VA/DoD Clinical Practice Guidelines

THE NON-SURGICAL MANAGEMENT OF HIP & KNEE OSTEOARTHRITIS

Provider Summary

Version 2.0 | 2020

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE NON-SURGICAL MANAGEMENT OF HIP & KNEE OSTEOARTHRITIS

Department of Veterans Affairs

Department of Defense

Provider Summary

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs or TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

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Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the Health Executive Committee "…on the use of clinical and epidemiological evidence to improve the health of the population…" across the Veterans Health Administration (VHA) and Military Health System, by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide healthcare providers with a framework to evaluate, treat, and manage the individual needs and preferences of adults with osteoarthritis (OA), thereby leading to improved clinical outcomes.

In 2014, the VA and DoD published a CPG for the Non-surgical Management of Hip & Knee Osteoarthritis (2014 VA/DoD OA CPG), which was based on evidence reviewed through December 2012. Since the release of that guideline, a growing body of research has expanded the general knowledge and understanding of OA. Consequently, a recommendation to update the 2014 VA/DoD OA CPG was initiated in 2019. The updated CPG includes objective, evidence-based information on the management of OA of the hip and the knee. It is intended to assist healthcare providers in all aspects of patient care and the non-surgical management of OA. The system-wide goal of evidence-based guidelines is to improve the patient's health and well-being by guiding healthcare providers who are caring for patients with OA along management pathways that are supported by evidence. The expected outcome of the successful implementation of this guideline is to:

- Assess the patient's condition and determine, in collaboration with the patient, the best treatment method
- Optimize health outcomes and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care (PCC)

Recommendations

The following recommendations were made using a systematic approach considering four domains as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, as detailed in the section on Methods and Appendix A in the full text OA CPG. These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications, as appropriate (e.g., resource use, equity, acceptability).

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Diagnosis		1.	We suggest against obtaining magnetic resonance imaging for the diagnosis of osteoarthritis of the hip and knee.	Weak against	Reviewed, New- replaced
Self-management		2.	We suggest a self-management program, including exercise and weight loss for osteoarthritis of the hip and knee, and bracing for osteoarthritis of the knee.	Weak for	Reviewed, New-replaced
Physical Therapy		3.	We suggest offering physical therapy as part of a comprehensive management plan for patients with osteoarthritis of the hip or knee.	Weak for	Reviewed, Amended
Pharmacotherapy	*a. Topical Pharmacotherapy*	4.	We recommend offering topical non-steroidal anti-inflammatory drugs for patients with pain associated with osteoarthritis of the knee.	Strong for	Reviewed, New-added
		5.	There is insufficient evidence to recommend for or against the use of topical non-steroidal anti-inflammatory drugs for patients with pain associated with osteoarthritis of the hip.	Neither for nor against	Reviewed, New-added
		6.	We suggest offering topical capsaicin for patients with pain associated with osteoarthritis of the knee.	Weak for	Reviewed, Amended
		7.	There is insufficient evidence to recommend for or against the use of topical capsaicin for patients with pain associated with osteoarthritis of the hip.	Neither for nor against	Reviewed, Amended
	b. Oral Pharmacotherapy	8.	We suggest offering acetaminophen and/or oral non-steroidal anti-inflammatory drugs for pain associated with osteoarthritis of the hip and knee.	Weak for	Reviewed, New-replaced
		9.	We suggest offering duloxetine as an alternative or adjunctive therapy for patients with an inadequate response or contraindications to acetaminophen or non-steroidal anti-inflammatory drugs for pain associated with osteoarthritis of the knee.	Weak for	Reviewed, New-replaced
		10.	We suggest against initiating opioids (including tramadol) for pain associated with osteoarthritis of the hip and knee. For patients already on long-term opioid therapy, refer to the current VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain.[c]	Weak against	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Pharmacotherapy (cont.)	***c. Intra-articular Injections***	11.	We suggest offering an intra-articular corticosteroid injection for patients with persistent pain due to osteoarthritis of the knee inadequately relieved by other interventions.	Weak for	Reviewed, New-replaced
		12.	We suggest offering an intra-articular, image-guided corticosteroid injection for patients with persistent pain due to osteoarthritis of the hip inadequately relieved by other interventions.	Weak for	Reviewed, New-replaced
		13.	We suggest offering intra-articular viscosupplementation injection(s) for patients with persistent pain due to osteoarthritis of the knee inadequately relieved by other interventions.	Weak for	Reviewed, New-replaced
		14.	We suggest against the use of intra-articular viscosupplementation injection(s) of the hip.	Weak against	Reviewed, New-replaced
Orthobiologics		15.	There is insufficient evidence to recommend for or against platelet-rich plasma injections for the treatment of osteoarthritis of the hip or knee.	Neither for nor against	Reviewed, New-added
		16.	We suggest against stem cell injections (e.g., mesenchymal, adipose-derived, and bone marrow-derived) for the treatment of osteoarthritis of the knee.	Weak against	Reviewed, New-added
Complementary and Integrative Health, Dietary Supplements, and Nutraceuticals		17.	There is insufficient evidence to recommend for or against the use of the following dietary supplements or nutraceuticals for the treatment of osteoarthritis of the hip or knee: • Avocado and soybean extract • Boswellia serrata • Cannabidiol (CBD oil) • Chondroitin • Curcumin (active component of turmeric) • Collagen • Glucosamine • Glucosamine plus chondroitin • Methylsulfonylmethane • Omega-3 fatty acid • Pycnogenol (pine bark) • Rosehip • Traditional Chinese medicine • Vitamin D • Vitamin E • Willow bark extract	Neither for nor against	Reviewed, New-replaced

