

Intra-Articular Platelet-Rich Plasma versus Hyaluronic Acid in the Treatment of Hip Osteoarthritis: A Cross-Sectional Analysis of the Overlapping Systematic Reviews

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Purpose: The debate over the effectiveness of platelet-rich plasma (PRP) versus hyaluronic acid (HA) in treating hip osteoarthritis (HOA) continues. This cross-sectional analysis of overlapping systematic reviews aims to evaluate the efficacy of intra-articular PRP compared to HA for HOA treatment. The goal is to guide decision-makers in selecting the most reliable systematic reviews and to provide treatment recommendations based on the best available evidence.

Methods: We conducted comprehensive searches of PubMed, EMBASE, and Cochrane Library databases to identify systematic reviews comparing intra-articular PRP and HA for HOA treatment. The methodological quality of these reviews was assessed, and relevant data were extracted. The Jadad algorithm was applied to determine which reviews provided the most robust evidence.

Results: Five systematic reviews were included, all categorized as Level-II evidence. The Assessment of Multiple Systematic Reviews scores ranged from 4 to 9, with a median score of 8. A high-quality systematic review was chosen according to the Jadad algorithm. It is suggested that there were no significant differences observed in the improvement of any short-term outcome scores (mean follow-up of 12.2 months for PRP, 11.9 months for HA), including the Western Ontario and McMaster Universities Osteoarthritis Index, the Visual Analog Scale for pain, and the Harris Hip Score, from pre-injection to post-injection between the groups.

Conclusion: There is inconsistency among the conclusions of the overlapping systematic reviews comparing intra-articular PRP and HA for HOA treatment. The best evidence indicates that PRP and HA injections yield similar short-term clinical benefits for patients with HOA. Further studies with larger sample sizes and longer follow-up periods are needed to provide more definitive conclusions.

Keywords: platelet-rich plasma, hyaluronic acid, Hip osteoarthritis, systematic review

Introduction

Osteoarthritis (OA) is a common degenerative disorder characterized by joint pain and dysfunction. It typically affects weight-bearing joints, with the hip being the second most frequently involved. Approximately 40% of individuals over 65 years old suffer from hip osteoarthritis (HOA).¹

Although there is no cure for HOA, various management strategies are employed to relieve symptoms and prevent functional decline. Non-surgical interventions include conservative measures such as weight loss and physiotherapy, as well as pharmacological treatments. Among these therapies, hyaluronic acid (HA) and platelet-rich plasma (PRP) injections have gained increasing attention. HA, a high molecular weight polysaccharide present in joint fluid, has been proven to relieve pain and improve function by reducing inflammation and stimulating chondrocyte metabolism.^{2,3}

Currently, intra-articular HA is considered a reliable treatment for HOA.⁴ PRP, an increasingly popular treatment for HOA, was first reported for therapeutic use in the 1980s.⁵ It is a natural concentrate of platelets obtained through the centrifugation of autologous whole blood. PRP is known to reduce inflammation and promote healing by releasing cytokines and growth factors.^{6–8}

The comparison between PRP and HA for treating HOA remains a topic of debate. Numerous randomized controlled trials (RCTs) and non-randomized controlled trials (non-RCTs) have been conducted, yielding controversial results.^{9–17} Additionally, multiple systematic reviews have been published, showing discordant findings.^{18–22} For instance, a study by Sambe et al²² found that the PRP group experienced significantly lower Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index pain scores and better visual analogue scale (VAS) scores than the HA group at six months. However, Belk et al²¹ concluded that both treatments had similarly short-term clinical outcomes (mean follow-up 12.2 months for PRP, 11.9 months for HA).

Cross-sectional analyses of systematic reviews have proven valuable for decision-makers in selecting the best treatment strategies by evaluating overlapping reviews on the same topic.^{23,24} To date, no cross-sectional analysis of overlapping systematic reviews has been conducted to compare intra-articular PRP and HA for HOA treatment. Therefore, this analysis aims to assist decision-makers in choosing among systematic reviews and provide treatment recommendations based on the best available evidence.

