Detailed project description

1. Title: 12/201/09 Stratified Care for Patients with Sciatica and Suspected Sciatica in Primary Care: A randomised trial (the SCOPiC trial - **SC**iatica **O**utcomes in **P**r**i**mary **C**are)

3. Summary of Research: We propose a full-scale, pragmatic, multi-centre, randomised controlled trial (RCT), with internal pilot, of stratified care versus usual, non-stratified care for primary care patients consulting with sciatica or suspected sciatica. Stratified care is a new model of care that uses systematic criteria from patient self-report and clinical assessment findings to classify patients into one of three subgroups (low risk, medium risk or high risk) in order to provide matched treatments for each subgroup. Patients at low risk will received brief education and self-management support in up to 2 treatment visits, patients at medium risk will receive a course of evidence-based conservative care led by physiotherapists, and patients at high risk will have a fast-track referral (including MRI scan) to spinal specialist assessment and opinion regarding suitability for more invasive treatments. The trial is planned over 4 years in total. We will determine whether stratified care leads to faster resolution of symptoms compared to usual, non-stratified care. We will also compare patients' function, leg pain and back pain, quality of life, days lost from work and productivity loss, healthcare utilisation, pain medication and satisfaction. We will investigate the impact of stratified care on service delivery and its cost-effectiveness compared to usual, non-stratified care.

We will use two previously successful methods to identify potentially eligible participants: i) electronic 'pop-up' prompts within GP computer software fired by appropriate Read codes entered by the GP during patient consultations and ii) regular retrospective reviews of practice consultation records. Potentially eligible participants will be invited to a community sciatica clinic for assessment and those with sciatica or suspected sciatica will be invited to participate in the trial and provide informed consent. In total, 470 adults aged 18 years and over consulting their GP with sciatica or suspected sciatica will be recruited from approximately 29 general practices. Individual patients will be randomised, using 1:1 telephone based, third-party randomisation, ensuring allocation concealment, stratified by treatment site and risk subgroup, using random permuted blocks of varying size, to either stratified care or usual, non-stratified care. The primary outcome, informed by our user involvement, is time to patient-reported resolution of symptoms (either 'completely recovered' or 'much better'), collected using SMS text messages (with options of brief phone calls for those not using text messaging). Secondary outcomes at 4 and 12 months will be collected via postal questionnaire with reminders and minimum data collection over the telephone by research nurses blind to treatment allocation. Process data (proportions of patients appropriately referred and treated relative to their risk subgroup) will help determine the impact of stratified care on service delivery. In addition, the cost-effectiveness of stratified care compared with usual, non-stratified care will be evaluated from NHS and societal perspectives.

We will conduct linked qualitative research, using face-to-face and telephone semi-structured interviews, to explore and understand the acceptability of the fast-track pathway to patients and clinicians. The SCOPiC trial has been directly informed from recent research by our team, in particular two intervention studies of stratified care for the broader group of patients in primary care with LBP with and without leg pain (STarT Back (1) and IMPaCT Back studies (2)), and a large observational cohort study of primary care patients consulting with back-related leg pain (ATLAS). These studies demonstrate that our planned methods of patient identification, assessment and recruitment are successful and that a RCT of stratified care is possible with primary care patients. We recruited 851 patients in our STarT Back trial, 922 in IMPaCT Back and 610 in ATLAS.

4. Background and Rationale:

4.1 Sciatica symptoms, pathology and terminology: Sciatica is a symptom of radiating leg pain, usually following a dermatomal distribution and often extending to the foot. Patients may also have other leg symptoms such as pins and needles, numbness or muscle weakness. It usually but not always occurs alongside symptoms of low back pain (LBP) and the leg pain is often worse than the LBP. The term sciatica therefore refers to a broad set of symptoms rather than a single condition (3). The most common reasons for sciatica are compression or irritation of the lumbar spinal nerve roots (the place where the spinal nerves branch off from the spinal cord) by a prolapsed or bulging disc, or tightening of the spinal or lateral canal (spinal stenosis). There are also some very rare reasons for sciatica such as tumours, cysts, or other extraspinal causes.

The term sciatica has been in use from Greek times, derived from the 'ischias' or pain around or coming from the hip and thigh. Modern understanding of pathology meant that the term has come to denote pain in the distribution of the sciatic nerve (4). Confusingly, the term sciatica is used in different ways by different clinicians (and patients), with some calling all leg pain referred from the back 'sciatica', and others using it more specifically to mean pain arising from the lumbar nerve root. Some clinicians prefer to only use the terms lumbar nerve root pain or lumbar radiculopathy to distinguish it from referred leg pain (usually a dull, poorly localised ache that spreads into the buttocks and thighs, that can be referred from many other back structures including muscles, ligaments, facet joints and so on).

4.2 Sciatica epidemiology and costs: About 60% of patients with LBP report pain in the leg(s) (5) although not all will be diagnosed as having sciatica or nerve root pain. In a recent systematic review, we showed that back-related leg pain is associated with greater pain and disability, poorer quality of life and increased use of healthcare resources compared to LBP alone (6). Accurate diagnosis and triage of patients can be challenging, especially in primary care where most patients are managed, and diagnosis is primarily based on clinical history and a brief clinical assessment rather than imaging tests such as MRI (7). This application focuses on patients with sciatica or suspected sciatica consulting in primary care. Sciatica is most common in adults aged 30 to 50 years old (8). Reports estimate that the annual prevalence in the general population is 2-3% with a lifetime prevalence of 49-70% (9). Prevalence estimates, however, vary widely from 1.2-43% as each study uses different diagnostic criteria and sampling methods (10). For example, Deyo et al (11) estimated the US lifetime prevalence of surgically important disc herniation at 2% and Heliovaara et al (12), in a Finnish population survey using strict criteria indicating nerve root pain, estimated a lifetime prevalence of 5.3% in men and 3.7% in women. These studies focus on very narrow definitions of sciatica, not appropriate for use in primary care. Our research shows that, although not confirmed by imaging, up to 70% of primary care patients consulting with back-related leg pain are considered or suspected to have a clinical diagnosis of sciatica.

It is generally believed that many patients with sciatica have a favourable outcome and experience natural resolution of symptoms within 12 weeks from onset (9, 13). Studies have shown that the herniated portion of the disc tends to regress over time, with partial to complete resolution after 6 months in two-thirds of people (14, 15). However, a substantial proportion (estimated at up to 30%) continues to suffer with pain for a year or more (9). A recent secondary care Norwegian study showed that recovery after 1 year was poor, varying from 49-58%, depending on the definition of recovery (16). Male patients, those who smoked, had more severe pain, or other health complaints, were more likely to have a poor outcome at 12 months follow-up (17). A Dutch study reported that leg pain intensity significantly predicted subsequent surgery for sciatica (18). Overall, however, the heterogeneity of available prognostic studies makes it difficult to draw firm conclusions about the prognosis of patients who are not treated surgically (19).

The literature clearly indicates that compared to LBP alone, sciatica has a more significant impact on patients, with longer and more frequent pain episodes (20, 21). The pain can lead to problems with everyday activities, including time off work, and even unemployment, leading to financial burdens for families as well as health and social services (6, 22, 23). Sciatica is responsible for much of the indirect costs and lost workdays associated with LBP. A Dutch study estimated that the cost of sciatica to society represents 13% of all LBP related costs (22), which translates to an annual impact to the UK economy of £268 million in direct medical costs and £1.9 billion in indirect costs.

4.3 Treatment for sciatica: In contrast to LBP, there is no UK National Institute of Health and Clinical Excellence (NICE) guidance about the best way to treat sciatica patients, and little previous research specifically on this patient population in the setting where most patients are managed – in primary care. Systematic reviews (eg. 24-27) and randomised trials (eg. 28, 29), summarise results from a range of treatments for sciatica. Overall they highlight the poor quality of the evidence to date, based mostly on small trials with only short-term follow-up. They conclude that the efficacy and tolerability of drugs commonly prescribed in primary care for sciatica (such as non-steriodal anti-inflammatory drugs (NSAIDs), corticosteroids, antidepressants, anitconvulsants, muscle relaxants and opioid analgesics) is unclear (26). They provide evidence that active physiotherapy increases the proportion of sciatica patients that improve and is especially effective for those with severe symptoms (28). Available reviews reach conflicting conclusions about the role of spinal injections for sciatica, although these appear to help pain relief in the short-term (30). There is some trial evidence for the benefits of epidural injections of local anaesthetic and corticosteriod (31) for leg pain, although larger studies are needed

with longer-term follow-up and there is little evidence to recommend specific types of injection methods over others. A recent prospective case series highlighted that 32% of non-radiologically guided caudal epidurals may fail to deliver the therapeutic agents to the site of pathology (32). In addition, national recommendations about the use of epidural injections propose confirming accurate needle placement and spread of injectate by conducting spinal epidurals under fluoroscopic guidance (33). Surgery for spinal stenosis has been shown to provide better pain relief than non-surgical interventions (34). Surgery for disc herniation has been the subject of 9 systematic reviews, and whilst the quality of included studies is mostly poor, they suggest that surgery brings short-term benefits in comparison with conservative care. Surgery provides faster relief and more rapid recovery from sciatica (13,35) even though outcomes are similar to those of non-surgical care 1 or 2 years later. Surgery and spinal injections are associated with more frequent and more severe adverse events (25), there is insufficient research evidence to suggest that one particular type of surgical technique is superior over others for sciatica due to herniated disc (27) and the optimal selection criteria for eligible patients for surgery is lacking (36). In addition, the most recent decision analytic model from an HTA systematic review (25) showed that immediate referral to disc surgery for all patients is not a cost-effective model of care. A commissioning guide for spinal services by the National Spinal Taskforce was published in January 2013 (37) and the Taskforce has made a submission to NICE regarding the need for a formal quality standard for radicular pain.