Topic	Sub-topic	#	Recommendation	Strength[a]	Category[b]
Complementary and Integrative Health, Dietary Supplements, and Nutraceuticals (cont.)		18.	There is insufficient evidence to recommend for or against the use of complementary and integrative health interventions for the treatment of osteoarthritis of the hip or knee, including: • Acupuncture • Massage • Light touch • Meditation • Tai chi • Yoga	Neither for nor against	Reviewed, New-replaced
		19.	There is insufficient evidence to recommend for or against the use of transcutaneous electrical nerve stimulation for the treatment of pain in osteoarthritis of the knee.	Neither for nor against	Reviewed, New-added

[a] For additional information, please refer to the section on Grading Recommendations in the full text OA CPG.

[b] For additional information, please refer to the section on Recommendation Categorization and Appendix A in the full text OA CPG.

[c] See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: https://www.healthquality.va.gov/guidelines/Pain/cot/

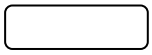
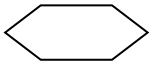
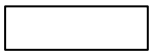
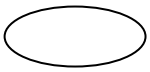
Abbreviations: DoD: Department of Defense; VA: Department of Veterans Affairs

Algorithm

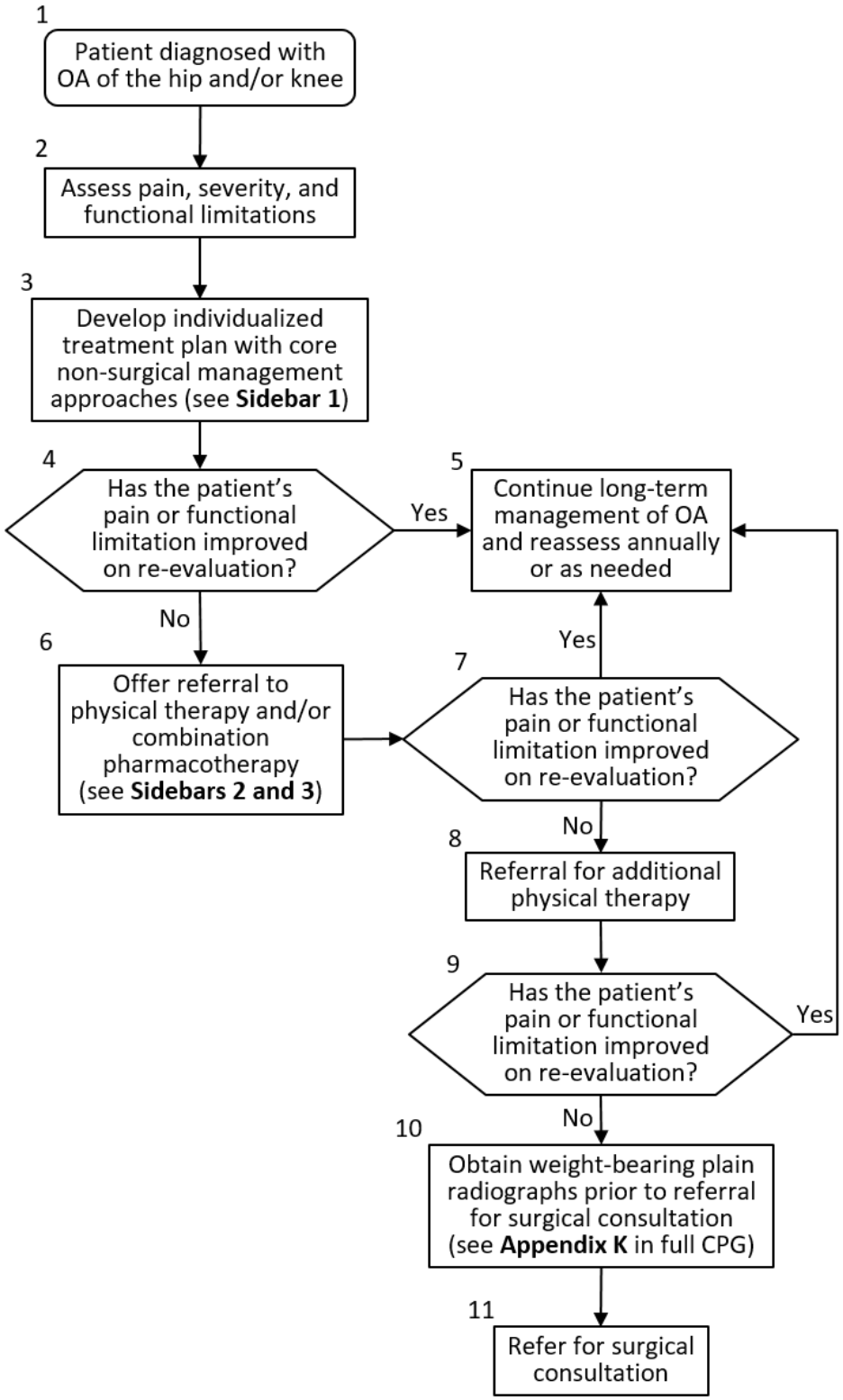
This CPG's algorithm is designed to facilitate understanding of the clinical pathways and decision-making process used in managing patients with OA. This algorithm format represents a simplified flow of the management of patients with OA and helps foster efficient decision making by providers. It includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[2] Sidebars provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered "Yes" or "No"
	Rectangles represent an action in the process of care
	Ovals represent a link to another section within the guideline

