Survey Report

Perception mapping of Indian Physicians on Role of Collagens in management of OA

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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1 INTRODUCTION

Osteoarthritis (OA) is the most prevalent joint disorder and a significant public health challenge in the modern era [1]. As life expectancy rises, particularly in developed nations, the global prevalence of OA is increasing rapidly. This condition places a substantial economic burden on healthcare systems [2]. OA primarily affects the weight-bearing joints, causing chronic pain and restricted mobility, which severely diminishes the quality of life for millions. These functional limitations accelerate aging and may even contribute to premature mortality in those affected [3].

OA is marked by the gradual breakdown of articular cartilage, with collagen being a key structural element. It has been suggested that taking collagen hydrolysates could support cartilage matrix production by activating chondrocytes [4]. This occurs after the collagen is absorbed in the intestines and transported via the bloodstream to the joints. Studies have shown that peptides from orally consumed collagen hydrolysates accumulate in cartilage just a few hours after ingestion [5]. Preclinical research on animals has shown encouraging results with collagen derivatives, indicating potential for cartilage repair in OA patients [6]. These findings have led scientists to explore whether collagen supplementation can help alleviate OA symptoms in humans.

Chondrocytes in the superficial and mid layers are responsible for producing the extracellular matrix (ECM), which consists mainly of collagen types II, IX, and XI, along with proteoglycans. This ECM supports the cartilage's ability to handle compressive and tensile stress in joints [7]. Collagen is the predominant macromolecule in the ECM, accounting for 60% of cartilage's dry weight and providing structural strength and stability. Type II collagen comprises 90%–95% of the total collagen in the ECM, forming fibrils and fibers intertwined with proteoglycans like aggrecans. Types IX and XI collagens, although making up only 5%–10%, are crucial for reinforcing the crosslinking between fibrils [8]. In the deeper cartilage zones, chondrocytes reach their final differentiation stage and predominantly synthesize collagen type X. Proteoglycans are the second largest ECM component and are highly glycosylated, enabling them to resist compression by attracting water [9]. These proteoglycans include aggrecan, decorin, biglycan, and fibromodulin, with aggrecan being the largest. Growth factors regulate the

development of chondrocytes from mesenchymal stem cells (MSCs) and also stimulate the production of specific ECM proteins. The production of collagen type X is associated with the regulation of proteolytic enzymes that clear the ECM, facilitating tissue calcification and vascularization [10].

2 RATIONALE OF THE STUDY

Collagen-based therapies have emerged as promising treatment options for OA, primarily due to collagen's role in maintaining cartilage structure and function. Recent research emphasized the therapeutic potential of collagen hydrolysates, which were believed to improve joint health by promoting cartilage repair and reducing pain and inflammation in OA patients. Studies showed that oral administration of undenatured type II collagen helped alleviate OA symptoms, with higher doses providing faster improvements in mobility and reducing disease progression. Additionally, collagen peptide supplementation was shown to significantly reduce pain in knee OA patients compared to placebo, offering a valuable non-invasive option for symptom management. These findings highlighted the need for further research and development of collagen-based treatments to better personalize OA therapy and improve patient outcomes.

This survey was designed to explore and map physicians' perceptions of the role of collagens in the management of OA. By assessing physician perspectives, the survey aimed to identify the effectiveness of collagens in OA management, as well as any barriers that may have hindered its wider application in clinical practice. This provided valuable insights into optimizing OA management and improving patient outcomes.

3 STUDY OBJECTIVE

To assess the perception of Indian physicians regarding the role of collagens in management of OA.

4 METHODS

The study was designed as a cross-sectional, questionnaire-based survey aimed at assessing the perceptions, practices, and clinical experiences of Indian physicians regarding the role of collagens in the management of OA. A structured questionnaire was distributed to a representative sample of physicians across various regions in India, including general practitioners who encountered OA in their routine practice.

The questionnaire captured data on the role of collagens in OA management, treatment protocols, and factors influencing physicians' decisions on collagen use. The data collected provided insights into the real-world application of collagen therapies, informing potential future guidelines and best practices. Participants received detailed information before deciding to participate, and a 10-question survey was administered electronically.

The cross-sectional design was deemed appropriate for capturing a snapshot of current practices and perceptions among physicians at a specific point in time. This questionnaire-based approach allowed the study to gather a wide range of data from a diverse group of practitioners, ensuring the findings were representative of the broader medical community in India. This design enabled the exploration of various factors, including treatment preferences, clinical outcomes, and safety concerns, without the need for longitudinal follow-up. Furthermore, the cross-sectional nature of the study allowed for the identification of trends and patterns in physicians' perspectives on the role of collagens in OA management, which may be further explored in future studies or clinical trials. The survey's structured format ensured comprehensive coverage of all relevant aspects of collagen use in OA patients, thereby providing an in-depth understanding of its role in clinical practice.

The study included general practitioners and specialists (e.g., orthopedists, rheumatologists) who encountered OA in their clinical practice, those knowledgeable about collagen therapy in OA management, and physicians from various regions of India to ensure a representative sample. Only those who provided consent and completed the questionnaire were included. Exclusion criteria encompassed retired or non-practicing physicians, those who did not manage OA, incomplete questionnaires, and those who did not provide informed consent.

A target sample size of 100 Indian physicians was set to ensure a diverse and representative sample, allowing for meaningful statistical analysis. The study adhered to ethical principles outlined in the Declaration of Helsinki, and ethical approval was obtained from an Independent Ethics Committee. The collected data were analyzed using descriptive and inferential statistics. Descriptive statistics summarized demographic information and response frequencies, providing a comprehensive view of the findings.

5 RESULTS

A total of 116 HCPs participated in the survey. Below is the summary of the responses.

