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## **Immobilisation versus early ankle movement for treating acute lateral ankle ligament injuries in adults (Protocol)**

Keene DJ, Williams MA, Segar AH, Byrne C, Lamb SE

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# Immobilisation versus early ankle movement for treating acute lateral ankle ligament injuries in adults

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## ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effects (benefits and harms) of immobilisation compared with early movement protocols for acute lateral ankle ligament injuries.

## BACKGROUND

### Description of the condition

Ligaments are fibrous connective tissues attaching bones. They perform a stabilising role for the joints, preventing excessive movements. If a ligament is forcibly overstretched, a sprain may occur. Ankle ligament sprains are among the commonest of all injuries, accounting for an estimated 300,000 admissions to UK Emergency Departments each year (Bridgman 2003). In the US general population the incidence is 215 per 100,000 person-years, half of which occur during sporting activities (Waterman 2010). The vast majority of ankle sprains involve the ligament complex on the lateral (outer side) of the ankle, and result from inversion injuries (in lay terms, 'going over on the ankle'). These lateral ligament sprains are graded according to clinical criteria that estimate the extent of ligamentous disruption (Cooke 2009; Martin 2013);

namely, Grade I (a mild sprain with some fibres of the ligament damaged), Grade II (a partial ligament tear) and Grade III (a complete ligament tear). Of the three ligaments (anterior talofibular ligament (ATFL), calcaneofibular ligament and posterior talofibular ligament) comprising the lateral ligament complex, the ATFL is the most commonly injured. Pain, loss of ankle range of motion and deficits in muscle function are major clinical features of acute ankle sprains; these result in reduced function and inability to weight-bear in more severe sprains (Bleakley 2008; Martin 2013; Terada 2013).

People with acute ankle sprains may present to primary or secondary care for diagnosis and management, especially if concerned about fracture or in excessive pain. Use of radiographs has been effectively controlled through the Ottawa Ankle Rules (Stiell 1995), with only the most concerning injuries being imaged to check for fracture. Treatment guidelines advocate a delayed examination of the ankle to allow more accurate diagnosis of sprain severity (Polzer

2012; Van Dijk 1996). Delaying examination allows some reduction in swelling, and allows more accurate assessment of injury severity and associated derangement (Van Dijk 1996). Management options at this stage include further watchful waiting, diagnostics, intensive physiotherapy or immobilisation. Surgery may also be considered, although most healthcare providers would try conservative treatment first.

Recovery may be protracted, particularly for more severe injuries. A systematic review including 31 studies found that after ankle sprain, up to 30% of people were experiencing pain one year after injury and only 36% to 85% reported full recovery within three years (Van Rijn 2008). The average absence from work in the UK is more than one week, which has substantial economic implications given the high incidence of ankle sprains (Cooke 2009). The approximate proportion of individuals who have not returned to sport within six weeks is 50% and within one year is 10% (Kerkhoffs 2002). Many of those with persistent symptoms have ankle instability, which is more likely after more severe ankle sprains (Pourkazemi 2014). Chronic ankle instability is implicated in the development of ankle osteoarthritis, even without an acute osteochondral lesion (Wikstrom 2013). Based on 2005 prices, the mean direct health costs of managing moderate to severe sprains with a tubular bandage were estimated at GBP 135 per sprain; when including sick leave, amounting to a mean absence of seven days off work, total costs were over GBP 900 per patient (Cooke 2009).

## Description of the intervention

Thorough assessment of the injury in the first couple of days is often prevented by swelling and pain. For the first few days after injury, people with acute ankle sprains are generally advised to rest, elevate the injured limb, apply ice and compression to the ankle, and are often issued with crutches if they are having difficulty with weight-bearing on the injured limb. One of the key dilemmas in early management of ankle sprains is whether to immobilise the ankle joint or to allow or promote ankle joint motion. Immobilisation of the ankle joint is achieved by means of externally applied splints, plaster or fibreglass casts, or rigid walking boots. Early ankle motion interventions can range from allowing ankle joint motion without specific guidance on exercise through to prescription of intensive exercise programmes. These protocols may or may not also involve the use of splints or braces that allow a degree of ankle motion, often termed 'functional treatment'.

