In October 2020 we corrected the wording in research recommendation 14.

Appendix K: Research recommendations

K.1 Referral criteria for suspected axial spondyloarthritis

Research recommendation 1	What are the optimal referral criteria for people with suspected spondyloarthritis?
Population	People presenting to primary care with low back pain of at least 3 months' duration that started before the age of 45
Relevant factors	Signs, symptoms, risk factors and results of tests available in primary care which may be associated with spondyloarthritis, individually or in combination, including: • Current and past symptoms • Comorbidities (including inflammatory bowel disease, psoriasis, uveitis) • Family history of spondyloarthritis and associated conditions • Blood tests (including CRP, ESR and HLA-B27)
Reference standard	Rheumatologist diagnosis of spondyloarthritis (for all participants, whether they meet any proposed referral criteria or not)
Outcomes	• Sensitivity • Specificity • Positive/negative predictive value • Positive/negative likelihood ratios • Resource use and costs • Estimated lifetime cost per QALY for each potential referral strategy
Study design	Prospective diagnostic accuracy study with subsequent economic evaluation. The methods adopted in the Dutch CaFaSpA study (van Hoeven et al. 2014, 2015) would be appropriate for the diagnostic accuracy component: participants were identified from GP databases and invited for full rheumatological work-up, leading to a reference-standard diagnosis of presence or absence of axial spondyloarthritis. Optimal rules for case-finding should be judged according to expected cost per QALY gained. The NICE model could be used to estimate these without the requirement for additional original economic work (although it would be valuable to collect data on resource use and costs associated with the strategies themselves, e.g. test costs).

Criterion	Explanation
Importance to patients, service users or the population	Diagnostic delay is a major problem in axial spondyloarthritis, with a mean interval between presentation and diagnosis of 8.5 years (Hamilton et al., 2011), during which time patients' quality of life is significantly impaired and irreversible pathological damage can occur. Therefore, it is critical that sensitive strategies are developed to prompt the recognition of possible cases and their appropriate referral to specialist rheumatology teams. However, it is not feasible to refer everyone with low back pain to a rheumatologist, so strategies also need to be specific enough to rule out cases that will not benefit from referral. As a result of the large number of permutations of possible referral strategies, it is impractical to run separate validation studies for all referral criteria that could be developed. Therefore, a single large, representative cross-sectional study would, provided it measured the predictor variables for all reasonable referral strategies, provide the ability to develop and validate any number of possible referral strategies. The study would need to be large enough that

Criterion	Explanation
	sufficient data are available to derive new referral rules and to validate those rules in a separate, independent subset of the data.
Relevance to NICE guidance	High priority: whilst referral recommendations have been made based on the currently available evidence, these are not UK specific, and the current large delays to diagnosis highlight the need for more robust evidence in this area.
Current evidence base	The proposed study is essentially a UK-specific repeat of a recent Dutch study, CaFaSpA (van Hoeven et al. 2014, 2015). Despite the methodological strengths of the CaFaSpA study, it is particularly important to derive UK-specific data because there are potentially critical anomalies in the Dutch evidence. For example, it found an HLA-B27 prevalence of 20% in people with axial spondyloarthritis and 2% in people without; much lower than estimates found elsewhere (75% and 20%, respectively). This lowers the validity of extrapolating any results found to the UK, and reinforces the need for UK-specific data to address this question. Other studies have explored different referral strategies, including in randomised designs (Poddubnyy et al., 2011; Sieper et al., 2013); however, these have the critical shortcoming that they provide no information on people who did not meet referral criteria. Therefore, it is not possible to know what rates of false-negative diagnosis the strategies were subject to, and this is an essential determinant of the value of any potential approach.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	The CaFaSpA study has already shown this type of research to be feasible in Holland; there is no reason why it should not be repeatable in the UK.