Materials and Methods

Literature Search

Two reviewers (XL and ZX) independently conducted comprehensive searches of the PubMed, EMBASE, and Cochrane Library databases from their inception to March 2024. The search utilized the following keywords: "hip osteoarthritis", "HOA", "hyaluronic acid", "HA", "platelet-rich plasma", "PRP", "systematic review" and "meta-analysis". Initial screening involved reviewing titles and abstracts, with full texts examined as necessary. References from included studies were also screened, and a manual search was performed to ensure all relevant studies were captured. Any disagreements were resolved through group discussion, with a third reviewer (HT) consulted as needed.

Eligibility Criteria

To be included, studies had to meet the following criteria: (1) comparison of intra-articular PRP with HA for HOA treatment; (2) systematic review format; (3) reporting at least one outcome measure, such as VAS or adverse events; (4) published in English. Narrative reviews, meeting abstracts, editorials, case reports, and correspondence articles were excluded.

Data Extraction

Two reviewers (XL and ZX) independently extracted data from the included systematic reviews. Collected data included: first author, publication date, date of last literature search, language restrictions, search databases, primary study design, number of included trials, software used for analysis, Grading of Recommendations Assessment, Development, and Evaluation (GRADE) summary, publication bias analysis, conflict of interest, I^2 statistic value, and meta-analysis results. Discrepancies were resolved through discussion, with a third reviewer (HT) consulted as needed.

Quality Assessment

The methodological quality of the systematic reviews was independently assessed by two reviewers (XL and ZX) using the Oxford Levels of Evidence²⁵ and the Assessment of Multiple Systematic Reviews (AMSTAR) instrument.²⁶ The AMSTAR tool is recognized for its reliability, validity, and responsiveness in evaluating systematic reviews.²⁷ Disagreements were resolved through discussion, with a third reviewer (HT) consulted if necessary.

Application of Jadad Decision Algorithm

Three reviewers (SY, XZ and TL) independently examined the sources of discordance among the systematic reviews using the Jadad decision algorithm and reached a consensus. The Jadad decision algorithm, developed by Jadad et al,²⁸ is a tool designed to select the highest quality evidence from overlapping systematic reviews with discordant conclusions.^{23,29–33} Discordance might arise from differences in clinical questions, inclusion and exclusion criteria, data extraction methods, study quality assessments, data pooling techniques, and statistical methods for data synthesis. The algorithm helped determine which systematic reviews provided the best available evidence and allowed us to generate recommendations despite discordant results.^{34–36}

Results

Literature Search

The Figure 1 outlines the study selection process. Out of 51 titles and abstracts reviewed, 5 systematic reviews met the inclusion criteria for this cross-sectional analysis.^{18–22} The characteristics of these systematic reviews are summarized in Table 1. These reviews were published between 2018 and 2023, each including 4–7 primary trials (Table 2). All primary trials were RCTs except for one non-RCT in Berney et al.²⁰ Sambe et al²² included the most primary studies (n=7) and conducted the most recent review, while Ye et al¹⁸ conducted the earliest review.

Search Methodology

Three systematic reviews restricted their search to English-language publications,^{20–22} one included both English and Spanish literature,¹⁹ and one had no language restrictions.¹⁸ Only Medina-Porqueres et al¹⁹ searched for grey literature. All systematic reviews included PubMed in their search strategies, but there was inconsistency in the use of Embase, Web of Science, Cochrane Library, and other databases. Detailed search methodologies are shown in Table 3.

