

# 2014 Update of the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada Treatment Recommendations for the Management of Spondyloarthritis. Part I: Principles of the Management of Spondyloarthritis in Canada

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**ABSTRACT. Objective.** The Canadian Rheumatology Association (CRA) and the Spondyloarthritis Research Consortium of Canada (SPARCC) have collaborated to update the recommendations for the management of spondyloarthritis (SpA).

**Methods.** A working group was assembled and consisted of the SPARCC executive committee, rheumatologist leaders from SPARCC collaborating sites, Canadian rheumatologists from across the country with an interest in SpA (both academic and community), a rheumatology trainee with an interest in SpA, an epidemiologist/health services researcher, a member of the CRA executive, a member of the CRA therapeutics committee, and a patient representative from the Canadian Spondylitis Association. An extensive review was conducted of literature published from 2007 to 2014 involving the management of SpA. The working group created draft recommendations using multiple rounds of Web-based surveys and an in-person conference. A survey was sent to the membership of the CRA to obtain an extended review that was used to finalize the recommendations.

**Results.** Guidelines for the management of SpA were created. Part I focuses on the principles of management of SpA in Canada and includes 6 general management principles, 5 ethical considerations, target groups for treatment recommendations, 2 wait time recommendations, and recommendations for disease monitoring. Also included are 6 modifications for application to juvenile SpA.

**Conclusion.** These recommendations were developed based on current literature and applied to a Canadian healthcare context. It is hoped that the implementation of these recommendations will promote best practices in the treatment of SpA. (First Release Feb 15 2015; J Rheumatol 2015;42:654–64; doi:10.3899/jrheum.141000)

## Key Indexing Terms:

SPONDYLOARTHRITIS

ANKYLOSING SPONDYLITIS

PSORIATIC ARTHRITIS

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Accepted for publication December 22, 2014.

The management of spondyloarthritis (SpA) is complex. The Spondyloarthritis Research Consortium of Canada (SPARCC) and the Canadian Rheumatology Association (CRA) have created treatment recommendations for the management of SpA. Initial recommendations were published in 2003 and subsequently updated in 2007<sup>1,2</sup>.

Since 2007, there has been a continued and rapid evolution in the diagnosis, management, and monitoring of SpA. The role of traditional disease-modifying anti-rheumatic drugs in the treatment of axial SpA (axSpA) has become tenuous<sup>3,4,5,6</sup>. Conversely, new evidence has established that nonsteroidal antiinflammatories (NSAID) may have a disease-modifying effect<sup>7,8,9</sup>. The potential for tumor necrosis factor inhibitors (TNFi) to prevent the progression of axial disease has been presented<sup>10</sup>. New biologic agents have emerged in the Canadian market, and their role in SpA has not yet been formally addressed. Magnetic resonance imaging (MRI) has emerged as a key diagnostic tool for the diagnosis of axSpA, particularly nonradiographic axSpA (nr-axSpA)<sup>11,12,13,14</sup>. Owing to the ongoing limitations that many clinicians face in accessing MRI for their patients with SpA in a timely manner, it is appropriate that CRA/SPARCC addresses MRI wait times, which was not done in 2007. Additionally, the 2007 recommendations did not address the management of juvenile spondyloarthritis (JSpA).

For clarity, these recommendations have been divided into 2 parts: Part I, Principles of the Management of SpA in Canada, and Part II, Specific Management Recommendations. Part I addresses optimal SpA management in Canada, as well as barriers to the implementation of these recommendations. This is largely derived from expert opinion. Part II consists of specific recommendations for SpA treatment and has a larger body of literature support.

Recommendations were based upon the highest quality of evidence available at the time the working group undertook this review. They are intended to promote best practices and improve delivery of healthcare for those with SpA. Recommendations, however, should not be interpreted as rigid or legal standards, nor are they intended to replace the clinical judgment of rheumatologists and other trained SpA healthcare providers acting according to the individual needs of the patient and the unique clinical circumstance.

## MATERIALS AND METHODS

**Participants.** The working group included the SPARCC executive committee, SPARCC rheumatologists, rheumatologists with an SpA interest (community and academic), an epidemiologist, a rheumatology trainee, a CRA representative, and a patient representative from the Canadian Spondylitis Association. There was no pharmaceutical or industry involvement.