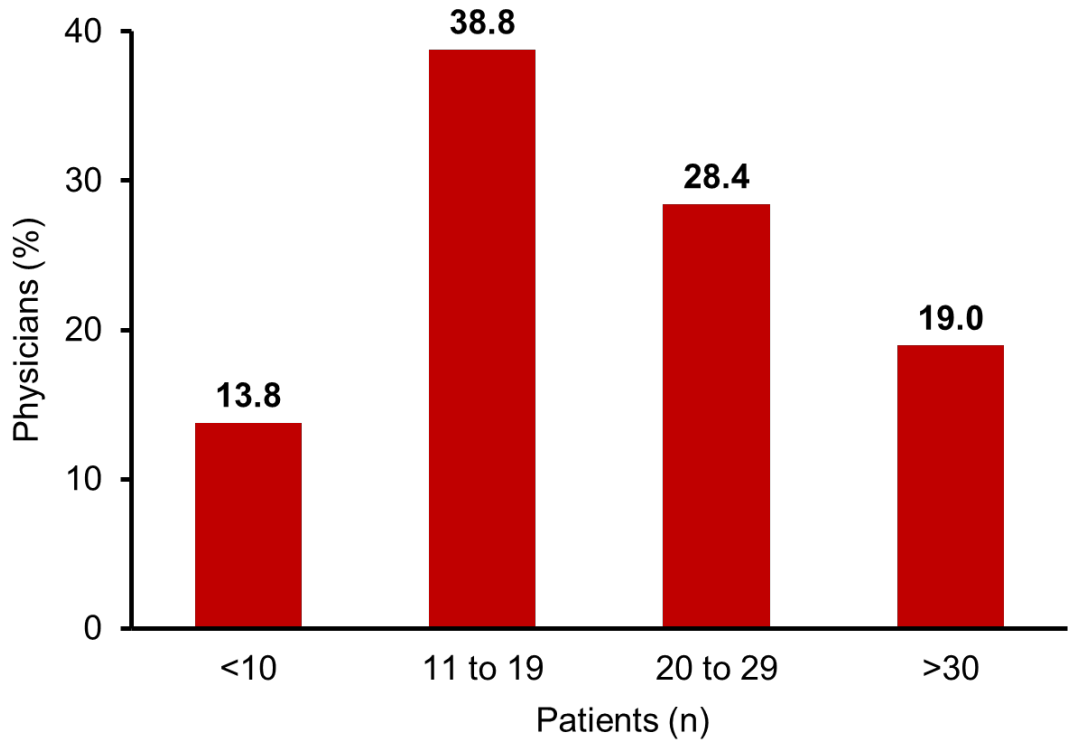
Question 1. In your clinical practice, how many patients of Osteoarthritis do you treat in a week?

A. < 10

B. 11 To 19

C. 20 To 29

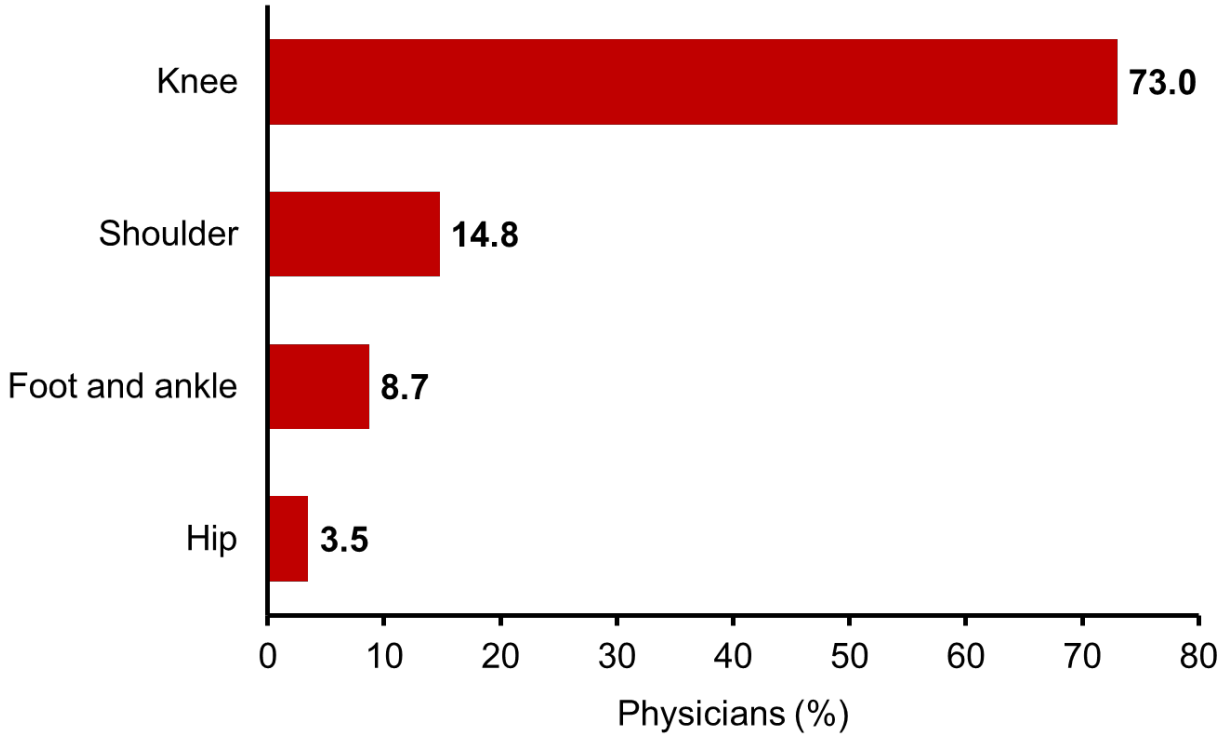
D. > 30



- The majority (38.8%) of physicians reported treating 11 to 19 osteoarthritis partients in a week.
- A significant proportion (28.4%) indicated they treat 20 to 29 patients of osteoarthritis per week in their clinical practice.
- Around 19.0% of physicians reported treating more than 30 osteoarthitis patients in a week.
- A small portion (13.8%) of physicians treated less than 10 patients with osteoarthritis per week in routine clinical practice.

