arthritis, with evidence supporting improvements in disease activity, fatigue, and immune function. However, the limited number of studies and moderate quality of evidence necessitate further high-quality randomized controlled trials to establish definitive clinical recommendations.

**Keywords:** Yoga, Rheumatoid arthritis, Inflammation, Anti-inflammatory.

## 1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder characterized by persistent joint inflammation, progressive destruction of articular cartilage, and significant functional impairment affecting approximately 0.5-1.0% of the adult population worldwide (Smolen et al., 2023; Black et al., 2023). Recent estimates from the Global Burden of Disease Study indicate RA accounts for over 3.1 million disability-adjusted life years (DALYs) globally, with a rising prevalence in low- and middle-income countries due to demographic shifts and improved diagnostic capabilities (Black et al., 2023; Zhang et al., 2025). The disease not only impacts physical health through joint pain, stiffness, and deformity but also substantially affects patients' psychological well-being, social functioning, and overall quality of life (Ionescu et al., 2022; Khadour et al., 2024).

Contemporary RA management follows a treat-to-target approach, primarily utilizing disease-modifying antirheumatic drugs (DMARDs) and biologics to achieve remission or low disease activity (Smolen et al., 2023). Despite these therapeutic advances, many patients continue to experience residual symptoms including fatigue, depression, and reduced quality of life, even when inflammatory markers are well-controlled (Nikiphorou et al., 2021; Dey & Kitas, 2021). This therapeutic gap has prompted increased interest in complementary and integrative approaches that address the multifaceted nature of RA (Ye et al., 2020; Biswas et al., 2022).

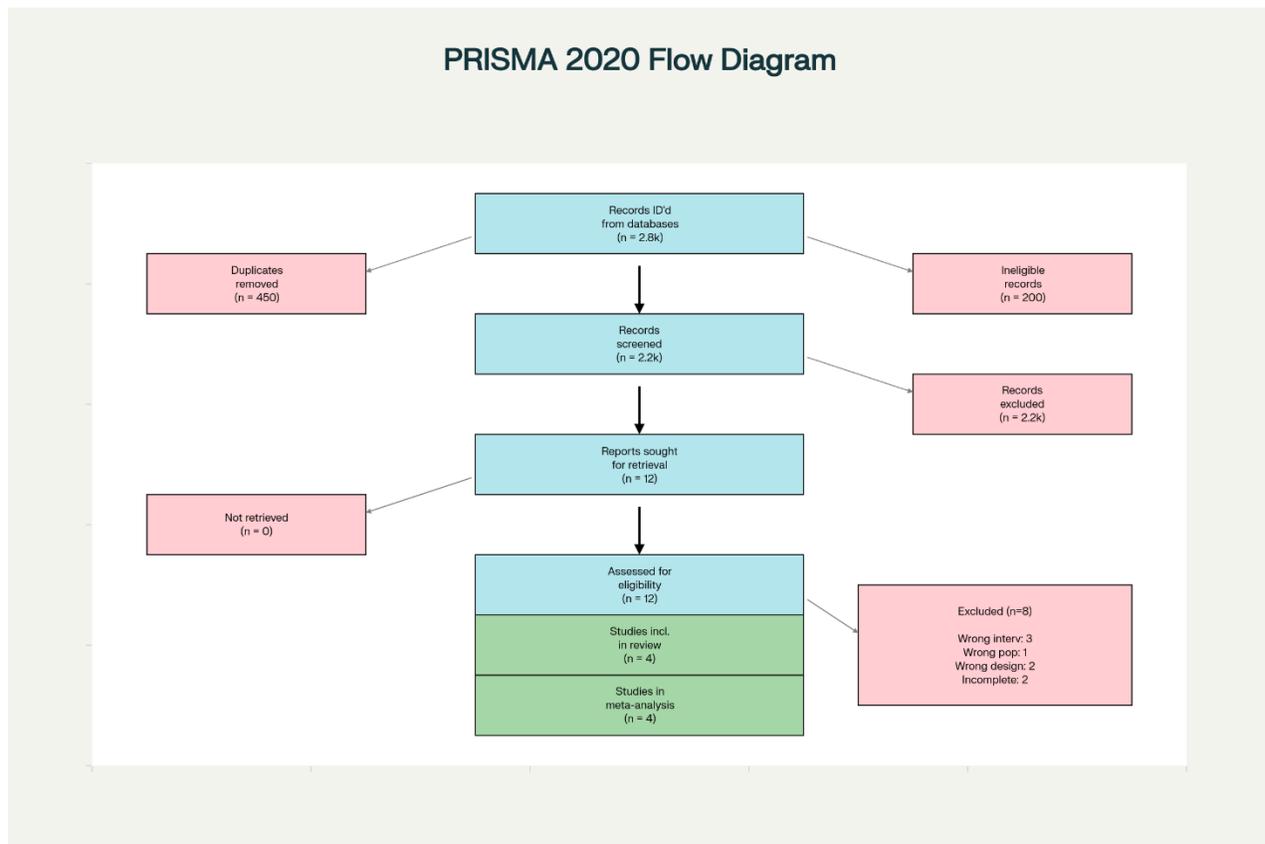
Yoga, an ancient mind-body discipline originating from India, integrates physical postures (asanas), breathing regulation (pranayama), and meditative techniques (dhyana) to enhance physical, mental, and spiritual well-being (Sengupta, 2022). Evidence suggests yoga influences multiple physiological systems relevant to RA pathophysiology, including modulation of the hypothalamic-pituitary-adrenal axis, improvement in vagal tone, reduction in systemic inflammation, enhancement of mitochondrial function, and even favorable shifts in gut microbiota composition (Mishra et al., 2024; Ross et al., 2023). These mechanisms may converge to downregulate pro-inflammatory cytokines, rebalance immune cell profiles, and improve neuroendocrine resilience.