In practical terms, current treatments range from information and advice, medications, exercise, traction, acupuncture and manual therapy, to more invasive treatments such as spinal injections and surgery. Although there is variation across clinicians, generally the current model of care followed for sciatica is 'stepped'. This typically means that initially there is a 'wait and see' policy in primary care, then for those patients not improving after a number of weeks or months, referral to a clinician such as a physiotherapist might be considered. Subsequently, patients failing to improve might be referred to specialist spinal services for investigations and spinal specialist management (9). Currently the only patients who are fast-tracked from primary care to spinal specialist opinion are those with suspected cauda equina syndrome or profound, widespread or progressive neurological deficit, who are treated as emergency cases. There are no robust estimates about the proportion of patients consulting in UK primary care with sciatica who proceed to spinal injection or spinal surgery, although some old reports estimate that between 5-15% of patients with sciatica proceed to disc surgery (14, 38), most often discectomy to remove part of the disc material. Our own primary care data from the NIHR funded ATLAS (Assessment and Treatment of Leg pain Associated with the Spine) observational cohort study shows that 13% of patients consulting in primary care are referred to secondary care spinal specialists at some point during the 12 months following their initial primary care consultation. The UK Spinal Taskforce (37) highlighted problems in the management of sciatica caused by variation in clinical practice, treatment delays and confusion between radiating non-specific LBP and true sciatica. The Taskforce made recommendations for improving care, but acknowledged that these were based largely on expert opinion rather than research evidence, highlighting the urgent need for good quality trial evidence about treatments for sciatica, including better information about the clinical and cost effectiveness of early referral of patients with severe symptoms for consideration of secondary care treatments such as surgery or spinal injections. A draft commissioning guide for radicular pain developed by a group led by the British Orthopaedic Association (39) in May 2013 is out for consultation and a key research recommendation is 'optimisation of the care pathway for radicular pain patients to ensure it is cost-effective. A model of care that does not over-treat those with a good natural history yet spots the patients who do need more active treatment to help with symptoms, prevent chronicity and return to work is needed' (39). We believe that better, and earlier, identification of patient subgroups in primary care for matched treatments (stratified care) is key to improving sciatica outcomes.

4.4 Relevant previous research: The stratified care model in this new trial is directly informed by our previous LBP and sciatica research (eg. 6,8,10,19), specifically i) our previous intervention studies in which we successfully demonstrated the clinical and cost-effectiveness of stratified care for the broader population of patients with LBP with or without leg pain in primary care (STarT Back (1), IMPaCT Back (2)) and ii) our current prospective cohort study of patients with back-related leg pain consulting in primary care, in which we have carefully characterised those with sciatica and suspected sciatica (ATLAS (44)). The following paragraphs explain the relevance of these studies, and how their findings provide the basis for our new stratified care model for sciatica patients.

In (i) a randomised trial of stratified care based on prognosis in patients with LBP (with or without leg pain) we demonstrated superior clinical and cost benefits of stratified care compared to best current care (1, 40) and usual primary care (2). Our stratified care model comprised both subgrouping patients according to risk of persistent disability in the long term (low, medium, high risk) using a brief screening tool (the STarT Back tool, 41) and matching each patient subgroup to treatments appropriate for their risk status. The STarT Back tool was developed for, and validated with, primary care patients with LBP (with and without leg pain) and captures 8 key modifiable physical and psychological prognostic indicators for persistent disabling symptoms in 9 simple questions. The score (from 0 to 9) is used to allocate patients to one of the three subgroups (41). Patients classified at low risk received a brief intervention focused on advice, reassurance and self-management guidance; those as medium risk received a course of up to 6 treatments of evidence-based physiotherapy (exercise, manual therapy, support to return to work); and those classified as high risk of poor outcome (the most complex patients in primary care) received a course of up to 6 treatments of psychologically-informed physiotherapy that integrated physical management with cognitive-behavioural principles (42, 43). In the STarT Back trial (n=851 patients), the subgroup of patients with leg pain who had sciatica or suspected sciatica (26%, based on assessment of clinical features) had worse scores on the STarT back tool than patients without sciatica. Sciatica was present in 10% of patients classified at low risk of poor outcome, 26% of patients at medium risk and 38% of patients at high risk, in comparison to patients with LBP alone, which accounted for 70% of the patients classified at low risk, 45% medium risk and 33% high risk. In the stratified care arm of the STarT Back trial, whilst the protocol defined that treatment was determined by the STarT Back tool's risk subgroup, clinicians could over-rule the tool if they felt strongly that the matched treatment was inappropriate for the individual patient. Reassuringly, the screening tool's treatment recommendation was only over-ruled by clinicians in 7% of patient cases at low risk, 2% at medium risk, and none among high risk patients. Therefore, we believe that using the STarT Back tool to inform treatment allocation warrants further testing as part of a new stratified care model specifically for patients with sciatica and suspected sciatica. However, we want to take the opportunity to extend our prognosis-based model of stratified care for the group of patients with a specific diagnosis of sciatica by combining prognostic information from the STarT Back tool with key information from the patient's clinical assessment so that the new stratified care model combines the best information about patient prognosis and the best information about the severity indicators of sciatica (clinical indicators).

In (ii) the ATLAS observational cohort (44), funded within our current NIHR Applied Programme Grant on Spinal Pain 2009-2014 (CI: Hay) we are describing the clinical course, characteristics and prognostic indicators of patients consulting in primary care with back-related leg pain including true sciatica. The study completed recruitment in March 2013 and is currently in 12-month follow-up. We recruited 610 patients from 16 general practices in 24 months. ATLAS provides the best available data in the UK on the characteristics of patients with sciatica and suspected sciatica consulting in primary care. Trained study physiotherapists, working to a detailed assessment informed by literature reviews and expert consensus (45), assessed patients in community clinics and reached a diagnosis for each patient. Given the challenge of diagnosing sciatica accurately in primary care, without MRI confirmation of pathology, they were also asked to rate their level of confidence in their clinical diagnosis. Analyses show that 70% (429 of 610 patients) were diagnosed with sciatica or suspected sciatica (with ≥70% diagnostic confidence). Of these, the assessing clinicians considered that 55% had sciatica due to a disc herniation, 11% due to spinal stenosis and the rest were unsure/unclear. The primary care patients diagnosed with sciatica had a mean age of 50 years, 60% were female, 61% were currently in a paid job and 30% had taken time off work for the current episode (unpublished data from ATLAS). On a scale of 0-24, where 24 is maximal functional disability (measured using the sciatica version of the Roland Morris Disability Questionnaire (RMDQ, 46)), patients in the cohort had a mean score of 12 (SD 5.7) and moderate leg pain intensity (mean of 5.7 (SD 2.9) out of 10). Of those with sciatica, 44% reported leg pain for 6 weeks or less, 22% between 6-12 weeks, 22% between 3-12 months, and 12% for more than 12 months. This was the first ever episode of sciatica for only 11% of patients. Amongst the group with a clinical diagnosis (of ≥70% diagnostic confidence) of sciatica in the ATLAS cohort, the STarT Back screening tool classified 11% as low risk and hence as having a good prognosis, 49% as medium risk and 40% as high risk for persistent disability (unpublished ATLAS data). Our preliminary analysis confirms that the STarT Back tool subgroup allocation (low, medium and high risk) significantly predicts functional outcomes over 12 months for patients with a clinical diagnosis of sciatica, as it did in all patients with LBP in our earlier studies. The proportions of those

with sciatica who report persistent high disability (defined as ≥7 on RMDQ) at 12 months follow-up were: 10% for those classified as low risk at baseline, 39% for those at medium risk at baseline, and 64% for those at high risk at baseline. Among sciatica patients classified at high risk by the STarT Back tool at baseline, persistent disability at 4 months was almost 10 times as likely compared to those at low risk (OR 9.79 95%CI 3.70, 25.92). ATLAS also provides the best available UK data on the proportion and characteristics of patients with sciatica or suspected sciatica in primary care who are currently referred, at some point over 12 months from primary care consultation, to spinal specialists for further assessment and consideration of treatments such as spinal injections and surgery. These patients represent those who are appropriate for 'fast-track' referral for early specialist assessment, and therefore, we have used these data as the best available proxy for which patients should be fast-tracked in the SCOPiC trial. We conducted multivariable regression analyses to identify the key factors in each of the following five blocks – demographic and occupational factors (eg. age, work loss, affecting performance at work), pain factors (eg. duration, intensity, bothersomeness), co-morbidities (eg. general health, pain self-efficacy), self-report pain response factors (eg. cough/sneeze response, tingling/numbness) and clinical assessment findings (eg. muscle weakness, reflex tests, sensation tests, neural tests) - predicting referral to spinal specialists in the ATLAS cohort. Four variables strongly and independently predicted referral; interference with ability to work (including work around the house), pain below the knee, intense leg pain, loss of or reduced pin prick sensation. These four factors were also considered to be clinically important and have therefore been combined with the STarTBack tool into the stratification algorithm for patients in primary care with sciatica and suspected sciatica. Full details of the new stratified care model are given in section 6 below and summarised in figure 2. We propose that matching treatments to subgroups of patients in primary care, using information on both prognosis and clinical severity, will improve the efficiency and effectiveness of care, by ensuring the right patients access the right treatments at the right time. An RCT is now needed to investigate the effectiveness of our new stratified care model tailored for the more specific group of patients with sciatica and suspected sciatica in primary care – the SCOPiC trial.

