Health Technology Assessment Programme

National Institute for Health Research

NETSCC, HTA

11 January 2013

The Health Technology Assessment programme is managed by NETSCC, HTA as part of the NIHR Evaluation, Trials and Studies Coordinating Centre at the University of Southampton.

Alpha House, University of Southampton Science Park
Southampton SO16 7NS
Suggest a topic for research via our online form at www.hta.ac.uk/suggest

tel: +44(0)23 8059 5586
fax: +44(0)23 8059 5639
email: hta@hta.ac.uk

www.hta.ac.uk

The NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), based at the University of Southampton, manages evaluation research programmes and activities for the NIHR

Health Technology Assessment Programme
National Institute for Health Research
Evaluation, Trials and Studies Coordinating Centre
University of Southampton, Alpha House
Enterprise Road, Southampton, SO16 7NS

tel: +44(0)23 8059 5586
fax: +44(0)23 8059 5639

email: hta@hta.ac.uk
web: www.hta.ac.uk

Protocol

1. Project title

What is the clinical and cost-effectiveness of conservative interventions for elbow tendinopathy?

1.1. HTA reference

Technology assessment report commissioned by the NIHR HTA programme, December 2012. HTA reference no. 12/73.[1]

2. TAR team and project 'lead'

TAR Team Peninsula Technology Assessment Group (PenTAG)

Project Lead **Louise Crathorne**
Research Fellow Health Technology Assessment
Peninsula Technology Assessment Group
University of Exeter Medical School
Veysey Building
Salmon Pool Lane
Exeter EX2 7SG

3. Plain English Summary

This project will review evidence for the effectiveness of conservative interventions for elbow tendinopathy such as tennis or golfer's elbow. "Conservative" covers most commonly used interventions with the exception of surgery. The evidence will come from well designed research studies, particularly randomised controlled trials (RCT) and systematic reviews of RCTs. The evidence will be brought together to find out which interventions produce the best results. We will also summarise any evidence on which interventions give the best value for money.

.

4. Decision problem

4.1. Background

The prevalence of tendon injuries is increasing. Medical management of elbow tendinopathy has historically included non-steroidal anti-inflammatory drugs (NSAIDs), advice regarding rest, use of an elbow counterforce brace, and corticosteroid injection(s). Current treatment usually begins with traditional non-invasive measures that include activity modification; orthotics (to correct malalignment); stretching; massage; heat and cold therapy; traditional strengthening exercises; ultrasound. Generally favourable outcomes have been reported for traditional non-invasive methods, but in about 30% of patients these are ineffective. Surgery remains the last option due to the morbidity and inconsistent outcomes.

Newer treatments include physical therapy such as iontophoresis (topical introduction of ionized drugs into the skin using electrical current), phonophoresis (ultrasound-enhanced delivery of topical drugs), and low-level laser treatment. These are however thought to lack sufficient evidence of their efficacy at this time, suggesting they are not used in the NHS.

A background search has revealed that although there are already systematic reviews of RCTs, including Cochrane reviews, on many common interventions for elbow tendinopathy, many of these are out-of-date by up to 10 years. Further there is also no recent overview of these reviews, making it difficult for a practitioner or a commissioner of health care or research to easily identify where there is uncertainty about alternative treatment options. This in turn makes it difficult to identify which of the existing systematic reviews are most likely benefit from further development. Also there have been no apparent attempts to summarise evidence on cost-effectiveness despite there being a number of primary studies examining this issue.

4.2. Purpose

The purpose is to evaluate evidence for the effectiveness and cost-effectiveness of conservative interventions for elbow tendinopathy.

Given the findings of the background search and the limited amount of time available for this project, we propose to address the general purpose by:

a) Performing an overview of systematic reviews

b) Quantifying the number of RCTs not already incorporated into the most recent systematic reviews identified in the overview

c) Performing a systematic review of cost-effectiveness studies

Although a number of other important potential objectives will not be addressed, such as a mixed treatment comparison of alternative treatments for elbow tendinopthy and a health economic model of cost-effectiveness, we believe that the three proposed objectives will provide essential preliminary work for such further research activity.

4.3. General approach

This will be secondary research. We will adhere to the general guidance on conduct of systematic reviews provided by the Cochrane Collaboration and NHS Centre for Reviews and Dissemination (CRD).[2] We will conduct the work with reference to a predefined protocol which will be available on the PROSPERO database.

We will work in close collaboration with the Cochrane Musculoskeletal Group who will provide content expertise. We have included a member of the group in our review team to facilitate this. We anticipate that the overview of systematic reviews will be a Cochrane Overview, but this will require approval from the Cochrane Musculoskeletal Group which we are currently pursuing.

