research

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ORIGINAL RESEARCH Multicentre randomised controlled trial

Use of cast immobilisation versus removable brace in adults with an ankle fracture

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Study question How superior is a removable brace compared with plaster cast immobilisation on function, quality of life, resource use, and complications in adults with an ankle fracture?

Methods Pragmatic, multicentre, superiority randomised controlled trial in 20 trauma centres in the UK National Health Service. People aged 18 years or older with an acute closed ankle fracture, suitable for cast immobilisation, were potentially eligible. Randomisation was on a 1:1 basis to either a plaster cast (n=334) or a removable brace (n=335). Participants receiving cast immobilisation could only complete ankle range of movement exercises once the cast was removed.Participants receiving a removable brace could complete ankle range of movement exercises immediately. The primary outcome was the Olerud Molander ankle score at 16 weeks, analysed by intention to treat. Secondary outcomes were leg specific function (Manchester-Oxford foot questionnaire, disability rating index), quality of life, and complications at 6, 10, and 16 weeks.

Study answer and limitations No statistically significant difference was found in the Olerud Molander ankle score between the cast and removable brace groups at 16 weeks (favours brace: 1.8, 95% confidence interval −2.0 to 5.6). No clinically significant differences were found in the Olerud Molander ankle scores at other time points, in the secondary unadjusted, imputed, or per protocol analyses. The main limitation of this study was the 25% loss to follow-up; however, the minimum sample size was exceeded by a large margin, and post hoc sensitivity analysis, accounting for missing data, gave similar results.

What this study adds This study found that cast immobilisation was not superior to a removable brace at 16 weeks in adults with ankle fracture. Other factors will need to be considered in deciding optimal management of ankle fractures.

Funding, competing interests, and data sharing This trial was funded by the National Institute for Health Research (NIHR). Authors have received funding from NIHR. Trial data are not publicly available but access to the anonymised dataset can be obtained on reasonable request.

Trial registration ISRCTN registry ISRCTN15537280.

Olerud Molander ankle score (OMAS) in adults with ankle fracture allocated to plaster cast or removable brace in intention-to-treat population*

	Cast (n=334)		Removable brace (n=335)		Between group difference (95% CI)		
	No	Mean (SD) OMAS	No	Mean (SD) OMAS	Unadjusted	Adjusted†	P value
6 weeks	241	37.2 (22.1	256	39.6 (20.6)	2.4 (−1.4 to 6.2)	2.2 (−1.4 to 5.8)	0.23
10 weeks	229	47.1 (21.7)	239	51.5 (23.0)	4.5 (0.4 to 8.5)	4.5 (0.6 to 8.3)	0.02
16 weeks	242	62.4 (23.4)	260	64.5 (22.4)	2.1 (−1.9 to 6.2)	1.8 (−2.0 to 5.6)	0.35

*Positive values in favour of removable brace.
†Estimates are from linear regression model adjusted for patient sex, age group, and fracture management at baseline.

Efficacy, acceptability, and safety of muscle relaxants for adults with non-specific low back pain

Cashin AG, Folly T, Bagg MK, et al

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Study question Are muscle relaxants effective and safe compared with placebo, usual care, a waiting list, or no treatment in adults with non-specific low back pain?

Methods Systematic review and meta-analysis of randomised controlled trials investigating the efficacy and safety of muscle relaxants compared with control in adults reporting non-specific low back pain. Eight databases including three clinical trial registries were searched from inception to 23 February 2021. Two reviewers independently identified studies, extracted data, and assessed the risk of bias and certainty in the evidence using the Cochrane risk-of-bias tool and Grading of Recommendations, Assessment, Development and Evaluations, respectively. Random effects meta-analyses were used to estimate pooled effects and 95% confidence intervals.