## How the intervention might work

Immobilisation is often used in clinical practice to manage acute soft tissue injuries, with the aim of reducing the risk of bleeding and disruption of new collagen formation, and controlling inflammation during the acute phase (Kannus 2003; Karlsson 2007).

The acute phase of ligament healing is approximately 10 days in duration (Kannus 2003). Immobilisation of the injured joint after ligament rupture aims to limit strain and damage to the healing ligament. This is especially indicated after partial or complete ligament tears, in order to control motion in an otherwise unstable joint during the initial phase of healing (Cooke 2009).

In contrast, basic research suggests that there are many negative effects of immobilisation on musculoskeletal tissues. It is increasingly recognised that there are significant cellular benefits from mechanical loading. Specifically, mechanistic basic research has shown that loading of musculoskeletal tissues stimulates up-regulation of growth factors associated with cellular proliferation and matrix remodelling (Khan 2009). In addition, immobilisation has been linked with deleterious effects relating to muscle function, including atrophy and weakness (Santos 2013). These findings have led to recommendations for mobilising injured tissues early after injury (Bleakley 2012; Kannus 2003). However, the applicability of basic research to human injury is contentious (Pound 2014).

## Why it is important to do this review

The previous version of this Cochrane review concluded that early ankle movement was the favourable strategy (Kerkhoffs 2002); however, there have been numerous trials since with inconsistent findings. This inconsistency is reflected in more recent reviews (Lin 2010; Petersen 2013; Seah 2011), treatment algorithms (Polzer 2012) and clinical guidelines (Martin 2013). Some of these favour early mobilisation (Lin 2010; Polzer 2012), while others, for severe sprains at least, favour a short period of immobilisation (Martin 2013; Petersen 2013; Seah 2011). An up-to-date Cochrane review is therefore timely.

## OBJECTIVES

To assess the effects (benefits and harms) of immobilisation compared with early movement protocols for acute lateral ankle ligament injuries.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We will include randomised controlled trials and quasi-randomised (method of allocating participants to a treatment which

is not strictly random: e.g. by hospital number) controlled trials evaluating immobilisation versus early ankle movement for treating acute lateral ankle ligament injuries in adults.

### Types of participants

We will include studies involving adults (16 years or older) reporting an acute injury (equal to or less than seven days old) to the lateral ligament complex of the ankle.

We will exclude studies where participants are children (aged under 16), unless separate data for adults are available, or the proportion of children is small (less than 10%) and, preferably, the numbers are balanced between the groups.

We will include studies that include people with avulsion fractures, provided these injuries are no more than a bony flake (and therefore commensurate with clinical management as severe sprains).

### Types of interventions

We will include trials comparing externally applied non-invasive immobilisation of the ankle joint (for example, rigid casting or full-time use of a fixed walking boot or brace) with early ankle movement. Early ankle movement will involve the following.

- No immobilisation.
- Ankle motion exercises.
- Physical therapies (involving joint movement such as exercise prescription, manual therapy).
- Use of splint/ankle brace that allows restricted ankle movement.
- Ankle taping and strapping not intended to immobilise the ankle.
- A shorter period of immobilisation of the ankle joint.

We will exclude studies comparing immobilisation with early ankle movement following surgical repair of ankle ligaments.

Our main comparison will be any immobilisation versus any form of early ankle movement. Within this comparison, we will initially stratify trials by the type of early movement: no restriction (including active movement), restricted ankle movement (e.g. functional bracing) and shorter-term immobilisation (up to two weeks).

### Types of outcome measures

#### Primary outcomes

1. Ankle-related function (patient-reported outcome measures (e.g. the Foot and Ankle Outcome Score (Roos 2001), and the Karlsson Ankle Function Score (Karlsson 1991)) or clinical function scores (e.g. the Kaikkonen functional scale (Kaikkonen 1994)). We will report validated measures in preference to non-validated measures, and validated patient-reported outcome measures (PROMS) in preference to clinical function measures.

