Appendix C: Review protocols

	Details	Additional comments
Review question 1	What signs and symptoms should prompt a healthcare professional to think of spondyloarthritis?	
Objectives	To identify clinical signs and symptoms which indicate that a patient presenting in any healthcare setting may have spondyloarthritis	
Type of review	Diagnostic review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis, or people with diagnosed spondyloarthritis whose presenting symptoms are being studied	GDG made post-hoc decision to give equal inclusion priority to retrospective and prospective studies
Intervention	Signs and symptoms including: Axial • Low/general back pain (>3 months) • Onset of back pain age<45 • Spinal fusion • Neck pain • Morning stiffness • Stiffness • Limited mobility • Inflammatory bowel disease • Psoriasis • Uveitis • Site-specific inflammation/pain • Enthesitis • Fatigue • Signs on imaging • Response to NSAIDs • Buttock pain Peripheral • Joint pain and swelling • Oligoarthritis • enthesitis • Dactylitis • Inflammatory bowel disease • Psoriasis • Uveitis • Examination showing suspected persistent synovitis of undetermined cause • Site-specific inflammation/pain	Including signs and symptoms as specified in diagnostic scores Back pain to included inflammatory back pain e.g. as defined by ASAS, Calin criteria, Berlin criteria

	Details	Additional comments
	• Nail involvement • Fatigue • (ReA) Urethritis, keratoderma blennorrhagica, conjunctivitis, balanitis, soft palate ulceration • Morning stiffness • Signs on imaging	
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	No universal gold standard exists with which to compare
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	Intent 1. Primary care – to get assessment (sensitivity and specificity) 2. Secondary care – to get diagnosis GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded • Case studies • Anything other than cohort or cross-sectional studies	
Review strategies	Study quality will be assessed in GRADE framework	

	Details	Additional comments
Review question 2	What risk factors should increase suspicion of spondyloarthritis?	
Objectives	To identify risk factors which indicate that a patient presenting in any healthcare setting may have spondyloarthritis	
Type of review	diagnostic review	
Language	English	
Study design	e.g. Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis , or people with diagnosed spondyloarthritis whose presenting symptoms are being studied	GDG made post-hoc decision to give equal inclusion priority to retrospective and prospective studies
Intervention	Risk factors Family history HLA-B27 +ve History of psoriasis History of IBD History of uveitis History of ReA History of JIA (enthesitis/psoriatic) Recent enteric or genitourinal infection Onset under age 45 (axial)	
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	No universal gold standard exists with which to compare
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case studies Anything other than cohort or cross-sectional studies	
Review strategies	Study quality will be assessed in GRADE framework	

	Details	Additional comments
Review question 3	What are the obstacles to a prompt diagnosis of spondyloarthritis?	
Objectives	To identify the potential obstacles that prevent people with spondyloarthritis receiving a prompt diagnosis of their condition	
Type of review	Descriptive	
Language	English	
Study design	Qualitative studies	Include survey, focus groups, case study
Status	No date restriction	
Population	People (aged 16 years and over) with a suspected or confirmed diagnosis of spondyloarthritis Healthcare professionals	GDG agree that views of healthcare professionals may be useful in this instance
Intervention	Barriers such as • Lack of patient awareness leading to delayed diagnosis • Patients deterred by lack of diagnosis at earlier consultation • Lack of health-care professional awareness of chronic inflammatory conditions • Lack of health-care professional awareness of complications/co-morbid manifestations of pre-existing inflammatory conditions • High consultation rate of lower back pain (mostly mechanical) • Lack of cross referrals in secondary care between relevant specialities • Over-specialism within rheumatology leading to consultations where relevant comorbidities are not assessed. • Lack of multidisciplinary team assessment • Lack of access from GPs to (i) HLA-B27 testing (ii) appropriate MRI equipment or protocol • Patient gender (under-diagnosis in women) • Lack of a biological marker in SpA	These are examples; this list is not exhaustive
Comparator	Prompt diagnosis of SpA	
Outcomes	Specific barriers to care identified	
Other criteria for inclusion / exclusion of studies	NA	
Search strategies	Studies looking at delays to diagnosis, early vs late diagnosis etc. See appendix D	
Review strategies	Study quality will be assessed using the NICE Methodology checklist: qualitative studies Themes relating to barriers to diagnosis will be identified and presented with supporting quotations	

	Details	Additional comments
	Details	**Additional comments**
Review question 4	What is the diagnostic utility of a risk assessment score for identifying spondyloarthritis?	
Objectives	To identify the diagnostic utility of using different risk assessment scores to diagnose spondyloarthritis	
Type of review	Diagnostic test accuracy review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis	
Intervention	Any risk assessment score/rule/model presenting at least two characteristics in combination Clinical diagnostic scores/tools such as: • Axial ○ Modified New York criteria ○ Bennett's criteria etc. ○ ASAS criteria (axial) ○ AMOR criteria ○ Calin criteria ○ European Spondyloarthropathy Study Group criteria • Peripheral ○ CASPAR criteria ○ ASAS criteria (peripheral) ○ Modified McGonagle criteria • Both ○ Moll and Wright ○ Vasey and Espinoza	Consider also: ○ Modified Stoke Ankylosing Spondylitis Spinal Score ○ Some diagnostic criteria used as scores ○ Combinations of diagnostic tests ○ Enthesitis scores ○ Delphi/consensus ○ Clinical diagnosis+imaging (axial) ○ Clinical diagnosis+imaging (peripheral) ○ PEST ○ Inflammatory back pain questionnaires (NASS, Spondyloarthritis Society of America) ○ Prognostic risk factors in combination
Comparator	Clinician diagnosis	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies Where data exists for both, preference will be given to prospective studies over	

