



British Association for Sexual Health and HIV National Guideline on the Management of Sexually Acquired Reactive Arthritis 2020

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What is new in the 2020 guideline

- Changing incidence of Sexually Acquired Reactive Arthritis (SARA)
- Pathogens that are newly recognised as linked to SARA
- The emerging importance of enteric pathogens that may be acquired sexually
- New treatments for seronegative spondyloarthritis, although their effect on SARA is as yet unknown
- Clear graded recommendations using the GRADE system

Introduction and Methodology

Objectives:

The aim is to reduce the number of sexually transmitted infections (STIs) and, therefore, their complications. Pertinent to this guideline, is to consider STIs in anyone presenting with a suspected reactive arthritis (ReA), particularly if they also have symptoms or signs suggestive of an STI.

1
2 This guideline discusses the aetiology and clinical features of sexually acquired
3 reactive arthritis (SARA), and makes recommendations on the diagnostic tests
4 and treatment for effective management with the aim of improving health
5 outcomes for people with SARA. This will include appropriate partner
6 notification and prevention of onward transmission when an STI is identified.
7

8 The guideline is aimed at those over the age of 16 years, presenting to health
9 care professionals working in sexual health services. The recommendations are
10 primarily aimed at services offering level 3 care in STI management within the
11 United Kingdom. However, the principles will apply to those presenting to level
12 1 and 2 services, and appropriate local referral pathways will need to be
13 developed. The guideline will also be of use to rheumatologists assessing and
14 managing patients presenting with possible SARA. Again local pathways
15 between rheumatology and sexual health services should be available.
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17 18 **Search strategy:**

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20 This guideline was produced according to specifications set out in the CEG
21 document 'Framework for guideline development and assessment' (2015,
22 updated 2019) accessed at
23 [https://www.bashhguidelines.org/media/1229/2015-guidelines-framework-](https://www.bashhguidelines.org/media/1229/2015-guidelines-framework-amended-dec-2019.pdf)
24 [amended-dec-2019.pdf](https://www.bashhguidelines.org/media/1229/2015-guidelines-framework-amended-dec-2019.pdf). It has been updated by reviewing the previous SARA
25 guideline (2008) and medical literature since its publication using abstracts and
26 articles in the English language. Where there was a paucity of randomised
27 control trials and high quality evidence expert judgement was considered.
28

29 Search terms: Reactive arthritis, sexually acquired reactive arthritis, SARA,
30 Reiters, Spondyloarthropathy, Spondyloarthritides, Spondyloarthritis, Infectious
31 arthritis.

32 Sources: OVID, Medline, PubMed, National Institute for Health and Clinical
33 Excellence (NICE), Cochrane Library

34 Guidelines produced by: IUSTI, BASHH, CDC
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37 **Equality impact assessment:**

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39 An assessment of the guideline and its recommendations was undertaken to
40 ensure the principles of equality and diversity were adhered to. See Appendix 1.
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43 **Stakeholder involvement, piloting and feedback:**

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45 The document was reviewed by the Clinical Effectiveness Group of BASHH, and
46 their comments incorporated.
47

1 The draft guideline was placed on the BASHH website and any comments
2 received during the consultation period were reviewed by the authors and acted
3 on appropriately.

4
5 The document was also reviewed by a patient representative, target users and
6 the public panel of BASHH, and their feedback considered by the authors and
7 used to inform the guideline.
8

11 **Aetiology**

12
13 Reactive arthritis is one of the seronegative spondyloarthropathies. It is a sterile
14 inflammation of the synovial membranes, fascia, and tendons triggered by an
15 infection at a distal site. This can be enteric infection with gastro-intestinal
16 pathogens (eg *Salmonella*, *Shigella*, *Campylobacter*), or a sexually transmitted
17 infection (STI), when it is termed sexually acquired reactive arthritis (SARA).
18 Reactive arthritis also encompasses Reiter's syndrome, with its classic triad of
19 arthritis, conjunctivitis, and urethritis, with or without cutaneous manifestations
20 such as keratoderma blenorrhagica or circinate balanitis/vulvitis. The term
21 Reiter's syndrome is no longer used in clinical practice.
22

23 Reactive arthritis must be distinguished from septic arthritis, which has a
24 different aetiology and specific management requirements.
25

26 **Infective pathogens**

27
28 The precise mechanisms linking infective pathogens with SARA are not fully
29 understood, nor is it clear why some individuals develop SARA as a result of an
30 STI and others do not. It is thought that SARA is caused by an immune response
31 to the infective agent, with DNA and/or surface pathogens being identified in the
32 joint material of patients with SARA.¹⁻⁹ *Chlamydia trachomatis* has been shown
33 to exist in an unusual and persistent state in patients with SARA. This aberrant
34 form represses synthesis of the major outer membrane protein (MOMP) and
35 produces heat shock proteins, which contribute to the inflammatory response.<sup>10-
36 12</sup>
37

38 STIs with a link to SARA include:

- 39 • *Chlamydia trachomatis* - this has the strongest association with SARA, and
40 has been identified in up to two thirds of cases. It has been suggested that
41 ocular serovars of *C. trachomatis* (trachoma), rather than genital strains,
42 may be preferentially associated with SARA.¹³ The theory being that in a
43 minority of cases the genital inoculum includes both ocular and genital
44 strains, and that the ocular strains then travel to the joint and are
45 responsible for the development of SARA. However, this is unproven and
46 more work is needed to determine this. There have also been some
47 recent case reports of SARA associated with other chlamydia types,
48 namely lymphogranuloma venereum (LGV).¹⁴ More recently a decline in
49 the incidence of SARA has been observed despite rising *C. trachomatis*

1 diagnoses. This may reflect detection and treatment of the genital
2 infection at early stage or represent a more complex picture than
3 previously thought.¹⁵

- 4 • *Neisseria gonorrhoeae* - associated in up to 16% of cases, and distinct
5 from its role in septic arthritis.¹⁶⁻²⁰
- 6 • *Mycoplasma genitalium* - this is a well-recognised cause of urethritis but
7 has only been identified in the joints in a few cases so its arthritogenic
8 potential is not yet fully known.²¹⁻²³ Similarly, *Ureaplasma urealyticum*
9 has been reported in a few cases of arthritis but a causal role in the
10 development of SARA has not been established.²⁴⁻²⁵
- 11 • Sexual transmission of enteric pathogens triggering SARA have been
12 reported²⁶⁻²⁷ and Shigella outbreaks have been identified in men that are
13 independent of travel history, thus raising the likelihood of sexual
14 transmission.²⁸ Therefore, ReA due to *Shigella* could be acquired through
15 the enteric or sexual route. Whether other enteric pathogens may also
16 have this potential is unclear.
- 17 • There is insufficient evidence to suggest a causal role for other genital
18 tract pathogens and commensals.

21 Risk factors and associations

22
23 SARA is more commonly seen in men, with a ratio of over 10 to 1, although under
24 recognition or a different disease phenotype in women may be a possible
25 explanation.^{16,20,29,30} Possession of the HLA-B27 gene increases susceptibility to
26 SARA and is associated with increased severity of the condition.^{18,30-35}

27
28 ReA has been increasing in incidence in the sub-Saharan HIV positive population,
29 where almost all cases of HIV-associated ReA are HLA-B27-negative, but similar
30 observations have not been documented in Caucasian populations with HIV.³⁶⁻³⁸

31
32 SARA may be associated with other spondyloarthritides, most commonly axial
33 spondyloarthritis, ranging from the non-radiographic form to the established,
34 radiographic subset known as ankylosing spondylitis; sometimes psoriatic
35 arthritis; occasionally inflammatory bowel arthritis; and SAPHO (synovitis, acne,
36 pustulosis, hyperostosis, osteitis).

40 Clinical features

42 History

43
44 It is important to ask about genital and urinary symptoms, joint and other
45 musculoskeletal symptoms and extra-articular features. There may also be a past
46 or family history of spondyloarthritis, iritis, psoriasis, inflammatory bowel
47 disease or SAPHO.^{16,19,29,33,39}

1 It is essential to take a thorough sexual history. There is usually a history of
2 sexual intercourse with a new partner within 3 months of the onset of the
3 arthritis symptoms^{30,32,34} and on average genital symptoms occur 14 days before
4 the arthritis.^{16,19,29,30,32}

6 **Symptoms and signs**

8 Women are more likely than men to be asymptomatic in terms of genital
9 symptoms. However, they may report altered vaginal discharge, pelvic pain,
10 deep dyspareunia, inter-menstrual or post-coital bleeding. Clinical examination
11 may reveal mucopurulent cervicitis, with or without cervical contact bleeding,
12 and/or tenderness on abdominal or bimanual examination.