K.2 Referral criteria for people with inflammatory bowel disease

Research recommendation 2	At what stage and using what criteria should people with inflammatory bowel disease be referred to a rheumatologist for a spondyloarthritis assessment?
Population	People with inflammatory bowel disease but no diagnosis of spondyloarthritis
Index test	Defined criteria for a referral to a rheumatologist
Reference standard	Rheumatologist diagnosis
Outcomes	• Sensitivity • Specificity • Positive/negative predictive value • Positive/negative likelihood ratios
Study design	Prospective diagnostic accuracy study, which should follow up all individuals, regardless of whether the algorithm says they need to be referred or not

Potential criterion	Explanation
Importance to patients, service users or the population	The guideline committee noted that people with inflammatory bowel disease (Crohn's disease or ulcerative colitis) are more likely to have or develop spondyloarthritis than those without. An inflammatory bowel disease-specific referral rule would provide value as the diagnostic importance of other spondyloarthritis associated features may be different in the presence of inflammatory bowel disease, something which is not possible to judge from the currently available data. Better referral rules should result in a reduction in the current large delay between onset of symptoms and diagnosis for people with spondyloarthritis.
Relevance to NICE guidance	Medium priority: no recommendations were made in this guideline due to the lack of evidence, and studies would allow for recommendations to be possible in future guideline updates.
Current evidence base	During the development of this guideline specific, validated referral rules were identified for people with inflammatory back pain or acute anterior uveitis, but not for people with inflammatory bowel disease.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	The fact that similar studies have been conducted for people with inflammatory back pain and uveitis implies they should also be possible for people with inflammatory bowel disease.

K.3 Educational interventions

Research recommendation 3	What is the effectiveness and cost-effectiveness of educational interventions for healthcare professionals in order to increase the number of prompt diagnoses of spondyloarthritis?
Population	Healthcare professionals likely to encounter people with possible spondyloarthritis (e.g. GPs, physiotherapists, ophthalmologists, dermatologists, gastroenterologists)
Intervention	Educational interventions (e.g. written materials, web-based training, in-person courses, individual or group training)
Comparator	Standard clinical practice
Outcomes	• Time to referral/diagnosis • Number of contacts with health care professionals • Patient satisfaction • Health-related quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	One of the major reasons identified during this guideline for the delays in diagnosis of spondyloarthritis is a lack of awareness of the condition on behalf of by healthcare professionals. This can take many forms, such as a lack of awareness of different spondyloarthritis subtypes, lack of knowledge about associated clinical features (for example, the differences between inflammatory and mechanical back pain) or characteristics of the patient populations (for example, that spondyloarthritis affects similar numbers of men and women, or that a substantial proportion of people with spondyloarthritis are HLA-B27 negative). Educational interventions to improve the level of awareness may therefore lead to reductions in diagnosis delays.
Relevance to NICE guidance	High priority: it is currently not possible to provide recommendations about educational interventions for healthcare professionals likely to encounter people with spondyloarthritis, and these studies would enable this gap to be filled.
Current evidence base	There are currently very few studies assessing the effectiveness and cost-effectiveness of educational interventions for healthcare professionals likely to encounter people with spondyloarthritis.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	Similar educational intervention studies have been undertaken in other clinical areas, and there is no reason to suppose they should be more difficult to undertake in this area.

K.4 CASPAR criteria

Research recommendation 4	What is the diagnostic utility of the CASPAR criteria in people with suspected (not confirmed) psoriatic arthritis, compared with clinician diagnosis as the gold standard?
Population	People with suspected psoriatic arthritis who have not been refered to a rheumatologist
Index test	CASPAR criteria
Reference standard	Rheumatologist diagnosis
Outcomes	• Sensitivity • Specificity • Positive/negative predictive value • Positive/negative likelihood ratios
Study design	Prospective diagnostic accuracy study

Potential criterion	Explanation
Importance to patients, service users or the population	The CASPAR criteria for diagnosis of psoriatic arthritis are widely used, both in specialist clinical setting as well as during recruitment to randomised clinical trials of interventions for people with this condition. An evaluation of the diagnostic accuracy of these criteria would help to inform how they can best be used in the future as part of both the referral and diagnostic processes.
Relevance to NICE guidance	Medium priority: a consensus based recommendation has been made to support the use of CASPAR, but future updates of the guideline would benefit from prospectively collected data.
Current evidence base	Although the criteria have been validated in case-control studies (i.e. by comparing people with an existing diagnosis of psoriatic arthritis vs people who have had psoriatic arthritis ruled out), this is not the optimal approach to validating a diagnostic tool. Research which evaluated the diagnostic utility of the CASPAR tool in people who have suspected, but not yet confirmed, psoriatic arthritis would be less prone to selection bias, particularly among the non-cases. This would also enable evaluation of how well the tool performs in people who have an uncertain or mixed presentation, who would been excluded from case-control studies.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	The fact that similar studies have been conducted for many other diagnostic and classification tools implies it should also be possible to do so for the CASPAR criteria.

