



Comparison between radiography and magnetic resonance imaging for the detection of sacroiliitis in the initial diagnosis of axial spondyloarthritis: a cost-effectiveness study

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Abstract

Objective The purpose of our study was to determine the cost-effectiveness of radiography and MRI-based imaging strategies for the initial diagnosis of sacroiliitis in a hypothetical population with suspected axial spondyloarthritis.

Materials and methods A decision analytic model from the health care system perspective for patients with inflammatory back pain suggestive of axial spondyloarthritis was used to evaluate the incremental cost-effectiveness of 3 imaging strategies for the sacroiliac joints over a 3-year horizon: radiography, MRI, and radiography followed by MRI. Comprehensive literature search and expert opinion provided input data on cost, probability, and utility estimates. The primary effectiveness outcome was quality-adjusted life-years (QALYs), with a willingness-to-pay threshold set to \$100,000/QALY gained (2018 American dollars).

Results Radiography was the least costly strategy (\$46,220). Radiography followed by MRI was the most effective strategy over a 3-year course (2.64 QALYs). Radiography was the most cost-effective strategy. MRI-based and radiography followed by MRI-based strategies were not found to be cost-effective imaging options for this patient population. Radiography remained the most cost-effective strategy over all willingness-to-pay thresholds up to \$100,000.

Conclusion Radiography is the most cost-effective imaging strategy for the initial diagnosis of sacroiliitis in patients with inflammatory back pain suspicious for axial spondyloarthritis.

Keywords Cost-effectiveness · Sacroiliitis · Axial spondyloarthritis · Radiography · Magnetic resonance imaging

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Introduction

Axial spondyloarthritis (axSpA) is a rheumatic disease of the axial skeleton which affects about 0.7% of the US population [2]. Imaging of the sacroiliac joints plays a major role in the diagnosis of axSpA, since the disease usually begins in the sacroiliac joints [3]. AxSpA can be classified as radiographic or non-radiographic, which may represent a continuous disease spectrum [4]. According to the Assessment in SpondyloArthritis international Society (ASAS) criteria for axSpA, patients with back pain for at least 3 months starting at <45 years of age with sacroiliitis on imaging plus ≥ 1 axSpA feature or with positive human leukocyte antigen B27 (HLA-B27) plus ≥ 2 additional axSpA features may be classified as having axSpA [5].

Radiography is generally the first recommended imaging modality for the evaluation of axSpA [4, 6], unless the patient is young with a short duration of symptoms, in which case MRI may be considered as the first modality of choice [7]. If clinical features and radiographs fail to establish the suspected diagnosis of axSpA, MRI of the sacroiliac joints is recommended [7]. Sacroiliitis can be diagnosed by radiographs, when at least grade 2 bilaterally or grade 3 unilaterally according to the modified New York grading [3], or on MRI when active inflammation is present. According to the modified New York grading system, grade 0 signifies normal sacroiliac joints, grade 1 shows suspicious changes such as blurring of the joint margins, grade 2 demonstrates minimal abnormalities (small areas of sclerosis or localized erosion, with preserved joint space), grade 3 implies unequivocal abnormalities (sclerosis, erosions, joint space widening, narrowing or partial ankylosis), and grade 4 means complete ankylosis [8, 9]. Active sacroiliitis on MRI is defined according to the ASAS criteria as: (1) bone marrow edema on fluid-sensitive sequence or bone marrow enhancement, (2) inflammation in a typical anatomical area, i.e. the subchondral bone, and (3) MRI appearance highly suggestive of axSpA [10].

While radiography is less expensive than MRI, it is also less sensitive and may not reveal early disease [11]. It may also be a less reliable examination, with reported large intra- and inter-observer variability [9, 12–14]. It remains unclear which imaging modality is most cost-effective in the evaluation of axSpA. The purpose of our study was to determine the cost-effectiveness of radiography and MRI-based imaging strategies for the initial diagnosis of sacroiliitis in a hypothetical population with suspected axial spondyloarthritis.

Materials and methods

Our study did not require Institutional Review Board review as it does not constitute human subjects research.

