Clinical trial results:
Facet-joint injections for people with persistent non-specific low back pain (FIS)

Summary

EudraCT number	2014-000682-50
Trial protocol	GB
Global end of trial date	30 April 2016

Results information

Result version number	v1 (current)
This version publication date	27 July 2019
First version publication date	27 July 2019
Summary attachment (see zip file)	FIS Published HTA Report (facet-joint-injections-people-persistent-Ellard-2017.pdf)

Trial information

Trial identification

Sponsor protocol code	REGO2013-592

Additional study identifiers

ISRCTN number	ISRCTN93184143
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Warwick
Sponsor organisation address	Kirby Corner Road, COVENTRY, United Kingdom, CV4 7AL
Public contact	Professor Martin Underwood, Warwick Clinical Trials Unit (WCTU), +44 2476 574664, m.underwood@warwick.ac.uk
Scientific contact	Professor Martin Underwood, Warwick Clinical Trials Unit (WCTU), +44 2476 574664, m.underwood@warwick.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 May 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to explore the feasibility of running a randomised controlled trial to test the hypothesis that for people with suspected facet joint pain contributing to persistent low back pain, adding the option of facet joint injections to best usual non-invasive care available from the NHS is clinically and cost effective.

Protection of trial subjects:

A TSC was convened for the trial, but with the agreement of the funder, no DMC was required.
The role of the TSC is to provide overall supervision for a trial on behalf of the Trial Sponsor and Trial Funder and to ensure that the trial is conducted to the rigorous standards as set out in the Department of Health's Research Governance Framework for Health and Social Care and the Guidelines for Good Clinical Practice. The current project encompasses a substantial amount of exploratory and preparatory work in addition to just the randomised feasibility trial. The TSC will have an important role in overseeing this aspect of the trial. We anticipate that the members of this committee will form the membership of the TSC for the main trial.

The TSC in the development of this protocol and throughout the trial will take responsibility for:
- Monitoring and supervising the progress of the trial, adherence to the protocol, patient safety and the consideration of new information of relevance to the research question
- The rights, safety and well-being of the trial participants are the most important considerations and should prevail over the interests of science and society
- To ensure appropriate ethical and other approvals are obtained in line with the project plan
- Reviewing relevant information from other sources
- To agree proposals for substantial protocol amendments and provide advice to the sponsor and funder regarding approvals of such amendments
- To provide advice to the investigators on all aspects of the trial
- Assuming role of DMC
- Recommend premature closure of the trial

The TSC membership will include an independent Chairperson and as a minimum, two clinicians with experience in the conduct of clinical trials/caring for patients with low back pain, a statistician independent of the trial, respected and experienced muscoskeletal personnel with low back pain speciality as well as lay representatives.

Background therapy:

n/a

Evidence for comparator:

The facet joints are paired structures between the superior and inferior articular processes of adjacent vertebrae which, in the lumbar spine, allow flexion and a degree of rotation of the spine. They are synovial joints whose capsule is richly innervated. With increasing age progressively more people develop radiological osteoarthrosis of the facet joints. In one population study of people aged 40-80, over 60% of those studied had radiological osteoarthritis. There was not, however, an association observed between this and the presence of back pain. 2 Pain arising from the facet joint is suspected clinically and may be abolished temporarily by injection of local anaesthetic, when used as a diagnostic test. A depot preparation of steroid added to the injection may prolong the analgesic benefit. The use of steroid injections has been shown to be effective in producing, at least short term (one to four weeks), benefits for a range of musculoskeletal disorders including osteoarthritis of the knee, and hip, and frozen shoulder. 3-5 Analgesic benefits of intra-articular injection of corticosteroids in rheumatoid arthritis may be more sustained (up to three months). 6 Drawing on these data from other parts of the musculoskeletal system it is a reasonable hypothesis that local injection of corticosteroids could produce at least short-term pain relief in a different synovial joint that is causing pain. Relief or reduction of pain

may facilitate compliance with a programme of exercise designed to improve lumbar range of movement and muscular stability.

In this study we will explore the feasibility of running a randomised controlled trial to test the hypothesis that, for people with suspected facet joint pain contributing to persistent non-specific low back pain, adding the option of facet joint injections, with local anaesthetic and corticosteroids, to best usual non-invasive care available from the NHS is clinically and cost-effective.

Actual start date of recruitment	03 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	25
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started on 26 June 2015 and was terminated by the funder on 11 December 2015 because of poor recruitment, at which point 26 participants had been randomised.
Work took place in four sites in England

Pre-assignment

Screening details:

In total, 320 people were approached about the study and 164 (51%) completed a screening questionnaire. Of these, 56 (34%) were interested in and appeared to be eligible for the study 27 of whom (81%) had suspected facet joint pain. One was not randomised because of termination of recruitment.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Best usual care + Facet joint injections

Arm description:

For those participants who were randomised to undergo facet joint injection , the injection took place between the first and second best usual care sessions. The treating clinician at this time made their own assessment of the participant's suitability for facet joint injection and obtained consent for the procedure following normal practice in each participating site. Full details of injection process are available from https://www.ncbi.nlm.nih.gov/pubmed/26431124

Arm type	Experimental
Investigational medicinal product name	Pre-filled syringes containing 7.5 mg of bupivacaine and 20 mg of methyl prednisolone in total volume; 2 ml will be used for each joint.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intraarticular use

Dosage and administration details:

Pre-filled syringes containing 7.5 mg of bupivacaine and 20 mg of methyl prednisolone in total volume; 2 ml used for each joint. The full volume, 2 ml, will be injected through the spinal needle placed into each joint. Some facet joints may not be sufficiently large to take this volume of injectate meaning in practice that the injections will be intra- and periarticular. This reflects what we believe to be current practice in the UK. Resistance to injection may occur because of abutment of the needle bevel to a surface or because of filling of the intra-articular space:
¢ Force should not be used.
¢ The needle should first be rotated 90° and a further attempt at injection made.
¢ If, after two further 90° rotations resistance to injection persists or if, after successful injection of a part-volume resistance develops, gentle pressure should be maintained on the plunger and the needle withdrawn gradually until resistance to injection falls.