2. Adverse events: These are complications that require substantive treatment such as deep vein thrombosis, pulmonary embolism, complex regional pain syndrome type 1, treatment failure, or chronic instability resulting in surgery, and recurrence.

#### Secondary outcomes

1. Pain (e.g. Visual Analogue Score)
2. Health-related quality of life (e.g. Short-Form 12, EuroQol EQ-5D)
3. Return to physical recreational activities including sport
4. Return to work
5. Recurrent injury
6. Minor adverse reactions (e.g. skin complications)
7. Chronic ankle instability (subjective symptoms with or without clinical objective measures of joint laxity). We will not include ankle joint laxity detected during clinical tests (e.g. talar tilt) in the absence of symptoms of ankle instability.
8. Swelling
9. Ankle motion
10. Patient satisfaction
11. Intervention adherence/acceptability

We will also collect data reported on intervention costs, resource use, days off work and other costs, as well as report on the results of any cost-effectiveness analyses associated with the included trials.

#### Timing of outcome measurement

We will group this into the following categories.

1. Acute: randomisation up to and including six weeks.
2. Subacute: beyond six weeks and up to and including 12 weeks.
3. Intermediate: beyond 12 weeks and up to (but not including) 12 months.
4. Long-term: equal to or greater than 12 months.

#### Outcomes for 'Summary of findings' table

1. Ankle-related function (patient-reported outcome measures or clinical function scores)
2. Adverse events
3. Pain
4. Health-related quality of life
5. Return to physical recreational activities including sport
6. Chronic ankle instability
7. Recurrent injury

Preferably, long-term results for function, pain, quality of life, chronic ankle instability and recurrent injury will be presented.

### Search methods for identification of studies

## Electronic searches

We will search the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (to present), the Cochrane Central Register of Controlled Trials (CENTRAL) (current issue), MEDLINE (1946 to present), EMBASE (1980 to present), the Allied and Complementary Medicine Database (AMED) (1985 to present), Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1937 to present), SPORTDiscus (1985 to present) and the [Physiotherapy Evidence Database \(PEDro\)](#) (1929 to present). We will also search the [WHO International Clinical Trials Registry Platform Search Portal](#) and [Clinicaltrials.gov](#) for ongoing and recently completed trials. We will not apply any language restrictions in the searches.

In MEDLINE, we will combine subject-specific terms with the sensitivity-maximising version of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials ([Lefebvre 2011](#)). The search strategies for CENTRAL, MEDLINE and EMBASE are reported in [Appendix 1](#).

## Searching other resources

We will check reference lists of included trials and relevant systematic reviews for potentially eligible studies. We will search grey literature using [OpenGrey](#).

## Data collection and analysis

### Selection of studies

Pairs of four review authors (DK, MW, AS, CB) will independently screen the titles and, where available, abstracts through database searches. We will obtain full reports of potentially eligible studies, and pairs of authors will independently perform study selection. If agreement is not achieved at any stage, a third review author will adjudicate.

### Data extraction and management

Pairs of four review authors (DK, MW, AS, CB) will independently extract data using a standard data extraction form developed for this review. A third review author will adjudicate where necessary. The following information will be systematically extracted: sample size, sample demographics (age, sex, injury characteristics, time since injury), recruitment method, selection criteria, descriptions of intervention and control groups, detailed descriptions of the interventions (also including setting, timing, care personnel involved, extent of immobilisation, devices used, weight-bearing restrictions, prescription of assistive devices, exercises used, advice and instructions), supervision and delivery of interventions, other methods, outcome assessment and results. We will extract data after translation from the non-English language, where required.

Where necessary, we will contact study authors for additional information.

### Assessment of risk of bias in included studies

Pairs of four review authors (DK, MW, AS, CB) will assess the risk of bias using Cochrane's 'Risk of bias' tool ([Higgins 2011](#)). We will use the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.
4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective reporting.
7. Other bias.

We will assess patient-reported outcomes and objective outcomes separately when assessing for blinding and completeness of outcomes. We will resolve disagreements by discussion. If disagreement persists, a final decision will be facilitated by a third review author.