K.5 Standard DMARDs for peripheral spondyloarthritis

Research recommendation 5	What is the comparative effectiveness and cost-effectiveness of standard DMARDs for the management of peripheral spondyloarthritis, and is this effectiveness affected by differences in dose escalation protocols?
Population	People with a confirmed diagnosis of peripheral spondyloarthritis (psoriatic arthritis, reactive arthritis, enteropathic spondyloarthritis)
Intervention	• Standard DMARDs (singly or in combination) • Dose escalation protocols
Comparator	• Other standard DMARDs (singly or in combination) • Alternative dose escalations
Outcomes	• Pain • Disease activity • Functional capacity • Joint stiffness/mobility • Adverse events • Health-related quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	The current lack of evidence makes it difficult to optimise initial therapy for peripheral spondyloarthritis, either by specifying specific drugs within the class of standard DMARDs or optimising dose, administration and monitoring protocols. There is therefore the need for randomised controlled trials looking at alternative drug and dosing strategies for the administration of standard DMARDs of for managing peripheral spondyloarthritis.
Relevance to NICE guidance	High priority: it is currently not possible to provide recommendations about the comparative effectiveness of standard DMARDs for the first-line treatment of peripheral spondyloarthritis, and these studies would enable this gap to be filled.
Current evidence base	Whilst there are a number of randomised controlled trials comparing standard DMARDs with placebo for the management of peripheral spondyloarthritis, there is a lack of evidence comparing individual standard DMARDs to other standard DMARDs.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.6 Switching and augmenting pharmacological therapy

Research recommendation 6	When first-line treatment for spondyloarthritis has failed, what is the most effective and cost-effective ordering of systemic biological disease-modifying anti-rheumatic drugs to treat with and does this ordering change based on particular patient characteristics?
Population	People with a confirmed diagnosis of spondyloarthritis for whom first-line treatment has failed
Intervention	Sequences of biological DMARDs
Comparator	Alternative sequences of biological DMARDs
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Well conducted RCTs comparing different possible alternatives for second-line treatment, and looking at whether the optimum second-line treatment differs based on patient characteristics, would enable more specific and individually tailored treatment choices to be made in the future.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations for switching and sequencing based on the available evidence.
Current evidence base	Only a limited amount of low-quality evidence was found looking at the effectiveness of switching or augmenting treatment when first-line treatment is not providing adequate symptom control, and therefore it was only possible to make very general, class level, recommendations.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.7 Biological DMARDs for peripheral spondyloarthritis

Research recommendation 7	What is the effectiveness and cost-effectiveness of biological DMARDs in people with persistent peripheral spondyloarthritis (excluding psoriatic arthritis) or undifferentiated spondyloarthritis?
Population	People with a confirmed diagnosis reactive arthritis, enteropathic spondyloarthritis or undifferentiated spondyloarthritis
Intervention	Biological DMARDs
Comparator	Standard care (which may include NSAIDs, standard DMARDs, steroids)
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	The substantial side effects possible with biological DMARDs, and their significant cost, means it is difficult to justify offering them to these groups without good evidence of efficacy. There is therefore the need for randomised controlled trials, with a sufficient sample size to identify possible benefits, in these 3 populations. If trials were to recruit participants from multiple spondyloarthritis subpopulations, results should be clearly stratified by diagnosis to enable any differences in benefits or harms between the groups to be identified.
Relevance to NICE guidance	High priority: it is currently not possible to provide recommendations about the effectiveness of biological DMARDs for types of peripheral spondyloarthritis other than psoriatic arthritis, and these studies would enable this gap to be filled.
Current evidence base	Although there have been trials conducted of biological DMARDs for psoriatic arthritis, which have led to positive recommendations in NICE technology appraisals, no such good quality evidence exists in enteropathic arthritis, reactive arthritis or undifferentiated spondyloarthritis.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.8 Manual therapies