	Details	Additional comments
	retrospective studies as these are less open to selection bias	
Review strategies	If 3 or fewer studies are identified data from 2 x 2 tables will be pooled using Meta-Disc for univariate analysis If 4 or more studies are identified, data from 2 x 2 tables will be pooled in STATA using the metandi function for bivariate analysis	

	Details	Additional comments
Review question 5	What is the usefulness of information gathering (for example family history, self-report questionnaires, and screening criteria) in improving early diagnosis of spondyloarthritis?	Information gathering not restricted by setting (could occur in primary care, intermediate services or secondary care)
Objectives	To ascertain the utility of routinely collecting information prior to making a diagnosis	
Type of review	Descriptive	
Language	English	
Study design	Any study type	Patient-survey, HCP-survey, focus-groups, interview, thematic analysis, grounded theory, case study
Status	No date restriction	
Population	People suspected of having spondyloarthritis or people with inflammatory back pain symptoms	NB: axial and peripheral
Information	Family history Self-report questionnaires Screening criteria	
Comparator	Absence of information gathering	
Outcomes	Clinical utility of information • Percentage of referrals correctly diagnosed as spondyloarthritis • Time taken from symptoms to diagnosis (not time from referral) • Resource use and costs • Health-related quality of life • Improvement in disease specific outcomes • Reduced long term complications and /or skeletal damage	The clinical utility of information is its capacity to • help rule diagnosis in and/or out and • make a decision on intervention options possible. Outcomes will differ for axial, peripheral and other forms of spondyloarthritis
Other criteria for inclusion / exclusion of studies	Non-qualitative study designs	
Review strategies	Standard qualitative review Study quality will be assessed using the NICE Methodology checklist: qualitative studies	

	Details	Additional comments
Review question 6	What is the comparative effectiveness of different referral strategies in diagnosing spondyloarthritis?	
Objectives	To compare the effectiveness of different referral strategies for people suspected of having spondyloarthritis	There will be value in differentiating between referral strategies for different forms of spondyloarthritis
Type of review	Intervention review	
Language	English	
Study design	RCT only	
Status	No date restriction	
Population	People suspected of having spondyloarthritis or people with inflammatory back pain symptoms	NB: peripheral and axial
Intervention	Referral strategy/ protocol/proforma/pathway	Examples of referral strategy could include • Referral on presentation with low back pain or joint pain • Referral with low back pain/joint pain and serological test results • Referral with multiples of diagnostic criteria items • other combinations Diagnosis and referrals not restricted by setting (primary care, intermediate services or secondary care)
Comparator	Any other referral strategy	
Outcomes	• Percentage of referrals correctly diagnosed as spondyloarthritis • Time taken from symptoms to diagnosis (not time from referral) • Resource use and costs • Health-related quality of life • Improvement in disease specific outcomes • Reduced long term complications and/or skeletal damage	Correct diagnosis should not be purely defined as the ASAS criteria, as this would exclude older papers
Other criteria for inclusion / exclusion of studies	NA	
Review strategies	Standard intervention review. Study quality will be assessed in GRADE framework	

	Details	Additional comments
Review question 7	What is the diagnostic utility of a HLA B27 test for investigating suspected spondyloarthritis?	
Objectives	To identify the diagnostic utility of using the HLA B27 test to diagnose spondyloarthritis	
Type of review	Diagnostic test accuracy review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis	
Intervention	Human leucocyte antigen (HLA)-B27	Also search for Human lymphocyte antigen B27, human leukocyte (A) antigen, white blood cell antigens, histocompatibility leukocyte A antigen
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies	
Review strategies	If 3 or fewer studies are identified data from 2 x 2 tables will be pooled using Meta-Disc for univariate analysis If 4 or more studies are identified, data from 2 x 2 tables will be pooled in STATA using the metandi function for bivariate analysis	

	Details	Additional comments
Review question 8	What is the diagnostic utility of an erythrocyte sedimentation rate test for investigating suspected spondyloarthritis?	
Objectives	To identify the diagnostic utility of using the erythrocyte sedimentation rate test to diagnose spondyloarthritis	
Type of review	Diagnostic test accuracy review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis	
Intervention	Erythrocyte sedimentation rate test	Also search for Sed* test Sedimentation rate ESR
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies Where data exists for both, preference will be given to prospective studies over retrospective studies as these are less open to selection bias	ESR varies with time and other conditions and activity
Review strategies	If 3 or fewer studies are identified data from 2 x 2 tables will be pooled using Meta-Disc for univariate analysis If 4 or more studies are identified, data from 2 x 2 tables will be pooled in STATA using the metandi function for bivariate analysis	

	Details	Additional comments
Review question 9	What is the diagnostic utility of a C-reactive protein test for investigating suspected spondyloarthritis?	
Objectives	To identify the diagnostic utility of using the C-reactive protein test to diagnose spondyloarthritis	
Type of review	Diagnostic test accuracy review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis	
Intervention	C-reactive protein test	Search also CRP; High-sensitivity C-reactive protein; hs-CRP
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies Where data exists for both, preference will be given to prospective studies over retrospective studies as these are less open to selection bias	
Review strategies	If 3 or fewer studies are identified data from 2 x 2 tables will be pooled using Meta-Disc for univariate analysis If 4 or more studies are identified, data from 2 x 2 tables will be pooled in STATA using the metandi function for bivariate analysis	

	Details	Additional comments
Review question 10	What is the diagnostic utility of imaging (alone or in sequence) for investigating suspected spondyloarthritis?	
Objectives	To identify the diagnostic utility of using different imaging methods to diagnose spondyloarthritis	
Type of review	Diagnostic test accuracy review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis	
Intervention	• MRI • X-ray • Ultrasound • Isotope bone scan • PET CT • PET MRI • Sequential combinations of the above	One-off or repeat
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies Where data exists for both, preference will be given to prospective studies over retrospective studies as these are less open to selection bias	
Review strategies	If 3 or fewer studies are identified data from 2 x 2 tables will be pooled using Meta-Disc for univariate analysis If 4 or more studies are identified, data from 2 x 2 tables will be pooled in STATA using the metandi function for bivariate analysis	