### Measures of treatment effect

We will calculate risk ratios (RRs) and 95% confidence intervals (CIs) for dichotomous outcomes, and mean differences (MDs) and 95% CIs for continuous outcomes. Where different measurement scores or scales are used for the same continuous outcome measure, we will pool data using standardised mean differences (SMDs) and 95% CIs. We will consider using the Peto odds ratio (OR) for dichotomous outcomes with rare events (low event rates and a high frequency of zero events). We will also calculate numbers needed to treat for one additional beneficial outcome (NNTB) or harmful outcome (NNTH), where appropriate.

### Unit of analysis issues

It is unlikely that cluster or cross-over trial designs will be used in included studies, or that there will be treatment comparisons of multiple body parts (i.e. bilateral ankle sprains). One likely unit of analyses issue can arise from the inclusion of studies with more than two relevant treatment groups. If more than two intervention groups are relevant to a single analysis, we will seek advice of a statistician and follow Cochrane guidance ([Higgins 2011b](#)). We will also remain aware of potential unit of analyses issues arising from multiple observations, such as at different times, for the same outcome.

### Dealing with missing data

If data are missing from trial reports, we will attempt to contact trial authors. We will undertake analysis with the available data. We will consider the potential impact of missing data on the findings of the review in the interpretation of incomplete outcome bias. Where

possible, we will calculate missing standard deviations from other statistics, such as standard errors, CIs or P values, according to the methods recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

### Assessment of heterogeneity

We will judge heterogeneity from both clinical and statistical perspectives. We will judge clinical heterogeneity on the basis of the similarities of study participants, intervention protocols and outcome measures. The evaluation of statistical heterogeneity will include visual inspection, and consideration of the  $\chi^2$  test and the  $I^2$  statistic. We will interpret the findings of the  $I^2$  statistic as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% considerable heterogeneity (Deeks 2011).

### Assessment of reporting biases

To assess the potential for reporting bias, we will screen the WHO International Clinical Trials Registry Platform Search Portal for prospective trial registration in trials published after 1 July 2005, and check on the availability of trial protocols that were published at minimum prior to completion of trial recruitment. We will report the potential for selective reporting of outcomes in the 'Risk of bias' assessment.

If data are pooled from 10 or more studies, we will explore the potential for publication bias using funnel plots. If there is bias because smaller studies without statistically significant effects remain unpublished, this should reveal an asymmetrical appearance of the funnel plot (Sterne 2011). We will consider the presence of small-study bias in the overall analysis through comparison of the results of the fixed-effect and random-effects models. If the random-effects estimate suggests greater effectiveness, we will consider whether it is reasonable to conclude that the intervention was more effective in smaller studies (Sterne 2011).

### Data synthesis

When considered appropriate, we will pool results of comparable groups of trials using both the fixed-effect and the random-effects models. Our choice of the model to report will be guided by careful consideration of the extent of heterogeneity and whether it can be explained, in addition to other factors, such as the number and size of included studies. We will use 95% CIs throughout. We will consider not pooling data where there is considerable heterogeneity ( $I^2 > 75\%$ ) that cannot be explained by the diversity of methodological or clinical features among trials. Where it is inappropriate to pool data, we will still present trial data in the analyses or tables for illustrative purposes and will report these in the text.

We will adjust differences in the direction of different outcome scales included within the meta-analysis by multiplying data values by -1 where necessary.

### Subgroup analysis and investigation of heterogeneity

Where data allow, we plan to conduct the following subgroup analyses.

1. Injury severity (Grade I versus Grade II and III sprains): injury severity can be a prognostic factor and/or mediator of treatment effect.
2. Duration of immobilisation (greater or less than two weeks): soft tissue healing within two weeks represents the acute phase and the start of the proliferation phase. Ending immobilisation before this time may influence these early physiological responses to injury.
3. Type of early movement (with or without functional brace): a functional brace can allow movement, but will still restrict motion in certain directions and influence function, for example, walking performance.

We will investigate whether the results of subgroups are significantly different by inspecting the overlap of confidence intervals and performing the test for subgroup differences available in [Review Manager 2014](#).

