

# Randomized Controlled Trials for Platelet-Rich Plasma Use in Knee Osteoarthritis Rarely Report Key Sociodemographic Patient Variables: A Scoping Review



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**Purpose:** To investigate the characteristics and rate of sociodemographic variables reported in randomized controlled trials (RCTs) studying platelet-rich plasma (PRP) injections in the treatment of knee osteoarthritis (OA). **Methods:** In January 2024, PubMed, Scopus, and Web of Science databases were queried for the phrase “Platelet-Rich Plasma Knee Osteoarthritis.” Included studies were RCTs investigating PRP use in knee OA published in English between 2012 and 2023. Each RCT was inspected for patient age and sex or gender as well as the following sociodemographic variables: race, ethnicity, insurance status, income, housing status, work status, and education. Data were presented in a descriptive fashion and analyzed using  $\chi^2$  test and Fisher’s exact test to compare 2 and 3 categorical variables, respectively, with significance defined as  $P < .05$ . **Results:** From 2012 through 2023, 71 RCTs met inclusion criteria. Included publications reported both age and sex or gender in 71/71 papers (100%). Reporting rates for other sociodemographic variables were as follows: race (3/71, 4.23%), work status (5/71, 7.04%), and education (3/71, 4.23%). No studies included the ethnicity, insurance status, income, or housing status of the enrolled patients. There was no difference in reporting sociodemographic variables by journal ( $P = .083$ ) or by year of publication ( $P = .340$ ). Sociodemographic variables were reported significantly less frequently than age and sex or gender ( $P < .001$ ). **Conclusions:** In this study, we found that age and sex or gender are always reported in RCTs of PRP use for knee OA. However, other sociodemographic variables, such as race, work status, and education, that may be important to understand are rarely reported. **Clinical Relevance:** Sociodemographic variables may affect outcomes in knee osteoarthritis. It is important to understand which of these variables are most studied and which variables are most overlooked. This will help us better understand the quality of the available information.

Platelet-rich plasma (PRP) is an autologous blood product created by centrifuging whole blood and removing the red blood cell and platelet-poor fractions.<sup>1</sup> The resulting product is rich in cytokines and growth factors and can be injected back into the body. PRP has been studied as a potential therapy across wide

range of pathologies. Specifically in orthopaedics, PRP has been the subject of many recent randomized control trials (RCTs) investigating its use as a therapy for knee osteoarthritis (OA).

Social determinants of health are the key components of health equity. Notably, in PRP and OA literature, variables such as race and ethnicity,<sup>2-4</sup> work status,<sup>5,6</sup> income level,<sup>7</sup> educational attainment,<sup>6,8,9</sup> and insurance status<sup>10,11</sup> have been demonstrated to have an important influence on health outcomes. It is well documented that sociodemographic variables affect baseline symptom profiles of patients with knee OA,<sup>3,8,12,13</sup> which is important because evidence suggests that outcomes of PRP use for knee OA are associated with baseline symptoms.<sup>14</sup> Therefore, information on the sociodemographics of a study population should be provided for RCTs on PRP use for

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knee OA to better contextualize findings, given how these variables affect both the baseline disease and the outcomes of this treatment. However, in RCTs across a variety of medical and surgical specialties, such variables are often underreported.<sup>15,16</sup> This is especially true in the orthopaedic surgery literature.<sup>17-21</sup>

The absence of sociodemographic variables in RCTs creates a notable problem. Limited demographic information makes it difficult to generalize study results across patient populations, which makes it harder for physicians to contextualize results and counsel patients accordingly. Furthermore, although the random allocation of RCTs minimizes confounding variables, without a proper understanding of the baseline characteristics of the population being studied, it is more difficult to ensure that all potential confounding variables are controlled for. RCTs continue to be the standard for medical research and the studies off which clinical practice guidelines are based; therefore, it is necessary that these studies incorporate the socioeconomic and demographic variables of the included patients.

The purpose of this scoping review was to investigate the characteristics and rate of sociodemographic variables reported in RCTs studying PRP injections in the treatment of knee OA. We hypothesized that sociodemographic variables would appear infrequently in RCTs investigating the use of PRP for knee OA.

## Methods

### Literature Review

This was designed in adherence with the extension of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for scoping reviews. PubMed, Scopus, and Web of Science databases were queried for the phrase "Platelet-Rich Plasma Knee Osteoarthritis." The initial search was performed by 1 author (J.K.). Included studies were Level I and Level II RCTs investigating PRP use in knee OA published in English between 2012 and 2023. Excluded studies were those of all other study design, studies not published in English, and those lacking a full text. After removal of duplicates, the title and abstract and then full texts were screened independently by 2 authors (J.K. and A.F.) for final inclusion. If disagreements arose, a third author (A.Y.) reviewed to help resolve them.

### Data Collection

Each included RCT was examined by 2 authors (J.K. and A.F.) for the following sociodemographic variables: age, sex or gender, race, ethnicity, insurance status, income, housing status, work status, and education. Data were recorded in a binary manner (e.g., "included"/"not included") and tabulated in a categorical manner for each variable and compiled in tables for this paper.

## Statistical Analysis

Journal and year of each publication were reported using descriptive statistics. The proportion of RCTs reporting sociodemographic variables according to journal and year of publication was calculated; the relative frequency of reporting of different variables were compared.  $\chi^2$  tests were used when comparing 2 categorical variables, and Fisher's exact tests were used when comparing more than 2 categorical variables with alpha defined as  $P < .05$ . All statistical analyses were performed in STATA (version 17.0; StataCorp, College Station, TX). No meta-analysis was performed.

## Results

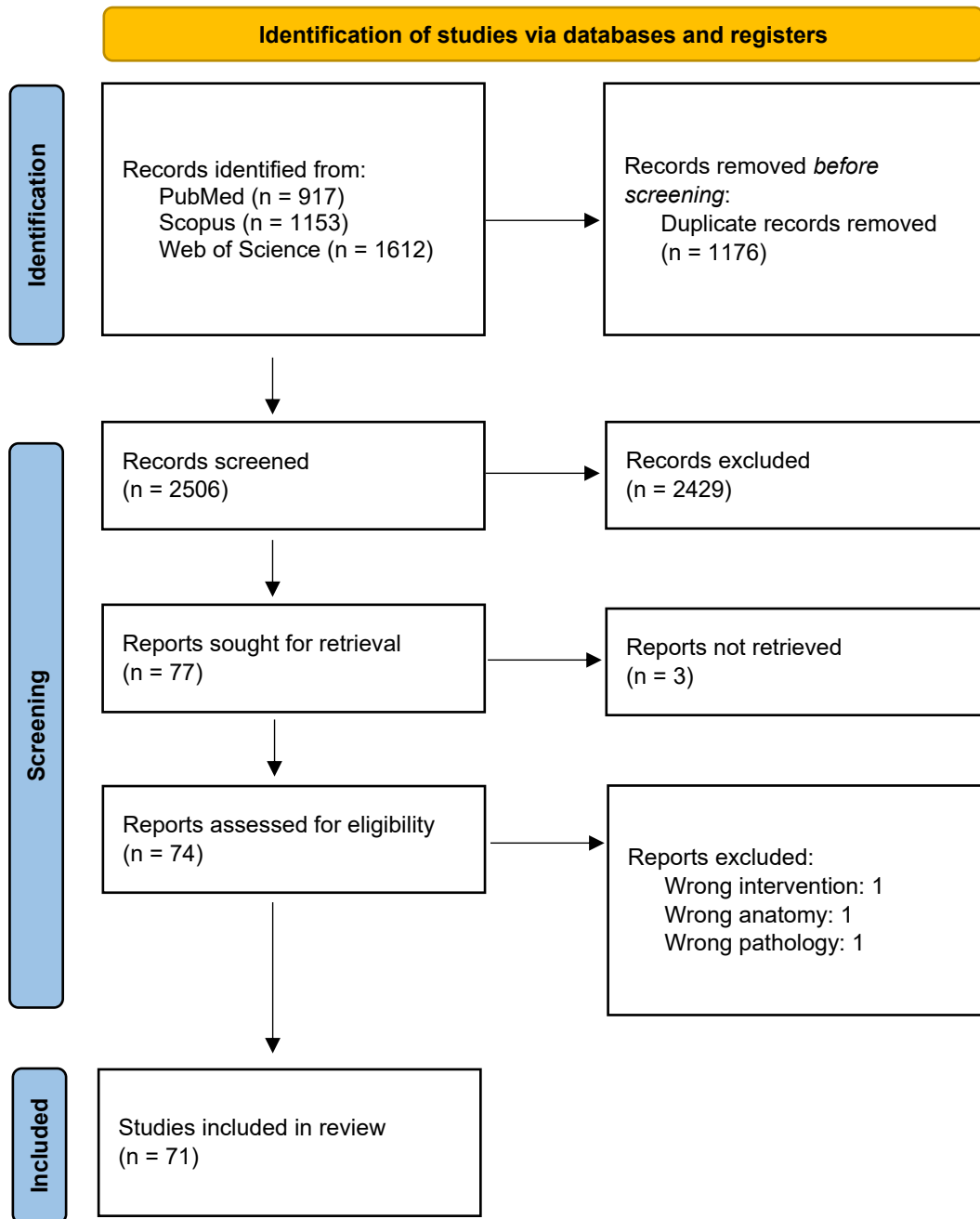
The literature search identified 71 RCTs published in 41 journals.<sup>22-92</sup> A PRISMA table demonstrating full search results and study screening can be found in [Figure 1](#). The *American Journal of Sports Medicine* was the source of the most included studies (10/71, 14.1%) followed by *Knee Surgery, Sports Traumatology, Arthroscopy* (6/71, 8.45%) and then by *BMC Musculoskeletal Disorders and Arthroscopy* (5/71, 7.04%). Most publications came from 2022 (18/71, 25.4%). Complete information on included journals and year of publication can be found in [Tables 1](#) and [2](#). All included studies can be found in [Supplementary Table 1](#).