	Details	Additional comments
Review question 11	What is the diagnostic utility of testing for infection such as salmonella, shigella, yersinia, campylobacter and chlamydia in cases of suspected reactive arthritis?	
Objectives	To identify the diagnostic utility of using testing for specific infections to diagnose reactive arthritis.	
Type of review	Diagnostic test accuracy review	
Language	English	
Study design	Cohort, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected reactive arthritis	
Intervention	Specific testing/culture methods e.g. • Urine testing (Chlamydia) • Swabbing (Chlamydia) • Anal swabs (Chlamydia) • Blood cultures (all) • PCR (fragments of bacterial DNA) (all) • Faecal samples (GI infections)	
Comparator	Clinical opinion of spondyloarthritis was considered the preferred reference standard, with diagnosis using any specified criteria as the next preference.	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies Where data exists for both, preference will be given to prospective studies over retrospective studies as these are less open to selection bias	
Review strategies	If 3 or fewer studies are identified data from 2 x 2 tables will be pooled using Meta-Disc for univariate analysis If 4 or more studies are identified, data from 2 x 2 tables will be pooled in STATA using the metandi function for bivariate analysis	

	Details	Additional comments
Review question 12	What are the indications (signs, risk factors, test or scan findings) for referral for specialist advice at initial diagnosis?	
Objectives	To identify which variables from the above list are able to accurately predict a subsequent diagnosis of spondyloarthritis	
Type of review	Descriptive	
Language	English	
Study design	Cohort studies, cross-sectional studies	
Status	No date restrictions	
Population	People (aged 16 years and over) with suspected spondyloarthritis	
Intervention	Indications to include: • inflammatory lower back pain (axial) of at least 3 months duration often with insidious onset • Joint/tendon pain (axial or peripheral)/swelling (peripheral) • Morning stiffness or stiffness improving with exercise • Elevated ESR/CRP • HLA-B27 positive • Family history • Presence of extra-articular symptoms (uveitis, psoriasis, IBD) • Radiographic/imaging signs if available • NSAID responsiveness • Reactive arthritis	Core features are the first three on the list
Comparator	People presenting suspected SpA who are not positive for (some of) the above signs/symptoms/risk factors	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value Diagnostic odds ratio	GDG indicated that positive and negative likelihood ratios would be the most useful measure, with a positive likelihood ratio value >=2 or a negative likelihood ratio value <=0.5 representing a clinically useful result
Other criteria for inclusion / exclusion of studies	The following study types will be excluded Case-control studies Case studies Where data exists for both, preference will be given to prospective studies over retrospective studies as these are less open to selection bias	
Review strategies	Prospective consecutive cross-sectional studies are the preferred study type. If none are available we will examine retrospective cross-sectional studies	

	Details	Additional comments
Review question 13	How should transition from specialist paediatric services to specialist adult rheumatology services be managed for young people between the ages of 16 and 18?	The GDG opted to refer to Transition care guideline (anticipated publication date: February 2016) The GDG did not feel there would be any substantial differences between general transition care and that for people with spondyloarthritis. Therefore this review question was not carried out

	Details	Additional comments
Review question 14	What is the effectiveness of manual therapies compared with standard care for managing spondyloarthritis?	Changed at GDG1 to focus on what is done rather than the professional doing it
Objectives	To determine the effectiveness of each of these therapies for managing the symptoms and structural outcomes associated with spondyloarthritis	
Type of review	Intervention review	
Language	English	
Study design	RCTs for short term outcomes Observational studies for long term outcomes	Changed from RCT only at GDG1 as GDG felt that RCTs were unlikely to have adequate follow up to examine the long term outcomes needed to evaluate these interventions. Observational studies: include case series ≥10 people. Exclude case reports/case reviews
Status	No date restriction	
Population	People (aged 16 years and over) 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)	Number of sessions, intensity, frequency etc. to be determined
Comparator	Standard care	Standard care to include usual care, treatment as usual, waiting list, delayed start of treatment, no treatment and placebo exercise
Outcomes	Pain Adverse events Joint mobility Physical function Quality of life Imaging Composite measures	AEs to be reported as number of events per person year Composites measures: scales to be pooled as they are all measuring the same thing – GDG to provide a list of outcome scales
Other criteria for inclusion / exclusion of studies	Minimum length/duration of treatment - effect should be expected at 8-12 sessions or 3 months	
Review strategies	If RCTs/systematic review are available these are the preferred option If not other study designs are to be used (see above for restrictions on eligible observational study designs)	

