INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

"Cross-talk" Between Gut Microbiome Dysbiosis and Osteoarthritis Progression: A Systematic Review

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Review question / Objective: **The systematic review aims to methodically summarize and analyze the latest evidence on gut microbiome and osteoarthritis in human and animal studies, systematically elaborate the "Gut-Joint" axis, and explore the underlying mechanisms by which gut microbiome dysbiosis contributes to the progression of osteoarthritis. With future research expected to deepen understanding of the correlation between gut microbiome and osteoarthritis, gut microbiome dysbiosis may be a new target for the prevention or early treatment of osteoarthritis.**
Information sources: **XWe will search the studies published in PubMed, Embase, Cochrane, and Web of Science from database inception to July 31, 2022. Only articles in English will be included.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 March 2023 and was last updated on 11 March 2023 (registration number INPLASY202330039).

INTRODUCTION

Review question / Objective: **The systematic review aims to methodically summarize and analyze the latest evidence on gut microbiome and osteoarthritis in human and animal studies, systematically elaborate the "Gut-Joint" axis, and explore the underlying mechanisms by which gut microbiome dysbiosis contributes to the progression of osteoarthritis. With future research expected to deepen understanding of the correlation between gut microbiome and osteoarthritis, gut microbiome dysbiosis may be a new target for the prevention or early treatment of osteoarthritis.**

Condition being studied: **Osteoarthritis (OA) is a common musculoskeletal disease that is predominantly characterized by joint pain, swelling, morning stiffness, and limb**

dysfunction. OA is the main cause of disability and quality-of-life decline in middle-aged and elderly people. The aging global population and high incidence of obesity and joint injuries have increased the socioeconomic burden of OA, with an estimated 250 million people affected worldwide. Based on different exposure factors, OA is considered to be a collection of multiple phenotypes, each with specific pathophysiological and clinical features, such as metabolic OA, traumatic OA, and aging-related OA. These exposures alone or in concert contribute to the complex cross-talk between mechanical, biochemical, and cellular factors that ultimately lead to OA. Although OA is a typical joint degenerative disease, the role of inflammatory factors in its occurrence and development has attracted the attention of researchers. OA is characterized by chronic and low-grade inflammation, primarily mediated by the innate immune system. As the pathogenesis of OA has not been completely elucidated, there is no recognized therapeutic target for advanced OA except pain management or joint replacement.

METHODS

Participant or population: Patients and animals with osteoarthritis will be addressed in the review.

Intervention: Any intervention that affects the gut microbiota will be included in the review.

Comparator: Patients and animals with or without osteoarthritis, but not received gut microbiome intervention.

Study designs to be included: No restrictions on the types of study sesign.No restriction in study types.

Eligibility criteria: 1. Interventions that affect the gut microbiome will be included. 2. Patients and animals only with other arthritic diseases, such as rheumatoid arthritis, will be excluded.

Information sources: We will search the studies published in PubMed, Embase, Cochrane, and Web of Science from database inception to July 31, 2022. Only articles in English will be included.

Main outcome(s): 1. Gut microbiome analysis; 2. osteoarthritis evaluation.

Additional outcome(s): X1. Inflammatory factors; 2. intestinal permeability.

Quality assessment / Risk of bias analysis: The quality of human studies was evaluated by Agency for Healthcare Research and Quality (AHRQ) scale on five aspects: selection bias, performance bias, attrition bias, detection bias, and reporting bias. The quality of animal studies was evaluated by the CAMARADES checklist on seven aspects: sample size calculation, random allocation, blinded evaluation of outcomes, appropriate animal model, animal welfare, peer review, and conflict of interest declaration.

Strategy of data synthesis: All data from the studies were extracted and evaluated in the same way. The narrative synthesis will be planned in the systematic review.

Subgroup analysis: None planned.

Sensitivity analysis: None planned.

Language restriction: English.

Country(ies) involved: China.

Keywords: Gut microbiome, Osteoarthritis, Cartilage, Inflammation, Immune response.

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