Question 2. Which joint is the most commonly involved in your patients in your routine clinical practice?

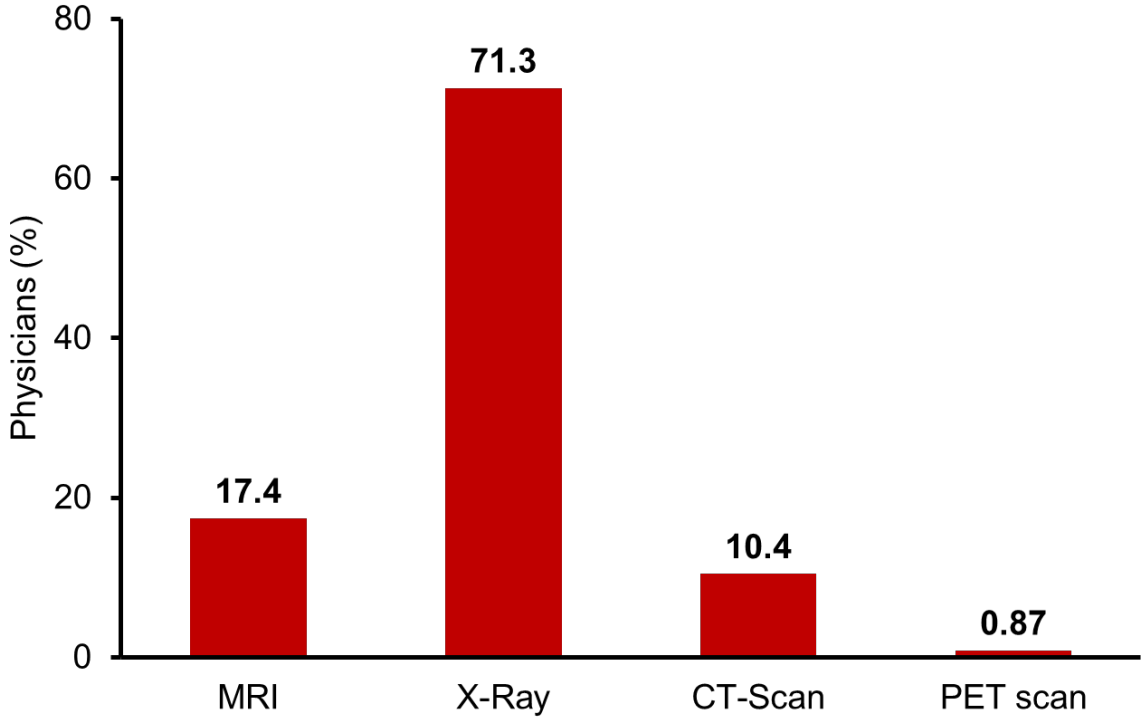
A. Hip
B. Knee
C. Shoulder
D. Foot and ankle



- The majority of physicians (73.0%) reported that the knee is the most commonly involved joint in their clinical practice.
- A significant proportion (14.8%) indicated that the shoulder is frequently affected in routine practice.
- Approximately 8.7% of physicians noted that the foot and ankle are commonly involved joints.
- A small proportion (3.5%) observed the hip as a commonly affected joint in their clinical practice.

Question 3. What is the most practical investigational criteria for assessment of an OA patient in your practice?

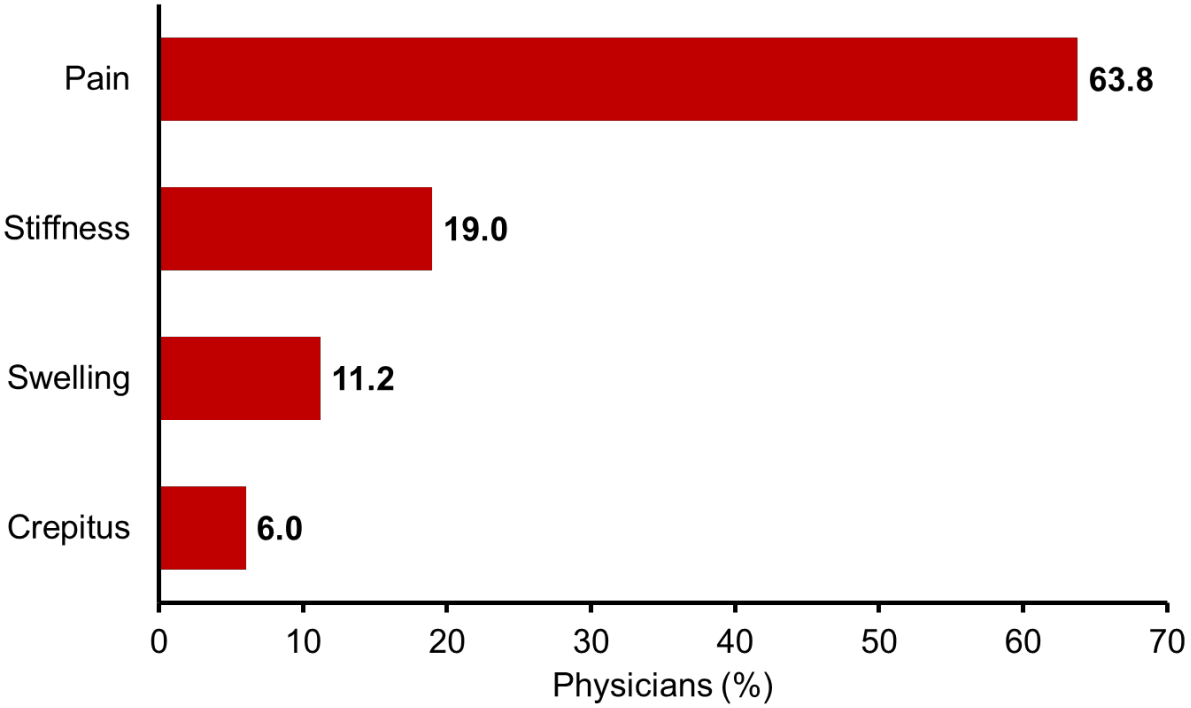
A. MRI
B. X-Ray
C. CT-Scan
D. PET scan



- The majority (71.3%) of physicians considered X-ray to be the most practical investigative tool for assessing OA patients.
- Approximately 17.4% of physicians viewed MRI as the most practical diagnostic modality for evaluating OA.
- Around 10.4% of physicians used CT scans as a common investigative tool in their clinical practice for OA assessment.
- A very small proportion (0.87%) of physicians reported using PET scans as a practical investigative tool for osteoarthritis.

