



## Complete Summary

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### GUIDELINE TITLE

The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints.

### BIBLIOGRAPHIC SOURCE(S)

National Institute for Clinical Excellence (NICE). The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints. London (UK): National Institute for Clinical Excellence (NICE); 2005 May. 28 p. (Technology appraisal; no. 89).

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Cartilage defects in knee joints due to sporting injury, osteochondritis dissecans, or chondromalacia patellae

### GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness  
Treatment

### CLINICAL SPECIALTY

Family Practice  
Internal Medicine  
Orthopedic Surgery

### **INTENDED USERS**

Advanced Practice Nurses  
Physician Assistants  
Physicians

### **GUIDELINE OBJECTIVE(S)**

To assess the effectiveness and cost-effectiveness of autologous chondrocyte implantation (ACI) by examining the current evidence

### **TARGET POPULATION**

Patients with symptomatic knee cartilage defects

### **INTERVENTIONS AND PRACTICES CONSIDERED**

Autologous chondrocyte implantation

**Note:** This procedure is not recommended for the treatment of articular cartilage defects except in the context of ongoing or new clinical trials.

### **MAJOR OUTCOMES CONSIDERED**

- Knee joint function following autologous chondrocyte implantation
- Complication rate following autologous chondrocyte implantation
- Treatment success and failure rate
- Pain
- Quality of life
- Cost effectiveness

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases  
Searches of Unpublished Data

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

**Note from the National Guideline Clearinghouse (NGC):** The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment

report for this technology appraisal was prepared by the Aberdeen Health Technology Assessment Group (see the "Companion Documents" field).

## **Search Strategy**

Papers were identified using the following search strategies:

1. Electronic databases searched included MEDLINE (Ovid, 2000 to June 2004 for autologous chondrocyte implantation [ACI] search, 1996 to June 2004 for search of other techniques for repairing cartilage defects, and for economic search, 1966 to June 2004 for quality of life search), EMBASE (Ovid, 2000 to June 2004 for ACI search, 1996 to June 2004 for search of other techniques for repairing cartilage defects, and for economic search, 1980 to June 2004 for quality of life search), Sports Discus (2000 to 2004), The Cochrane Library (issue 2, 2004), National Health Service (NHS) Centre of Reviews and Dissemination Databases (May 2004), BIOSIS (2000 to 6 June 2004), EBSCO Biomedical Reference Collection (6 June 2004), HSTAT (6 June 2004), Science Citation Index (6 June 2004), Social Science Citation Index (6 June 2004), Department of Health Research Findings Register ReFeR (6 June 2004). Medical Subject Headings (MeSH) and keywords encompassing cartilage diseases, chondrocytes, knee diseases, knee injury, costs, quality of life, autologous implantation, and other repair techniques were sought. Details of the search strategies used are shown in appendix 3 of the systematic review companion document.
2. Databases of ongoing trials: [www.controlled-trials.com](http://www.controlled-trials.com) (June 2004), National Research Register (6 June 2004).
3. Abstracts from the meetings of the American Academy of Orthopaedic Surgeons (2000-2004) were searched.
4. Broad internet searches were performed using a metasearch engine (Dogpile).
5. Reference lists of relevant studies and reviews identified were scanned, as well as studies reported in industry submissions to the National Institute for Health and Clinical Excellence (NICE).

## **Inclusion and Exclusion Criteria**

Studies were included if they were prospective controlled trials (randomised controlled trials or controlled clinical trials) of ACI for localised defects of the knee, in comparison to any other or no treatment, in any patient group. Abstracts were included, provided that relevant data were shown and that publication of the abstract was not superseded by publication as a full paper. Long term (follow-up of at least two years) uncontrolled studies of interventions for localised knee defects - or natural history - were also included to enable a comparison of long term outcomes across studies. Studies in all languages were included.

## **Data Extraction**

Two reviewers extracted data regarding study design and characteristics, details of the intervention, and patient characteristics and outcomes into a specially designed form, which was piloted before use. Differences in data extraction were resolved by discussion, referring back to the original paper. Data extraction for German studies was done by one reviewer only.

## **Quality Assessment**

To assess the quality of controlled trials, the following criteria were assessed: 1. Method of randomisation, 2. Allocation concealment, 3. Handling of missing data/complete description of losses to follow-up, 4. Intention-to-treat analysis, 5. Power calculation, 6. Blinding of patients (if possible), 7. Blinding of carers, 8. Blinding of outcome assessors, 9. Comparable timing of outcome assessment between groups, 10. Comparable post-operative rehabilitation between groups, 11. Specification of eligibility criteria, 12. Similarity at baseline with respect to prognostic factors, 13. Presentation of point estimates and measure of variability for primary outcome measure, 14. Sponsoring by manufacturer.

## **NUMBER OF SOURCE DOCUMENTS**

Four randomised controlled trials were included, as well as long term observational data from selected case series.

## **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Expert Consensus

## **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

Overall study quality was rated as follows:

- A. All quality criteria met
- B. One or more of the quality criteria only partially met
- C. One or more criteria not met

## **METHODS USED TO ANALYZE THE EVIDENCE**

Systematic Review with Evidence Tables

## **DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

## **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

### **Considerations**

Technology appraisal recommendations are based on a review of clinical and economic evidence.