5. Evidence explaining why this research is needed now: This trial addresses key recommendations from i) the National Spinal Taskforce (37) and ii) the Commissioning Guide for Radicular Pain (39). The Taskforce recommended that commissioners of healthcare ensure appropriate levels of service provision and pathways that enable timely, sound clinical decision-making. The Commissioning Guide recommended optimisation of care pathways, working out how to prevent over-treating those with good natural history whilst providing access to treatment for those that need it. Despite these recommendations, there is little evidence upon which to base pathways and clinical decisions for sciatica in primary care. A logical next step in our research, the SCOPiC trial is specifically designed to test a new model of care (stratified care) that systematically matches patients with sciatica and suspected sciatica to treatment pathways with clear referral criteria. It combines key prognostic indicators with key clinical indicators of sciatica severity and allocates patients into one of three subgroups, for matched treatment. It will provide clinical and cost-effectiveness data to inform development of future guidelines for practitioners and improve patient options. This application is also timely given the growing national and international interest in stratified medicine (47), which aims to tailor therapeutic decisions in ways that maximise treatment benefit, reduce harm and increase healthcare efficiency by offering the right treatment to the right patient at the right time. Stratified care is particularly suited to sciatica and suspected sciatica patients in primary care given that the numbers of patients make it inappropriate and unsustainable to offer intensive or expensive treatments to all. Stratified care for patients with back pain has been a top international research priority for over 17 years (48,49).

6. Health Technology being assessed: The Health Technology being assessed is stratified care for primary care consulters with sciatica. This new model of stratified care combines key physical, psychological and clinical assessment information to ensure that patients with mild and self-limiting sciatica symptoms are reassured and supported to self-manage, whilst those with moderate symptoms and impact (medium risk) receive a course of evidence based physiotherapy-led care, and those with the greatest difficulties and clinical indicators of severe sciatica (high risk) are fast-tracked for spinal specialist opinion about suitability of other treatments. Using stratified care to route patients to appropriate and timely treatment matched to their profile is well suited to primary care, where the numbers of patients make it inappropriate and unaffordable to offer more intensive or expensive treatments to all. There is a growing literature on stratified medicine (eg. 47) and stratified care for

back pain specifically (eg. 50-52) that emphasises the potential for improved patient outcomes when subgroups of patients with different profiles are matched to different treatments.

Our stratified care model combines subgrouping patients, using clear criteria, into one of three subgroups each of which receives one of three matched treatments. The criteria combine 4 key clinical indicators (interference with ability to do work (including work around the house), pain below the knee, intense leg pain, loss of or reduced pin prick sensation) that predict referral to secondary care over 12 months with 8 key prognostic indicators (using the validated STarT Back tool (41)). The 8 prognostic factors are physical function (2 questions), pain elsewhere, pain in the leg, fear of movement, catastrophising, anxiety, low mood and pain bothersomeness, combined in one score to give an overall risk index. The latter 5 factors form the psychosocial subscale of the STarT Back tool. Informed by empirical data from the ATLAS cohort, we have combined the prognostic information (from the STarT Back tool) and the clinical indicators of sciatica severity (from the clinical assessment) to construct a stratified care algorithm for use in the SCOPiC trial. Using this algorithm, patients randomised to the intervention arm will be stratified into one of three strata or subgroups (low risk, medium risk, high risk). The algorithm is shown in figure 2 and the three subgroups summarised as follows:

i) Low risk: Patients will be allocated to the low risk subgroup if they score 3 or less on the STarT Back screening tool, irrespective of clinical indicators. We know from our ATLAS data that only 2% of patients who scored 3 or less were referred to spinal specialists in secondary care. These patients have a very good prognosis in primary care. We expect 12% of primary care patients with sciatica and suspected sciatica will be at low risk (unpublished ATLAS data). In the SCOPiC trial, these patients will receive a brief intervention tailored to patient need, in up to 2 treatment visits with a physiotherapist, comprising advice and education, reassurance, support for self-management and advise on use of analgesia.

ii) Medium risk: Patients will be allocated to the medium risk subgroup in the SCOPiC trial if they have either of the following combinations of STarT Back tool scores and clinical indicators; a) STarT Back score of 4 or more overall but with 3 or less on the psychosocial subscale, and 3 or fewer of the clinical indicators; or b) STarT Back psychosocial subscale score of 4 or more, but only 2 or fewer clinical indicators. We expect 57% of primary care patients with sciatica and suspected sciatica will be in this subgroup (unpublished ATLAS data). These patients will receive a course of evidence-based, physiotherapist-led treatment, tailored to patient need, including patient education, individualised exercise and manual therapy. The package will include efforts to optimise pain medication, support for return to work and continuation of everyday activities.

iii) High risk: Patients will be allocated to the high risk subgroup if; a) they score 4 or more of the 5 items in the psychosocial subscale and they have 3 or more of the 4 clinical indicators; or b) they score 4 or more on the STarT Back tool and are positive on all 4 clinical indicators. We expect 31% of patients in primary care with sciatica and suspected sciatica to be in this subgroup (unpublished ATLAS data). The matched treatment is a fast-track pathway that refers these patients for spinal specialist assessment and opinion about suitability for more invasive treatments, including spinal injections or surgery. 'Fast-track' is defined as immediate referral to spinal specialist assessment and spinal specialist assessment within 4 weeks from the community sciatica clinic visit. An MRI scan will be part of the pathway for patients in this subgroup.

7. Aims and objectives: The overall aim is to investigate whether the management of primary care patients with sciatica and suspected sciatica can be improved through stratified care. The specific objectives are:

7.1 Primary objective: To compare the clinical effectiveness of stratified care compared to usual, non-stratified care, in terms of patient-reported time to resolution of symptoms, for adults consulting in primary care with sciatica and suspected sciatica.

7.2 Secondary objectives:

- To compare the cost effectiveness of stratified care compared to non-stratified care over 12 months
- To compare the clinical effectiveness of stratified care compared to usual, non-stratified care, on a range of important secondary outcomes, including function, pain, quality of life, work loss, healthcare use and patient satisfaction
- To investigate the impact of stratified care on service delivery, specifically proportions of patients receiving risk-appropriate referrals and treatments
- To determine, and understand, the acceptability of the fast-track pathway to patients and clinicians

8. Research Plan:

8.1 Design: A multicentre, pragmatic, assessor-blind, two-arm, randomised controlled trial (RCT), with internal pilot, comparing stratified care versus usual, non-stratified care, with concurrent health economic evaluation and linked qualitative interviews. Figure 1 summarises the SCOPiC trial design and flow-chart.

8.2 Setting: Primary and community NHS care, with a fast-track pathway to NHS specialist spinal services (that include existing primary/secondary care interface services, spinal orthopaedics, and pain services in participating NHS Trusts). We will work with approximately 29 GP practices in total to identify patients across two geographical centres (North Staffordshire and North Shropshire) with support from the Primary Care Research Network Central England (PCRN-CE). We will work with two physiotherapy services, a community hospital (the Haywood) in Stoke-on-Trent, and two NHS Trust specialist spinal services (University Hospital of North Staffordshire in Stoke-on-Trent and the Roger Jones and Agnes Hunt Orthopaedic Hospital in Oswestry), to deliver treatment to trial participants.

8.3 Target Population: Adults consulting in general practice with sciatica or suspected sciatica irrespective of duration or severity of symptoms. **Inclusions:** Adults aged 18 years and over consulting in general practice, who following clinical assessment in community sciatica clinics, have a clinical diagnosis of sciatica or suspected sciatica; who either have a mobile phone that can receive and send SMS texts or have access to a land-line telephone; willing to participate and able to give full informed consent. **Exclusions:** Suspected serious spinal pathology or 'red-flags' (eg. cauda equina syndrome, progressive/ widespread neurological deficit, acute spinal cord compression, suspicion of spinal tumours, infection or fractures). Fewer than 1% of primary care patients with acute back pain have serious medical pathologies (53), with estimates of 0.0-0.7% spinal malignancy, 0.7-4% spinal fractures, and 0.0-0.01% spinal infection, 0.1% cauda equine, and 0.2% inflammatory disorder (53, 54). Other exclusions include previous lumbar spine surgery, ongoing care from or consultation with a secondary care doctor or physiotherapist for same problem in the last 3 months, serious co-morbidity preventing a patient attending the community sciatica clinic, severe enduring mental health condition, pregnancy, and those unable to communicate in English. We are deliberately choosing not to restrict our trial to people with disc herniation or spinal stenosis confirmed through MRI findings, reflecting current practice in which primary care decisions are made on the basis of symptoms rather than on the basis of imaging findings. We are thus including people typical of those seen in primary care and seeking healthcare by using a selection of frequent diagnostic and symptom Read Codes informed from our previous research.