14 Male genital symptoms include urethral discharge, dysuria and/or testicular
15 pain or swelling. On examination there may be visible urethral discharge,
16 testicular pain and/or swelling.^{19,20,30,34,40}

18 Depending on the sexual history, STIs at extra-genital sites may produce rectal
19 discharge, bleeding, discomfort and tenesmus. However rectal infection may be
20 asymptomatic, and pharyngeal infections frequently are. Rectal discharge,
21 bleeding and/or inflammation may be visible on proctoscopy examination in the
22 presence of a rectal STI.

24 The arthritis is inflammatory in nature, with joint pain, often at night, possible
25 swelling, and early morning stiffness. Peripheral joint involvement typically
26 occurs as an asymmetrical arthritis, typically an oligoarthritis, primarily
27 involving the lower limbs - knees, ankles and feet.^{19,29-31,33,41}

29 Other musculoskeletal symptoms include pain or difficulty on walking due to
30 enthesitis and/or plantar fasciitis (20-40%),^{16,18,20,29,30,41} painful movements due
31 tenosynovitis (30%), fusiform swelling of a finger or toe with dactylitis
32 (16%),^{29,30,41} and lower back pain and stiffness if sacro-iliitis is present in an
33 acute episode (10%).^{16,18-20,30,31,41-43}

35 Examination of the articular system may reveal multiple swollen joints, with pain
36 on active or passive movement. Specific entheses to examine are the Achilles
37 tendon and plantar fascial attachments to the calcaneum.^{16,18,20,29,30,33} In the
38 presence of enthesopathy there may be tenderness with or without swelling.
39 Tenosynovitis may produce crepitus on movement over tendon sheaths,^{29,30} with
40 associated tenderness and or swelling. Tenderness on direct sacral pressure
41 may indicate sacro-iliitis,^{16,18,20,29,30} though can also be present with lumbosacral
42 disc disease and other pathologies.

44 Irritable and red eyes with photophobia may occur with conjunctivitis (20-50%)
45 or iritis (2-11%), and less commonly disturbance of visual acuity and ocular pain
46 with uveitis. Any individual with eye symptoms should undergo formal slit-lamp
47 examination to identify iritis, corneal ulceration, keratitis, intra-ocular
48 haemorrhage, optic neuritis, and posterior uveitis. These are all rare but
49 reported manifestations.^{16,18-20,29,30,33,43}

1
2 Circinate balanitis or vulvitis are present in 14-40% of patients.^{16,18,20,29,30,35,43}
3 Extra-genital muco-cutaneous features include psoriasiform eruptions (12%),¹⁹
4 keratoderma blennorrhagica (5-33%)^{16,18-20,29,30,33,35,43} and nail dystrophy (6-
5 12%).^{19,43} Inspection of the oral cavity may reveal oral ulceration or
6 geographical tongue which are both reported in a minority of cases.⁴³
7

8 Other rare extra-articular features which may have few or no symptoms or signs:

- 9 • Cardiovascular: tachycardia, left ventricular dilatation, aortic valve
10 disease, cardiac conduction delays^{18-20,29,35,44}
- 11 • Renal: proteinuria, microscopic haematuria, aseptic pyuria,
12 glomerulonephritis^{31,45}
- 13 • Others: cranial nerve palsies, meningoencephalitis, thrombophlebitis of
14 the lower limbs, subcutaneous nodules.^{16,19,20,29}

15
16 Non-specific systemic symptoms of malaise, fatigue, weight loss, and fever are
17 seen in some patients.^{30,41,42}
18
19
20

21 **Diagnosis**

22
23 The diagnosis of SARA is based on clinical findings - namely typical features of
24 spondyloarthritis with a sexually transmitted genital infection. There are no
25 specific diagnostic criteria.
26

27 All patients should be offered screening for STIs (Grade 1A), as per BASHH
28 guidelines⁴⁶ and as follows:
29

30 Male genital samples:

- 31 • Urine NAAT for *C. trachomatis* and *N. gonorrhoeae*
- 32 • Urethral gram stained smear (if urethral symptoms)
- 33 • Urethral culture and sensitivity testing for *N. gonorrhoeae*

34
35 Female genital samples:

- 36 • Vulvovaginal NAAT for *C. trachomatis* and *N. gonorrhoeae*
- 37 • Endocervical culture and sensitivity testing for *N. gonorrhoeae* (if
38 microscopy or NAAT positive)

39
40 Genital samples in trans people:

- 41 • Urine NAAT for *C. trachomatis* and *N. gonorrhoeae* in all patients
- 42 • If the patient has a vagina (including post genital reconstruction
43 surgery) and is using it for sex, vulvovaginal NAAT for *C. trachomatis*
44 and *N. gonorrhoeae*
- 45 • Urethral and/or endocervical gram stained smear and culture for *N.*
46 *gonorrhoeae* as appropriate (depending on symptoms, genital
47 configuration and any reconstructive surgery)

- 1 • More details on STI screening in trans people are available from the
2 BASHH guideline at [https://www.bashh.org/media/4400/bashh-](https://www.bashh.org/media/4400/bashh-recommendations-for-integrated-sexual-health-services-for-trans-including-non-binary-people-2019pdf.pdf)
3 [recommendations-for-integrated-sexual-health-services-for-trans-](https://www.bashh.org/media/4400/bashh-recommendations-for-integrated-sexual-health-services-for-trans-including-non-binary-people-2019pdf.pdf)
4 [including-non-binary-people-2019pdf.pdf](https://www.bashh.org/media/4400/bashh-recommendations-for-integrated-sexual-health-services-for-trans-including-non-binary-people-2019pdf.pdf)
5

6 Samples in both men and women:

- 7 • Pharyngeal and rectal NAAT samples for *C. trachomatis* and *N.*
8 *gonorrhoeae* where indicated by the sexual history.
9 • Screening for HIV and syphilis
10 • Screening for hepatitis B and C based on risk factors in the sexual
11 history
12 • Consider *M. genitalium* NAAT (urine in men/vulvovaginal sample in
13 women)
14

15 The following are also useful initial investigations:

- 16 • Acute phase response - erythrocyte sedimentation rate (ESR), C-
17 reactive protein (CRP) or plasma viscosity (PLV)
18 • Full blood count (FBC)
19 • Urinalysis
20

21 Further investigations

22

23 The following tests may be useful in some situations, but are not necessarily
24 always required. Close liaison with relevant pathology departments is advisable
25 to ensure that the correct samples are obtained.
26

27 Biochemistry:

- 28 • Liver and kidney function tests
29

30 Microbiology:

- 31 • Blood cultures
32 • Stool culture
33 • Synovial fluid aspirate for cell count, gram stain crystals and culture (to
34 exclude septic arthritis and gout)

35 Radiology

- 36 • X-rays of affected joints
37 • Ultrasonography of affected joints or entheses
38 • Magnetic resonance imaging of sacro-iliac joints

39 Others:

- 40 • HLA-B27
41 • Electrocardiogram (ECG)
42 • Echocardiogram
43 • Synovial biopsy
44 • Exclusion tests for other rheumatological diseases
45 Rheumatoid factor (rheumatoid arthritis)
46 Autoantibodies (systemic lupus erythematosus)
47 Plasma urate (gout)
48 Chest x-ray and serum angiotensin-converting enzyme level
 (sarcoidosis)

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Management

General advice

In the majority of cases SARA may be self-limiting and the principles of management reflect this. However, this is not always the case. Patients should receive a detailed explanation of their condition and the likely prognosis. This should be supported by appropriate written information and online resources. Patient information leaflets are available via the BASHH website.

As with all sexually transmitted infections, patients should be advised to abstain from all sexual contact until they and their partner(s) have completed treatment and follow up.

Patients should be advised to avoid potentially 'triggering infections' in the future, either urogenital or enteric, to avoid a new flare of SARA. Therefore, safer sexual practice should be discussed and the importance of food hygiene stressed.³¹

Close liaison between relevant specialists, depending on the clinical features, is advised. This may include GUM physicians, rheumatologists, dermatologists, ophthalmologists and microbiologists.

Treatment

Therapy is directed at the distinct elements of the condition with specialist advice being obtained depending on the individual's symptoms and signs.

All patients with eye symptoms should be urgently referred for specialist ophthalmological advice.

In those cases where significant peripheral joint or spinal joint symptoms are present, prompt liaison with the rheumatologists and/or a referral to an Early Arthritis Clinic is recommended.