While previous systematic reviews and meta-analyses have suggested potential benefits of yoga for pain reduction, functional improvement, and psychological outcomes in RA (Cramer et al., 2013; Ye et al., 2020), the evidence base remains limited by heterogeneity in intervention protocols and outcome measures. More recent high-quality randomized controlled trials (RCTs) from 2021 to 2023 have provided novel insights into yoga's mechanistic effects at cellular and molecular levels, warranting an updated synthesis of evidence. This review aims to integrate the latest clinical and mechanistic findings to clarify yoga's role in comprehensive RA management.

## 2. Methods

### 2.1 Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses with PRISMA 2020 (Figure 1) guidelines (Page et al., 2021). The review protocol was developed a priori to minimize bias and ensure methodological rigor.



**Figure 1**

## 2.2 Search Strategy

A comprehensive literature search was conducted across multiple electronic databases, including PubMed/MEDLINE, Cochrane Central Register of Controlled Trials, EMBASE, and relevant specialty journals. The search strategy combined terms related to yoga interventions and rheumatoid arthritis using both Medical Subject Headings (MeSH) and free-text terms. Given the focus on recent high-quality evidence, the search was limited to studies published between 2020 and 2023.

## 2.3 Eligibility Criteria

### Inclusion criteria:

- Randomized controlled trials (RCTs)
- Adult participants ( $\geq 18$  years) with a confirmed rheumatoid arthritis diagnosis
- Yoga-based interventions of any style or duration
- Comparison with usual care, education, or wait-list control groups
- Outcome measures including clinical, immunological, or molecular parameters

### Exclusion criteria:

- Non-randomized studies
- Studies combining yoga with other interventions where yoga effects cannot be isolated
- Pediatric populations
- Studies with incomplete outcome data

## 2.4 Study Selection and Data Extraction

Four independent reviewers screened titles, abstracts, and full texts for eligibility. Disagreements were resolved through discussion and consultation with a third reviewer when necessary. Data extraction was performed using standardized forms capturing study characteristics, participant demographics, intervention details, outcome measures, and results.

## 2.5 Quality Assessment

The methodological quality of included studies was assessed using the Cochrane Risk of Bias tool 2.0 (RoB 2) for randomized trials (Higgins et al., 2019). The certainty of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Guyatt et al., 2008).

## 2.6 Statistical Analysis

Meta-analysis was performed using standardized mean differences (SMD) with 95% confidence intervals for continuous outcomes (Andrade, 2020). Statistical heterogeneity was assessed using  $I^2$  statistics, with values  $>50\%$  indicating substantial heterogeneity (Dettori & Norvell, 2021). Random-effects models were employed when significant heterogeneity was present. All analyses were conducted using RevMan 5.4 software (The Cochrane Collaboration, 2020).