	Details	Additional comments
	Where one or more studies are available, data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 15	What is the effectiveness of structured exercise compared with standard care for managing spondyloarthritis?	
Objectives	To ascertain the clinical effectiveness of structured exercise in the management of symptoms related to spondyloarthritis	
Type of review	Intervention review	
Language	English	
Study design	RCTs for short term outcomes Observational studies for long term outcomes	Changed from RCT only at GDG1 as GDG felt that RCTs were unlikely to have adequate follow up to examine the long term outcomes needed to evaluate these interventions. Observational studies: include case series ≥10 people. Exclude case reports/case reviews
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	Structured exercise • Individual • Group • Home • Hospital • symptom/disease specific	Number of sessions, intensity, frequency etc. to be determined
Comparator	Standard care Unstructured / unsupervised exercise	Standard care to include usual care, treatment as usual, waiting list, delayed start of treatment and no treatment as well as placebo exercise
Outcomes	Pain Adverse events Joint mobility Physical function Quality of life Imaging Composite measures	AEs to be reported as number of events per person year Composites measures, Also scales to be pooled as they are all measuring the same ting – GDG to provide a list of outcome scales
Other criteria for inclusion / exclusion of studies	Inclusion: No addition criteria Exclusion Non-consecutive case series, case-studies	
Review strategies	If RCTs/systematic review are available these are the preferred option If not other study designs are to be used Where one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
	If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 16	What is the effectiveness of hydrotherapy compared with standard care for managing spondyloarthritis?	
Objectives	To ascertain the clinical effectiveness of hydrotherapy in the management of symptoms related to spondyloarthritis	
Type of review	Intervention review	
Language	English	
Study design	RCTs for short term outcomes Observational studies for long term outcomes	Change from SR/RCTs as GDG felt that RCTs were unlikely to have adequate follow up to examine the long term outcomes needed to evaluate these interventions.
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	Structured hydrotherapy programme with patient specific goas guided by a therapist	Spa therapy not included
Comparator	Standard care	Standard care to include usual care, treatment as usual, waiting list, delayed start of treatment and no treatment as well as placebo hydrotherapy
Outcomes	Pain Adverse events Joint / Spinal mobility Physical function Quality of life Imaging Composite measures	AEs to be reported as number of events per person year Composites measures, Also scales to be pooled as they are all measuring the same ting – GDG to provide a list of outcome scales
Other criteria for inclusion / exclusion of studies	Inclusion: No addition criteria Exclusion Non–consecutive case series, case-studies	
Review strategies	If RCTs/systematic review are available these are the preferred option If not other study designs are to be used. Where one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 17	What is the effectiveness of acupuncture compared with sham acupuncture and standard care for managing spondyloarthritis?	Standard care also accepted by GDG as a comparator
Objectives	To ascertain the clinical effectiveness of acupuncture in the management of spondyloarthritis symptoms	
Type of review	Intervention review	
Language	English	
Study design	Systematic reviews and/or randomised controlled trials	GDG expected that any benefits of these interventions would be observed in the short term so did not extend the study type to include observational studies
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	Acupuncture	Any particular type of acupuncture , electro-acupuncture, acupressure, etc., number of sessions, duration of sessions, frequency etc.
Comparator	Sham acupuncture Standard care	Standard care to include usual care, treatment as usual, waiting list, delayed start of treatment and no treatment
Outcomes	Pain Adverse events Joint / Spinal mobility Physical function Quality of life Imaging Composite measures	AEs to be reported as number of events per person year Composites measures, Also scales to be pooled as they are all measuring the same ting – GDG to provide a list of outcome scales
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion: Study design: Case-control Cohort study Narrative review Case-study Qualitative review	
Review strategies	IF RCTs/systematic review are available these are the preferred option Where one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
	Details	**Additional comments**
Review question 18	What is the effectiveness of physical aids (for example, braces) compared with standard care for managing spondyloarthritis?	
Objectives	To ascertain the clinical effectiveness of physical aids in the management of spondyloarthritis symptoms	
Type of review	Intervention	
Language	English	
Study design	RCTs and systematic reviews only	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	Physical aids	e.g. braces, walking aids, hand splints, hot wax baths, sheepskin protectors for elbows, driving aids, mirrors, assisted daily living devices
Comparator	Standard care	Standard care to include usual care, treatment as usual, waiting list, delayed start of treatment and no treatment
Outcomes	Pain Adverse events Joint / Spinal mobility Physical function Quality of life Imaging Composite measures Fatigue	
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion (study design): Case-control Cohort study Narrative review Case-study Qualitative review	
Review strategies	If RCTs/systematic review are available these are the preferred option Where one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 19	What is the effectiveness of long-term (4 weeks or longer) treatment with antibiotics for first-line management of reactive arthritis compared with standard treatment?	
Objectives	To determine the effectiveness of long term (4 weeks or longer) treatment with antibiotics as first line treatment for reactive arthritis.	
Type of review	Intervention	
Language	English	
Study design	RCTs and systematic reviews	
Status	No date restriction	
Population	People (aged 16 or above) with confirmed or suspected reactive arthritis	
Intervention	Long term (4 weeks or more) antibiotic therapy as first line treatment	Consider combination therapies
Comparator	Standard treatment	Standard treatment to include placebo, and non-antibiotic first line therapies
Outcomes	Pain Adverse events Joint count Sacroiliitis imaging Physical function Inflammatory markers (CRP, ESR) Fatigue	

Other criteria for inclusion / exclusion of studies	Inclusion:
	No additional criteria
	
	Exclusion:
	• Intervention:
	  ○ RCTs where duration of intervention is less than 4 weeks
	
	• Study design:
	  ○ Case-control
	  ○ Cohort study
	  ○ Narrative review
	  ○ Case-study
	  ○ Qualitative review	

Review strategies	If RCTs/systematic review are available these are the preferred option Where one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 20	What is the comparative effectiveness of the following pharmacological interventions for management of axial spondyloarthritis: • corticosteroids • non-steroidal anti-inflammatory drugs • standard disease-modifying anti-rheumatic drugs?	Apremilast not yet licensed – likely to be classified as DMARD JAK-STAT is a 'small molecule' drug
Objectives	To ascertain the absolute and relative effectiveness of pharmaceutical management of axial spondyloarthritis with a range of non-biologic drugs	
Type of review	Intervention	
Language	English	
Study design	Systematic reviews and RCTs only	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	NSAIDs Corticosteroids Standard disease-modifying anti-rheumatic drugs	GDG have indicated the following as potentially relevant (BNF (Sep 2014)): NSAIDs (ibuprofen, naproxen, fenoprofen, flurbiprofen, ketoprofen, diclofenac, aceclofenac, etodolac, indomethacin, meloxicam, nabumetone, phenylbutazone, sulindac, etoricoxib, celecoxib) Corticosteroids (prednisolone, prednisolone modified release, betamethasone, hydrocortisone (acetate), solu-corta (soluble), methylprednisolone [acetate], methylprednisolone sodium succinate (soluble), triamcinolone acetonide, triamcinolone hexacetonide) Standard DMARDs (methotrexate, sulfasalazine, hydroxychloroquine, ciclosporin, leflunamide)
Comparator	Each of the above Comparisons with placebo may be incorporated into network meta-analysis	
Outcomes	Pain Adverse events Spinal mobility Physical function Quality of life Imaging Composite measures Fatigue ESR+CRP	
Other criteria for inclusion /	Inclusion: No additional criteria	DMARDs may not show effect until at least 3 months of treatments