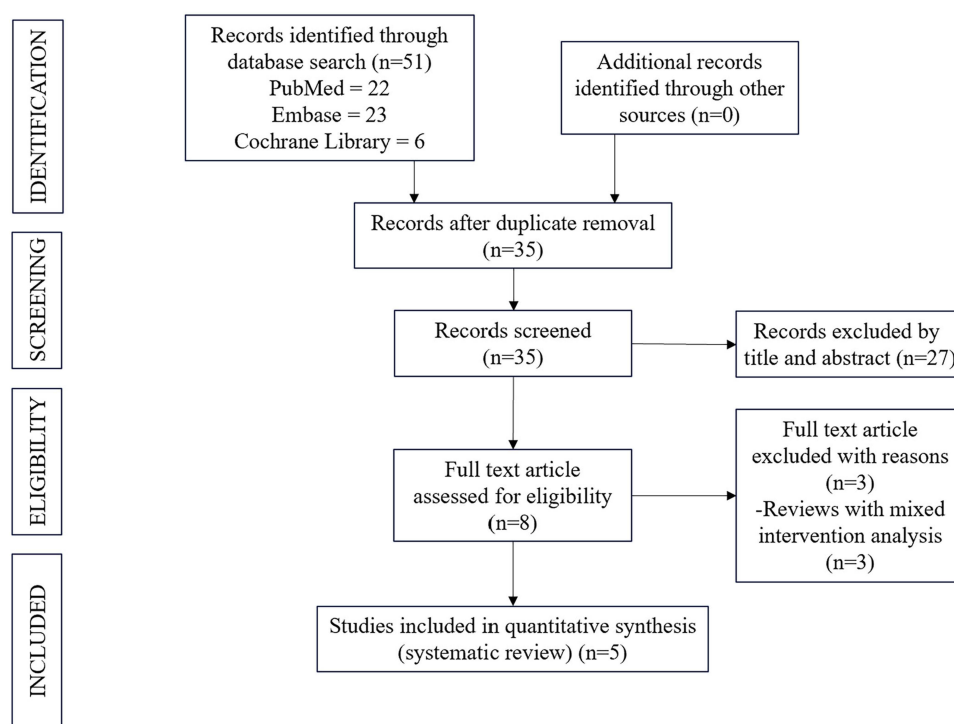


Figure 1 The flow chart of study selection.

Table 1 The Characteristics of the Included Studies

First author	Date of publication	Journal	Impact factor	Date of last literature search	No. of included studies	No. of included RCTs
Ye Y ¹⁸	2018.4	International Journal of Surgery	15.3	2017.8	4	4
Medina-Porqueres I ¹⁹	2020.6	Clinical Rheumatology	3.4	2017.8	4	4
Berney M ²⁰	2020.10	Irish Journal of Medical Science	2.1	2017.8	5	4
Belk JW ²¹	2022.6	The Journal of Arthroscopic and Related Surgery	4.7	2021.1	6	6
Sambe HG ²²	2023.10	Curēus	1.2	2022.9	7	7

Table 2 Included Primary Studies

First author (year)	Sanchez (2012)	Battaglia (2013)	Dallari (2016)	Di Sante (2016)	Doria (2017)	Villanova-López (2020)	Kraeutler (2021)	Nouri (2022)
Ye Y (2018) ¹⁸		+	+	+	+			
Medina-Porqueres I (2020) ¹⁹		+	+	+	+			
Berney M (2020) ²⁰	+	+	+	+	+			
Belk JW (2022) ²¹		+	+	+	+	+	+	
Sambe HG (2023) ²²		+	+	+	+	+	+	+

Table 3 Search Methodology of the Included Studies

First author (year)	Restriction of publication language	Restriction of publication status	Search database				
			PubMed	Embase	Web of science	Cochrane Library	others
Ye Y (2018) ¹⁸	No English & Spanish	Yes	+	+	+	+	
Medina-Porqueres I (2020) ¹⁹		No	+			+	+
Berney M (2020) ²⁰	English	Yes	+	+			+
Belk JW (2022) ²¹	English	Yes	+	+		+	
Sambe HG (2023) ²²	English	Yes	+			+	+

Table 4 Methodological Information About the Included Studies

First author (year)	Design of included studies	Level of evidence	Software	GRADE use	Sensitivity analysis
Ye Y (2018) ¹⁸	RCT	Level II	STATA	No	No
Medina-Porqueres I (2020) ¹⁹	RCT	Level II	NA	Yes	No
Berney M (2020) ²⁰	RCT and non-RCT	Level II	NA	No	No
Belk JW (2022) ²¹	RCT	Level II	RevMan	No	No
Sambe HG (2023) ²²	RCT	Level II	RevMan	No	No

Abbreviations: RCT, randomized controlled trial. non-RCT, non-randomized controlled trial.

