Washington State Health Care Authority

Final Key Questions and Background

Treatments for Patients with Chondral Defects of the Knee

Background

Chondral defects refer to damage of the surface cartilage lining the bones where they connect, or articular cartilage. Chondral defects can cause pain, reduce function, and may decrease quality of life as much as severe osteoarthritis.[1] Articular cartilage has a limited ability to regenerate and over time is associated with scarring, progressive cartilage degeneration, and increased risk for osteoarthritis.[2,3] One treatment for chondral defects is debridement of damaged cartilage tissue, although this treatment does not replace the cartilage. Chondral restoration procedures aim to replace damaged tissue with healthier cartilage.

This health technology assessment (HTA) reviews the efficacy, safety, and cost-effectiveness of selected chondral defect restoration procedures of the knee, including microfracture, drilling, osteochondral autologous transplantation (OATS), osteochondral allograft transplantation (OCA), and matrix-induced autologous chondrocyte implantation (MACI).

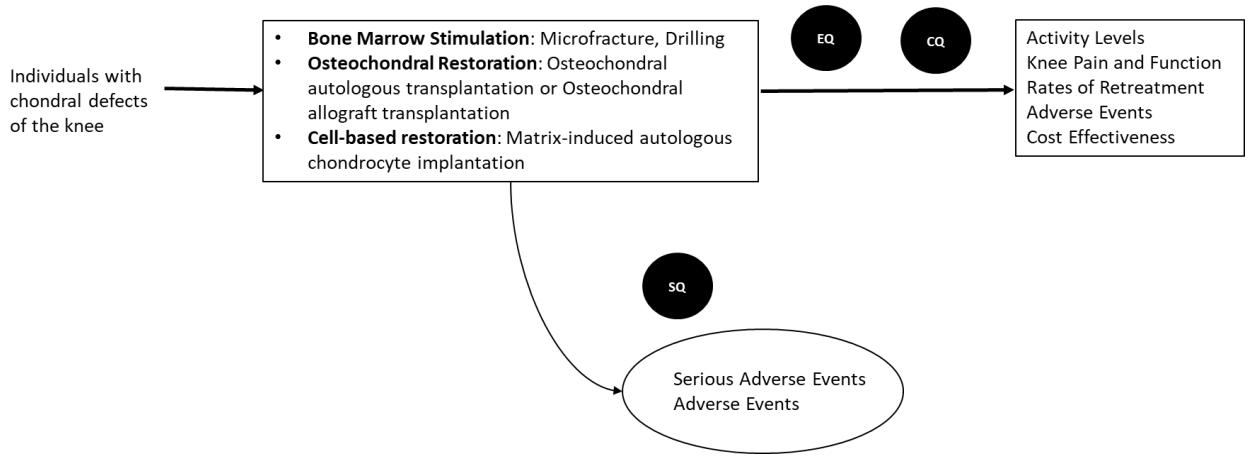
Policy Context

The State of Washington Health Care Authority selected treatment of chondral defects of the knee for a HTA because of medium concerns of efficacy and high concerns for safety and cost.

Scope of this HTA

The analytic framework (***Figure 1***), research questions, and key study selection criteria (***Table 1***) are listed in this section.

Figure 1. Analytic Framework Depicting Scope of This Health Technology Assessment



Abbreviations: CQ = cost question; EQ = efficacy question; SQ = safety question

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Research Questions

Efficacy Question. What is the efficacy of the following cartilage restoration treatments for chondral defects of the knee?

- Bone marrow stimulation procedures
  - Microfracture
  - Drilling
- Osteochondral restoration
  - Osteochondral autologous transplantation (OATS)
  - Osteochondral allograft transplantation (OCA)
- Cell-based restoration
  - Matrix-induced autologous chondrocyte implantation (MACI)

Safety Question. What are the harms associated with treatments for chondral defects of the knee listed above?

Cost Question. What is the cost-effectiveness of cartilage restoration treatments for chondral defects of the knee listed above?

Study Selection Criteria

Table 1 provides the study selection criteria we will use to include studies in the HTA and are organized by population, intervention, comparator, outcomes, timing, setting, and study design (PICOTS) criteria.

Table 1. Proposed Population, Intervention, Comparator, Outcome, Timing, and Setting (PICOTS) for Health Technology Assessment

PICOTS	Include	Exclude
Population	• Individuals with a focal defect of the articular cartilage of the knee—specifically of the femur, tibia, or patella • Any age	• Individuals receiving a restorative procedure for a chondral defect in a joint other than the knee • Studies conducted in animals, *in vitro*, or *in silico*
Intervention	• Microfracture surgery (including drilling) • Osteochondral autologous transplantation (OATS) • Osteochondral allograft transplantation (OCA) • Matrix-induced autologous chondrocyte implantation (MACI; 3rd-generation ACI) Interventions that use biologic or synthetic materials will be included if the materials are FDA-approved or there is evidence that they are in advanced commercial development for the US (e.g. Phase 3 trials; FDA-designation as a Regenerative Medicine Advanced Therapy (RMAT), Fast Track, or	• Other treatments not specifically listed as included • Procedures using materials that are not in advanced commercial developmentAutologous chondrocyte implantation (1st and 2nd generation ACI)