General model overview

A decision analytic model from the US health care system perspective for a hypothetical population of 36-year-old male patients with suspected axSpA was designed to assess the incremental cost-effectiveness of 3 imaging strategies for the sacroiliac joints during a 3-year horizon: radiography, MRI, and radiography followed by MRI. For the base case, patients were assumed to have failed 12 weeks of full-dose non-steroidal anti-inflammatory drugs (NSAIDs) treatment and were presenting to a rheumatologist for assessment. Imaging of the sacroiliac joints was obtained to evaluate the diagnosis of axSpA, as per current recommendations [4, 6, 7]. The probabilities of response to treatment, treatment-related complications, and recovery in the absence of treatment were included in the model. The model focused on axial spondyloarthritis and did not evaluate peripheral spondyloarthritis.

In our model, patients underwent either radiography alone, MRI alone, or radiography followed by MRI, if the radiographs were negative. Additional imaging strategies for sacroiliitis, including computed tomography, ultrasound, or nuclear medicine scans, were not considered for this model as they are not recommended in the current guidelines for the diagnosis of axial spondyloarthritis, unless the patient cannot undergo MRI [6, 7].

Treatment was initiated based on positive imaging findings on either imaging modality. Patients who were not diagnosed with sacroiliitis on imaging did not receive treatment with biological disease-modifying antirheumatic drugs (bDMARDs). All patients were initially naïve to bDMARD therapy. Patients with axSpA were treated according to the standard of practice of rheumatologists at our institution, which is similar to the Assessment in SpondyloArthritis International Society-European League Against Rheumatism (ASAS-EULAR) 2016 recommendations for the management of axial spondyloarthritis [3]: Patients diagnosed with sacroiliitis on imaging underwent treatment with a tumor necrosis factor inhibitor (TNFi) and were reassessed in 3 months. If they responded to therapy, TNFi was continued for the remainder of the follow-up duration. If they failed to achieve a good response, they were treated with another TNFi and re-evaluated in another 3 months. If the second TNFi failed, Interleukin-17 inhibitor (IL-17i) therapy was initiated, and a good response was assumed for all patients. It was assumed that all patients eventually improved with the third-line bDMARD treatment and that all patients survived the follow-up period.

The primary effectiveness outcome was quality-adjusted life-years (QALYs). Costs were estimated in 2018 American dollars. The costs and health benefits were discounted at the recommended 3% rate to reflect their present value. The model was created using a decision analysis software (TreeAge Pro 2016, Williamstown, MA, USA).

Probabilities

Values for probability estimates were determined through a comprehensive literature search and consensus expert opinion and are summarized in Table 1. Weighted averages of MRI sensitivity and specificity (0.67 and 0.79, respectively) were calculated from prior studies, including 517 patients [15], 187 patients [11], 69 and 88 patients [16], and 101 patients [8]. Weighted averages of radiography sensitivity and specificity, (0.40 [8, 9, 12, 17] and 0.87 [8, 12, 17], respectively), were derived from prior studies of 50 radiographs [12], 104 patients [9], 101 patients [8], and 58 patients [17].

The probability of axSpA in our population was estimated at 0.51 from a weighted average of results from 4 studies, including 751 patients [18], 517 patients [15], 350 patients [19], and 816 patients [2].

The probability of obtaining an MRI after negative radiographs was estimated at 0.73 based on the frequency at which MRI of the sacroiliac joints was obtained in a prior study with 79 patients with pre-radiographic axSpA evaluated in a rheumatology clinic [19].

The probability of recovery with NSAIDs therapy in true positive patients was estimated at 0.33 based on ASDAS clinically important improvement in a cohort study of 100 patients with axSpA [20]. The probability of recovery with NSAIDs in true negative patients was obtained from a weighted average of 0.57 from two randomized controlled studies in patients with chronic low back pain including 293 patients [21] and 220 patients [22], respectively.

The probability of recovery after the first line TNFi in true positive patients was 0.45 according to a Cochrane systematic review [23]. The probability of recovery after the second-line TNFi in true positive was 0.31 from a longitudinal observational multicenter Norwegian study of 514 patients from the NOR-DMARD register [24].

The probability of symptoms persistence without treatment was derived from placebo trials, with a weighted average input value of 0.87 estimated from a Cochrane systematic review article [23] and a randomized controlled trial of 316 patients [25]. No relevant literature on the probability of recovery after TNFi in false-positive and true-negative patients was found, and the input value was estimated at 0.1 based on consensus expert opinion.

The probability of any adverse events from NSAIDs was estimated at 0.43 according to a Cochrane systemic review [26]. The probability of any adverse events from TNFi was estimated at 0.41, representing a weighted average from prior studies, including a cohort study of 402 patients [27], a randomized controlled trial of 215 patients [28], a randomized controlled trial of 185 patients [29], and a randomized controlled trial of 213 patients [30].