8.4 Recruitment procedures:

8.4.1 Identification and invitation: We will use two previously successful methods to identify potentially eligible participants: i) electronic 'pop-up' prompts within GP computer software fired by appropriate Read codes entered by the GP during patient consultations and, ii) regular retrospective reviews of practice consultation records. In method i) when a patient with back and/or leg pain consults their GP, and the GP enters an appropriate diagnostic or symptomatic Read Code on the computer system, a 'pop-up' prompt screen will ask the GP if he or she thinks the patient might have sciatica or suspected sciatica, and if so to consider whether the patient is suitable to be invited to the community sciatica clinic, taking into account trial inclusion/exclusion criteria. Entering 'yes' on the computer system will flag those patients thought to be suitable for invitation to the clinic and allows the GP to briefly inform the patient about the trial. In order to maximise recruitment, in method ii) potentially eligible participants will also be identified by regular (weekly) retrospective review of GP consultation records. Patients for whom the GP has entered one of the agreed Read Codes will have an electronic tag attached to their computer record, so that if GPs overlook or do not have time to invite the patient to the community sciatica clinic, this method will ensure these patients are identified and also invited. On a weekly basis PCRN-CE staff will facilitate the mailing of letters to all potentially eligible patients. Duplication checks will avoid the same patient being invited twice. Letters inviting patients to the clinic will be posted to all potentially eligible patients identified using both methods. The letter will explain that there is a research study being hosted at the clinic but that attendance at the clinic in no way obliges them to take part in the research. Patients will be invited to telephone the clinic administrator to make an appointment at the community sciatica clinic. The administrator will carry out a brief check for suitability for the clinic (presence of leg pain, aged 18 and over, ability to communicate in English, not seen a secondary care doctor or physiotherapist for the same problem in the last 3 months) and will then make the clinic appointment within 10 working days. A letter will be sent to patients to confirm their appointment details, together with a study baseline questionnaire and participant

information sheet giving details of the trial. Approximately two days before the clinic, a clinic administrator will telephone patients to remind them about their appointment time and ask those who are interested in taking part in the research to bring their completed questionnaire. These processes have been successful in both the STarT Back RCT (n=851 patients) and ATLAS cohort study (n=610 patients).

8.4.2 Full eligibility screening and informed consent: The community sciatica clinics will operate as integrated research/service clinics, with NHS treating clinicians being fully supported by PCRN clinical and administrative staff working as a single team (replicating the approach we took in ATLAS). Trained, study physiotherapists will welcome patients, explain the purpose of the clinic, and answer any questions patients have about the research. Patients expressing interest in the research will proceed with a standardised assessment for sciatica and suspected sciatica by trained, study physiotherapists to establish full eligibility. The standardised clinical assessment to determine whether patients have sciatica or suspected sciatica will use the assessment developed and tested in ATLAS (see 45 and 55 for full details) and informed by available guidelines for identification of nerve root syndrome and spinal stenosis (54,56). Eligibility for the trial will be based on the assessing physiotherapists being ≥70% confident of a diagnosis of sciatica (due to either nerve root pain or spinal stenosis).This decision will be made by combining information from the patient's subjective and objective clinical assessment, including checking for red flags and neurological testing (including tests for strength, reflexes, sensation in legs and neural tension tests), which has been shown to be a feasible and reliable approach in our ATLAS cohort. Leg pain thought to be due to causes other than sciatica and suspected sciatica will be excluded (for example: hip pathology, peripheral neuropathy, vascular pain, referred pain), as will patients where there is significant diagnostic uncertainty regarding the diagnosis of sciatica. Hence, patients included in the trial will have pain in one or both legs, plus at least one of the following self-reported symptoms or clinical findings; leg pain approximating a dermatomal distribution, leg pain worse or as bad as the back pain, leg pain made worse by coughing/sneezing/straining, subjective sensory symptoms approximating a dermatomal distribution, any degree of objective neurological findings relating to spinal nerve root(s) involvement such as sensory or reflex changes or myotomal weakness, or positive neural tension. The assessing physiotherapist will record the clinical assessment, including presence or absence of the 4 clinical indicators on a standard proforma. As part of this assessment all patients will also be asked to complete the STarT Back tool. Therefore, prior to randomisation, the subgroup classification of all patients (low risk, medium risk, high risk) will be determined.

For those patients eligible and willing to participate, a research nurse will explain the trial in detail, gain written informed consent, check completion of all baseline information and undertake randomisation. Patients not eligible or not wanting to take part in the research will receive a session of advice and education about their problem from a physiotherapist in the clinic and advised to seek further advice or treatment from their GP, as in usual care. For these patients, we will inform their GP in writing that they were either not suitable for, or did not wish to participate in the SCOPiC trial.

8.5 Randomisation: Eligible patients who consent to take part will be randomised to one of the two trial arms using a 1:1 telephone-based, third-party randomisation, ensuring allocation concealment, operated by the research nurse. The research nurse will telephone the Keele CTU randomisation service, find out the random allocation for the participants and inform the appropriate physiotherapist in the clinic. Individual patients will be randomised, stratified by treatment site and risk subgroup, using random permuted blocks of varying size, to either stratified care or usual, non-stratified care. We will inform the patients' GP, in writing, that the patient is participating in the trial. Delivery of the allocated treatment will commence within the same community sciatica clinic visit. Patients randomised to usual, non-stratified care will be seen by physiotherapists who have NOT carried out the clinical assessment and eligibility screen, and who are blind to the stratification algorithm, in order to make sure that there is no contamination between treatment arms.

8.6 Interventions:

8.6.1 Stratified care: Stratified care is a model of care with two components: i) clear identification and subgrouping of patients with different characteristics, and ii) matching of patient subgroups to different treatments. Our stratified care approach combines systematic information about individual patients' likelihood of persistent disability (prognostic information) with information about the severity of sciatica from their clinical history and physical examination (clinical indicators). This combined information is used in order to allocate patients into one of three subgroups (low, medium or high risk), in order to receive matched treatment in ways that support self-management for patients at low risk, yet ensure that patients at medium and high risk

receive rapid access to the treatments that are most likely to help them, including evidence-based interventions led by physiotherapists and fast-track access to spinal specialist clinicians. Figure 2 provides the stratification algorithm.

Low risk subgroup: Patients scoring 3 or less on the STarT Back Tool (out of a total possible 9), irrespective of the 4 clinical indicators, have a good prognosis in primary care and will receive a brief treatment package tailored to the patients' needs delivered by study physiotherapists, in up to 2 treatment visits, comprising advice, information and education about sciatica, pain relief and appropriate activity levels, and reassurance about their good prognosis without further tests or investigations, in order to support self-management. Patients' individual concerns will be identified and addressed. To reinforce these key messages a brief sciatica booklet will be given to the patient along with an information sheet of local contacts for exercise venues such as swimming pools, exercise classes and inexpensive physical activity opportunities. Patients allocated to the low risk subgroup will receive up to 2 treatment sessions with a physiotherapist, in order to permit review where needed but no further treatment will be offered. Patients will, of course, be able to seek other care from their GP or other health professionals and this healthcare use will be collected in follow-up questionnaires and analysed. **Justification:** This treatment package has been directly informed by our previous stratified care treatment package for patients at low risk in both the STarT Back and IMPaCT Back studies (1,2), with the amendment here of up to 2 treatment sessions rather than only 1. Our ATLAS data showed that 12% of primary care patients with sciatica and suspected sciatica will be at low risk and, of these, only 2% were referred to secondary care specialist opinion. Whilst there are no trials testing the effect of information and education for sciatica patients, adequately informing patients about sciatica (causes, no need to perform diagnostic imaging, expected good prognosis and recovery without surgery) plays an important role in improving patient satisfaction and likely recovery (9).

Medium risk subgroup: Patients scoring 4 or more on the STarT Back tool AND who have 3 or fewer of the clinical indicators are at medium risk of persistent disabling symptoms. Patients scoring 4 or more on the psychosocial subscale of the STarT Back tool AND who have 2 or fewer clinical indicators are also in this subgroup. They will receive a course of physiotherapist-led treatment, tailored to the patients' needs, that provides secondary prevention of disabling sciatica. The STarT Back tool and clinical assessment will guide the treating physiotherapist in targeting management towards the physical and psychosocial factors that are particular problems for each patient. These are likely to include, for example, problems with everyday functional tasks, low mood related to the pain, and fear of physical activity. The physiotherapist will negotiate an individualised treatment plan with the patient according to their need and best current evidence. The physiotherapist will address any worries or fears and unhelpful beliefs patients may have about their back and sciatic pain, and explain the overall favourable natural healing process without the need for invasive procedures such as injections and/or surgery. They will emphasise messages about promoting speedy return to normal activity, avoiding rest whilst respecting an increase in leg pain to guide physical activities, appropriate use of pain relieving modalities (such as painkillers), and return to work issues, and will use a range of pre-agreed physiotherapy techniques, including exercise (and home exercise), manual therapy and techniques including goal setting where appropriate. This matched treatment package will be delivered in one 45-minute session with up to 6 further 30-minute sessions (tailored according to clinical need) over 6 to 8 weeks. We will provide a short training package (3 days in duration; see Section 8.8) for physiotherapists treating this subgroup of patients in the trial, adapting our previous training programmes used in STarT Back, IMPaCT Back and ATLAS studies to ensure it is appropriate for patients with sciatica. Procedures will be in place to direct patients who fail to improve, or who worsen, or who develop 'red flag' symptoms such as cauda equine to spinal specialists, for further assessment and management. **Justification:** This treatment package has been directly informed by the matched treatments we developed and tested in STarT Back and IMPaCT Back (in which physiotherapists provided education, exercise and manual therapy as well as a combined physiotherapy/psychological intervention termed 'psychologically-informed physiotherapy'). The matched treatment is also underpinned by theories of self-efficacy (57) and fear avoidance (58), by current best evidence for physiotherapy-led treatments for sciatica (8,28) including spinal stenosis (59) and by recent consensus-based recommendations (39). For example, spinal manual therapy is effective at 6 months at relieving local or radiating pain in people with acute back pain and sciatica with disc protrusion (8). Whilst systematic reviews have suggested there is insufficient evidence about exercise therapy for sciatica, trials have shown that adding physiotherapy-led active exercise to GP care for sciatica provides better outcomes than GP care alone (28). A further trial has shown that

physiotherapy-led, symptom-guided, exercise (using directional preference, manual therapy techniques and muscle stability training) led to less work absence, neurological deficit and greater patient ratings of improvement compared with exercises not focused on the back (29). Recent consensus-based recommendations (39) also recommend a low-intensity, combined physical and psychological program involving physiotherapy.

