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Diagnostic delay in axial spondylarthritis: A lost battle?

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A B S T R A C T

Diagnostic delay in axial spondylarthritis (axSpA) remains an unacceptable worldwide problem; with evidence suggesting significant detrimental impact both clinically on the individual, and economically on society. There is therefore, a need for global action across various healthcare professions that come into contact with patients living, and suffering, with undiagnosed axSpA. Recent estimates of the median diagnostic delay suggest that globally, individuals with axSpA wait between 2 and 6 years for a diagnosis – revealing a clear benchmark for improvement. This timespan presents a window of opportunity for earlier diagnosis and intervention, which will likely improve patient outcomes. This review describes the current diagnostic delay as estimated across countries and over time, before presenting evidence from published strategies that may be implemented to improve this delay across primary and secondary care, including for specialties treating extra-musculoskeletal manifestations of axSpA (ophthalmology, gastroenterology, dermatology). Ongoing campaigns tackling delayed diagnosis in axSpA are also highlighted.

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Introduction

Delay to diagnosis in axial spondyloarthritis (axSpA) remains an extensive worldwide problem; the estimated mean diagnostic delay being 6.7 years globally [1]. With regard to the median, an individual with axSpA will likely wait between 2 and 6 years for a diagnosis—providing the rheumatology community a clear benchmark of this unacceptable global problem [2]. This delay to diagnosis can have a significant impact on those living with the condition, with evidence indicating that delay is associated with increased likelihood for worse quality of life and negative psychological consequences, higher disease activity, worse physical function, increased structural damage, poorer treatment response, greater likelihood of work disability and higher direct and indirect healthcare costs compared to timely diagnosis [3,4]. Fatigue, difficulty sleeping, and a prevalence of psychosomatic disorders have also been associated with longer diagnostic delay in axSpA [5]. Growing evidence thus suggests that earlier diagnosis and treatment facilitates better disease outcomes.

Qualitative studies have further highlighted the detrimental psychological consequences of diagnostic delay in axSpA. In a recent study in the US, most participants described significant suffering before axSpA was diagnosed, which could have been avoided with earlier intervention and treatment [6]. In particular, doctors "giving up" on attempting to determine an appropriate diagnosis left a profoundly negative impact. Similarly, in other qualitative studies, patients have described having to truly fight for their diagnosis, reporting of doctors minimizing or dismissing complaints about symptoms or telling them that their issues were psychosomatic – resulting in distress, sadness, frustration, and anger [7,8]. The emotional impact of having to repeatedly engage with healthcare providers while describing hard-to-explain symptoms was evident, with the lack of diagnosis leading to depression in some patients, and negatively impacting their relationships and professional lives [7]. Patients have reported not feeling "listened to" or "believed" about their symptoms, leading to feelings of helplessness and in some cases resulting in patients withdrawing from care completely, further increasing the diagnostic delay [9].

A recent systematic literature review (Yi et al., 2020) highlighted the need for further robust research, to gain a more comprehensive understanding of the factors that contribute to diagnostic delay in axSpA, and of the impact of this delay on disease burden across different countries and healthcare settings [3]. In this 2020 review, a search for all original research articles published up to July 2018 yielded 21 studies reporting associations of diagnostic delay with clinical (15 studies), economic (9 studies), or humanistic (6 studies) burden, wherby only 4 studies included over 200 patients. Across all studies, the majority of patients were male and exhibited radiographic disease. Due to the limited number of identified studies and small sample sizes, a meaningful meta-analysis was not possible. Data corresponding to economic and humanistic outcomes were particularly lacking. Further studies exploring the long-term impact of diagnostic delay on the axSpA disease burden are therefore warranted.

Although 2 recent systematic reviews have indicated potential improvements in the diagnostic delay over recent decades, this delay remains unacceptably long and may have plateaued in recent years [1,2]. There is therefore a need for global action and initiatives to strive to improve the long and detrimental journey to diagnosis often experienced by patients, to likely result in improved outcomes. In this review, we describe the current diagnostic delay as estimated across countries and over time, before presenting published strategies for improving this delay. We also highlight ongoing campaigns tackling delayed diagnosis in axSpA. Although diagnostic delay remains a topical and unacceptable problem in axSpA, it is not a lost battle. It is thus our responsibility as clinicians to continue to strive toward earlier diagnosis and treatment for people living with axSpA.

Diagnostic delay across countries and over time

A recent systematic review and meta-analysis by Zhao et al. identified a total of 64 studies reporting the mean diagnostic delay for axSpA [1]. Data were pooled to calculate a mean diagnostic delay of 6.7 years worldwide. The mean diagnostic delay did not differ significantly across regions. However, when stratified by World Bank economic class, the high-income group demonstrated significantly longer delays than those demonstrated by the upper-middle-income (by 2.5 years; $P < 0.01$) and lower-

middle-income (by 3.7 years; $P = 0.03$) countries. Of the countries in which 3 or more studies were conducted (UK, Turkey, Italy, Iran, China), the UK was reported as having the longest mean diagnostic delay (8.65 years, calculated from 9 studies), and China the shortest (4.32 years, estimated from 4 studies) (Fig. 1). The meta-analysis reported no meaningful change in diagnostic delay over time (using the year of publication as a proxy for calendar time, due to the lack of reported recruitment period in some studies). By country, this finding was consistent with results from the UK, France, and Germany. However, the delay in diagnosis was reported to dramatically improve in 4 studies reporting diagnostic delay over time in Japan (pre-*vs* post-2000: 7.5 *vs* 3.6 years), Italy (1990s *vs* 2000s: 7.4 *vs* 2.1 years), Egypt (pre-*vs* post-2010: 11 *vs* 4.6 years), and Australia (pre-1978 *vs* 1978–1985, 1986–1993, and 1994–2005: 13.8 *vs* 9.4, 5.3, and 4.3, respectively).

A systematic review by Hay et al. recently explored the median diagnostic delay for axSpA [2]. Although median data cannot be pooled for meta-analysis, it is generally recommended for the analysis of skewed data, whereby diagnostic delay data is known to be skewed by outliers, resulting in a mean that is inflated above the median by a high proportion of individuals with extremely long delays. Zhao et al. justified their use of mean values in order to conduct a meta-analysis, and because reporting the median takes the emphasis away from people with unusually long diagnostic delays, thus reducing the emphasis placed on precisely those individuals who require an improvement in diagnosis. Across the 25 studies included by Hay et al. although one study in Denmark reported a median delay of 0.67 years, the vast majority (80%) reported diagnostic delays of 2–6 years. Of note, methodological concerns have been highlighted regarding the study from Denmark, which might have skewed the results to reflect the shorter delay of 0.67 years [10]. The remaining 3 studies in South Korea, Czech Republic and Norway, reported median diagnostic delays of 8, 7.5, and 7 years, respectively. The authors propose that evidence from an included study by Garrido-Cumbrera et al. (2019) supports the suggestion that a 2–6 year diagnostic delay range is "typical," as this large study of 2,846 patients across 13 European countries found a median delay of 4 years (mean delay: 7.4 years) in 2017–2018. Estimates from 4 studies reporting the median diagnostic delay over time (conducted in Italy [published in 2012], the UK [published in 1988], Australia [published in 2008], and the US [published in 2015]) suggest that diagnostic delay has been reducing since the mid-20th century – potentially due to increased disease awareness and understanding, and advances in diagnostic imaging technology, specifically in magnetic resonance imaging (MRI).

Beyond the aforementioned 2 systematic reviews, studies from China [11] and the UK [12] have reported changes in diagnostic delay over time. In the UK, data from 12,333 patients diagnosed with ankylosing spondylitis (AS) in the Clinical Practice Research Datalink (CPRD) revealed an increase in median time from first coded non-specific back pain symptom to diagnosis between 1998 and 2017, from 3.62 to 8.31 years [12]. The time to diagnosis was longer in women than in men – 6.71 versus 5.65 years, respectively. These findings are consistent with those derived from UK survey data; revealing an increase in median diagnostic delay from 6 to 8.5 years between 2010 and 2016 [13,14]. In contrast, a single-center study of 566 patients in China diagnosed with axSpA demonstrated an improvement in median diagnostic delay (time from the first symptoms to the correct diagnosis) after the introduction of the 2009 Assessment of Spondyloarthritis International Society (ASAS) criteria, from 4.5 to 1.1 years [11].

Two recent studies report variations in diagnostic delay between countries. A survey study reported that the mean time from the onset of symptoms to the final axSpA diagnosis was longer in Central Eastern European countries compared to that in the US (4.2 vs. 2.7 years, $P < 0.05$) [15]. Within Europe, a study reporting the results of two surveys (European Map of Axial Spondyloarthritis [EMAS] and the Atlas of Axial Spondyloarthritis in Spain) suggested a greater mean diagnostic delay in Spanish patients compared to those reported in other European countries (8.5 vs. 7.2 years; $P < 0.001$) [16].

