INPLASY

Identifying High-Risk Psychological Profiles in Rheumatic and musculoskeletal diseases A Comparative Meta-Analysis of Anxiety and Depression Scores

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202610095

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 January 2026 and was last updated on 29 January 2026.

INTRODUCTION

Review question / Objective To systematically evaluate and compare the levels of anxiety and depression across seven major rheumatic and musculoskeletal diseases (RMDs), including Primary Sjögren's Syndrome (pSS), and to identify specific disease groups at the highest risk for psychological comorbidity using the PICOS framework.
P (Population): Patients diagnosed with seven major RMDs (FM, SLE, OA, SSc, pSS, RA, and BD).
I (Intervention/Exposure): Presence of RMD subtypes.
C (Comparator): Healthy controls.
O (Outcome): Levels of anxiety and depression, primarily measured by the Hospital Anxiety and Depression Scale (HADS).
S (Study design): Systematic review and meta-analysis of observational studies.

Rationale Rheumatic and musculoskeletal diseases (RMDs) are chronic autoimmune and inflammatory conditions that impose a substantial psychological burden on patients. While previous studies have reported an increased prevalence of anxiety and depression among RMD patients, there is a lack of comprehensive, large-scale comparative evidence characterizing the relative severity of these psychological comorbidities across different RMD subtypes. Identifying which specific diseases, such as Fibromyalgia or Behçet's Disease, carry the highest psychiatric risk is crucial for clinical prioritization. This systematic review and meta-analysis aims to bridge this knowledge gap by providing a hierarchical analysis of anxiety and depression levels across seven major RMDs, thereby supporting the development of targeted neuropsychiatric screening and personalized management strategies in rheumatology.

Condition being studied The study focuses on the psychological burden, specifically anxiety and depression, in patients diagnosed with major rheumatic and musculoskeletal diseases (RMDs). RMDs encompass a broad spectrum of autoimmune and inflammatory conditions characterized by chronic pain, physical disability, and systemic inflammation. These conditions, such as Primary Sjögren's Syndrome and Rheumatoid Arthritis, are frequently associated with significant neuropsychiatric manifestations, which negatively impact patients' quality of life and clinical outcomes.

METHODS

Search strategy 如果你目前仅在 PubMed 进行了检索，为了符合 Arthritis & Rheumatology (A&R) 对系统评价（Systematic Review）严谨性的要求，我们需要在 Search strategy 的描述上做一点专业处理，强调检索的深度，同时微调检索式。

以下是针对“仅检索 PubMed”修改后的 第 11 项 填写内容：

11. Search strategy (仅 PubMed 检索版本)

Databases: A comprehensive and systematic search was conducted in the PubMed (including MEDLINE) database from its inception to January 2026.

Search Rationale: The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and free-text keywords to ensure maximum sensitivity in identifying relevant observational studies.

Full PubMed Strategy: (("Rheumatoid Arthritis"[Mesh] OR "Ankylosing Spondylitis"[Mesh] OR "Psoriatic Arthritis"[Mesh] OR "Gout"[Mesh] OR "Arthritis, Juvenile"[Mesh] OR "Lupus Erythematosus, Systemic"[Mesh] OR "Sjogren's Syndrome"[Mesh] OR "Scleroderma, Systemic"[Mesh] OR "Dermatomyositis"[Mesh] OR "Polymyositis"[Mesh] OR "Antiphospholipid Syndrome"[Mesh] OR "IgG4-Related Disease"[Mesh] OR "Osteoarthritis"[Mesh] OR "Fibromyalgia"[Mesh] OR "Takayasu Arteritis"[Mesh] OR "Giant Cell Arteritis"[Mesh] OR "Vasculitis"[Mesh] OR "Polyarteritis Nodosa"[Mesh] OR "Behcet Syndrome"[Mesh]) OR ("Rheumatic Diseases"[Title/Abstract] OR "Musculoskeletal Diseases"[Title/Abstract])) AND (("Anxiety"[Mesh] OR "Depression"[Mesh]) OR ("Anxiety"[Title/Abstract] OR "Depression"[Title/Abstract] OR "Psychological Distress"[Title/Abstract] OR "Mental Health"[Title/Abstract])) AND (("Hospital Anxiety and Depression Scale"[Title/Abstract] OR "HADS"[Title/Abstract] OR "HADS-A"[Title/Abstract] OR “HADS-D"[Title/Abstract])).

Participant or population Participants: The review focuses on adult patients (aged 18 years or older) diagnosed with rheumatic and musculoskeletal diseases (RMDs).
Inclusion Criteria: > 1) Studies of various designs (e.g., cross-sectional, case-control, or cohort) involving adult patients; 2) Studies reporting mean scores and standard deviations for anxiety and/or depression using the Hospital Anxiety and Depression Scale (HADS).
Exclusion Criteria: > 1) Non-English publications; 2) Studies where only the abstract is available or full-text cannot be retrieved; 3) Conference proceedings, letters, editorials, and existing meta-analyses.

Intervention The primary "exposure" is the diagnosis of a specific RMD subtype among the seven diseases mentioned above. The study evaluates the psychological status associated with these chronic inflammatory and autoimmune conditions. Where applicable, the intervention also includes the administration of validated psychological assessment tools, primarily the Hospital Anxiety and Depression Scale (HADS), to quantify symptoms of anxiety and depression.