Question 4. Which is the most common symptom do you observe in patients suffering from OA in your clinical practice?

A. Pain
B. Stiffness
C. Crepitus
D. Swelling



- Pain is the most commonly reported symptom of osteoarthritis, observed by a significant majority of physicians (63.8%).
- Stiffness is the second most frequently observed symptom, reported by 19.0% of physicians.
- Swelling is noted as a common symptom by approximately 11.2% of physicians in their clinical practice.
- A small proportion (6.0%) of physicians reported crepitus as a common symptom in patients with osteoarthritis.

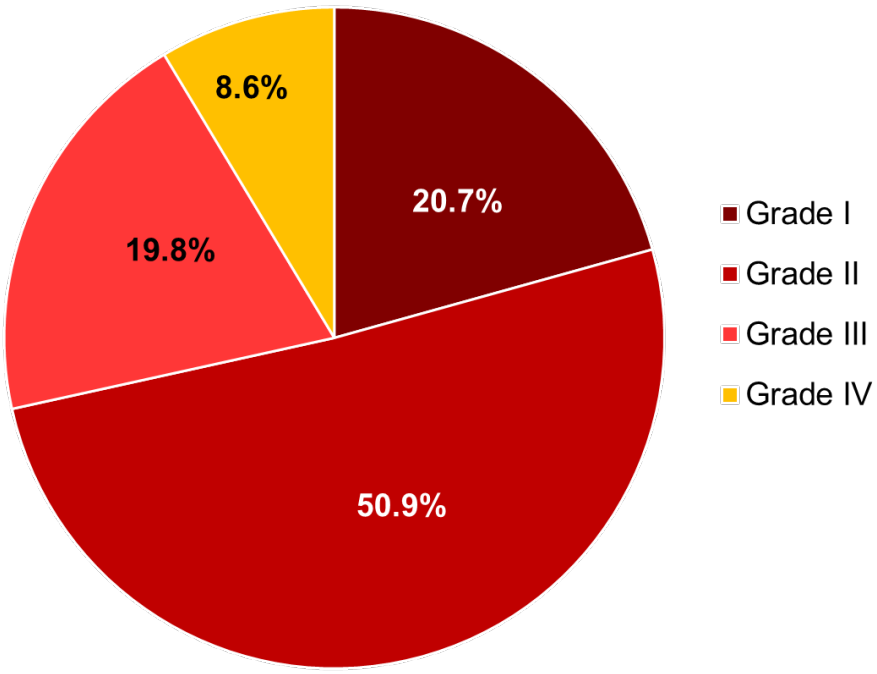
Question 5. In which grade of OA do you consider prescribing nutritional supplements?

A. Grade I

B. Grade II

C. Grade III

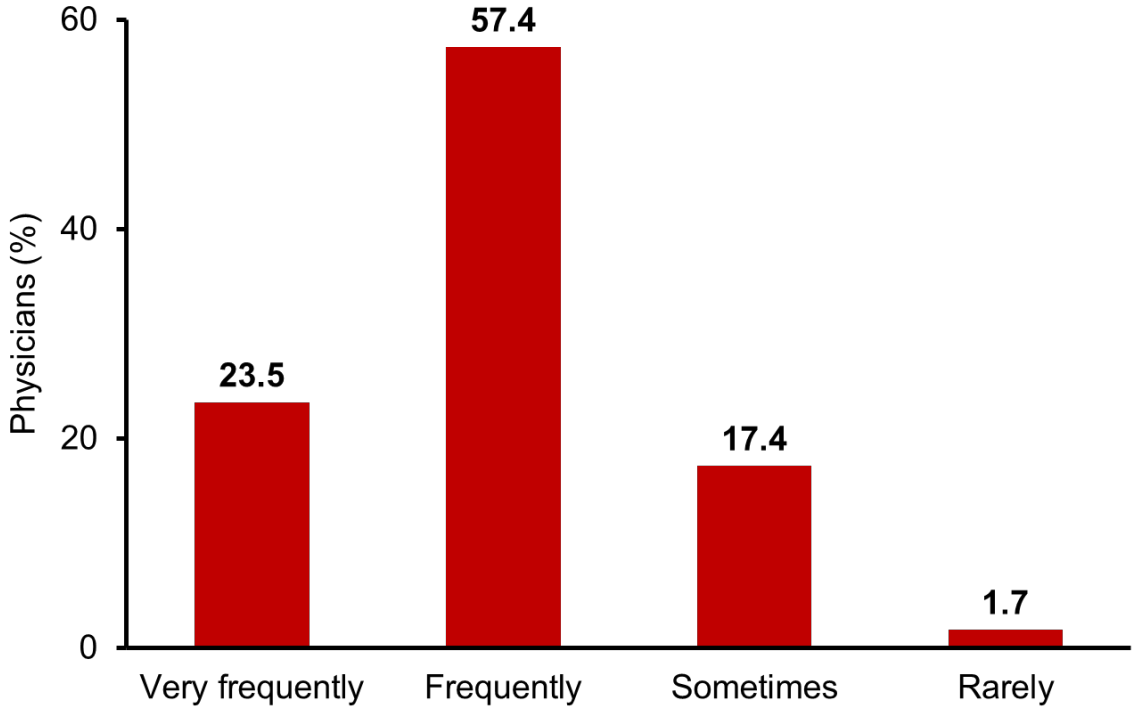
D. Grade IV



- Approximately 50.9% of physicians prescribed nutritional supplements for patients with Grade II osteoarthritis.
- About 20.7% of physicians considered Grade I osteoarthritis as an indication for prescribing nutritional supplements.
- Nutritional supplements are prescribed by 19.8% of physicians for patients with Grade III osteoarthritis.
- A small proportion (8.6%) of physicians prescribed nutritional supplements for patients with Grade IV osteoarthritis.