Several factors have been independently associated with a longer diagnostic delay: including female sex, HLA-B27 negativity, presence of psoriasis, and young age at symptom onset [17,18]. Presence of peripheral arthritis and IBD have been associated with earlier diagnosis [19–21]. However, results from the aforementioned systematic reviews (Zhao et al., 2021; Hay et al., 2022) suggest that the extent (if at all) to and direction with which these factors are associated with diagnostic delay differs between countries, potentially indicating differing diagnostic practices [1,2]. Zhao et al. reported conflicting associations of gender, HLA-B27 and peripheral arthritis with diagnostic delay. The consensus was better regarding the absence of extra-musculoskeletal manifestations (EMMs), lower educational

Fig. 1. Mean diagnostic delay across World Health Organization regions and countries, as estimated by Zhao et al., 2021 [1]
n studies were included to calculate the estimates: Europe (n = 39), West Pacific (n = 9), Eastern Mediterranean (n = 8), Americas (n = 5), Southeast Asia (n = 3); Turkey (n = 10), UK (n = 9), Iran (n = 4), China (n = 4), Italy (n = 3).

attainment, and younger age of onset – all associated with longer diagnostic delays. Hay et al. reported that only gender (20 studies) and family history of axSpA (5 studies) were associated with sufficient data concordance to explore their association with diagnostic delay; whereby non-significant relationships were reported across the majority of studies. These two reviews indicated contradictory or limited evidence supporting the associations between patient characteristics and diagnostic delay, and further research is required to establish with greater certainty the patient groups most vulnerable to experiencing diagnostic delay. Nevertheless, results from the EMAS 2017–2018 survey study revealed a much longer and arduous journey to diagnosis in females with axSpA across Europe, with a higher number of visits to physiotherapists and osteopaths before being diagnosed, and lower proportion of HLA-B27-positive patients [22]. EMAS females also reported higher disease activity, greater psychological distress, and greater use of alternative therapies. The greater delay to diagnosis in females may be due to possible bias from physicians (AS historically thought of as a predominantly male disease), or different pattern of clinical presentations across genders—females typically more arthritis than enthesitis-related symptomatology, and less likely to test positive in HLA-B27 or imaging investigations [22,23]. It is thus crucial to sensitize physicians to gender differences in axSpA presentation and disease course, in order to prompt earlier referral to a rheumatologist.

Published strategies to improve diagnostic delay – window of opportunity

Recent evidence has highlighted shortcomings at both the primary and secondary care level, which contribute to the delayed diagnosis of axSpA [24,25]. Indeed, 62% of patients report contacting a healthcare practitioner within the first year of developing axSpA symptoms [13], thus significant diagnostic delay occurs after presentation to a healthcare provider. Despite the existence of various published guidelines for appropriate referral and investigations in patients with chronic lower back pain (CLBP), recommendations are not always implemented in clinical practice; especially referral for appropriate imaging when axSpA is suspected [24,26,27]. Evidence suggests that the knowledge, awareness, and confidence in assessing and identifying the key features and risk factors of suspected axSpA is often poor among healthcare professionals (HCPs) across primary and secondary care [28–33], even among musculoskeletal radiologists who are often responsible for acquiring and interpreting imaging results [27,34,35].

Nevertheless, these shortcomings represent a window of opportunity for the improved recognition, referral, and ultimately diagnosis of axSpA. Fig. 2 provides a high-level summary of the unique challenges to prompt referral, diagnosis, and treatment initiation in axSpA, as well as proposed solutions to overcome these challenges. Far-reaching mobilization, education, and training are required across the various healthcare professions that come into contact with patients living with and suffering from undiagnosed axSpA—from HCPs in primary care to whom patients with chronic back pain (CBP) will likely first present, all the way to the specialist physiotherapists, musculoskeletal radiologists and rheumatologists ultimately involved in triage and diagnosis of axSpA (Fig. 3). It is also important to note that whilst the implementation of simple, non-burdensome tools, algorithms and referral strategies will be critical for reducing diagnostic delay in axSpA, we must ensure a balance between not missing suspected axSpA diagnoses, versus not overwhelming rheumatology services with inappropriate referrals. We must also remain vigilant regarding the potential over-diagnosis of axSpA; it is thus important to recognize other conditions that may present with similar symptoms or provide an alternative diagnosis, in order to prevent potential misdiagnosis and inappropriate treatment [36,37].

Improved referral via primary care

Most patients experiencing CLBP or other axSpA symptoms will initially seek care from primary care physicians such as general physicians (GPs), physiotherapists, or complementary/alternative medicine practitioners (e.g., acupuncturists, chiropractors, osteopaths, massage therapists), only stimulating rheumatology referral if displaying musculoskeletal symptoms or features indicating rheumatological disease. It is therefore crucial for HCPs in primary care to be aware of and be able to recognize the hallmark features of axSpA. However, distinguishing axSpA from other forms of CLBP, an extremely common musculoskeletal complaint, can be challenging [29,31,33,38–41]. Evidence suggests that this

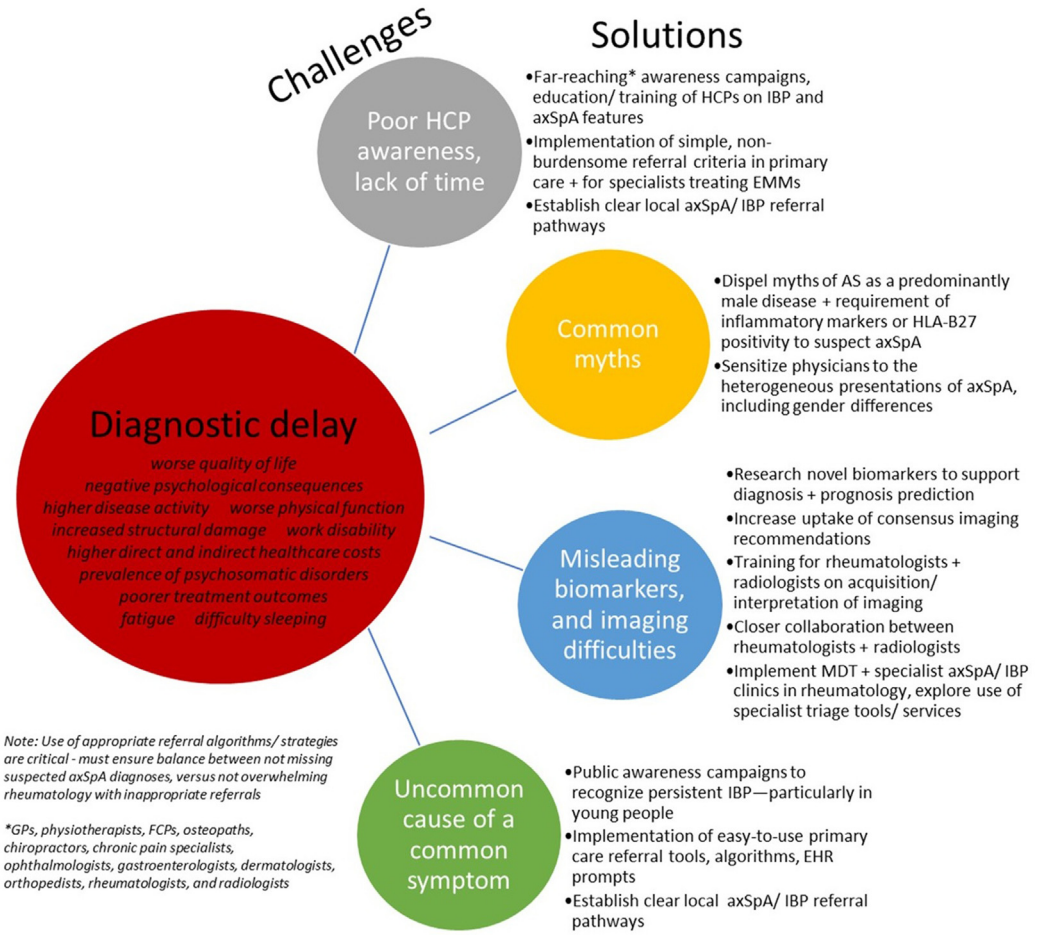

Fig. 2. Challenges and proposed solutions to improve diagnostic delay in axSpA.

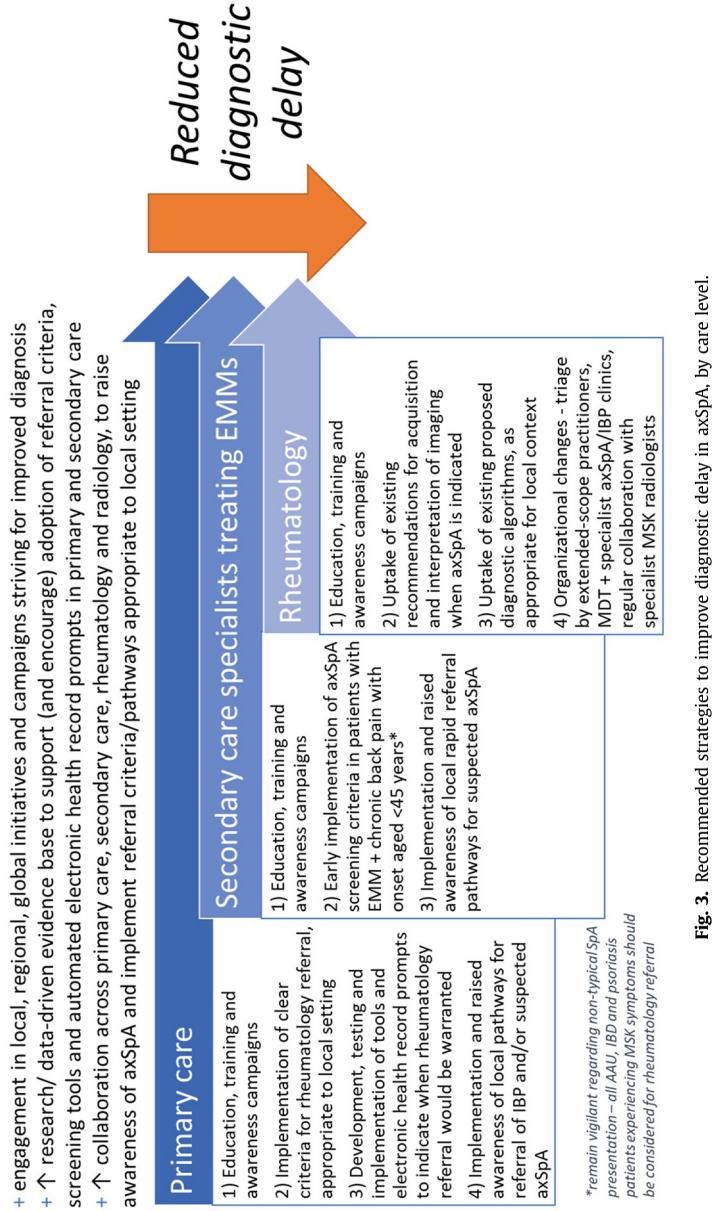

Fig. 3. Recommended strategies to improve diagnostic delay in axSpA, by care level.

challenge is exacerbated by a concerning lack of awareness of axSpA features/EMMs among primary care professionals, and common myths regarding axSpA are still prevalent (e.g., axSpA as a predominantly male disease, or misplaced importance/requirement of positive inflammatory markers/HLA-B27 to suspect axSpA) [29,30,33,39,41,42]. Collaboration between practitioners may also be lacking. In a recent UK survey, chiropractors and osteopaths reported that the main perceived barrier to subsequent rheumatology referral was reluctance by the GP to accept their professional opinion [30].