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PICOTS	Include	Exclude
	Breakthrough Therapy candidate (e.g.Prochondrix CR [AlloSource], Novocart 3D® [Aesculap Biologics])	
Comparator	For Microfracture: • Chondroplasty • Knee replacement (total or partial) • Sham surgery • Non-surgical interventions or conservative therapy (e.g., physical therapy, injections, oral analgesics) For OATS, OCA: • Microfracture or drilling • MACI • Chondroplasty • Knee replacement (total or partial) • Sham surgery • Non-surgical interventions or conservative therapy (e.g., physical therapy, injections, oral analgesics) For MACI: • Microfracture or drilling • OATS • OCA • Chondroplasty • Knee replacement (total or partial) • Sham surgery • Non-surgical interventions or conservative therapy (e.g., physical therapy, injections, oral analgesics)	• Head-to-head comparisons of the same procedure with different techniques (e.g., MACI with scaffold A vs. MACI with scaffold B, OCA with cadaveric tissue vs synthetic tissue) with the exception of studies comparing first line procedure with second line procedure (e.g. first line OCA vs second line OCA after failed microfracture) • Waitlist control • No comparator

Outcomes	EQ:
	• Activity levels:
	  ○ Time to return to work or sport
	  ○ Rehabilitation time
	  ○ Activities of daily living
	• Patient-reported outcomes
	• Rates of retreatment
	• Avoidance of osteoarthritis and knee replacement
	
	SQ:
	• Serious adverse events (e.g., death, disability, cartilage or meniscal injury)
	• Adverse events (e.g., infection, bleeding, nerve damage, tendonitis, joint swelling or effusion)
	
	CQ: (U.S.-based cost inputs only)
	• Cost-effectiveness
	• Cost-utility
		• Intermediate outcomes, (e.g., imaging outcomes, pathology findings)
		• Non-validated measurement tool
		• Non-U.S. cost inputs

Timing & Language	• No timing restrictions • English-language articles	• No timing exclusions • Non–English language articles
Study Design	• EQ: RCTs, NRSI[a] • SQ: RCTs, NRSI • CQ: CEA, CUA, or CBA performed from the societal or payor perspective	• Editorials, commentaries, narrative reviews, or letters; conference abstracts; case reports or case series;; case-control studies; other observational study designs without a comparator group not already specified

PICOTS	Include	Exclude
		• Relevant systematic reviews will be excluded but will be hand searched to identify potentially eligible primary studies
Setting	• Countries categorized as "very high human development" on the United Nations Development Programme's 2018 Human Development Index Report[b]	• Countries not categorized as "very high human development" according to the United Nations Development Programme's 2018 Human Development Index Report[b]

Notes: [a]If insufficient RCT evidence is identified for the EQ, NRSIs will be included.
[b] Andorra, Argentina, Australia, Austria, Bahamas, Bahrain, Barbados, Belarus, Belgium, Brunei Darussalam, Bulgaria, Canada, Chile, Costa Rica, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hong Kong China (SAR), Hungary, Iceland, Ireland, Israel, Italy, Japan, Kazakhstan, Korea (Republic of), Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Mauritius, Montenegro, Netherlands, New Zealand, Norway, Oman, Palau, Panama, Poland, Portugal, Qatar, Romania, Russian Federation, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Arab Emirates, United Kingdom, United States, and Uruguay.
Abbreviations: CBA = cost-benefit analysis; CEA = cost-effectiveness analysis; CQ = cost question; CUA = cost-utility analysis; EQ = efficacy question; FDA= Food and Drug Administration; NRSI = nonrandomized study of intervention (e.g., prospective or retrospectively conducted comparative cohort study); RCT = randomized controlled trial; SQ = safety question

What is Excluded from this HTA

First and second generation ACI will not be an eligible procedure for this HTA as its use of a periosteal patch has evolved into MACI, which uses a porcine or synthetic matrix, reducing complications from ACI.[4,5] Exclusion of ACI limits the review to procedures typically performed in contemporary clinical practice. Studies that evaluate focal chondral defect procedures to restore the type of cartilage damage present in degenerative osteoarthritis will not be included. Case-control studies, case series, and case reports will not be included to ensure adequate comparative evidence is used in the evidence synthesis. While we will include comparative cohorts for the safety question, we will assess the body of trial evidence before considering the inclusion of comparative cohorts for efficacy.

Public Comments

The State of Washington's Health Technology Assessment Program posted for public comment the draft key questions and proposed scope for a health technology assessment (HTA) on the topic of "Treatment for Patients with Chondral Defects of the Knee" between December 22, 2023 and January 5, 2024. No public comments were received.

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References

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