From 2012 through 2023, the 71 included RCTs' reporting rates for sociodemographic variables were age 71/71 (100%), sex or gender in 71/71 (100%), race (3/71, 4.23%),<sup>34,59,65</sup> work status (5/71, 7.04%),<sup>37,54,65</sup> and education (3/71, 4.23%)<sup>65,75</sup> in any section ([Tables 3](#) and [4](#)). No studies included ethnicity, insurance status, income, or housing status of the enrolled patients. Reporting rates for sociodemographic variables in the results section of the RCTs were age (59/71, 83.1%), sex or gender (58/71, 81.7%), race (3/71, 4.23%), work status (3/71, 4.23%), and education (3/71, 4.23%) ([Table 2](#)).

Using  $\chi^2$  it was found that there was no difference in reporting sociodemographic variables by journal ( $P = .083$ ) or by year of publication ( $P = .340$ ) ([Table 5](#)). Furthermore, using Fisher's exact test, we found race, work status, and education were reported significantly less frequently than age and sex or gender ( $P < .001$ ).

## Discussion

Our study reveals a deficit in sociodemographic variable reporting. Of the 71 included RCTs, all reported the age and sex or gender of their participants. However, other sociodemographic variables were documented much less frequently. Only 4.23% of the 71 RCTs included race, 4.23% included education, and 7.04% included work status. Further sociodemographic data such as income, insurance status, and housing status were omitted from all included RCTs. The results of our study demonstrate why it is difficult



**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Flow Chart for Study Selection

to generalize study results of RCTs on PRP use in knee OA. Without all relevant sociodemographic information on the population in question, it is impossible to contextualize results of these studies and to facilitate the ability of physicians to apply findings to their practice.

When designing studies, we must ensure baseline characteristics are similar between treatment groups because these characteristics have been shown to affect outcomes, and significant differences could jeopardize study validity.<sup>93</sup> Age and sex represent 2 such variables;

their reporting has become standard in scientific studies because we know they have a great influence on how patients respond to disease and therapy. For example, the impact of age on knee OA progression is well accepted; radiographic evidence of knee OA increases with age, and for younger patients with OA who have decades to live, there is more time for greater disability to develop.<sup>94-96</sup> Several large cohort studies have also noted a greater prevalence of knee OA in female patients<sup>94,97</sup> and have shown women to have a predilection for more severe knee OA.<sup>12,98</sup> It is standard to

**Table 1.** Randomized Controlled Trials by Journal

Journal	n	%
Acta Orthopaedica Belgica	2	2.82
American Journal of Sports Medicine	10	14.1
Archives of Orthopedic and Trauma Surgery	3	4.23
Archives of Rheumatology	1	1.41
Arthroscopy	5	7.04
BMC Musculoskeletal Disorders	5	7.04
Biomedicines	1	1.41
The Bone and Joint Journal	1	1.41
Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders	1	1.41
Clinical Rehabilitation	1	1.41
Clinical Rheumatology	2	2.82
Cureus	2	2.82
Frontiers in Bioengineering and Biotechnology	1	1.41
Frontiers in Medicine	1	1.41
Injury	2	2.82
International Journal of Molecular Sciences	2	2.82
Investigative Radiology	1	1.41
Iranian Journal of Allergy, Asthma and Immunology	1	1.41
The Journal of Applied Biomedicine	1	1.41
Journal of Back and Musculoskeletal Rehabilitation	1	1.41
Journal of Clinical Medicine	1	1.41
Journal of Orthopaedic Research	1	1.41
Journal of Orthopaedic Surgery and Research	1	1.41
Journal of Orthopaedics and Traumatology	1	1.41
Journal of Pain Research	2	2.82
Journal of Stem Cells & Regenerative Medicine	1	1.41
Journal of Translational Medicine	1	1.41
Journal of the American Medical Association	1	1.41
Journal of Cartilage & Joint Preservation	1	1.41
Knee Surgery, Sports Traumatology, Arthroscopy	6	8.45
Medicina	1	1.41
Orthopedic Journal of Sports Medicine	2	2.82
Orthopedic Reviews	1	1.41
Orthopaedic Surgery	1	1.41
Orthopade	1	1.41
PM&R	1	1.41
Pain Physician	1	1.41
Scientific Reports	1	1.41
Stem Cells and Development	1	1.41
World Journal of Orthopedics	1	1.41

include these variables in RCTs, which facilitates the ability of the reader to apply the findings of these studies to their individual patients.<sup>12,15</sup>

In contrast, sociodemographic variables other than age and sex are poorly reported in the literature. Examining 158 orthopedic RCTs Somerson et al. found only 20.3% included race or ethnicity.<sup>17</sup> A 2023 study by Kirchner et al. found race and ethnicity to be reported in 37% and 27.8%, respectively, of spine surgery RCTs.<sup>18</sup> Outside of orthopaedics, one study demonstrated that 48.5% of 231 RCTs in 5 high-impact medical journals reported race and less than 15% reported other sociodemographic variables.<sup>15</sup> This prior research is consistent with our findings that sociodemographic variables appear infrequently in RCTs on PRP use in knee OA.

**Table 2.** Publication Year of Randomized Controlled Trials

Year of Publication	n	%
2023 <sup>38,58,60,81,90</sup>	5	7.04
2022 <sup>22,24,34-36,40,43,54,65,70,79,84-86,88,89,91,92</sup>	18	25.4
2021 <sup>23,25,26,37,42,45,48,62,66,71,78,82,87</sup>	13	18.3
2020 <sup>27-29,49,69,72,73,76</sup>	8	11.3
2019 <sup>30,44,55,57,61,80</sup>	6	8.45
2018 <sup>31,39,63</sup>	3	4.23
2017 <sup>41,47,56,83</sup>	4	5.63
2016 <sup>33,59,64,68,77</sup>	5	7.04
2015 <sup>46,50,52,53,74</sup>	5	7.04
2014 <sup>75</sup>	1	1.41
2013 <sup>67</sup>	1	1.41
2012 <sup>32,51</sup>	2	2.82

This absence of sociodemographic variables presents many difficulties because these variables have been shown to have an effect on a variety of study outcome measures. For example, with regard to race, a 2021 study by Callahan et al. found that Black patients with knee osteoarthritis were more likely to report severe pain and worse function compared with White patients.<sup>3</sup> A meta-analysis by Vaughn et al. reported that Black patients reported higher pain severity with a standard mean difference of 0.57 (95% confidence interval [CI], 0.54-0.61) in studies using the Western Ontario and McMaster Universities Osteoarthritis Index.<sup>13</sup> Vaughn et al. also demonstrated the Black patients had higher self-reported disability (0.38, 95% CI, 0.22-0.54) and performed worse on functional tests (-0.5, 95% CI, -0.72 to -0.44). These results are echoed by a number of recent studies.<sup>99,100</sup> Despite these findings, only 1 of 60 RCTs included in our study reported the race of its participants. Considering the evidence that exists in the literature for how race influences the baseline disease of OA, including symptom profiles, providing readers of RCTs on PRP use as a treatment modality for knee OA with the sociodemographic variables of their study's population is important for contextualizing how to apply their findings to individual patients.