High risk subgroup: Patients who score 4 or more on the psychosocial subscale of the STarT Back tool AND have 3 of 4 of the clinical indicators as well, as patients who score 4 or more on the STarT Back tool AND have all 4 clinical indicators, are in this subgroup. These patients have the most severe difficulties and clinical indications for further treatment options and, in the SCOPiC trial, they will be fast-tracked to specialist assessment and opinion about suitability for other treatments, including spinal injections or surgery. 'Fast-track' is defined as immediate referral to secondary care assessment with that secondary care assessment occurring within 4 weeks of the community sciatica clinic visit. We will work with existing services in participating NHS Trusts, including spinal specialist clinics, spinal orthopaedics and pain clinics. An MRI scan will be part of the consideration for secondary care treatment in fast-track patients, in line with recent guidelines that recommend a selective approach to imaging (60). MRI is the best available diagnostic imaging modality for LBP and leg pain as it provides excellent resolutions of nerve roots (allowing for assessment of nerve root compression) and bony structures. MRI is non-invasive for the patient and does not involve any ionising radiation exposure. The MRI processes will follow those we used in the ATLAS study (44) and a summary report on the scan will be provided by a consultant radiologist at participating NHS Trusts, completed within 10 working days of the clinic appointment. The spinal specialist clinicians can access the MRI results electronically, as part of their assessment of patients in this fast-track pathway. It is important to note that the fast-track pathway is to *specialist assessment and opinion* and not to surgery or injection. It is the specialist clinician, in negotiation with the patient, who will determine the most appropriate secondary care treatment based on assessment findings and patient preference. **Justification:** Whilst this fast-track pathway is new and is specifically for patients with the most severe sciatica, the spinal specialist services and treatments they offer are not new. This subgroup of patients has severe sciatica symptoms (positive on 3 or 4 of our clinical indicators) and they are at risk of persistent disabling symptoms. These are the patients who need to be identified early in primary care and referred to a spinal specialist for further assessment about suitability for treatments in secondary care, including surgery and spinal injections. Whilst long-term outcomes from surgery and conservative care are similar, the timing of surgery for severe sciatica is important. Relief of symptoms has been shown to be twice as fast among patients with severe sciatica who are treated with early surgery compared with those treated conservatively (35). In addition, surgery has been shown to be superior to conservative care for lumbar spinal stenosis (61). Hence, patient choice is likely to favour surgery if they wish a faster time to recovery and pain relief (25). Injection therapy is an appropriate treatment for severe radicular pain (37,54) shown to provide short-term relief and moderate long-term improvement (25). We know, however, that not all patients who might be suitable for surgery or spinal injections will wish to proceed with these treatments, and that some patients in this pathway may be deemed unsuitable for surgery or spinal injections when they are assessed by spinal specialists. For these patients, the spinal specialist may recommend other treatment approaches, including conservative care. It is fast-tracking to specialist assessment and opinion that is key in this matched treatment pathway. We will capture data on time to specialist assessment, time to any treatments that follow and type of treatment(s).

8.6.2 Usual, non-stratified care: The control arm of our trial (usual, non-stratified care) is based on current usual primary care. However, in response to feedback from our Research User Group and multidisciplinary Clinical Advisory Group, and in order to operationalize the trial and avoid demoralising patients, we have decided to include limited contact with a physiotherapist in the control arm. Prior to randomisation all patients in this arm will have received the same comprehensive assessment (including the 4 clinical indicators and the STarT Back tool) as those in the intervention arm (stratified care), but the physiotherapists delivering the usual care intervention will not be informed about the patients' STarT Back results, or the presence or absence of clinical indicators. For these patients, treatment will include a one-off session (at the same clinic visit) of advice and education. If the treating physiotherapist considers that the patient needs further physiotherapy or medical treatment this will be arranged in consultation with their GP. A letter to the GP will inform him or her about the care the patient received at the clinic. Care received at the clinic will be recorded using case report forms, and any additional onward care received following the clinic visit (e.g. initiated by the GP during follow-up) will be captured using questions seeking healthcare use data in the follow-up questionnaires. In order to avoid

contamination at the community sciatica clinic, we will ensure that the therapists overseeing the control treatment will not be made aware of the details of the stratification algorithm during the trial, and that patients will be aware that they will be treated according to two models of primary care, one based on matching subgroups of patients to treatments and one based on current practice. This replicates the methods used in the STarT Back trial (1). The key difference between treatment arms is the systematic use of the stratification algorithm to determine treatment and referral decision-making.

8.7 Audit of interventions: All physiotherapists who deliver care to patients in the SCOPiC trial will complete case report forms in order to fully record the detail of the interventions provided. With participants' consent, record reviews of the secondary care treatments provided will be reviewed by members of the trial team. Thus we will document the treatments received and the number of treatment sessions. Patients in both arms of the trial will be advised that they can access their GP for ongoing care in the usual way and that they should contact their GP if their condition worsens.

8.8 Workshops for participating clinicians: Up to 20 musculoskeletal physiotherapists will undertake training workshops to support the trial. Those overseeing care for the control group will receive 1 half-day workshop about trial procedures and use of case report forms. Those overseeing assessment of eligibility and the use of the stratification algorithm and matched treatments will attend 3 days of training led by the study team and collaborating surgeons and pain consultant. The focus of the training will be on the procedures of the trial, including use of case report forms, carrying out the standardised assessment according to agreed protocols to identify patients with sciatica/suspected sciatica for participation in the trial, and stratified care. The training will facilitate the physiotherapists to target back and sciatic pain along with co-morbid pain, disability and psychological risk factors for chronicity such as pain-related distress, fear of movement, unhelpful beliefs and expectations, for those patients receiving physiotherapy treatment. The training will include the evidence-based assessment and treatment of back pain and sciatica/suspected sciatica, including the use and interpretation of the STarT Back tool and clinical indicators. Current guidelines for managing LBP and sciatica in primary care will be discussed, including appropriate reassurance and advice about analgesia, the maintenance of, or return to, usual activities (including work) and patients who present a clinical or management concern (e.g. those with signs of potential serious pathology or red flags). The training will include current best physiotherapy practice for the management of disability, back pain and sciatica, including the role of exercise and manual therapy as well as strategies for equipping patients with the skills to manage future recurrences. Goal setting, pacing, graded exercise and manual therapy will also be covered. The training will be supplemented by a comprehensive manual, providing clear guidelines and treatment algorithms for the evidence based assessment and treatment of patients with back pain and sciatica/suspected sciatica. Mentoring and supervision will be provided by the study team and the spinal physiotherapy specialists working in the specialist spinal services. Up to 10 secondary care specialists (spinal orthopaedic surgeons, pain consultants, and interventional radiologists who provide spinal injections for sciatica patients) will attend up to 2 half-day workshops to discuss the trial and agree the smooth operation of the fast-track pathway, including accessing MRI reports for these patients and recording of timing and types of interventions provided.

8.9 Outcome measures and data collection:

8.9.1 Primary outcome: The primary outcome measure is time to resolution of symptoms of sciatica, measured on a 7-point ordered categorical scale: 'completely recovered', 'much better', 'quite a bit better', 'a little better', 'same/ no change', 'worse' and 'much worse' – the anchor being against baseline clinic presentation of symptoms. This is a commonly used outcome in primary care research of musculoskeletal disorders and was used in a recent trial comparing early surgery with conservative care for patients with severe sciatica (35). Primary evaluation of this measure is time to patient-reported resolution of symptoms (either 'completely recovered' or 'much better'), collected using regular SMS text messages (with the option of brief phone calls for those not using text messaging). These will occur weekly for the first 16 weeks or until patient reports resolution of symptoms. If no resolution occurs within the first 16 weeks then the primary outcome measure will be collected monthly from months 4 to 12 or until the patient reports resolution. 94% of UK adults have a mobile phone (http://media.ofcom.org.uk/facts/) and previous research has shown that weekly text messages are a useful method of data collection to examine the clinical course of back pain in primary care, with high mean response rate of 83% (62). Even in patients with severe sciatica, the greatest improvements take place in the first 12 weeks (35) so we expect key differences in outcome between trial arms to be evident early in follow-up and

within 4 months from randomisation. Our Research User Group stressed the importance of time to resolution as their key outcome of interest, given the particular impact and severity of symptoms of sciatica.

8.9.2 Secondary outcomes:

Secondary clinical outcomes will evaluate health status at 4 and 12 months using participant self-completed postal questionnaires with reminders and telephone minimum data collection for non-responders by research nurses who are blind to treatment allocation. Measures will include numerical rating scales of leg and back pain, function (sciatica version of the RMDQ, 46), self-rated global perceived recovery (as in primary outcome), fear of movement (Tampa Scale of Kinesiophobia, 58), self-efficacy (63,64), anxiety and depression (Hospital Anxiety and Depression Scale, 65), risk of poor outcome (STarT Back tool, 41), quality of life using EQ5D-5L and SF12 (66,67), sick days lost from work and productivity loss, proportions of patients accessing secondary care assessment and interventions including timing of interventions, healthcare utilisation, pain medication, adverse events and patient satisfaction with care and with treatment outcome.