Education and training

Education and training of GPs has been found to substantially improve the recognition and referral of patients with suspected axSpA [43,44]. A recent multi-center study conducted in the Netherlands demonstrated >40% improvement in referral after receiving SpA education/training [43]. Among UK physiotherapists, Steen et al. (2021) demonstrated that good awareness of national SpA guidance and continued professional development were associated with better awareness and knowledge of axSpA features [33]. A follow-up study published in 2023 demonstrated improved knowledge/awareness of axSpA features compared to those reported in the aforementioned 2021 study, likely reflecting the increased professional education on axSpA in recent years in the UK (largely pioneered and led by the National Axial Spondyloarthritis Society, NASS, see section*: Campaigns tackling diagnostic delay*) and widespread introduction of first contact practitioners (FCPs), who are key in supporting earlier recognition in UK primary care [42]. Finally, peripheral disease has been associated with reduced diagnostic delay in axSpA [19–21] – likely due to the fact that GPs have been trained and consistently prompted via early arthritis initiatives about the importance of early referral for patients with swollen joints [19]. This evidence indicates the potential impact that primary care education and training programs could have on reducing diagnostic delay in axSpA, through ensuring that axSpA remains a higher priority in practitioner's clinical reasoning. The effectiveness of such initiatives should be further investigated (and disseminated) through future research, to facilitate knowledge sharing and to help justify their wider implementation.

Referral strategies and algorithms

There are an extensive number of published referral strategies for patients with suspected axSpA, developed for and tested within primary care settings (Table 1, although the performance of imaging for suspected axSpA is generally not recommended in primary care) [45,46]. These strategies attempt to strike a delicate balance between not missing suspected axSpA diagnoses, while not overwhelming rheumatology with inappropriate referrals. The most appropriate/preferred referral strategy and criteria will vary depending on the local setting and service availability. Simpler strategies will likely yield better uptake, and prevent delays caused by the use of unnecessary resources in primary care or challenges interpreting tests that may be better implemented and interpreted in rheumatology [41,45].

Most of the published referral algorithms use inflammatory back pain (IBP) as a cornerstone criterion for referral; whereby the presence of IBP should indicate referral to rheumatology. However, it is important to note that although IBP is an important feature for the screening of axSpA in primary care, it is estimated that only 75% of patients with axSpA present with typical IBP symptoms [45]. Absence of IBP thus does not necessarily exclude a suspected diagnosis of axSpA. As a heterogeneous disease with differing presentations and lack of diagnostic criteria, knowledge of all hallmark axSpA features is vital to facilitate early identification and referral, again highlighting the importance of education and training for HCPs throughout primary and secondary care. It is also worth noting that low awareness of the differences between mechanical and IBP has been reported across both primary and secondary care – likely contributing to delayed diagnosis for axSpA [29,31,33,38–41].

Online tools and electronic health record prompts

To our knowledge, there is little published evidence regarding the implementation of online tools and automated electronic health record (EHR) flags/prompts (based on presence of key axSpA/IBP features) to aid the identification of suspected axSpA in primary care – highlighting a gap for future research. Nevertheless, in the UK examples such as the PRIMIS pop-up alert tool (https://www.nottingham.ac.uk/primis/projects/axspa.aspx) and online SPADE tool (SPondyloArthritis Diagnosis Evaluation tool - http://www.spadetool.co.uk/), could be useful in supporting primary care providers

Table 1
Summary of published axSpA referral strategies developed for use in primary care settings, and number of patients diagnosed with axSpA in their respective validation studies.

Strategy	Clinical parameters	Laboratory or imaging parameters	Referral rule	Patients diagnosed with axSpA/referred
Brandt I Germany, 2007	· IBP defined by: (≥1/3) - Morning stiffness >30 min - Pain at night/early morning - Improvement with exercise	HLA-B27 Sacroiliitis (imaging not recommended in primary care)	≥1/3	159/350 45%
Brandt II Germany, 2007	· IBP defined by: (≥2/3) - Morning stiffness >30 min - Pain at night/early morning - Improvement with exercise	HLA-B27 Sacroiliitis	≥2/3	
Brandt III Germany, 2007	· IBP defined by: (≥3/3) - Morning stiffness >30 min - Pain at night/early morning - Improvement with exercise	HLA-B27 Sacroiliitis	≥3/3	
Hermann Austria, 2009	· IBP defined by Calin classification criteria: (≥4/5): - Persistent back pain for ≥3 months - Age of onset <40 years - Insidious onset of back pain - Back pain relieved by exercise - Back stiffness especially in the morning		1/1	30/92 33%
MASTER Germany, 2011	· IBP defined by: - Morning stiffness in lower part of the spine >30 min - Improvement with exercise not with rest - Waking at night due to back pain, which improves with exercise · Good response to NSAIDs · Family history of AS	HLA-B27 Sacroiliitis on imaging	≥2/5	90/242 37%
Braun IBP Germany, 2011	· IBP defined by: - Improvement with exercise not with rest - Waking in second half of the night - Alternating buttock pain · Good response to NSAIDs · CBP onset ≤35 years		≥2/5	113/322 35%
RADAR International, 2013	· IBP defined by any set of criteria · Good response to NSAIDs · Family history of SpA · EMMs	HLA-B27 Sacroiliitis on imaging	≥2/6	226/568 40%
RADAR 2/3 International, 2013	· IBP defined by any set of criteria · Good response to NSAIDs · EMMs		≥2/3	226/568 40%
Braun 2-step Germany, 2013	· IBP defined by: - Improvement with exercise not with rest - Buttock pain · Psoriasis	HLA-B27 (only if ≤ 1/3 clinical parameters +)	≥2 or HLA- B27+	342/950 36%
CaFaSpA The Netherlands, 2014	· IBP defined by the ASAS criteria: (≥4/5) - Age of onset <40 years - Insidious onset		≥1/3	87/364 24%

(*continued on next page*)

Table 1 (*continued*)

Strategy	Clinical parameters	Laboratory or imaging parameters	Referral rule	Patients diagnosed with axSpA/referred
	- Improvement with exercise - No improvement with rest - Pain at night (with improvement on getting up) · Good response to NSAIDs · Family history of SpA			
ASAS International, 2015	· IBP defined by any set of criteria, preferably ASAS · Good response to NSAIDs · Family history of SpA · EMMs · Peripheral manifestations (arthritis, enthesitis and/or dactylitis)	HLA-B27 Elevated acute-phase reactants Sacroiliitis	≥1/8	
NICE Clinical Guideline UK, 2017	· Low back pain onset <35 years · Improvement with exercise not with rest · Waking at night due to symptoms · Buttock pain · Good response to NSAIDs within 48 h · Family history of SpA · Current or past arthritis · Current or past enthesitis · Current or past psoriasis	HLA-B27 (prescribed only if exactly 3 clinical parameters +)	≥4 or 3 and HLA-B27+	

All primary care referral strategies require presence of chronic back pain (>3 months), with an age of onset <45 years. Of note, performance of imaging is not generally recommended in primary care for suspected axSpA.

in identifying and referring suspected axSpA. The implementation of such tools should be underpinned by robust data collection, to evaluate their impact and collate an evidence base for others to draw upon.

Several recent studies have explored the application of machine learning algorithms to predict/identify diagnoses of axSpA within administrative claims and EHR data [47–51]. Although showing good predictive value in test data with artificially high prevalence and useful for understanding and profiling the characteristics of patients who develop axSpA, when applied to a population with low prevalence rates (such as primary care), the positive predictive value can be low and multiple models may be required to more effectively identify suspected axSpA [48]. While not yet implementable in clinical practice, such advances may provide a future avenue for the improved identification of suspected axSpA, and ultimately hasten diagnosis by a rheumatologist.

Whilst the focus of this article is on physician-based strategies to improve axSpA diagnosis, it is worth mentioning the recent development of online patient symptom checkers and self-referral tools to support prompt referral of suspected axSpA to rheumatology for further investigation. An online patient self-referral tool was recently developed and evaluated by Proft et al. in Germany, as part of the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) study [52]. The online tool was developed in alignment with the ASAS recommendations for rheumatology referral of patients with CBP and axSpA features [46]. Patients were asked 13 questions pertaining to CBP, IBP, and other indicators of SpA. To prompt rheumatology referral, patients had to report CBP (lasting >3 months) with an age of onset <45 years, and at least one additional IBP (slow onset, morning stiffness, improvement with exercise but not with rest, night-time waking due to pain, or alternating buttock pain) or axSpA feature (pain improvement with NSAID use, tendonitis, HLA-B27 positivity, raised inflammatory markers with no alternative explanation such as infection, presence of axSpA EMM [acute anterior uveitis [AAU], psoriasis, or inflammatory bowel disease [IBD]], or a family history of AS, psoriasis, or IBD). Proft et al. compared the performance of the novel self-referral tool, with performance of the established physician-based Berlin tool (Table 1, Brandt I), whereby 19.4% (35/180) of self-

referred patients were ultimately diagnosed with axSpA. This figure was, expectedly, less than the 39.2% (71/181) of physician-referred patients, but substantially greater than the assumed 5% probability of axSpA among patients with CBP. Of note, the self-referral tool had been developed in order to maximize sensitivity; only requiring fulfillment of one IBP or axSpA feature in patients with CBP with an age of onset <45 years to trigger rheumatology referral. The requirement of ≥2 IBP features and one SpA parameter could improve the specificity and reduce the number of patients referred to rheumatology. However, the authors estimate that this approach would miss approximately 10% of diagnoses. True estimation of the sensitivity of the tool and the proportion of SpA patients missed was not possible, as patients who did not fulfill the self-referral criteria were not evaluated.

