AAOS
American Academy of Orthopaedic Surgeons

Platelet-Rich Plasma (PRP) for Knee Osteoarthritis Technology Overview

Review Period Report

Disclaimer: This Technology Overview was prepared using systematic review methodology and summarizes the findings of studies published as of August 25, 2021 on the use of platelet rich plasma for the treatment of knee osteoarthritis. As a summary, this document does not make recommendations for or against the use of platelet rich plasma. It should not be construed as an official position of the American Academy of Orthopaedic Surgeons. Readers are encouraged to consider the information presented in this document and reach their own conclusions about platelet rich plasma for the treatment of knee osteoarthritis

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Platelet-Rich Plasma for Knee Osteoarthritis

Overview of the Review Period

The reviews and comments related to this technology overview are reprinted in this document and posted on the AAOS website. All reviewers are required to disclose their conflict of interests.

Review Process:

AAOS contacted 5 organizations with content expertise to review a draft of the technology overview during the three-week peer review period in February 2022.

Additionally, the draft was also provided to members of the AAOS Board of Directors (BOD), members of the Council on Research and Quality (CORQ), members of the Board of Councilors (BOC), members of the Board of Specialty Societies (BOS) and members of the Committee on Devices, Biologics, and Technology (DBT) for review and comment.

- Eight (8) individuals provided comments via the electronic structured peer review form. No reviewers asked to remain anonymous.
- All eight reviews were on behalf of a society and/or committee.
- The work group considered all comments and made some modifications when they were consistent with the evidence.

Reviewer Key

Each reviewer was assigned a number (see below). All responses in this document are listed by the assigned peer reviewer's number.

Table 1. Reviewer Key

Reviewer Number	Name of Reviewer	Society/ Committee Being Represented
1	Gregory Pinkowsky, MD, FAAOS	American Academy of Orthopaedic Surgeons
2	Peter Amadio, MD, FAAOS	American Academy of Orthopaedic Surgeons, Board of Specialty Societies
3	Julie Dodds, MD, FAAOS	American Academy of Orthopaedic Surgeons, Board of Specialty Societies
4	Matthew Austin, MD, FAAOS	American Association of Hip and Knee Surgeons
5	Kevin Shea, MD, FAAOS	American Academy of Orthopaedic Surgeons, Quality Research Council
6	Ajay Srivastava, MD	American Academy of Orthopaedic Surgeons, Committee on Evidence Based Quality and Value
7	Lutul Farrow, MD, FAAOS	American Academy of Orthopaedic Surgeons, Board of Specialty Societies
8	Matthew Abdel, MD, FAAOS	American Academy of Orthopaedic Surgeons, Board of Directors

Reviewer Demographics

Table 2: Reviewer Demographics

Reviewer Number	Name of Reviewer	Primary Specialty	Work Setting
1	Gregory Pinkowsky, MD, FAAOS	Sports Medicine	Private Group or Practice
2	Peter Amadio, MD, FAAOS	Hand	Academic Practice
3	Julie Dodds, MD, FAAOS	Arthroscopy	Private Group or Practice
4	Matthew Austin, MD, FAAOS	Total Joint	Private Group or Practice
5	Kevin Shea, MD, FAAOS	Sports Medicine	
6	Ajay Srivastava, MD	Adult Knee	Private Group or Practice
7	Lutul Farrow, MD, FAAOS	Sports Medicine	Clinical Hospital
8	Matthew Abdel, MD, FAAOS	Adult Hip	Academic Practice

Reviewers' Disclosure Information

All reviewers are required to disclose any possible conflicts that would bias their review via a series of 10 questions (see Table 3). For any positive responses to the questions (i.e., "Yes"), the reviewer was asked to provide details on their possible conflict.

Table 3. Disclosure Question Key

Disclosure Question	Disclosure Question Details
A	A) Do you or a member of your immediate family receive royalties for any pharmaceutical, biomaterial or orthopaedic product or device?
B	B) Within the past twelve months, have you or a member of your immediate family served on the speakers bureau or have you been paid an honorarium to present by any pharmaceutical, biomaterial or orthopaedic product or device company?
C	C) Are you or a member of your immediate family a PAID EMPLOYEE for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
D	D) Are you or a member of your immediate family a PAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
E	E) Are you or a member of your immediate family an UNPAID CONSULTANT for any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
F	F) Do you or a member of your immediate family own stock or stock options in any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier (excluding mutual funds)
G	G) Do you or a member of your immediate family receive research or institutional support as a principal investigator from any pharmaceutical, biomaterial or orthopaedic device or equipment company, or supplier?
H	H) Do you or a member of your immediate family receive any other financial or material support from any pharmaceutical, biomaterial or orthopaedic device and equipment company or supplier?
I	I) Do you or a member of your immediate family receive any royalties, financial or material support from any medical and/or orthopaedic publishers?
J	J) Do you or a member of your immediate family serve on the editorial or governing board of any medical and/or orthopaedic publication?