Utility values

QALY value of 0.77 for untreated axSpA was derived from the mean EQ-5D index score for the International Classification of Diseases, Ninth Revision (ICD-9) code of joint disorder not elsewhere classified [31]. For treated axSpA, a QALY value of 0.92 was obtained from the mean reported EQ-5D US value for males age 30–39 from nationally representative surveys of the non-institutionalized civilian population in the USA [32]. Literature on disutility values for NSAIDs and anti-TNF adverse events was limited, and these inputs were estimated at 0.05 each by consensus expert opinion.

Diagnostic imaging costs

The cost of 2-views sacroiliac joints radiographs (Current Procedural Terminology [CPT] 7220) of \$29 and the cost of MRI of the pelvis without contrast for the sacroiliac joints of \$323 (CPT 72195) were obtained from the national average Medicare reimbursements (facility price) in 2018 American dollars [33].

Treatment costs

The costs of medication were taken from the website GoodRx for prescription drug prices in the USA [34]. The cost of physiotherapy was estimated at \$453 from the facility price for one session of physiotherapy evaluation (CPT 97162), 6 sessions of manual therapy (CPT 97140), 4 sessions of therapeutic exercises (CPT 97110), and 2 sessions of neuromuscular re-education (CPT 97112) [33]. There was limited literature on the average cost of treatment of NSAIDs and TNFi adverse events; therefore, they were estimated at \$20 and \$40, respectively, by consensus expert opinion.

Analysis

The primary outcomes were costs, effectiveness (QALYs), and incremental cost-effectiveness ratios (ICERs). The willingness-to-pay threshold was set to \$100,000/QALY gained. All inputs were tested with one-way sensitivity analysis over a broad range of reasonable values, testing one variable at a time while keeping all other variables fixed. Variables to which the model's results were sensitive were further evaluated with a threshold analysis. Probabilistic sensitivity analysis was performed using the Monte Carlo simulation method over 100,000 simulations. A cost-effectiveness acceptability curve was obtained from the probabilistic sensitivity analysis up to a willingness-to-pay of \$100,000.

Table 1 Input variables for sacroiliitis imaging model with one-way sensitivity analysis ranges and results

	Base case value	One-way sensitivity analysis range	One-way sensitivity analysis results for 3-year horizon	Reference
Imaging test performance				
MRI sensitivity	0.67	0.1–0.9	Sensitive: MRI is favored at or below 0.32	[8, 11, 15, 16]
MRI specificity	0.79	0.1–0.9	Robust	[8, 11, 15, 16]
Radiography sensitivity	0.40	0.1–0.9	Sensitive: MRI is favored above 0.74	[8, 9, 12, 17]
Radiography specificity	0.87	0.1–0.9	Sensitive: MRI is favored at or below 0.52	[8, 12, 17]
Clinical probabilities (%)				
Probability of sacroiliitis in hypothetical population	0.51	0.1–0.9	Robust	[2, 15, 18, 19]
Probability of getting an MRI after negative radiographs	0.73	0.1–0.9	Robust	[19]
Probability of NSAIDs complication	0.43	0.1–0.9	Robust	[26]
Probability of bDMARD complication	0.41	0.1–0.9	Robust	[27–30]
Probability of recovery with NSAIDs in true positive patients	0.33	0.1–0.9	Robust	[20]
Probability of recovery with NSAIDs in true negative patients	0.57	0.1–0.9	Robust	[21, 22]
Probability of recovery after first line TNFi if false positive patients	0.1	0.1–0.9	Robust	Consensus expert opinion
Probability of recovery after first line TNFi in true negative patients	0.1	0.1–0.9	Robust	Consensus expert opinion
Probability of recovery after second line TNFi in true negative patients	0.1	0.1–0.9	Robust	Consensus expert opinion
Probability of recovery after first line TNFi in true positive patients	0.45	0.1–0.9	Robust	[23]
Probability of recovery after second line TNFi in true positive patients	0.31	0.1–0.9	Robust	[24]
Probability of recovery without treatment in true positive patients	0.13	0.1–0.9	Robust	[23, 25]
Costs (\$)				
Cost for sacroiliac joints radiographs	29	5–200	Robust	[33]
Cost of MRI of the sacroiliac joints (pelvis)	323	100–5000	Robust	[33]
Cost for 3 months of NSAIDs	48	15–600	Robust	[34]
Cost for 3 months of first line TNFi (adalimumab)	14,539	3000–30,000	Robust	[34]
Cost for 3 months of second line TNFi (etanercept)	14,539	3000–30,000	Robust	[34]
Cost for 3 months of IL-17i (secukinumab)	14,063	3000–30,000	Robust	[34]
Cost of physiotherapy	453	200–2000	Robust	[33]
Cost of NSAIDs complication	20	5–50,000	Robust	Consensus expert opinion
Cost of TNFi complication	40	5–50,000	Robust	Consensus expert opinion
Utilities				
Utility of untreated sacroiliitis	0.77	0.50–0.92	Robust	[31]
Utility of treated sacroiliitis	0.92	0.81–0.99	Robust	[32]
Disutility of NSAIDs complication	0.05	0.01–0.50	Robust	Consensus expert opinion
Disutility of TNFi complication	0.05	0.01–0.50	Robust	Consensus expert opinion