Other online symptom checkers are available for use by the public (e.g., https://www.actonaxialspa.com/symptoms-checker/; https://monsterpainintheas.com/; https://spondylitis.org/about-spondylitis/could-i-have-spondyloarthritis/), although these were developed by charities/patient organizations and do not prompt direct referral to a rheumatologist. Whilst potentially useful for patients, primary care physicians have expressed concern that patients using an online screening tool may request unnecessary referrals [41].

Implementation of local pathways for referral

Implementation of clear, appropriate healthcare infrastructure and referral pathways within local settings are critical to operationalize existing proposed referral algorithms/strategies and facilitate prompt referral of suspected axSpA to rheumatology for further investigation. Exact management pathways and recommended investigations prior to referral will vary between and within countries, and be specific to the very local context in many cases. All HCPs within primary care should be aware of their local processes and pathways for referring suspected axSpA or IBP to rheumatology. Primary care service providers (such as GP practices and musculoskeletal interface services, physiotherapy services) should ensure that all practicing HCPs within the service are aware of the signs, symptoms, and risk factors of SpA or IBP, and work with local rheumatology services to develop appropriate referral criteria and pathways. Development of clear graphics, handouts, or digital reminders of these pathways can be useful – see examples for the Low Back Assessment Clinical Pathway in Alberta, Canada (https://www.albertahealthservices.ca/assets/about/scn/ahs-scn-bjh-spine-low-back-assess-clinical-pathways.pdf); IBP Pathway in Cornwall and Isles of Scilly, UK (https://rms.cornwall.nhs.uk/primary_care_clinical_referral_criteria/primary_care_clinical_referral_criteria/rheumatology/inflammatory_back_pain_in_adults); National Institute for Health and Care Excellence (NICE) guidance for primary care – identifying and referring SpA, UK (https://www.bmj.com/content/bmj/suppl/2017/02/28/bmj.j839.DC1/mcak020217.wi.pdf) [53]).

Improved referral via secondary care specialists treating EMMs

Although primarily affecting the axial skeleton and sacroiliac joints, axSpA is frequently associated with a number of peripheral (arthritis, enthesitis and dactylitis) and EMMs – including AAU, psoriasis, and IBD. Ophthalmologists, dermatologists and gastroenterologists are thus in a strategic position to screen patients living with EMMs and at-risk of axSpA.

Within the multicenter Screening for AxSpA in Psoriasis, Iritis, and Colitis (SAPSIC) cohort, almost half of patients with psoriasis, AAU or colitis ≤45 years of age with ≥3 months undiagnosed back pain were diagnosed with axSpA when using a 3-stage evaluation approach comprising clinical evaluation, laboratory tests (HLA-B27, CRP) and radiography, and MRI [54]. 68.7% were diagnosed after the clinical evaluation alone [55]. Closer collaboration is thus recommended between rheumatology and specialists presented with EMMs (e.g. ophthalmology, gastroenterology, dermatology); to improve referral of suspected axSpA to rheumatology.

Several different tools and referral strategies/algorithms have been tested and published within these specialist care settings (Table 2). A referral strategy of all patients treated for EMMs reporting CBP with an age of onset <45 years could be the preferred strategy, to reduce the need for imaging/genetic testing outside of rheumatology. However, the exact strategy will vary depending on what is most appropriate in that specific healthcare setting/local context. As for primary care service providers, ophthalmology, dermatology and gastroenterology service providers should ensure that treating HCPs

Table 2
Summary of published axSpA referral tools and strategies developed for use in secondary care settings treating EMMs.

	Strategy	Referral algorithm/tool	Sensitivity	Specificity	Likelihood ratio (LR) or area under curve (AUC)	Patients diagnosed with axSpA/referred
AAU	DUET algorithm Ireland, 2015	· Chronic back pain (>3 months) with an age of onset <45 years OR those with joint pain requiring medical care AND · HLA−B27+ OR psoriasis	96% in validation cohort *(52.9% England, Sykes 2018; 77.9% Germany, Rademacher 2022)*	97% in validation cohort *(67.9% England, Sykes 2018; 42.2% Germany, Rademacher 2022)*	- positive LR 41.5 - negative LR 0.03 *(positive LR 1.3, negative LR 0.5 Germany, Rademacher 2022)*	29/72 40%
	SENTINEL Spain, 2016	· HLA−B27+ OR HLA-B27- with more than 1 episode of AU separated by at least 3 months				401/798 (50.2%) axSpA, 140/798 (17.5%) peripheral SpA *HLA-B27+ more frequently diagnosed with axial (69.8% vs. 27.3%, P < 0.0001) and peripheral SpA (21.9% vs. 11.1%, P < 0.0001)*
	ASAS International, 2015 *(assessed in England, Sykes 2018; Netherlands, Bentum 2022; Germany, Rademacher 2022)*	· Chronic back pain (>3 months) with an age of onset <45 years	*- 79.8% (Germany, Rademacher 2022)*	*- 27.7% (Germany, Rademacher 2022)*	*- positive LR 1.1, negative LR 0.7 (Germany, Rademacher 2022)*	*- 17/73, 23.3% (England, Sykes 2018)* *- 19/81 23% definite axSpA (10/19 AS); 32/81 40% suspected axSpA (Netherlands, Bentum 2022)*
	Rademacher Germany, 2022	· None − all patients with AAU referred				106/189 56%
IBD	TASQ-IBD Canada, 2013 *Not validated, and only tested in sample of axSpA patients*	· Chronic back pain or stiffness persisting for ≥3 months AND · 16 questions regarding IBD, back pain and stiffness, extra-axial features *No referral rule − TBD during validation*				
	Queiro Axial Spain, 2018	· Aged ≤45 AND ≥2/3: · Back pain · Morning stiffness in back ≥30 min · Current or ever waking/interrupted	87.5%,	89.8%	LR 8.6	24/30 (diagnosed with axial inflammatory arthritis, not axSpA) 80%

	sleep due to back pain				
Queiro Peripheral Spain, 2018	· Aged ≤45 AND ≥2/3: · Joint pain · Morning stiffness in joints ≥30 min · Current or ever swollen joints	82.8%	87.4%	LR 6.6	26/36 (diagnosed with peripheral inflammatory arthritis, not axSpA) 72%
IBIS-Q Italy, 2020	· Chronic joint symptoms (for ≥3 months) AND ≥3/14 ever: · Heel pain · Back pain ≥3 months, not injury related · Swollen wrist without trauma · Night waking and walking due to back pain · Morning stiffness in back >30 min · Stiff neck for weeks · Pain in thigh to knee · Difficulty picking things up from floor without flexing knees · Dactylitis (fingers) lasting days · Difficulty tying laces · Difficulty buttoning shirt · Difficulty walking due to foot pain · Swollen, painful hands · Swollen, painful feet	92.7%	76.8%	AUC 0.88 positive predictive value 77%	56/181 with chronic joint symptoms 30%
DETAIL Italy, 2021	≥3/6: · Finger, toe, and/or other joint swollen, painful ever · Occasional dactylitis · Heel pain ever · Back pain ever ≥3 months, not injury related · Low back pain in morning and/or after resting, improves with exercise · Night waking due to low back pain			Post-test probability of SpA of 80% or more	
Lim UK, 2022	· Patients with CT-identified sacroiliitis AND · Chronic back pain (>3 months) and age of onset <45				11/27 with sacroiliitis 40.7%
Lim UK, 2023	· Chronic back pain (>3 months) and age of onset <45				4/82 4.9%

(*continued on next page*)

Table 2 (*continued*)

	Strategy	Referral algorithm/tool	Sensitivity	Specificity	Likelihood ratio (LR) or area under curve (AUC)	Patients diagnosed with axSpA/referred
	(equivalent to ASAS International, 2015)					
	ProSpA-CD UK, 2022	· Evidence of axSpA via scoring system on MRE images	0.60	0.85	AUC 0.78	
Psoriasis	Proft Germany, 2022	· Chronic back pain (≥3 months) and age of onset <45 AND · No treatment with biologics or targeted synthetic DMARD within last 12 weeks				14/100 (diagnosed with axSpA − 9 fulfilling ASAS criteria for axSpA, 13 fulfilling CASPAR for PsA)
CBP presenting to physical medicine and rehabilitation physicians, orthopedists, ophthalmologists	SUSPECT Belgium, 2017	· Chronic back pain (≥3 months) with onset <45 years and back pain at night AND · 1 ASAS SpA feature AND · ≥4/5: · Onset <40 years · Insidious onset · Improvement with exercise · No improvement with rest · Pain at night (improvement by getting up)				37/85 43.5% (15 had not met the referral criteria, but were referred based on clinical judgment)

are aware of SpA features, and develop referral criteria/pathways in collaboration with local rheumatology services. Knowledge of axSpA EMMs is continually advancing and specialists should remain up-to-date with the latest research. Within dermatology, hidradenitis suppurativa (acne inversa) has been newly associated with axSpA as a possible EMM [56,57].

Acute anterior uveitis

Prevalence estimates for SpA within AAU patients varies greatly between studies, from 20% to 78%, due to variations in study design, evaluation approach and characteristics of the AAU source population [58–68].