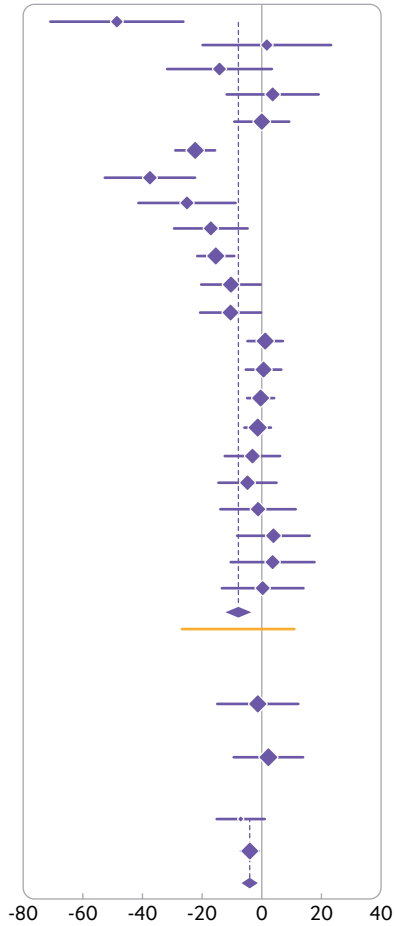
Study answer and limitations Very low and low certainty evidence shows that non-benzodiazepine antispasmodics might offer a small (<8 points on a 0–100 point scale), non-clinically important reduction in pain intensity (mean difference −7.7, 95% confidence interval −12.1 to −3.3; 16 trials, 4546 participants) at two weeks or less for acute low back pain and they might increase the risk of an adverse event (relative risk 1.6, 95% confidence interval 1.2 to 2.0; 16 trials, 3404 participants) but not a serious adverse event (2.3, 0.3 to 20.8; 2 trials, 830 participants; very low certainty evidence). The number of trials investigating other muscle relaxants and different durations of low back pain were small and the certainty of evidence was reduced because most trials were at high risk of bias.

What this study adds This review found considerable uncertainty in the clinical efficacy and safety of muscle relaxants to treat acute low back pain in adults. Large, definitive, placebo controlled trials are urgently needed to resolve these uncertainties.

Funding, competing interests, and data sharing This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. All authors declare no competing interests. The dataset and accompanying code used in this study are available from the corresponding author (j.mcauley@neura.edu.au).

Review registration PROSPERO CRD42019126820 and Open Science Framework https://osf.io/mu2f5/.

Reference, drug	Muscle relaxants No	Mean	SD	Control No	Mean	SD	Weight (%)	Mean difference (95% CI)
Acute low back pain								
Non-benzodiazepine antispasmodics								
Hindle 1972,[59] carisoprodol	14	15.5	30.0	14	64.0	30.0	2.4	-48.5 (-70.7 to -26.3)
Lepisto 1979,[64] tizanidine	15	-51.0	30.0	15	-52.7	30.0	2.5	1.7 (-19.8 to 23.2)
Baratta 1982,[69] cyclobenzaprine	58	-55.0	48.5	59	-40.0	48.9	3.2	-15.0 (-32.6 to 2.6)
Berry 1988,[77] tizanidine	46	-29.0	43.3	52	-33.0	32.9	3.6	4.0 (-11.4 to 19.4)
Berry 1988,[78] tizanidine	51	19.0	23.2	45	19.0	22.9	5.1	0.0 (-9.2 to 9.2)
Tüzün 2003,[75] thiocolchicoside	73	25.1	20.9	68	47.4	19.8	5.7	-22.3 (-29.0 to -15.6)
Ketenci 2005,[62] thiocolchicoside	38	6.3	11.7	14	43.7	27.9	3.7	-37.4 (-52.5 to -22.3)
Ketenci 2005,[62] tizanidine	32	18.6	16.6	13	43.7	27.9	3.4	-25.1 (-41.3 to -8.9)
Ralph 2008,[68] carisoprodol	269	-47.0	77.9	278	-30.0	66.7	4.3	-17.0 (-29.2 to -4.8)
Pareek 2009,[67] tizanidine	94	-58.8	21.4	91	-43.5	20.6	5.8	-15.3 (-21.4 to -9.2)
Serfer 2010,[72] carisoprodol	260	-44.5	48.4	128	-34.2	44.0	5.0	-10.3 (-19.9 to -0.7)
Serfer 2010,[72] carisoprodol	251	-44.5	47.5	128	-34.2	44.0	5.0	-10.3 (-19.9 to -0.7)
NCT00671502 2011,[90] carisoprodol	280	-27.5	30.0	140	-28.6	30.0	5.8	1.1 (-5.0 to 7.2)
NCT00671502 2011,[90] carisoprodol	281	-28.0	30.0	139	-28.6	30.0	5.8	0.6 (-5.5 to 6.7)
NCT00671879 2012,[89] carisoprodol	271	-15.5	22.1	132	-15.2	21.4	6.1	-0.3 (-4.8 to 4.2)
NCT00671879 2012,[89] carisoprodol	270	-16.4	21.4	132	-15.2	21.4	6.1	-1.2 (-5.7 to 3.3)
Friedman 2015,[51] cyclobenzaprine	103	36.0	35.8	104	39.0	30.9	5.1	-3.0 (-12.1 to 6.1)
Aparna 2016,[58] thiocolchicoside	79	6.7	30.0	74	11.5	30.0	5.0	-4.8 (-14.3 to 4.7)
Friedman 2018,[53] orphenadrine	78	38.0	33.0	38	39.0	32.0	4.2	-1.0 (-13.5 to 11.5)
Friedman 2018,[53] methocarbamol	80	43.0	32.7	38	39.0	32.0	4.3	4.0 (-8.4 to 16.4)
Friedman 2019,[54] metaxalone	76	42.0	33.3	24	38.3	29.3	3.9	3.7 (-10.2 to 17.6)
Friedman 2019,[54] tizanidine	76	38.7	31.7	25	38.3	29.3	4.0	0.4 (-13.1 to 13.9)
Overall effect							100.0	-7.7 (-12.1 to -3.3)
Prediction interval								(-26.5 to 11.1)
Test for heterogeneity: ^{2}=76.19; P<0.01; I^2=80% (70%; 86%)								
Antispastic								
Friedman 2019,[54] baclofen	79	36.7	32.0	24	38.3	29.3	100.0	-1.6 (-15.3 to 12.1)
Benzodiazepine								
Friedman 2017,[52] diazepam	57	31.7	31.7	55	29.7	32.0	100.0	2.0 (-9.8 to 13.8)
Mixed low back pain								
Non-benzodiazepine antispasmodic								
Aksoy 2002,[47] thiocolchicoside	174	33.0	36.2	155	40.0	37.4	10.0	-7.0 (-15.0 to 1.0)
Akhter 2017,[46] thiocolchicoside	144	9.4	11.5	144	13.5	11.5	90.0	-4.1 (-6.8 to -1.4)
Overall effect							100.0	-4.4 (-6.9 to -1.9)
Test for heterogeneity: ^{2}=0; P=0.50; I^2=0%								