Research recommendation 8	What is the long-term effectiveness and cost-effectiveness of manual therapy as an intervention (without other concurrent physiotherapy) for both axial and peripheral spondyloarthritis, and does this effectiveness and cost-effectiveness change in different settings or between different delivery strategies?
Population	People with a confirmed diagnosis of spondyloarthritis
Intervention	Manual therapies • Soft tissue techniques (including massage, muscle energy technique and myofascial release) • Traction • Manipulation/mobilisation (including Spinal Manipulation Therapy (SMT) and Maitland Technique) • Mixed modality manual therapy (soft tissue techniques +/- traction +/- manipulation/mobilisation)
Comparator	Standard care
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Well conducted randomised controlled trials (in both axial and peripheral spondyloarthritis) comparing manual therapy interventions plus standard care to standard care alone would fill an important gap in the evidence base around which interventions provide effective symptom relief for people with spondyloarthritis, and allow for more effective support to be provided.
Relevance to NICE guidance	Medium priority: it was not possible to make recommendations as part of this guideline due to the lack of evidence, and randomised controlled trials would enable recommendations to be made in future updates of the guideline.
Current evidence base	Only a limited amount of low-quality evidence was found looking at the effectiveness of manual therapies, and therefore it was not felt possible to make any recommendations.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.9 Structured exercise

Research recommendation 9	What is the short- and long-term effectiveness and cost-effectiveness of structured exercise programs for peripheral spondyloarthritis, and does this effectiveness and cost-effectiveness change in different settings or between different delivery strategies?
Population	People with a confirmed diagnosis of peripheral spondyloarthritis
Intervention	Structured exercise programs
Comparator	Standard care
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	It is believed that structured exercise programs may provide benefits for people with peripheral spondyloarthritis, particularly in people with axial involvement. Well conducted long-term randomised controlled trials comparing structured exercise programs interventions plus standard care to standard care alone would fill an important gap in the evidence base around which interventions provide effective symptom relief for people with peripheral spondyloarthritis.
Relevance to NICE guidance	Medium priority: it was not possible to make recommendations as part of this guideline due to the lack of evidence, and randomised controlled trials would enable recommendations to be made in future updates of the guideline.
Current evidence base	Whilst evidence was found for structured exercise programs in axial spondyloarthritis, the same evidence was not found for peripheral spondyloarthritis
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.10 Hydrotherapy

Research recommendation 10	What is the short- and long-term effectiveness and cost-effectiveness of hydrotherapy in improving patient-reported outcomes in spondyloarthritis, and does this effectiveness and cost-effectiveness differ between hydrotherapy in a hydro pool or a standard swimming pool?
Population	People with a confirmed diagnosis of spondyloarthritis
Intervention	• Hydrotherapy in a hydro pool • Hydrotherapy in a standard swimming pool
Comparator	Standard care
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Well conducted long-term RCTs (in both axial and peripheral spondyloarthritis) comparing hydrotherapy plus standard care to standard care alone would fill an important gap in the evidence base around which interventions provide effective symptom relief for people with spondyloarthritis. Further, the majority of the concerns around the affordability of hydrotherapy as an intervention are based on it having to be conducted in a specialist hydrotherapy pool. It would therefore be important to know whether a much cheaper and more available hydrotherapy intervention, using a standard swimming pool, offers equivalent benefits.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations for hydrotherapy based on the available evidence.
Current evidence base	Whilst evidence around hydrotherapy does exist in the form of short-term randomised controlled trials and longer-term observational studies, there is currently a lack of long-term randomised controlled trials which have been conducted looking at the effectiveness of hydrotherapy for people with spondyloarthritis.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.11 Hydrotherapy for managing flares

Research recommendation 11	What is the effectiveness and cost-effectiveness of hydrotherapy in managing flares in people with spondyloarthritis, and does this effectiveness and cost-effectiveness differ between hydrotherapy in a hydro pool or a standard swimming pool?
Population	People with a confirmed diagnosis of spondyloarthritis experiencing a flare episode
Intervention	• Hydrotherapy in a hydro pool • Hydrotherapy in a standard swimming pool
Comparator	Standard care
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	There is a need for randomised controlled trials (following people up for at least the entire duration of their flare) comparing hydrotherapy plus standard care to standard care alone, as it may provide an effective way of managing flares for people with spondyloarthritis. Further, the majority of the concerns around the affordability of hydrotherapy as an intervention are based on it having to be conducted in a specialist hydrotherapy pool. It would therefore be important to know whether a much cheaper and more available hydrotherapy intervention, using a standard swimming pool, offers equivalent benefits.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations for hydrotherapy based on the available evidence.
Current evidence base	No evidence was identified about the benefits of hydrotherapy for managing flares, an important gap in the evidence base as this is one of the situations it is felt likely to have the greatest benefits.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.12 Acupuncture