Adverse events, defined as any serious morbidity or events causing unwarranted distress to a participant that were potentially related to either intervention or trial processes, will be identified by treating clinicians, participating GPs and from patients' questionnaires. There were no adverse events in our STarT Back trial with LBP patients (using conservative treatments). Adverse events are expected to be higher in patients receiving more invasive treatments of spinal injection and surgery. Expected adverse events include fever, headache, severe back pain, prolonged numbness/weakness or urinary retention (for epidural injections) and cerebrospinal fluid leak, neurological damage, cauda equina syndrome, deep-vein thrombosis, pulmonary embolism, myocardial infarction, urinary tract infection, urinary retention and discitis for surgery (68). There is an 8% rate of medical and surgical complication rates from surgery (68) and a 5-10% chance of revision surgery (68,69).

Health economic outcomes will be collected within the trial to determine the cost of the intervention, control and other sciatica-specific health care utilisation. Resource use information will be obtained on primary care consultations, prescriptions, tests and investigations, and on NHS-based and private healthcare, physiotherapy, injections, outpatient visits, A&E attendances, nature and length of inpatient stays, surgery and over-the-counter purchases by patients, and will be collected via participant questionnaires at 4 and 12 months and review of primary care and hospital records (with participants' permission). Unit costs will be obtained from standard sources and health care providers. Given that many sciatica-related costs are due to loss of productivity, information will also be collected from participants on occupation status, sciatica-related time off work and reduced work performance (presenteeism) to enable the calculation of productivity costs, allowing analysis from a societal cost perspective. The outcome of interest for the economic analysis is quality-adjusted life years (QALYs) and these will be calculated using EQ5D-5L responses at baseline, 4 and 12 months.

Process outcomes will be collected to investigate the impact of stratified care on service delivery. Numbers and proportions of patients in each arm of the trial receiving risk-appropriate referrals and treatments, and the timings of treatments, will be collected from case report forms, patient questionnaires and record reviews from GP practices and secondary care services. We want to find out if stratified care results in greater proportions of patients accessing appropriate care, and whether they access that care more quickly, than in usual care.

8.10 Sample size: The sample size is 470 patients in total, in order to compare stratified care to usual, non-stratified care, for time to resolution of symptoms. In our previous trial of stratified care for LBP (STarT Back, 1), 69% of patients in the intervention group had a clinically important improvement on the primary outcome measure at 4 months compared to 56% in the control group; an absolute difference of 13% that corresponds to a point hazard ratio (HR) of 1.55. The primary interest in this new trial, directly informed by user involvement, is time to resolution of symptoms (defined as being 'completely recovered' or 'much better' according to self-reported assessment of sciatica during follow up compared to baseline) as opposed to improvement or not at a fixed time-interval. As such, the evaluation focuses on survival analysis testing the null hypothesis of equality of survival curves. Assumptions are made in respect of the exponential distribution of the survival times and proportionality of hazard ratios across the duration of follow-up, and uniformity in patient entry criteria and levels of censorship. Sample size for detecting a HR denoted by the ratio of mean survival times (μ_I/μ_C) is given by the following equation: $n=2(Z_\alpha+Z_\beta)^2/[\log_e(\mu_I/\mu_C)]^2$, which focuses on comparison of number of events (70). Using this, and in order to be conservative, to detect a hazard ratio of at least 1.4 in mean survival times (time to resolution of symptoms) with power of 90%, two-tailed statistical significance of 5% and 1:1 allocation would require a sample size of 188 per treatment group (376 in total) for evaluation. These are the required

figures for full analysis and do not allow for loss to follow up. Taking into account loss to follow up, we assume that right-censorship rates will be similar between trial arms and no greater than 20%. Thus, we inflate our sample size requirement to the magnitude of ×1.25 to account for the anticipated reduction in total participants followed up for the primary outcome. Hence, the total sample requirement is 470 (235 per treatment group). Thus, in terms of time to resolution and by way of example, our trial will be powered to detect differences between trial arms in the region of a mean of 28 days to resolution versus 20 days, or 56 days versus 40 days. This sample size will also provide more than 80% power to detect a small standardised effect size (0.3) between arms in our key secondary outcome at 12 months follow-up (everyday functional disability measured using the sciatica version of the RMDQ).

8.11 Estimated recruitment rates: To recruit 470 patients in the trial, we will need to identify 8,774 patients in 22 months from approximately 29 GP practices (average practice size of 5,000 adults, so total adult practice population of 146,232). The figure of 8,774 is based on estimated consultation prevalence for LBP with or without leg pain in general practice of 6% over the recruitment period. Of these, 5,440 (62%) are expected to have leg pain (based on the point prevalence of self-reported leg pain from STarT Back trial participants). Of these, we expect 3,264 (60%) to be invited to one of our community sciatica clinics (we expect no sciatica or suspected sciatica in 40% of patients) and 1,958 (60%) to attend the clinic for detailed screening for eligibility. We plan two recruitment centres, each running approximately 2 to 3 half-day clinics per week. We expect 1,175 (60%) to have sciatica or suspected sciatica at the community clinic (with at least 70% diagnostic confidence) and meet the trial eligibility criteria and 40% of these to consent to participate in the trial (n=470). These estimates are based on our previous studies and are conservative, as we have estimated lower rates than those we have observed before (60% considered to have sciatica or suspected sciatica in comparison to 70% in ATLAS; 40% consent rate in the trial in comparison with 63% of those eligible in the STarT Back trial). We assessed 1310 patients in the ATLAS study from 16 GP practices in 24 months, based on one site running three half-day clinics per week. Hence the SCOPiC trial requires just under twice the number of community clinics and GP practices than the ATLAS study. Figure 1 summarises the SCOPiC trial design and flow-chart.

9. Blinding and protection against bias: Selection bias at recruitment will be avoided by separating the processes of determining patient eligibility and treatment allocation and by using random permuted blocks overseen by our CTU, not allowing physiotherapists assessing and treating patients to predict the next allocation in their clinic. Blinding of patients and clinicians is not possible. Patients will be told that the trial is comparing two primary care approaches for the treatment of sciatica and suspected sciatica, one based on matching patients to treatment using specific criteria and one based on current care. Research nurses blinded to treatment allocation (and different to the community sciatica clinic research nurse who telephones the CTU randomisation service) will oversee the collection of patient-reported outcomes and conduct minimum data collection over the telephone at 4 and 12 months follow-up for patients who do not respond to questionnaires or reminders. The trial databases will be password protected to ensure that the research nurses and trial statistician remain blind to treatment allocation. Comparing available variables across, for example, consenting and non-consenting individuals, dropouts and completers will be carried out to evaluate external validity. Using validated outcome measures with established reliability will reduce measurement error. Treatment will be recorded by clinicians in a standardised format on Case Report Forms (CRFs), as is usual practice in our trials, and audits of these CRFs will be undertaken throughout the trial. Each intervention will adhere to a specific protocol with supporting documentation, developed for the trial and informed by our previous studies (1,2,44).

10. Data analysis:

10.1 Internal pilot: In an internal pilot study, we will assess recruitment and follow-up rates over the first 8 months of recruitment (just over one third of the anticipated total recruitment period). The considered stopping criteria based on this pilot phase will be if, from the start of the study recruitment period: (i) observed monthly recruitment rate falls short of 70% of that anticipated, (ii) loss to follow up is in excess of 25%. This takes into account that further measures can be taken to increase both recruitment and follow up (if needed) for the remaining study timeline. No formal interim analysis of outcomes is proposed for this study (hence no adjustment is required to the parameters of the end analysis). The Data Monitoring Committee will review the data on recruitment and follow-up from the internal pilot and make recommendations to the Trial Steering

Committee and the HTA manager in respect of continuation (without change), continuation (in view that adjustments will be needed to meet the required shortfall in recruitment/follow-up), or to stop the trial. The internal pilot study over the first 8 months of recruitment will also provide information on the following key aspects: success of GP practice recruitment and retention; success of physiotherapy site recruitment, training and engagement; suitability of the patient selection criteria; proportion of patients allocated to each of the three stratified care subgroups (low, medium and high risk); time to fast-track MRI and specialist opinion.

10.2 Clinical outcomes: The primary analysis will compare time to self-reported resolution between stratified care and usual, non-stratified care, on an intention-to-treat basis. A Kaplan-Meier survival analysis will estimate the time from randomisation until resolution of symptoms. Patients lost to follow-up will be censored at the time interval this occurs. This will provide us with the data for comparing the relative mean survival times of the two trial arms. Cox regression analysis will compare time to recovery between arms by calculation of a hazard ratio of rates of resolution along with 95% confidence interval estimates (and corresponding p-value of testing against a 2-tailed 5% significance level), adjusted for age, gender and baseline pain severity.

Sensitivity analyses will be carried out on the primary outcome evaluation based on evaluation of subgroups of participants that: (i) complete follow up and, (ii) adhere to the matched treatment pathway. We will analyse differences in secondary outcomes at 4 and 12 months and provide point and 95% interval estimates from linear and logistic regression analyses as appropriate to the data being analysed. A small number of pre-specified sensitivity analyses of the primary outcome measure, using Cox regression, will include testing the effectiveness of stratified care for those with suspected disc-related radiculopathy as determined by clinical assessment, and for patients in each of the subgroups in both arms of the trial (low risk, medium risk, fast-track patients).

A graphical and statistical examination of the proportional hazards assumption will be carried out (i.e. hazard ratio is constant over the duration of follow-up). If this assumption is not met, we will model time-interaction effects. A statistical analysis plan (SAP) will be agreed with the Data Monitoring Committee (DMC) and published in a trial protocol paper.