Table 4. Reviewer's Disclosure Information

Reviewer Number	Name of Reviewer	Disclosure Available via AAOS Disclosure System	A	B	C	D	E	F	G	H	I	J
1	Gregory Pinkowsky, MD, FAAOS	No	No	No	No	No	No	No	No	No	No	No
2	Peter Amadio, MD, FAAOS	Yes										
3	Julie Dodds, MD, FAAOS	Yes										
4	Matthew Austin, MD, FAAOS	Yes										
5	Kevin Shea, MD, FAAOS	Yes										
6	Ajay Srivastava, MD	No	No	No	No	No	No	No	No	No	No	No
7	Lutul Farrow, MD, FAAOS	Yes										
8	Matthew Abdel, MD, FAAOS	Yes										

Reviewer Responses to Structured Review Form Questions

All reviewers are asked 15 structured review questions which have been adapted from the Appraisal of Guidelines for Research and Evaluation (AGREE) II Criteria*. Their responses to these questions are listed on the next few pages.

Table 5. Reviewer Responses to Structured Review Questions 1-4

Reviewer Number	Name of Reviewer	1. The overall objective(s) of the technology overview is (are) specifically described.	2. The research covered by the technology overview is (are) specifically described.	3. The technology overview's target audience is clearly described.	4. Given the nature of the topic and the data, all clinically important outcomes are considered.
1	Gregory Pinkowsky, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
2	Peter Amadio, MD, FAAOS	Agree	Agree	Agree	Agree
3	Julie Dodds, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
4	Matthew Austin, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Disagree
5	Kevin Shea, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Ajay Srivastava, MD	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
7	Lutul Farrow, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
8	Matthew Abdel, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

Table 6. Reviewer Responses to Structured Review Questions 5-8

Reviewer Number	Name of Reviewer	5. The patients to whom this technology overview is meant to apply are specifically described.	6. The criteria used to select articles for inclusion are appropriate.	7. The reasons why some studies were excluded are clearly described.	8. All important studies that met the article inclusion criteria are included
1	Gregory Pinkowsky, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
2	Peter Amadio, MD, FAAOS	Disagree	Agree	Neutral	Neutral
3	Julie Dodds, MD, FAAOS	Agree	Strongly Agree	Strongly Agree	Strongly Agree
4	Matthew Austin, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
5	Kevin Shea, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Ajay Srivastava, MD	Agree	Agree	Agree	Agree
7	Lutul Farrow, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
8	Matthew Abdel, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

Table 7. Reviewer Responses to Structured Review Questions 9-12

Reviewer Number	Name of Reviewer	9. The validity of the studies is appropriately appraised.	10. The methods are described in such a way as to be reproducible	11. The statistical methods are appropriate to the material and the objectives of this technology overview	12. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed.
1	Gregory Pinkowsky, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
2	Peter Amadio, MD, FAAOS	Neutral	Neutral	Neutral	Disagree
3	Julie Dodds, MD, FAAOS	Agree	Strongly Agree	Strongly Agree	Strongly Agree
4	Matthew Austin, MD, FAAOS	Strongly Agree	Strongly Agree	Disagree	Agree
5	Kevin Shea, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
6	Ajay Srivastava, MD	Agree	Agree	Agree	Agree
7	Lutul Farrow, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree
8	Matthew Abdel, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree	Strongly Agree

Table 8. Reviewer Responses to Structured Review Questions 13-15

Reviewer Number	Name of Reviewer	13. Health benefits, side effects, and risks are adequately addressed.	14. Areas for future research are adequately addressed.	15. The writing style is appropriate for health care professionals.
1	Gregory Pinkowsky, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree
2	Peter Amadio, MD, FAAOS	Neutral	Neutral	Agree
3	Julie Dodds, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree
4	Matthew Austin, MD, FAAOS	Agree	Strongly Agree	Strongly Agree
5	Kevin Shea, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree
6	Ajay Srivastava, MD	Agree	Agree	Agree
7	Lutul Farrow, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree
8	Matthew Abdel, MD, FAAOS	Strongly Agree	Strongly Agree	Strongly Agree

Reviewers' Recommendation for use of this technology overview in Clinical Practice

Would you recommend this technology overview be used to inform clinical practice?