Other sociodemographic variables including work status, educational attainment, income, housing status, and insurance status have also been shown to have a substantial effect on knee OA outcomes. Studies examining the relationship between work status on outcomes in knee OA found that patients with knee OA are significantly more likely to experience work loss and that unemployed patients are significantly more likely to have radiographic evidence of knee OA.<sup>5,6</sup> Patients with lower levels of education are more likely to demonstrate radiographic evidence of knee OA,<sup>6</sup> to develop knee OA, and to experience more severe symptoms.<sup>8,9,101</sup> With respect to income, Jørgensen et al. found lower income level to be significantly associated with an increased risk of knee

**Table 3.** Publication Details of the 60 Included Studies and the Sociodemographic Variables They Reported in Any Section

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Bone Marrow Aspirate Concentrate Is Equivalent to Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis at 2 Years: A Prospective Randomized Trial	Anz et al. <sup>22</sup>	Am J Sports Med	2022	I	Age, Sex or gender
Hyaluronic Acid Versus Platelet-Rich Plasma: A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis	Cole et al. <sup>41</sup>	Am J Sports Med	2017	I	Age, Sex or gender
Leukocyte-Rich versus Leukocyte-Poor Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis: A Double-Blind Randomized Trial	Di Martino et al. <sup>43</sup>	Am J Sports Med	2022	I	Age, Sex or gender
Platelet-Rich Plasma Versus Hyaluronic Acid Injections for the Treatment of Knee Osteoarthritis: Results at 5 Years of a Double-Blind, Randomized Controlled Trial	Di Martino et al. <sup>44</sup>	Am J Sports Med	2019	I	Age, Sex or gender
Platelet-Rich Plasma Intra-articular Knee Injections Show No Superiority Versus Viscosupplementation: A Randomized Controlled Trial	Filardo et al. <sup>50</sup>	Am J Sports Med	2015	I	Age, Sex or gender
Clinical Efficacy of Platelet-Rich Plasma Injection and Its Association With Growth Factors in the Treatment of Mild to Moderate Knee Osteoarthritis: A Randomized Double-Blind Controlled Clinical Trial As Compared With Hyaluronic Acid	Park et al. <sup>66</sup>	Am J Sports Med	2021	I	Age, Sex or gender
Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial	Patel et al. <sup>67</sup>	Am J Sports Med	2013	I	Age, Sex or gender
Microfragmented Adipose Tissue Versus Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis: A Prospective Randomized Controlled Trial at 2-Year Follow-up	Zaffagnini et al. <sup>89</sup>	Am J Sports Med	2022	I	Age, Sex or gender
Does intraoperative application of leukocyte-poor platelet-rich plasma during arthroscopy for knee degeneration affect postoperative pain, function and quality of life? A 12-month randomized controlled double-blind trial	Duif et al. <sup>46</sup>	Arch Orthop Trauma Surg	2015	II	Age, Sex or gender

(continued)

**Table 3.** Continued

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Leukocyte-poor platelet-rich plasma is more effective than the conventional therapy with acetaminophen for the treatment of early knee osteoarthritis	Simental-Mendía et al. <sup>77</sup>	Arch Orthop Trauma Surg	2016	II	Age, Sex or gender
Multiple platelet-rich plasma injections are superior to single PRP injections or saline in osteoarthritis of the knee: the 2-year results of a randomized, double-blind, placebo-controlled clinical trial	Yurtbay et al. <sup>88</sup>	Arch Orthop Trauma Surg	2022	I	Age, Sex or gender
Single versus multi-dose intra-articular injection of platelet rich plasma in early stages of osteoarthritis of the knee: A single-blind, randomized, superiority trial	Subramanyam et al. <sup>78</sup>	Arch Rheumatol	2021	I	Age, Sex or gender
Intra-articular Injection of Platelet-Rich Plasma Is Superior to Hyaluronic Acid or Saline Solution in the Treatment of Mild to Moderate Knee Osteoarthritis: A Randomized, Double-Blind, Triple-Parallel, Placebo-Controlled Clinical Trial	Lin et al. <sup>61</sup>	Arthroscopy	2019	I	Age, Sex or gender
Intra-Articular Injection of Autologous Microfat and Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Double-Blind Randomized Comparative Study	Louis et al. <sup>62</sup>	Arthroscopy	2021	II	Age, Sex or gender
Intra-Articular Platelet-Rich Plasma Combined With Hyaluronic Acid Injection for Knee Osteoarthritis Is Superior to Platelet-Rich Plasma or Hyaluronic Acid Alone in Inhibiting Inflammation and Improving Pain and Function	Xu et al. <sup>87</sup>	Arthroscopy	2021	II	Age, Sex or gender
Growth Factors Levels Determine Efficacy of Platelets Rich Plasma Injection in Knee Osteoarthritis: A Randomized Double Blind Noninferiority Trial Compared With Viscosupplementation	Louis et al. <sup>63</sup>	Arthroscopy	2018	II	Age, Sex or gender
Intra-Articular Injection of Platelet-Rich Plasma Is More Effective than Hyaluronic Acid or Steroid Injection in the Treatment of Mild to Moderate Knee Osteoarthritis: A Prospective, Randomized, Triple-Parallel Clinical Trial	Szwedowski et al. <sup>79</sup>	Biomedicines	2022	II	Age, Sex or gender

(continued)

Table 3. Continued

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Efficacy of platelet-rich plasma and plasma for symptomatic treatment of knee osteoarthritis: a double-blinded placebo-controlled randomized clinical trial	Dório et al. <sup>45</sup>	BMC Musculoskelet Disord	2021	II	Age, Sex or gender
Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial	Filardo et al. <sup>51</sup>	BMC Musculoskelet Disord	2012	I	Age, Sex or gender
Comparing efficacy of a single intraarticular injection of platelet-rich plasma (PRP) combined with different hyaluronans for knee osteoarthritis: a randomized-controlled clinical trial	Huang et al. <sup>54</sup>	BMC Musculoskelet Disord	2022	I	Age, Sex or gender
Intra-articular injection of photo-activated platelet-rich plasma in patients with knee osteoarthritis: a double-blind, randomized controlled pilot study	Paterson et al. <sup>68</sup>	BMC Musculoskelet Disord	2016	II	Age, Sex or gender
The comparison effects of intra-articular injection of Platelet Rich Plasma (PRP), Plasma Rich in Growth Factor (PRGF), Hyaluronic Acid (HA), and ozone in knee osteoarthritis; a one year randomized clinical trial	Raeissadat et al. <sup>71</sup>	BMC Musculoskelet Disord	2021	I	Age, Sex or gender
The effectiveness of leucocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: the PEAK randomized controlled trial	Lewis et al. <sup>92</sup>	Bone Joint J	2022	I	Age, Sex or gender
Knee Osteoarthritis Injection Choices: Platelet- Rich Plasma (PRP) Versus Hyaluronic Acid (A one-year randomized clinical trial)	Raeissadat et al. <sup>74</sup>	Clin Med Insights Arthritis Musculoskelet Disord	2015	I	Age, Sex or gender
Intra-articular injection with platelet-rich plasma compared to triamcinolone hexacetonide or saline solution in knee osteoarthritis: A double blinded randomized controlled trial with one year follow-up	Nunes-Tamshiro et al. <sup>65</sup>	Clin Rehabil	2022	I	Age, Sex or gender, Race, Work status, Education
Outcome of Intra-articular Injection of Total Stromal Cells and Platelet-Rich Plasma in Primary Knee Osteoarthritis: A Randomized Clinical Trial	Khasru et al. <sup>58</sup>	Cureus	2023	II	Age, Sex or gender
Double-Blind Randomized Controlled Trial Comparing Platelet-Rich Plasma With Intra-Articular Corticosteroid Injections in Patients With Bilateral Knee Osteoarthritis	Pretorius et al. <sup>70</sup>	Cureus	2022	II	Age, Sex or gender

(continued)