Recommended and Alternative regimens

Antibiotics

- Antimicrobial therapy for any genital infection identified is essential and should be as in uncomplicated infection, as directed by relevant infection guidelines.⁴⁷⁻⁴⁹
- Whether short course antibiotic treatment for the acute genital infection influences the non-genital aspects of SARA is controversial. It may reduce the risk of recurrent arthritis developing in individuals

1 with a history of ReA but is unlikely to affect the arthritis once it is
2 manifest.^{30,41,43,50,51} (Grade IB)

- 3 • Longer course antibiotic therapy for joint symptoms has been
4 considered as some have anti-collagenolytic properties.⁵² Many
5 studies had small numbers of individuals with SARA and mostly the
6 antibiotic therapy had been commenced after the arthritis had become
7 established. Conflicting results have been obtained, with various
8 antibiotic regimens including combination antibiotic therapy.⁵³⁻⁶⁴
9 Similarly, the effect of antibiotic therapy on the late prognosis of
10 arthritis has not been confirmed.^{65,66} The role of longer term
11 antimicrobial therapy in SARA has not been proven and is therefore
12 not recommended.^{33,41,53-60,62-70} (Grade 1C)

13 14 Physical therapy

- 15 • Rest is helpful for constitutional symptoms, enthesitis and arthritis,
16 particularly in weight bearing joints and tendons where restriction of
17 activity is part of first-line treatment.
18 • Physiotherapy should be used, as necessary, to prevent muscle wasting
19 and, when symptoms improve, to strengthen muscles and improve the
20 range of movement in the affected joints and tendons. Physiotherapy
21 and exercise are particularly important where there is axial
22 involvement.^{11,33,69,71-74} (Grade 1D)
23 • Cold pads may be used to alleviate joint pain and oedema,⁷²⁻⁷⁴ and
24 ultrasound³³ and orthotics with insoles, cushioning and heel supports
25 may help with enthesitis.^{11,33} (Grade 1D)

26 27 Non-Steroidal Anti-inflammatory drugs (NSAIDs)

- 28 • NSAIDs are well established as the main stay of therapeutic
29 management for many inflammatory arthritides. It is important that
30 they are used regularly for the maximum anti-inflammatory benefit.
31 No specific NSAID has benefits over others in these circumstances, and
32 individual responses will vary.^{31,33,35,41,71-78} (Grade 1B)
33 • NSAIDs may also be useful for associated constitutional symptoms and
34 oral or topical options exist for symptoms of enthesitis^{11,31,33,79} (Grade
35 1D)
36 • Potential side effects of NSAIDs should be considered – namely
37 gastrointestinal, renal and cardiovascular. NSAIDs should be given for
38 the shortest possible time period, particularly in those with other
39 underlying risks factors for toxicity.^{33,71,75,79-81} (Grade 1A)
40 • For individuals at high risk of gastrointestinal bleeding, a cyclo-
41 oxygenase (COX)-2 selective drug should be used. (Grade 1A)
42 Risk factors for gastrointestinal bleeding include previous history of
43 the same, age over 65 years, male gender, cigarette smoking, excessive
44 alcohol intake, concomitant oral glucocorticoids, antiplatelet agents
45 and anticoagulants.⁷⁵ Gastro-protective agents such as proton pump
46 inhibitors or histamine-2 receptor blockers can reduce the
47 gastrointestinal risks.
48 • COX-2 selective drugs have been linked with increased cardiovascular
49 risk independent of baseline cardiovascular risk factors.⁸² The greatest

1 risk may be with high doses taken long-term and in those with multiple
2 risk factors for cardiovascular or cerebrovascular disease. Naproxen
3 appears to have the best cardiovascular safety profile.^{75, 83-85}
4

5 Corticosteroids

- 6 • For single troublesome joints, intra-articular corticosteroid injections
7 are especially valuable. There are no randomised placebo-controlled
8 trials (RPCTs) of their use in SARA.^{31,33,35,41,71,72,74,79,86-89} ((Grade 1C)
- 9 • Local corticosteroid injections can be used for enthesitis, although
10 should be used judiciously at weight-bearing sites.^{11,31,41,74,87,88} (Grade
11 2C)
- 12 • Topical corticosteroid preparations can be used for cutaneous or
13 mucosal lesions. Low potency options are preferable for mucosal
14 lesions.^{9,30} (Grade 1C) Alternative options for mild to moderate lesions
15 include topical salicylic acid ointments, vitamin D3 analogues such as
16 calcitriol,⁹⁰ (Grade 1C) and for more severe lesions retinoids such as
17 acitretin.^{31,35,91} (Grade 1C)
- 18 • Topical corticosteroid eye drops, or oral corticosteroids, and
19 mydriatics are used to treat uveitis. Posterior uveitis usually requires
20 more aggressive therapy.³¹ All patients with eye symptoms should
21 have a slit lamp examination and be managed with specialist
22 ophthalmological advice. (Grade 1A)
- 23 • Systemic corticosteroids may be valuable where there are several
24 joints involved, or where severe constitutional symptoms arise. They
25 can be given orally, as a single intramuscular injection, or occasionally
26 as an intravenous bolus. There are no RPCTs of use of corticosteroids
27 in SARA, but they have been demonstrated to reduce inflammation in
28 rheumatoid arthritis.^{31,33,71,72} (Grade 2D) If systemic corticosteroids are
29 used consideration should be given to osteoporosis prophylaxis,
30 although this is unlikely to be required if a short course or single
31 injection is used.⁹²⁻⁹⁴
32

33 Disease Modifying Anti-Rheumatic Drugs (DMARDs)

- 34 • These are indicated where there are disabling joint symptoms that
35 have persisted for over 3 months, earlier where there is severe disease,
36 or where erosive joint damage is identified.
- 37 • Sulphasalazine has been shown to reduce the severity and duration of
38 peripheral joint synovitis, although it may not influence long term
39 recovery. There may also be some benefits in early sacroilitis but not
40 in established ankylosing spondylitis. High doses of 3g daily are
41 associated with significant toxicity, particularly gastrointestinal,
42 whereas 2g daily appears to be equally effective and better tolerated.
43 The dose of sulphasalazine should be titrated upwards until an
44 effective dose is reached.^{31,35,72,79,95-99} (Grade 1B)
- 45 • Methotrexate is favoured by many physicians because of the ease of
46 weekly oral administration and the favourable responses seen in
47 rheumatoid disease and psoriatic arthritis. The main effect of
48 methotrexate is seen in the peripheral joints and entheses. It may be
49 helpful with severe mucous membrane and skin lesions, although its

1 side effects also include mouth ulceration and gastro-intestinal
2 intolerance. There is no proven efficacy of methotrexate in the
3 treatment of axial or spinal joint disease. In addition, there are no
4 published RPCTs of its use in SARA. Doses range from 7.5-15mg orally
5 as a single weekly dose. This can be increased to 25mg orally in
6 resistant arthritis. It may also be given as an intramuscular
7 preparation. It is important to give oral folic acid, usually as a single 5-
8 15 mg dose weekly, at 24 hours following the methotrexate dose.
9 31,35,71-73,79,91 (Grade 1B)

10 Biologic agents

- 12 • Tumour necrosis factor (TNF) alpha blockers, of which there are a
13 number, are highly effective in the treatment of rheumatoid
14 arthritis,^{81,100-103} ankylosing spondylitis,^{11,69,81,103-109} psoriatic
15 arthritis^{11,69,81,103,104,107,109-112} and skin lesions,^{69,103,107,109-112} other
16 spondyloarthritides,^{79,107,113,114} and related enthesitis.^{109,111} They have
17 also been reported to reduce the frequency of episodes of uveitis when
18 treating ankylosing spondylitis.^{31,103,107,109,115-118}
- 19 • There are side effects with TNF alpha blockers including infusion
20 reactions; an increased risk of infection, including tuberculosis;
21 development of autoantibodies; systemic lupus erythematosus and
22 vasculitis; demyelinating disease; and worsening congestive cardiac
23 failure. There is no proven risk for solid cancer and lymphoma
24 development but caution is necessary for cutaneous malignancies and
25 frequent skin examination is required.^{79,103,105,107,119,120}
- 26 • Experience of the use of biological agents in the treatment of ReA,
27 including SARA, is limited and no large or controlled studies are
28 available. Early reports are encouraging and it does not appear that
29 they re-activate the infective trigger in patients with ReA.^{31,121}
30 However, the place of such therapy in SARA is not yet
31 established.^{11,33,35,79,107,122-129} (Grade 2C)
- 32 • New treatments for seronegative spondyloarthritis including axial
33 spondyloarthritis and psoriatic arthritis include IL-17A inhibitors^{130, 131}
34 and JAK inhibitors¹³² have shown effectiveness in rheumatoid arthritis.
35 No data are currently available on their potential effect in SARA.