Reviewer Number	Name of Reviewer	Would you recommend this technology overview be used to inform clinical practice?
1	Gregory Pinkowsky, MD, FAAOS	Strongly Recommend
2	Peter Amadio, MD, FAAOS	
3	Julie Dodds, MD, FAAOS	Strongly Recommend
4	Matthew Austin, MD, FAAOS	Strongly Recommend
5	Kevin Shea, MD, FAAOS	
6	Ajay Srivastava, MD	
7	Lutul Farrow, MD, FAAOS	
8	Matthew Abdel, MD, FAAOS	Strongly Recommend

Reviewer Detailed Responses and Editorial Suggestions

Reviewer #1, Gregory Pinkowsky, M.D., FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
1	Gregory Pinkowsky, M.D., FAAOS	American Academy of Orthopaedic Surgeons	A. Appropriate selection of articles reviewed. PRP has been evaluated versus an appropriate amount of other treatments. Well written and concise conclusions.

Workgroup Response to Reviewer #1

Dear Gregory Pinkowsky, M.D., FAAOS,

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. Thank you for the positive feedback.

Reviewer #2, Peter Amadio, M.D., FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
2	Peter Amadio, M.D., FAAOS	American Academy of Orthopaedic Surgeons, Board of Specialty Societies	A. While the tables are comprehensive, the written summary, to which most readers will refer, is incomplete, and do not address outcome time frames, type or method of preparation of PRP, or sex differences in response.

Workgroup Response to Reviewer #2

Dear Peter Amadio, M.D., FAAOS

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. This workgroup spent considerable time evaluating the timing of outcomes, method of preparation of PRP and differences in patient characteristics in the development of this Technology Overview. Unfortunately, they were limited by heterogeniety of these factors both in comparable studies and in reporting within those studies, limiting the comparability for the final report.

Reviewer #3, Julie Dodds, M.D., FAAOS

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
3	Julie Dodds, M.D., FAAOS	American Academy of Orthopaedic Surgeons, Board of Specialty Societies	A. Line 177 - PRP vs Prolo - confused why this is considered insufficient evidence, in spite of 1 high level study. I would rephrase the conclusion "Due to the presence of only 1 high level study, PRP cannot be considered superior to prolo" or something like that. B. Otherwise, topic well covered.

Workgroup Response to Reviewer #3

Dear Julie Dodds, M.D., FAAOS

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. Thank you for your comment. The work group believes there is insufficient evidence to change the section as it is written. Further high quality randomized controlled studies could be useful to bring future clarity.
B. Thank you for the positive feedback.

Reviewer #4, Matthew Austin, M.D., FAAOS,

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
4	Matthew Austin, M.D., FAAOS	American Association of Hip and Knee Surgeons	A. One of the main limitations in the studies, particularly in the comparison of PRP vs HA injections, is the lack of inclusion of the severity of the knee OA. B. As we know insurances don't cover PRP, we need to consider inherent selection bias in the patient population who are using PRP. They are more likely to be affluent and higher socioeconomic class. They are more likely to be motivated and therefore more likely to show better results. C. All the studies which show better results at less than 12 weeks should not be included because standard of care for cortisone shot is roughly 3 months and insurance covers hyaluronic acid injections at six months. PRP injection should relieve pain for at least six months. D. Recent guidelines published by AAOS in 2021 on nonoperative management of knee arthritis has PRP at lower strength of evidence and low grade of recommendation. Hopefully our recommendations align otherwise it gets mixed signals to the public. E. One of the major limitations is that while the review focuses on "statistically significant differences" it does not mention those differences reaching the MCID for the outcome measures examined. This is particularly important given the the cost of the PRP intervention. F. Some mention of the range of costs associated with PRP and other treatment modalities would be worthwhile to the reader. G. One major recommendation for improvement would be the conclusion. As written, the conclusion is a little strong saying that PRP demonstrated statistically significant improvement in several PROs compared to some other treatments. The data is so mixed particularly when compared to corticosteroids, which I believe should be the gold standard comparison. I think the conclusion should be tempered and state that the data is mixed with some studies showing benefit to PRP and others finding no difference.

Workgroup Response to Reviewer #4

Dear Matthew Austin, M.D., FAAOS,

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. This workgroup spent considerable time evaluating the timing of outcomes, method of preparation of PRP and differences in patient characteristics in the development of this TO. Unfortunately, they were limited by heterogeniety of these factors both in comparable studies and in reporting within those studies, limiting the comparability for the final report.
B. The workgroup shares this reasonable observation among the general population, although hopefully mitigated in the study design by double-blind randomization in the studies where the design is possible.
C. The feedback is appreciated, and we will take it under advisement in developing PICO questions and inclusion criteria for future updates.
D. This workgroup appreciates the consideration and can confirm that there is internal consistency to the documents.
E. The work group was unable to apply MCID to the situations included within this report due to a lack of validated and published MCID values.
F. Thank you for your comment. This was outside the scope of the current TO but would be important to include in a future paper.
G. Thank you for your comment. An edit was made to the conclusion to improve clarity.