Algorithm: Management and Treatment of Osteoarthritis of the Hip and/or the Knee



Abbreviations: OA: osteoarthritis

Sidebar 1: Initial Individualized Treatment Plan

Discuss a self-management program:

- Regular self-directed exercise
- Comprehensive lifestyle intervention for weight reduction: refer to the current VA/DoD CPG for the Management of Adult Overweight and Obesity[a]
- Bracing for OA of the knee (prescription of adaptive equipment such as a cane and knee braces may also be offered in conjunction with the above to help decrease weight burden/provide stability for knee OA)
- Offer referral for physical therapy[b]

Pharmacotherapy:

- Initial treatments:
  - Topical agents for OA of the knee (e.g., NSAIDs, capsaicin)
  - Acetaminophen
  - NSAIDs or COX-2 inhibitors

[a] See the VA/DoD Clinical Practice Guidelines for the Management of Adult Overweight and Obesity. Available at: https://www.healthquality.va.gov/guidelines/CD/obesity

[b] Consider early referral to physical therapy based on pain severity, functional limitations, and adherence

Abbreviations: COX-2: cyclooxygenase-2; CPG: Clinical Practice Guideline; DoD: Department of Defense; NSAIDs: non-steroidal anti-inflammatory drugs; OA: osteoarthritis; VA: Department of Veterans Affairs

Sidebar 2: Second-line and Combination Pharmacotherapy

Second-line or combination treatments:

- Consider combining two initial treatments (see **Sidebar 1**)
- Consider intra-articular CSI for knee and hip OA:
  - CSI should be avoided for the three months preceding joint replacement surgery
  - CSI for the hip should be image-guided
- Duloxetine: consider adding duloxetine as an alternative or adjunct to initial treatments (see **Sidebar 1**)
- Consider intra-articular VSI in patients with inadequately controlled knee pain with core pharmacologic and non-pharmacologic treatments