Question 6. How frequently do you prescribe nutraceutical supplements in the management of osteoarthritis?

A. Very frequently
B. Frequently
C. Sometimes
D. Rarely



- The majority (57.4%) of physicians prescribed nutritional supplement frequently in the management of osteoarthritis.
- A smaller proportion (23.5%) of physicians prescribed them very frequently in the management of osteoarthritis.
- Around 17.4% of physicians prescribed nutraceutical supplements only sometimes in the management of osteoarthritis.
- A very small percentage of physicians (1.7%) reported prescribing nutritional supplement rarely.

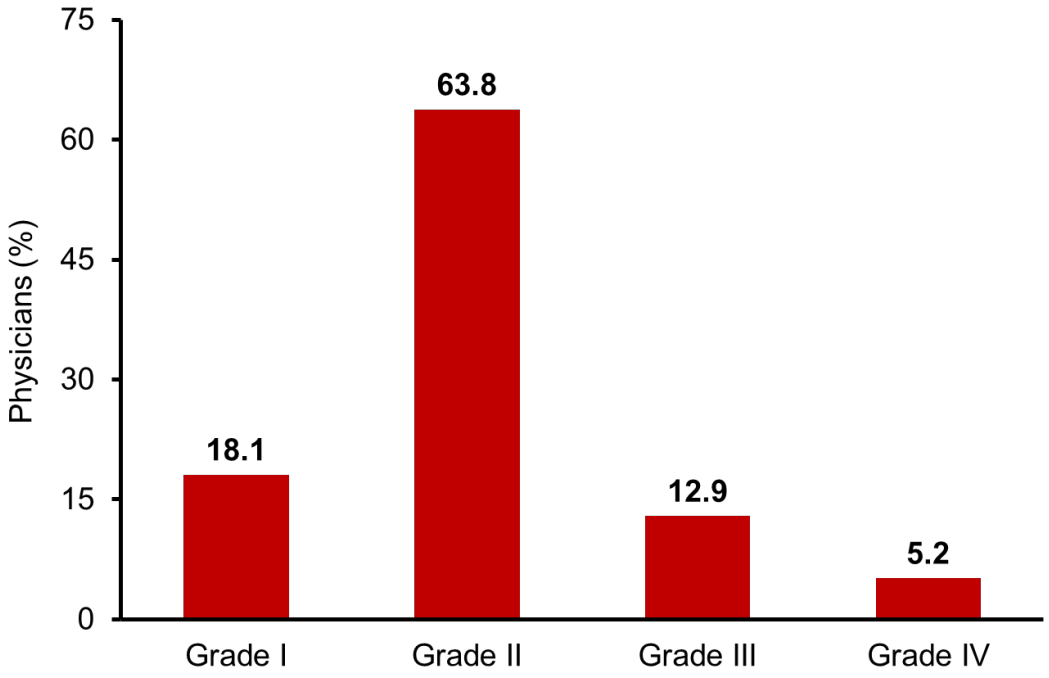
Question 7. In which severity of OA you prescribe combination of Sodium Hyalurnoate, Native collagen type II, Aflapin and Curcumin fixed dose combination (FDC)?

A. Grade I

B. Grade II

C. Grade III

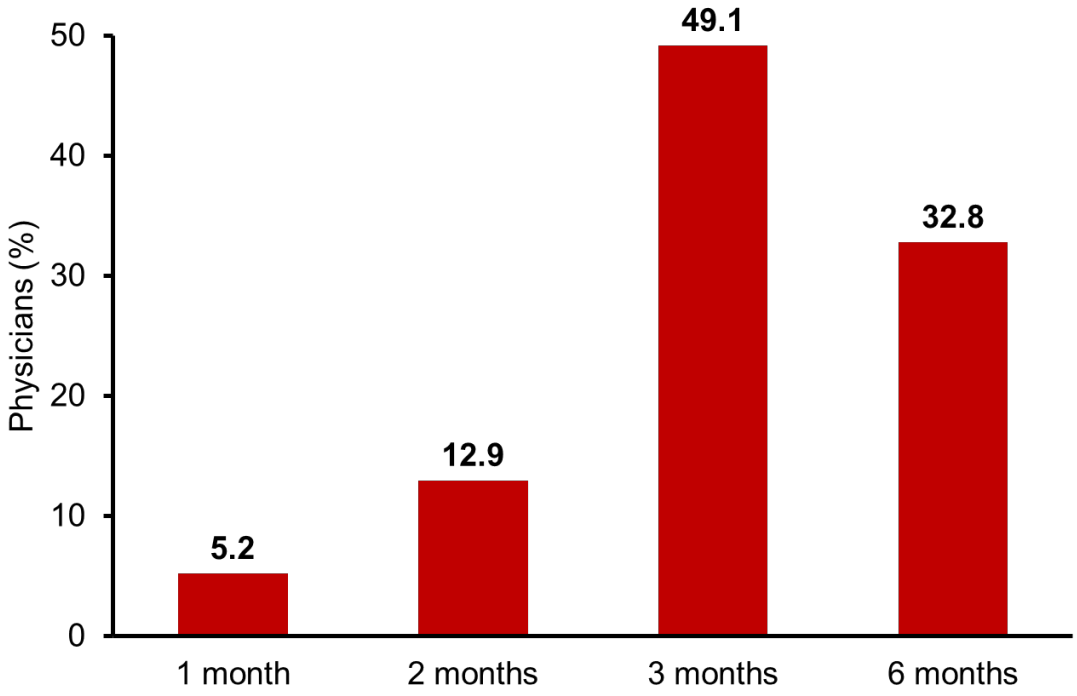
D. Grade IV



- The majority (63.8%) of physicians prescribed a combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin in Grade II osteoarthritis.
- A significant portion (18.1%) of physicians prescribed this fixed-dose combination in Grade I osteoarthritis.
- Approximately 12.9% of physicians choose to prescribed a combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin in Grade III osteoarthritis.
- Only a small percentage (5.2%) of physicians prescribed the combination in Grade IV osteoarthritis.