### Sensitivity analysis

If there are sufficient data, we will conduct sensitivity analyses on various aspects of trial and review methodology. These will include sensitivity analyses to explore: (i) the effects on primary outcomes of excluding trials at high or unclear risk of selection bias (thus restricting the analysis to studies with low risk of selection bias due to the use of adequate methods of allocation concealment); (ii) the effects of excluding trials reported only in conference proceedings or other short reports; and (iii) the choice of statistical model for pooling data (fixed-effect versus random-effects).

### 'Summary of findings' tables

Where there is sufficient evidence, we will prepare 'Summary of findings' tables. We will use the GRADE approach to assess the quality of evidence related to the two primary and the five secondary outcomes listed under 'Outcomes for 'Summary of findings' tables' in [Types of outcome measures](#) (Schünemann 2011).

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- \* Indicates the major publication for the study

## APPENDICES

### Appendix I. Search strategies

#### CENTRAL (Wiley Online Library)

- #1 MeSH descriptor: [Lateral Ligament, Ankle] this term only
- #2 MeSH descriptor: [Ankle Injuries] this term only
- #3 ((ankle or talo-fibular or talofibular or calcaneo-fibular or calcaneofibular or fibular) near/4 ligament\*):ti,ab,kw (Word variations have been searched)
- #4 #1 or #2 or #3
- #5 MeSH descriptor: [Joint Instability] this term only
- #6 MeSH descriptor: [Rupture] this term only
- #7 MeSH descriptor: [Sprains and Strains] this term only
- #8 sprain\* or strain\* or injur\* or rupture\* or tear or torn or trauma\* or lesion\* or distort?ion:ti,ab,kw (Word variations have been searched)
- #9 #5 or #6 or #7 or #8
- #10 #4 and #9
- #11 (ankle\* near/4 (sprain\* or inversion\*)):ti,ab,kw (Word variations have been searched)
- #12 #10 or #11
- #13 MeSH descriptor: [Immobilization] explode all trees
- #14 MeSH descriptor: [Casts, Surgical] this term only
- #15 MeSH descriptor: [Splints] this term only
- #16 MeSH descriptor: [Bandages] explode all trees
- #17 MeSH descriptor: [Braces] this term only
- #18 MeSH descriptor: [Physical Therapy Modalities] explode all trees
- #19 MeSH descriptor: [Exercise] explode all trees
- #20 MeSH descriptor: [Early Ambulation] this term only
- #21 mobil\* or immobil\* or movement\* or exercis\* or "physical therapy" or physiotherapy or cast or casts or splint\* or bandag\* or strap\* or plaster\*:ti,ab,kw (Word variations have been searched)
- #22 (functional near/1 (treatment or therapy)):ti,ab,kw (Word variations have been searched)
- #23 #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
- #24 #12 and #23 [Trials]

#### MEDLINE (Ovid Online)

- 1 Lateral Ligament, Ankle/
- 2 Ankle Injuries/
- 3 ((ankle or talo-fibular or talofibular or calcaneo-fibular or calcaneofibular or fibular) adj4 ligament\*).tw.
- 4 or/1-3
- 5 Joint Instability/
- 6 Rupture/
- 7 "Sprains and Strains"/
- 8 (sprain\* or strain\* or injur\* or rupture\* or tear or torn or trauma\* or lesion\* or distort?ion).tw.
- 9 or/5-8
- 10 4 and 9
- 11 (ankle\* adj4 (sprain\* or inversion\*)).tw.
- 12 10 or 11
- 13 Immobilization/
- 14 Casts, Surgical/
- 15 Splints/

16 Bandages/  
 17 Braces/  
 18 exp Physical Therapy Modalities/  
 19 exp Exercise/  
 20 Early Ambulation/  
 21 (mobil\* or immobil\* or movement\* or exercis\* or "physical therapy" or physiotherapy or cast\*1 or splint\* or bandag\* or strap\* or plaster\*).tw.  
 22 (functional adj1 (treatment or therapy)).tw.  
 23 or/13-22  
 24 12 and 23  
 25 Randomized controlled trial.pt.  
 26 Controlled clinical trial.pt.  
 27 randomized.ab.  
 28 placebo.ab.  
 29 Drug therapy.fs.  
 30 randomly.ab.  
 31 trial.ab.  
 32 groups.ab.  
 33 or/25-32  
 34 exp Animals/ not Humans/  
 35 33 not 34  
 36 24 and 35