Abbreviations: CSI: corticosteroid injection; OA: osteoarthritis; VSI: viscosupplementation injections

Sidebar 3: Pharmacotherapy Considerations

- Acetaminophen: because of safety concerns (e.g., hepatotoxicity), the lowest clinically effective dose should be used; in addition, a maximum of 4 g/day should never be exceeded
- NSAIDs or COX-2 inhibitors: should generally be avoided in patients with or at risk for CVD, CKD, and in those patients at risk for serious UGI toxicity
  - Consider adding a PPI or misoprostol in patients at risk for UGI events who require treatment with NSAIDs or COX-2 inhibitors
  - Assessment of renal function should occur and NSAIDs and COX-2 inhibitors should be avoided in patients with eGFR <30 ml/min/1.73 m^2
- Opioids: in most patients, treatment with an opioid should be avoided; for those already on opioids, refer to the current VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain[a]

[a] See the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain. Available at: https://www.healthquality.va.gov/guidelines/Pain/cot/

Abbreviations: CKD: chronic kidney disease; COX-2: cyclooxygenase-2; CVD: cardiovascular disease; DoD: Department of Defense; eGFR: estimated glomerular filtration rate; g: grams; m^2: square meters; min: minute; ml: milliliters; NSAIDs: non-steroidal anti-inflammatory drugs; OA: osteoarthritis; PPI: proton-pump inhibitor; UGI: upper gastrointestinal tract; VA: Department of Veterans Affairs

Scope of the CPG

Regardless of the setting, any patient in the VA and DoD healthcare systems should have access to the interventions recommended in this guideline after taking into consideration the patient's specific circumstances.

Guideline recommendations are intended to be patient-centered. Thus, treatment and care should consider a patient's needs and preferences. Effective, open communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. The use of an empathetic and non-judgmental approach facilitates discussions sensitive to sex, culture, ethnicity, and other considerations. The information that patients are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. Treatment information should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family and caregiver involvement should be considered, if appropriate.

This CPG is designed to assist providers in managing or co-managing adult patients with a confirmed diagnosis of OA of the hip and/or knee. Moreover, this CPG's patient population of interest is those with OA who are eligible for care in the VA and DoD healthcare systems and those in the community who receive care from community-based providers. It includes Veterans as well as deployed and non-deployed active duty Service, Guard, and Reserve Members and their dependents.

Methods

The 2020 VA/DoD OA CPG is an update to the 2014 VA/DoD OA CPG. The methodology used in developing the 2020 CPG follows the *Guideline for Guidelines,*[a] an internal document of the VA and DoD EBPWG that was updated in January 2019.[3] This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from the VA and DoD (known as the Work Group) and the development and submission of an updated OA CPG.

This CPG's Work Group was charged with developing evidence-based clinical practice recommendations and publishing a guideline to be used by primary care providers within the VA/DoD healthcare systems as well as those within the community who treat patients within the VA and DoD. Specifically, the Work Group was responsible for identifying the key questions (KQs) of the most clinical relevance, importance, and interest for the diagnosis and management of patients with OA. The Work Group also provided direction on inclusion and exclusion criteria for the systematic evidence review and assessed the level and quality of the evidence. The amount of scientific evidence that had accumulated since the 2014 VA/DoD OA CPG was also considered when identifying the KQs. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included in the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

[a] See the *Guideline for Guidelines*. Available at: http://www.healthquality.va.gov/policy/index.asp.

The VA Office of Quality and Patient Safety, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command – the DoD proponents for CPGs – identified three clinical leaders as Champions for the 2020 CPG: Anil Krishnamurthy, MD from the VA and MAJ John Cody, MD and COL Jess Edison, MD, from the DoD.

The Lewin Team, including The Lewin Group, Duty First Consulting, ECRI, Sigma Health Consulting, and Anjali Jain Research & Consulting, was contracted by the VA and DoD to support the development of this CPG and conduct the systematic evidence review. The first conference call was held in February 2019, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality and Patient Safety and the DoD Office of Evidence Based Practice, and the Champions. During this call, participants discussed the guideline's scope, the Champions' roles and responsibilities, the project timeline, and the approach for developing specific research questions on which to base a systematic evidence review. The group also identified a list of clinical specialties and areas of expertise that are important and relevant to the management of OA, from which Work Group members were recruited. The specialties and clinical areas of interest included: primary care, nursing, physical therapy, clinical pharmacology, internal medicine, dietetics, orthopedic surgery, rheumatology, family medicine, sports medicine, physical medicine and rehabilitation, and pain management.

