Classification Criteria for Symptomatic Knee OA at an Early Structural Stage (EsSKOA)

OARSI Initiative Status Report – *October 2025*

Dear Members of the EsSKOA Advisory Committee and Initiative Sponsors,

We are now reaching the end of the third year of funding for this initiative to develop and test classification criteria for **symptomatic knee OA at an early structural stage** (EsSKOA). As a reminder, our goal is to expand the construct of symptomatic knee OA to include those earlier in the course of disease who have not yet developed established radiographic OA.

We are guided by the established four-phase American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) methodology for classification criteria development: 1) Generating a list of candidate items (variables) that should be considered for classification. 2) Data acquisition and analyses to examine the ability of the candidate items to discriminate the condition of interest from other conditions (mimickers). 3) Establishing the criteria, weights and provisional classification threshold through an evidence-informed consensus approach, including multi-criteria decision analysis; and 4) Assessing the criteria's performance characteristics in an independent sample.

The past three years have been tremendously thought-provoking. There continues to be much debate about the construct 'early OA'. We thought it would be useful to provide you with a summary of our responses to frequently asked questions regarding the EsSKOA initiative.

Q1. Why focus on people with symptoms – why not just 'early OA'?

In the early stages of OA, people may have knee symptoms with little or no OA structural abnormalities on radiographs. While not all these people will progress radiographically, those with symptoms deserve care. Furthermore, enrollment of people with symptomatic knee OA into DMOAD clinical trials earlier in the disease course may enhance the likelihood of trial success. Our goal is not to define 'pre-clinical' OA, i.e., people with imaging markers or biochemical markers indicating an increased risk for developing OA, but without symptoms. Regulatory approval of disease-modifying therapies requires evidence of improvement in patient-relevant outcomes. Thus, the effort to develop classification criteria currently focuses on those with symptoms rather than asymptomatic individuals with risk factors for knee OA. After the EsSKOA criteria are developed, studies will be able to identify risk factors for progression (symptomatic, structural or other biomarkers) and risk factors for development of incident EsSKOA.

Q2. How will 'structural stage' be defined?

Structural stage will be defined using weight-bearing radiography of the tibiofemoral and patellofemoral compartments of the knee. Radiography is simple, widely accepted, and available in most countries. Radiography has many limitations, but it is still a proxy for structural OA stage.

Q3. Will fulfillment of the criteria require a minimum level of knee symptom severity?

In developing the classification criteria, many aspects of the symptoms, including duration and severity, are being considered. We do not yet know what the criteria will look like. Regardless, this does not preclude setting a threshold level requirement for a specific trial to reduce knee OA symptoms. Assuming regulatory approval of

the EsSKOA criteria as an indication, trial inclusion would be based on fulfilling the EsSKOA criteria *and* possibly additional specific criteria, as for any clinical trial. For example, a DMOAD trial would likely want to recruit individuals who meet the EsSKOA criteria and have identified risk factors for progression (to be determined) or a specific mechanistic phenotype, e.g. certain clinical characteristics or an endotype. A symptom treatment trial may recruit individuals with EsSKOA who have at least X/10 on a pain numeric rating scale for there to be opportunity to improve.

Q4. Will MRI findings be included in the criteria?

Findings on MRI are among our potential candidate items and are being considered in criteria development. However, we must also consider the feasibility of requiring MRI, based on costs and availability. If MRI features are determined to be useful in discriminating EsSKOA from mimickers, they can be included in the criteria as optional measures since the criteria methods allow for computation of a score in the absence of data regarding certain features. That's how it's been handled in other criteria for advanced imaging that may not be feasible to perform universally.

The above information is currently being compiled into an infographic for our website and an abstract for submission to the upcoming OARSI and EULAR conferences on the EsSKOA construct.