**Patient population.** These recommendations apply to both axial and peripheral SpA (Figure 1). Included in axSpA is ankylosing spondylitis (AS) as well as nr-axSpA; diagnosed axSpA is based upon MRI findings at the sacroiliac (SI) joints and/or spine without radiographic evidence of sacroiliitis, according to the Assessment of SpA international Society

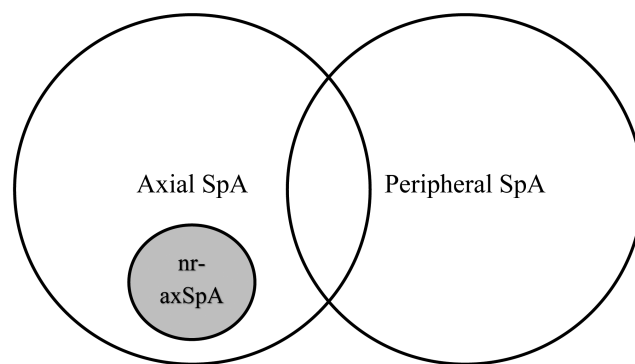


Figure 1. Defining the patient population. SpA: spondyloarthritis; nr-axSpA: nonradiographic axial SpA.

(ASAS) criteria<sup>15,16</sup>. Peripheral SpA is classified by ASAS criteria; accordingly, axial involvement is not required<sup>17</sup>. Psoriatic arthritis (PsA) is included, and may be predominantly axial or predominantly peripheral.

SpA in children, referred to as JSpA, more commonly presents as undifferentiated disease and is commonly referred to as enthesitis-related arthritis (ERA) under the International League of Associations for Rheumatology classification criteria for juvenile idiopathic arthritis (JIA). Consequently, the target population in children will focus and be referred to as JSpA(ERA). In contrast to adults, children are more likely to have peripheral arthritis and enthesitis rather than axial involvement at disease onset. Spinal involvement is uncommon early in the disease course, but axial involvement of the SI joints is possible and generally becomes more clinically evident as the child ages.

These recommendations are not intended for the diagnosis or classification of SpA; the diagnosis of SpA is made based upon physician clinical judgment. Classification criteria for axial and peripheral SpA have been proposed by ASAS, and the CASPAR criteria may be used for PsA<sup>16,17,18</sup>.

**Development process.** The recommendations were updated through a nominal group process (Supplementary data available online at jrheum.org).

**Evidence-based literature review.** Literature published since the last recommendations was reviewed (Figure 2; Supplementary data available online at jrheum.org).

**Grading evidence.** We used a simplified version of the Scottish Intercollegiate Guideline Network for consistency with the CRA Recommendations for Rheumatoid Arthritis (Table 1)<sup>19,20</sup>.

**Extended review.** After the recommendations were drafted, they were reviewed by the CRA Therapeutics Committee in March–April 2014. A need for extended review by the CRA membership was identified. Active members and emeritus members of the CRA were sent an electronic survey in which they were asked to provide input on recommendations identified as controversial or based on expert opinion alone. Feedback from survey respondents (n = 136, response rate 35%) was used to finalize recommendations and discussion.

## RESULTS

The CRA/SPARCC Principles for the Management of SpA in Canada encompass general management principles, ethical considerations, target groups for treatment recommendations, wait time recommendations, and disease monitoring. These are summarized in Table 2. These management principles may also be applied to JSpA(ERA) using a series of modifications summarized in Table 3. The

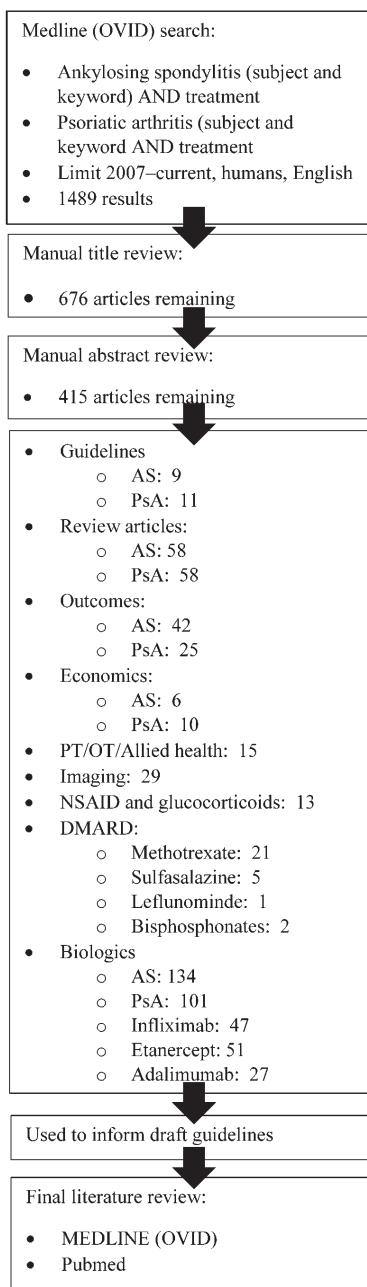


Figure 2. Initial literature review process. SpA: spondyloarthritis; AS: ankylosing spondylitis; PsA: psoriatic arthritis; PT: physiotherapy; OT: occupational therapy; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

level of evidence (LOE), strength of recommendation (SOR), and expert opinion score (EO) are listed for each recommendation specifically. EO was evaluated on a 5-point Likert scale ranging from “disagree completely” to “agree completely”. Barriers to the implementation of the individual recommendations are also described. These recommendations address factors in the Canadian healthcare system that may affect the applicability of the recommendations.