Effect of muscle relaxants compared with control on pain intensity (0-100 scale) at immediate term (≤2 weeks) post-randomisation for adults with low back pain. Negative values for mean differences indicate that effects favour muscle relaxants compared with control, whereas negative values for trial observations indicate change from baseline

Clinical effectiveness of common elective orthopaedic procedures

Blom AW, Donovan RL, Beswick AD, Whitehouse MR, Kunutsor SK

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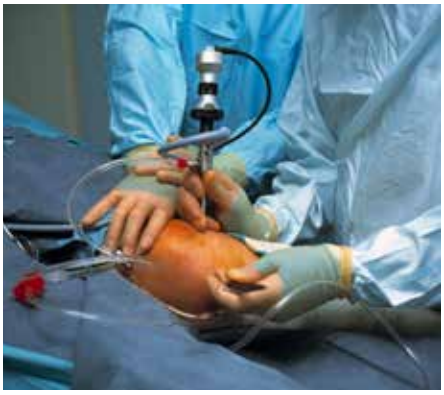
Find this at: http://dx.doi.org/10.1136/bmj.n1511

Study question Does level 1 evidence exist to show that common elective orthopaedic procedures are clinically effective compared with no treatment, placebo, or non-operative care?

Methods This umbrella review of meta-analyses of randomised controlled trials studied 10 of the most common orthopaedic procedures—arthroscopic anterior cruciate ligament reconstruction, arthroscopic meniscal repair of the knee, arthroscopic partial meniscectomy of the knee, arthroscopic rotator cuff repair, arthroscopic subacromial decompression, carpal tunnel decompression, lumbar spine decompression, lumbar spine fusion, total hip replacement, and total knee replacement. Medline, Embase, and the Cochrane Library were searched until September 2020 for meta-analyses of randomised controlled trials that compared the clinical effectiveness of these orthopaedic procedures with no treatment, placebo, or non-operative care. The quality and quantity of the evidence behind the interventions were assessed, and comparisons were made with the strength of the recommendations in relevant national clinical guidelines.

Study answer and limitations Evidence from randomised controlled trials supports the superiority of carpal tunnel decompression and total knee replacement over non-operative care. No randomised controlled trials specifically compared total hip replacement or meniscal repair of the knee with non-operative care. Trial evidence for the other six procedures showed no benefit over non-operative care. Some procedures lacked sufficient level 1 evidence.

