



# BMJ Open OASIS – a randomised, placebo-controlled trial of oral glucocorticoids for leg pain in patients with acute sciatica: trial protocol

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## ABSTRACT

**Introduction** Sciatica is a lower spine condition characterised by radiating leg pain below the knee. It may be accompanied by motor and sensory loss in the distribution of a spinal nerve. There are few effective treatments for sciatica. Orally administered glucocorticoids have shown some promise, however, any beneficial effects need to be confirmed and weighed against drug safety and cost-effectiveness, in a high-quality, definitive trial.

**Methods and analysis** The Oral Steroids In Sciatica (OASIS) trial is a randomised, placebo-controlled, double-blind trial that will evaluate a tapering regimen of oral prednisolone in 200 participants with acute sciatica. Participants will be recruited on presentation to general practice, specialist outpatient clinics or hospital emergency departments and randomised to receive orally administered prednisolone 50 mg per day, up to 3 days then tapering to cessation over 10 days, or placebo, for a maximum of 13 days, in addition to guideline advice. Participants will be followed for 1 year. The primary endpoint will be leg pain intensity at 2 weeks. Secondary outcomes will include back pain intensity, disability, time to recovery, quality of life and treatment success rate. Adverse events will be assessed and a cost-effectiveness analysis will be conducted.

**Ethics and dissemination** Ethical approval has been granted from the Human Research Ethics Committee, The University of Sydney. Trial results will be disseminated by publications and conference presentations and via the media.

**Trial registration number** ACTRN12619001716156.

## INTRODUCTION

Sciatica is a symptom characterised by pain radiating down the back of the leg, in the distribution of a lumbar nerve (radicular pain), most often due to compression of a nerve root (L4 to S3) by a herniated intervertebral disc. It may be accompanied by back pain, motor or sensory deficits and changes in reflexes. Most cases occur in the fourth and fifth decades of life.<sup>1</sup> With a lifetime

## Strengths and limitations of this study

- The OASIS trial is a two arm, participant-blinded, clinician-blinded and assessor-blinded, randomised controlled trial of oral glucocorticoids compared with placebo for reducing leg pain in patients with acute sciatica.
- This trial is adequately powered and will inform the appropriate and judicious use of oral glucocorticoids for sciatica.
- While we anticipate adequate blinding of participants in this study, there is still a risk that patients may suspect they were randomised to the active treatment arm given the known effects of prednisolone (insomnia, mood changes, anxiety, a sense of fullness, weight gain and stomach upset).

prevalence reported between 12.2% and 43.0% and point prevalence between 1.5% and 13.4%, sciatica is a common condition that has important physical, psychological and economic impacts.<sup>2–5</sup> While back pain is the leading cause of disability worldwide,<sup>6</sup> the subset of people with sciatica has greater disability, higher pain, longer absence from work and consume more health resources than people with back pain but no sciatica.<sup>1,7</sup>

There are few effective treatments to alleviate sciatica, irrespective of symptom duration (acute or chronic).<sup>8–12</sup> Our previously published trial showed that pregabalin, a drug used to treat neuropathic pain, did not improve outcomes compared with placebo in people with sciatica, but significantly increased the risk of adverse events.<sup>13</sup> A review also showed that common analgesics such as paracetamol, non-steroidal anti-inflammatory drugs or opioid analgesics (and their combination) are no more effective than placebo in reducing pain or disability caused by

sciatica.<sup>14 15</sup> In addition, there is also little evidence that non-pharmacological, non-invasive interventions (eg, physical therapy) are effective for people with sciatica. However, exercise (isometric trunk and lower limb exercises) has been shown to provide a small treatment effect in the short term (compared with advice) for people with chronic sciatica, but there is no clear benefit of exercise for acute sciatica (<3 months duration).<sup>16</sup>