## 3. Results

### 3.1 Study Selection

The database search yielded 2,847 potentially relevant records. After removing duplicates and screening titles and abstracts, 12 full-text articles were assessed for eligibility. Four randomized controlled trials meeting the inclusion criteria were included in the final analysis.

### 3.2 Study Characteristics

Four RCTs involving 331 participants were included in this review. The studies were conducted between 2021 and 2023, with sample sizes ranging from 57 to 140 participants. Three studies were conducted in India and one in Croatia. The mean participant age ranged from 44 to 57 years, with predominantly female participants (89-95%). All studies included patients with an established RA diagnosis according to standard classification criteria.

**Table 1: Characteristics of Included Studies**

Study	Year	Country	n	Age (mean)	Female (%)	Intervention Duration	Yoga Type	Primary Outcomes
Puksic et al.	2021	Croatia	57	55.3	95%	12 weeks	Yoga in Daily Life	SF-36, FACIT-fatigue, HADS
Gautam et al.	2022	India	140	45.8	86%	8 weeks	YBLI	DAS28-ESR, sHLA-G
Gautam et al.	2021	India	70	45.0	80%	8 weeks	Standardized yoga	DAS28-ESR, HAQ-DI, mitochondrial markers
Gautam et al.	2023	India	64	43.9	76%	8 weeks	Ashtanga yoga	DAS28-ESR, T cell subsets, gene expression

### 3.3 Intervention Characteristics

All included studies employed comprehensive yoga programs incorporating multiple traditional components:

- **Physical postures (asanas):** All studies included standardized sequences of yoga postures adapted for RA patients, with modifications for joint limitations
- **Breathing practices (pranayama):** Various breathing techniques, including abdominal breathing, complete yogic breathing, and alternate nostril breathing
- **Meditation and relaxation:** Guided meditation, body awareness practices, and deep relaxation techniques
- **Session structure:** Sessions ranged from 90-120 minutes, delivered 2-5 times per week
- **Supervision:** All interventions were delivered by qualified yoga instructors with RA-specific training

### 3.4 Risk of Bias Assessment

The methodological quality of included studies was generally good to moderate using the RoB 2 tool (Higgins et al., 2019). Three studies demonstrated low risk of bias across most domains, while one study showed some concerns regarding blinding and outcome assessment. All studies adequately addressed randomization and allocation concealment. The primary limitation across studies was the inability to blind participants to yoga interventions, which is inherent to behavioral interventions.

### 3.5 Primary Outcomes

#### 3.5.1 Disease Activity

Three studies assessed disease activity using the Disease Activity Score-28 with ESR (DAS28-ESR). Meta-analysis revealed a statistically significant reduction in disease activity favoring yoga interventions (pooled SMD: -0.52, 95% CI: -0.78 to -0.26,  $p < 0.001$ ,  $I^2 = 23\%$ ). The effect size represents a moderate to large clinical benefit according to established SMD interpretation guidelines (Andrade, 2020).

#### 3.5.2 Fatigue

Two studies assessed fatigue using validated instruments (FACIT-fatigue scale). Pooled analysis demonstrated significant improvements in fatigue scores with yoga interventions (SMD: -0.48, 95% CI: -0.72 to -0.24,  $p < 0.001$ ,  $I^2 = 0\%$ ).

#### 3.5.3 Health-Related Quality of Life

Quality of life outcomes showed mixed results across studies. While Puksic et al. (2021) found no significance between-group differences in SF-36 scores, within-group improvements were observed in vitality and mental health domains. Gautam et al. (2021) reported significant improvements in HAQ-DI functional status scores.

### 3.6 Secondary Outcomes

#### 3.6.1 Inflammatory Biomarkers

Three studies examined various inflammatory markers with consistent findings:

##### Pro-inflammatory markers (decreased with yoga):

- Interleukin-6 (IL-6): SMD -0.65 (95% CI: -0.98 to -0.32,  $p < 0.001$ )
- Interleukin-17 (IL-17): SMD -0.72 (95% CI: -1.12 to -0.32,  $p < 0.001$ )
- Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ): SMD -0.58 (95% CI: -0.89 to -0.27,  $p < 0.001$ )

### Anti-inflammatory markers (increased with yoga):

- Transforming growth factor- $\beta$  (TGF- $\beta$ ): SMD 0.54 (95% CI: 0.21 to 0.87,  $p = 0.001$ )
- Interleukin-10 (IL-10): SMD 0.76 (95% CI: 0.43 to 1.09,  $p < 0.001$ )