What this study adds Although they may be effective overall or in certain subgroups, no strong high quality evidence base shows that many commonly performed orthopaedic procedures are better than non-operative alternatives. Despite the lack of strong evidence, some of these procedures are still recommended by national guidelines in certain situations.



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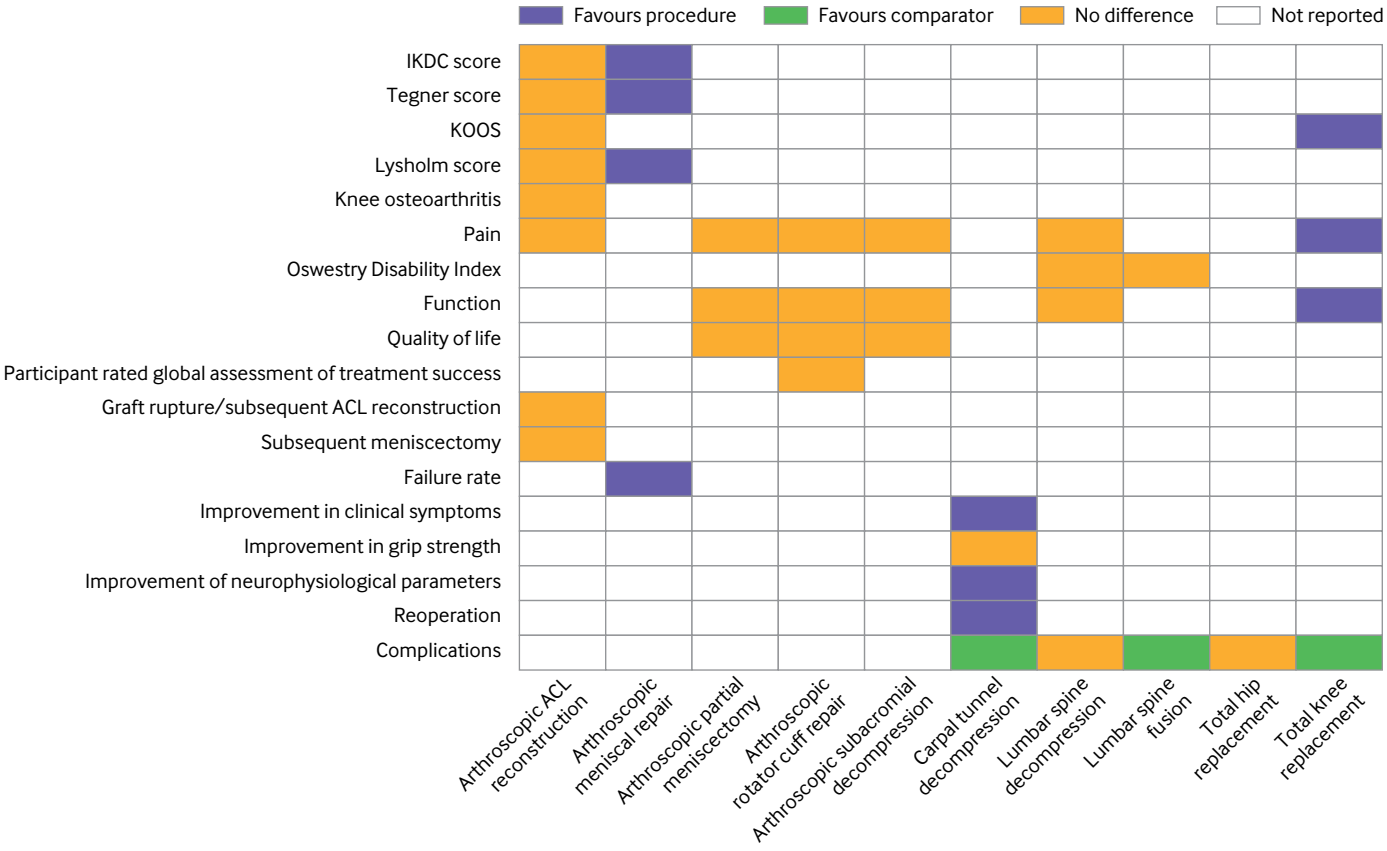
Systematic review registration PROSPERO CRD42018115917.