## General Management Principles

**Recommendation 1.** Target disease is defined and terminology established (LOE IV, SOR D). Barriers to implementation include rapidly evolving terminology that is not well established with some agencies not recognizing the terminology at all. Many provincial formularies do not recognize axial and peripheral SpA as diseases or that nr-axSpA is a unique disease subset. Instead, the indications for the use of some medications are only for AS and PsA, which may inappropriately classify patients.

**Recommendation 2.** Treatment goal is remission or minimal disease activity (MDA) using a treat-to-target approach. Expert review of SpA literature defined remission as the “absence of clinical and laboratory evidence of significant inflammatory disease activity” (LOE IV, SOR D)<sup>21</sup>.

A validated MDA definition does exist for PsA<sup>22,23</sup>. Patients achieve MDA if they fulfill 5/7 outcome measures (LOE II, SOR B)<sup>22</sup>.

There are no barriers to the implementation of this recommendation.

**Recommendation 3.** Optimal management includes pharmacological and nonpharmacological treatment and patient education. Patient education has randomized controlled trial evidence in both axial and peripheral SpA, but it should be noted that high-quality, large trials are lacking (LOE I, SOR A)<sup>24,25,26</sup>.

Implementation of this recommendation is restricted by variable access to nonpharmacological therapies by the Canadian population.

**Recommendations 4–6.** Based upon expert opinion and address several management issues in SpA (LOE IV, SOR D).

These recommendations do not have any specific barriers to implementation, but the dearth of evidence suggests additional funding should be allocated to risk-benefit analysis, pharmacoeconomic studies, and postmarketing surveillance.

## Ethical Considerations

**Recommendations 7–11.** This section is largely unchanged from the 2007 Recommendations (LOE IV, SOR D)<sup>2</sup>.

There are no barriers to the implementation of ethical considerations in SpA.

## Target Groups for Treatment Recommendations

**Recommendation 12.** Defines target groups for these recommendations (LOE IV, SOR D).

There are no identified barriers to the implementation of this recommendation.

## Wait Time Recommendations

**Recommendation 13.** Focuses on axSpA, which has a diagnostic delay of 5–10 years<sup>12,27</sup>. Those at highest risk of SpA should be assessed by a rheumatologist within 3 months.

Table 1. Custom system for assigning LOE and SOR.

LOE	SOR
I: Metaanalysis, systematic reviews of RCT, or an individual RCT	A: Strong recommendation: <ul style="list-style-type: none"> <li>• Direct level 1 evidence</li> </ul>
II: Metaanalysis, systematic reviews of observational studies (cohort/case control studies), or individual observational studies, OR RCT subgroup/posthoc analysis	B: Moderate recommendation: <ul style="list-style-type: none"> <li>• Direct level 2 or extrapolated level 1 evidence</li> </ul>
III: Nonanalytic studies (case reports, case series)	C: Weak recommendation: <ul style="list-style-type: none"> <li>• Direct level 3 or extrapolated level 2 evidence</li> </ul>
IV: Expert opinion	D: Consensus recommendation: <ul style="list-style-type: none"> <li>• Expert opinion based on very little evidence</li> </ul>
NR: Recommendation is not linked to evidence	

LOE: level of evidence; SOR: strength of recommendation; RCT: randomized controlled trial; NR: not reported.

For PsA, evidence suggests that a diagnostic delay of 6 months results in poorer outcomes. Therefore, patients at risk of peripheral SpA should be assessed by a rheumatologist within 6 weeks of referral (LOE IV, SOR D)<sup>28</sup>.

**Recommendation 14.** Timely MRI access is critical for diagnosing nr-axSpA (LOE IV, SOR D)<sup>12,15</sup>.

Diagnostic MRI should include whole spine and pelvis scans with appropriate sequencing. Over 5% of patients have MRI evidence of inflammation in the spine without the involvement of the SI joint (LOE II, SOR B)<sup>16</sup>.

Unfortunately, there are several barriers to the implementation of wait time recommendations. Access to rheumatologists remains difficult with great variability between geographic and health regions. Screening all patients under the age of 45 with back pain for SpA would quickly overwhelm the current workforce. The number of MRI machines is also highly variable across the country, and often reflects poor accessibility and long wait times. Many radiology departments do not allow the entire spine and SI joints to be imaged in a single procedure. In such circumstances, it was felt that it was appropriate to image the SI joints first and to proceed to other areas of the spine if clinically indicated.