Treating sciatica with glucocorticoids is based on a pharmacologically plausible rationale. Sciatica is the most commonly caused by compression of a lumbar nerve root due to disc herniation,<sup>3</sup> but mechanical compression alone may not be sufficient to cause symptoms.<sup>17</sup> Emerging data suggest that both compression and a secondary inflammatory response may be required to provoke leg pain, especially in acute cases<sup>18</sup> as pain severity is more closely linked to inflammatory changes than in chronic sciatica.<sup>19</sup> Glucocorticoids are inhibitors of inflammatory processes and are believed to exert their anti-inflammatory actions via repression of proinflammatory mediators.<sup>20</sup> Thus the rationale for using glucocorticoids such as prednisone or prednisolone in acute sciatica is to reduce the inflammation and oedema associated with the inflammatory changes around the nerve root<sup>21</sup> and alleviating symptoms and signs.<sup>18</sup>

Most systematic review evidence evaluating the efficacy of glucocorticoid therapy for sciatica focused on epidural administration. These reviews reported epidural glucocorticoid injections have a small, but short-term treatment benefit (mean difference against placebo=−6.2 on a 100-point pain scale, 95% CI=−9.4 to −3.0).<sup>10–12</sup> Importantly, epidural injections are comparatively more complex and generally more expensive, second-line treatments. Furthermore, the invasive nature of this procedure means that there is potential for serious although rare adverse events.<sup>22</sup> In contrast, short-term systemic glucocorticoid could be a simple, low-cost, first-line treatment option for sciatica with an acceptable risk profile and may have a longer duration of effect at the target site than a single, one-off epidural injection.<sup>23 24</sup>

However, current clinical evidence of systemic glucocorticoids for sciatica is inconclusive. The 2017 back pain guideline from the American College of Physicians does not recommend systemic glucocorticoids be used to treat acute sciatica, based on a review of six trials that found no effect on acute pain and none to a small effect on disability.<sup>8</sup> In contrast, a 2017 *British Medical Journal* review reported that glucocorticoids have some effects on pain and disability.<sup>14</sup> The challenge with existing evidence in the area is that the doses and drug formulations of glucocorticoids vary considerably across trials and at times patients with any symptom duration were combined in the analyses. This provides little meaningful guidance on issues such as optimal formulation and duration of glucocorticoid treatment or the ideal time to initiate therapy with respect to symptom duration.

In our 2019 review,<sup>9</sup> we identified a total of nine trials (n=717 participants) and found inconclusive, mostly

low-quality evidence on the efficacy of glucocorticoids administered via the oral, intramuscular or intravenous routes. We identified some promise of a short (15-day) course of oral prednisone for acute sciatica, with one trial showing reductions in pain and disability in the long term with such a regimen.<sup>25 26</sup> Short-term glucocorticoid therapy is generally considered safe, and any adverse events are usually reversible on cessation of drug treatment.<sup>27</sup> Long-term use of glucocorticoids is associated with serious risks including osteoporotic fractures, dyslipidaemia, glucose intolerance and glucocorticoid-induced avascular bone necrosis.<sup>28</sup> Such risks are less relevant in the treatment of sciatica, where glucocorticoids are typically used as short-term therapy.<sup>9</sup>

Nevertheless, there are potential harms associated with short-term glucocorticoid therapy.<sup>29</sup> Our systematic review found that those who received oral glucocorticoids had an almost twofold greater risk of adverse events such as nausea or light-headedness compared with placebo (risk ratio=2.1, 95% CI 1.4 to 3.1, one study).<sup>9</sup> Because glucocorticoids are already used in routine care to treat sciatica (spinal conditions are one of the main indications for adults to be prescribed glucocorticoids in the USA),<sup>29</sup> and their benefits are largely unclear, we need to establish whether they have benefits that outweigh the possible harms of these medicines for people with sciatica.

Finding a simple, effective and low-cost, first-line treatment option for acute sciatica is a priority. Our review findings suggest a possible benefit of early glucocorticoid therapy for sciatica as more notable benefits were seen when treatment was commenced early (ie, in acute cases).<sup>9</sup> Oral glucocorticoids in particular have the potential to provide a simple, low-cost treatment solution in acute sciatica. However, as questions remain around whether oral glucocorticoids can provide clinically worthwhile benefit, effectiveness needs to be confirmed and considered against drug safety and cost-effectiveness, in a high-quality, definitive trial. We propose a randomised placebo-controlled trial to investigate the efficacy and safety of oral glucocorticoids compared with placebo in people with acute sciatica. Informed by previous trials, we will use glucocorticoids administered early in the course of sciatica.<sup>9</sup> If found to be efficacious and safe, oral glucocorticoids would be a conservative treatment for patients with acute sciatica.