bDMARD biological disease-modifying antirheumatic drug, *IL-17i* Interleukin-17 inhibitor, *MRI* magnetic resonance imaging, *NSAIDs* non-steroidal anti-inflammatory drugs, *TNFi* tumor necrosis factor inhibitor

Results

Cost-effectiveness analysis

The least expensive imaging strategy was radiography alone (\$46,220), followed by MRI alone (\$77,004), and then radiography combined with MRI (\$95,114) (Table 2). The most effective imaging strategy was radiography combined with MRI (2.64 QALYs), followed by MRI alone (2.61 QALYs), and then radiography alone (2.56 QALYs). Radiography alone was the most cost-effective strategy (Fig. 1); the ICERs for the two other strategies were above the conventional willingness-to-pay threshold of \$100,000 and thus were not considered cost-effective.

Sensitivity analyses

One-way sensitivity analysis demonstrated that the results of our cost-effectiveness model were sensitive only to the sensitivity and specificity of radiography and the sensitivity of MRI; the model's results were robust to alterations in all other variables. Threshold analyses showed that MRI became the most cost-effective strategy when the sensitivity of radiographs was > 0.74 , the specificity of radiography was ≤ 0.52 , or the sensitivity of MRI was ≤ 0.32 .

Probabilistic sensitivity analysis showed that radiography alone was the most cost-effective strategy in 100% of simulations.

The cost-effectiveness acceptability curve depicted that radiography remained the most cost-effective strategy for all willingness-to-pay thresholds up to \$100,000 per QALY gained.

Discussion

According to our cost-effectiveness analysis, a radiography-based strategy is the most cost-effective for the detection of sacroiliitis in the initial diagnosis of axSpA when evaluated from the health care system perspective over a 3-year duration. This was considered the favored rather than dominant

strategy because, while it was the cheapest, it was not the most effective.

The variables which impacted the cost-effectiveness of the proposed strategies were the imaging diagnostic accuracy. When the sensitivity of radiography increased above a certain threshold or when the specificity of radiography or the sensitivity of MRI decreased below a certain threshold, then MRI became the favored strategy. While these findings may seem counterintuitive, this suggests that the model favors treating fewer patients, either true or false positive, in the short term. The reason for this being high costs of treatment with relatively small improvements in quality of life for the selected, commonly accepted willingness-to-pay threshold of \$100,000.

Imaging plays an essential role in the diagnosis of axSpA: sacroiliitis on imaging along with at least 1 SpA feature meets the ASAS criteria for axSpA [5]. Radiography is recommended as the first-line imaging modality for the initial evaluation of inflammatory sacroiliac or back symptoms in the context of suspected axSpA [4, 6, 7]. Evaluation with MRI is the recommended next step in the setting of negative radiographs. CT can be helpful for patients who cannot undergo MRI. Radiography and CT depict structural changes, while MRI can reveal signs of inflammation, sometimes years before the appearance of structural changes [10]. The interpretation of MRI also appears to be more reliable than radiographs, with a reported kappa statistic for MRI inter-observer variation of 0.65–0.98 [35, 36] compared to 0.19–0.79 for radiographs [12].