Question 8. What is the optimum duration you prescribe combination of Sodium Hyaluronate, Native collagen type II, Aflapin and Curcumin FDC?

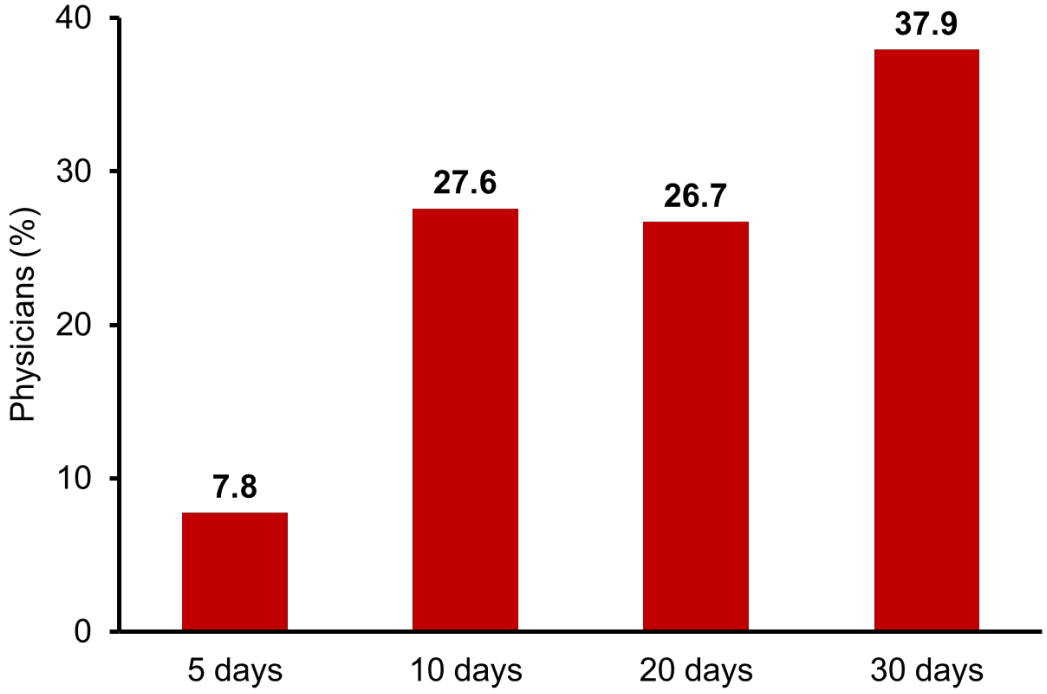
A. 1 month
B. 2 months
C. 3 months
D. 6 months



- The majority (49.1%) of physicians prescribed the combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin for 3 months.
- A significant portion (32.8%) of physicians opt for a duration of 6 months for prescribing this fixed-dose combination.
- Around 12.9% of physicians preferred a 2-month duration for prescribing this combination.
- Only a small percentage of physicians (5.2%) prescribe the combination for 1 month duration.

Question 9. According to your clinical practice, in how many days does Aflapin improve joint function and relieves pain?

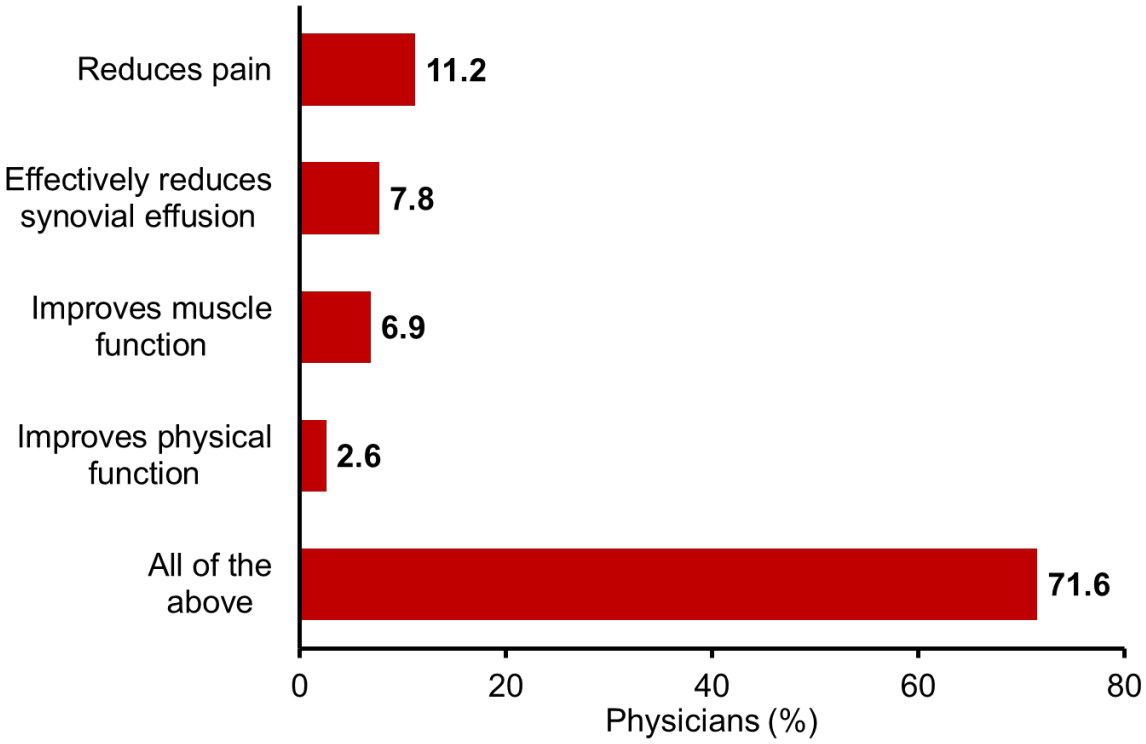
A. 5 days
B. 10 days
C. 20 days
D. 30 days