Different screening and referral strategies have been proposed for suspected axSpA in AAU. The Dublin Uveitis Evaluation Tool (DUET) algorithm developed by Haroon et al. prompts referral to rheumatology in AAU patients with CBP (>3 months) with an age of onset <45 years or those with joint pain requiring medical care, if testing positive for HLA–B27 or with presence of psoriasis [66]. The DUET algorithm reported high sensitivity and specificity (96% and 97% respectively, positive likelihood ratio 41.5 and negative likelihood ratio 0.03) for diagnosing SpA. Nevertheless, due to the high prevalence of axSpA among individuals presenting with AAU, other authors recommend that all patients with AAU and CBP with an age of onset <45 years should be referred to rheumatology, irrespective of HLA-B27 status [67,68]. This is in alignment with ASAS recommendations for the referral of patients with suspected axSpA by non–rheumatology specialists [46]. Sykes et al. estimated that in their cohort of AAU patients in Norwich, England, the sensitivity and specificity of the DUET algorithm were 52.9% and 67.9%, respectively – highlighting the variation in algorithm appropriateness based on local setting [67]. Almost half of new diagnoses referred via ASAS criteria were HLA-B27 negative without psoriasis or history of joint pains requiring a medical visit, and thus would have been missed via the DUET algorithm. A recent study by Rademacher et al. (2022) recommended that all AAU patients experiencing musculoskeletal symptoms should be referred to rheumatology for further evaluation, and that rheumatologists should consider that SpA may present atypically in AAU patients; with no/mild back pain starting >45 years, lasting for <3 months [58]. In this study, >20% of AAU patients ultimately diagnosed with SpA would have been missed if using the DUET (sensitivity 77.9%, specificity 42.2%) or ASAS (sensitivity 79.8%, specificity 27.7%) strategies.

Inflammatory bowel disease

A 2016 systematic review and meta-analysis reported that SpA may occur in up to 13% of individuals with IBD [69]. However, a more recent systematic review and meta-analysis (2019) highlighted the need for larger, more robust study designs harnessing sensitive imaging techniques and multivariable modeling to provide more accurate estimates [70]. Pooled prevalence of sacroiliitis, the most commonly reported axSpA feature, in IBD was reported as 21.0% (95% confidence interval, 17–26%; range 2%–68%) [70].

In the UK, a recent study by Lim et al. harnessed a validated computed tomography screening tool to prospectively identify sacroiliitis [71]. All patients with sacroiliitis were sent a screening questionnaire, with self-reported CBP (>3 months) and age of onset <45 years indicating rheumatology review. Of 27 patients with sacroiliitis, just 5 did not report CBP with an age of onset <45 years. 8 had a pre-existing axSpA diagnosis, and 3 had undiagnosed axSpA; thus, a total of 40.7% (11/27) had a rheumatologist-verified axSpA diagnosis.

A recent study explored the potential of magnetic resonance enterography (MRE) as a screening tool for axSpA in patients with IBD (ProSpA-CD) [72]. The authors concluded that MRE had good specificity (0.85), but poor sensitivity (0.60), suggesting that its use as a screening tool is limited. No significant association was found between the location of Crohn's disease or the presence of extra-intestinal manifestations and the occurrence of axSpA.

Two studies have been published in Italy, developing and testing novel screening questionnaires (IBIS-Q, DETAIL) to identify SpA in IBD, without the need for imaging prior to rheumatology referral. The IBIS-Q (IBD Identification of Spondyloarthritis Questionnaire, 14 items) was recently developed to identify SpA in IBD patients within an integrated combined multidisciplinary rheumatological-gastroenterology clinic [73]. The IBIS-Q could be completed quickly (maximum 5 minutes), and performed well for detection of axial and peripheral SpA (area under the curve 0.88 with 95% confidence

interval 0.83–0.93). A cut-off of 3 positive questions had a sensitivity of 92.7% and specificity of 76.8%, although further validation is needed. The DETection of Arthritis in Inflammatory bowel diseases (DETAIL, 6-items) questionnaire was recently validated in a multicenter cohort of patients with IBD enrolled at 11 gastroenterology units, whereby the combination of at least 3 questions yielded a post-test probability of SpA ≥80% [74]. The questionnaire was quick to administer (range 0.6–2.2 minutes), however, the presence of alternative diagnoses (e.g., osteoarthritis, fibromyalgia) represented a minor confounder. In Spain, Queiro et al. have proposed 2 promising, short screening questionnaires (3-items) to detect axial and peripheral inflammatory arthritis in patients with IBD [75]. The axial questionnaire yielded sensitivity of 87.5%, specificity of 89.8% and likelihood ratio of 8.6 in a population aged ≤45 years. For the peripheral questionnaire, the sensitivity, specificity and likelihood ratio were 82.8%, 87.4%, and 6.6, respectively.

Psoriasis and psoriatic arthritis

Although psoriasis is a frequent EMM of axSpA (prevalence estimated at 9.3% [76]), studies reporting prevalence of undiagnosed axSpA within psoriasis patients are lacking, outside of the aforementioned SASPIC cohort. With regards to psoriatic arthritis (PsA), depending on the definition used, evidence suggests that between 20% and 70% of individuals with PsA may experience axial disease (axPsA) [77–79]. In the ADIPSA (Axial Disease In PSoriatic Arthritis) study, 23.9% (49/201) of PsA patients fulfilled Modified New York criteria for AS; 72% (85/118) of psoriatic SpA cases and 7% (9/127) of peripheral PsA cases fulfilled the ASAS clinical or radiographic imaging criteria (full criteria not assessed due to lack of MRI) [79].

Until recently, algorithms for identifying axial involvement in psoriasis patients were lacking. However, a simple dermatologist-centered screening tool has recently been proposed in a study by Proft et al. in Germany, to identify suspected PsA and axPsA [80]. Patients were eligible for rheumatology referral if aged ≥18 years, with a confirmed diagnosis of psoriasis, CBP (≥3 months) with onset <45 years, and no treatment with biologic/targeted synthetic DMARD within the last 12 weeks. Of those qualifying for referral, 14% (14/100, including 3 with axial and peripheral involvement) were ultimately diagnosed with axPsA by the treating rheumatologist after clinical examination and interrogation of imaging, genetic and laboratory results. All patients with axPsA presented with active inflammatory and/or structural changes in the sacroiliac joints and/or spine on imaging. ASAS criteria for axSpA were fulfilled in 9/14 (64.3%) axPsA patients. 5% (5/100) of those referred were diagnosed with peripheral PsA solely. Of these 19 patients diagnosed with PsA, all but one (with axPsA) fulfilled the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria for PsA.

A consensus definition of axPsA remains lacking, as do robust longitudinal evaluations and comparisons of the natural history of varying axSpA/axPsA/peripheral PsA disease entities, which should be a priority on the future research agenda [81]. Recent work from Regierer et al. in Germany suggests that axPsA (fulfilling clinical and/or imaging definitions) differs significantly from axSpA + psoriasis in its clinical manifestations and thus the two should be considered distinct entities [82].

Improved assessment in rheumatology

Uptake of existing diagnostic algorithms to support clinical judgment

Although improved identification and referral of axSpA in primary and secondary care will no doubt reduce diagnostic delay in axSpA, swift referral to rheumatology does not guarantee swift diagnosis. The complex, heterogeneous nature of the disease makes diagnosis challenging, and there is no single definitive test or diagnostic criteria that can be used for axSpA. Diagnosis must be led by clinical judgment, informed by physical examination, investigations such as blood tests (for inflammatory markers, HLA-B27) and imaging (x-rays and MRI scans), and interpretation of reported symptoms and clinical history. Nevertheless, uptake of existing, practical, evidence-based algorithms, may be useful to inform diagnostic investigations (e.g., Carvalho & Machado, 2019 [83]). The OptiRef study in Germany has recently informed development of a data-driven calculator that can be used by rheumatologists to support a diagnosis through estimating disease probability, based on presence or absence of clinical, laboratory and imaging parameters and anticipated local prevalence of axSpA in those referred (https://www.axspa.de/calculator.html) [84].

Uptake of recommendations for acquisition and interpretation of imaging

Interpretation of MRI remains challenging in suspected axSpA, and will depend on the expertise of the radiologist. Promising evidence from the UK suggests that development and uptake of consensus imaging recommendations is likely to improve/standardize acquisition and interpretation of appropriate imaging in suspected axSpA, and thus facilitate more timely axSpA diagnosis (Table 3) [27,35,85–89]. Close collaboration between rheumatologists and musculoskeletal radiologists is vital [34,86], and additional training of rheumatologists and radiologists may be required [90]. The implementation of specialist axSpA clinics that regularly collaborate with specialist musculoskeletal radiologists would improve awareness of axSpA features and implementation of rheumatology/radiology multidisciplinary teams are useful for discussing challenging cases [71,88,89]. ASAS have recently developed consensus recommendations to improve and standardize communication between radiologists and rheumatologists around requesting and reporting imaging in suspected axSpA, to improve diagnoses [85]. Future solutions to support the interpretation of imaging may include a move towards the use quantitative imaging biomarkers or the development of algorithms/tools to support the semi-automated detection of key axSpA features [91–95]. However, further research is needed before they can be translated to or used in clinical practice.

Table 3
Improvements in UK rheumatology/radiology services following the introduction of national consensus imaging recommendations for axSpA [86].