Research recommendation 12	What is the effectiveness and cost-effectiveness of acupuncture, as standardly performed in the UK, versus sham acupuncture for the management of symptoms in axial and peripheral spondyloarthritis?
Population	People with a confirmed diagnosis of spondyloarthritis
Intervention	Acupuncture (as performed in the UK)
Comparator	Sham acupuncture
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	If maintenance of access to acupuncture is going to be justified for people with spondyloarthritis, well-conducted long-term randomised controlled trials (in both axial and peripheral spondyloarthritis) comparing acupuncture plus standard care to standard care alone are necessary, given the sparse and low-quality evidence base that currently exists.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base for people with spondyloarthritis.
Current evidence base	Until recently some people with spondyloarthritis have received acupuncture as a treatment for pain in spondyloarthritis, as these treatments have been available through many NHS services. However, there is currently a lack of evidence of efficacy of acupuncture in this population.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.13 Spinal surgery

Research recommendation 13	Is pre-operative disease activity/stability a predictor of outcomes after spinal surgery for people with spondyloarthritis and axial inflammation?
Population	People with a confirmed diagnosis of spondyloarthritis who or are going to undergo spinal surgery
Predictive factors	• Duration of disease • Duration of delay in diagnosis • Severity of disease • Comorbidities • Osteoporosis • Site of surgery • Indication for surgery • Elective/non-elective • Current treatment • Fitness for surgery • Pre-surgical functional status • Type of centre delivering surgery • Smoking • NSAID use
Outcomes	Good (or poor) surgical outcome
Study design	Prospective cohort study

Criterion	Explanation
Importance to patients, service users or the population	Spinal surgery is only considered for a small subset of people with spondyloarthritis. To maximise the benefit-risk balance from surgery, it is necessary to identify in advance those individuals who will gain the greatest benefit, which in turns requires evidence linking pre-surgical characteristics to outcomes.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations on the predictors for spinal surgery success based on the available evidence.
Current evidence base	Pre-operative disease activity is felt to be one of the factors most likely to correlate to surgical outcomes, but there is currently no evidence to support or refute this belief. Cohort studies would provide evidence which could help to identify cut-offs for the appropriate people to refer for surgery, which is not currently possible.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort studies in this area should be feasible.

K.14 Joint replacement surgery

Research recommendation 14	Is pre-operative disease activity/stability a predictor of outcomes after joint replacement surgery for people with spondyloarthritis?
Population	People with a confirmed diagnosis of spondyloarthritis who or are going to undergo joint replacement surgery
Predictive factors	• Duration of disease • Duration of delay in diagnosis • Severity of disease • Comorbidities • Osteoporosis • Site of surgery • Indication for surgery • Elective/non-elective • Current treatment • Fitness for surgery • Pre-surgical functional status • Type of centre delivering surgery • Smoking • NSAID use
Outcomes	Good (or poor) surgical outcome
Study design	Prospective cohort study

Criterion	Explanation
Importance to patients, service users or the population	Joint replacement surgery is only considered for a small subset of people with spondyloarthritis. To maximise the benefit-risk balance from surgery, it is necessary to identify in advance those individuals who will gain the greatest benefit, which in turns requires evidence linking pre-surgical characteristics to outcomes.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations on the predictors for joint replacement surgery success based on the available evidence.
Current evidence base	Pre-operative disease activity is felt to be one of the factors most likely to correlate to surgical outcomes, but there is currently no evidence to support or refute this belief. Cohort studies would provide evidence which could help to identify cut-offs for the appropriate people to refer for surgery, which is not currently possible.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort studies in this area should be feasible.