	Details	Additional comments
exclusion of studies	Exclusion: Study design: Case-control Cohort study Narrative review Case-study Qualitative review	Corticosteroids may be administered short term/one off
Review strategies	If RCTs/systematic reviews are available these are the preferred option Where sufficient and suitable data are available, network meta-analysis will be used If network meta-analysis is not a suitable strategy, and one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile with accompanying evidence statements If only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 21	What is the comparative effectiveness of the following pharmacological interventions for management of peripheral spondyloarthritis: • corticosteroids • non-steroidal anti-inflammatory drugs • standard disease-modifying anti-rheumatic drugs?	
Objectives	To ascertain the absolute and relative effectiveness of pharmaceutical management of peripheral spondyloarthritis with a range of non-biologic drugs	
Type of review	Intervention	
Language	English	
Study design	Systematic reviews and RCTs only	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	NSAIDs Corticosteroids Standard disease-modifying anti-rheumatic drugs	GDG have indicated the following as potentially relevant (BNF (Sep 2014)) NSAIDs (ibuprofen, naproxen, fenoprofen, flurbiprofen, ketoprofen, diclofenac, aceclofenac, etodolac, indometacin, meloxicam, nabumetone, phenylbutazone sulindac, etoricoxib, celecoxib) Corticosteroids (prednisolone, prednisolone modified release, betamethasone, hydrocortisone (acetate), solucorta (soluble), methylprednisolone (acetate), methylprednisolone sodium succinate (soluble), triamcinolone acetonide, triamcinolone hexacetonide) Standard DMARDs (methotrexate, sulfasalazine, intramuscular gold, leflunomide, azathioprine, ciclosporin)
Comparator	Each of the above Comparisons with placebo may be incorporated into network meta-analysis	
Outcomes	Pain Adverse events (additional related to methotrexate) Joint count Physical function Quality of life Imaging Composite measures Fatigue CRP	

	Details	Additional comments
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion: Study design: Case-control Cohort study Narrative review Case-study Qualitative review	
Review strategies	If RCTs/systematic review are available these are the preferred option Where • Sufficient and suitable data are available, network meta-analysis will be used • If network meta-analysis is not a suitable strategy, and one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile will accompanying evidence statements • Only a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 22	(a) How often should people receiving pharmacological interventions for managing spondyloarthritis be monitored? (b) How often should people with spondyloarthritis be offered specialist review?	
Objectives	To determine the frequency with which people with spondylitis should have their medication monitored and/or reviewed	Frequency may depend on type of drug
Type of review	Intervention	
Language	English	
Study design	RCT and systematic review	
Status	No date restrictions	
Population	People (aged 16 or over) with a confirmed diagnosis of spondyloarthritis	People with comorbidities may have different baseline risk of complications/adverse events
Intervention	Frequency of medication monitoring or review	
Comparator	No monitoring, different monitoring frequencies	
Outcomes	Outcomes for Q22(a) • Tolerability • Adverse events • adherence Outcomes for Q22(b) • standard outcomes for SpA intervention reviews	
Other criteria for inclusion / exclusion of studies	No exclusions	
Review strategies	If RCTs/systematic reviews are available these are the preferred option Where • one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile will accompanying evidence statements • a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 23	When a first-line treatment has failed, what is the effectiveness of the following for managing spondyloarthritis: • switching to a different pharmacological intervention? • augmenting with a second pharmacological intervention?	
Objectives	To ascertain the absolute and relative effectiveness of second line treatment options once a first line option has failed.	
Type of review	Interventional review	
Language	English	
Study design	RCT only	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis who did not respond to first-line therapy	
Intervention	NSAIDs Corticosteroids Standard disease-modifying anti-rheumatic drugs Biologics (in AS only) – cross refer to TAs	Please indicate if any of the drugs listed below are to be excluded BNF (Sep 2014) list the following as NSAIDs (ibuprofen, dexibuprofen, naproxen, fenoprofen, flurbiprofen, ketoprofen, dexketoprofen, tiaprofenic acid, diclofenac, aceclofenac, etodolac, indomethacin, mefenamic acid, meloxicam, nabumetone, phenylbutazone, piroxicam, sulindac, tenoxicam, tolfenamic acid, ketorolac, parecoxib, etoricoxib, celecoxib) As Corticosteroids (prednisolone, prednisolone modified release, betamethasone, dexamethasone, hydrocortisone acetate, methylprednisolone acetate, triamcinolone acetonide) As Standard DMARDs (methotrexate, ci(y)closporin, sulf(ph)asalazine, intramuscular gold, penicillamine, leflunomide, azathioprine, hydroxychloroquine)
Comparator	Each of the above when one first line treatment option has failed, or as augmented therapy with a first line treatment.	
Outcomes	Pain Adverse events Joint count/Spinal mobility Physical function Quality of life Imaging Composite measures Inflammatory markers (ESR, CRP)	