Table 3. Continued

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Assessment of the effectiveness and satisfaction of platelet-rich plasma compared with hyaluronic acid in knee osteoarthritis at minimum 7-year follow-up: A post hoc analysis of a randomized controlled trial	Wang et al. <sup>85</sup>	Front Bioeng Biotechnol	2022	II	Age, Sex or gender
Impact of autologous platelet-rich plasma therapy vs. hyaluronic acid on synovial fluid biomarkers in knee osteoarthritis: a randomized controlled clinical trial	Li et al. <sup>60</sup>	Front Med (Lausanne)	2023	I	Age, Sex or gender
Comparison of clinical outcome, cartilage turnover, and inflammatory activity following either intra-articular or a combination of intra-articular with intra-osseous platelet-rich plasma injections in osteoarthritis knee: A randomized, clinical trial	Barman et al. <sup>35</sup>	Injury	2022	I	Age, Sex or gender
Single intra-articular injection with or without intra-osseous injections of platelet-rich plasma in the treatment of osteoarthritis knee: A single-blind, randomized clinical trial	Barman et al. <sup>36</sup>	Injury	2022	II	Age, Sex or gender
Intra-Articular Injections of Platelet-Rich Plasma versus Hyaluronic Acid in the Treatment of Osteoarthritic Knee Pain: A Randomized Clinical Trial in the Context of the Spanish National Health Care System	Montañez-Heredia et al. <sup>64</sup>	Int J Mol Sci	2016	II	Age, Sex or gender
Short-Term Outcomes of Percutaneous Trephination with a Platelet Rich Plasma Intrameniscal Injection for the Repair of Degenerative Meniscal Lesions. A Prospective, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study	Kaminski et al. <sup>57</sup>	Int J Mol Sci	2019	II	Age, Sex or gender
A Randomized Trial of Intra-articular Injection Therapy for Knee Osteoarthritis	Tschopp et al. <sup>81</sup>	Invest Radiol	2023	I	Age, Sex or gender
Effect of Dextrose Prolotherapy, Platelet Rich Plasma and Autologous Conditioned Serum on Knee Osteoarthritis: A Randomized Clinical Trial	Pishgahi et al. <sup>69</sup>	Iran J Allergy Asthma Immunol	2020	II	Age, Sex or gender
Clinical comparison of platelet-rich plasma injection and daily celecoxib administration in the treatment of early knee osteoarthritis: A randomized clinical trial	Reyes-Sosa et al. <sup>76</sup>	J Appl Biomed	2020	II	Age, Sex or gender

(continued)



Table 3. Continued

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Efficacy of a Novel Intra-Articular Administration of Platelet-Rich Plasma One-Week Prior to Hyaluronic Acid versus Platelet-Rich Plasma Alone in Knee Osteoarthritis: A Prospective, Randomized, Double-Blind, Controlled Trial	Wu et al. <sup>86</sup>	J Clin Med	2022	II	Age, Sex or gender
A prospective randomized double-blind clinical trial to assess the effects of leukocyte-reduced platelet-rich plasma on pro-inflammatory, degradative, and anabolic biomarkers after closed pilon fractures	Zitsch et al. <sup>91</sup>	J Orthop Res	2022	II	Age, Sex or gender
Intra-articular platelet-rich plasma vs corticosteroids in the treatment of moderate knee osteoarthritis: a single-center prospective randomized controlled study with a 1-year follow up	Elksniņš-Finogejevs et al. <sup>49</sup>	J Orthop Surg Res	2020	II	Age, Sex or gender
Clinical and radiographic comparison of a single LP-PRP injection, a single hyaluronic acid injection and daily NSAID administration with a 52-week follow-up: a randomized controlled trial	Buendía-López et al. <sup>39</sup>	J Orthop Traumatol	2018	II	Age, Sex or gender
Platelet-rich plasma-derived growth factor vs hyaluronic acid injection in the individuals with knee osteoarthritis: A one year randomized clinical trial	Raeissadat et al. <sup>72</sup>	J Pain Res	2020	II	Age, Sex or gender
MRI Changes After Platelet Rich Plasma Injection in Knee Osteoarthritis (Randomized Clinical Trial)	Raeissadat et al. <sup>73</sup>	J Pain Res	2020	II	Age, Sex or gender
Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee	Lana et al. <sup>59</sup>	J Stem Cells Regen Med	2016	I	Age, Sex or Gender, Race
Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis: The RESTORE Randomized Clinical Trial	Bennell et al. <sup>37</sup>	JAMA	2021	I	Age, Sex or gender, Work status
Platelet-rich plasma is similar to platelet-rich plasma plus hyaluronic acid for the treatment of knee osteoarthritis at 2 years: a randomized controlled trial	Branch et al. <sup>38</sup>	JCJP	2023	I	Age, Sex or gender

(continued)

**Table 3.** Continued

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options	Duymus et al. <sup>47</sup>	Knee Surg Sports Traumatol Arthrosc	2017	I	Age, Sex or gender
Intra-articular injections of platelet-rich plasma decrease pain and improve functional outcomes than sham saline in patients with knee osteoarthritis	Chu et al. <sup>40</sup>	Knee Surg Sports Traumatol Arthrosc	2022	I	Age, Sex or gender
Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial	Görmeli et al. <sup>53</sup>	Knee Surg Sports Traumatol Arthrosc	2015	I	Age, Sex or gender
The effects of repeated intra-articular PRP injections on clinical outcomes of early osteoarthritis of the knee	Gobbi et al. <sup>52</sup>	Knee Surg Sports Traumatol Arthrosc	2015	II	Age, Sex or gender
Two cycles of plasma rich in growth factors (PRGF-Endoret) intra-articular injections improve stiffness and activities of daily living but not pain compared to one cycle on patients with symptomatic knee osteoarthritis	Vaquerizo et al. <sup>83</sup>	Knee Surg Sports Traumatol Arthrosc	2017	II	Age, Sex or gender
Comparing the Efficacy of Intra-Articular Single Platelet-Rich Plasma (PRP) versus Oovel Crosslinked Hyaluronic Acid for Early-Stage Knee Osteoarthritis: A Prospective, Double-Blind, Randomized Controlled Trial	Wang et al. <sup>84</sup>	Medicina (Kaunas)	2022	I	Age, Sex or gender
Platelet-Rich Plasma Versus Microfragmented Adipose Tissue for Knee Osteoarthritis: A Randomized Controlled Trial	Baria et al. <sup>34</sup>	Orthop J Sports Med	2022	II	Age, Sex or Gender, Race
Platelet-Rich Plasma Injections for Advanced Knee Osteoarthritis: A Prospective, Randomized, Double-Blinded Clinical Trial	Jubert et al. <sup>56</sup>	Orthop J Sports Med	2017	II	Age, Sex or gender
Does intra articular platelet rich plasma injection improve function, pain and quality of life in patients with osteoarthritis of the knee? A randomized clinical trial	Rayegani et al. <sup>75</sup>	Orthop Rev (Pavia)	2014	II	Age, Sex or gender, Education
Clinical Efficacy of Intra-Articular Injection with P-PRP Versus that of L-PRP in Treating Knee Cartilage Lesion: A Randomized Controlled Trial	Zhou et al. <sup>90</sup>	Orthop Surg	2023	II	Age, Sex or gender
Intra-articular injections of platelet-rich plasma, hyaluronic acid or corticosteroids for knee osteoarthritis : A prospective randomized controlled study	Huang et al. <sup>55</sup>	Orthopade	2019	I	Age, Sex or gender, Work status

(continued)

**Table 3.** Continued

Article	Author	Journal	Year of Publication	Level of Evidence	Sociodemographic Variables Reported
Efficacy of Genicular Nerve Radiofrequency Ablation Versus Intra-Articular Platelet Rich Plasma in Chronic Knee Osteoarthritis: A Single-Blind Randomized Clinical Trial	Elawamy et al. <sup>48</sup>	Pain Physician	2021	II	Age, Sex or gender
Randomized, Placebo-Controlled Analysis of the Knee Synovial Environment Following Platelet-Rich Plasma Treatment for Knee Osteoarthritis	Tucker et al. <sup>82</sup>	PM R	2021	II	Age, Sex or gender
A Prospective Study Comparing Leukocyte-Poor Platelet-Rich Plasma Combined with Hyaluronic Acid and Autologous Microfragmented Adipose Tissue in Patients with Early Knee Osteoarthritis	Dallo et al. <sup>42</sup>	Stem Cells Dev	2021	II	Age, Sex or gender
Single- and double-dose of platelet-rich plasma versus hyaluronic acid for treatment of knee osteoarthritis: A randomized controlled trial	Tavassoli et al. <sup>80</sup>	World J Orthop	2019	II	Age, Sex or gender

OA in a cohort of 4.6 million Danish patients.<sup>101</sup> Finally, Medicaid patients with knee OA are known to have significantly worse symptoms, pain, and knee function than privately insured patients.<sup>102</sup> Furthermore, given that the populations in which PRP is used is likely to be different from the population that is diagnosed with knee OA with regard to insurance status, employment status, and income, reporting of these variables is important in allowing physicians to contextualize study outcomes and decide how to counsel individual patients.