Reviewer #5, Kevin Shea, M.D., FAAOS,

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
5	Kevin Shea, M.D., FAAOS	American Academy of Orthopaedic Surgeons, Quality Research Council	A. No comment.

Workgroup Response to Reviewer #5

Dear Kevin Shea, M.D., FAAOS,

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. No comment.

Reviewer #6, Ajay Srivastava, M.D.,

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
6	Ajay Srivastava, M.D.	American Academy of Orthopaedic Surgeons, Committee on Evidence Based Quality and Value	A. I would like to congratulate DBT committee for their hard work. B. Here are my suggestions: I would suggest that we should exclude the study who have which has looked for outcome at less than 12 weeks. It is generally accepted to repeat Cortisone shot at 12 weeks and insurances will mandate hyaluronic acid injections at 24 weeks. Therefore, only the studies which match the time for cortisone and hyaluronic acid should be included. C. I'm concerned about inherent selection bias in PRP group because that's supposed to be affluent socioeconomic class with motivation to do better. This group of patients are likely to show a better outcome as compared to all pair type of insurance patient mix. D. Final recommendation should be written in a way that PRP versus Cortisone or PIP versus hyaluronic acid. In other words, a general statement that PRP is effective could be misleading.

Workgroup Response to Reviewer #6

Dear Ajay Srivastava, M.D.,

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. Thank you for the positive feedback.
B. Thank you for the feedback. We will take it under advisement in developing PICO questions and inclusion criteria for future updates.
C. The workgroup shares this reasonable observation among the general population, although hopefully mitigated in the study design by double-blind randomization in the studies where the design is possible.
D. Thank you for your comment. An edit was made to the conclusion to improve clarity.

Reviewer #7, Lutul Farrow, M.D., FAAOS,

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
5	Lutul Farrow, M.D., FAAOS	American Academy of Orthopaedic Surgeons, Board of Specialty Societies	A. Great summary of the data. delivered clearly. will be useful.

Workgroup Response to Reviewer #7

Dear Lutul Farrow, M.D., FAAOS,

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. Thank you for the positive feedback.

Reviewer #8, Matthew Abdel, M.D., FAAOS,

Reviewer Number	Reviewer Name	Society or committee you are representing	Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the technology overview; The response(s) below also include all editing suggestions received from the Additional Comments section of the structured review form.
8	Matthew Abdel, M.D., FAAOS	American Academy of Orthopaedic Surgeons, Board of Directors	A. See above.

Workgroup Response to Reviewer #8

Dear Matthew Abdel, M.D., FAAOS,

Thank you for your expert review of the Platelet-Rich Plasma for Knee Osteoarthritis Technology Overview. We will address your comments in the order that you listed them.

A. No comment.

Appendix A – Structured Review Form

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
1. The overall objective(s) of the technology overview is (are) specifically described.	○	○	○	○	○
2. The research covered by the technology overview is (are) specifically described.	○	○	○	○	○
3. The technology overview's target audience is clearly described.	○	○	○	○	○
4. Given the nature of the topic and the data, all clinically important outcomes are considered.	○	○	○	○	○
5. The patients to whom this technology overview is meant to apply are specifically described.	○	○	○	○	○
6. The criteria used to select articles for inclusion are appropriate.	○	○	○	○	○
7. The reasons why some studies were excluded are clearly described.	○	○	○	○	○
8. All important studies that met the article inclusion criteria are included.	○	○	○	○	○
9. The validity of the studies is appropriately appraised.	○	○	○	○	○
10. The methods are described in such a way as to be reproducible.	○	○	○	○	○
11. The statistical methods are appropriate to the material and the objectives of this technology overview.	○	○	○	○	○
12. Important parameters (e.g., setting, study population, study design) that could affect study results are systematically addressed.	○	○	○	○	○
13. Health benefits, side effects, and risks are adequately addressed.	○	○	○	○	○
14. Areas for future research are adequately addressed.	○	○	○	○	○
15. The writing style is appropriate for health care professionals.	○	○	○	○	○

Please provide a brief explanation of both your positive and negative answers in the preceding section. If applicable, please specify the draft page and line numbers in your comments. Please feel free to also comment on the overall structure and content of the draft:

Would you recommend this technology overview be used to inform clinical practice? (REQUIRED)

- ○ Strongly Recommend
- ○ Recommend
- ○ Would Not Recommend
- ○ Unsure

Additional Comments regarding this technology overview?