Update on Team Composition

In the past year, we revisited the roles and responsibilities of the Methods Working Group and Steering Committee to enhance clarity and reduce duplication of efforts. As a result, Dr. Ida K. Haugen now chairs the EsSKOA Steering Committee and Dr. Gillian Hawker now co-chairs the EsSKOA Methods Working Group with Dr. Tuhina Neogi. In June, we said goodbye to Project Manager Ngozi Ekeleme. On October 14th 2025, we welcomed Arin Deveci to the Project Manager role. We wish to thank Ian Stanaitis for his support during this transition! Finally, we have recruited two Patient Research Partners (PRPs) to the team: Andrea Hampson (Toronto, Canada) and Janny Kok (Rotterdam, Netherlands).

Summary of Progress to Date and Plans for 2026[1]

In **Phase I**, we identified **over 70 candidate items** that our community feels should be considered in classification criteria development (King et al, 2025) and identified **key mimic conditions** that need to be differentiated from EsSKOA (mimic conditions: traumatic collateral ligament strain, patellofemoral pain syndrome, patellar tendonitis, meniscal tear, bursitis, undiagnosed immune-mediated inflammatory arthritis, undiagnosed crystal-induced inflammatory arthritis, Baker's cyst [Hawker et al, 2025]).

We are currently mid-way through **Phase 2**. The goal here is to determine the usefulness of the candidate items, alone or in combination, to discriminate individuals with EsSKOA from those with a mimic condition (primary aim). We also hope to better understand if and how the candidate items distinguish people with EsSKOA from those with established radiographic knee OA (secondary aim).

[1] Please note that additional information regarding the initiative and publications / presentations may be found on the OARSI website at https://oarsi.org/research/member-update-esskoa-initiative

Phase 2 requires data on the candidate items from participants with possible EsSKOA and mimic conditions (primary aim). We are obtaining this information through two concurrent processes: **a)** primary data collection; and **b)** secondary data analysis of existing cohorts.

Primary Data Collection:

An operating grant has been submitted to the Canadian Institutes of Health Research, CIHR, in September 2025, to enable recruitment and assessment of ~600 individuals (200 each with EsSKOA, a mimic condition or established knee OA) in the province of Ontario, Canada. Half of the recruits will be held for criteria validation in Phase 4. Grant results are expected in January; if successful, funding will begin April 1, 2026. *We require 100 participants with EsSKOA and 100 with a mimic condition to commence Phase 2 analysis.*

Data will be collected using standardized patient and expert clinician assessments and laboratory and imaging tests. Expert clinician assessors will assign a 'probable case status' to each participant following the assessment. Once all candidate item information is obtained, it will be summarized and subjected to a blinded adjudication process by expert clinicians who will assign the 'gold standard case status' (EsSKOA versus mimic condition – dependent variable). Data analyses will then examine the association of candidate items (independent variables) to gold standard case status (dependent variable).

We are anxious to begin recruitment. Study materials have been finalized and questionnaires pilot tested. The adjudication protocol and members of the adjudication team are being formalized. The analysis plan has been developed. Ethics approval is pending.

Secondary Data Abstraction:

An environmental scan of existing datasets identified 19 cohorts for review. Their data code books, inclusion/exclusion criteria, etc. were searched to determine potential availability of information on our candidate items and participants with EsSKOA, established OA, and mimic conditions. Most cohorts lacked the required information for the primary study aim. The Incident OAI cohort was identified as having the highest potential for usefulness in this initiative. Before proceeding, there was agreement that a pilot study should be undertaken to assess the prevalence of participants with possible EsSKOA and mimic conditions. Should this pilot indicate sufficient information on candidate items in the two populations, the information will be summarized for each study subject and subjected to the same blinded adjudication process to determine gold standard case status.

Results will inform **Phase 3**, criteria elucidation and confirmation of the target population in which the criteria will be applied.

Budget Update

We are extremely grateful to sponsors Viatris Inc. and Grünenthal, each donating $90,000 USD total in grant funding to support this initiative. We are also grateful for the OARSI Board's funding of $30,000 supporting 0.5 FTE for a research fellow in the start-up phase.

A summary of funds spent to date and proposed use of remaining funds is below. In brief, expenses were $15,768 in 2023, $30,667 in 2024, and $41,845 in 2025 (expected to December 31). These were for project

manager support and to cover the costs of knowledge dissemination, including abstract submission, poster printing and manuscript publication.