K.15 Monitoring of pharmacological treatment

Research recommendation 15	What are the most effective doses and monitoring arrangements for people treated with anti-tumour necrosis factor (TNF) drugs both for spondyloarthritis as well as a comorbidity (e.g. inflammatory bowel disease) simultaneously?
Population	People with a confirmed diagnosis of spondyloarthritis and a related comorbidity (psoriasis, inflammatory bowel disease, recurrent uveitis) being treated with anti-TNF drugs
Intervention	Anti-TNF drugs
Comparator	• Alternative doses • Alternative treatment and monitoring schedules
Outcomes	• Pain • Joint mobility • Physical function • Imaging results • Adverse events • Quality of life • Resource use and costs
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Anti-TNF therapy is indicated for a number of conditions, and it is therefore not uncommon for people to be treated with anti-TNFs for more than one condition simultaneously. This means it is not possible to follow the optimum dosing or monitoring strategy for both conditions, as these will frequently be different, leading to uncertainties in the correct management for that individual. There is therefore the need for studies of people on anti-TNF therapy for spondyloarthritis and a common anti-TNF treated comorbidity (e.g. inflammatory bowel disease) to identify the optimum treatment arrangements for each relevant pair of conditions.
Relevance to NICE guidance	Medium priority: it was not possible to make recommendations as part of this guideline due to the lack of evidence, and randomised controlled trials would enable recommendations to be made in future updates of the guideline.
Current evidence base	There is currently no evidence from randomised controlled trials available to address this question, and therefore it represents a noticeable gap in the evidence base on treatment options for people with spondyloarthritis.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.16 Specialist care during flares

Research recommendation 16	What is the comparative effectiveness and cost-effectiveness of direct access to specialist care versus access via primary care for reducing the risk of complications during flare episodes?
Population	People with a confirmed diagnosis of spondyloarthritis experiencing a flare episode
Intervention	Direct access to specialist care
Comparator	Access to specialist care via primary care
Outcomes	• Improvement in severity, duration, frequency of flare episodes • Time to receiving appropriate care • Number of contacts with health care professionals • Satisfaction with care received • Health-related quality of life • Resource use and cost
Study design	Cluster randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Cluster randomised RCTs comparing direct access to specialist care versus access to primary care could enable a greater standardisation of services, by demonstrating which of these two outcomes produces better outcomes for individuals experiencing a flare.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations on flare management based on the available evidence.
Current evidence base	There is currently no evidence about the optimal setting for managing flares and the most appropriate route for accessing specialist care, and there is considerable variation in practice across the UK.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	Whilst trials of service organisation are inherently complex, designing it as a cluster randomised trial should mean that it is practical to undertake.

K.17 Management of flares

Research recommendation 17	What is the comparative effectiveness and cost-effectiveness of healthcare professional led management and self-help plans for the management of flare episodes in people with spondyloarthritis?
Population	People with a confirmed diagnosis of spondyloarthritis experiencing a flare episode
Intervention	Professional-led management
Comparator	Self-help plans
Outcomes	• Improvement in severity, duration, frequency of flare episodes • Time to receiving appropriate care • Number of contacts with health care professionals • Satisfaction with care received • Health-related quality of life • Resource use and cost
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Randomised controlled trials comparing healthcare professional led and self-help plans for managing flares (which would need to follow people up for at least the entire duration of their flare) could help to demonstrate whether there are additional benefits of healthcare professional led management which would justify the higher costs of such an approach.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations on flare management based on the available evidence.
Current evidence base	There is currently no evidence about the relative effectiveness of self-management versus healthcare professional management of flares in people with spondyloarthritis, and there is considerable variation in practice across the UK.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.

K.18 Managing osteoporosis and fracture risk

Research recommendation 18	What is the optimum approach for identifying and managing osteoporosis and fracture risk in axial spondyloarthritis?
Population	People with a confirmed diagnosis of spondyloarthritis
Intervention	Osteoporosis and fracture screening
Comparator	• Different settings for screening • Different approaches to screening • Standard care
Study design	Prospective cohort study

Criterion	Explanation
Importance to patients, service users or the population	Risks of osteoporosis and fracture are known to be higher in people with axial spondyloarthritis than the general population. However, few studies have looked at whether this higher risk means it is appropriate to adopt a different strategy for identifying and monitoring these conditions in this group (e.g. is more intensive monitoring justified). Prospective cohort studies addressing questions about the frequency of monitoring could help to improve outcomes for this high-risk group.
Relevance to NICE guidance	Low priority: the research would fill relevant gaps in the evidence base, but it is possible to make recommendations on the predictors for spinal surgery success based on the available evidence.
Current evidence base	There is currently very little evidence available to address questions around the optimal approaches to risk management for people with spondyloarthritis.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort studies in this area should be feasible.