	Details	Additional comments
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion: Study design: Case-control Cohort study Narrative review Case-study Qualitative review	
Review strategies	If RCTs/systematic reviews are available these are the preferred option Where: • one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile will accompanying evidence statements • a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 24	What is the effectiveness of systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of enteropathic arthritis?	
Objectives	To determine the effectiveness of using systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of enteropathic arthritis	
Type of review	Intervention	
Language	English	
Study design	RCTs and systematic reviews	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of enteropathic spondyloarthritis	
Intervention	Biologic DMARDs, to include: • Abatacept • Adalimumab • Anakinra • Secukinumab (currently unlicensed) • Certolizumab pegol • Etanercept • Golimumab • Infliximab • Rituximab • Ustekinumab (From BNF November 2014)	None currently licensed for this indication so studies would be on off-label use. Exception is Secukinumab which is completely unlicensed presently
Comparator	Any of the above, plus placebo, or other classes of systemic drugs used to treat this group (NSAIDs, DMARDs, corticosteroids)	
Outcomes	Pain Adverse events Joint count/ Spinal mobility Physical function Quality of life Imaging Composite measures ESR, CRP	
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion: Study design: Case-control Cohort study Narrative review Case-study Qualitative review	

	Details	Additional comments
Review strategies	If RCTs/systematic reviews are available these are the preferred option Where: • one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile will accompanying evidence statements • a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 25	What is the effectiveness of systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of reactive arthritis?	
Objectives	To determine the effectiveness of using systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of reactive arthritis.	
Type of review	Intervention	
Language	English	
Study design	RCTs and systematic reviews	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of undifferentiated spondyloarthritis, excluding non-radiographic ankylosing spondylitis	
Intervention	Biologic DMARDs, to include: • Abatacept • Adalimumab • Anakinra • Certolizumab pegol • Etanercept • Golimumab • Infliximab • Rituximab • Secukinumab • Tocilizumab • Ustekinumab (From BNF November 2014)	None currently licensed for this indication so studies would be on off-label use. Exception is Secukinumab which is completely unlicensed presently
Comparator	Any of the above, plus placebo, or other classes of systemic drugs used to treat this group (NSAIDs, DMARDs, corticosteroids)	
Outcomes	Pain Adverse events Joint count Physical function Quality of life Imaging ESR, CRP Composite measures	
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion: Study design: Case-control Cohort study Narrative review Case-study Qualitative review	

	Details	Additional comments
Review strategies	If RCTs/systematic reviews are available these are the preferred option Where: • one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile will accompanying evidence statements • a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 26	What is the effectiveness of systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of undifferentiated spondyloarthritis, excluding non-radiographic ankylosing spondylitis?	
Objectives	To determine the effectiveness of using systemic biological disease-modifying anti-rheumatic drugs for managing symptoms of undifferentiated spondyloarthritis.	
Type of review	Intervention	
Language	English	
Study design	RCTs and systematic reviews	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of undifferentiated spondyloarthritis, excluding non-radiographic ankylosing spondylitis	
Intervention	Biologic DMARDs, to include: • Abatacept • Adalimumab • Anakinra • Certolizumab pegol • Etanercept • Golimumab • Infliximab • Rituximab • Secukinumab • Tocilizumab • Ustekinumab (From BNF November 2014)	None currently licensed for this indication so studies would be on off-label use. Exception is Secukinumab which is completely unlicensed presently
Comparator	Any of the above, plus placebo, or other classes of systemic drugs used to treat this group (NSAIDs, DMARDs, corticosteroids)	
Outcomes	Pain Adverse events Joint count / Spinal mobility Physical function Quality of life Imaging Composite measures ESR, CRP	
Other criteria for inclusion / exclusion of studies	Inclusion: No additional criteria Exclusion: Study design: Case-control Cohort study Narrative review	

	Details	Additional comments
	Case-study Qualitative review	
Review strategies	If RCTs/systematic reviews are available these are the preferred option Where: • one or more studies are available data will be pooled in a standard pairwise meta-analysis and presented to the GDG in a GRADE profile will accompanying evidence statements • a single study is available, the data will be presented in a GRADE profile with accompanying evidence statements	

	Details	Additional comments
Review question 27	What information on treatment, long-term complications and self-management do young people and adults with spondyloarthritis find useful?	
Objectives	To identify the content (and format) of information provided to people with spondyloarthritis which is most useful.	GDG may be able to supplement this review with information from other reviews e.g. long-term complications etc.
Type of review	Qualitative and/quantitative	
Language	English	
Study design	For qualitative, interview, survey, focus groups For quantitative, RCT	
Status	No date restrictions	
Population	People with a confirmed diagnosis of spondyloarthritis (aged 16 and over)	
Intervention	Information on: • Treatment (options) • Treatment (access) • Treatment (adverse events) • Management (patient-led) • Management (clinician-led) • Complications and comorbidities • Access to support groups • Sexual wellbeing/relationship wellbeing • Psychological interventions • Work capability (support to continue, advice as to adaptations, whether type of work is appropriate) • Driving (including adaptations) • Access to supports for daily living activities (including walking aids/podiatry support) • Citizens advice/adult social services/ benefit eligibility • Educational support • Travel advice (e.g. insurance, travel vaccinations, ability, long haul flight, storing medications, drug access) • Pregnancy and family planning • Diet and alcohol • Supplements and CAM (including chiropractice and osteopathy) • Changing GP or other services	
Comparator	• Different formats of information • Different content of information • Timing of provision of information • Delivery setting	
Outcomes	Patient reported outcomes to include: • Usefulness (including accessibility/ comprehension)	

	Details	Additional comments
	• Accuracy • Clinician reported outcomes to include: • Usefulness (including accessibility/comprehension) • Accuracy	
Other criteria for inclusion / exclusion of studies	N/A	
Review strategies	Study quality will be assessed within the GRADE framework and/or the NICE checklist for qualitative studies will be used as appropriate	