10.3 Economic analysis: The within-trial health economic analysis will determine the cost-effectiveness of a stratified care model for sciatica in primary care compared with usual, non-stratified care. A cost-consequence analysis will initially be reported, describing all the important results relating to costs and outcomes. An incremental cost-utility analysis will then be undertaken using patient responses to the EQ-5D-5L questionnaire (converted to tariff values using the UK Crosswalk value set), to calculate the cost per additional quality-adjusted life year (QALY) gained. The base-case analysis will adopt a health care perspective. However, analysis from a wider societal perspective will also be undertaken, to explore the impact on the results when productivity costs are taken into account. Additional analyses will consider the cost-effectiveness for low, medium and high risk subgroups separately, as we have done for stratified care for LBP (40). Deterministic and probabilistic sensitivity analyses will be conducted to test the robustness of the results and overall uncertainty in the trial cost and outcome data respectively.

10.4 Analysis of process outcomes: This will involve cross-tabulating risk subgroup by different healthcare resource utilisation such physiotherapy, GP consultations, secondary care consultations and treatments. For example, patients at low risk are expected to have no more than 2 physiotherapy sessions and we anticipate this low level attendance to occur more frequently in stratified care than usual care. Secondary care specialist opinion is expected to occur more frequently in stratified care, than usual care, for patients at high risk.

11. Linked qualitative interviews: The aim of the linked qualitative research is to determine, and understand, the acceptability of the fast-track pathway to patients and clinicians. **Justification:** Qualitative research on patients' experiences of living with and managing sciatica is scarce (71,72) and qualitative studies that report clinicians' views of managing this condition are even less common (73). The few qualitative studies that do exist have investigated patients' experiences of sciatica (71,72), with no studies as far as we are aware investigating the most severe group of sciatica patients (those in the high risk group in the SCOPiC trial). We have previously conducted in-depth qualitative interviews with 37 patients consulting in primary care with LBP with and without leg pain (16 of whom had pain below the knee) (71) to more fully understand the experience of sciatica. Results highlighted the impact of the intense nature of sciatica pain, the desire of patients for clinicians to appreciate the pain intensity, the desire to have the pain diagnosed, and the importance of clear information about treatment and prognosis. The importance of offering a credible clinical assessment, explanation and

diagnosis of the condition was clear. Expectations about treatment options varied between patients and they balanced the need for pain relief with the possibility of adverse effects. Qualitative research within our current ATLAS cohort study (as yet unpublished) has explored the experiences of primary care patients with back-related leg pain (including those with a diagnosis of sciatica and suspected sciatica). We therefore already have rich data across the spectrum of consulting patients, including those with mild, moderate and severe symptoms, comprising 20 in-depth interviews with patients and 56 audio-recorded consultations between clinicians and patients attending a mix of initial assessment and follow-up appointments. Early indications are that the clinical explanation of the diagnosis and symptoms has an important impact on patients' self-management strategies and response to treatment. Given that the novel addition in the SCOPiC trial involves fast-tracking to spinal specialist assessment and opinion about suitability for more invasive treatments, we have decided to focus our linked qualitative research in this new trial *only* on patients in this high risk subgroup (and clinicians who manage them) in order to determine, and understand, the acceptability of this fast-track pathway. We will build on the findings from the ATLAS study to help understand the acceptability of the fast-track pathway in the SCOPiC trial, and draw on experiences from our previous qualitative study exploring the acceptability and implementation of stratified care for LBP (74,75). We will use Normalisation Process Theory (76) to investigate sense making processes of patients and clinicians regarding the acceptability (and potential future utility) of the fast-track pathway, and adopt Allen's (77) 'critical pathway analysis' to guide the enquiry.

Sample: A purposive sample of patients in the high risk subgroup will be interviewed based on their time to resolution (from their SMS text results), treatment centre, and range of patient demographics including age, gender and baseline leg pain severity. All participating spinal specialist clinicians and a sample of participating physiotherapists and GPs will be invited for interview.

Methods: Up to 25 semi-structured interviews with patients at high risk will be conducted (we anticipate there being a total of approx. 72 patients suitable for invitation for interview or 31% of those randomised to stratified care). We are particularly interested in patients' views about their clinical care, its appropriateness for addressing their problem and the time taken to symptom resolution and treatment(s). We will also conduct up to 20 semi-structured interviews with participating clinicians (GPs, physiotherapists and spinal specialists to whom the fast-track patients are referred), in order to understand their views about the suitability of this patient subgroup for onward referral and the acceptability of the fast-track pathway to clinicians.

Analysis: Audio recordings of interviews will be transcribed verbatim, checked, anonymised and analysed thematically using methods of constant comparison derived from grounded theory (78). Data will be managed and shared using N-Vivo analysis software. Emerging themes will be explored, and discussed at regular trial team meetings including clinicians and researchers. The analysis will be informed by the emergent themes arising from the data. We are particularly interested in the experiences of patients and clinicians of the fast-track pathway, and will analyse the interviews iteratively so that key insights from patients and clinicians are directly fed into the on-going data collection and analysis process. We believe this linked, focused, qualitative research is important as it will explain if, and why, the new fast-track pathway is acceptable to patients and clinicians.

12. Dissemination and projected outputs:

12.1 Outputs: The recent NHS Spinal Task Force (37) recommended that appropriate levels of service provision and pathways are in place for patients with sciatica, to enable good decision-making. Our proposed trial specifically addresses two of the Taskforce's research recommendations for sciatica patients: i) the need for better guidance about which patients should be referred for specialist opinion, including early surgical opinion and ii) the need for earlier diagnosis to differentiate between non-specific spinal pain and patients with radicular pain, for whom other interventions might be successful and cost-effective options.

We expect the following outputs: important and faster improvements in patients' pain and daily activity restrictions as well as a reduction in days lost from work; high-quality, generalisable data on the clinical and cost-effectiveness of stratified primary care for patients with sciatica and suspected sciatica, that can directly inform NHS service commissioning and delivery; detailed information on patients' and clinicians' experiences of the fast-track pathway in comparison to usual care, that can directly inform dissemination strategies; a feasible model for delivering stratified care that combines prognostic information with clinical indicators of sciatica severity, with agreed matched treatments; support packages and materials that facilitate the delivery of stratified care, ready for use in the NHS.

The following summarises how we will seek to translate our findings into practice: uploading a DVD summarising stratified care, key findings and tips for implementation on our website (see www.keele.ac.uk/sbst/ for a previous example from our stratified care research for low back pain); hosting a national conference at Keele (we did this to support roll-out of stratified care for LBP in April 2012, and 150 delegates from the NHS attended); offering training programmes for clinicians; working with the Department of Health to embed the stratified care approach within key workstreams such as: QiPP Right Care Workstream, AHP QiPP Website, Any Qualified Provider documentation, Musculoskeletal commissioning online toolkit; contributing to NICE guidelines and Map of Medicine Pain Management Guidelines (RCGP/British Pain Society); developing educational materials for national bodies such as Arthritis Research UK's training mechanisms (e.g. "Hands On") and e-learning modules to support postgraduate curricula developed by professional bodies such as the Royal Colleges of Physicians, Surgeons and General Practitioners, and the Chartered Society of Physiotherapy; delivering evidence based workshops at national conferences of the professional bodies; working with collaborators internationally to facilitate rapid translation and use of stratified care for sciatica patients.

12.2 Dissemination and implementation: We are committed to the translation of our results in ways that positively impact on primary care and patient outcomes. We previously supported the implementation of stratified care for back pain, made the screening tool and training available, and supported stakeholder events for clinicians and commissioners. In supporting roll-out of stratified care for back pain (eg. with NHS South Central, Heart of England, Scotland, Sheffield, AXA PPP, BUPA, Map of Medicine) we have developed networks that support implementation, and we will expand on these to ensure translation of results from this trial. These networks are facilitated by our team's involvement in the West Midlands CLAHRC (Mallen, Hay) and our lead role for primary care in the developing Academic Health Sciences Networks (AHSN). There is real demand from clinicians, service managers and commissioners for stratified care for other patient groups, with many requests from NHS partners about whether our existing approach for patients with back pain could be used for patients with other pain problems. This shows real potential for meaningful translation into NHS practice of a new stratified care approach for patients with sciatica and suspected sciatica.

Dissemination will include publishing in peer reviewed journals (with open access) and presentations at academic and professional conferences. Through our local and national NHS partnerships, the CLAHRC and AHSN, and our involvement in professional bodies, we will disseminate our outputs in more practical ways to ensure rollout in the NHS. We will provide free and open access for public bodies to all aspects of IP arising from this research, disseminating our outputs via our website, through the networks of patient bodies such as Back Care and Arthritis Research UK, and the education and training mechanisms of professional bodies (Royal Colleges and Chartered Society of Physiotherapy). We plan a national conference to disseminate the findings to stakeholders including patient groups, clinicians, service leads, commissioners, professional body musculoskeletal champions, research funders and the Department of Health (similar to our national STarT Back conference in 2012). We will provide, freely available on our website, practical tools to support commissioners and clinicians to adopt stratified care, clearly defined matched treatments which target different patient profiles, clinician support packages, and information about how to access training in stratified care. We will work with our Research User Group (RUG) to provide patient self-management materials and summaries, laying out the implications and choices for patients. We intend our results to be incorporated rapidly into national and international guidelines (e.g. NICE), with easy access for managers, clinicians and patients to a set of practical guides to support implementation.