There is $91,720 remaining. From this, we must support our Project Manager (salary + benefits + annual cost of living raise = $40,000) and have budgeted $1,500 for costs of publication/knowledge dissemination and $900 to compensate our PRPs for their time and efforts. This leaves $49,320 remaining[2]. We propose to use the latter in 2026 to fund primary data collection *during point of care* by two team members (Lauren King, Toronto, and Tom Appleton, London, Ontario, Canada). Should external funding be received to support data collection, we will use the existing funding to enable primary recruitment beyond Canada.

Timeline

We estimate that full recruitment of the ~600 study subjects required for Phases 2-4 will require two to two and a half years, depending on the number of sites that are willing and able to participate and of course procurement of the necessary funds. We are optimistic that our OARSI community will be keen to participate.

We are aiming for the Expert Panel discussion to be held in conjunction with the 2027 OARSI Congress.

Publications

2025

King LK, Mahmoudian A, Liew JW, Wang Q, Stanaitis I, Schiphof D, Callahan LF, Hunter DJ, Appleton CT, Turkiewicz A, Englund M, Lohmander LS, Haugen IK, Hawker GA, Neogi T, Runhaar J; OARSI Early-stage Symptomatic Knee Osteoarthritis Initiative. Elucidating the initial symptoms and experiences of knee osteoarthritis: An international patient survey. Osteoarthritis Cartilage. 2025;33(9):1147-1152. doi: 10.1016/j.joca.2025.05.008.

Hawker GA, King LK, Liew JW, Wang Q, Mahmoudian A, Jansen NEJ, Stanaitis I, Berenbaum F, Das S, Ding C, Emery CA, Filbay SR, Hochberg MC, Ishijima M, Kloppenburg M, Lane NE, Losina E, Mobasheri A, Runhaar J, Appleton CT, Turkiewicz A, Englund M, Lohmander LS, Haugen IK, Neogi T; OARSI Early-stage Symptomatic Knee Osteoarthritis Initiative. OARSI initiative to develop classification criteria for early-stage symptomatic knee OA (EsSKOA): What conditions should be considered in the differential diagnosis of EsSKOA? Osteoarthritis Cartilage. 2025 Sep;33(9):1141-1146. doi: 10.1016/j.joca.2025.05.005.

King LK, Liew JW, Mahmoudian A, Wang Q, Jansen NEJ, Stanaitis I, Hung V, Berenbaum F, Das S, Ding C, Emery CA, Filbay SR, Hochberg MC, Ishijima M, Kloppenburg M, Lane NE, Losina E, Mobasheri A, Turkiewicz A, Runhaar J, Haugen IK, Appleton CT, Lohmander LS, Englund M, Neogi T, Hawker GA; OARSI Early-stage Symptomatic Knee Osteoarthritis Initiative. Multi-centre modified Delphi exercise to identify candidate items for classifying early-stage symptomatic knee osteoarthritis. Osteoarthritis Cartilage. 2025;33(1):155-165. doi: 10.1016/j.joca.2024.10.016.

[2] We had proposed to begin data collection in 2025, but since we are delayed we have not used this (thus: 0 for 2025 actual). Data collection for the remaining participants will require new funding; we expect to use all remaining Viatris and Grunenthal funding in 2026.

Mahmoudian A, King LK, Liew JW, Wang Q, Berenbaum F, Das S, Ding C, Emery CA, Filbay SR, Hochberg MC, Ishijima M, Kloppenburg M, Lane NE, Losina E, Mobasheri A, Appleton CT, Englund M, Lohmander LS, Runhaar J, Turkiewicz A, Hawker GA, Neogi T, Haugen IK; OARSI Early-stage Symptomatic Knee Osteoarthritis Initiative. Reframing Early-stage Symptomatic Knee Osteoarthritis (EsSKOA): A Strategic Lens for Trial Design. Osteoarthritis Cartilage, *Under Review*.