## Disease Monitoring

**Recommendation 15.** Outlines specific components for monitoring in SpA. Few studies examine the utility of patient history in monitoring, but it remains a critical part of the assessment of patients (LOE IV, SOR D). Physical examinations should be relevant to the patient's predominant presenting features, but all patients should have a tender joint count, swollen joint count, and enthesal assessment (LOE IV, SOR D). Enthesitis in SpA has been associated with poorer outcomes and increased disease activity<sup>29,30</sup>. Specific metrology of the spine is not included because the clinical utility and prognostic value of spinal metrology remains under study (LOE IV, SOR D). Baseline laboratory screening should be completed with regard to further management and potential toxicities (LOE IV, SOR

D). Patients should be screened for extraarticular manifestations and comorbid conditions (LOE IV, SOR D).

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), a reliable and valid outcome measure, was included in the monitoring recommendations<sup>31,32,33</sup>. In Canada, the BASDAI is often a mandatory component of the application process for biologic agents, and was thus felt to be worthy of inclusion. This recommendation is based on expert opinion (LOE IV, SOR D).

Also included was functional assessment. One potential measure of function could be the Bath Ankylosing Spondylitis Functional Index that is used in the ASAS recommendations for record keeping<sup>34</sup>. The working group felt that it was important to assess patient function regularly, but left the specific tool for assessment to the discretion of the treating physician. Patient assessment of global well-being was included for similar reasons (LOE IV, SOR D for both recommendations).

Elevated acute-phase reactant (APR) was included because it may indicate propensity for radiographic progression or response to therapy. Patients with elevated APR have been shown to have the greatest benefit from NSAID therapy and TNFi in multiple studies<sup>8,35,36,37,38</sup>. C-reactive protein (CRP) has been associated with outcomes in AS and has been incorporated into a matrix model for treatment<sup>39</sup>. Patients with an elevated CRP had greater structural damage on radiographs, radiographic progression, and had greater progression from nr-axSpA to axSpA<sup>10,40,41,42</sup>. In PsA, an elevated baseline CRP was an independent risk factor for radiographic progression<sup>43</sup>. Patients with PsA with higher erythrocyte sedimentation rates had greater rates of damage progression and less likelihood of reaching a minimal disease activity state<sup>44</sup>. Patients with PsA who were beginning TNFi treatment were found to have a better response to therapy if their baseline CRP was elevated<sup>45</sup>. Elevated CRP has also been shown to differentiate patients with PsA from those with psoriasis without arthritis<sup>46</sup> (LOE II, SOR B for this component of Recommendation 15).

The working group agreed that patients with SpA should



Table 2. 2014 Update on the CRA/SPARCC Treatment Recommendations for the Management of SpA.

Recommendation	LOE	SOR	EO
<b>General management principles</b>			
1. Management recommendations for SpA will be organized under the categories of axSpA (including nr-axSpA) and peripheral SpA.	IV	D	4.9
2. The goal of treatment is remission. When remission is not possible, the goal is minimal disease activity and control of symptoms, prevention of damage, and improvement in quality of life. Therapy should be adjusted until these goals are reached.	IV (SpA) II (PsA)	D (SpA) B (PsA)	4.9
3. Optimal management of SpA includes a combination of nonpharmacological and pharmacological treatments, as well as patient education.	I	A	5.0
4. Patient preferences, including risk-benefit balances, must be incorporated into regulatory decision-making and prescribing of arthritis medications.	IV	D	5.0
5. It is appropriate to consider pharmacoeconomic data in formulating decisions on management strategies. The particular aim is to identify subgroups of patients with the highest burden of disease for whom the additional benefits merit the additional costs.	IV	D	4.5
6. Postmarketing evaluation of new therapies for SpA should be implemented to ensure appropriate access and utilization of these agents, and to ensure their safety in an unselected population with longer periods of observation.	IV	D	5.0
<b>Ethical considerations</b>			
7. A Formulary Committee has a duty to represent the public's interests in promoting the greatest health benefits possible (ethical principle of Beneficence) as fairly as possible within society's limited shared resources (Justice) through an open and transparent process and in accordance with the best available evidence (Accountability).	IV	D	4.7
8. Economic evaluations should be comprehensive with a clear analysis of the direct and indirect costs of suboptimal treatment. Ethically, suboptimal treatment is always questionable (principle of Nonmaleficence).	IV	D	4.5
9. Fairness across all patient groups and illness categories is mandatory, and is enshrined in the Canada Health Act. <i>Ad hoc</i> decisions that favor some groups but not others are not ethically acceptable.	IV	D	4.9
10. Resource limitations may require that qualifications be placed on access to some extremely expensive therapies. Physicians must be enabled to practice the highest standard of evidence-based medicine for the benefit of their patients, and thus even extremely expensive therapies that are clinically effective must not be excluded on principle. Formulary committees should be encouraged to <i>work in conjunction with clinical specialists</i> to develop guidelines for access that promote safe and effective interventions at lower cost where possible, but that allow clinicians and patients to access necessary therapeutics when other options are not medically appropriate.	IV	D	4.9
11. In a Canadian context, the delivery of healthcare is a provincial rather than federal responsibility. However, the principles of universality, transferability, and comprehensiveness of the Canada Health Act, and the underlying ethical principle of Justice, indicate that treatments approved in 1 province should generally be available to patients in all provinces.	IV	D	4.9
<b>Target groups for treatment recommendations</b>			
12. These management recommendations are intended for: a. Rheumatologists b. Primary care physicians, internists, and other healthcare providers c. Persons with SpA d. Insurance payers e. Government agencies f. Formularies	IV	D	4.9
<b>Wait time recommendations</b>			
13. Patients with chronic back pain with an age of onset prior to 45 should be screened for the presence of SpA and assessed by a rheumatologist within 3 mos of referral. Patients at risk of peripheral SpA should be assessed by a rheumatologist within 6 weeks of referral.	IV	D	4.1
14. MRI frequently plays an important role in the diagnosis of SpA. When a rheumatologist orders an MRI to diagnose SpA, the whole spine and pelvis should be imaged. MRI imaging should occur within 6 weeks of being ordered by the rheumatologist.	IV (timing) II (whole spine)	D (timing) B (whole spine)	4.5