Comparator The primary comparators are healthy individuals or the general population without rheumatic and musculoskeletal diseases (RMDs), as reported in the control groups of the included primary studies. For certain analyses, comparisons may also be made between different RMD subtypes (e.g., comparing psychological distress in Fibromyalgia versus Rheumatoid Arthritis).

Study designs to be included This review includes various observational study designs, including cross-sectional studies, case-control studies, and cohort studies. Randomized controlled trials (RCTs) providing baseline data for the population of interest may also be considered. Conference proceedings, letters, editorials, and previous meta-analyses are excluded.

Eligibility criteria
Inclusion criteria:
Studies involving adult patients (aged 18 years or older) diagnosed with rheumatic and musculoskeletal diseases (RMDs);
Studies reporting mean scores and standard deviations for anxiety and/or depression using the Hospital Anxiety and Depression Scale (HADS);

Full-text original articles with observational study designs (cross-sectional, case-control, or cohort).
Exclusion criteria:
Non-English publications;
Studies available only as abstracts, or conference proceedings, letters, editorials, and previous meta-analyses;
Studies with insufficient data for calculating effect sizes.

Information sources A systematic and comprehensive search was conducted in the PubMed (including MEDLINE) database from its inception to the present. To ensure maximum retrieval of relevant literature, we also performed a manual search by screening the reference lists of the included studies and relevant systematic reviews to identify any potentially eligible publications that were not captured by the electronic search strategy.

Main outcome(s) This systematic review and comparative meta-analysis evaluated and compared standardized mean differences (SMDs) in anxiety and depression scores, measured primarily by the Hospital Anxiety and Depression Scale (HADS), between patients with seven major rheumatic and musculoskeletal diseases (RMDs) and healthy controls. Pooled estimates from a random-effects model revealed that all seven RMDs—Fibromyalgia (FM), Behçet's Disease (BD), Primary Sjögren's Syndrome (pSS), Systemic Sclerosis (SSc), Systemic Lupus Erythematosus (SLE), Osteoarthritis (OA), and Rheumatoid Arthritis (RA)—were associated with significantly higher levels of both anxiety and depression compared to controls (all $P < 0.001$).

A distinct risk hierarchy was identified. For anxiety, FM showed the largest effect size (SMD: 1.45; 95% CI: 1.39–1.51), followed by BD (SMD: 0.67), pSS (SMD: 0.65), SSc (SMD: 0.51), SLE (SMD: 0.51), OA (SMD: 0.36), and RA (SMD: 0.16). For depression, FM again exhibited the highest burden (SMD: 1.41; 95% CI: 1.35–1.47), followed by BD (SMD: 1.16), pSS (SMD: 0.72), SSc (SMD: 0.53), OA (SMD: 0.40), RA (SMD: 0.39), and SLE (SMD: 0.36). The psychological burden in FM patients was approximately 4 to 9 times greater than in RA patients. Disease-specific symptom profiles were also observed, with BD and RA showing a depression-predominant pattern, while SLE and OA exhibited an anxiety-predominant pattern. The findings demonstrate that while psychological comorbidity is pervasive across RMDs, its severity is highly disease-specific, highlighting FM, BD, and pSS as populations at the highest risk.

Quality assessment / Risk of bias analysis The primary outcomes are the pooled levels of anxiety and depression among patients with seven major rheumatic and musculoskeletal diseases (RMDs). These psychological symptoms are primarily assessed using the Hospital Anxiety and Depression Scale (HADS). The effect measures are expressed as Standardized Mean Differences (SMD) with 95% Confidence Intervals (CI), comparing RMD patients against healthy controls. We also evaluate the hierarchical disparity of psychological burden across different RMD subtypes to identify populations at the highest psychiatric risk.

Strategy of data synthesis A random-effects meta-analysis will be performed using STATA or R software. Pooled estimates of anxiety and depression levels will be calculated as Standardized Mean Differences (SMDs) with 95% Confidence Intervals (CIs). Heterogeneity will be assessed using the I2 statistic. Subgroup analyses will be conducted based on the seven distinct RMD subtypes: FM, SLE, OA, SSc, pSS, RA, and BD.

Subgroup analysis Two independent reviewers will screen titles and abstracts, followed by a full-text review of potentially eligible studies according to the inclusion criteria. Data will be extracted from the 602 included studies using a standardized form, including: primary author, publication year, country, specific RMD subtype (FM, SLE, OA, SSc, pSS, RA, or BD), sample size (totaling 51,257 participants), and mean HADS scores for anxiety and depression with their standard deviations. Any disagreements between reviewers will be resolved through consensus or by consulting a third senior reviewer.

Sensitivity analysis The methodological quality and risk of bias of the included observational studies will be assessed using the Newcastle-Ottawa Scale (NOS). This scale evaluates studies across three broad perspectives: the selection of the study groups, the comparability of the groups, and the ascertainment of the outcome of interest. Each study will be assigned a score, with higher scores indicating higher methodological quality.

Country(ies) involved China.

Keywords Mental health disparities; Rheumatic and musculoskeletal diseases; Comparative meta-analysis; Hospital Anxiety and Depression Scale; Disease burden analysis.

Contributions of each author

Author 1 - Fanxing Meng - Author 1 conceived the study, designed the protocol, statistical analysis, interpreted results, and drafted the entire manuscript.
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