- The majority (37.9%) of physicians believed that Aflapin improves joint function and relieves pain within 30 days.
- A significant portion (27.6%) of physicians reported that improvement in joint function and pain occurs within 10 days.
- Around 26.7% of physicians feel that Aflapin provides relief and improves joint function in 20 days.
- A smaller percentage (7.8%) of physicians believed that Aflapin takes only 5 days to show improvement.

Question 10. What do you think are the advantages of Sodium Hyaluronate in Osteoarthritis?

A. Effectively reduces synovial effusion
B. Improves muscle function
C. Reduces pain
D. Improves physical function
E. All of the above



- The majority (71.6%) of physicians believed that all the listed advantages of Sodium Hyaluronate i.e., reducing synovial effusion, improving muscle function, reducing pain, and improving physical function are beneficial in the management of osteoarthritis.
- A smaller group (11.2%) of physicians reported pain reduction as a primary advantage of Sodium Hyaluronate in the osteoarthritis management.
- Effective reduction in synovial effusion is highlighted by 7.8% of physicians as a key benefit of Sodium Hyaaluronate.
- A smaller proportion of physicians (6.9%) believed that Sodium Hyaluronate improves muscle function.
- Only 2.6% of physicians see improvement in physical function as a significant advantage.

6 SUMMARY

A survey of physicians' practices and preferences in the management of OA revealed several key findings. The majority of physicians (38.8%) reported treating 11 to 19 OA patients per week, while a significant proportion (28.4%) treated 20 to 29 patients weekly. Around 19.0% of physicians indicated that they treat more than 30 OA patients per week, whereas a smaller portion (13.8%) treated fewer than 10 OA patients weekly.

Regarding the commonly involved joints, the majority of physicians (73.0%) reported the knee as the most frequently affected joint in their clinical practice. The shoulder was the second most commonly involved joint, as indicated by 14.8% of physicians. Approximately 8.7% noted the foot and ankle as commonly affected joints, while a small proportion (3.5%) observed the hip as commonly involved. When it comes to diagnostic tools, the majority of physicians (71.3%) considered X-ray to be the most practical for assessing OA patients. MRI was viewed as the most practical diagnostic modality by 17.4% of physicians, and CT scans were commonly used by 10.4%. A very small proportion (0.87%) reported using PET scans for OA assessment.

In terms of symptoms, pain was the most commonly reported symptom of OA, observed by 63.8% of physicians. Stiffness was the second most frequently reported symptom (19.0%), followed by swelling (11.2%), and crepitus (6.0%). Additionally, a majority of physicians (57.4%) frequently prescribed nutritional supplements for managing OA, with a significant portion (23.5%) prescribing them very frequently, and a smaller percentage (1.7%) reporting rare prescription of these supplements.

The survey also revealed that a majority (63.8%) of physicians prescribed a combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin for Grade II osteoarthritis, with smaller proportions prescribing this combination for other OA grades. The preferred duration for this fixed-dose combination was 3 months (49.1%), followed by 6 months (32.8%), 2 months (12.9%), and 1 month (5.2%). Lastly, the majority (71.6%) of physicians believed that the combination of Sodium Hyaluronate's benefits, such as reducing synovial effusion, improving muscle function, reducing pain, and improving physical function, were advantageous in managing OA.

7 DISCUSSION

The survey results highlight significant trends in osteoarthritis (OA) management among physicians, with a substantial focus on practical diagnostic tools and commonly involved joints. The preference for X-rays (71.3%) as the primary diagnostic modality underscores its practicality and accessibility in clinical settings. Despite the advanced imaging capabilities of MRIs and CT scans, their higher costs and limited availability might explain their secondary roles. This preference for X-rays aligns with current clinical guidelines that recommend cost-effective and readily available diagnostic tools for initial OA assessment.

In terms of symptoms, pain emerged as the most commonly reported symptom of OA, cited by 63.8% of physicians, followed by stiffness (19.0%) and swelling (11.2%). This symptomatology informs the therapeutic strategies adopted by physicians, emphasizing the need for effective pain management and inflammation control. The frequent prescription of nutritional supplements, particularly the combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin, for Grade II OA (63.8%) reflects a targeted approach to symptom relief and joint function improvement. The preferred treatment duration of three months suggests a balance between achieving therapeutic efficacy and minimizing long-term medication burden.

Lastly, the survey underscores the importance of a multifaceted treatment approach in OA management. The combination of various supplements and the perceived benefits of Sodium Hyaluronate in reducing synovial effusion, improving muscle function, and alleviating pain highlight a comprehensive strategy to address the multifactorial nature of OA. The strong trust in these combinations and their prescribed durations (49.1% for three months) suggest that physicians are guided by both clinical evidence and practical outcomes observed in their patients. Overall, the survey provides valuable insights into current clinical practices and preferences, emphasizing the need for accessible diagnostics, effective symptom management, and comprehensive therapeutic approaches in the management of osteoarthritis.