## **Technology Appraisal Process**

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

### **Who is on the Appraisal Committee?**

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

## **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

Not applicable

## **COST ANALYSIS**

## **Literature Search**

The literature search undertaken by the Assessment Group identified a number of published economic studies of autologous chondrocyte implantation (ACI), although the available data appeared limited. In addition, Verigen UK Ltd submitted unpublished cost-effectiveness data in confidence. The Assessment Group undertook some illustrative modeling, comparing ACI with mosaicplasty and microfracture for patients previously treated with lavage and debridement.

## **Cost-Effectiveness Summary**

The data on the relative effectiveness of autologous chondrocyte implantation (ACI) compared with microfracture and the still relatively experimental mosaicplasty technique were inconsistent. Furthermore, there was a lack of long-term follow-up, and the quality of life gain from treating with ACI compared with other alternatives remained unclear.

Details of the cost analysis are found in section 4.2 of the original guideline document.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

## **RECOMMENDATIONS**

### **MAJOR RECOMMENDATIONS**

Autologous chondrocyte implantation (ACI) is not recommended for the treatment of articular cartilage defects of the knee joint except in the context of ongoing or new clinical studies that are designed to generate robust and relevant outcome data, including the measurement of health-related quality of life and long-term follow-up. Patients should be fully informed of the uncertainties about the long-term effectiveness and the potential adverse effects of this procedure.

## **CLINICAL ALGORITHM(S)**

None provided

## **EVIDENCE SUPPORTING THE RECOMMENDATIONS**

### **TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS**

The type of evidence supporting the recommendations is not specifically stated.

## **BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS**

### **POTENTIAL BENEFITS**

Appropriate use of autologous chondrocyte implantation (ACI) for the treatment of articular cartilage defects of the knee joint

### **POTENTIAL HARMS**

Not stated

## **QUALIFYING STATEMENTS**

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- This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- The trials published in the literature thus far all compare autologous chondrocyte implantation (ACI) with a different treatment. Therefore, data on each comparison are limited and no trial data are available for comparing ACI with no treatment. Follow-up from the trials so far has only been up to two years, with longer-term outcomes being uncertain.

## **IMPLEMENTATION OF THE GUIDELINE**

### **DESCRIPTION OF IMPLEMENTATION STRATEGY**

#### **Implementation and Audit**

- National Health Service (NHS) hospitals and clinicians who care for people who have articular cartilage defects of the knee joint should review their current practice and policies to take account of the guidance set out in Section 1 of the original guideline document and in the "Major Recommendations" section of this summary.

- Autologous chondrocyte implantation (ACI) should be performed only within the context of ongoing or new clinical studies that are designed to generate robust and relevant outcome data. Patients should be fully informed of the uncertainties about the long-term effectiveness and the potential adverse effects of this procedure.

## **IMPLEMENTATION TOOLS**

Patient Resources  
Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

## **INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES**

### **IOM CARE NEED**

Getting Better

### **IOM DOMAIN**

Effectiveness  
Patient-centeredness

## **IDENTIFYING INFORMATION AND AVAILABILITY**

### **BIBLIOGRAPHIC SOURCE(S)**

National Institute for Clinical Excellence (NICE). The use of autologous chondrocyte implantation for the treatment of cartilage defects in knee joints. London (UK): National Institute for Clinical Excellence (NICE); 2005 May. 28 p. (Technology appraisal; no. 89).

### **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

### **DATE RELEASED**

2000 Dec (revised 2005 May)

### **GUIDELINE DEVELOPER(S)**

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

### **SOURCE(S) OF FUNDING**

National Institute for Health and Clinical Excellence (NICE)

## **GUIDELINE COMMITTEE**

Appraisal Committee

## **COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE**

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## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

## **GUIDELINE STATUS**

This is the current release of the guideline.

## **GUIDELINE AVAILABILITY**

Electronic copies: Available in Portable Document Format (PDF) format from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

## **AVAILABILITY OF COMPANION DOCUMENTS**

The following are available:

- The use of autologous chondrocyte implantation (ACI) for the treatment of cartilage defects in knee joints. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 2 p. (Technology appraisal 89). Available in Portable Document Format (PDF) from the [National Institute for Clinical Excellence \(NICE\) Web site](#).
- Clinical and cost-effectiveness of autologous chondrocyte implantation for cartilage defects in knee joints; technology assessment report. Aberdeen (UK): Aberdeen Health Technology Assessment Group; 2004 Aug. 101 p. (Technology appraisal 89). Available in Portable Document Format (PDF) from the [National Institute for Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N870. 11 Strand, London, WC2N 5HR.

## **PATIENT RESOURCES**

The following is available:

- Autologous chondrocyte implantation (ACI) for treating cartilage damage in the knee. Understanding NICE guidance - information for people with cartilage damage in the knee, their families and carers, and the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 May. 7 p.

Electronic copies: Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N0871. 11 Strand, London, WC2N 5HR.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## **NGC STATUS**

This summary was completed by ECRI on November 29, 2005.

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