Sociodemographic variables have been shown to affect not only baseline scores for patients with knee OA but may also affect outcome scores specific to OA treated with PRP. A meta-analysis conducted by Zhao et al. found that efficacy of PRP is related to sample gender composition; in a subgroup analysis of large trials and trials with less than 50% women, the treatment’s therapeutic effects were insignificant, whereas the analysis of all the included studies demonstrated statistically significant improvement and pain relief.<sup>103</sup> Furthermore, Cao et al. demonstrated in a meta-analysis that PRP is more effective in treating OA in those with higher symptom baseline scores, which are affected by sociodemographic variables, as discussed previously, but also in those with older age and higher body mass index.<sup>14</sup> Women have also been shown to respond well to PRP for knee OA despite the association of female sex with worse symptom profiles in knee OA.<sup>104</sup> Interestingly, the highest incidences of PRP

injection for OA of the knee and hip was seen in patients aged 44 and younger.<sup>105</sup> These studies are an example of how increased reporting of sociodemographic variables in RCTs studying PRP injections for knee OA may help to ensure this treatment modality is being offered to the patient populations for which it may be the most beneficial.

Importantly, it has also been shown that reporting bias is highly prevalent in systematic reviews and meta-analyses of PRP use for OA.<sup>106</sup> Knowing this, along with our findings demonstrating low reporting rates of sociodemographic variables besides age and sex or gender, the field should push for more transparency

**Table 4.** Sociodemographic Variable Inclusion Rates in Platelet-Rich Plasma for Knee Osteoarthritis Randomized Controlled Trials for Results Section and Any Section

Factor	Included in Results, n (%)	Included in Any Section, n (%)
Total	59 (83.1)	71 (100)
Age	59 (83.1)	71 (100)
Sex or gender	58 (81.7)	71 (100)
Race	3 (4.23)	3 (4.23)
Ethnicity	0 (0.00)	0 (0.00)
Work status	3 (4.23)	5 (7.04)
Insurance status	0 (0.00)	0 (0.00)
Income	0 (0.00)	0 (0.00)
Housing status	0 (0.00)	0 (0.00)
Education	3 (4.23)	3 (4.23)

**Table 5.** Any Sociodemographic Variable Inclusion in Any Section of the Manuscript by Journal and Year of Publication and Comparison With  $\chi^2$ 

Journal	n/total	%	P Value
			.083
American Journal of Sports Medicine	0/10	0.00	
Acta Orthopaedia Belgica	0/2	0.00	
Archives of Orthopedic and Trauma Surgery	0/3	0.00	
Archives of Rheumatology	0/1	0.00	
Arthroscopy	0/5	0.00	
BMC Musculoskeletal Disorders	1/5	20.0	
Biomedicines	0/1	0.00	
The Bone and Joint Journal	0/1	0.00	
Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders	0/1	0.00	
Clinical Rheumatology	1/2	0.50	
Clinical Rehabilitation	1/1	100	
Cureus	0/2	0.00	
Frontiers in Bioengineering and Biotechnology	0/1	0.00	
Frontiers in Medicine	0/1	0.00	
Injury	0/1	0.00	
International Journal of Molecular Sciences	0/1	0.00	
Investigative Radiology	0/1	0.00	
Iranian Journal of Allergy, Asthma and Immunology	0/1	0.00	
The Journal of Applied Biomedicine	0/1	0.00	
Journal of Back and Musculoskeletal Rehabilitation	0/1	0.00	
Journal of Clinical Medicine	0/1	0.00	
Journal of Orthopaedic Research	0/1	0.00	
Journal of Orthopaedic Surgery and Research	0/1	0.00	
Journal of Orthopaedics and Traumatology	0/1	0.00	
Journal of Pain Research	0/2	0.00	
Journal of Stem Cells & Regenerative Medicine	1/1	100	
Journal of Translational Medicine	0/1	0.00	
Journal of the American Medical Association	1/1	100	
Journal of Cartilage & Joint Preservation	0/1	0.00	
Knee Surgery, Sports Traumatology, Arthroscopy	0/6	0.00	
Medicina	0/1	0.00	
Orthopedic Journal of Sports Medicine	1/2	50.0	
Orthopedic Reviews	1/1	100	
Orthopaedic Surgery	0/1	0.00	
Orthopade	0/1	0.00	
PM R	0/1	0.00	
Pain Physician	0/1	0.00	
Scientific Reports	1/1	100	
Stem Cells and Development	0/1	0.00	
World Journal of Orthopedics	0/1	0.00	

(continued)

**Table 5.** Continued

Journal	n/total	%	P Value
Year of Publication			.340
2023	0/5	0.00	
2022	3/18	16.7	
2021	2/13	15.4	
2020	1/8	12.5	
2019	0/6	0.00	
2018	0/3	0.00	
2017	0/4	0.00	
2016	1/5	20.0	
2015	0/5	0.00	
2014	1/1	100	
2013	0/1	0.00	
2012	0/2	0.00	

and a greater focus on inclusion of study details such as the sociodemographic variables of the study population.

It is also of note that when sociodemographic variables were reported, they were not always reported in the results sections of included publications. This suggests that even when deemed important enough to include, they were not the subject of study analyses.

All included sociodemographic variables were infrequently or never reported in the included RCTs. Without these data, we cannot ensure that these study results are generalizable. To allow study results to be applied appropriately and to provide physicians with the information they need to best counsel patients, we suggest that RCTs report the sociodemographic data of included participants. Future research should examine the associations between sociodemographic variables and the outcomes of treating knee OA with PRP.

### Limitations

This study has several limitations. One is the sample size of 71 RCTs; including more RCTs would have given us greater power. Second, in examining RCTs only from the past 10 years, we may have overlooked information from the years before 2012. Third, RCTs were not evaluated for overlapping populations. Fourth, the included studies were not evaluated for a declaration that their findings may not be generalizable to other populations.

### Conclusions

In this study, we found that age and sex or gender are always reported in RCTs of PRP use for knee OA. However, other sociodemographic variables, such as race, work status, and education, that may be important to understand are rarely reported.

### Disclosures

The authors declare the following financial interests/ personal relationships which may be considered as