36 Rare treatments

37 Medical synovectomy

- 38 • Procedures involving Yttrium-90, Osmic acid, Samarium-153 or
39 Rhenium-186 have shown short term benefit in symptomatic chronic
40 single joint synovitis, but their advantage over intra-articular
41 corticosteroids has not been confirmed.¹³³ (Grade 2D)

42 Radiotherapy

- 43 • This is exceptionally used for severe, disabling heel pain from
44 enthesitis.¹¹ (Grade 2D)

45 Surgery

- 46 • In certain circumstances surgical procedures such as synovectomy and
47 arthroplasty may be valuable. It has been suggested that a 3 month
48 course of azithromycin be given alongside the synovectomy, but this
49

1 trial did not include a placebo arm so benefit can not be confirmed.^{72,134}
2 (Grade 2D)

3 Low dose TCAs

- 4 • Severe post-inflammatory pain and fatigue can be treated with low
5 dose tricyclic drugs such as amitriptyline 10-25mg nocte. (Grade 2D)

7 **Pregnancy and breast feeding**

- 9 • Many drugs are not licensed in pregnancy or during breastfeeding, and
10 should be avoided unless the potential benefit outweighs the risk.
- 11 • Recommended and alternative treatment regimens for individual STIs
12 in pregnancy can be found in the relevant STI guidelines on the BASHH
13 website (www.bashh.org/guidelines)
- 14 • NSAIDs have the potential to cause reversible sub-fertility by the
15 leuteinised unruptured ovarian follicle syndrome.¹³⁵ If used regularly
16 during pregnancy, particularly in the third trimester, they may result in
17 premature closure of the foetal ductus arteriosus, oligohydramnios,
18 delayed onset and increased duration of labour.^{136,137} Advice on
19 breastfeeding depends on the specific NSAID being used.¹³⁸
- 20 • Prolonged use of corticosteroids carries a risk of intrauterine growth
21 restriction and fetal adrenal suppression. Systemic effects to the baby
22 from breastfeeding are unlikely unless the mother is taking more than
23 40mg of prednisolone (or equivalent) a day. With higher doses,
24 appropriate monitoring of infant adrenal function is recommended.¹³⁷
25 (Grade 1A)
- 26 • Sulphasalazine carries a theoretical risk of neonatal haemolysis in the
27 third trimester so should be used with caution in pregnancy and during
28 breastfeeding, and with maternal folate supplementation.¹³⁷ (Grade
29 1A)
- 30 • Methotrexate and retinoids are both teratogenic and therefore
31 contraindicated in pregnancy and breastfeeding. Men should also avoid
32 conception in their female partners for at least 3 months after
33 methotrexate use. Women taking retinoids should be advised about
34 use of effective contraception for 1 month before, during, and for 3
35 years after any retinoid therapy.¹³⁷ (Grade 1A)
- 36 • TNF blockers and other biologic therapies should only be used under
37 advice of the appropriate specialist as advice varies depending on the
38 specific medication.¹³⁸

40 **In HIV positive individuals**

- 41 • There is no evidence to suggest that treatments should be any different
42 in HIV positive individuals. Drug interactions and overlapping
43 toxicities with antiretrovirals should be considered. ([www.hiv-
44 druginteraction.org/checker](http://www.hiv-druginteraction.org/checker))

47 **Reactions to treatment**

- There are many treatment options described in this guideline with key side effects highlighted. However, we recommend referring to the British National Formulary (BNF) (<https://www.medicinescomplete.com>) or Summary of Product Characteristics (SPC) for full details and to check on interactions with other concomitant medications.

10 Follow up

11 Follow up for specific STIs should be as for uncomplicated infections. In certain cases this will include follow up for test of cure, or repeat screening. See BASHH STI guidelines for further information (www.bashh.org/guidelines).

12 Follow up may be useful to confirm adherence to treatment, and clarify the risk of reinfection. Where a test of cure is not required, this follow up could be done over the telephone.

13 Follow up for extra-genital features should be under the guidance of the relevant specialist.

14 SARA is a self-limiting disease in the majority of individuals, with mean duration of symptoms of 4-6 months. However, 50% of patients may experience recurrent episodes at variable time intervals, particularly those individuals who are HLA-B27 positive, which is a recognised predictor of disease chronicity and severity in spondyloarthritis.^{16,18,19,29,30,33,35,39,41,43,104, 139}

15 Up to 17% will develop chronic symptoms lasting over 12 months,²⁹ and 15% will experience persistent locomotor disability. The latter is principally due to erosive joint damage and resultant deformity.^{18,39}

16 Ocular involvement with uveitis may lead to cataracts and rapid loss of vision in a minority,^{18-20,39} hence the need for expert ophthalmological input.

38 Contact tracing and treatment

39 Contact tracing for specific STIs should be performed according to BASHH guidelines (www.bashh.org/guidelines), with reference to look back periods. Patients should be informed of the importance of partner notification, and supported to do this by appropriately trained professionals.

40 Patients who present as a sexual contact of a known STI should be offered epidemiological treatment, and screening for all STIs.

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Auditable outcomes

- Proportion of patients with clinical diagnosis of SARA tested for sexually transmitted infections (chlamydia, gonorrhoea, HIV and syphilis as a minimum). Performance standard 97%
- Proportion of patients treated with recommended regimen for confirmed STI. Performance standard 97%
- Proportion of patients offered information (written or digital) about their diagnosis and management. Performance standard 97%

Recommendations for further research

Investigation of the significance of *M.genitalium* and SARA.

Elucidation of the current frequency and type of *C. trachomatis* and *N. gonorrhoeae* in synovial fluid of individuals with SARA.

A protocol for a Cochrane systematic review has been established to evaluate this contentious area and this needs to be progressed.¹⁴⁰

Qualifying statement

Decisions to follow these recommendations must be based on professional clinical judgement, consideration of individual patient circumstances and available resources.

All possible care has been undertaken to ensure specification of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

Review arrangements

An author group will be invited by the BASHH CEG to review and revise the guideline in 2025 using the BASHH framework for guideline development. However, addenda may be issued sooner than 2025, particularly if relevant new data are available relating to testing or treatment options.

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2

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5

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8

9 **Editorial independence**

10 This guideline was commissioned, edited and endorsed by the BASHH CEG
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12

13 All members of the guideline writing committee completed the BASHH conflict of
14 interest declaration detailed below at the time the guideline's final draft was
15 submitted to the CEG.

16

17 **Conflict of interest**

18

19 All members of the guideline writing committee completed the BASHH conflict of
20 interest declaration form at the time the guideline's final draft was submitted to
21 the CEG. No authors have any conflicts of interest to declare and the content of
22 the guideline is not attributed to any organisation they are associated with.

23

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25 **Membership of the Clinical Effectiveness Group**

26

27 Current membership of the BASHH Clinical effectiveness group is available at

28 <https://www.bashh.org/guidelines>

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1 **References**

- 2
- 3 1. Schumacher HR Jr, Magge S, Cherian PV, Sleckman J, Rothfuss S,
4 Clayburne G et al. Light and electron microscopic studies on the
5 synovial membrane in Reiter's syndrome: immunocytochemical
6 identification of chlamydial antigen in patients with early disease.
7 Arthr Rheum 1988; 31: 937-46.
- 8 2. Taylor-Robinson D, Gilroy CB, Thomas BJ, Keat ACS. Detection of
9 Chlamydia trachomatis DNA in joints of reactive arthritis patients by
10 polymerase chain reaction. Lancet 1992; 340: 81-2.
- 11 3. Rahman MU, Cheema MA, Schumacher HR, Hudson AP. Molecular
12 evidence for the presence of chlamydia in the synovium of patients
13 with Reiter's syndrome. Arthr Rheum 1992; 35: 521-9.
- 14 4. Bas S, Griffais R, Kvein TK, Glennås A, Melby K, Vischer TL.
15 Amplification of plasmid and chromosome chlamydia DNA in synovial
16 fluid of patients with reactive arthritis and undifferentiated
17 seronegative oligoarthropathies. Arthr Rheum 1995; 38: 1005-13.
- 18 5. Branigan PJ, Gérard HC, Hudson AP, Schumacher HR Jr. Comparison of
19 synovial tissue and synovial fluid as the source of nucleic acids for
20 detection of Chlamydia trachomatis by polymerase chain reaction.
21 Arthr Rheum 1996; 39: 1740-6.
- 22 6. Li F, Bulbul R, Schumacher HR Jr, Keiber-Emmons T, Callegari PE, Von
23 Feldt JM et al. Molecular detection of bacterial DNA in venereal-
24 associated arthritis. Arthr Rheum 1996; 39: 950-8.
- 25 7. Nikkari S, Puolakkainen M, Yli-Kerttula U, Luukkainen R, Lehtonen O-P,
26 Toivanen P. Ligase chain reaction in detection of chlamydia DNA in
27 synovial fluid cells. Br J Rheumatol 1997; 36: 763-5.
- 28 8. Vittecoq O, Schaefferbeke T, Favre S, Daragon A, Biga N, Cambon-
29 Michot C et al. Molecular diagnosis of Ureaplasma urealyticum in an
30 immunocompetent patient with destructive reactive polyarthritis.
31 Arthr Rheum 1997; 40: 2084-9.
- 32 9. Tully JG, Rose DL, Baseman JB, Dallo SF, Lazzell AL, Davis CP.
33 Mycoplasma pneumoniae and Mycoplasma genitalium mixture in
34 synovial fluid isolate. J ClinMicrobiol 1995; 33: 1851-5.
- 35 10. Gérard HC, Branigan PJ, Schumacher HR Jnr, Hudson AP. Synovial
36 *Chlamydia trachomatis* in patients with reactive arthritis/Reiter's
37 syndrome are viable but show aberrant gene expression. J Rheumatol
38 1998;25:734-42.
- 39 11. Rihl M, Klos A, Köhler L, Kuipers JG. Reactive arthritis. Best Practice &
40 Research Clinical Rheumatology 2006; 20: 1119-37.
- 41 12. Gerard HC, Whittum-Hudson JA, Carter JD, Hudson AP. The pathogenic
42 role of Chlamydia in spondyloarthritis. Curr Opin Rheumatol
43 2010;22:363-7.
- 44 13. Gerard HC, Stanich JA, Whittum-Hudson JA, Schumacher HR, Carter JC,
45 Hudson AP. Patients with Chlamydia-associated arthritis have ocular