## METHODS AND ANALYSIS

### Design

OASIS—Oral Steroids In Sciatica—is a randomised, placebo-controlled, participant-blinded, clinician-blinded and assessor-blinded superiority trial, with two parallel groups randomised at a 1:1 allocation. We have chosen a randomised, placebo-controlled design in order to provide high-level evidence on the efficacy. The current report describes the detailed trial protocol and follows the SPIRIT 2013 Statement.<sup>30</sup>

## Setting

The OASIS trial will be conducted in general practice, specialist (eg, rheumatology) outpatient clinics and hospital emergency departments. Registered medical practitioners will be invited to participate as study doctors. Participants will be recruited when they present to a study doctor with acute sciatica. All sites will follow the same study procedures.

## Eligibility criteria

Adults with acute sciatica (with or without concomitant low back pain) will be screened for eligibility as they present to a study doctor. Study doctors will complete a screening form to determine eligibility for the study.

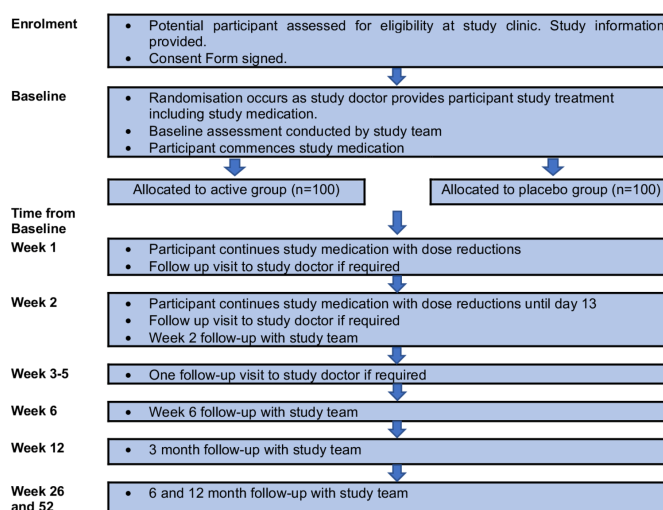
Inclusion criteria are as follows:

- ▶ Adults ( $\geq 18$  years old) with radiating pain into one leg below the knee, accompanied by nerve root or spinal nerve involvement as indicated by the presence of at least one of these clinical features: dermatomal leg pain, myotomal weakness, sensory deficits or diminished reflex.
- ▶ Pain duration not greater than 6 weeks (no minimum duration).
- ▶ Leg pain that is at least moderate in intensity or results in at least moderate interference with daily activities during the previous week (as measured by modification of 7 and 8 in the Medical Outcomes Study 36-Item Short-Form Health Survey).
- ▶ An adequate understanding of English or the availability of interpreter services for the participant to complete the trial outcomes.

Exclusion criteria are as follows:

- ▶ Known or suspected serious disease of the spine (eg, cauda equina syndrome).
- ▶ Planning to undergo spinal surgery or other interventional procedures (eg, an epidural injection) for sciatica during the treatment period.
- ▶ Having had spinal surgery or other interventional procedure (eg, an epidural injection) in the preceding 6 months.
- ▶ Having used a systemic glucocorticoid (for any condition) via any method of administration since the start of this episode of sciatica.
- ▶ Contraindications to glucocorticoids or precaution to glucocorticoids where risks outweigh potential benefits, including known allergy to prednisolone, active infection, active gastrointestinal bleeding (peptic ulcer), uncontrolled hypertension and heart failure, psychosis, immunosuppression and significant adverse event likely due to the previous use of equivalent dose steroid (eg, psychotic reaction).
- ▶ Known diabetes, prediabetes and the previous history of gestational diabetes, as glucocorticoids might affect blood sugar levels and lead to an unmasking of group allocation.