Table 2. Continued.

Recommendation	LOE	SOR	EO
Disease monitoring			
15. Specific disease monitoring of patients with SpA in clinical practice should ideally include:			
a. Patient history	IV	D	4.8
b. Relevant clinical exam (axial or peripheral). For axSpA, spinal mobility should be assessed. All patients should have an assessment of tender joints, swollen joints, and enthesitis.	IV	D	4.8
c. Baseline screening for hepatitis B virus and other chronic infection, liver disease, renal disease, and malignancy.	IV	D	4.8
d. Assessment for signs and symptoms of extraarticular manifestations of SpA (in particular, inflammatory bowel disease, uveitis, and psoriasis).	IV	D	4.8
e. Assessment for signs and symptoms of comorbid conditions associated with inflammatory arthritis (i.e., CV disease, hypertension, hyperlipidemia, DM, and osteoporosis).	IV	D	4.8
f. BASDAI questionnaire.	IV	D	4.8
g. Assessment of function.	IV	D	4.8
h. Patient assessment of global well-being.	IV	D	4.8
i. CRP/ESR.	II	B	4.8
j. Drug toxicity (including infection and malignancy) and adherence.	IV	D	4.8
k. Appropriate imaging, including plain radiographs and/or MRI of the axial skeleton and involved peripheral joints.	II	B	4.8
l. Quality of life assessment.	IV	D	4.8
m. Participation in activities and work disability.	IV	D	4.9
n. Frequency of disease monitoring will depend on disease severity, treatment type, and patient preference.	IV	D	5.0
o. Monitoring and management of extraarticular manifestations of SpA (i.e., IBD, uveitis, psoriasis) should be in collaboration with respective specialists as needed.	IV	D	5.0
p. Monitoring and management of comorbid conditions associated with inflammatory arthritis (i.e., CV disease, hypertension, hyperlipidemia, DM, osteoporosis) should be in collaboration with primary care physicians and respective specialists as needed.	IV	D	4.9

CRA: Canadian Rheumatology Association; SPARCC: Spondyloarthritis Research Consortium of Canada; SpA: spondyloarthritis; LOE: level of evidence; SOR: strength of recommendation; EO: expert opinion; axSpA: axial SpA; PsA: psoriatic arthritis; nr-axSpA: nonradiographic axSpA; MRI: magnetic resonance imaging; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IBD: inflammatory bowel disease; CV: cardiovascular; DM: diabetes mellitus.

be monitored for drug toxicity and adherence, but there is no trial data to support that this monitoring improves outcomes in SpA (LOE IV, SOR D).

Appropriate imaging is included in this recommendation. The ASAS recommendations include both plain radiographs and MRI as acceptable<sup>16</sup>. A systematic review suggested that the utility of MRI in the diagnosis of SpA was limited because of a lack of high-quality studies<sup>47</sup>. There is 1 high-quality study showing that standardized evaluation of the MRI of SI joints in patients with SpA had high diagnostic utility<sup>48</sup>. Another evaluated the diagnostic utility of MRI of spinal inflammatory lesions<sup>49</sup>. The utility of imaging for monitoring SpA is under debate, with some studies supporting MRI monitoring in response to NSAID<sup>8,42</sup> or TNFi<sup>50</sup> treatments. The use of MRI and ultrasound for the diagnosis and monitoring of PsA has been reviewed, and an MRI scoring system has been developed<sup>51,52,53</sup>. Appropriate imaging should also be performed in peripheral arthritis. In PsA, baseline joint damage increased the risk of damage progression<sup>44</sup>. Thus, radiographic assessment of peripheral joints is an important

component of the monitoring of peripheral SpA. (LOE II, SOR B for this component of the recommendation.)