	Details	Additional comments
Review question 28	What is the effectiveness of information and education in the management of flare episodes?	
Objectives	To identify how effective information and education may be in the management of flare.	
Type of review	Quantitative review	
Language	English	
Study design	RCT	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	Education/Information for patients: could include • Variation in medication (and safety) • Information on access to flare care e.g. who to contact, advice lines direct to clinical nurse specialists • Information on how to manage flare prior to specialist consultation • When not to consult specialist e.g. not flare • Education/information for clinicians – could include • Distinction between true flare and poorly managed disease (or complications such as fracture) • Assigned specialist (i.e. named nurse) • Awareness of need for rapid specialist referral	Information can include leaflets of flare episodes, who to contact in the event of flare, how to self-manage Education can include structured education on the conditions given by support groups/HCPs etc. to people with SpA
Comparator	• No information • Standard information given to patients • Comparison of the above	
Outcomes	Patient reported outcomes to include: • Usefulness of information in terms of being able to access care or self-management • Number of flare episodes (i.e. poorly controlled disease) • Duration of flare episodes • Number of contacts with HCP • Patient satisfaction	
Other criteria for inclusion / exclusion of studies	Studies which are not RCTs/SRs	
Review strategies	Study quality will be assessed in the GRADE framework	

	Details	Additional comments
Review question 29	What is the usefulness of direct access to specialist care, compared with initial primary care access followed by specialist rheumatological care, in the management of flare episodes?	NB: Be aware that definition of flare may vary across studies/patients/specialists
Objectives	To identify the most appropriate health care professional to access in the event of flare episodes	
Type of review	Quantitative and if necessary qualitative	GDG not aware of any quantitative evidence, but were aware of some applicable ongoing work that may be available by the time re-run searches are undertaken
Language	English	
Study design	For Quantitative review • RCT • Observational intervention For qualitative review • Any qualitative study design	Qualitative to include patient-survey, HCP-survey, focus-groups, interview, thematic analysis, grounded theory, case study
Status	No date restrictions	
Population	People with diagnosed spondyloarthritis	Population should include any people with diagnosed spondyloarthritis, as qualitative work may ask people about previous rather than current flares. The GDG were unaware of any clinical definitions of flare episodes and noted what constitutes a flare episode is specific to individuals
Intervention	Care by health care professional in primary care settings	
Comparator	Care by health care professional in specialist setting	
Outcomes	• Time to care received • Number of contacts with health care professionals • Satisfaction with care received • Health-related quality of life • Resource use and cost • Improvement in severity, duration, frequency of flare episodes	Need to ensure flares are musculoskeletal flares (as opposed to any other comorbidities e.g. uveitis) or have a musculoskeletal component (which may include fatigue) If a patient is recurrently flaring then treatment may be escalated. Be aware that different studies may use different baselines or standards for comparison.
Other criteria for inclusion / exclusion of studies	N/A	
Review strategies	If quantitative studies are identified we will following hierarchy of evidence rules	

	Details	Additional comments
	If no quantitative studies are identified we will use qualitative evidence if identified	

	Details	Additional comments
Review question 30	What is the effectiveness of specialist-led long-term management of spondyloarthritis compared with primary-care-led long-term management?	Review question should focus on the health care professional responsible for long-term care, not the setting or location of care
Objectives	To ascertain if the care of people with spondyloarthritis is best situated in specialist centres or in primary care	
Type of review	Quantitative review	No qualitative but must include patient reported outcomes e.g. ratings
Language	English	
Study design	For Quantitative review RCT Observational intervention	
Status	No date restriction	
Population	People diagnosed with spondyloarthritis	
Intervention	Specialist-led management	
Comparator	Primary-care led management	
Outcomes	• Number of contacts with health care professionals • Number, severity, duration of flare episodes • Resource use and costs • Health-related quality of life • Disease progression • Long term morbidity and extra-articular symptoms and mortality (including but not limited to: uveitis, psoriasis, inflammatory bowel disease, enthesitis, oligoarthritis, site specific inflammation, dactylitis, osteoporosis (and fracture), spinal fractures, spinal cord injuries, blindness, aortic regurgitation, cardiovascular complications, joint replacement) Access to different therapy options (including, but not limited to, drug therapies) Access to specialist therapies (e.g. specialist rheumatology physiotherapy)	High number of contacts may be a positive or negative indicator i.e. it may indicate careful management, or it may indicate person has unstable/poorly managed condition Not all therapies may be accessible to GPs
Other criteria for inclusion / exclusion of studies	Non-interventional study designs	
Review strategies	Study quality will be assessed in the GRADE framework	

	Details	Additional comments
Review question 31	How should the cross-speciality care for people with spondyloarthritis be organised?	There is currently variation in how this is organised See TA on PsA management that recommends cross speciality care between Rheum and Dermatology
Objectives	To establish how cross-speciality care for people with spondyloarthritis should be organised	
Type of review	Prospective observational	
Language	English	
Study design	Observational intervention	
Status	No date restriction	
Population	People with diagnosed spondyloarthritis	Includes all types of spondyloarthritis
Intervention	Cross-speciality care, which could include: • Combined clinics • Cross-speciality referrals • Cross-speciality treatment management • Multiple drug management	Potential for combined clinics may be limited in smaller hospitals Dermatology, ophthalmology, gastroenterology are main specialities that work in conjunction with rheumatology
Comparator	Comparison with interventions listed above	
Outcomes	• Time to appointment • Number of contacts with health care professionals • Health related quality of life • Resource use and costs • Patient satisfaction • Disease burden reduced from both spondyloarthritis and associated conditions • Service delivery/organisation	Health related quality of life will include impact of multiple appointments
Other criteria for inclusion / exclusion of studies	Exclude RCTs	
Review strategies	Study quality will be assessed in the GRADE framework	