Overall findings of umbrella review by outcome measures and orthopaedic procedures. ACL=anterior cruciate ligament; IKDC=International Knee Documentation Committee; KOOS=Knee Injury and Osteoarthritis Outcome Score

Recommendations for including or reviewing patient reported outcome endpoints in grant applications

Snyder C, Gilbert A, Moher D, et al; on behalf of the PROTEUS consortium

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Patients, clinicians, regulators, policy makers, and clinical guideline developers value information regarding the impact of disease and treatment from the perspective of patients. Thus, patient reported outcome (PRO) assessments that collect this information are a critical aspect of research studies. The PRO results from research studies can most effectively be used if they are measured appropriately and reported clearly. However, a recent review of 160 international clinical trials with PRO endpoints found frequent suboptimal reporting, and more than a third of trials failed to report PRO findings at all.

Several methodological tools have been developed using rigorous, stakeholder engaged methods to improve the design, analysis, reporting, and interpretation of PROs in research studies. However, given the space constraints in most grant applications, not all the recommended information from these documents can be included. The PROTEUS consortium (patient reported outcomes tools: engaging users and stakeholders; TheProteusConsortium.org) undertook an effort to identify the key information regarding PRO methods to include in grant applications. By following these recommendations, investigators can demonstrate, and reviewers evaluate, preparedness to conduct the PRO aspects of the study rigorously, and ensure that adequate resources have been budgeted.

The online paper and technical appendix describe the four step, informal consensus development process used to develop these recommendations and the specific results from the recommendation-development process. Box 1 presents the final recommendations for information always to include, and box 2 presents the information to include if the PRO is a primary endpoint or if a second paragraph of PRO content can be included. The full paper includes example text for the topics in boxes 1 and 2 and additional topics to include if space is not a limitation. By following these recommendations at the formative, grant application phase, research teams can successfully report their results meaningfully at the completion of the study.

Box 1 | Topics related to patient reported outcomes (PRO) that should always be covered in grant applications*

1 Describe the rationale for PRO assessment
2 State the PRO specific research question(s)
3 Specify the PRO concepts or domains used to evaluate the research question(s) (eg, overall health related quality of life, specific domain, specific symptom), and the questionnaire(s) selected to assess them
4 Describe the time points for PRO assessment
5 Include a data collection plan outlining the permitted mode(s) of administration (eg, paper, telephone, electronic, other) and setting (eg, clinic, home, other)
6 State the PRO analysis method(s), in relation to the objective(s). State the broad PRO objectives, specifying if they are exploratory/descriptive or aim to evaluate treatment efficacy/clinical benefit. If they are to evaluate treatment efficacy/clinical benefit, state specific hypotheses (including relevant PRO concepts or domains) and include whether the between group comparison tests for superiority, equivalence, or non-inferiority. If the broad PRO objectives include within patient or within treatment group comparisons, clearly state the assumption (ie, improvement, worsening, stable state, overall effect), specific objective (eg, proportion of responders, time to PRO event, magnitude of improvement or worsening), and principal time point of interest

*The topics might be included in a dedicated section or could be described throughout the grant application.

Box 2 | Topics that should be included in grant applications if a patient reported outcome (PRO) is a primary endpoint or if a second paragraph of PRO content can be included*

Background and rationale for PRO assessment
1 Summarise PRO findings in relevant studies

Data collection and management
2 Justify the PRO instrument selected and provide or cite evidence of PRO instrument measurement properties and patient acceptability or burden, ideally in the population of interest
3 If PROs will not be collected from the entire study sample, provide a rationale and describe the PRO specific eligibility criteria (eg, PRO substudy, language or reading requirements, or pre-randomisation completion of PRO assessment)
4 When the study context requires someone other than a study participant to answer on his or her behalf (a proxy reported outcome), state and justify the use of a proxy respondent
5 Specify PRO data collection and management strategies to minimise missing data
6 State whether PRO data will be monitored during the study to inform the clinical care of individual study participants

Analysis
7 When a PRO is the primary endpoint, state the required sample size (and how it was determined) and recruitment target (accounting for expected loss to follow-up)
8 Outline the methods for handling missing items or entire assessments (eg, approach to imputation and sensitivity analyses)
9 Specify whether more than one language version will be used
10 Include PRO analysis plans for addressing multiplicity or type I (α) error

*This content is in addition to the content described in box 1. These additional topics might be included in a dedicated section or could be described throughout the grant application.