Assess quality of life (QoL) with appropriate referrals to allied health if needed. Several studies have demonstrated poor QoL in PsA<sup>54,55,56</sup> and AS<sup>57,58</sup>. In AS, poor QoL has been correlated with poor metrology and patient-reported outcomes<sup>59,60,61</sup> (LOE IV, SOR D).

Tailor the therapeutic approach to the patient's individual characteristics. Clinical status may affect frequency and intensity of monitoring. Those with poor prognostic features (older age, number of comorbidities, involvement of peripheral joints, and female sex) may warrant closer followup<sup>62,63,64</sup>. Hip involvement in AS is also associated with worse function and radiographic progression<sup>65,66,67</sup>. Conversely, disease activity levels in patients with established AS may clinically and functionally plateau, warranting less assessment<sup>68</sup>. Patients with psoriatic SpA have worse outcomes than those without, and obese patients with PsA may need closer monitoring<sup>69,70</sup> (LOE IV, SOR D).

Specific structural lesions should be monitored. Hip involvement in AS has been shown to be associated with

Table 3. The 2014 Update on the CRA/SPARCC Treatment Recommendations for the Management of SpA for application to JSpA(ERA).

Recommendation	LOE	SOR
General management principles		
1. JSpA(ERA) additionally requires a multidisciplinary family-centered approach to promote normal growth, social development, and physical function in the child or adolescent.	IV	D
Ethical considerations		
2. In consideration of the limited clinical trials in the pediatric population compared to adults, access to therapeutics including some extremely expensive therapies should be based on the highest available standard of evidence-based medicine as well as the best interests of the child.	IV	D
Target groups for treatment recommendations		
3. In JSpA(ERA), these management recommendations are additionally intended for: a. Pediatricians	IV	D
Wait time recommendations		
4. As peripheral SpA is more common in JSpA(ERA), persistent joint or enthesal symptoms > 4 weeks should be screened for the presence of JSpA by a pediatric rheumatologist within 6 weeks of referral.	IV	D
5. axSpA symptoms in JSpA(ERA) should be expanded to include back or buttock pain. Patients with axial symptoms > 4 weeks duration should be screened for the presence of JSpA(ERA) by a pediatric rheumatologist within 6 weeks of referral.	IV	D
Disease monitoring		
6. Radiologic findings in the spine at disease onset is infrequent in JSpA(ERA). Hip involvement is also more common in JSpA(ERA) and confers a poor prognostic factor. Initial MRI imaging should include the pelvis and hips. Additional sites to be imaged by MRI to be determined by pediatric rheumatologist. Whole-body MRI should be considered for early detection of peripheral and axial involvement in JSpA(ERA).	I (MRI SI joints) III (whole-body MRI)	A (MRI SI joints) C (whole-body MRI)

CRA: Canadian Rheumatology Association; SPARCC: Spondyloarthritis Research Consortium of Canada; SpA: spondyloarthritis; JSpA: juvenile SpA; ERA: enthesitis-related arthritis; LOE: level of evidence; SOR: strength of recommendation; axSpA: axial SpA; MRI: magnetic resonance imaging; SI: sacroiliac.

worse functional and radiographic progression<sup>65,66,67</sup>. As with clinical monitoring, there has not been a specific study assessing the effect of monitoring structural damage on outcomes in SpA.

These monitoring recommendations have many barriers to implementation. Many Canadian rheumatologists are providing care for a large patient population, thus reducing the time available to assess an individual patient. Assessments of function, QoL, and work are usually cumbersome and may not be practical for many to perform on a regular basis. Access to specialists and primary care physicians may also be limited based on local availability.

Juvenile SpA

JSpA typically presents with more peripheral and enthesal involvement compared with adults<sup>71</sup>. It includes several overlapping subtypes: juvenile ankylosing spondylitis, juvenile PsA, reactive arthritis, enteropathic arthritis, and undifferentiated disease called ERA<sup>71</sup>. Currently, ERA is the most common form of SpA seen among children with JIA<sup>71</sup>, and the recommendations will address this population specifically. Because of shared familial and genetic predispositions, JSpA(ERA) may be thought of as an on-a-continuum-of disease with adult SpA<sup>71</sup>. Indeed, many adult rheumatologists in Canada will manage patients with

JSpA(ERA) who have passed the age of 18. This section of the 2014 Update of the CRA/SPARCC Recommendations for the Management of SpA will address adaptations of the adult SpA recommendations (Table 3) that may be applied to JSpA(ERA).

General Management Principles

Recommendation 1. JSpA(ERA) requires a multidisciplinary family-centered approach to promote normal growth, social development, and physical function (LOE IV, SOR D).

There are no barriers to the implementation of this recommendation modification.

Ethical Considerations

Recommendation 2. In light of scarce clinical trial data, decision-making should incorporate the best interests of the child (LOE IV, SOR D).

There are no barriers to the implementation of this recommendation modification.

Target Groups for Treatment Recommendations

Recommendation 3. Pediatricians are included (LOE IV, SOR D).