#### **EMBASE (Ovid Online)**

1 Ankle lateral ligament/  
 2 Ankle injury/  
 3 Ankle instability/  
 4 ((ankle or talo-fibular or talofibular or calcaneo-fibular or calcaneofibular or fibular) adj4 ligament\*).tw.  
 5 or/1-4  
 6 Joint Instability/  
 7 Ligament Rupture/  
 8 Sprain/  
 9 (sprain\* or strain\* or injur\* or rupture\* or tear or torn or trauma\* or lesion\* or distort?ion).tw.  
 10 or/6-9  
 11 5 and 10  
 12 Ankle sprain/  
 13 (ankle\* adj4 (sprain\* or inversion\*)).tw.  
 14 12 or 13  
 15 11 or 14  
 16 Mobilization/ or Immobilization/  
 17 Orthopedic cast/ or Plaster cast/  
 18 Splint/  
 19 Bandage/  
 20 Brace/  
 21 exp Physiotherapy/  
 22 Manipulative medicine/  
 23 exp Kinesiotherapy/  
 24 exp Exercise/  
 25 Functional Training/  
 26 (mobil\* or immobil\* or movement\* or exercis\* or "physical therapy" or physiotherapy or cast\*1 or splint\* or bandag\* or strap\* or plaster\*).tw.  
 27 (functional adj1 (treatment or therapy)).tw.

28 or/16-27  
 29 15 and 28  
 30 Randomized controlled trial/  
 31 Clinical trial/  
 32 Controlled clinical trial/  
 33 Randomization/  
 34 Single blind procedure/  
 35 Double blind procedure/  
 36 Crossover procedure/  
 37 Placebo/  
 38 Prospective study/  
 39 ((clinical or controlled or comparative or placebo or prospective\* or randomi#ed) adj3 (trial or study)).tw.  
 40 (random\* adj7 (allocat\* or allot\* or assign\* or basis\* or divid\* or order\*)).tw.  
 41 ((singl\* or doubl\* or trebl\* or tripl\*) adj7 (blind\* or mask\*)).tw.  
 42 (cross?over\* or (cross adj1 over\*)).tw.  
 43 ((allocat\* or allot\* or assign\* or divid\*) adj3 (condition\* or experiment\* or intervention\* or treatment\* or therap\* or control\* or group\*)).tw.  
 44 RCT.tw.  
 45 or/30-44  
 46 Case Study/ or Abstract Report/ or Letter/  
 47 45 not 46  
 48 29 and 47

## CONTRIBUTIONS OF AUTHORS

MW: Initiator of review, design and drafting of protocol.

DK: Initiator of review, design and drafting of protocol.

AS: Design and drafting of protocol.

CB: Design and drafting of protocol.

SL: Oversee design and drafting of protocol, guarantor.

## DECLARATIONS OF INTEREST

MW: Worked as a research physiotherapist on the Collaborative Ankle Support Trial (CAST), a pragmatic randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of three types of mechanical ankle support with tubular bandage, conducted between 2003 and 2006. CAST was funded by the UK National Institute for Health Research Health Technology Assessment Programme.

DK: None declared.

AS: None declared.

CB: None declared.

SL: Was the chief investigator of the Collaborative Ankle Support Trial (CAST), a pragmatic randomised controlled trial comparing the clinical effectiveness and cost-effectiveness of three types of mechanical ankle support with tubular bandage, conducted between 2003 and 2006. CAST was funded by the UK National Institute for Health Research Health Technology Assessment Programme.

Review authors who were not investigators on CAST will carry out independent trial selection and evaluation of this trial.

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- National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research & Care (CLAHRC), Oxford, UK.

This protocol has been developed in association with the NIHR Collaboration for Leadership in Applied Health Research & Care (CLAHRC) (Keene, Williams, Byrne, Lamb). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NIHR, NHS or the UK Department of Health.

### External sources

- No sources of support supplied