Participants will have an initial consultation with a study doctor and up to three follow-up consultations, if required. Questionnaires will be completed with the



**Figure 1** Participant timeline.

research team via phone or online. A participant timeline is shown in [figure 1](#).

## Intervention

All participants will receive guideline-recommended advice from a study doctor. This advice includes reassurance (of the benign pathology and prognosis), advice to stay active and to avoid bed rest and commonly recommended medicines. Study doctors will be trained on the trial protocol and receive regular monitoring visits from the trial team to ensure adherence to the trial protocol.

## Trial medication

Study doctors will prescribe and supply the study medication (either oral prednisolone or placebo). We have selected a dosing regimen which is similar to that used in the Goldberg *et al*'s trial<sup>26</sup> as our early preparatory work for the current trial found no consensus on glucocorticoid dosing recommendations. We conducted a number of consultations with clinicians (including primary care general practitioners, rheumatologists and sports physicians) but there was no clear consensus on an appropriate dose and duration of treatment. Our chosen regimen also balances the need for an adequate anti-inflammatory dose while mitigating the risk of adverse events.

The proposed medication regimen is pragmatic and involves a short tapering course of oral prednisolone, commencing with a high dose and tapering to cessation over 13 days. In our trial, participants will receive prednisolone 50 mg for up to 3 days, followed by 25 mg for up to 5 days, followed by 12.5 mg for up to 5 days. Trial medicines will be provided as 16 whole tablets of 25 mg prednisolone (or identical placebo) for each participant to complete the study dosing regimen: in order to maintain the stability and integrity of the study medication, only whole tablets will be provided. Participants will be supplied with a pill cutter to allow for halving of tablets during the final 5 days of the tapering regimen. The maximum duration from commencement to cessation will be 13 days with the maximum cumulative dose of 337.5 mg. The dose



can be adjusted by the study doctor depending on individual progress and tolerability. For example, if a participant experiences side effects (eg, difficulty sleeping), the initial prednisolone dose can be lowered to 25 mg per day. If a participant reaches 'adequate improvement' (0 to 1 out of 10 pain for 3 consecutive days),<sup>13</sup> dose reduction can start earlier.

The decreasing dose regimen will be communicated by the study doctor to the participant on the day of their enrolment into the study. The doctor will provide this advice verbally and will also write it down for the participant.

To monitor adherence to the study medicines, study doctors will be asked to record the study medication prescribed and participants will be asked to record their intake in a daily diary, plus return any unused medicines for counting at the end of the trial.

### Concomitant treatments

All participants may receive additional care during the treatment period as deemed appropriate by their study doctor. This may include physical or manual therapies or other medications except systemic glucocorticoids (oral or injection by any route). Concomitant use of inhaled and topical corticosteroids is permitted. We will record the use of concomitant analgesia/therapies. The efficacy of common analgesics (paracetamol, Nonsteroidal anti-inflammatory drugs, anticonvulsants and opioids) is either minimal or unclear in the context of acute sciatica.<sup>14 31</sup> Furthermore, due to the randomised nature of our study, we expect concomitant use of analgesics will be similar in both groups. Therefore, we have permitted concomitant analgesic use in this trial.

Participants will be asked to inform their study doctor regarding any concomitant medicines that are, or recommended, to be commenced. This provision does not apply if a medical emergency needs urgent pharmacotherapy.

### Outcomes

The outcomes were chosen to incorporate the core outcomes recommended by consensus of international experts.<sup>32 33</sup> Outcomes will be collected at 2, 6, 12, 26 and 52 weeks, unless otherwise stated.

#### Primary outcome

Leg pain intensity measured on a 0–10 Numerical Rating Scale (NRS) will be the primary outcome. This scale is valid, reliable and responsive for this population<sup>34</sup> and is a recommended measurement tool for pain intensity in back pain research.<sup>32</sup>

#### Secondary outcomes

The key secondary outcome is disability measured with the Roland Morris Disability Scale for sciatica.<sup>35</sup> We will also measure: (1) back pain intensity measured by the NRS<sup>36 37</sup>; (2) time to recovery measured by a pain diary or questionnaire. Participants will be asked to record the average daily leg pain score in a pain diary, or online, for a minimum of 3 weeks using the Numerical Rating Scale.