Consideration of costs related to the disease and its treatment for the patient, health care system, and society are deemed important in the management decisions of treating rheumatologist, which is stated as one of the five overarching principles of the ASAS-EULAR management recommendations, recently added in 2016 [3]. While there have been several prior studies evaluating the accuracy of different imaging techniques and treatment options for axSpA, we were unable to find a study that took into account these factors along with costs in the published literature. In this present study, we therefore attempted to create a cost-effectiveness model evaluating the three most commonly used imaging strategies in our practice, which included radiography alone, MRI alone, and

Table 2 Results of cost-effectiveness analysis of three imaging strategies for the for the detection of sacroiliitis in the initial diagnosis of axial spondyloarthritis with a 3-year follow-up

Time horizon (years)	Strategy	Expected Cost (US\$)	Incremental Cost (US \$)	Effectiveness (QALY)	Incremental effectiveness	ICER (cost per QALY gained) (US\$)
3	Radiography	46,220	–	2.56	–	–
	MRI	77,004	30,784	2.61	0.05	569,792
	Radiography and MRI	95,114	48,893	2.64	0.09	569,742

QALY quality-adjusted life-year

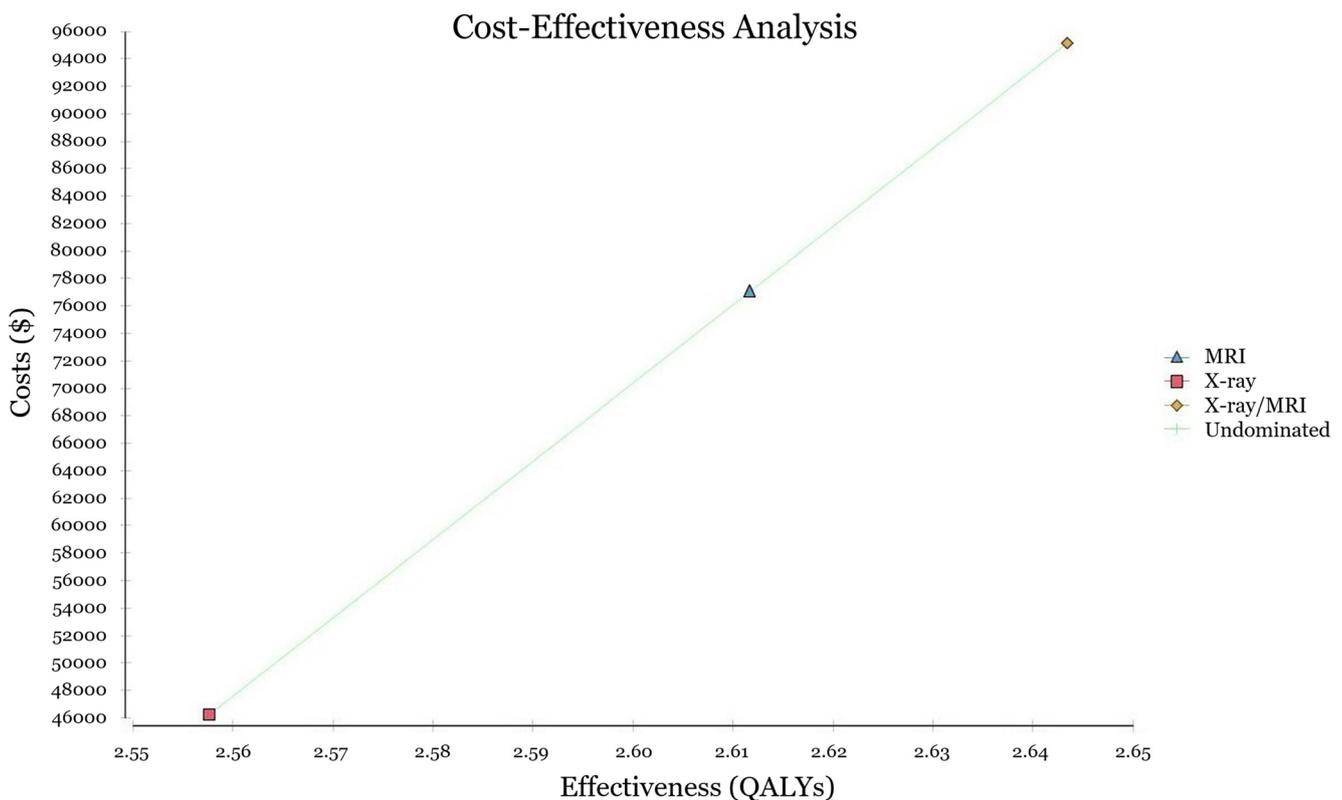


Fig. 1 Cost-effectiveness analysis depicting that radiography alone is the least effective and costly, whereas radiography followed by MRI is the most effective but also most costly strategy. QALY quality-adjusted life-year

radiography followed by MRI. Such an evaluation is useful when considering health care expenses on a population scale, particularly when health care resources are limited. While radiography is already the first-line imaging modality recommended for the evaluation of axSpA, our results provide a health economics argument to support this recommendation, despite known important limitations of radiography, including lower sensitivity and large intra- and inter-observer variability.