There are no barriers to the implementation of this recommendation modification.

## Wait Time Recommendations

**Recommendation 4.** Peripheral symptoms predominate in JSpA(ERA). Patients with symptoms for greater than 4 weeks should be assessed by a pediatric rheumatologist within 6 weeks (LOE IV, SOR D).

**Recommendation 5.** Patients with axial symptoms (including back or buttock pain) of > 4 weeks should be assessed by a pediatric rheumatologist within 6 weeks (LOE IV, SOR D).

The wait time recommendations for JSpA(ERA) have many of the same barriers to implementation as the adult population. There are even fewer pediatric rheumatologists than adult rheumatologists, leading to prolonged wait times. Again, evaluation of all children with persistent buttock or back pain would likely overwhelm pediatric rheumatologists with patients. In some areas of Canada, there is no pediatric rheumatologist at all within a reasonable geographic distance. Traveling far distances is more challenging for younger children who cannot travel independently to appointments.

## Disease Monitoring

**Recommendation 6.** Consider whole-body MRI for assessing widespread enthesal, axial, and peripheral disease. Whole-body MRI with specialized protocols for JSpA(ERA) was used in a series of patients with ERA and was able to identify the expected characteristic lesions<sup>72</sup>. This study demonstrated good agreement with clinical examination for peripheral arthritis, but MRI superiority for assessment of the hips, SI joints, and spine<sup>72</sup>. Clinical examination was found to overestimate enthesitis activity, suggesting that whole-body MRI may have an important role in quantifying enthesal disease<sup>72</sup> [LOE I, SOR A for MRI of SI joints in JSpA(ERA). LOE III, SOR C for whole-body MRI].

There are significant barriers to the implementation of this recommendation in Canada. Currently, a validated whole-body MRI protocol is only available at 1 academic center (The Hospital for Sick Children, Toronto, Ontario).

## DISCUSSION

Part I of the 2014 Update on the CRA/SPARCC Treatment Recommendations for the Management of SpA addresses principles of the management of SpA in Canada as well as barriers to their implementation. These consist of 15 recommendations as well as 6 modifications of these recommendations for application to a JSpA(ERA) population. Figure 3 illustrates a proposed algorithm for assessment.

The intent of these recommendations is to inform Canadian rheumatologists, primary care physicians, internists and other healthcare providers, persons with SpA, insurance payers, government agency staff, and formularies. It is recognized that each patient is unique and that recommendations cannot be blindly applied to all. Each treating

physician should use these recommendations along with their clinical judgment and in partnership with their patients. Ideal SpA management is individualized and specific to each particular patient.

In developing these recommendations, it is apparent that there are many clinical questions about the management of SpA that remain unanswered. Monitoring of axial disease and response to treatment with MRI, for example, remains a topic of debate. It is also clear that there are many barriers to the implementation of these SpA management principles in the current Canadian context. As the field of SpA advances, it is expected that new updates to these recommendations will be required.

## ONLINE SUPPLEMENT

Supplementary data for this article are available at [jrheum.org](http://jrheum.org).

## REFERENCES

1. Maksymowych WP, Inman RD, Gladman D, Thomson G, Stone M, Karsh J, et al. Canadian Rheumatology Association Consensus on the use of anti-tumor necrosis factor- $\alpha$  directed therapies in the treatment of spondyloarthritis. *J Rheumatol* 2003;30:1356-63.
2. Maksymowych WP, Gladman D, Rahman P, Boonen A, Bykerk V, Choquette D, et al. The Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada treatment recommendations for the management of spondyloarthritis: A national multidisciplinary stakeholder project. *J Rheumatol* 2007;34:2273-84.
3. Chen J, Veras MM, Liu C, Lin J. Methotrexate for ankylosing spondylitis. *Cochrane Database Syst Rev* 2013;2:CD004524.
4. Chen J, Liu C. Is sulfasalazine effective in ankylosing spondylitis? A systematic review of randomized controlled trials. *J Rheumatol* 2006;33:722-31.
5. van Denderen JC, van der Paardt M, Nurmohamed MT, de Ryck YM, Dijkmans BA, van der Horst-Bruinsma IE. Double blind, randomised, placebo controlled study of leflunomide in the treatment of active ankylosing spondylitis. *Ann Rheum Dis* 2005;64:1761-4.
6. Haibel H, Rudwaleit M, Braun J, Sieper J. Six months open label trial of leflunomide in active ankylosing spondylitis. *Ann Rheum Dis* 2005;64:124-6.
7. Wanders A, Heijde Dv, Landewé R, Béhier JM, Calin A, Olivieri I, et al. Nonsteroidal antiinflammatory drugs reduce radiographic progression in patients with ankylosing spondylitis: a randomized clinical trial. *Arthritis Rheum* 2005;52:1756-65.
8. Kroon F, Landewé R, Dougados M, van der Heijde D. Continuous NSAID use reverts the effects of inflammation on radiographic progression in patients with ankylosing spondylitis. *Ann Rheum Dis* 2012;71:1623-9.
9. Poddubnyy D, Rudwaleit M, Haibel H, Listing J, Märker-Hermann E, Zeidler H, et al. Effect of non-steroidal anti-inflammatory drugs on radiographic spinal progression in patients with axial spondyloarthritis: results from The German Spondyloarthritis Inception Cohort. *Ann Rheum Dis* 2012;71:1616-22.
10. Haroon N, Inman RD, Learch TJ, Weisman MH, Lee M, Rahbar MH, et al. The impact of tumor necrosis factor  $\alpha$  inhibitors on radiographic progression in ankylosing spondylitis. *Arthritis Rheum* 2013;65:2645-54.
11. Rudwaleit M, Jurik AG, Hermann KG, Landewé R, van der Heijde D, Baraliakos X, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/OMERACT