If recovery has not occurred after 3 weeks, the daily diary will be recorded until 7 days after recovery from sciatica (defined as the first of 7 consecutive days of 0 to 1 out of 10 pain),<sup>38</sup> or up to 12 weeks, whichever occurs earlier. If recovery has not occurred by 12 weeks, participants will be asked at each subsequent follow-up assessment (26 and 52 weeks) whether they have reached recovery or not, and the recovery date (if available); (3) quality of life will be measured with the Short Form-12<sup>39</sup> and (4) treatment success rate will be calculated according to the proportion of patients with 30% improvement in leg pain (compare baseline pain scores with final pain scores).

The following data will also be collected:

- ▶ Adverse events (described in detail under the Harms section) will be collected by self-report at 2, 6 and 12 weeks for all adverse events that occur between baseline and 12 weeks. At 26 and 52 weeks, we will ask participants if they have been diagnosed with a new medical condition, experienced fracture or experienced a worsening of an existing medical condition.
- ▶ Work absenteeism and use of other treatments or healthcare services will be collected in a questionnaire on healthcare utilisation.
- ▶ Adherence to study medication will be measured by participants' self-report of daily medication intake, recorded in a diary or online and by counting the returned medications, against the doctor's prescription record.
- ▶ Success of blinding will be measured in a questionnaire at the 2-week follow-up.

### Sample size

A sample size of 200 participants (100 per group) will provide 90% power to detect a difference of 1 on a 10-point scale for leg pain intensity between the oral glucocorticoid and placebo groups at the 2-week follow-up, assuming an SD of 1.8,<sup>13</sup> a two-tailed alpha of 5% and allowing for 10% of dropouts and 20% non-compliance.

We have chosen 1 out of a 0–10 NRS in leg pain intensity as a clinically worthwhile difference. Previous research showed that patients with back pain need to see a median of 30% more reduction in pain than would occur without intervention to perceive the effect of a drug intervention as worthwhile,<sup>40</sup> estimated to be one point based on the 4-week pain score in our previous sciatica study.<sup>13</sup>

The sample size will also provide 90% power to detect a difference of 3 on a 24-point scale for disability (Roland Morris Disability Scale for sciatica<sup>35</sup>; key secondary outcome) at the 2-week follow-up, assuming an SD of 5,<sup>13</sup> a two-tailed alpha of 5%, 10% dropouts and 20% non-compliance.

### Strategies for achieving adequate participant enrolment

We plan to recruit 200 sites (for participant screening, recruitment and provision of trial treatment) during the OASIS trial to complete recruitment. In order to enrol our target sample size, a series of strategies will be adopted, including regular site monitoring visits and

support from our team, introducing streamlined procedures (screening, recruitment and follow-up) to reduce the workload of clinicians and participants, applying continuing education credit points with relevant professional bodies for trial participation and reimbursing clinicians for the time they spend on trial-related tasks.

### Assignment of interventions: allocation

Allocation sequence will be prepared a priori using a computerised random number generator by an independent statistician not involved in participant recruitment, data collection or analysis, in permuted blocks sizes of 4 and 6. Study medication packs will be prepared according to the allocation sequence. The participant will be enrolled into the study after the informed consent process has been completed and the participant has met all inclusion criteria and none of the exclusion criteria. The participant will receive a study medication pack with a unique study enrolment number. This is where randomisation will occur.

### Blinding

Allocation to group will be concealed and the active and placebo medicines will be identical in appearance, texture and taste, allowing blinding to the participant, treatment provider, assessor and all study personnel including the Steering Committee. Statistical analysis and interpretation will also be conducted blinded to group allocation. While we anticipate adequate blinding of participants in this study based on previous, similar research,<sup>26</sup> there is a risk that patients may suspect they were randomised to the active treatment arm given the known effects of prednisolone (insomnia, mood changes, anxiety, a sense of fullness, weight gain and stomach upset).<sup>27</sup>

To maintain the overall quality and rigour of the study design, unblinding to the blinded study personnel should only occur in exceptional circumstances when knowledge of the actual treatment is absolutely essential for further management of the participant. The decision for this will be made in consultation with the clinicians involved in the participant's management (including the study doctor) and the Steering Committee.