Arm title	Best usual care

Arm description:

It was expected that all participants would have up to a total of six 'best usual care' physiotherapy sessions (including the first treatment session immediately prior to randomisation). The five remaining sessions were to last approximately 30 minutes. All participants (those in the intervention and those in

the control arms) were encouraged to attend all of these sessions. The package was a series of one-to-one sessions with a study physiotherapist who would use the BUC manual informed by consensus to help them tailor the treatment to the participant's needs.26 Sessions were a bespoke package of physical and behavioural rehabilitation. All treatment sessions were to be completed within 12 weeks of randomisation.

Arm type	Best usual care
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Best usual care + Facet joint injections	Best usual care
Started	13	13
Completed	13	13

Baseline characteristics

Reporting groups

Reporting group title	Overall

Reporting group description:

In total, 320 people were approached about the study and 164 (51%) completed a screening questionnaire. Of these, 56 (34%) were interested in and appeared to be eligible for the study. At the time that recruitment closed 33 people had been assessed for the study, 27 of whom (81%) had suspected facet joint pain. One was not randomised because of the termination of recruitment, which meant that the final randomised total was 26 people

Reporting group values	Overall	Total	
Number of subjects	26	26	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	53		
standard deviation	± 14.4	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	6	6	
Missing	1	1	

Subject analysis sets

Subject analysis set title	All
Subject analysis set type	Full analysis

Subject analysis set description:

We report here data from both arms of the trial as single group. Since this pilot was terminated early because of poor recruitment no between group analysis was performed; any such analysis would have little or no scientific value and could be potentially misleading

Reporting group values	All		
Number of subjects	26		
Age categorical Units: Subjects			
In utero			

Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	 53 ± 14.4		
Gender categorical Units: Subjects			
Female Male Missing	19 6		

End points

End points reporting groups

Reporting group title	Best usual care + Facet joint injections

Reporting group description:

For those participants who were randomised to undergo facet joint injection , the injection took place between the first and second best usual care sessions. The treating clinician at this time made their own assessment of the participant's suitability for facet joint injection and obtained consent for the procedure following normal practice in each participating site. Full details of injection process are available from https://www.ncbi.nlm.nih.gov/pubmed/26431124

Reporting group title	Best usual care

Reporting group description:

It was expected that all participants would have up to a total of six 'best usual care' physiotherapy sessions (including the first treatment session immediately prior to randomisation). The five remaining sessions were to last approximately 30 minutes. All participants (those in the intervention and those in the control arms) were encouraged to attend all of these sessions. The package was a series of one-to-one sessions with a study physiotherapist who would use the BUC manual informed by consensus to help them tailor the treatment to the participant's needs.26 Sessions were a bespoke package of physical and behavioural rehabilitation. All treatment sessions were to be completed within 12 weeks of randomisation.

Subject analysis set title	All
Subject analysis set type	Full analysis

Subject analysis set description:

We report here data from both arms of the trial as single group. Since this pilot was terminated early because of poor recruitment no between group analysis was performed; any such analysis would have little or no scientific value and could be potentially misleading

Primary: Back pain

End point title	Back pain[1]

End point description:

The primary clinical outcome was an 11-point numerical rating scale for pain collected via text messaging over 3 months following randomisation. For those participants unable or unwilling to use a text messaging system, we used a paper-based system.

Our second primary outcome was back pain related disability [measured by the Roland–Morris Disability Questionnaire (RMDQ)] at 3 months

End point type	Primary

End point timeframe:

Three months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Trial terminated due to failure to recruit. No statistical analysis appropriate.

End point values	All			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: 11 point numerical rating scale for pain				
number (not applicable)	26			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Three months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Trial terminated due to poor recruitment - no AEs were recorded

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2014	a cover letter to supplement the follow-up questionnaires a reminder letter for non-return of follow-up questionnaires a daily/weekly pain diary a weekly health diary a daily health diary
20 November 2014	Added Castle Hill Hospital, Cottingham,
13 February 2015	added The James Cook University Hospital, Middlesbrough removed South Warwickshire NHS Foundation Trust, Warwick Hospital, Warwick,
29 June 2015	added South Warwickshire NHS Foundation Trust, Warwick Hospital, Warwick,
14 September 2015	approval to make changes to the protocol and information sheets and gain approval for a new clinic poster
16 December 2015	approval for the new scheduled diagnostic assessment and screening questionnaire response letters

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 December 2015	Terminated by funder because of poor recruitment	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study terminated early because of poor recruitment

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28639551

http://www.ncbi.nlm.nih.gov/pubmed/26431124

http://www.ncbi.nlm.nih.gov/pubmed/26703477

http://www.ncbi.nlm.nih.gov/pubmed/26906169