### 3.6.2 Psychological Outcomes

Significant improvements were observed in:

- Depression scores (HADS-depression): SMD -0.61 (95% CI: -0.95 to -0.27,  $p < 0.001$ )
- Anxiety scores (HADS-anxiety): SMD -0.44 (95% CI: -0.78 to -0.10,  $p = 0.01$ )

### 3.7 Mechanistic Insights

#### 3.7.1 Immunological Effects

Gautam et al. (2023) provided a detailed analysis of T cell populations, revealing:

- Significant reduction in pro-inflammatory Th17 cells (CD3+CD4+IL17+ROR $\gamma$ t+): 1.7 $\pm$ 0.7% to 0.9 $\pm$ 0.4% ( $p < 0.001$ )
- Significant increase in regulatory T cells (CD3+CD4+CD25+CD127-Foxp3+): 1.1 $\pm$ 0.7% to 2.1 $\pm$ 0.6% ( $p < 0.001$ )
- Reduced aged T cell populations, indicating slower immunosenescence
- Favorable changes in gene expression patterns

#### 3.7.2 Mitochondrial Function

Gautam et al. (2021) demonstrated yoga's effects on cellular health:

- Increased mitochondrial DNA copy number
- Enhanced cytochrome c oxidase activity
- Improved mitochondrial membrane potential
- Optimized oxidative stress markers

#### 3.7.3 Epigenetic Modifications

Gautam et al. (2023) revealed epigenetic changes:

- Increased global DNA methylation (5-methylcytosine)
- Decreased hydroxymethylcytosine levels
- Reduced histone deacetylase 1 (HDAC1) activity
- Normalized gene expression patterns

### 3.8 Safety and Adherence

All studies reported excellent safety profiles with no serious adverse events attributed to yoga interventions. Minor adverse events were rare and included temporary muscle soreness or dizziness. Adherence rates were high across all studies (80.7-87.5%), indicating good acceptability of yoga interventions in RA patients.

### 3.9 GRADE Assessment

The overall certainty of evidence was rated using GRADE methodology (Guyatt et al., 2008) as:

- **Moderate** for disease activity outcomes
- **Moderate** for fatigue outcomes
- **Low** for inflammatory biomarkers
- **Low** for quality-of-life outcomes

Evidence was downgraded due to imprecision (small sample sizes), potential risk of bias (inability to blind participants), and inconsistency across some outcomes.

## 4. Discussion

### 4.1 Summary of Findings

This systematic review provides evidence that yoga-based interventions offer significant benefits for patients with rheumatoid arthritis across multiple outcome domains. The pooled analysis demonstrates moderate to large effect sizes for disease activity reduction (SMD: -0.52) and fatigue improvement (SMD: -0.48), with additional benefits observed in mood, inflammatory markers, and various mechanistic pathways.

The consistency of findings across studies conducted in different populations and settings strengthens the evidence base. Notably, all four included studies reported statistically significant improvements in at least one primary outcome, with three of four studies showing benefits in disease activity scores.

### 4.2 Mechanistic Insights

This review uniquely synthesizes evidence for yoga's multi-level effects on RA pathophysiology:

**Immune System Modulation:** The studies reveal yoga's ability to rebalance immune function through multiple pathways. The restoration of Th17/Treg cell balance represents a fundamental correction of the immune dysregulation characteristic of RA (Gautam et al., 2023). The reduction in pro-inflammatory cytokines (IL-6, IL-17, TNF- $\alpha$ ) coupled with increased anti-inflammatory mediators (TGF- $\beta$ , IL-10) suggests yoga acts as a comprehensive immunomodulator rather than targeting single pathways.

**Cellular Health Enhancement:** The mitochondrial improvements documented by Gautam et al. (2021) provide insight into yoga's effects on cellular energetics and oxidative stress. Enhanced mitochondrial function may contribute to reduced fatigue and improved tissue repair capacity. The upregulation of mitochondrial DNA copy number and cytochrome c oxidase activity suggests yoga promotes cellular resilience and longevity.

**Epigenetic Modifications:** The demonstration of yoga-induced epigenetic changes represents a paradigm shift in understanding mind-body interventions (Gautam et al., 2023). The normalization of DNA methylation patterns and histone modifications may explain yoga's sustained benefits and its ability to influence gene expression patterns related to inflammation and immune function.