potential competing interests: F.A.P. reports consulting or advisory relationships with Exactech, Stryker Orthopaedics, and OSSIO. J.N.L. reports speaking and lecture fees from Stryker Orthopaedics and travel reimbursement with Innocoll Biotherapeutics. All other authors (J.L.K., A.F., C.L.F., E.H.L., A.Y., D.P., C.K.M.) declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- Fice MP, Miller JC, Christian R, et al. The role of platelet-rich plasma in cartilage pathology: An updated systematic review of the basic science evidence. *Arthroscopy* 2019;35:961-976.e963.
- Johnson AJ, Vasilopoulos T, Booker SQ, et al. Knee pain trajectories over 18 months in non-Hispanic Black and non-Hispanic White adults with or at risk for knee osteoarthritis. *BMC Musculoskelet Disord* 2021;22:415.
- Callahan LF, Cleveland RJ, Allen KD, Golightly Y. Racial/ethnic, socioeconomic, and geographic disparities in the epidemiology of knee and hip osteoarthritis. *Rheum Dis Clin North Am* 2021;47:1-20.
- Reyes AM, Katz JN. Racial/ethnic and socioeconomic disparities in osteoarthritis management. *Rheum Dis Clin North Am* 2021;47:21-40.
- Sharif B, Garner R, Sanmartin C, Flanagan WM, Hennessy D, Marshall DA. Risk of work loss due to illness or disability in patients with osteoarthritis: A population-based cohort study. *Rheumatology (Oxford)* 2016;55:861-868.
- Lee J, Han K, Park Y, Park S-H. Effects of education, income, and occupation on prevalence and symptoms of knee osteoarthritis. *Sci Rep* 2021;11:13983.
- Mickle AM, Domenico LH, Tanner JJ, et al. Elucidating factors contributing to disparities in pain-related experiences among adults with or at risk for knee osteoarthritis. *Front Pain Res (Lausanne)* 2023;4:1058476.
- Callahan LF, Cleveland RJ, Shreffler J, et al. Associations of educational attainment, occupation and community poverty with knee osteoarthritis in the Johnston County (North Carolina) osteoarthritis project. *Arthritis Res Ther* 2011;13:R169.
- Hannan M, Anderson J, Pincus T, Felson D. Educational attainment and osteoarthritis: Differential associations with radiographic changes and symptom reporting. *J Clin Epidemiol* 1992;45:139-147.
- Labrum J, Paziuk Rign T, et al. Does Medicaid insurance confer adequate access to adult orthopaedic care in the era of the patient protection and Affordable Care Act? *Clin Orthop Relat Res* 2021;475:1527-1536.
- Werner B, Cancienne J, Browning R, Verma N, Cole B. An analysis of current treatment trends in platelet-rich plasma therapy in the Medicare database. *Orthop J Sports Med* 2020;8:2325967119900811.
- Tschon M, Contartese D, Pagani S, Borsari V, Fini M. Gender and sex are key determinants in osteoarthritis not only confounding variables. A systematic review of clinical data. *J Clin Med* 2021;10:3178.
- Vaughn I, Terry E, Bartley E, Schaefer N, Fillingim R. Racial-ethnic differences in osteoarthritis pain and disability: A meta-analysis. *J Pain* 2019;20:629-644.
- Cao Y, Luo J, Han S, Li Z, Fan T, et al. A model-based quantitative analysis of efficacy and associated factors of platelet rich plasma treatment for osteoarthritis. *Int J Surg* 2023;109:1742-1752.
- Orkin AM, Nicoll G, Persaud N, Pinto AD. Reporting of sociodemographic variables in randomized clinical trials, 2014-2020. *JAMA Netw Open* 2021;4:e2110700.
- Stadeli KM, Hantouli MN, Brewer EG, et al. Beyond demographics: Missing sociodemographics in surgical research. *Am J Surg* 2020;219:926-931.
- Somerson JS, Bhandari M, Vaughan CT, Smith CS, Zelle BA. Lack of diversity in orthopaedic trials conducted in the United States. *J Bone Joint Surg Am* 2014;96:e56.
- Kirchner GJ, Kim AH, Smith NP, et al. Few randomized controlled trials in spine surgery in the United States include sociodemographic patient data: A systematic review. *J Am Acad Orthop Surg* 2023;31:421-427.
- Paul RW, Lee D, Brutico J, Tjoumakaris FP, Ciccotti MG, Freedman KB. Reporting and analyzing race and ethnicity in orthopaedic clinical trials: A systematic review. *J Am Acad Orthop Surg Glob Res Rev* 2021;5.
- Kotlier J, Fathi A, Kumaran P, et al. Demographic and socioeconomic patient data are rarely included in randomized controlled trials for femoral acetabular impingement and hip arthroscopy: A systematic review. *Arthrosc Sports Med Rehabil* 2024;6:100901.
- Kotlier J, Fathi A, Kumaran P, et al. Randomized controlled trials in the shoulder arthroplasty literature rarely include key demographic and socioeconomic patient data. *J Shoulder Elbow Surg* 2024;33:e296-e301.
- Anz AW, Plummer HA, Cohen H, Everts PA, Andrews JA, Hackel JG. Bone marrow aspirate concentrate is equivalent to platelet-rich plasma for the treatment of knee osteoarthritis at 2 years: A prospective randomized trial. *Am J Sports Med* 2022;50:618-629.
- Sdeek M, Sabry D, El-Sdeek H, Darweash A. Intra-articular injection of platelet rich plasma versus hyaluronic acid for moderate knee osteoarthritis. A prospective, double-blind randomized controlled trial on 189 patients with follow-up for three years. *Acta Orthop Belg* 2021;87:729-734.
- Zhang Q, Xu W, Wu K, Fu W, Yang H, Guo J. Intra-articular pure platelet-rich plasma combined with open-wedge high tibial osteotomy improves clinical outcomes and minimal joint space width compared with high tibial osteotomy alone in knee osteoarthritis: A prospective study. *Arthroscopy* 2022;38:476-485.
- Küçükakkaş O, Aydın T, Yurdakul O. Evaluation of the effect of intra-articular platelet-rich plasma and hyaluronic acid injections on femoral cartilage thickness in chronic knee osteoarthritis. *Acta Orthop Belg* 2021;88:811-819. Xu Sun.
- Sun S, Lin G, Hsu C, Lin H, Liou I, Wu S. Comparing efficacy of intraarticular single crosslinked Hyaluronan (HYAJOINT Plus) and platelet-rich plasma (PRP) versus PRP alone for treating knee osteoarthritis. *Sci Rep* 2021;11:140.
- Kesiktas F, Dernek B, Sen E, Albayrak H, Aydın T, Yildiz M. Comparison of the short-term results of single-

- dose intra-articular peptide with hyaluronic acid and platelet-rich plasma injections in knee osteoarthritis: A randomized study. *Clin Rheumatol* 2020;39:3057-3064.
28. Lamo-Espinosa J, Blanco J, Sánchez M, et al. Phase II multicenter randomized controlled clinical trial on the efficacy of intra-articular injection of autologous bone marrow mesenchymal stem cells with platelet rich plasma for the treatment of knee osteoarthritis. *J Transl Med* 2020;18:356.
  29. Elik H, Doğu B, Yılmaz F, Begoğlu F, Kuran B. The efficiency of platelet-rich plasma treatment in patients with knee osteoarthritis. *J Back Musculoskelet Rehabil* 2020;33:127-138.
  30. Bastos R, Mathias M, Andrade R, et al. Intra-articular injection of culture-expanded mesenchymal stem cells with or without addition of platelet-rich plasma is effective in decreasing pain and symptoms in knee osteoarthritis: A controlled, double-blind clinical trial. *Knee Surg Sports Traumatol Arthrosc* 2020;28:1989-1999.
  31. Su K, Bai Y, Wang J, Zhang H, Liu H, Ma S. Comparison of hyaluronic acid and PRP intra-articular injection with combined intra-articular and intraosseous PRP injections to treat patients with knee osteoarthritis. *Clin Rheumatol* 2018;37:1341-1350.
  32. Cerza F, Carnì S, Carcangiu A, et al. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. *Am J Sports Med* 2012;40:2822-2827.
  33. Smith P. Intra-articular autologous conditioned plasma injections provide safe and efficacious treatment for knee osteoarthritis: An FDA-sanctioned, randomized, double-blind, placebo-controlled clinical trial. *Am J Sports Med* 2016;44:884-891.
  34. Baria M, Pedroza A, Kaeding C, et al. Platelet-rich plasma versus microfragmented adipose tissue for knee osteoarthritis: A randomized controlled trial. *Orthop J Sports Med* 2022;10:23259671221120678.
  35. Barman A, Bandyopadhyay D, Mohakud S, et al. Comparison of clinical outcome, cartilage turnover, and inflammatory activity following either intra-articular or a combination of intra-articular with intra-osseous platelet-rich plasma injections in osteoarthritis knee: A randomized, clinical trial. *Injury* 2023;54:728-737.
  36. Barman A, Prakash S, Sahoo J, Mukherjee S, Maiti R, Roy SS. Single intra-articular injection with or without intra-osseous injections of platelet-rich plasma in the treatment of osteoarthritis knee: A single-blind, randomized clinical trial. *Injury* 2022;53:1247-1253.
  37. Bennell KL, Paterson KL, Metcalf BR, et al. Effect of intra-articular platelet-rich plasma vs placebo injection on pain and medial tibial cartilage volume in patients with knee osteoarthritis: The RESTORE randomized clinical trial. *JAMA* 2021;326:2021-2030.
  38. Branch EA, Cook JJ, Cohen A, et al. Platelet-rich plasma is similar to platelet-rich plasma plus hyaluronic acid for the treatment of knee osteoarthritis at 2 years: A randomized controlled trial. *JCJP* 2023;3:100129.
  39. Buendía-López DM, Medina Quirós M, Fernández-Villacañas Marín MÁ. Clinical and radiographic comparison of a single LP-PRP injection, a single hyaluronic acid injection and daily NSAID administration with a 52-week follow-up: A randomized controlled trial. *J Orthop Traumatol* 2018;19:3.
  40. Chu J, Duan W, Yu Z, et al. Intra-articular injections of platelet-rich plasma decrease pain and improve functional outcomes than sham saline in patients with knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2022;30:4063-4071.
  41. Cole BJ, Karas V, Hussey K, Pilz K, Fortier LA. Hyaluronic acid versus platelet-rich plasma: A prospective, double-blind randomized controlled trial comparing clinical outcomes and effects on intra-articular biology for the treatment of knee osteoarthritis. *Am J Sports Med* 2017;45:339-346.
  42. Dallo I, Szwedowski D, Mobasher A, Irlandini E, Gobbi A. A prospective study comparing leukocyte-poor platelet-rich plasma combined with hyaluronic acid and autologous microfragmented adipose tissue in patients with early knee osteoarthritis. *Stem Cells Dev* 2021;30:651-659.
  43. Di Martino A, Boffa A, Andriolo L, et al. Leukocyte-rich versus leukocyte-poor platelet-rich plasma for the treatment of knee osteoarthritis: A double-blind randomized trial. *Am J Sports Med* 2022;50:609-617.
  44. Di Martino A, Di Matteo B, Papio T, et al. Platelet-rich plasma versus hyaluronic acid injections for the treatment of knee osteoarthritis: Results at 5 years of a double-blind, randomized controlled trial. *Am J Sports Med* 2019;47:347-354.
  45. Dório M, Rodrigues Pereira RM, Branco Luz AG, Alle Deveza L, de Oliveira RM, Fuller R. Efficacy of platelet-rich plasma and plasma for symptomatic treatment of knee osteoarthritis: A double-blinded placebo-controlled randomized clinical trial. *BMC Musculoskelet Disord* 2021;22:822.
  46. Duif C, Vogel T, Topcuoglu F, Spyrou G, von Schulze Pellingahr C, Lahner M. Does intraoperative application of leukocyte-poor platelet-rich plasma during arthroscopy for knee degeneration affect postoperative pain, function and quality of life? A 12-month randomized controlled double-blind trial. *Arch Orthop Trauma Surg* 2015;135:971-977.
  47. Duymus TM, Mutlu S, Dernek B, Komur B, Aydogmus S, Kesiktas FN. Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options. *Knee Surg Sports Traumatol Arthrosc* 2017;25:485-492.
  48. Elawamy A, Kamel EZ, Mahran SA, Abdellatif H, Hassanien M. Efficacy of genicular nerve radiofrequency ablation versus intra-articular platelet rich plasma in chronic knee osteoarthritis: A single-blind randomized clinical trial. *Pain Physician* 2021;24:127-134.
  49. Elksniņš-Finogejevs A, Vidal L, Peredistijs A. Intra-articular platelet-rich plasma vs corticosteroids in the treatment of moderate knee osteoarthritis: A single-center prospective randomized controlled study with a 1-year follow up. *J Orthop Surg Res* 2020;15:257.
  50. Filardo G, Di Martino B, Merli A, et al. Platelet-rich plasma intra-articular knee injections show no superiority versus viscosupplementation: A randomized controlled trial. *Am J Sports Med* 2015;43:1575-1582.