K.19 Long term complications of spondyloarthritis

Research recommendation 19	What is the incidence of long-term complications, in particular osteoporosis, cardiovascular disease (CVD) and metabolic syndrome, in people with spondyloarthritis, and how does this compare with the general population? Are any specific spondyloarthritis features or risk factors associated with the incidence and outcomes of these complications
Population	People with a confirmed diagnosis of spondyloarthritis
Outcome to measure	• Osteoporosis incidence • Fracture rates • Cardiovascular disease incidence • Metabolic syndrome incidence • Mortality
Comparator	• Osteoporosis incidence in the general population • Fracture rates in the general population • Cardiovascular disease incidence in the general population • Metabolic syndrome incidence in the general population • Mortality in the general population
Study design	Prospective cohort study

Criterion	Explanation
Importance to patients, service users or the population	Spondyloarthritides are a group of systemic inflammatory conditions, and as such it is thought that people with these conditions may have an elevated risk of CVD, particularly if their disease is not adequately controlled. This may have direct vascular effects as well as precluding maintenance of a good level of cardiovascular fitness. There is also clinical uncertainty around the long-term use of non-steroidal anti-inflammatory drugs (NSAIDs): whether the long-term CVD risks associated with this class of drugs are observed in this population, or whether the suppression of inflammation with these drugs mitigates some of the CVD risks associated with these conditions. In addition, risks of osteoporosis and fracture are known to be higher in people with axial spondyloarthritis than the general population, and the prevalence of axial manifestations in people diagnosed with peripheral disease implies they may also be high in peripheral spondyloarthritis. The longer term complication rates in the spondyloarthritides need to be established, as well as whether standard biological disease modifying anti-rheumatic drug (DMARD) therapies and biological DMARDs influence these outcomes.
Relevance to NICE guidance	High priority: it is currently not possible to provide recommendations about appropriate monitoring for cardiovascular complications in people with spondyloarthritis, and these studies would enable this gap to be filled.
Current evidence base	There is currently little robust evidence available to address questions around the comparative incidence and severity of osteoporis and cardiovascular complications in people with spondyloarthritis.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that cohort studies in this area should be feasible.

K.20 Information on flares

Research recommendation 20	What approaches to signposting people with spondyloarthritis to appropriate services for managing their flares are found most useful by people with spondyloarthritis?
Population	People with a confirmed diagnosis of spondyloarthritis experiencing or who have experienced a flare episode
Phenomena of interest	Information on managing flare episodes, including: • Who to contact • How to self-manage • When to contact a healthcare professional • Identification of flare episodes
Study design	Qualitative study

Criterion	Explanation
Importance to patients, service users or the population	Being provided with appropriate information about flares is important for people with spondyloarthritis, but there is a lack of evidence about the most appropriate ways to ensure people have access to this information, and whether this differences between different subgroups of the population. Qualitative studies of preferences for information in people with spondyloarthritis who have experience of flares would enable the optimisation of support services for people at risk of having flares.
Relevance to NICE guidance	Medium priority: it was not possible to make recommendations as part of this guideline due to the lack of evidence, and randomised controlled trials would enable recommendations to be made in future updates of the guideline.
Current evidence base	There is currently little robust evidence available to address questions around the information needs of people with spondyloarthritis during flare episodes.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that qualitative studies in this area should be feasible.

K.21 Management of flares

Research recommendation 21	What is the effectiveness and cost-effectiveness of information provision in reducing the incidence and severity of flare episodes?
Population	Information for people provided in different formats (printed, online, helplines, flare management plans)
Intervention	Professional-led management
Comparator	• Alternative forms of information provision • Standard care
Outcomes	• Improvement in severity, duration, frequency of flare episodes • Time to receiving appropriate care • Number of contacts with health care professionals • Satisfaction with care received • Health-related quality of life • Resource use and cost
Study design	Randomised controlled trial

Potential criterion	Explanation
Importance to patients, service users or the population	Providing structured information about flares may help to reduce their incidence and severity, but there is a cost attached to providing these services. Well conducted randomised controlled trials would help to show whether there are any benefits from such an approach, and if these benefits are sufficiently large to justify the cost of providing this information prospectively.
Relevance to NICE guidance	Medium priority: it was not possible to make recommendations as part of this guideline due to the lack of evidence, and randomised controlled trials would enable recommendations to be made in future updates of the guideline.
Current evidence base	There is currently no evidence from randomised controlled trials about the effectiveness of information provision in reducing the incidence and severity of flare episodes.
Equality	No specific equality concerns are relevant to this research recommendation.
Feasibility	There is a sufficiently large and well defined population available that randomised controlled trials in this area should be feasible.