If unblinding is deemed necessary, the study team will facilitate contact between the clinicians involved in the participant's management and the independent statistician who generated the randomisation sequence, and care will be made to ensure that only the study personnel who will be involved in further management of that participant will be unblinded. Unblinding should not necessarily be a reason for study discontinuation.

At the completion of the study, unblinding will occur once data analysis and interpretation are complete.

### Data collection methods

After a participant has given consent for the study, the study doctor will notify the research team. For a participant to be officially enrolled in the study, a blinded research assistant will collect baseline data directly from

the participant before the participant starts the study medication and within 72 hours of visiting the study doctor. Follow-up data will be collected by a research assistant by phone or by the participant online. Research assistants will be trained to maintain blinding and ensure data accuracy, consistency and completeness.

### Other data collected

Questions will be asked regarding blinding and satisfaction at week 2. The blinding question will ask the participant to guess to which study treatment they were randomised, that is whether they have been randomised to prednisolone or placebo, or do not know. The satisfaction question will ask the participant to rate how satisfied they felt with the study treatment overall on a 5-point scale (extremely dissatisfied, dissatisfied, neutral, satisfied or extremely satisfied).

### Data management

The integrity of data will be closely monitored for omissions and errors in a custom-built and secure database hosted by The University of Sydney. We will use electronic data capture where data collected by phone will be directly entered into the database by research assistants and data completed by participants online (via a secure website) will be automatically transcribed into the database.

### Statistical methods

Data analysis will be blinded, by intention-to-treat and guided by a prespecified and detailed statistical analysis plan. Analysis will be conducted by the research team and by an independent biostatistician and checked for accuracy.

### Primary analysis

A linear regression model will be used to assess the effect of treatment group on leg pain intensity at week 2 with baseline leg pain as a covariate (analysis of covariance).

### Secondary analysis

For all secondary continuous outcomes measured at week 2, linear regression models will be used as per the primary analysis. For effects on the primary and all secondary continuous outcomes at weeks 6, 12, 26 and 52, longitudinal linear models will be used with the baseline value included as a covariate. These timepoints have been selected to allow a comparison with a previous trial which had similar follow-up timepoints.<sup>26</sup> Correlations between repeated measures will be accounted for using generalised estimating equations.<sup>41</sup> Time to recovery of pain will be analysed using a survival model.

### Tertiary analysis

For the analysis of the moderating effect of symptom duration, additional terms will be included in the model to investigate the interaction between symptom duration and treatment group. This will be conducted on the primary and key secondary outcomes only. Additionally, daily pain scores recorded in the pain diary will be plotted

in a mean plot to assess the effects on pain intensity at relevant time points.

### Cost-effectiveness analysis

Two analyses will be conducted from the health sector's perspective: a cost-effectiveness analysis using the primary outcome as a measure of effectiveness and a cost-utility analysis where utilities (quality-adjusted life-years) will be calculated from the 12-Item short Form Survey and transformed into utilities via the Short Form-6 dimension algorithm.<sup>42</sup> To obtain costs, health services will be valued at published standard rates (eg, the Medical Benefits Scheme standard fees) if available, or as reported by participants. Bootstrapping will be used to calculate the confidence intervals around the incremental cost-effectiveness ratios. Sensitivity analysis will test uncertainty in key parameters such as the selection of cost weights.

### Data monitoring

A Data Safety Monitoring Committee (DSMC) will be appointed by the Steering Committee, comprised of experts with skills relevant to the trial (eg, management of musculoskeletal conditions, use of glucocorticoids). The primary objective of the DSMC is to review unblinded safety (adverse event and serious adverse events) data and advise the OASIS Steering Committee Chair if any change to the study is recommended. An initial meeting of the DSMC will be held around 6 months after commencement of participant recruitment and subsequent meetings will be scheduled at the discretion of the DSMC or at the request of the OASIS Steering Committee. A suggested schedule is for the DSMC to meet when one-third of the participants (n=66) have been recruited, then when two-third of the participants (n=133) have been recruited, or yearly from the time of the initial meeting whichever is more frequent.