51. Filardo G, Kon E, Di Martino A, et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: Study design and preliminary results of a randomized controlled trial. *BMC Musculoskelet Disord* 2012;13:229.
52. Gobbi A, Lad D, Karnatzikos G. The effects of repeated intra-articular PRP injections on clinical outcomes of early osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc* 2015;23:2170-2177.
53. Görmeli G, Görmeli CA, Ataoglu B, Çolak C, Aslantürk O, Ertem K. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: A randomized, double-blind, placebo-controlled trial. *Knee Surg Sports Traumatol Arthrosc* 2017;25:958-965.
54. Huang-Ya H, Hsu C-W, Lin G-C, Lin H-S, Chou Y-J, Liou I-H, Sun S-F. Comparing efficacy of a single intra-articular injection of platelet-rich plasma (PRP) combined with different hyaluronans for knee osteoarthritis: A randomized-controlled clinical trial. *BMC Musculoskelet Disord* 2022;23:954.
55. Huang Y, Liu X, Xu X, Liu J. Intra-articular injections of platelet-rich plasma, hyaluronic acid or corticosteroids for knee osteoarthritis: A prospective randomized controlled study. *Orthopade* 2019;48:239-247.
56. Jubert NJ, Rodríguez L, Reverté-Vinaixa MM, Navarro A. Platelet-rich plasma injections for advanced knee osteoarthritis: A prospective, randomized, double-blinded clinical trial. *Orthop J Sports Med* 2017;5.
57. Kaminski R, Maksymowicz-Wleklik M, Kulinski K, Kozar-Kaminska K, Dabrowska-Thing A, Pomianowski S. Short-term outcomes of percutaneous trephination with a platelet rich plasma intrameniscal injection for the repair of degenerative meniscal lesions. A prospective, randomized, double-blind, parallel-group, placebo-controlled study. *Int J Mol Sci* 2019;20.
58. Khasru MR, Siddiq MAB, Jubery TAGMZN, et al. Outcome of intra-articular injection of total stromal cells and platelet-rich plasma in primary knee osteoarthritis: A randomized clinical trial. *Cureus* 2023;15:e34595.
59. Lana JFSD, Weglein A, Sampson SE, et al. Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee. *J Stem Cells Regen Med* 2016;12:69-78.
60. Li T, Li Y, Li W, et al. Impact of autologous platelet-rich plasma therapy vs. hyaluronic acid on synovial fluid biomarkers in knee osteoarthritis: A randomized controlled clinical trial. *Front Med (Lausanne)* 2023;10:1258727.
61. Lin K-Y, Yang CC, Hsu C-J, Yeh ML, Renn J-H. Intra-articular injection of platelet-rich plasma is superior to hyaluronic acid or saline solution in the treatment of mild to moderate knee osteoarthritis: A randomized, double-blind, triple-parallel, placebo-controlled clinical trial. *Arthroscopy* 2019;35:106-117.
62. Louis ML, Dumonceau RG, Jouve E, et al. Intra-articular injection of autologous microfat and platelet-rich plasma in the treatment of knee osteoarthritis: A double-blind randomized comparative study. *Arthroscopy* 2021;37:3125-3137.e3123.
63. Louis ML, Magalon J, Jouve E, et al. Growth factors levels determine efficacy of platelets rich plasma injection in knee osteoarthritis: A randomized double blind non-inferiority trial compared with viscosupplementation. *Arthroscopy* 2018;34:1530-1540.e1532.
64. Montañez-Heredia E, Irizar S, Huertas PJ, et al. Intra-articular injections of platelet-rich plasma versus hyaluronic acid in the treatment of osteoarthritic knee pain: A randomized clinical trial in the context of the Spanish national health care system. *Int J Mol Sci* 2016;17.
65. Nunes-Tamashiro JC, Natour J, Ramuth FM, et al. Intra-articular injection with platelet-rich plasma compared to triamcinolone hexacetonide or saline solution in knee osteoarthritis: A double blinded randomized controlled trial with one year follow-up. *Clin Rehabil* 2022;36:900-915.
66. Park Y-B, Kim J-H, Ha C-W, Lee D-H. Clinical efficacy of platelet-rich plasma injection and its association with growth factors in the treatment of mild to moderate knee osteoarthritis: A randomized double-blind controlled clinical trial as compared with hyaluronic acid. *Am J Sports Med* 2021;49:487-496.
67. Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: A prospective, double-blind, randomized trial. *Am J Sports Med* 2013;41:356-364.
68. Paterson KL, Nicholls M, Bennell KL, Bates D. Intra-articular injection of photo-activated platelet-rich plasma in patients with knee osteoarthritis: A double-blind, randomized controlled pilot study. *BMC Musculoskelet Disord* 2016;17:67.
69. Pishgahi A, Abolhasan R, Shakouri SK, et al. Effect of dextrose prolotherapy, platelet rich plasma and autologous conditioned serum on knee osteoarthritis: A randomized clinical trial. *Iran J Allergy Asthma Immunol* 2020;19:243-252.
70. Pretorius J, Nemat N, Alsayed A, et al. Double-blind randomized controlled trial comparing platelet-rich plasma with intra-articular corticosteroid injections in patients with bilateral knee osteoarthritis. *Cureus* 2022;14:e29744.
71. Raeissadat SA, Ghazi Hosseini P, Bahrami MH, et al. The comparison effects of intra-articular injection of platelet rich plasma (PRP), plasma rich in growth factor (PRGF), hyaluronic acid (HA), and ozone in knee osteoarthritis; a one year randomized clinical trial. *BMC Musculoskelet Disord* 2021;22:134.
72. Raeissadat SA, Ahangar AG, Rayegani SM, Sajjadi MM, Ebrahimpour A, Yavari P. Platelet-rich plasma-derived growth factor vs hyaluronic acid injection in the individuals with knee osteoarthritis: A one year randomized clinical trial. *J Pain Res* 2020;13:1699-1711.
73. Raeissadat SA, Ghorbani E, Sanei Taheri M, et al. MRI changes after platelet rich plasma injection in knee osteoarthritis (randomized clinical trial). *J Pain Res* 2020;13:65-73.
74. Raeissadat SA, Raygani SM, Hassanabadi H, et al. Knee osteoarthritis injection choices: Platelet-rich plasma (PRP) versus hyaluronic acid (a one-year randomized clinical trial). *Clin Med Insights Arthritis Musculoskelet Disord* 2015;8:1-8.
75. Rayegani SM, Raeissadat SA, Taheri MS, et al. Does intra articular platelet rich plasma injection improve function,