2024

Mahmoudian A, King LK, Liew JW, Wang Q, Appleton CT, Englund M, Haugen IK, Lohmander LS, Runhaar J, Turkiewicz A, Neogi T, Hawker GA; OARSI Early-stage Symptomatic Knee Osteoarthritis Initiative. Timing is everything: Towards classification criteria for early-stage symptomatic knee osteoarthritis. Osteoarthritis Cartilage. 2024;32(6):649-653. doi: 10.1016/j.joca.2024.02.888.

2023

King LK, Mahmoudian A, Waugh EJ, Stanaitis I, Gomes M, Hung V, MacKay C, Liew JW, Wang Q, Turkiewicz A, Haugen IK, Appleton CT, Lohmander S, Englund M, Runhaar J, Neogi T, Hawker GA; OARSI Early-stage Symptomatic Knee Osteoarthritis Initiative. "You don't put it down to arthritis": A qualitative study of the first symptoms recalled by individuals with knee osteoarthritis. Osteoarthr Cartil Open. 2023;6(1):100428. doi: 10.1016/j.ocarto.2023.100428.

Liew JW, King LK, Mahmoudian A, Wang Q, Atkinson HF, Flynn DB, Appleton CT, Englund M, Haugen IK, Lohmander LS, Runhaar J, Neogi T, Hawker G; OARSI Early Osteoarthritis Classification Criteria Task Force. A scoping review of how early-stage knee osteoarthritis has been defined. Osteoarthritis Cartilage. 2023;31(9):1234-1241. doi: 10.1016/j.joca.2023.04.015.

Pre-Initiative Publication

Hawker GA, Lohmander LS. What an earlier recognition of osteoarthritis can do for OA prevention. Osteoarthritis Cartilage 2021;29:1632-1634. doi: 10.1016/j.joca.2021.08.007.

Presentations

Title	Presenter(s)	Conference/Location	Date
Classification Criteria for Early-stage Symptomatic Knee OA —the why and the how and where are we now	Stefan Lohmander (Invited)	International Workshop on Osteoarthritis Imaging; Munich, Germany	*Future* – June 2026
ICRS Meets OARSI: Update of the Early-Stage Symptomatic Knee OA Classification Criteria Initiative	Armaghan Mahmoudian, Jean Liew (Invited)	International Cartilage Regeneration & Joint Preservation Society (ICRS) World Congress; Boston, MA, USA	13-Oct-2025
EsSKOA Update	Armaghan Mahmoudian, Jean Liew, Lauren King (Invited)	OARSI Live Webinar (Virtual) https://oarsi.org/education/oarsi-live-webinar-series	30-Sep-2025
Early Osteoarthritis Classification Criteria	Lauren King (Invited)	Symposium on Latest Innovations in Osteoarthritis; Toronto, Canada	16-Sep-2025

Classification Criteria of Early-stage Symptomatic Knee Osteoarthritis: Updates of the OARSI Initiative Presented as part of the ESCEO-OARSI Joint Symposium: Early knee osteoarthritis: Classification criteria for research and diagnostic criteria for clinical use (Chair: Martin Englund)	Armaghan Mahmoudian (Invited)	World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases; Rome, Italy	12-Apr-2025
Opportunities and Challenges of Early Knee Osteoarthritis	Lauren King (Invited)	Osteoarthritis Action Alliance - Lunch & Learn (Virtual) YouTube Recording	11-Dec-2024
Defining Early-Stage Symptomatic Knee Osteoarthritis – an OARSI Initiative Concurrent Session 1: Risk Factors, Prevention, and Early Disease	Lauren King, Armaghan Mahmoudian, Jean Liew (Invited)	OARSI 2024 World Congress on Osteoarthritis; Vienna, Austria	19-Apr-2024
Osteoarthritis: Highlights From the Past Informing the Future Rheumatology Research Foundation Roy Altman Memorial Lecture	Tuhina Neogi (Invited)	ACR Convergence 2023; San Diego, CA, USA	14-Nov-2023
Timing is everything! Towards classification criteria for Early-stage Symptomatic Knee OA	Armaghan Mahmoudian (Invited)	Asian Conference of Cartilage and Osteoarthritis 2023; Seoul, South Korea	20-Oct-2023