The guideline development process for the 2020 CPG update consisted of:

1. Formulating and prioritizing KQs and defining critical outcomes
2. Convening a patient focus group
3. Conducting the systematic evidence review
4. Convening a face-to-face meeting with the CPG Champions and Work Group members to develop recommendations
5. Drafting and submitting a final CPG on the management of OA to the VA/DoD EBPWG

A detailed description of these tasks is available in Appendix A in the full text OA CPG.

The Work Group used the GRADE system to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:[4]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Patient or provider values and preferences
- Other implications, as appropriate, e.g.:
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations

Additional information regarding these domains can be found in Appendix A in the full text OA CPG.

Using these four domains, the Work Group determined the relative strength of each recommendation ("Strong" or "Weak"). Generally, a "Strong" recommendation indicates high confidence in the quality of the available scientific evidence, a clear difference in magnitude between the benefits and harms of an intervention, similar patient or provider values and preferences, and understood influence of other implications (e.g., resource use, feasibility). Generally, if the Work Group has less confidence after the assessment across these domains and believes that additional evidence may change the recommendation, it assigns a "Weak" recommendation. It is important to note that the GRADE terminology used to indicate the assessment across the four domains (i.e., "Strong" versus "Weak") should not be confused with the clinical importance of the recommendation. A "Weak" recommendation may still be important to the clinical care of a patient with OA.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a therapy or preventive measure. This can occur when there is an absence of studies on a topic that met the systematic evidence review inclusion criteria, studies included in the systematic evidence review report conflicting results, or studies included in the systematic evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the relative strength of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend offering this option …")
- Weak for (or "We suggest offering this option …")
- No recommendation for or against (or "There is insufficient evidence …")
- Weak against (or "We suggest not offering this option …")
- Strong against (or "We recommend against offering this option …")

The rating of each recommendation made in the 2020 CPG can be found under Recommendations.

Evidence-based CPGs should be current, which typically requires revisions of previous guidelines based on new evidence or as scheduled and subject to time-based expirations.[5] The OA CPG Work Group largely focused on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Work Group considered, without complete review of the relevant evidence, the current applicability of other recommendations that were included in the 2014 VA/DoD OA CPG, subject to evolving practice in today's environment. Accordingly, some recommendations found in the 2014 VA/DoD OA CPG do not appear in this updated CPG.

A set of recommendation categories was adapted from those used by England's National Institute for Health and Care Excellence (NICE).[6,7] These categories, along with their corresponding definitions, were used to account for the various ways in which older recommendations could have been updated. In brief, the categories considered whether the evidence that related to a recommendation was systematically reviewed, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current care environment and within the scope of the CPG. Additional information regarding these categories and their definitions can be found in the Recommendation

Categorization section of the full text OA CPG. The categories for the recommendations carried forward from the 2014 VA/DoD OA CPG are noted in Appendix D in the full text OA CPG.

Recommendation Categories and Definitions*

Evidence Reviewed*	Recommendation Category	Definition
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from previous CPG that has been removed because it was deemed out of scope for the updated CPG

* Adapted from the NICE guideline manual (2012) [7] and Garcia et al. (2014) [6]

Abbreviation: CPG: clinical practice guideline

Guideline Work Group

Organization	Names*
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* Additional contributor contact information is available in Appendix H in the full text OA CPG.

Patient-centered Care

VA/DoD CPGs encourage providers to use a patient-centered care (PCC) approach that is individualized based on patient needs, characteristics, and preferences. Regardless of the setting, all patients in the healthcare system should be able to access evidence-based care appropriate to their specific needs or condition. When properly executed, PCC may decrease patient anxiety, increase trust in providers, and improve treatment adherence.[8,9] Improved patient-provider communication and a PCC approach conveys openness and supports disclosure of current and future concerns. As part of the PCC approach, providers should ask each patient about any concerns he or she has or barriers to high-quality care he or she has experienced.