Pre-BRITSpA consensus imaging recommendations [27,35,87]	Post-BRITSpA consensus imaging recommendations *NASS 2023 report* [88,89]
× In 2017, of 269 surveyed radiologists, just 75% were aware of the term axSpA; 31% and 25% were aware of ASAS definitions for positive MRI of the sacroiliac joints and spine, respectively [87] × In 2016, a survey indicated that just one-third of musculoskeletal radiologists performed the EULAR-recommended MRI protocol for axSpA [27,35]	*Promising improvements versus 2016/2017:* ✓ Significant improvements in awareness of axSpA among musculoskeletal radiologists: 97% now recognizing the term axSpA; 80% and 71% aware of ASAS definitions for positive MRI of the sacroiliac joints and spine, respectively ✓ Improved uptake of recommended imaging protocols (69%) *Outstanding room for improvement:* × Just 35% of responding Trusts/Health boards reported weekly meetings between radiology and rheumatology (20% meeting fortnightly) × Only 47% of Trusts offered a specialist axSpA clinic × Timely access to MRI had deteriorated and one-third of Trusts (34%, 33% and 29%, respectively) reported scans being interpreted internally by a non-musculoskeletal radiologist, outsourced to a specialist musculoskeletal radiologist or outsourced to a non-musculoskeletal radiologist *Evidence supporting our recommendations:* * Presence of a specialist axSpA clinic and at least fortnightly rheumatology/radiology meetings were associated with the following factors likely to improve timely diagnosis of axSpA: - greater familiarity with the term axSpA - greater familiarity with the national BRITSpA imaging guidance - greater awareness of features contributing to a positive MRI * Use of non-musculoskeletal radiologists (internal or outsourced) led to lower reported familiarity with the national imaging guidance or awareness of recommendations on positive MRI features – thus likely to have a detrimental impact on time to diagnosis

Implementation of multidisciplinary teams, musculoskeletal triage services, and specialist axSpA clinics

Organizational changes within rheumatology may help improve diagnostic delay in axSpA; whereby the implementation of multidisciplinary teams, musculoskeletal triage services, or early SpA/IBP clinics could raise awareness of axSpA and support timely diagnoses. In Italy, the "Early SpA Clinic" project across 19 rheumatology centers used in-depth organizational analyses to identify areas for improvement, ultimately resulting in changes such as increased collaboration with other hospital services for diagnostic slots (e.g., radiology) and the use of joint pathways with other departments (e.g., dermatology) [96]. Implemented changes resulted in a 23% decrease in waiting lists, a 22% decrease in referral time, and a 20% increase in rheumatology diagnoses (11% increase in SpA diagnoses, specifically). In Ontario, Canada, an interprofessional approach to axSpA screening via rapid access clinics for low back pain (https://www.lowbackrac.ca/) has demonstrated encouraging results in a recent study by Passalent et al. [97]. Since 2018, these clinics have facilitated early specialist screening/triage by extended-scope practitioners (advanced practice physiotherapists certified in arthritis care). Passalent et al. reported 82.7% agreement of axSpA risk assignment between rheumatologists and extended-scope practitioners. The reported sensitivity of the screening/triage process was 68%, the specificity was 90%, the positive predictive value was 80% (appropriate referrals to rheumatology), and the negative predictive value was 84% (appropriate diversions from rheumatology); demonstrating the potential of such roles in streamlining rheumatology services to facilitate earlier diagnoses.

In Germany, a recent study by Knitza et al. developed a machine learning algorithm to facilitate automated triaging of rheumatology referrals via the online referral system Rheport [98]. The authors reported that the diagnostic accuracy of the current Rheport algorithm for inflammatory rheumatic disease (area under the receiver operating curve [AUROC]: 0.534) could be improved with all developed machine learning models (AUROC: 0.630–0.737). Aiming for 90% sensitivity, the logistic regression model could double the specificity from 17% to 33%. Although the models were limited by patient-reported subjective data, with the incorporation of laboratory testing/imaging results, machine learning models could in the future improve and standardise the diagnostic accuracy of rheumatology triage services.

Campaigns tackling diagnostic delay

In the UK, in June 2021, the National Axial Spondyloarthritis Society (NASS) launched their pioneering Gold Standard Time to Diagnosis program; the world's first to set a gold standard for the diagnosis of axSpA. Their seminal program document outlines a roadmap to reducing diagnostic delay in the UK – developed through a national consultation process with people living with axSpA, HCPs, professional bodies, communication experts and commissioners [99]. The bold roadmap outlines 4 key contributors to diagnostic delay, and proposes solutions to tackle each. Governmental approaches, supported by the All Party Parliamentary Group for axSpA, will be harnessed, including the implementation of legislation, regulation, national care recommendations, and performance management systems; whilst simultaneously supporting hospital/HCP teams to improve care locally and develop best practice. Ensuring that awareness of axSpA permeates both public and HCP consciousness is a key part of the campaign. The Act on Axial SpA website provides resources for individuals who think they may have undiagnosed axSpA, and for HCPs in rheumatology, primary and secondary care (https://www.actonaxialspa.com/). By October 2021 (within 4 months of program launch), NASS' campaign had featured in 11 national media publications with a combined reach of over 101 million, and 1,264 people had used the online symptom checker (https://www.actonaxialspa.com/symptoms-checker/) [100].

Also in June 2021, the Axial Spondyloarthritis International Federation (ASIF) launched their global call to action and burden statement, as part of their international Delay to Diagnosis campaign [101]. In this document, ASIF propose key recommendations to be implemented worldwide but at a national/local level, to reduce diagnostic delay in axSpA. The report is a call to action for all stakeholders involved in the organization, delivery, and championing of axSpA care, to help reduce the delay to diagnosis for axSpA patients worldwide.

Summary

Recent estimates of median diagnostic delay suggest that globally, an individual with axSpA will wait between 2 and 6 years for a diagnosis. This time presents a window of opportunity for earlier diagnosis and earlier intervention; which would likely have a profound impact clinically, on the individual, and potentially societally in terms of work productivity and healthcare cost savings. There are many proposed/published strategies for improving diagnostic delay in axSpA, which require further testing in future research, across different healthcare settings. Simple, non-burdensome strategies or automated prompts via EHRs will be key. Rheumatology services should work directly with local service providers in primary (such as GP practices and musculoskeletal interface services, physiotherapy services) and secondary care (orthopedics, ophthalmology, gastroenterology, dermatology, radiology) to establish clear referral criteria and pathways for suspected axSpA, appropriate to the local setting. Barriers to improved diagnosis include lack of healthcare professional awareness of axSpA features, in addition to a lack of time/incentive to adopt proposed screening tools and strategies, highlighting the need for further robust data-driven evidence and national endorsement of these strategies to support/improve adoption. In coming years, it will be critical to assess the impact of recently introduced national, regional, and local initiatives and campaigns, to provide evidence for their impact on diagnostic delay and the individual journey for the patient. Although diagnostic delay in axSpA remains a global problem in rheumatology, it is not a lost battle. As clinicians, it is therefore of utmost importance to strive for improved education of HCPs across both primary and secondary care; to engage with initiatives/campaigns to improve diagnostic delay; and to advocate for the testing and implementation of published referral strategies, recommendations, and quality standards, to ultimately improve the lives of patients.

Practice points

- Delayed diagnosis in axSpA remains an extensive worldwide problem; recent estimates of the median diagnostic delay suggesting that an individual with axSpA will likely wait between 2 and 6 years for a diagnosis
- Evidence suggests that earlier identification and referral of suspected axSpA and the resultant earlier diagnosis and treatment, would likely improve both clinical outcomes for the individual and economic outcomes for the society
- Widespread implementation of education, training and simple non-burdensome referral strategies/prompts (within primary care and specialties treating EMMs) are recommended to improve diagnostic delay in axSpA
- Rheumatology services should work directly with local service providers in primary (such as GP practices and musculoskeletal interface services, physiotherapy services) and secondary care (orthopedics, ophthalmology, gastroenterology, dermatology, radiology) to establish clear referral criteria and pathways for suspected axSpA, appropriate to the local setting

Research agenda

- Further rigorous research is required to establish with greater certainty the patient groups most vulnerable to experiencing diagnostic delay, and to provide further robust data on the long-term impact of diagnostic delay on clinical and economic outcomes
- There are many published strategies for improving diagnostic delay in axSpA, which require further robust evaluation, to build a data-driven evidence base for others to draw upon and to support (and encourage) their widespread implementation
- In coming years, it will be critical to assess the impact of recently introduced national, regional, and local initiatives and campaigns, to provide evidence for their impact on diagnostic delay, clinical/economic outcomes, and most importantly, the individual journey for the patient

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References*

*[1] Zhao SS, Pittam B, Harrison NL, et al. Diagnostic delay in axial spondyloarthritis: a systematic review and meta-analysis. Rheumatology 2021;60(4):1620–8.

*[2] Hay CA, Packham J, Ryan S, et al. Diagnostic delay in axial spondyloarthritis: a systematic review. Clin Rheumatol 2022;41(7):1939–50.

*[3] Yi E, Ahuja A, Rajput T, et al. Clinical, economic, and humanistic burden associated with delayed diagnosis of axial spondyloarthritis: a systematic review. Rheumat Ther 2020.

[4] Milota T, Hurnakova J, Pavelka K, et al. Delayed treatment with a tumor necrosis factor alpha blocker associated with worse outcomes in patients with spondyloarthritis: data from the Czech National Registry ATTRA. Ther Adv Musculosk Dis 2022;14. 1759720X221081649.

[5] Ogdie A, Benjamin Nowell W, Reynolds R, et al. Real-world patient experience on the path to diagnosis of ankylosing spondylitis. Rheumatol Ther 2019;6(2):255–67.

*[6] Dube CE, Lapane KL, Ferrucci KA, et al. Personal experiences with diagnostic delay among axial spondyloarthritis patients: a qualitative study. Rheumatol Ther 2021;8(2):1015–30.

[7] Martindale J, Goodacre L. The journey to diagnosis in AS/axial SpA: the impact of delay. Muscoskel Care 2014;12(4):221–31.

[8] Lapane KL, Dubé C, Ferrucci K, et al. Patient perspectives on health care provider practices leading to an axial spondyloarthritis diagnosis: an exploratory qualitative research study. BMC Fam Pract 2021;22(1):251.

[9] Jordan A, Family H, Blaxall K, et al. Use of complementary and alternative medicine in axial spondyloarthritis: a qualitative exploration of self-management. J Clin Med 2019;8(5).

[10] Sykes M, Doll H, Gaffney K. Comment on: 'Diagnostic delay in patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis: results from the Danish nationwide DANBIO registry' by Sørensen et al</em&gt. Ann Rheum Dis 2014;73(7):e44–.

[11] Sun Y, Hu Z, Zhang X, et al. Improvement of delayed diagnosis of ankylosing spondylitis in a Chinese population. Chin Med J 2022;135(18):2256–7.

[12] Crossfield SSR, Marzo-Ortega H, Kingsbury SR, et al. Changes in ankylosing spondylitis incidence, prevalence and time to diagnosis over two decades. RMD Open 2021;7(3).

[13] Hamilton L, Gilbert A, Skerrett J, et al. Services for people with ankylosing spondylitis in the UK–a survey of rheumatologists and patients. Rheumatology 2011;50(11):1991–8.