- 1 (trachoma), not genital, serovars of *C trachomatis* in synovial tissue.
2 Microb Pathog 2010;**48**:62-68.
- 3 14. Perry M, White J. Three cases of Reactive Arthritis Secondary to
4 Lymphogranuloma Venereum. Journal of Clinical Rheumatology 2015;
5 21(1): 33-34 LGV.
- 6 15. Mason E, Wray L, Foster R, Jamil MS, Guy R, McNulty A et al. Reactive
7 arthritis et al. Sydney Sexual health Centre 1992-2012: declining
8 despite increasing chlamydia diagnosis. Int J STD & AIDS 2015;**27**:882-
9 889.
- 10 16. Csonka GW. The course of Reiter's Syndrome. Br Med J 1958; 1: 1088-
11 1090.
- 12 17. Rosenthal L, Olhagen B, Ek S. Aseptic arthritis after gonorrhoea. Ann
13 Rheum Dis 1980; 39: 141-6.
- 14 18. Leirisalo M, Skylv G, Kousa M, Voipio-Pulkki L-M, Suoranta H, Nissilä M
15 et al. Follow-up study on patients with Reiter's disease and reactive
16 arthritis with special reference to HLA-B27. Arthr Rheum 1982; 25:
17 249-59.
- 18 19. Kousa M. Clinical observations on Reiter's disease with special
19 reference to the venereal and non-venereal aetiology. Acta Derm
20 Venereol 1978; 58 Suppl S1: 5-36.
- 21 20. Csonka GW. Clinical aspects of Reiter's syndrome. Ann Rheum Dis
22 1979; 38 Suppl: 4-7.
- 23 21. Taylor-Robinson D and Keat A. Observations on *Chlamydia trachomatis*
24 and other microbes in reactive arthritis. It J STD AIDS 2015; 26(3):
25 139-144.
- 26 22. Horner PJ, Martin DH. Mycoplasma genitalium infection in men. J Infect
27 Dis 2017;**216**:S396-S405.
- 28 23. Taylor-Robinson D, Gilroy C, Horowitz S et al. *Mycoplasma genitalium*
29 in the joints of two patients with arthritis. Eur J Clin Microbiol Infec
30 Dis; 13(12): 1066-1069.
- 31 24. Schaeffer T, Renaudin H, Vernhes JP, de Barbeyrac B, Bannwarth B,
32 Bébéar C et al. Ureaplasma urealyticum and reactive arthritis. Clin
33 Rheumatol 1995; 14: 252.
- 34 25. Horowitz S, Horowitz J, Taylor-Robinson D, Sukenik S, Apte RN, Bar-
35 David J et al. Ureaplasma urealyticum in Reiter's syndrome. J
36 Rheumatol 1994; 21: 877-82.
- 37 26. Kennedy S, Murira J, Wenham C. A case of reactive arthritis secondary
38 to sexually acquired *Shigella flexneri*. Oxford Medical Case Reports
39 2017; 11: 210-211.
- 40 27. Chen M, Delpech V, O'Sullivan B et al. *Shigella sonnei*: another cause of
41 sexually acquired reactive arthritis. Int J STD AIDS 2002; 13(2) 135-
42 136.
- 43 28. Public Health England. Laboratory surveillance of non-travel
44 associated *Shigella* spp. infection in adult males, England: 2004 to
45 2017. Health Protection Report 2017; 11(42). Available at

1 [https://assets.publishing.service.gov.uk/government/uploads/system](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/662498/hpr4217_shgll-nntrvl.pdf)
2 [/uploads/attachment_data/file/662498/hpr4217_shgll-nntrvl.pdf](https://assets.publishing.service.gov.uk/government/uploads/attachment_data/file/662498/hpr4217_shgll-nntrvl.pdf)

- 3 29. Keat A. Reiter's syndrome and reactive arthritis in perspective. *N Engl*
4 *J Med* 1983;309:1606-15.
- 5 30. Keat AC, Maini RN, Pegrum GD, Scott JT. The clinical features and HLA
6 associations of reactive arthritis associated with non-gonococcal
7 urethritis. *QJM* 1979;48:323-42.
- 8 31. Leirisalo-Repo M, Repo H. Reactive arthritis: clinical features and
9 treatment in: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME,
10 Weisman MH (eds). *Rheumatology* 5th ed. Mosby Elsevier,
11 Philadelphia 2011. Section 8: Infection-related rheumatic diseases;
12 110: 1113-20.
- 13 32. Keat AC, Maini RN, Nkwazi GC et al. Role of *Chlamydia trachomatis* and
14 HLA-B27 in sexually acquired reactive arthritis. *Br Med J* 1978;1:605-
15 607.
- 16 33. Hamdulay SS, Glynne SJ, Keat A. When is arthritis reactive? *Postgrad*
17 *Med J* 2006; 82: 446-53.
- 18 34. Martin DH, Pollock S, Kuo C-C, Wang S-P, Brunham RC, Holmes KK.
19 *Chlamydia trachomatis* infections in men with Reiter's syndrome. *Ann*
20 *Intern Med* 1984;100:207-13.
- 21 35. Colmegna I, Cuchacovich R, Espinoza LR. HLA-B27-associated reactive
22 arthritis: pathogenetic and clinical considerations. *ClinMicrobiol Rev*
23 2004;17:348-69.
- 24 36. Stein CM, Davis P. Arthritis associated with HIV infection in Zimbabwe.
25 *J Rheumatol* 1996; 23: 506-511.
- 26 37. Clark MR, Solinger AM, Hochberg MC. Human immunodeficiency virus
27 infection is not associated with Reiter's syndrome. Data from three
28 large cohort studies. *Rheum Dis Clin North Am* 1992; 18: 267-276.
- 29 38. Adizie T, Moots RJ, Hodkinson B, French N, Adebajo AO. Inflammatory
30 arthritis in HIV positive patients: A practical guide. *BMC Infectious*
31 *Diseases* 2016; 16: 100.
- 32 39. Csonka GW. Long-term follow-up and prognosis of Reiter's syndrome.
33 *Ann Rheum Dis* 1979;38 Suppl:24-8.
- 34 40. Kousa M, Saikku P, Richmond S, Lassus A. Frequent association of
35 chlamydial infection with Reiter's syndrome. *Sex Transm Dis*
36 1978;5:57-61.
- 37 41. Flores D, Marquez J, Garza M, Espinoza LR. Reactive arthritis: newer
38 developments. *Rheum Dis Clin N Am* 2003;29:37-59.
- 39 42. Good AE. Reiter's syndrome: long-term follow-up in relation to
40 development of ankylosing spondylitis. *Ann Rheum Dis* 1979;38
41 Suppl:39-45.
- 42 43. Popert AJ, Gill AJ, Laird SM. A prospective study of Reiter's syndrome.
43 An interim report on the first 82 cases. *Br J Vener Dis* 1964;40:160-5.
- 44 44. Hannu T, Nieminen MS, Swan H, Leirisalo-Repo M. Cardiac findings of
45 reactive arthritis: an observational echocardiographic study.
46 *RheumatolInt* 2002;21:169-72.