Methodological Quality

As detailed in Table 4, all included systematic reviews were determined as Level II evidence according to the Oxford Levels of Evidence. Most reviews used only RCTs except for Berney et al.²⁰ Two reviews used RevMan for data analysis,^{21,22} one used STATA,¹⁸ and two did not specify their software.^{19,20} Only Medina-Porqueres et al¹⁹ utilized the

Table 5 AMSTAR Scores for the Included Studies

Items	Ye Y (2018) ¹⁸	Medina-Porqueres I (2020) ¹⁹	Berney M (2020) ²⁰	Belk JW (2022) ²¹	Sambe HG (2023) ²²
1. Was an a priori design provided?	1	0	1	1	1
2. Was there duplicate study selection and data extraction?	1	1	1	1	1
3. Was a comprehensive literature search performed?	0	1	0	1	1
4. Was the status of publication (ie grey literature) used as an inclusion criterion?	0	1	0	0	0
5. Was a list of studies (included and excluded) provided?	1	0	1	1	1
6. Were the characteristics of the included studies provided?	1	1	0	1	1
7. Was the scientific quality of the included studies assessed and documented?	1	1	0	1	1
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	1	1	0	1	1
9. Were the methods used to combine the findings of studies appropriate?	1	1	0	1	0
10. Was the likelihood of publication bias assessed?	0	0	0	0	0
11. Was the conflict of interest stated?	1	0	1	1	1
Total scores	8	7	4	9	8

GRADE system, and none conducted a sensitivity analysis. The AMSTAR scores ranged from 4 to 9, with a median score of 8 (Table 5). The review by Belk et al²¹ received the highest quality rating.

Heterogeneity Assessment

All included systematic reviews assessed heterogeneity, but one did not report the I^2 value.²⁰ The I^2 statistics are provided in Table 6. None of the reviews performed sensitivity analyses based on methodological quality (Table 4).

Table 6 I^2 Statistic Value of Each Variable in Each Meta-Analysis

Items	Ye Y (2018) ¹⁸	Medina-Porqueres I (2020) ¹⁹	Berney M (2020) ²⁰	Belk JW (2022) ²¹	Sambe HG (2023) ²²
VAS	0%		NA	83%	62%
VAS within 2 months	25%	96%			34%
VAS at 6 months	0%	98%			72%
VAS at 12 months	0%	97%			71%
HHS	84.1%		NA	88%	49%
HHS within 2 months	63.3%				
HHS at 6 months	91.2%				64%
HHS at 12 months	87.6%				47%
WOMAC	0%		NA	76%	68%
WOMAC within 2 months					30%
WOMAC at 6 months	0%				0%
WOMAC at 12 months	0%				87%
Adverse effects	0%	NA			NA
The growth factors' concentration		NA			

Abbreviations: WOMAC, Western Ontario and McMaster Universities Arthritis Index. VAS, visual analogue scale. HHS, Harris hip score.

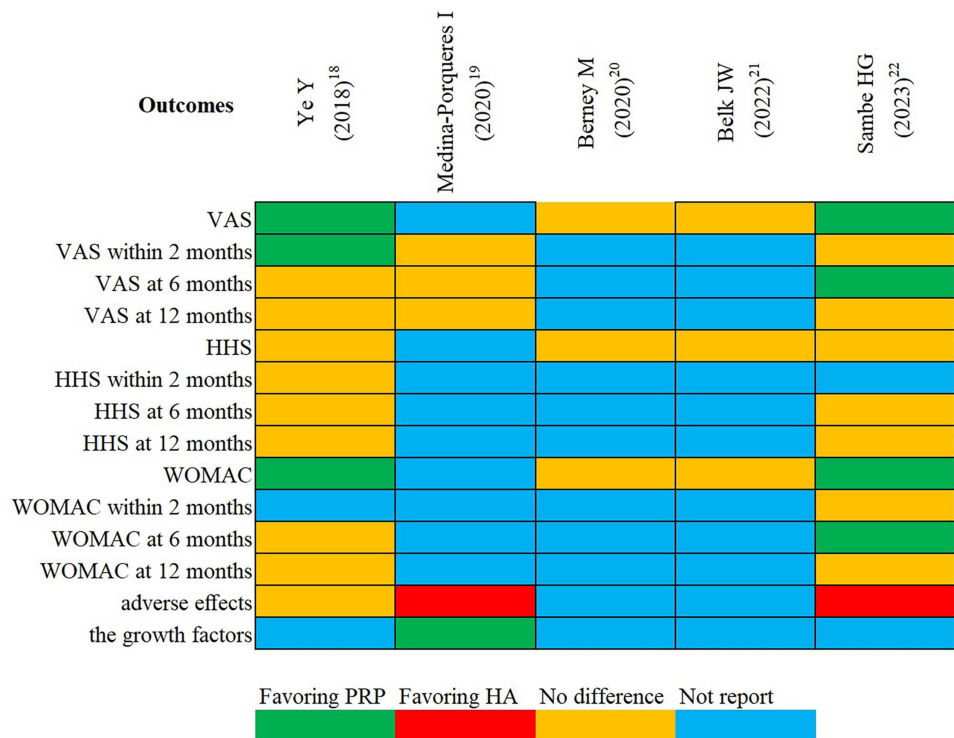


Figure 2 Results of the included meta-analyses.