	Details	Additional comments
Review question 32	What are the complications associated with spondyloarthritis?	
Objectives	To identify the long-term complications associated with spondyloarthritis so that these can be added to patient information and can be monitored for in any regular patient review and managing the risk where appropriate	
Type of review	Epidemiologic review (descriptive)	We will present the rates of each complication over a defined timeframe
Language	English	
Study design	Cohort studies with a priori defined follow-up time points	GDG made a post-hoc decision after presenting initial review to additionally include studies without a priori defined follow up time points
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis Missed diagnoses (false negatives)	
Complications	• Osteoporosis • Uveitis (Anterior) • Inflammation of the aorta/aortic valve • aortic regurgitation • Psoriasis • Inflammatory bowel disease • Spinal fractures • Spinal cord injuries • Cauda equina syndrome • erectile dysfunction • restrictive pulmonary disease • Ischemic heart disease • Stroke/CVA • Joint replacement • Hyperlipidaemia/metabolic syndrome • Surgery • Major depression • Alcoholism • Hospitalisation for the above or for disease symptoms • Spinal/joint deformity	
Comparator	People with SpA who do not develop the above complications	
Outcomes	Rates of each complication at pre-defined time points	See study design note above
Other criteria for inclusion / exclusion of studies	Follow-up of RCT's will be assessed as cohort studies if they have sufficiently long-follow up. Studies reported undefined time-points (such as median or follow-up) will be excluded	See study design note above

	Details	Additional comments
Review strategies	Study quality will be assessed within the GRADE framework	

	Details	Additional comments
Review question 33	What are the complications associated with the treatments for spondyloarthritis?	
Objectives	To identify the complications associated with the different treatment options for spondyloarthritis so that these can be added to patient information and can be monitored for in any regular patient review and managing the risk of the complications	
Type of review	Epidemiologic review (descriptive)	See RQ32
Language	English	
Study design	Cohort studies with a priori defined follow-up time points	GDG made a post-hoc decision after presenting initial review to additionally include studies without a priori defined follow up time points
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	NSAIDs • Gastritis • Ulcers • Bleeding • Cardiovascular events (potential risk reduction) • Renal • Hypertension Corticosteroids • Cataracts • Diabetes • Osteoporosis • Suppressed adrenal gland hormone production • Thin skin, easy bruising and slower wound healing • Weight gain • (wound) infection • Psychosis • Hypertension Standard DMARDs • Myelosuppression • Renal toxicity • Liver toxicity • Skin rash • Gastrointestinal disturbance • Malignancy • Hypertension • Haematological toxicity Biological DMARDs	Consider whether these complications are condition specific; in other words, would they occur in log-term use of these treatments in any condition, or are some more specific to how these treatments interact with spondyloarthritis Consider apremilast, tofactinib

	Details	Additional comments
	• Infection • Immunosuppression • Malignancy (especially skin) • Demyelination • Progressive Multifocal Leukoencephalopathy • Depression • Skin rash • Uveitis (etanercept only) Intra-articular and soft tissue injections • Infection • Local steroid effect • Skin depigmentation • Fat necrosis • Tendon rupture	
Comparator	People with SpA who do not develop the above complications	
Outcomes	Rates of each complication at pre-defined time points	See study design note above
Other criteria for inclusion / exclusion of studies	Follow-up of RCT's will be assessed as cohort studies if they have sufficiently long-follow up. Studies reported undefined time-points (such as median or follow-up) will be excluded	See study design note above
Review strategies	Study quality will be assessed within the GRADE framework	

	Details	Additional comments
Review question 34	What factors predict clinical improvement after spinal surgery (including osteotomy and fusion) in people with axial inflammation?	
Objectives	To identify the prognostic factors that predict clinical improvement following subsequent spinal surgery in axial inflammation	
Type of review	Prognostic	
Language	English	
Study design	Consecutive case series	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of axial spondyloarthritis	
Intervention	Variables could include • Duration of disease • Duration of delay in diagnosis • Severity of disease • Comorbidities (presence of / type of) • Osteoporosis • Site of surgery (e.g. lumbar may be more successful than cervical) • Indication for surgery (e.g. to fix fracture, to fix deformity, trauma) • Elective/non-elective • Current treatment • Fitness for surgery • Pre-surgical functional status • Type of centre delivering surgery • Occurrence of peri-/post-op complications	GDG indicated an interest in the type of centre delivering surgery, though this may be beyond the scope of this review
Comparator	People with SpA undergoing spinal surgery who are not positive for (some of) the above predictors	
Outcomes	Predictors assessed on: Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value	
Other criteria for inclusion / exclusion of studies	We will exclude case series where it is clear that they are not recruited consecutively	
Review strategies	Prospective consecutive case series are the preferred study type, If none are available we will examine other case series such as retrospective or where it is not clear is cases are consecutively recruited	

	Details	Additional comments
Review question 35	What factors predict clinical improvement after joint replacement surgery?	
Objectives	To identify the prognostic factors that predict clinical improvement after joint replacement	
Type of review	Prognostic	
Language	English	
Study design	Consecutive case series	
Status	No date restriction	
Population	People (aged 16 years and over) with a confirmed diagnosis of spondyloarthritis	
Intervention	Variable could include • Duration of disease • Duration of delay in diagnosis • Severity of disease • Comorbidities (presence of / type of) • Osteoporosis • Site of surgery • Indication for surgery (e.g. to fix fracture, to fix deformity, trauma) • Elective/non-elective • Current treatment • Fitness for surgery • Pre-surgical functional status • Type of implant • Previous joint replacement (same or different joint) • Type of centre delivering surgery • Occurrence of peri-/post-op complications	GDG indicated an interest in the type of centre delivering surgery, though this may be beyond the scope of this review
Comparator	People with SpA undergoing spinal surgery who are not positive for (some of) the above predictors	
Outcomes	Sensitivity Specificity Positive likelihood ratio Negative likelihood ratio Positive predictive value Negative predictive value	GDG to indicate which are more useful in clinical practice
Other criteria for inclusion/ exclusion of studies	We will exclude case series where it is clear that they are not recruited consecutively	
Review strategies	Prospective consecutive case series are the preferred study type, If none are available we will examine other case series such as retrospective or where it is not clear is cases are consecutively recruited	