General inclusion criteria, covering all three proposed objectives, are outlined below:

Criteria	Specification	Notes
Population	Patients with tendinopathy of the elbow in adults. Separate lateral and medial epicondylitis	Look for evidence on patients unresponsive to initial treatments
Intervention	Conservative treatments including orthotic devices, physiotherapy, NSAIDs, acupuncture, corticosteroid injections, low level laser	All treatments bar surgery
Comparator	Placebo or current practice or other conservative treatments	Current practice needs to be clearly defined
Outcomes	Function Pain Quality of life Remain/return to work Sport activity Harms of intervention Cost* Coat/QALY*	Outcomes at different time points will be differentiated clearly separating short-term (up to 1 month post onset) from long term (6 months or more from onset)
Setting	Primary or community care	
Study design	RCTs, SRs of RCTs, cost-effectiveness evaluations*	
Search dates	1990 onwards	
Language	English language only	

* Only relevant to systematic review of studies on cost and cost-effectiveness

5. Search Strategy

Refer to Appendix 1 for the draft search strategy for MEDLINE.

The search strategy will comprise the following main elements:

- Searching of electronic bibliographic databases
- Internet searches
- Scrutiny of references of included studies
- Contacting experts in the field

The following databases will be searched: MEDLINE (OVID); MEDLINE-in-Process (OVID); EMBASE (OVID); CINAHL (EBSCO); AMED (OVID); Cochrane (including CENTRAL, DARE and HTA); Web of Science (Thomson Reuters); PEDro (free); ClinicalTrials.gov.

A separate search for cost-effectiveness studies will be undertaken – see 7.

6. Methods for synthesis of evidence of clinical effectiveness

6.1. General

The assessment report will include an overview of systematic review of the evidence for the clinical effectiveness of conservative interventions for the treatment of elbow tendinopathy. We will use the approach to overviews suggested by the Cochrane Collaboration. We will indicate the number and general nature of the RCTs we identify which have not been included in the most valid and up-to-date systematic reviews included in the overview for each intervention. We do not anticipate that sufficient time will be available to perform any new systematic reviews or up-dates, but will reconsider this mid-way through the project. If time is available, we would have greatest interest in up-dating the systematic review of effectiveness on acupuncture because there is local expertise on the effectiveness of alternative medicine techniques.

6.2. Types of studies to be included

Systematic reviews of RCTs and RCTs meeting the other criteria mentioned in section 4. will be included.

6.3. Types of studies to be excluded

- Uncontrolled studies
- Animal models
- Narrative reviews, editorials, opinions
- Non English language papers
- Reports published as meeting abstracts only, or where insufficient methodological details are reported to allow critical appraisal of study quality.

6.4. Study selection process

Based on the above inclusion/exclusion criteria, papers will be selected for retrieval, independently by two reviewers (LC and LL), from the titles and abstracts generated by the search strategy. Discrepancies will be resolved by discussion. Retrieved papers will again be selected against the inclusion criteria by the same independent process.

6.5. Data extraction strategy

Data will be extracted from included studies by one reviewer using a standardised data extraction form and checked by another reviewer. Discrepancies will be resolved by discussion, with the involvement of a third reviewer if necessary.

6.6. Quality assessment strategy

The quality of the clinical effectiveness studies will be assessed for internal and external validity according to criteria suggested by the NHS CRD guidelines, according to study type. PRISMA will be the main tool for systematic reviews. RCTs will not be quality assessed in detail.

6.7. Methods of analysis/synthesis

The systematic reviews in the overview will be summarised narratively. Meta-analysis will not be employed.

We will use the approach suggested by GRADE to structure this summary. As well as recommendations for practice, particular attention will be paid to evidence gaps, separating

those where there appears to be RCTs which have not yet been incorporated into systematic reviews and those where there appear to be no RCTs.

7. Methods for synthesis of evidence of cost-effectiveness

7.1. Search

The range of sources searched will be the same as those for clinical effectiveness but also include NHS EED. A validated filter for studies on cost and cost-effectiveness will be applied.

7.2. Study selection criteria and procedures

The inclusion and exclusion criteria for the systematic review of economic evaluations will be identical to those for the systematic review of clinical effectiveness, except for study design. These will be full cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost consequence analyses. These can either be conducted as primary studies, particularly along-side RCTs, or be model based. Stand alone UK cost analyses will also be sought and appraised.