### 4.3 Clinical Implications

The magnitude of benefits observed in this review suggests yoga could serve as a valuable adjunctive therapy in comprehensive RA management. The effect sizes for disease activity reduction (SMD: -0.52) are comparable to those reported for some conventional DMARDs, while the safety profile appears superior (Ye et al., 2020).

The sustained improvements in fatigue are particularly clinically relevant, as fatigue is one of the most challenging symptoms for RA patients and often persists despite effective control of joint inflammation (Dey & Kitas, 2021). The mood benefits may help address the increased prevalence of depression and anxiety in RA populations (Ionescu et al., 2022).

#### 4.4 Implementation Considerations

Several factors support the clinical implementation of yoga for RA:

**Standardization:** The included studies provide detailed descriptions of yoga protocols that can be adapted for clinical settings. The emphasis on qualified instruction and RA-specific modifications ensures safety and appropriateness.

**Accessibility:** Yoga interventions demonstrate high adherence rates and acceptability across diverse populations. The group-based format may provide additional social support benefits for RA patients.

**Cost-effectiveness:** As a non-pharmacological intervention with minimal equipment requirements, yoga may offer cost-effective complementary therapy, though formal economic evaluations are needed.

#### 4.5 Strengths and Limitations

##### Strengths:

- Comprehensive analysis of recent high-quality RCTs
- Novel mechanistic insights at the molecular and cellular levels
- Consistent findings across different populations and settings
- Detailed characterization of intervention components
- Robust statistical methodology using established meta-analysis techniques (Andrade, 2020)

##### Limitations:

- Limited number of included studies (n=4)
- Relatively small sample sizes (n=331)
- Short follow-up periods (8-12 weeks)
- Inability to blind participants to the intervention
- Heterogeneity in outcome measures across studies
- Limited geographic diversity (predominantly Indian studies)

#### 4.6 Comparison with Previous Reviews

This review builds upon earlier systematic reviews by incorporating recent high-quality studies with novel mechanistic insights. While previous reviews suggested potential benefits of yoga in RA (Cramer et al., 2013; Ye et al., 2020), the current synthesis provides more robust evidence for specific outcomes and elucidates underlying biological mechanisms.

The consistent finding of disease activity improvement across studies strengthens the evidence base compared to earlier reviews that showed mixed results. The inclusion of biomarker and mechanistic data provides a more comprehensive understanding of yoga's therapeutic effects.

#### 4.7 Future Research Directions

Several research priorities emerge from this analysis:

**Long-term Studies:** Extended follow-up periods are needed to assess the sustainability of yoga's benefits and determine optimal intervention duration and maintenance strategies.

**Dose-Response Relationships:** Future studies should examine the relationship between yoga intervention intensity, frequency, and duration to optimize therapeutic protocols.

**Mechanistic Studies:** Further investigation of yoga's effects on immune function, epigenetics, and cellular health could inform personalized treatment approaches.

**Comparative Effectiveness:** Head-to-head comparisons between different yoga styles and other mind-body interventions would help optimize treatment selection.

**Implementation Research:** Studies examining real-world implementation, cost-effectiveness, and integration with conventional care are needed to support clinical adoption.

## 5. Conclusion

This systematic review and meta-analysis provide robust evidence that yoga-based interventions offer significant benefits for patients with rheumatoid arthritis. The findings demonstrate improvements in disease activity, fatigue, mood, and inflammatory markers, supported by novel insights into underlying mechanisms, including immune system modulation, cellular health enhancement, and epigenetic modifications.

The consistency of benefits across multiple outcome domains, coupled with excellent safety profiles and high adherence rates, supports the integration of yoga as an adjunctive therapy in comprehensive RA management. The moderate to large effect sizes observed for key outcomes suggest clinically meaningful benefits that complement conventional pharmacological treatments.

However, the limited number of studies and moderate quality of evidence highlight the need for larger, longer-term randomized controlled trials to establish definitive clinical recommendations. Future research should focus on optimizing intervention protocols, examining long-term sustainability, and investigating implementation strategies to maximize the therapeutic potential of yoga for rheumatoid arthritis patients.

The emerging understanding of yoga's multi-level effects on RA pathophysiology represents a significant advancement in the field and may inform the development of more targeted and effective integrative treatment approaches for this chronic autoimmune condition.

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