Shared Decision Making

Throughout this VA/DoD CPG, the authors encourage providers to focus on shared decision making (SDM). The SDM model was introduced in *Crossing the Quality Chasm*, an Institute of Medicine (now called the National Academy of Medicine) report, in 2001.[10] It is readily apparent that patients, together with their providers, make decisions regarding their plan of care and management options. Patients with OA require enough information and time to be able to make informed decisions. Providers must be adept at presenting information to their patients regarding treatments, expected outcomes, potential harms, and levels and/or locations of care. Providers are encouraged to use SDM to individualize treatment goals and plans based on patient capabilities, needs, goals, and preferences.

Pharmacotherapy Considerations

Pharmacologic Agents for the Treatment of OA[a,b] and their Selected Characteristics

Type	Generic Name	Brand	Formulations	Usual Starting Dose	Max Single Dose	Frequency	Notes
COX-2 Selective NSAIDs[c]	Celecoxib	Celebrex®, Elyxyb™/ Generics	C, Soln	100 – 200 mg	200 mg	Once or twice daily	Max 200 mg/day for OA
Partially Selective NSAIDs	Etodolac	Generics/ XR	C, T, T (XR)	200 mg (IR) 400 mg (XR)	IR 400 mg XR 1,000 mg	IR 2 – 4 times daily XR once daily	IR up to 1,000 mg daily XR up to 1,200 mg daily
	Meloxicam	Mobic®, Vivlodex®, Qmiiz® ODT/ Generics	C, T, ODT	Mobic, ODT 7.5 mg Vivlodex 5 – 10 mg	15 mg Vivlodex 10 mg	Once daily	Max dose is 15 mg daily Max dose is 10 mg (Vivlodex)
	Nabumetone	Generics	T	1,000 mg	2,000 mg	Once daily	May divide twice daily; max dose is 2,000 mg daily
Non-aspirin, Non-selective NSAIDs	Diclofenac potassium/ sodium	Generics	T, C, Soln	50 mg	75 mg	2 – 3 times daily	Max total daily dose is 150 mg; may divide up to 3 times daily
	Diclofenac sodium (XR)	Generics	T (XR)	100 mg	100 mg	Once daily	Max dose is 100 mg daily
	Fenoprofen	Nalfon®/ Generics	C, T	200 – 400 mg	600 mg	3 – 4 times daily	Higher renal risk; total daily dose should not exceed 3,200 mg
	Flurbiprofen	Ansaid®/ Generics	T	50 – 100 mg	100 mg	Twice daily	Max daily dose is 300 mg
	Ibuprofen	Generics	T, C, Susp	400 mg	800 mg	3 – 4 times daily	Max dose in chronic pain is 2,400 mg daily

[a] Refer to VA or DoD formularies for availability of agents or comparable agents. The list of available formulations may not be all-inclusive or may change with time as will generic availability. Combination products are not included in this figure.

[b] For additional details on warnings and precautions, drug-drug interactions, adverse events, dosing considerations and use in special populations, etc., refer to the prescribing information for the individual agents of interest.

[c] All NSAIDs have the potential to increase the risk for cardiovascular events and therefore should be used at the lowest effective dose for the shortest possible duration. Use with caution or avoid use of NSAIDs in patients with renal impairment, history of gastrointestinal bleeding, uncontrolled hypertension, congestive heart failure, advanced liver diseases, at high risk for or with known CVD, patients receiving anticoagulants or systemic corticosteroids, etc.

Type	Generic Name	Brand	Formulations	Usual Starting Dose	Max Single Dose	Frequency	Notes
Non-aspirin, Non-selective NSAIDs (cont.)	Indomethacin	Indocin® SR/ Tivorbex®/ Generics	C, C (XR), Supp, Susp	25 – 50 mg (IR) 75 mg (SR)	50 mg 75 mg	2 – 3 times daily 1 – 2 times daily	May divide up to 4 times daily (IR); max dose is 150 mg daily
	Ketoprofen IR	Generics	C, OTC T	50 mg	75 mg	3 – 4 times daily	Max dose is 300 mg daily
	Ketoprofen ER	Generics	C	200 mg	200 mg	Once daily	Max dose is 200 mg daily
	Meclofenamate sodium	Generics	C	50 mg	100 mg	4 times daily	May give 3 times daily; max dose is 400 mg daily
	Naproxen	Naprosyn®/ Generics	T, Susp	500 mg	500 mg	Twice daily	Max dose in chronic pain is 1,000 mg daily
		EC-Naprosyn®	T – EC (XR)	375 – 500 mg (EC)	500 mg	Twice daily	Max dose in chronic pain is 1,000 mg daily
	Naproxen sodium	Anaprox® DS/ Generics	T	550 mg	550 mg	Twice daily	Max dose in chronic pain is 1,100 mg daily
	Oxaprozin	Daypro®/ Generics	T	1,200 mg	1,200 mg	Once daily	Max dose is 1,200 mg daily
	Piroxicam	Feldene®/ Generics	C	20 mg	20 mg	Once daily	Max dose is 20 mg daily; may divide twice daily
	Sulindac	Generics	T	150 – 200 mg	200 mg	Twice daily	Max dose is 400 mg daily
	Tolmetin	Generics	T, C	400 – 600 mg	600 mg	3 times daily	Max dose is 1,800 mg daily
Non-acetylated Salicylates	Diflunisal	Generics only	T	250 – 500 mg	1,000 mg	2 – 3 times daily	Max dose is 1,500 mg daily
	Choline magnesium trisalicylate	Generics	T, Liquid	750 mg	1,500 mg	2 – 3 times daily	Max dose is 3,000 mg daily
	Salsalate	Generics	T	500 – 750 mg	1,000 mg	2 – 3 times daily	May increase to 3 times daily; max dose is 3,000 mg daily

Type	Generic Name	Brand	Formulations	Usual Starting Dose	Max Single Dose	Frequency	Notes
Acetaminophen	Acetaminophen	Generics	C, T, T (XR), Supp, Susp	650 mg	1,300 mg	3 – 4 times daily (max dose 2 – 4 g daily, depending upon the patient)	Max 3,000 mg/day in most patients. Consider lower total daily doses (e.g., 2 – 3 g) in elderly patients or those with heavy use of alcohol. In carefully selected patients, the max dose can be increased to no more than 4,000 mg/day. The total daily dose of acetaminophen from all sources (single and multiple ingredient products) must not exceed 4,000 mg/day.
Topical Therapies	Capsaicin	Generics	Cream, Gel, Liquid, Lotion Varied concentrations: 0.025 – 0.075%	–	–	Apply 3 – 4 times daily	Patients may experience burning/tingling sensation in the first few days of use; instruct patients to wash their hands with soap and water after application
	Diclofenac	Voltaren®	Gel 1%	2 – 4 g	4 g	Four times daily	Max dose is 32 g daily. Max of 16 g per lower extremity joint and 8 g per upper extremity joint daily. Single dose of 4 g applied to a lower extremity joint while 2 g applied to an upper extremity joint.
		Pennsaid®	Soln 2%	2 pumps (40 mg)	2 pumps (40 mg)	Twice daily	Spread the solution evenly around the front, back, and sides of the knee; local skin irritation
		Flector®	Patch 1.3%	1 patch (180 mg)	1 patch (180 mg)	Twice daily	Not FDA approved for OA; local skin irritation
		Solaraze®	Gel 3%	–	–	Twice daily	Not FDA approved for OA; local skin irritation

Type	Generic Name	Brand	Formulations	Usual Starting Dose	Max Single Dose	Frequency	Notes
Other Therapies	Duloxetine	Cymbalta®/ Generics	Delayed release C	30 mg for 1 week, increase to 60 mg once daily	60 mg	Once daily	Max dose is 60 mg daily; higher doses are not associated with improved outcomes, but a higher rate of adverse events is reported. Avoid in end-stage renal disease or CrCl <30 ml/min or in patients with substantial alcohol intake. Refer to prescribing information for other details including contraindications, drug-drug interactions, gradually reducing dose if withdrawing treatment, warnings and precautions, and adverse events.

Abbreviations: C: capsule; COX-2: cyclooxygenase-2; CrCl: creatinine clearance; CVD: cardiovascular disease; EC: enteric-coated; ER: extended release; FDA: Food and Drug Administration; g: grams; IR: immediate release; mg: milligrams; min: minute; ml: milliliters; NSAIDs: non-steroidal anti-inflammatory drugs; OA: osteoarthritis; ODT: oral disintegrating tablet; OTC: over-the-counter; Soln: solution; SR: sustained release; Supp: suppository; Susp: suspension; T: tablet; XR: extended release

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Access to the full guideline and additional resources are available at the following link:

https://www.healthquality.va.gov/guidelines/cd/oa/