13. Plan of investigation and timetable: The trial will be delivered over 4 years between 1st Sept 2014 and 31st Aug 2018. We will begin planning the trial, including communications with GP practices, PCRN staff and clinical teams prior to the Sept 2014 start date, in order to ensure we hold our first Trial Steering Committee and Data Monitoring Committee meetings in Sept 2014 and submit applications for research ethics and R&D approvals soon after that. Full detail is provided in Figure 3 (Gantt chart). The key milestones are:

Nov - Dec 2014	First set of Trial Steering & Data Monitoring Committee meetings
Jan – March 2015	Research ethical and global R&D approvals applications and processes
Nov 2014 - June 2015	GP practice recruitment and set-up as Patient Identification Centres
April 2015	Local R&D approvals for Centre 1

April 2015	Trial workshops and training of staff in community sciatica clinics
May 2015	Centre 1: Patient recruitment and treatment starts and weekly brief data collection starts (by SMS or phone, with reminders)
June 2015	Local R&D approvals for Centre 2
July 2015	Centre 2: Patient recruitment and treatment starts and weekly brief data collection starts (by SMS or phone, with reminders)
Sept 2015	4 month follow up (and reminders); qualitative interviews with patients begin
May 2016	12 month follow up (and reminders); qualitative interviews with clinicians begin
Feb 2017	End of participant recruitment at Centre 1
April 2017	End of participant recruitment at Centre 2 and to trial overall
Aug 2017	End of 4 month follow up data collection (including reminders)
April 2018	End of 12 month follow up data collection (including reminders)
May – Oct 2018	Final data analysis and completion of final report; peer-reviewed paper preparation

14. Project management: The trial will be overseen by a Trial Management Group chaired by the lead applicant (Foster) and consisting of representatives of all key groups involved in the design, operation and management of the trial. This group will meet monthly and will monitor progress along the planned timetable, discussing any issues as these arise and troubleshooting when required. Members of the PCRN-CE, including research facilitators who work within the clinical teams within participating NHS services, will be part of the Trial Management Group. Foster will be responsible for the overall delivery, to target and on budget, of the trial, with the support of the Trial Manager and trial team. A Trial Manager will be appointed to ensure the smooth running of the trial on a day-to-day basis. The trial will be supported by the Keele Primary Care Musculoskeletal Clinical Trials Unit (CTU), a UKCRC fully-registered CTU, and will be monitored by the CTU Operations Group. All trial procedures will adhere to the CTU Standard Operating Procedures (SOPs) and support will be provided by a Research Programme Manager. In addition to the project management within the CTU, an independent Trial Steering Committee (TSC), that will include 2 patient representatives, will be established to provide independent oversight of the trial, and reports will be submitted to one of the existing Data Monitoring Committees (which review all Keele CTU trials). The TSC and DMC will meet initially at the start of the trial to approve the trial protocol and subsequently at regular intervals as agreed by the committee.

15. Approval by ethics committees: We do not anticipate major ethical concerns with this trial, having previously obtained approvals for STarT Back and ATLAS. All patients in this trial will receive at least usual primary care management, and participants will be randomly allocated to either usual, non-stratified care or stratified care. Patients in both treatment arms will be able to consult for healthcare in addition to the care they receive within the trial, and this will be recorded and analysed. This trial requires the recruitment of patients identified within the NHS to an individually randomised trial involving the collection of primary patient-based data. Approval from an NHS Research Ethics Committee (REC) will therefore be obtained before commencing the trial. Local R&D committees of participating services will be approached to approve local involvement in the trial. Patients will be identified from their consultation with their GP, who will be able to exclude patients based on suitability. Potentially eligible patients will receive information about the trial and have time to consider this prior to attending the community sciatica clinic, where they will be able to discuss participating in the trial with a research nurse, prior to providing written, informed consent. This trial is evaluating a new treatment model of stratified care (subgrouping patients based on specific criteria and matching them to treatment pathways) and as such does not involve any treatments that are not currently used in clinical care. As in our previous stratified care RCT (1), clinicians will be able to override the stratification algorithm should this be felt important, but we will record if this happens and we expect only a small number of these cases. Safety reporting procedures will be in place to ensure any expected and unexpected serious adverse events which are deemed related to the trial are reported to the REC, sponsor, TSC and DMC. All data collected during the course of the trial will be handled and stored in line with the CTU Data Security procedures and SOPs, which are in accordance with the Data Protection Act 1998 and other relevant regulations and good practice guidelines. We will anonymise and archive the data for 20 years on a secure server at Keele University. Lewis and Foster will be the data custodians. We will make the data accessible to other researchers, in line with our CTU procedures.

16. Patient and Public Involvement: We have previously interviewed sciatica patients and these highlighted its impact, the need for clearer information on treatment and prognosis and patients' willingness to balance their desire for pain relief with adverse effects (71). Participants wanted patients with severe symptoms to be prioritised in order to reduce unnecessary delays in treatment. Secondly, we held a workshop with 3 users from our Research User Group (RUG). This highlighted the importance of early assessment and diagnosis (a patient had waited 5 years for a diagnosis), and the need to get patients to treatments that match their problem more quickly (a patient had tried multiple conservative treatments without benefit before being referred for specialist opinion after 15 years). Users liked the idea of stratified care. They all felt that early pain relief is the key outcome, given the severity of the pain and that regular, brief, SMS texts or phone calls that collect pain data were acceptable. They stressed that patients with very severe symptoms will try any treatment; if fast-tracked patients chose not to have surgery, they felt it was still appropriate to get a surgical opinion.
Stratified care for patients with sciatica and suspected sciatica combines the best information about diagnosis and prognosis currently available in order to improve early treatment decision-making. Thus we need to ensure that stratified care and trial processes are relevant and acceptable to patients. Two user representatives have helped with the application and have agreed to join the TSC. They will review the trial documentation. There will also be a wider RUG advising the team on the qualitative interviews with patients. This activity is well supported by the Patient and Public Involvement (PPI) infrastructure at Keele, which includes a user involvement co-ordinator (herself a patient), the RUG and a wider Virtual Users Panel that communicates electronically. Our PPI team hold regular support sessions and have helped patients to speak at national and international conferences and co-author peer reviewed papers. We host the West Midlands Research Design Service (RDS) at Keele and hold the lead role for PPI within it. Our partnership with the Primary Care Musculoskeletal Research Consortium provides a formal structure to support patient and clinician involvement in our research.

17. Expertise and justification of support required:
17.1 Expertise: Our team is internationally recognised for primary care research and the clinical impact of our research in back pain and sciatica, with trials funded from NIHR, MRC and medical charities. The team is led by Prof Foster, an NIHR Research Professor, with support from Prof Hay (NIHR Senior Investigator) and Dr Konstantinou (HEFCE Senior Clinical Lecturer). The trial requires considerable understanding of sciatica and suspected sciatica in the primary care setting. The co-applicant team and our spinal specialist clinical collaborators (Dr Julie Ashworth, Consultant in Anaesthesia and Pain Medicine, University Hospital of North Staffordshire, Clinical Lead for the IMPACT interdisciplinary chronic pain service and part time research fellow at Keele University; Mr Vinay Jasani, Consultant Orthopaedic Spinal Surgeon and Clinical Lead of Spinal Services at the University Hospital of North Staffordshire; Mr Birender Balain, Consultant Orthopaedic Surgeon, Centre for Spinal Disorder, RJAH Orthopaedic Hospital, Oswestry) have extensive expertise in the clinical care of patients with sciatica. We have published reviews of the prevalence and impact of sciatica, prognostic factors in sciatica, the best combination of items that discriminate sciatica in primary care and the physical examination of leg pain and radiculopathy. Our track record includes the only large cohort study of back-related leg pain in primary care with follow-up over 12 months to determine subgroups, outcomes and prognosis (ATLAS). This demonstrates our ability to recruit this patient group to research. We have conducted many primary care RCTs testing treatments for musculoskeletal patients, including the only trial of stratified care for patients with back pain. Our trials have high recruitment (over 6,000 patients) and follow-up (averaging 85%), with parallel economic evaluations, and are published in the top medical journals (Lancet, BMJ). Our recent trials (STarT Back n=851, PhysioDirect n=2250 and BEEP n=526), supported by Keele's CTU, recruited to target ahead of schedule, demonstrating our ability to deliver high quality trials in successful partnership with NHS clinicians, services and the PCRN. We have the expertise and established NHS/University links to deliver this trial. The PCRN-Central England has the highest accrual of NHS patients involved in research nationally, largely as a result of our Centre's musculoskeletal research.
Foster is internationally recognised for primary care RCTs testing treatments for musculoskeletal pain and together with Hay, Dunn and Hill has pioneered stratified primary care for low back pain. She is the CI of a recently awarded NIHR Applied Programme Grant on Stratified Care for Musculoskeletal Pain (2014-2019), and the SCOPiC trial forms part of her NIHR Research Professor 5 year research strategy to develop and test ways to match patients to treatments. She will provide overall leadership to the Trial Management Group.

Konstantinou is a HEFCE Senior Clinical Lecturer and a recognised expert in the assessment and management of spinal disorders, particularly sciatica. She leads the ATLAS cohort and will support Foster in the leadership of the SCOPiC trial, overseeing the delivery of stratified care, and together with Hay and Mallen provide clinical leadership. Konstantinou and Hill will lead the training programme for participating physiotherapists, supported by secondary care collaborators Jasani, Balain and Ashworth. Artus is an NIHR GP Clinical Lecturer and will lead communications with participating GP practices and ensure smooth delivery of usual, non-stratified care. Dunn and van der Windt are leading epidemiologists in musculoskeletal pain who provide methodological expertise for stratification, data collection and analyses. Lewis and Jowett bring extensive experience in the design, conduct and analysis of pragmatic RCTs with health economic evaluations and will supervise the junior statistician and health economist. Sanders has considerable experience of qualitative research, including previous qualitative research within IMPaCT Back (79) and ATLAS. He will supervise the qualitative researcher in this trial.