- pain and quality of life in patients with osteoarthritis of the knee? A randomized clinical trial. *Orthop Rev (Pavia)* 2014;6:5405.
76. Reyes-Sosa R, Lugo-Radillo A, Cruz-Santiago L, Garcia-Cruz CR, Mendoza-Cano O. Clinical comparison of platelet-rich plasma injection and daily celecoxib administration in the treatment of early knee osteoarthritis: A randomized clinical trial. *J Appl Biomed* 2020;18:41-45.
  77. Simental-Mendía M, Vílchez-Cavazos JF, Peña-Martínez VM, Said-Fernández S, Lara-Arias J, Martínez-Rodríguez HG. Leukocyte-poor platelet-rich plasma is more effective than the conventional therapy with acetaminophen for the treatment of early knee osteoarthritis. *Arch Orthop Trauma Surg* 2016;136:1723-1732.
  78. Subramanyam K, Alguvelly R, Mundargi A, Khanchandani P. Single versus multi-dose intra-articular injection of platelet rich plasma in early stages of osteoarthritis of the knee: A single-blind, randomized, superiority trial. *Arch Rheumatol* 2021;36:326-334.
  79. Szwedowski D, Mobasheri A, Moniuszko A, Zabrzyński J, Jeka S. Intra-articular injection of platelet-rich plasma is more effective than hyaluronic acid or steroid injection in the treatment of mild to moderate knee osteoarthritis: A prospective, randomized, triple-parallel clinical trial. *Biomedicines* 2022;10:991.
  80. Tavassoli M, Janmohammadi N, Hosseini A, Khafri S, Esmailnejad-Ganji SM. Single- and double-dose of platelet-rich plasma versus hyaluronic acid for treatment of knee osteoarthritis: A randomized controlled trial. *World J Orthop* 2019;10:310-326.
  81. Tschopp M, Pfirrmann CWA, Fucentese SF, et al. A randomized trial of intra-articular injection therapy for knee osteoarthritis. *Invest Radiol* 2023;58:355-362.
  82. Tucker JD, Goetz LL, Duncan MB, et al. Randomized, placebo-controlled analysis of the knee synovial environment following platelet-rich plasma treatment for knee osteoarthritis. *PM R* 2021;13:707-719.
  83. Vaquerizo V, Padilla S, Aguirre JJ, Begoña L, Orive G, Anitua E. Two cycles of plasma rich in growth factors (PRGF-Endoret) intra-articular injections improve stiffness and activities of daily living but not pain compared to one cycle on patients with symptomatic knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* 2018;26:2615-2621.
  84. Wang Y-C, Lee C-L, Chen Y-J, et al. Comparing the efficacy of intra-articular single platelet-rich plasma (PRP) versus novel crosslinked hyaluronic acid for early-stage knee osteoarthritis: A prospective, double-blind, randomized controlled trial. *Medicina (Kaunas)* 2022;58:1028.
  85. Wang Z, Wang R, Xiang S, et al. Assessment of the effectiveness and satisfaction of platelet-rich plasma compared with hyaluronic acid in knee osteoarthritis at minimum 7-year follow-up: A post hoc analysis of a randomized controlled trial. *Front Bioeng Biotechnol* 2022;10:1062371.
  86. Wu Y-T, Li T-Y, Lee K-C, et al. Efficacy of a novel intra-articular administration of platelet-rich plasma one-week prior to hyaluronic acid versus platelet-rich plasma alone in knee osteoarthritis: A prospective, randomized, double-blind, controlled trial. *J Clin Med* 2022;11:3241.
  87. Xu Z, He Z, Shu L, Li X, Ma M, Ye C. Intra-articular platelet-rich plasma combined with hyaluronic acid injection for knee osteoarthritis is superior to platelet-rich plasma or hyaluronic acid alone in inhibiting inflammation and improving pain and function. *Arthroscopy* 2021;37:903-915.
  88. Yurtbay A, Say F, Çinka H, Ersoy A. Multiple platelet-rich plasma injections are superior to single PRP injections or saline in osteoarthritis of the knee: The 2-year results of a randomized, double-blind, placebo-controlled clinical trial. *Arch Orthop Trauma Surg* 2022;142:2755-2768.
  89. Zaffagnini S, Andriolo L, Boffa A, et al. Microfragmented adipose tissue versus platelet-rich plasma for the treatment of knee osteoarthritis: A prospective randomized controlled trial at 2-year follow-up. *Am J Sports Med* 2022;50:2881-2892.
  90. Zhou Y, Li H, Cao S, et al. Clinical efficacy of intra-articular injection with P-PRP versus that of L-PRP in treating knee cartilage lesion: A randomized controlled trial. *Orthop Surg* 2023;15:740-749.
  91. Zitsch BP, James CR, Crist BD, Stoker AM, Della Rocca GJ, Cook JL. A prospective randomized double-blind clinical trial to assess the effects of leukocyte-reduced platelet-rich plasma on pro-inflammatory, degradative, and anabolic biomarkers after closed pilon fractures. *J Orthop Res* 2022;40:925-932.
  92. Lewis E, Merghani K, Robertson I, et al. The effectiveness of leucocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: The PEAK randomized controlled trial. *Bone Joint J* 2022;104-B:663-671.
  93. Roberts C. Baseline imbalance in randomised controlled trials. *BMJ* 1999;319:185.
  94. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum* 1987;30:914-918.
  95. Deshpande BR, Katz JN, Solomon DH, et al. Number of persons with symptomatic knee osteoarthritis in the US: Impact of race and ethnicity, age, sex, and obesity. *Arthritis Care Res (Hoboken)* 2016;68:1743-1750.
  96. Zhang JY, Fabricant PD, Ishmael CR, Wang JC, Petrigliano FA, Jones KJ. Utilization of platelet-rich plasma for musculoskeletal injuries: An analysis of current treatment trends in the United States. *Orthop J Sports Med* 2016;4:2325967116676241.
  97. Jordan JM, Helmick CG, Renner JB, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: The Johnston County Osteoarthritis Project. *J Rheumatol* 2007;34:172-180.
  98. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage* 2005;13:769-781.
  99. Simkin J, Valentino J, Cao W, et al. Quantifying mediators of racial disparities in Knee Osteoarthritis Outcome Scores: A cross-sectional analysis. *JBJS Open Access* 2021;6:e21.00004.
  100. Vega J, Emara A, Orr M, Klika A, Piuze N, the Cleveland Clinic Arthroplasty Group. Demographic and



- socioeconomic determinants are associated with poor preoperative patient-reported pain and function in primary TKA: A cohort study of 14,079 patients. *J Bone Joint Surg Am* 2023;105:286-292.
101. Jørgensen KT, Pedersen BV, Nielsen NM, Hansen AV, Jacobsen S, Frisch M. Socio-demographic factors, reproductive history and risk of osteoarthritis in a cohort of 4.6 million Danish women and men. *Osteoarthritis Cartilage* 2011;19:1176-1182.
  102. Schwartzberg HG, Roy R, Wilson K, et al. Patient characteristics independently associated with knee osteoarthritis symptom severity at initial orthopedic consultation. *J Clin Rheumatol* 2022;28:e359-e362.
  103. Zhao K, Liu Y, Nie L, et al. The influence of sample size and gender composition on the meta-analysis conclusion of platelet-rich plasma treatment for osteoarthritis. *J Orthop Translat* 2019;15:34-42.
  104. Sánchez M, Jorquera C, de Dicastillo L, et al. Women show a positive response to platelet-rich plasma despite presenting more painful knee osteoarthritis than men. *Knee Surg Sports Traumatol Arthrosc* February 16, 2024. [Epub ahead of print.].
  105. Li A, Stavrakis A, Photopoulos C. Platelet-rich plasma use for hip and knee osteoarthritis in the United States. *Knee* 2022;39:239-246.
  106. Kim D, Bashrum B, Kotlier J, et al. Reporting bias is highly prevalent in systematic reviews and meta-analyses of platelet rich plasma injections for hip osteoarthritis. *Arthrosc Sports Med Rehabil* 2024;6:100851.