[14] Derakhshan MH, Pathak H, Cook D, et al. Services for spondyloarthritis: a survey of patients and rheumatologists. Rheumatology 2018;57(6):987–96.

[15] Korotaeva T, Dina O, Holdsworth E, et al. Investigating diagnosis, treatment, and burden of disease in patients with ankylosing spondylitis in Central Eastern Europe and the United States: a real-world study. Clin Rheumatol 2021;40(12):4915–26.

[16] Garrido-Cumbrera M, Gratacós J, Collantes-Estevez E, et al. A benchmarking study evaluating axial spondyloarthritis burden in Spain and other European countries. Results from the Spanish Atlas and the European Map of axial spondyloarthritis (EMAS) studies. Int J Rheum Dis 2021;24(9):1127–36.

[17] Redeker I, Callhoff J, Hoffmann F, et al. Determinants of diagnostic delay in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. Rheumatology 2019;58(9):1634–8.

[18] Magrey M, Walsh JA, Flierl S, et al. The international Map of axial spondyloarthritis survey: a US patient perspective on diagnosis and burden of disease. ACR Open Rheumat 2023;5(5):264–76.

* The most important ten references have been denoted with asterisk.

[19] Sykes MP, Doll H, Sengupta R, Gaffney K. Delay to diagnosis in axial spondyloarthritis: are we improving in the UK? Rheumatology 2015;54(12):2283–4.
[20] Aggarwal R, Malaviya AN. Diagnosis delay in patients with ankylosing spondylitis: factors and outcomes–an Indian perspective. Clin Rheumatol 2009;28(3):327–31.
[21] Masson Behar V, Dougados M, Etcheto A, et al. Diagnostic delay in axial spondyloarthritis: a cross-sectional study of 432 patients. Joint Bone Spine 2017;84(4):467–71.
*[22] Garrido-Cumbrera M, Poddubnyy D, Gossec L, et al. Gender differences in patient journey to diagnosis and disease outcomes: results from the European Map of Axial Spondyloarthritis (EMAS). Clin Rheumatol 2021;40(7):2753–61.
[23] Chimenti M-S, Alten R, D'Agostino M-A, et al. Sex-associated and gender-associated differences in the diagnosis and management of axial spondyloarthritis: addressing the unmet needs of female patients. RMD Open 2021;7(3): e001681.
[24] Barnett R, Ingram T, Sengupta R. Axial spondyloarthritis 10 years on: still looking for the lost tribe. Rheumatology 2020;59(Suppl4):iv25–37.
[25] Gaffney K, Webb D, Sengupta R. Delayed diagnosis in axial spondyloarthritis—how can we do better? Rheumatology 2021;60(11):4951–2.
[26] Hall AM, Scurrey SR, Pike AE, et al. Physician-reported barriers to using evidence-based recommendations for low back pain in clinical practice: a systematic review and synthesis of qualitative studies using the Theoretical Domains Framework. Implement Sci 2019;14(1):49.
[27] Derakhshan MH, Pathak H, Cook D, et al. Services for spondyloarthritis: a survey of patients and rheumatologists. Rheumatology 2018;57(6):987–96.
[28] Mathieson HR, Merashli M, Gaffney K, et al. Poor awareness of inflammatory back pain and axial spondyloarthritis among secondary care specialists. Clin Rheumatol 2016;35(10):2627–8.
[29] Jois RN, Macgregor AJ, Gaffney K. Recognition of inflammatory back pain and ankylosing spondylitis in primary care. Rheumatology 2008;47(9):1364–6.
[30] Yong CY, Hamilton J, Benepal J, et al. Awareness of axial spondyloarthritis among chiropractors and osteopaths: findings from a UK Web-based survey. Rheumatol Adv Pract 2019;3.
[31] Danve A, Deodhar A. Axial spondyloarthritis in the USA: diagnostic challenges and missed opportunities. Clin Rheumatol 2019;38(3):625–34.
[32] Tant L, Delmotte N, Van den Enden M, et al. High prevalence of undiagnosed axial spondyloarthritis in patients with chronic low back pain consulting non-rheumatologist specialists in Belgium: SUSPECT study. Rheumat Ther 2017;4(1): 121–32.
[33] Steen E, McCrum C, Cairns M. Physiotherapists' awareness, knowledge and confidence in screening and referral of suspected axial spondyloarthritis: a survey of UK clinical practice. Muscoskel Care 2021;19(3):306–18.
[34] Bennett AN, Marzo-Ortega H, Kaur-Papadakis D, Rehman A. The use of magnetic resonance imaging in axial spondyloarthritis: time to bridge the gap between radiologists and rheumatologists. J Rheumatol 2017;44(6):780–5.
[35] Mandl P, Navarro-Compán V, Terslev L, et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheumat Dis 2015;74(7):1327–39.
[36] Bittar M, Khan MA, Magrey M. Axial spondyloarthritis and diagnostic challenges: over-diagnosis, misdiagnosis, and under-diagnosis. Curr Rheumatol Rep 2023;25(3):47–55.
[37] Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis 2023;82(1):19–34.
[38] Magrey M, Yi E, Wolin D, et al., editors. Recognition of inflammatory back pain by US healthcare providers and barriers to specialist referral. Wiley 111 River St, Hoboken 07030-5774, NJ USA: Arthritis & Rheumatology; 2019.
[39] van Onna M, Gorter S, van Meerendonk A, van Tubergen A. General practitioners' perceptions of their ability to identify and refer patients with suspected axial spondyloarthritis: a qualitative study. J Rheumatol 2014;41(5): 897–901.
[40] Adizie T, Elamanchi S, Prabu A, et al. Knowledge of features of inflammatory back pain in primary care in the West Midlands: a cross-sectional survey in the United Kingdom. Rheumatol Int 2018;38(10):1859–63.
[41] Lapane KL, Shridharmurthy D, Khan S, et al. Primary care physician perspectives on screening for axial spondyloarthritis: a qualitative study. PLoS One 2021;16(5):e0252018.
[42] Steen E, McCrum C, Cairns M. A UK survey evaluation of First Contact Practitioners' and musculoskeletal physiotherapists' confidence, recognition, and referral of suspected axial spondyloarthritis. Muscoskel Care 2023;21(2): 380–96.
[43] van Onna M, Gorter S, Maiburg B, et al. Education improves referral of patients suspected of having spondyloarthritis by general practitioners: a study with unannounced standardised patients in daily practice. RMD Open 2015;1(1): e000152.
[44] van Onna M, Gorter S, Maiburg B, et al. GPs' patterns of clinical assessment when faced with a patient suspected for spondyloarthritis: a prospective educational intervention study. BJGP Open 2017;1(1):bjgpopen17X100689.
[45] Coath FL, Gaffney K. Inflammatory back pain: a concept, not a diagnosis. Curr Opin Rheumatol 2021;33(4):319–25.
[46] Poddubnyy D, van Tubergen A, Landewé R, et al. Development of an ASAS-endorsed recommendation for the early referral of patients with a suspicion of axial spondyloarthritis. Ann Rheumat Dis 2015;74(8):1483–7.
[47] Walsh JA, Rozycki M, Yi E, Park Y. Application of machine learning in the diagnosis of axial spondyloarthritis. Curr Opin Rheumatol 2019;31(4):362–7.
[48] Kennedy J, Kennedy N, Cooksey R, et al. Predicting a diagnosis of ankylosing spondylitis using primary care health records-A machine learning approach. PLoS One 2023;18(3):e0279076.
[49] Zhao SS, Hong C, Cai T, et al. Incorporating natural language processing to improve classification of axial spondyloarthritis using electronic health records. Rheumatology 2020;59(5):1059–65.
[50] Sengupta R, Narasimham S, Mato BS, et al. P261 Early and accurate diagnosis of patients with axial spondyloarthritis using machine learning: a predictive analysis from electronic health records in the United Kingdom. Rheumatology 2022;61(Supplement_1). keac133.260.