- 1 45. Konttinen YT, Bergroth V, Nordström D, Tallgren LG, von Bonsdorff M,
2 Santavirta S. IgA nephropathy in reactive arthritis. *J Rheumatol*
3 1987;14:1070-1.
- 4 46. <https://www.bashh.org/guidelines>
5 47. <http://www.iusti.org/regions/Europe/euroguidelines.htm>
6 48. <http://www.bashh.org/guidelines>
7 49. <http://www.cdc.gov/std/>
- 8 50. Frydén A, Bengtsson A, Foberg U, Svenungsson B, Castor B, Kärnell A et
9 al. Early antibiotic treatment of reactive arthritis associated with
10 enteric infections: clinical and serological study. *Br Med J*
11 1990;301:1299-1302.
- 12 51. Bardin T, Enel C, Cornelis F, Salski C, Jorgensen C, Ward R et al.
13 Antibiotic treatment of venereal disease and Reiter's syndrome in a
14 Greenland population. *Arthr Rheum* 1992;35:190-4.
- 15 52. Nordström D, Lindy O, Lauhio A, Sorsa T, Santavirta S, Konttinen YT.
16 Anti-collagenolytic mechanism of action of doxycycline treatment in
17 rheumatoid arthritis. *RheumatolInt* 1998;17:175-80.
- 18 53. Lauhio A, Leirisalo-Repo M, Lähdevirta J, Saikku P, Repo H. Double-
19 blind, placebo-controlled study of three-month treatment with
20 lymecycline in reactive arthritis, with special reference to chlamydia
21 arthritis. *Arthr Rheum* 1991;34:6-14.
- 22 54. Sieper J, Fendler C, Laitka S, Sörensen H, Gripenberg-Lerche C, Hiepe F
23 et al. No benefit of long-term ciprofloxacin treatment in patients with
24 reactive arthritis and undifferentiated oligoarthritis: a three-month,
25 multicenter, double-blind, randomized, placebo-controlled study.
26 *Arthr Rheum* 1999;42:1386-96.
- 27 55. Yli-Kerttula T, Luukkainen R, Yli-Kerttula U et al. Effect of a three
28 month course of ciprofloxacin on the outcome of reactive arthritis. *Ann*
29 *Rheum Dis* 2000;59:565-70.
- 30 56. Kvien TK, Gaston JSH, Bardin T, Butrimiene I, Dijkmans BAC, Leirisalo-
31 Repo M et al. Three month treatment of reactive arthritis with
32 azithromycin: a EULAR double blind, placebo controlled study. *Ann*
33 *Rheum Dis* 2004;63:1113-9.
- 34 57. Smieja M, MacPherson DW, Kean W, Schmuck ML, Goldsmith CH,
35 Buchanan W et al. Randomised, blinded, placebo controlled trial of
36 doxycycline for chronic seronegative arthritis. *Ann Rheum Dis*
37 2001;60:1088-94.
- 38 58. Wakefield D, McCluskey P, Verma M, Aziz K, Gatus B, Carr G.
39 Ciprofloxacin treatment does not influence course or relapse rate of
40 reactive arthritis and anterior uveitis. *Arthr Rheum* 1999;42:1894-7.
- 41 59. Wollenhaupt J, Hammer M, Pott HG, Zeidler H. A double-blind, placebo-
42 controlled comparison of 2 weeks versus 4 months treatment with
43 doxycycline in chlamydia-induced reactive arthritis. *Arthr Rheum*
44 1997;40 suppl:S143.
- 45 60. Putschky N, Pott H-G, Kuipers JG, Ziedler H, Hammer M, Wollenhaupt J.
46 Comparing 10-day and 4-month doxycycline courses for treatment of

- 1 Chlamydia trachomatis-reactive arthritis: a prospective double-blind
2 trial. *Ann Rheum Dis* 2006;65:1521-4.
- 3 61. Dreses-Werringloer U, Padubrin I, Zeidler H, Kohler L. Effects of
4 azithromycin and rifampicin on Chlamydia trachomatis infection in
5 vitro. *Antimicrob Agents Chemother* 2001;45:3001-8.
- 6 62. Carter JD, Valeriano J, Vasey FB. Doxycycline versus doxycycline and
7 rifampicin in undifferentiated spondyloarthropathy, with special
8 reference to Chlamydia-induced arthritis. A prospective, randomised
9 9-month comparison. *J Rheumatol* 2004;31:1973-80.
- 10 63. Carter JD, Espinoza LR, Inman RD, Sneed KB, Ricca LR, Vasey FB et al.
11 Combination antibiotics as a treatment for chronic Chlamydia-induced
12 reactive arthritis: A double-blind, placebo-controlled, prospective trial.
13 *Arthritis Rheum* 2010; 62: 1298-307.
- 14 64. Leirisalo-Repo M, Paimela L, Julkunen H, Peltomaa R, Laasila K,
15 Kautiainen H et al. A 3-month, randomised, placebo-controlled study
16 with combination antimicrobial therapy in acute reactive arthritis.
17 *Arthritis Rheum* 2001;44 Suppl:S91.
- 18 65. Yli-Kerttula T, Luukkainen R, Yli-Kerttula U, Möttönen T, Hakola M,
19 Korpela M et al. Effect of a three month course of ciprofloxacin on the
20 late prognosis of reactive arthritis. *Ann Rheum Dis* 2003;62:880-4.
- 21 66. Laasila K, Laasonen L, Leirisalo-Repo M. Antibiotic treatment and long
22 term prognosis of reactive arthritis. *Ann Rheum Dis* 2003;62:655-8.
- 23 67. Pott HG, Wittenborg A, Junge-Hülsing G. Long-term antibiotic
24 treatment in reactive arthritis. *Lancet* 1988;1:245-6.
- 25 68. Barber CE, Kim J, Inman RD, Esdaile JM, James MT. Antibiotics for
26 treatment of reactive arthritis: a systemic review and meta analysis. *J*
27 *Rheumatol* 2013;40:916-28.
- 28 69. Anandarajah A, Ritchlin CT. Treatment update on spondyloarthropathy.
29 *Curr Opin Rheumatol* 2005;17:247-56.
- 30 70. NICE guideline [NG65]. Spondyloarthritis in over 16s: diagnosis and
31 management. Published February 2017. Available at
32 <https://www.nice.org.uk/guidance/ng65>
- 33 71. Combe B, Landewe R, Lukas C, Bolosiu HD, Breedveld F, Dougados M et
34 al. EULAR recommendations for the management of early arthritis:
35 report of a task force of the European Standing Committee for
36 International Clinical Studies Including Therapeutics (ESCISIT). *Ann*
37 *Rheum Dis* 2007;66:34-45.
- 38 72. Toivanen A, Toivanen P. Epidemiological, clinical, and therapeutic
39 aspects of reactive arthritis and ankylosing spondylitis.
40 *Curr Opin Rheumatol* 1995;7:279-83.
- 41 73. Cuellar ML, Espinoza LR. Management of spondyloarthropathies.
42 *Curr Opin Rheumatol* 1996;8:288-95.
- 43 74. Leirisalo-Repo M. Prognosis, course of disease, and treatment of the
44 spondyloarthropathies. *Rheum Dis Clin North Am* 1998;24:737-51.
- 45 75. Patrono C. Non-steroidal anti-inflammatory drugs in: Hochberg MC,
46 Silman AJ, Smolen JS, Weinblatt ME, Weisman MH (eds). *Rheumatology*

- 1 5th ed. Mosby Elsevier, Philadelphia 2011. Section 4: Principles of
2 management;50:485-93.
- 3 76. Juvakoski T, Lassus A. A double-blind cross-over evaluation of
4 ketoprofen and indomethacin in Reiter's disease. *Scand J Rheumatol*
5 1982;11:106-8.
- 6 77. Dougados M, Nguyen M, Caporal R, Legeais J, Bouxin-Sauzet A, Pellegrini-
7 Guegnault B et al. Ximoprofen in ankylosing spondylitis. A double
8 blind placebo controlled dose ranging study. *Scand J Rheumatol*
9 1994;23:243-8.
- 10 78. Wienecke T, Gotzsche PC. Paracetamol versus non steroidal anti-
11 inflammatory drugs for rheumatoid arthritis. *Cochrane Database of*
12 *Systematic Reviews* 2004, Issue 1. Art. No: CD003789.
- 13 79. Palazzi C, Olivieri I, D'Amico E, Pennese E, Petricca A. Management of
14 reactive arthritis. *Expert OpinPharmacother* 2004;5:61-70.
- 15 80. <http://www.mhra.gov.uk>
- 16 81. <http://nice.org.uk/guidance>
- 17 82. British National Formulary. Non-steroidal anti-inflammatory drugs –
18 NSAIDs and cardiovascular events. Available at
19 [https://bnf.nice.org.uk/treatment-summary/non-steroidal-anti-](https://bnf.nice.org.uk/treatment-summary/non-steroidal-anti-inflammatory-drugs.html)
20 [inflammatory-drugs.html](https://bnf.nice.org.uk/treatment-summary/non-steroidal-anti-inflammatory-drugs.html)
- 21 83. McGettigan P, Henry D. Cardiovascular risk and inhibition of
22 cyclooxygenase. *JAMA* 2006;296:1633-44.
- 23 84. Kearney PM, Baigent C, Godwin J, Halls H, Emberson JR, Patrono C. Do
24 selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal
25 anti-inflammatory drugs increase the risk of atherothrombosis? Meta-
26 analysis of randomised trials. *BMJ* 2006; 332: 1302
- 27 85. Ray WA, Varas-Lorenzo C, Chung CP, Castellsague J, Murray KT, Stein
28 CM et al. Cardiovascular risks of nonsteroidal anti-inflammatory drugs
29 in patients after hospitalization for serious coronary heart disease.
30 *Circ Cardiovasc Qual Outcomes* 2009; 2: 155-63.
- 31 86. Blyth T, Hunter JA, Stirling A. Pain relief in the rheumatoid knee after
32 steroid injection a single-blind comparison of hydrocortisone
33 succinate, and triamcinolone acetonide or hexacetonide. *Br J*
34 *Rheumatol* 1994; 33: 461-3.
- 35 87. Canoso JJ, Naredo E. Aspiration and injection of joints and periarticular
36 tissues and intralesional therapy in: Hochberg MC, Silman AJ, Smolen
37 JS, Weinblatt ME, Weisman MH (eds). *Rheumatology* 5th ed. Mosby
38 Elsevier, Philadelphia 2011. Section 4: Principles of management; 66:
39 617-28.
- 40 88. Calin A. Management of Reiter's syndrome. *Ann Rheum Dis* 1979; 38
41 Suppl: 96-7.
- 42 89. Günaydin I, Pereira PL, Daikeler T, Mohren M, Trübenbach J, Schick F et
43 al. Magnetic resonance imaging guided corticosteroid injection of the
44 sacroiliac joints in patients with therapy resistant
45 spondyloarthritis: a pilot study. *J Rheumatol* 2000; 27: 424-8.

- 1 90. Thiers BH. The use of topical calcipotriene/calcipotriol in conditions
2 other than plaque-type psoriasis. *J Am Acad Dermatol* 1997;37:S69-71.
- 3 91. Owen ET, Cohen ML. Methotrexate in Reiter's disease. *Ann Rheum Dis*
4 1979;38:48-50.
- 5 92. Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells GA, Tugwell P.
6 Calcium and vitamin D for corticosteroid-induced osteoporosis.
7 *Cochrane Database of Systematic Reviews* 1998, Issue 2. Art No:
8 CD000952.
- 9 93. Cranney A, Welch V, Adachi J, Shea B, Suarez-Almazor ME, Tugwell P et
10 al. Calcitonin for preventing and treating corticosteroid-induced
11 osteoporosis. *Cochrane Database of Systematic Reviews* 2000, Issue 1.
12 Art. No: CD001983.
- 13 94. Homik J, Cranney A, Shea B, Tugwell P, Wells GA, Adachi J et al.
14 Bisphosphonates for steroid induced osteoporosis. *Cochrane Database*
15 *of Systematic Reviews* 1999, Issue 1. Art. No: CD001347.
- 16 95. Dougados M, van der Linden S, Leirisalo-Repo M, Huitfeldt B, Juhlin R,
17 Veys E et al. Sulfasalazine in the treatment of spondyloarthritis: a
18 randomized, multicenter, double-blind, placebo-controlled study.
19 *Arthr Rheum* 1995; 38; 618-27.
- 20 96. Clegg DO, Reda DJ, Weisman MH, Cush JJ, Vasey FB, Schumacher HR et
21 al. Comparison of sulfasalazine and placebo in the treatment of
22 reactive arthritis (Reiter's syndrome): a Department of Veterans
23 Affairs Cooperative Study. *Arthr Rheum* 1996; 39: 2021-7.
- 24 97. Egsmose C, Hansen TM, Andersen LS, Beier JM, Christensen L, Ejstrup L
25 et al. Limited effect of sulphasalazine treatment in reactive arthritis. A
26 randomised double blind placebo controlled trial. *Ann Rheum Dis*
27 1997; 56: 32-6.
- 28 98. Clegg DO, Reda DJ, Abdellatif M. Comparison of sulfasalazine and
29 placebo for the treatment of axial and peripheral articular
30 manifestations of the seronegative spondyloarthropathies: a
31 Department of Veterans Affairs Cooperative Study. *Arthr Rheum* 1999;
32 42: 2325-9.
- 33 99. Braun J, Zochling J, Baraliakos X, Alten R, Burmester G, Grasedyck K et
34 al. Efficacy of sulfasalazine in patients with inflammatory back pain
35 due to undifferentiated spondyloarthritis and early ankylosing
36 spondylitis: a multicenter randomised controlled trial. *Ann Rheum Dis*
37 2006; 65: 1147-53.
- 38 100. Lipsky PE, van der Heijde DM, St Clair EW, Furst DE, Breedveld FC,
39 Kalden JR et al. Infliximab and methotrexate in the treatment of
40 rheumatoid arthritis. *N Engl J Med* 2000;343:1594-602.
- 41 101. Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, Keystone
42 EC et al. A comparison of etanercept and methotrexate in patients with
43 early rheumatoid arthritis. *N Engl J Med* 2000; 343: 1586-93.
- 44 102. Genovese MC, Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff
45 MH et al. Etanercept versus methotrexate in patients with early

- 1 rheumatoid arthritis. Two-year radiographic and clinical outcomes.
2 Arthritis Rheum 2002; 46: 1443-50.
- 3 103. Reimold AM. New indications for treatment of chronic inflammation
4 by TNF-(alpha) blockade. Am J Med Sci 2003; 325: 75-92.
- 5 104. Khan MA. Update on spondyloarthropathies. Ann Intern Med
6 2002;136:896-907.
- 7 105. Braun J, Brant J, Listing J, Zink A, Alten R, Golder W et al. Treatment of
8 active ankylosing spondylitis with infliximab: a randomised controlled
9 multicentre trial. Lancet 2002; 359: 1187-93.
- 10 106. Gorman JD, Sack KE, Davis JC Jr. Treatment of ankylosing spondylitis
11 by inhibition of tumour necrosis factor α . N Engl J Med 2002; 346:
12 1349-56.
- 13 107. Braun J, Sieper J. Biological therapies in the spondyloarthritides - the
14 current state. Rheumatology 2004; 43: 1072-84.
- 15 108. Van der Heijde D, Kivitz A, Schiff MH, Sieper J, Dijkmans BA, Braun J et
16 al. Efficacy and safety of adalimumab in ankylosing spondylitis: results
17 of a multicenter, randomised, double-blind, placebo-controlled trial.
18 Arthritis Rheum 2006; 54: 2136-46.
- 19 109. Kavanaugh A, Tutuncu Z, Catalan-Sanchez T. Update on anti-tumor
20 necrosis factor therapy in spondyloarthropathies including psoriatic
21 arthritis. Curr Opin Rheumatol 2006; 18: 347-53.
- 22 110. Mease PJ, Goffe BS, Metz J, Van der Stoep A, Finck B, Burge DJ.
23 Etanercept in the treatment of psoriatic arthritis and psoriasis: a
24 randomised trial. Lancet 2000; 356: 385-90.
- 25 111. Antoni CE, Krueger GG, de Vlam K, Birbara C, Beutler A, Guzzo C et al.
26 Infliximab therapy improves symptoms and signs of psoriatic arthritis:
27 results of the IMPACT 2 trial. Ann Rheum Dis 2005; 64: 1150-7.
- 28 112. Mease PJ, Gladman DD, Ritchlin CT, Ruderman EM, Steinfeld SD, Choy
29 EHS et al. Adalimumab for the treatment of moderately to severely
30 active psoriatic arthritis: results of a double-blind, randomized,
31 placebo-controlled trial. Arthritis Rheum 2005; 52: 3279-89.
- 32 113. Van der Bosch F, Kruithof E, Baeten D, Heressens A, De Keyser F,
33 Mielants H et al. Randomised double-blind comparison of chimeric
34 monoclonal antibody to tumour necrosis factor α (infliximab) versus
35 placebo in active spondyloarthropathy. Arthritis Rheum 2002; 46:
36 755-65.
- 37 114. Kruithof E, De Rycke L, Roth J, Mielants H, Van den Bosch F, De Keyser
38 F et al. Immunomodulatory effects of etanercept on peripheral joint
39 synovitis in the spondyloarthropathies. Arthritis Rheum 2005; 52:
40 3898-909.
- 41 115. Rosenbaum JT, Smith JR. Anti-TNF therapy for eye involvement in
42 spondyloarthropathy. Clin Exp Rheumatol 2002; 20 Suppl 28:S143-5.
- 43 116. Braun J, Baraliakos X, Listing J, Sieper J. Decreased incidence of
44 anterior uveitis in patients with ankylosing spondylitis treated with
45 anti-tumor necrosis factor agents. Arthritis Rheum 2005; 52: 2447-51.

- 1 117. Theodossiadis PG, Markomichelakis NN, Sfikakis PP. Tumor necrosis
2 factor antagonists: preliminary evidence for an emerging approach in
3 the treatment of ocular inflammation. *Retina* 2007; 27: 399-413.
- 4 118. Levy-Clarke G, Reed G, Nussenblatt R. Is anti-tumour necrosis factor
5 (TNF) agents effective in reducing uveitis flares in patients with
6 spondyloarthropathies? *Nature Clinical Practice Rheumatology* 2007;
7 3: 376-7.
- 8 119. Keane J, Gershon S, Wise RP, Mirabile-Levens E, Kasznica J,
9 Schwieterman WD et al. Tuberculosis associated with infliximab, a
10 tumour necrosis factor α -neutralising agent. *N Engl J Med* 2001; 345:
11 1098-104.
- 12 120. Baeten D, Kruithof E, Van den Bosch F, Van den Bossche N, Heressens A,
13 Mielants H et al. Systemic safety follow up in a cohort of 107 patients
14 with spondyloarthritis treated with infliximab: a new perspective
15 on the role of host defence in the pathogenesis of the disease? *Ann*
16 *Rheum Dis* 2003; 62: 829-34.
- 17 121. Mayer A, Chatelus E, Wendling D, Berthelot J-M, Dernis E, Houvenagel E
18 et al. Safety and efficacy of anti-tumor necrosis factor α therapy in ten
19 patients with recent-onset refractory reactive arthritis. *Arthritis*
20 *Rheum* 2011; 63: 1274-80.
- 21 122. Carter JD. Treating reactive arthritis: insights for the clinician.
22 *TherAdvMusculoskel Dis* 2010; 2: 45-54.
- 23 123. Flagg SD, Meador R, Hsia E, Kitumnuaypong T, Schumacher HR Jr.
24 Decreased pain and synovial inflammation after etanercept therapy in
25 patients with reactive and undifferentiated arthritis: an open-label
26 trial. *Arthritis Rheum* 2005; 53: 613-7.
- 27 124. Wechalekar MD, Rischmueller M, Whittle S, Burnet S, Hill CL.
28 Prolonged remission of chronic reactive arthritis treated with three
29 infusions of infliximab. *J ClinRheumatol* 2010; 16: 79-80.
- 30 125. Schafranski MD. Infliximab for reactive arthritis secondary to
31 *Chlamydia trachomatis* infection. *RheumatolInt* 2010; 30: 679-80.
- 32 126. Kaipainen-Seppänen O, Niinisalo H, Korpilähde T, Virolainen J.
33 Treatment of reactive arthritis with infliximab. *Scand J Rheumatol*
34 2003; 32: 122-4.
- 35 127. Meador RJ, Hsia EC, Kitumnuaypong T, Schumacher HR. Is etanercept
36 (ENBREL) effective in the treatment of reactive and undifferentiated
37 arthritis? *Arthritis Rheum* 2001; 44 Suppl: S348.
- 38 128. Gaylis N. Infliximab in the treatment of an HIV positive patient with
39 Reiter's syndrome. *J Rheumatol* 2003; 30: 407-11.
- 40 129. Carter JD, Gerard HC, Hudson AP. Psoriasiform lesions induced by
41 tumour necrosis factor antagonists: a skin-deep medical conundrum.
42 *Ann Rheum Dis* 2008; 67: 1181-83.
- 43 130. Van der Heijde D, Cheng-Chung Wei J, Dougados M et al. Ixekizumab, an
44 interleukin-17A antagonist in the treatment of ankylosing spondylitis
45 or radiographic axial spondyloarthritis in patients previously
46 untreated with biological disease-modifying anti-rheumatic drugs

- 1 (COAST-V): 16 week results of a phase 3 randomised, double-blind,
2 active-controlled and placebo-controlled trial. *Lancet* 2018; 8; 392:
3 2441-2451.
- 4 131. Mease PJ, Kavanaugh A, Reimold A et al. Secukinumab Provides
5 Sustained Improvements in the Signs and Symptoms of Psoriatic
6 Arthritis: Final 5-year Results from the Phase 3 FUTURE 1 Study. *ACR
7 Open Rheumatol* 2020; 2(1): 18-25.
- 8 132. Taylor PC. Clinical efficacy of launched JAK inhibitors in rheumatoid
9 arthritis. *Rheumatology (Oxford)* 2019; 1; 58 (Suppl 1): i17-i26.
- 10 133. O'Duffy EK, Clunie GPR, Lui D, Edwards JCW, Ell PJ. Double blind
11 glucocorticoid controlled trial of samarium-153 particulate
12 hydroxyapatite radiation synovectomy for chronic knee synovitis. *Ann
13 Rheum Dis* 1999; 58: 554-8.
- 14 134. Pavlica L, Nikolic D, Magic Z, Brajuskovic G, Strelac N, Milicic B et al.
15 Successful treatment of postvenereal reactive arthritis with
16 synovectomy and 3 months' azithromycin. *J Clin Rheumatol* 2005; 11:
17 257-63.
- 18 135. Smith G, Roberts R, Hall C, Nuki G. Reversible ovulatory failure
19 associated with the development of luteinized unruptured follicles in
20 women with inflammatory arthritis taking non-steroidal anti-
21 inflammatory drugs. *Br J Rheumatol* 1996; 35: 458-62.
- 22 136. de Wit W, van Mourik I, Wiesenhaan PF. Prolonged maternal
23 indomethacin therapy associated with oligohydramnios. Case reports.
24 *Br J Obstet Gynecol* 1988; 95: 303-5.
- 25 137. <http://www.bnf.org>
- 26 138. Flint J, Panchal S, Hurrell A et al. BSR and BHPR guideline on
27 prescribing drugs in pregnancy and breastfeeding – Part I: standard
28 and biologic disease modifying anti-rheumatic drugs and
29 corticosteroids. *Rheumatology*; 55 (9): 1693-1697
- 30 139. McGonagle, Aydin S Z, Gul A et al. 'MHC-I-opathy' – unified concept for
31 spondyloarthritis and Behcet disease. *Nature Reviews Rheumatology*
32 2015; 11: 731-740
- 33 140. Siva C, Tanjong GE, Zhou X, Choy EHS, Singh JA. Antibiotics for reactive
34 arthritis. (Protocol). *Cochrane Database of Systematic Reviews* 2013,
35 Issue 9. Art. No: CD006078.

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Appendix 1: NICE Equality Impact Assessment

BASHH Guideline Equality Impact Assessment <i>(based on NICE documentation shared with BASHH August 2019)</i>				
Guidance title: BASHH Guidelines for the Management of Sexually Acquired Reactive Arthritis		Completed by: E Carlin and S Flew		Date: 24.10.2019
How relevant is the topic to equality?	Inequalities in health impact of the condition or public health issue	Potential of guidance to add value	Priority for NHS or other government department	Topic relevance; conclusions and outcomes
	<ul style="list-style-type: none"> • Prevalence and impact of condition or public health problem • Prevalence of risk factors 	<ul style="list-style-type: none"> • Inequalities in access, uptake or impact • Timeliness • Equality issues identified by proposers of the topic • Equality issues identified by patient or lay organisations 	<ul style="list-style-type: none"> • Department of Health or other centralised NHS bodies such as NHS England • Local authorities • Home Office • Other agencies 	<ul style="list-style-type: none"> • If equality issues had impact on the guidance summarise these impacts
Sex/gender	SARA is more commonly identified in men	Guideline highlights under-recognition of SARA in females	N/A	N/A
Race	Potential for increased incidence in HIV positive Sub-Saharan population. HLA-B27 possession linked to the condition and increased severity	Guideline highlights association with selected populations	N/A	N/A

Disability	May cause locomotor or visual disability and be associated with other disabling spondyloarthropathies	Early detection, diagnosis and treatment may reduce the risk of progression and the development of disability	Collaborative working with affected specialties may reduce the development of disability and improve access for those with existing disability	Collaborative specialist working and early referral is essential to reduce the risk of long term disability
Age	Causative STIs are more common in young people but can occur in any age group. There is no direct age association with SARA.	Recommendations for STI screening are not age-specific	Importance of access to Sexual Health Services and STI and HIV testing	STI and HIV screening is advised regardless of age
Sexual orientation	Causative STIs are more common in MSM but no direct sexual orientation association with SARA	Appropriate STI screening depends on sexual practice as detailed in the guideline	As above	STI and HIV screening is advised and recommendations are given according to sexual practice
Gender reassignment	No known link with SARA	Guidance comments on sample taking in trans population	As above	STI and HIV screening is advised and recommendations are given for trans people
Religion/ belief	N/A	N/A	N/A	N/A
Pregnancy & maternity	No known link with SARA	Guidance mentions treatment options in pregnancy/breastfeeding	N/A	Guideline indicates need to consider treatment risks in pregnancy/breastfeeding
Other definable characteristics &	Geographical variation in HLA type means	Guideline indicates association with HLA-B27	N/A	N/A

<p>socioeconomic factors that may be affected by protected characteristics, including:</p> <ul style="list-style-type: none"> • Prisoners and young offenders • Refugees and asylum seekers • Migrant workers • Looked after children • Homeless people • Deprivation • Disadvantage associated with geographical distinctions 	<p>certain populations are more at risk due to increased HLA-B27 expression</p>	<p>but routine testing does not contribute to management</p>		
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