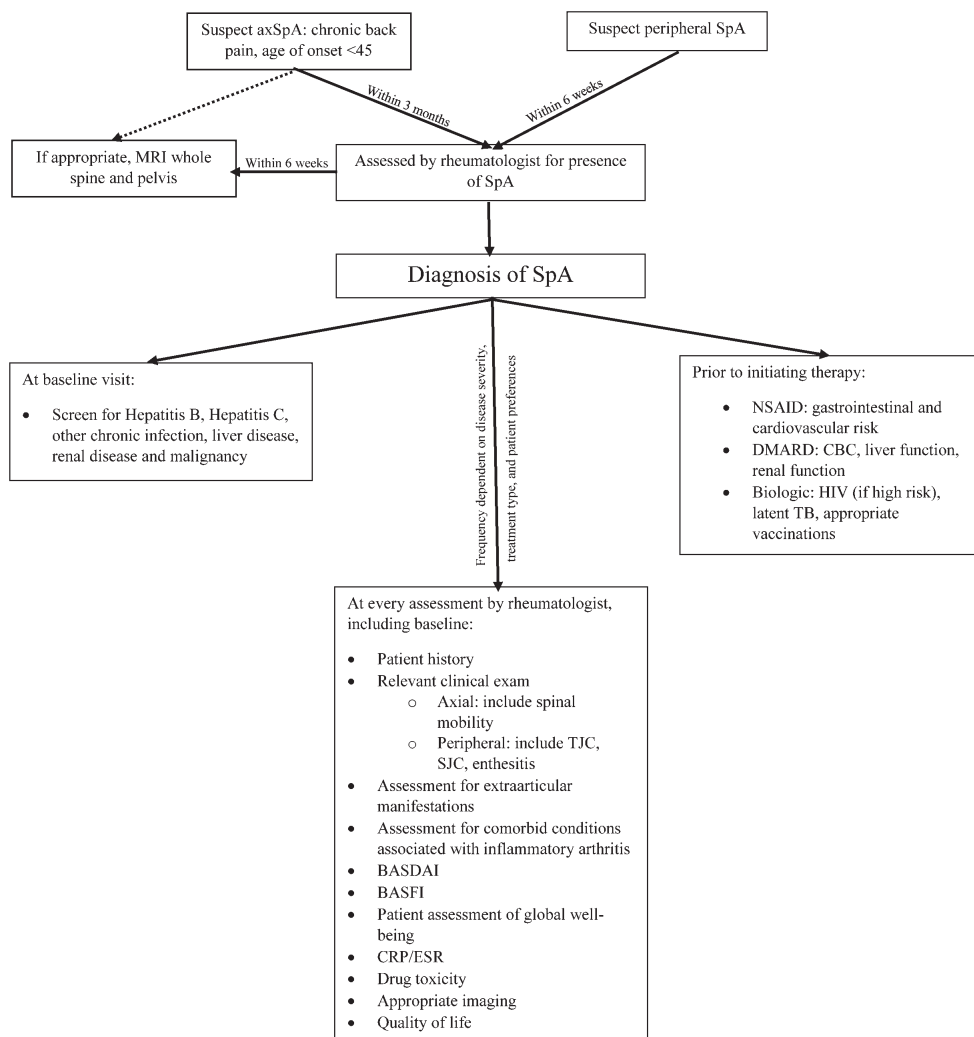


Figure 3. Algorithm for the assessment of SpA. SpA: spondyloarthritis; axSpA: axial SpA; MRI: magnetic resonance imaging; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; CBC: complete blood count; HIV: human immunodeficiency virus; TB: tuberculosis; TJC: tender joint count; SJC: swollen joint count; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

- MRI group. *Ann Rheum Dis* 2009;68:1520-7.
12. Rudwaleit M, Sieper J. Referral strategies for early diagnosis of axial spondyloarthritis. *Nat Rev Rheumatol* 2012;8:262-8.
13. Maksymowych WP, Dhillon SS, Park R, Salonen D, