

Classification Criteria for Early-stage Symptomatic Knee OA Status Report on the OARSI Initiative - September 2023

There are many reasons why efforts to change the course of osteoarthritis (OA) have failed, one of them that we have typically targeted patients in later stages of the disease. Intervening earlier in the disease process may provide a more permissive environment for changing the course of the disease to prevent the downstream consequences of chronic pain, depression, joint destruction, disability, and development of co-morbidities. The importance of identifying and treating early-stage disease is recognized in other chronic conditions such as diabetes, cardiovascular disease, Alzheimer's disease, and rheumatoid arthritis.

The development of knee OA represents a continuum. During the early-stage, patients may experience intermittent symptoms and minimal or no radiographic changes. This stage may offer a window of opportunity for interventions to slow or arrest the OA disease process before structural and biomechanical derangement become too severe and/or pain sensitization occurs. No widely accepted, validated criteria exist to define symptomatic early-stage knee OA. Classification criteria are standardized definitions intended to create well-defined, relatively homogeneous cohorts of patients for clinical research; they do not equal diagnostic criteria.

OARSI Initiative, workgroup structure, funding

In December 2021, the Osteoarthritis Research Society International (OARSI) Board of Directors voted to adopt an initiative to develop classification criteria for Early-stage Symptomatic Knee OA (EsSKOA). Initial funding was provided by OARSI in 2021, followed in 2023 by generous sponsorships from Grünenthal and Viatrix.



Work plan and where are we now?

The project is currently completing *Phase 1*. A survey of the OARSI membership found that knee symptoms and history were considered most helpful in determining if a patient has early-stage knee OA. A scoping review of the literature identified that “early OA” in most studies included people with persistent knee symptoms, and/or K&L radiographic grade 2, both of which suggest established OA. A qualitative study of people with knee OA about their pain experience found that initial symptoms are insidious, slow to progress, and generally explained away. This work informed the ongoing international Delphi Survey of knee OA clinicians and researchers.



What's next?

Phase 2 of this initiative will generate data to inform criteria development. An environmental scan will be conducted of existing datasets and ongoing studies that might be sources of data for the required analyses, though we anticipate primary data collection will be required. Through this work, we will identify the factors that increase or decrease the likelihood of an individual having “EsSKOA”.

Phase 3 will identify an Expert Panel of individuals who have clinical experience regarding the assessment, diagnosis and management of people presenting with undifferentiated knee symptoms. Panel members will commit to several tasks, including submission of cases from their practice with information about candidate items, review data from the prior phases, and participation in the multicriteria decision analysis process. We will establish consensus on the “gold standard” for EsSKOA. Consensus is also required on the definition of late-stage or established knee OA. Panel members will then be asked to complete case report forms capturing candidate items and other relevant information for patients in their practice who present with undifferentiated knee symptoms. They will be asked the probability, in their opinion, that the patient has EsSKOA based on the agreed construct. We will select a sub-sample of 30 cases, with a range of probabilities from 0 to 100%.

The expert panel will review the 30 paper cases and rank them in order of probability of EsSKOA; this exercise serves as the basis for identifying key positive and negative features that influenced experts’ rankings. Key inclusion, exclusion, and sufficient criteria will be defined. Through multicriteria decision analysis we will identify the features with the greatest influence on clinicians’ probability determinations and, in turn, the relative weights of the items. The total sum of the relative weights is scaled to provide a probability score ranging from 0-100. We then return to the paper cases to identify the threshold at which EsSKOA should be defined, typically determined through analysis of the score associated with the paper cases deemed to be appropriate vs. inappropriate for enrollment into a trial for EsSKOA to prevent progression to late-stage OA. At the end of Phase 3, we will have preliminary criteria ready for refinement and validation in independent datasets in *Phase 4*.

Publications to date that have resulted from the Initiative

Hawker GA, et al. What an earlier recognition of osteoarthritis can do for OA prevention. *Osteoarthritis Cartilage* 2021;29:1632. <https://doi.org/10.1016/j.joca.2021.08.007>

Liew J, et al. A scoping review of how early-stage osteoarthritis has been defined. *Osteoarthritis Cartilage* 2023;31:1234. <https://doi.org/10.1016/j.joca.2023.04.015>

Mahmoudian A, et al. Timing is everything. Towards classification criteria for Early-stage Symptomatic Knee OA. Manuscript submitted *Osteoarthritis Cartilage*.

King L, et al. “You Don’t Put It Down to Arthritis”: A Qualitative Study of the First Symptoms Recalled by Individuals with Knee Osteoarthritis. Draft, in preparation to submit to *Osteoarthritis Cartilage*.