Our study has several limitations. Firstly, there is uncertainty associated with the input estimates. The input values were derived from published studies, which have their own limitations, heterogeneity in study design, variability in outcome measures, and sometimes a limited sample size. Moreover, literature was limited or lacking for certain inputs; therefore, expert opinion had to be employed. Also, Medicare reimbursement rates were used as proxy for costs, whereas private insurances may reimburse different amounts. The effects of these uncertainties are mitigated by the sensitivity analysis, which demonstrated robustness of the results over wide tested ranges.

Second, there are limitations related to our model's design. The model is built based on the treatment algorithm followed by rheumatologists at our center, which is similar to, but slightly different than, the current EULAR-ASAS management recommendations for axSpA [3]. There is an assumption

that patients eventually improve after the third-line treatment and that all patients survived the follow-up period, which was based on our experts' expectations. The hypothetical population consisted of 36-year-old male patients with suspected axSpA, which may limit the generalizability of our model's results for patients of other ages or for female patients. This population was selected as the most common group of patients evaluated for axSpA, based on a study on the prevalence of axSpA in the USA [2]. Our model also does not include costs of tests that may be used for the diagnosis of axSpA such as HLA-B27, ESR, and CRP and potential harms of radiation exposure. It also does not address timing considerations, particularly with respect to the fact that MRI could provide an earlier diagnosis than radiography by detecting radiographically occult inflammatory lesions [10]. Early diagnosis and treatment may prevent irreversible structural damage and ensuing functional disability. It is possible that patients with a short duration of symptoms may be more likely to have non-radiographic axSpA and could benefit from MRI. While European League Against Rheumatism recommendations specify that MRI may be considered as an alternative first imaging strategy in patients who are young or who present with a short duration of symptoms [7], the American College of Radiology (ACR) appropriateness criteria do not take into account these specific situations [6]. Finally, the 3-year time

period does not consider longer-term outcomes, including the impact of delayed diagnosis with increased clinical complications. In our review of the literature, we did not find utility values for treated axSpA detected early versus later to account for this possibility. Moreover, our model focuses on the initial diagnosis scenario, which is the first rheumatology consultation. It is likely, in our opinion, that if a diagnosis of early axSpA is initially missed due to negative radiographs, the patient will return to seek medical attention with persistent symptoms and further workup at that time may lead to the correct diagnosis. The 3-year follow-up duration utilized in our model is longer than in most clinical trials and it would be difficult to use a lifetime horizon for our model given the uncertainties of what could happen to a patient after this initial diagnosis scenario [37].

Lastly, our model only addresses the cost-effectiveness of imaging for the initial detection of sacroiliitis and does not include any subsequent imaging, which may be performed for monitoring of disease activity. The role of MRI for this purpose remains uncertain, with at best moderate correlation between clinical symptoms and inflammatory changes on MRI [3].

Conclusion

Our model suggests that radiography is the most cost-effective imaging strategy for the detection of sacroiliitis in the initial diagnosis of axSpA, based on its lower cost. The decision to utilize a particular imaging strategy remains nevertheless dependent on additional factors such as clinical context, imaging modality availability, and budgetary constraints.

Compliance with ethical standards

Conflict of interest Author #5 declares a financial relationship with the Pfizer Psoriatic Arthritis Advisory Panel, outside the submitted work.

Author #6 declares a financial relationship with Abbvie (clinical trials, consulting fees), Amgen (clinical trials, consulting fees), UCB (consulting fees), Pfizer (clinical trials, consulting fees), Novartis (clinical trials, consulting fees), and Celgene (clinical trials), outside the submitted work.

The other authors declare that they have no relevant conflicts of interest.

Ethical approval This study did not require Institutional Review Board review as it does not constitute human subjects research.

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