8 CLINICAL RECOMMENDATIONS

- For the management of osteoarthritis (OA), the use of X-rays is highly recommended as the primary diagnostic tool due to its practicality and accessibility, as preferred by the majority of physicians.
- Pain management should be prioritized in OA treatment plans, as pain is the most commonly reported symptom. Physicians should consider incorporating a combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin, particularly for patients with Grade II OA, which is favored by 63.8% of physicians.
- Nutritional supplements should be prescribed with a standard treatment duration of three months, as this duration is preferred by 49.1% of physicians, balancing efficacy and long-term medication burden.
- A multifaceted approach to OA management is recommended, addressing symptoms such as pain, stiffness, and swelling. Sodium Hyaluronate should be included in treatment regimens for its benefits in reducing synovial effusion, improving muscle function, and alleviating pain, as supported by 71.6% of physicians.
- Regular monitoring and adjustment of treatment protocols are essential to ensure optimal patient outcomes. Physicians should tailor OA management strategies based on individual patient needs, symptom severity, and response to treatment.

9 CONSULTANT OPINION

Based on the survey results, it is clear that X-rays are the preferred diagnostic tool among physicians for the initial assessment of osteoarthritis (OA) due to their practicality and accessibility. This preference underscores the importance of cost-effective and widely available diagnostic options in clinical practice. The survey also highlights the critical need for effective pain management strategies in OA, with the combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin being favored, particularly for patients with Grade II OA. This combination is trusted for its ability to alleviate pain and improve joint function, suggesting its efficacy in routine clinical use.

The recommended three-month duration for prescribing these supplements aligns with clinical best practices, balancing therapeutic benefits with patient compliance. Physicians should consider integrating this approach into their treatment protocols, ensuring that patients receive consistent and effective management. Additionally, the multifaceted benefits of Sodium Hyaluronate, including reducing synovial effusion and improving muscle function, support its inclusion in comprehensive OA treatment plans.

Regular monitoring and individualized treatment adjustments are essential to optimize patient outcomes. The survey findings advocate for a tailored approach to OA management, addressing the diverse symptoms and severity levels presented by patients. By incorporating these insights, physicians can enhance the effectiveness of OA treatments and improve overall patient care.

10 MARKET OPPORTUNITIES

The survey results reveal significant market opportunities for diagnostic tools and treatment options for OA. The strong preference for X-rays as the primary diagnostic tool underscores the demand for accessible and practical imaging solutions. Effective pain management is crucial, with a notable market potential for the combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin, especially for Grade II OA patients. This combination's trusted efficacy in pain relief and joint function improvement highlights a need for products that address these therapeutic areas.

A three-month prescription duration for these supplements is favored, suggesting a market for formulations designed for optimal therapeutic benefits and patient compliance. Additionally, the multifaceted benefits of Sodium Hyaluronate, including reducing synovial effusion and improving muscle function, present opportunities for comprehensive OA treatment solutions. Marketing efforts should emphasize these benefits, targeting both healthcare providers and patients.

There is also potential for developing tailored OA management strategies, incorporating regular monitoring and individualized treatment adjustments. This approach can be supported by innovative solutions that enhance patient adherence and optimize clinical outcomes. Overall, the survey indicates promising avenues for market expansion and innovation in OA diagnostic and therapeutic products.

11 MARKET POSITIONING

- Position the combination of Sodium Hyaluronate, Native Collagen Type II, Aflapin, and Curcumin as the preferred choice for managing osteoarthritis, particularly for Grade II patients, reflecting its strong endorsement by physicians for its efficacy in pain relief and joint function improvement.
- Emphasize the combination's effectiveness for long-term treatment, with physicians prescribing it for durations of up to three months, aligning with standard clinical practices.
- Highlight the combination's multifaceted benefits, including its ability to reduce synovial effusion and improve muscle function, making it an essential treatment option for managing both pain and functional limitations in OA patients.
- Focus on the preferred dosage regimens, including a three-month prescription, to match physician preferences and optimize patient compliance.
- Develop and market fixed-dose combinations to improve convenience, enhance adherence, and provide a comprehensive solution for OA management.
- Showcase the combination’s versatility for treating a broad range of OA patients, from those with moderate symptoms to more complex cases, thereby capturing a larger market segment.

12 REFERENCES

1) Vos T, Abajobir AA, Abbafati C, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390:1211–1259.
2) Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis. 2014;73:1323–1330.
3) Berthelot G, Johnson S, Noirez P, et al. The age-performance relationship in the general population and strategies to delay age-related decline in performance. Arch Public Heal. 2019;77:1–9.
4) Deal CL, Moskowitz RW. Nutraceuticals as therapeutic agents in osteoarthritis. The role of glucosamine, chondroitin sulfate, and collagen hydrolysate. Rheum Dis Clin N Am. 1999;25:379–395.
5) Taga Y, Iwasaki Y, Shigemura Y, Mizuno K. Improved in vivo tracking of orally administered collagen hydrolysate using stable isotope labeling and LC–MS techniques. J Agric Food Chem. 2019;67:4671–4678.
6) Bagi CM, Berryman ER, Teo S, Lane NE. Oral administration of undenatured native chicken type II collagen (UC-II) diminished deterioration of articular cartilage in a rat model of osteoarthritis (OA) Osteoarthr Cartil. 2017;25:2080–2090.
7) Sophia Fox AJ, Bedi A, Rodeo SA. The basic science of articular cartilage: Structure, composition, and function. Sports Health. 2009;1:461–468.
8) Eyre D. Collagen of articular cartilage. Arthritis Res. 2002;4:30–35.
9) Roughley PJ, Lee ER. Cartilage proteoglycans: Structure and potential functions. Microsc Res. Tech. 1994;28:385–397.
10) Poole AR, Kobayashi M, Yasuda T, Laverty S, Mwale F, Kojima T, et al. Type II collagen degradation and its regulation in articular cartilage in osteoarthritis. Ann. Rheum. Dis. 2002;61(Suppl. 2):78–81.