### Harms

#### Adverse events

Adverse events will be collected by self-report at 2, 6 and 12 weeks for all adverse events (including serious) that occur between baseline and 12 weeks.

At 26 and 52 weeks, we will ask participants if they have been diagnosed with a new medical condition, experienced fracture or experienced a worsening of an existing medical condition.

#### Serious adverse events

Serious adverse events will be defined as any untoward medical occurrence that results in death; is life threatening; requires hospitalisation or prolongation of the existing hospitalisation; results in persistent or significant disability or incapacity; is a congenital abnormality or birth defect; is a medically significant or important event or reaction.

Serious adverse events will be reported to an independent medical monitor for assessment and relevant bodies (eg, ethics committee, regulatory body) within the required timeline. We will monitor the number and

severity of adverse events and consider tolerability when interpreting the results.

### Auditing

The OASIS is a trial endorsed by the Australia New Zealand Musculoskeletal (ANZMUSC) Clinical Trials Network. We plan to request an independent audit overseen by ANZMUSC to review core trial processes and documents in the first year after commencement of participant recruitment.

### Patient and public involvement

Trial idea was reviewed by the ANZMUSC consumer advisory group who provided feedback which was incorporated in the trial design.

## ETHICS AND DISSEMINATION

### Research ethic approval

Ethics approval has been granted from the Human Research Ethics Committee, The University of Sydney (Project number 2019/740).

### Protocol amendments

Any modifications to the protocol which may affect the trial design and conduct, or the potential benefits or harms to the participants, will require a formal amendment to the protocol. Such amendments will be agreed on by the Steering Committee and approved by the ethics committee prior to implementation.

### Consent or assent

Study doctors will be trained on the informed consent process and will introduce the study to potential participants who will also receive a patient information sheet and consent form (either in paper or electronic form). Study doctors, with assistance from the study team where necessary, will also answer any questions that are raised by potential participants, and obtain written consent from those willing to participate in the study. At any stage, participants can withdraw consent without repercussion.

### Confidentially

All study data will be stored securely in either locked file cabinets (paper files) or electronically (electronic database files) with access granted only to the study team. Where required, study doctors will have access to study data collected from the participants they are responsible for, only after consent from the participants.

### Access to data

The Steering Committee will have access to the final dataset, which may be provided to a statistician to assist with data analysis if required. To ensure confidentiality, the final dataset will contain deidentified information only.



## Ancillary and post-trial care

The cost of treatments outside the study treatment will not be borne by the study. Any post-trial care, including continuation or recommencement of a glucocorticoid, will be determined by the participants and their clinician; whether they are study doctors or other qualified clinicians.

If non-negligent harm associated with the protocol occurs, participants will be covered by professional indemnity and clinical trials insurance of the trial. This will include cover for additional healthcare, compensation or damages.

## Dissemination policy

The main study results will be submitted for publication in a scientific journal, presented at relevant professional conferences and incorporated into evidence syntheses, guidelines and point of care recommendations. The results will also be disseminated to the media, general public and policymakers.

Authorship eligibility guidelines of publications arising from the study will align with those outlined by the International Committee of Medical Journal Editors (<http://www.icmje.org/>). There are no plans to use professional writers.

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**Contributors** All authors conceived and/or refined the trial design. CAS, AM, JL, QL, RB, ROD, CM, BR and C-WCL procured funding. CAS and AM provided expertise in pharmacy. RB, ROD and BR provided expertise in medicine and rheumatology. QL provided statistical expertise. C-WCL was responsible for the design of the cost-effectiveness analysis. CL drafted the manuscript; all authors critically contributed to the writing and approved the final manuscript for publication.

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**Competing interests** The study has been awarded funding from the National Health and Medical Research Council (NHMRC), Australia. The investigators maintain full autonomy in the design, conduct and reporting of the study. We have ethics approval to reimburse study clinicians for their time spent on study-specific tasks.

**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the 'Methods' section for further details.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; peer reviewed for ethical and funding approval prior to submission.

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