Results of Jadad Decision Algorithm

The pooled results from the included studies are shown in Figure 2. The Jadad decision algorithm was employed to determine the best available evidence among the five included reviews. Despite varying primary study selections, all reviews addressed the same research question. The algorithm considered the methodological quality of primary trials, individual patient data analysis, publication status, and language restrictions. Ultimately, the systematic review by Belk et al²¹ was identified as the highest quality according to the Jadad decision algorithm (Figure 3). This review concluded that PRP and HA injections provide similarly beneficial short-term clinical outcomes (mean follow-up of 12.2 months for PRP, 11.9 months for HA) for patients with HOA.

Discussion

The increasing incidence of HOA presents a significant public health challenge, impacting quality of life and contributing to substantial healthcare costs. Risk factors for HOA include age, gender, bone mineral density, and nutritional status. The disease progresses through the loss of articular cartilage, narrowing of the hip joint space, and inflammation.³⁷ With no treatment currently available to halt this progression, management strategies aim to alleviate symptoms and prevent functional decline. The American College of Rheumatology recommends intra-articular injections, including HA and PRP.³⁸

Initial clinical evidence has suggested the efficacy and safety of both HA and PRP for treating HOA, leading to comparisons of these treatments.^{9–17} Multiple systematic reviews have evaluated the efficacy and safety of intra-articular HA versus PRP for HOA treatment, but their conclusions have varied, creating confusion for decision-makers.^{18–22}

To our knowledge, this study is the first cross-sectional analysis of overlapping systematic reviews comparing intra-articular PRP with HA for HOA treatment. This analysis aims to help decision-makers navigate conflicting reviews and determine the best available evidence.

After a comprehensive literature search, we identified five systematic reviews that met our inclusion criteria. Using the Jadad decision algorithm, we selected the highest-quality review by Belk et al,²¹ which concluded that PRP and HA

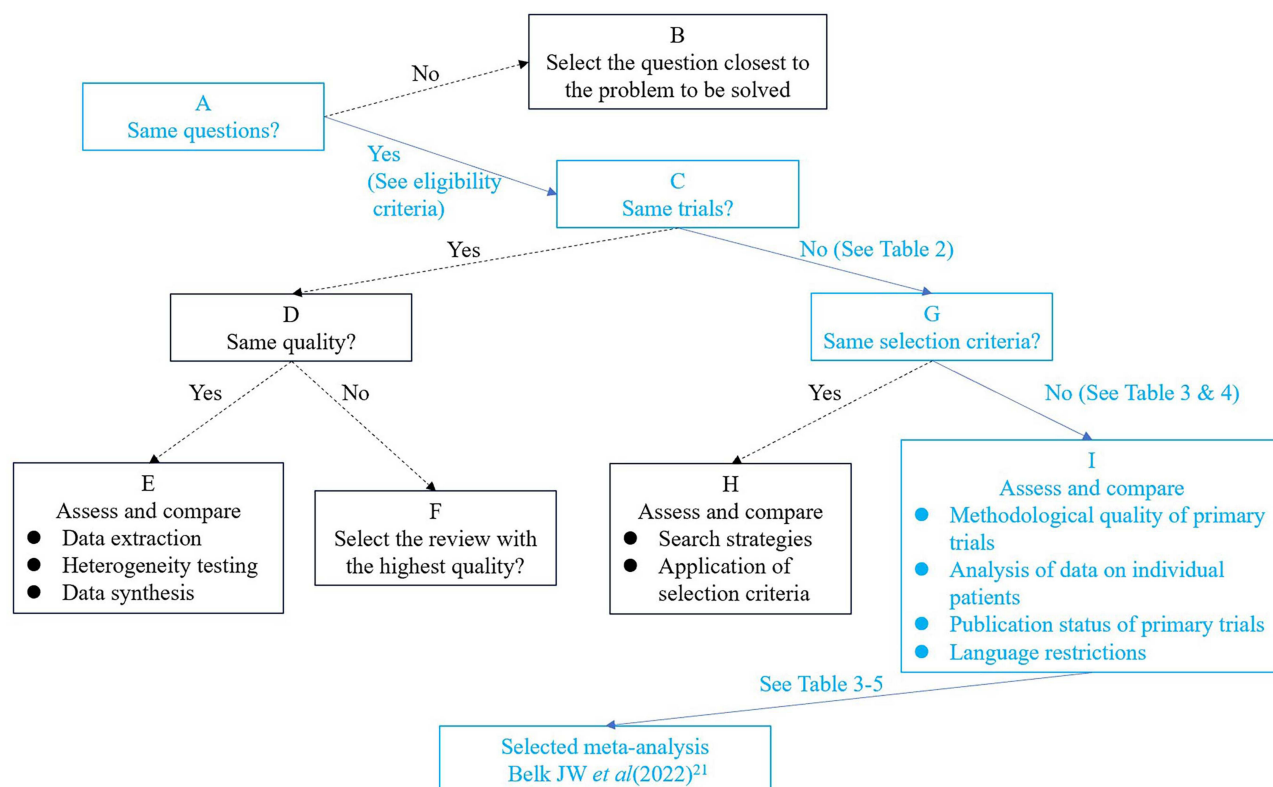


Figure 3 The flow chart of the Jadad decision algorithm.

injections provide similar short-term clinical outcomes (mean follow-up 12.2 months for PRP, 11.9 months for HA) for HOA patients. There were no statistically significant differences in WOMAC, VAS, or Harris hip scores (HHS) from pre-injection to post-injection between the groups, indicating that both injections are beneficial without clear superiority of one over the other.

Our study revealed discordant results among the included systematic reviews, despite their publication within a similar timeframe. Some reviews suggested that PRP offered greater benefits than HA.^{18,22} For instance, Ye et al¹⁸ found that PRP significantly reduced VAS scores at two months, but showed no significant advantage in WOMAC scores over HA at 12 months. This discrepancy may be due to Ye et al's review¹⁸ being the earliest published and including the fewest primary trials.

Three of the five systematic reviews reported no significant differences in HHS between PRP and HA at any time point, likely due to the chronic and slowly progressing nature of HOA requiring longer follow-up to detect functional improvements.^{18,21,22} Additionally, two reviews indicated that adverse effects were more common with PRP, particularly post-injection pain.^{19,22} However, these adverse effects were temporary and manageable with proper injection techniques.^{10,15}

Our study had several limitations. First, the literature search was restricted to English-language articles, excluding non-English studies despite a comprehensive search of multiple databases. Second, the systematic reviews included were all Level II evidence, preventing us from providing a Level I treatment recommendation. Third, we could not assess long-term results due to the scarcity of clinical trials evaluating PRP versus HA beyond one year.¹⁴ Future studies should extend follow-up durations to better understand the long-term efficacy of these treatments.

Conclusion

This cross-sectional analysis is the first to compare overlapping systematic reviews of intra-articular PRP versus HA for HOA treatment. The analysis highlighted discordant conclusions among the reviews. Based on the best available

evidence, PRP and HA injections yield similar short-term clinical outcomes for HOA patients. Further research with larger sample sizes and extended follow-up periods is necessary to provide more definitive recommendations.

Abbreviations

OA, osteoarthritis; HOA, hip osteoarthritis; HA, hyaluronic acid; PRP, platelet-rich plasma; RCTs, randomized controlled trials; non-RCTs, non-randomized controlled trials; VAS, visual analogue scale; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; AMSTAR, Assessment of Multiple Systematic Reviews; HHS, Harris hip scores.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Acknowledgments

We thank our colleagues for their cooperation with this study. We also would like to thank the reviewers for their constructive criticism and suggestions.

Funding

This work was supported by Beijing Tongzhou District Science and Technology Planning Project (KJ2023CX067), National Key R & D Program of China (2022YFC3502100), National Natural Science Foundation of China (82205089), Fundamental Research Funds for the Central Public Welfare Research Institutes (ZZ13-YQ-030), Scientific and Technological Innovation Project of China Academy of Chinese Medical Sciences (CI2021A01614), Clinical Research Center Construction Project of Guang'anmen Hospital, CACMS (2022LYJSZX13).

Disclosure

The authors report no conflicts of interest in this work.

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