[51] Deodhar A, Rozycki M, Garges C, et al. Use of machine learning techniques in the development and refinement of a predictive model for early diagnosis of ankylosing spondylitis. Clin Rheumatol 2020;39:975–82.
*[52] Proft F, Spiller L, Redeker I, et al. Comparison of an online self-referral tool with a physician-based referral strategy for early recognition of patients with a high probability of axial spa. Semin Arthritis Rheum 2020;50(5):1015–21.
[53] McAllister K, Goodson N, Warburton L, Rogers G. Spondyloarthritis: diagnosis and management: summary of NICE guidance. BMJ 2017;356:j839.
[54] Maksymowych WP, Carmona R, Yeung J, et al. THU0393 performance of the ASAS classification criteria presenting with undiagnosed back pain? Data from the screening in axial spondyloarthritis in psoriasis, iritis, and colitis (SASPIC) cohort. Ann Rheum Dis 2019;78(Suppl 2):482.
[55] Maksymowych WP, Carmona R, Yeung J, et al. SAT0339 what is the impact of imaging on diagnostic ascertainment of patients presenting with undiagnosed back pain and what is the impact of central evaluation? Data from the screening in axial spondyloarthritis in psoriasis, iritis, and colitis (SASPIC) cohort. Ann Rheum Dis 2019;78(Suppl 2):1248–9.
[56] Schneider-Burrus S, Witte-Haendel E, Christou D, et al. High prevalence of back pain and axial spondyloarthropathy in patients with hidradenitis suppurativa. Dermatology 2016;232(5):606–12.
[57] Rondags A, Arends S, Wink FR, et al. High prevalence of hidradenitis suppurativa symptoms in axial spondyloarthritis patients: a possible new extra-articular manifestation. Semin Arthritis Rheum 2019;48(4):611–7.
*[58] Rademacher J, Müllner H, Diekhoff T, et al. Keep an Eye on the back: spondyloarthritis in patients with acute anterior uveitis. Arthritis Rheumatol 2023;75(2):210–9.
[59] Juanola X, Santamaría EL, Cordero-Coma M, Group SW. Description and prevalence of spondyloarthritis in patients with anterior uveitis: the SENTINEL interdisciplinary collaborative project. Ophthalmology 2016;123(8):1632–6.
[60] Bubova K, Hasikova L, Mintalova K, et al. The prevalence of MRI-defined sacroiliitis and classification of spondyloarthritis in patients with acute anterior uveitis: a longitudinal single-centre cohort study. Diagnostics 2022;12(1):161.
[61] Bolletta E, Macchioni P, Citriniti G, et al. Clinical features and prevalence of spondyloarthritis in a cohort of Italian patients presenting with acute nongranulomatous anterior uveitis. J Immun Res 2022:2022.
[62] Wach J, Maucort-Boulch D, Kodjikian L, et al. Acute anterior uveitis and undiagnosed spondyloarthritis: usefulness of Berlin criteria. Graefes Arch Clin Exp Ophthalmol 2015;253:115–20.
[63] Monnet D, Breban M, Hudry C, et al. Ophthalmic findings and frequency of extraocular manifestations in patients with HLA-B27 uveitis: a study of 175 cases. Ophthalmology 2004;111(4):802–9.
[64] Chung YM, Liao HT, Lin KC, et al. Prevalence of spondyloarthritis in 504 Chinese patients with HLA-B27-associated acute anterior uveitis. Scand J Rheumatol 2009;38(2):84–90.
[65] Oliveira TL, Maksymowych WP, Lambert RG, et al. Sacroiliac joint magnetic resonance imaging in asymptomatic patients with recurrent acute anterior uveitis: a proof-of-concept study. J Rheumatol 2017;44(12):1833–40.
[66] Haroon M, O'Rourke M, Ramasamy P, et al. A novel evidence-based detection of undiagnosed spondyloarthritis in patients presenting with acute anterior uveitis: the DUET (Dublin Uveitis Evaluation Tool). Ann Rheumat Dis 2015;74(11):1990–5.
[67] Sykes MP, Hamilton L, Jones C, Gaffney K. Prevalence of axial spondyloarthritis in patients with acute anterior uveitis: a cross-sectional study utilising MRI. RMD Open 2018;4(1):e000553.
[68] van Bentum RE, Verbraak FD, Wolf S, et al. High prevalence of previously undiagnosed axial spondyloarthritis in patients referred with anterior uveitis and chronic back pain: the SpEYE study. J Rheumatol 2022;49(7):680–7.
[69] Karreman MC, Luime JJ, Hazes JMW, Weel AEAM. The prevalence and incidence of axial and peripheral spondyloarthritis in inflammatory bowel disease: a systematic review and meta-analysis. J. Crohn's Colitis 2016;11(5):631–42.
[70] Evans J, Sapsford M, McDonald S, et al. Prevalence of axial spondyloarthritis in patients with inflammatory bowel disease using cross-sectional imaging: a systematic literature review. Ther Adv MusculoskelDis 2021;13.1759720x21996973.
[71] Lim CSE, Hamilton L, Low SBL, et al. Identifying axial spondyloarthritis in patients with inflammatory bowel disease using computed tomography. J Rheumatol 2022. jrheum.220362.
[72] Evans J, Raine T, Mcdonald S, et al. POS0965 magnetic resonance enterography as a screening tool for axial spondyloarthritis in crohn's disease: a prospective single-center cross-sectional observational study using mre screening followed by clinical assessment (ProSpA-CD). Ann Rheum Dis 2022;81(Suppl 1):789–90.
[73] Variola A, Zanolin ME, Cipriano G, et al. The IBIS-Q [IBd identification of spondyloarthritis questionnaire]: a novel tool to detect both axial and peripheral arthritis in inflammatory bowel disease patients. J Crohns Colitis 2020;14(12):1680–6.
[74] Benfaremo D, Luchetti MM, Carlo MD, et al. Multicenter validation of the DETAIL questionnaire for the screening of spondyloarthritis in patients with inflammatory bowel diseases. J Rheumatol 2021;48(2):179–87.
[75] Queiro R, Rodríguez-Caminero S, Riestra S, et al. Performance of two screening questionnaires for inflammatory arthritis in patients with inflammatory bowel disease. BioMed Res Int 2018;2018:8618703.
[76] Stolwijk C, van Tubergen A, Castillo-Ortiz JD, Boonen A. Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis. Ann Rheumat Dis 2015;74(1):65–73.
[77] Gottlieb AB, Merola JF. Axial psoriatic arthritis: an update for dermatologists. J Am Acad Dermatol 2021;84(1):92–101.
[78] Mease PJ, Palmer JB, Liu M, et al. Influence of axial involvement on clinical characteristics of psoriatic arthritis: analysis from the corrona psoriatic arthritis/spondyloarthritis registry. J Rheumatol 2018;45(10):1389–96.
[79] Jadon DR, Sengupta R, Nightingale A, et al. Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis. Ann Rheumat Dis 2017;76(4):701–7.
[80] Proft F, Lüders S, Hunter T, et al. Early identification of axial psoriatic arthritis among patients with psoriasis: a prospective multicentre study. Ann Rheum Dis 2022;81(11):1534–40.
[81] Proft F, Käding H. Same, same or different? Commonalities and differences between spondyloarthritis and its subsets of axial and peripheral spondyloarthritis with psoriatic arthritis and its diverse phenotypes. RMD Open 2023;9(2).

[82] Regierer AC, Weiß A, Proft F, et al. Comparison of patients with axial PsA and patients with axSpA and concomitant psoriasis: an analysis of the German register RABBIT-SpA. RMD Open 2023;9(1).
[83] Carvalho PD, Machado PM. How to investigate: early axial spondyloarthritis. Best Pract Res Clin Rheumatol 2019; 33(4):101427.
[84] Poddubnyy D, Proft F, Spiller L, et al. Diagnosing axial spondyloarthritis: estimation of the disease probability in patients with a priori different likelihoods of the diagnosis. Rheumatology 2021;60(11):5098–104.
[85] Diekhoff T, Eshed I, Giraudo C, et al. ASAS recommendations for requesting and reporting imaging in patients with suspected axial spondyloarthritis. 74(Suppl. 9).. In: ABSTRACT SUPPLEMENT ACR convergence 2022, November 10–14, 2022, Philadelphia, PA; 2022.
[86] Bray TJP, Jones A, Bennett AN, et al. Recommendations for acquisition and interpretation of MRI of the spine and sacroiliac joints in the diagnosis of axial spondyloarthritis in the UK. Rheumatology 2019;58(10):1831–8.
[87] Bennett AN, Marzo-Ortega H, Kaur-Papadakis D, Rehman A. The use of magnetic resonance imaging in axial spondyloarthritis: time to bridge the gap between radiologists and rheumatologists. J Rheumatol 2017;44(6):780–5.
[88] National Axial Spondyloarthritis Society. The use of MRI in the diagnosis of axial SpA: a UK survey of protocols for Magnetic Resonance Imaging (MRI) in the diagnostic process of Axial Spondyloarthritis (axial SpA). Last accessed 28th June 2023, https://nass.co.uk/wp-content/uploads/2023/04/NASS-uses-of-MRI-DIGITAL-version.pdf. 2023.
[89] National Axial Spondyloarthritis Society & All-Party Parliamentary Group for Axial Spondyloarthritis. Axial SpA in England: are NHS services improving?. Last accessed 6th July 2023, https://nass.co.uk/wp-content/uploads/2022/11/NASS_APPG-report_FINAL.pdf. 2023.
[90] Poddubnyy D, Sieper J. Current unmet needs in spondyloarthritis. Curr Rheumatol Rep 2019;21(9):43.
[91] Van Den Berghe T, Babin D, Chen M, et al. Neural network algorithm for detection of erosions and ankylosis on CT of the sacroiliac joints: multicentre development and validation of diagnostic accuracy. European radiology; 2023.
[92] Kucybała I, Tabor Z, Polak J, et al. The semi-automated algorithm for the detection of bone marrow oedema lesions in patients with axial spondyloarthritis. Rheumatol Int 2020;40(4):625–33.
[93] Lin KYY, Peng C, Lee KH, et al. Deep learning algorithms for magnetic resonance imaging of inflammatory sacroiliitis in axial spondyloarthritis. Rheumatology 2022;61(10):4198–206.
[94] Thorley N, Jones A, Ciurtin C, et al. Quantitative magnetic resonance imaging (qMRI) in axial spondyloarthritis. Br J Radiol 2023;96(1144):20220675.
[95] Bressem KK, Vahldiek JL, Adams L, et al. Deep learning for detection of radiographic sacroiliitis: achieving expert-level performance. Arthritis Res Ther 2021;23(1):106.
[96] D'Angelo S, Afeltra A, Atzeni F, et al. Early spondyloarthritis clinic: organizational improvements in the patient journey. Front Med 2022;9.
*[97] Passalent L, Sundararajan K, Perruccio AV, et al. Bridging the gap between symptom onset and diagnosis in axial spondyloarthritis. Arthritis Care Res 2022;74(6):997–1005.
[98] Knitza J, Janousek L, Kluge F, et al. Machine learning-based improvement of an online rheumatology referral and triage system. Front Med 2022;9:954056.
*[99] Webb D, Swingler L, Barnett R, et al. Act on axial SpA: a gold standard time to diagnosis. Last Accessed 28th June 2023, https://www.actonaxialspa.com/wp-content/uploads/2021/06/NASS_A-Gold-Standard-time-to-diagnosis_DIGITAL_28pp_compressed.pdf. 2021.
[100] Marshall L, Webb D, MacAulay F, et al. P270 'Act on Axial SpA': a gold standard time to diagnosis. Rheumatology 2022; 61(Supplement_1). keac133.269.
*[101] Axial Spondyloarthritis International Federation. The unacceptable delay in axial spondyloarthritis diagnosis: a global call to action. Last accessed 28th June 2023, https://jointhealth.org/pdfs/ASIF-Delay-to-Diagnosis-Report.pdf. 2021.