Based on the inclusion/exclusion criteria, study selection will be made independently by two reviewers. Discrepancies will be resolved by discussion, with involvement of third reviewer when necessary.

7.3. Study quality assessment

The methodological quality of the economic evaluations will be assessed according to internationally accepted criteria such as the CHEC list questions developed by Evers et al.[3] Any studies based on decision models will also be assessed against the ISPOR guidelines for good practice in decision analytic modelling.[4]

7.4. Data extraction and analysis

Data will be extracted by one researcher into two types of summary tables: one to describe the study design of each economic evaluation and the other to describe the main results.

The study design table will include: author and year; model type or trial based; study design (e.g. CEA, CUA or cost-analysis); service setting/country; study population; comparators; research question; perspective, time horizon, and discounting; main costs included; main outcomes included; sensitivity analyses conducted; and other notable design features.

The results table will reflect the outcomes used in the studies. The original authors' conclusions will be noted, and also any issues they raise concerning the generalisability of results. Finally the reviewers' comments on study quality and generalisability of their results will be recorded.

The conclusions on costs and cost-effectiveness concerning each intervention whose cost-effectiveness has been assessed will be based on the patterns of results in the included studies taking into account provisos arising from limitations identified in the studies.

8. Expertise in this TAR team

Name	Institution	Expertise
Louise Crathorne	**PenTAG, University of Exeter Medical School**	**Systematic reviewing and project management**
Linda Long	**PenTAG, University of Exeter Medical School**	**Systematic reviewing and child health**
Simon Briscoe	**PenTAG, University of Exeter Medical School**	**Information science**
Chris Cooper	**PenTAG, University of Exeter Medical School**	**Information science**
Prof Chris Hyde	**PenTAG, University of Exeter Medical School**	**Systematic reviewing and economic evaluation. Project guarantor**
Prof Rachelle Buchbinder	**Joint Coordinating Editor, Cochrane Musculoskeletal Group**	**Liaison with Cochrane Group and authorsof previous Cochrane Reviews on elbow tendinopathy**
Prof Paul Dieppe	**University of Exeter Medical School**	**Liaison with local clinical experts**

In addition to the research team, we will be receiving expert advice on subject content from the Cochrane Musculoskeletal Group mediated via Professor Rachelle Buchbinder. Local subject experts identified with the assistance of Professor Paul Dieppe may also be involved.

TAR Centre

PenTAG is part of the Institute of Health Service Research at the University of Exeter Medical School. PenTAG was established in 2000 and currently has two major work streams: independent health technology assessments (HTAs) for NICE and the NIHR HTA

programme, and evidence synthesis work in relation to the needs of the SW Peninsula Collaboration for Applied Health Research and Care (PenCLAHRC), as well as for other local and national decision-makers.

The group is multi-disciplinary and draws on individuals' backgrounds in public health, health services research, computing and decision analysis, systematic reviewing, statistics and health economics. The Institute of Health Research is made up of discrete by methodologically related research groups, among which HTA is a strong and recurring theme.

Recent projects include:

- Bendamustine for the first-line treatment of chronic lymphocytic leukaemia (Binet stage B or C) in patients for whom fludarabine combination chemotherapy is not appropriate: a critique of the submission from Napp
- The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of TA111): a systematic review and economic model
- Ofatumumab (Arzerra®) for the treatment of chronic lymphocytic leukaemia in patients who are refractory to fludarabine and alemtuzumab: a critique of the submission from GSK
- Everolimus for the second-line treatment of advanced and/or metastatic renal cell carcinoma
- The clinical and cost-effectiveness of sunitinib for the treatment of gastrointestinal stromal tumours: a critique of the submission from Pfizer
- The clinical- and cost-effectiveness of lenalidomide for multiple myeloma in people who have received at least one prior therapy: an evidence review of the submission from Celgene
- Bevacizumab, sorafenib tosylate, sunitinib and temsirolimus for renal cell carcinoma: a systematic review and economic model
- Machine perfusion systems and cold static storage of kidneys from deceased donors.
- The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults
- The harmful health effects of recreational Ecstasy: A systematic review of observational evidence
- Assessment of surrogate outcomes in model-based cost effectiveness analyses within UK health technology reports: a methodological review

- Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting $beta_2$-agonists for the treatment of chronic asthma in adults and children aged 12 years and over.
- Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting $beta_2$-agonists for the treatment of chronic asthma in children under the age of 12 years.
- The effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure: a systematic review and economic model.
- The effectiveness and cost-effectiveness of cinacalcet for secondary hyperparathyroidism in end stage renal disease: a systematic review and economic model
- The effectiveness and cost-effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma: a systematic review and economic evaluation.
- Surveillance of cirrhosis for the development of hepatocellular carcinoma: systematic review and economic analysis.
- Surveillance of Barrett's oesophagus: exploring the uncertainty.
- The cost effectiveness of testing for hepatitis C in former injecting drug users.
- Do the findings of case series vary systematically by methodological characteristics.
- The effectiveness and cost effectiveness of dual chamber pacemakers compared to single chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation.
- The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema: a systematic review and economic evaluation.
- The effectiveness and cost-effectiveness of microwave and thermal balloon endometrical ablation for heavy menstrual bleeding: a systematic review and economic modelling.
- Effectiveness and cost-effectiveness of imatinib for first-line treatment of chronic myeloid leukaemia in chronic phase: a systematic review and economic analysis.
- Systematic review of endoscopic Sinus Surgery for Nasal Polyps.
- Screening for hepatitis C in GUM clinic attenders and injecting drug users.

- The effectiveness and cost effectiveness of imatinib in chronic myeloid leukaemia: a systematic review.

Team members' contribution

Name	Job title	Contribution
Louise Crathorne	**Research Fellow in Health Technology Assessment**	**Providing overall project management. Contributing to the protocol. Assessing abstracts and titles and papers for inclusion and exclusion in both reviews. Leading the overview and cost-effectiveness systematic reviews. Leading the writing and editing the report.**
Linda Long	**Associate Research Fellow Health Technology Assessment**	**Assessing abstracts and titles and papers for inclusion and exclusion in the effectiveness oveview. Contributing to the clinical effectiveness overview. Contributing to the writing and editing the report.**
Simon Briscoe	**Information Scientist**	**Writing and running the search strategies for all reviews.**
Chris Cooper	**Senior Information Scientist**	**Overseeing the development of the search strategy.**
Chris Hyde	**Professor**	**Drafting the protocol. Assessing abstracts and titles and papers for inclusion and exclusion in the cost-effectiveness systematic review. Contributing to the writing and editing the report. Overall director of the project and guarantor of the report.**
Rachelle Buchbinder	**Professor**	**Liaison with Cochrane Musculoskeletal Group. Assistance with Cochrane overview of systematic reviews**
Paul Dieppe	**Professor**	**Assistance identifying local clinical experts**

9. Competing interests of authors

None

10. Timetable

This is a Short Report, which means that the final report should be handed in 12 weeks from signing-off the protocol. However, this project may be extended if the size of the searches, or other unforeseen circumstances, means that this short time frame needs extending.

11. Appendices

11.1. Draft Medline search strategy

MEDLINE search strategy

1. (tend?nopath* or paratend?nopath*).tw.
2. (tend?n?s?s or tend?nitis or p?r?ten???itis).tw.
3. tendinopathy/
4. bursitis*.tw.
5. bursitis/
6. or/1-5
7. (elbow? or "common extensor origin").tw.
8. elbow/
9. elbow joint/
10. or/7-9
11. 6 and 10
12. ("lateral epicondylitis" or "medial epicondylitis" or "elbow pain?").tw.
13. ((tennis or golfer* or row* or shooter* or archer*) adj1 elbow?).tw.
14. tennis elbow/
15. or/11-14
16. (random* or "controlled trial?" or "clinical trial?" or rct?).tw.
17. Randomized controlled trial.pt.
18. ("systematic review?" or "meta-analys?s" or "meta analys?s" or metaanalys?s).tw.
19. meta-analysis.pt.
20. or/16-19
21. 15 and 20
22. limit 21 to (english language and yr="1990 -Current")

Costs filter

1. exp "Costs and Cost Analysis"/
2. exp Economics/
3. exp models, economic/
4. (pharmacoeconomic* or economic* or price* or cost* or cba or cea or cua or "health utilit*").tw.
5. ec.fs.
6. or/1-5

12. References

1. National Institute for Health and Clinical Excellence. Conservative interventions for elbow tendinopathy (HTA No 12/73). London: NICE; 2012.
2. Reviews NHSCf, Dissemination. Systematic Reviews: CRD's guidance for undertaking reviews in healthcare. York: NHS Centre for Reviews and Dissemination; 2009.
3. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. *Int J Technol Assess Health Care* 2005; **21:** 240-245.
4. Weinstein MC, O'Brien B, Hornberger J *et al*. Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR Task Force on Good Research Practices--Modeling Studies. *Value Health* 2003; **6:** 9-17.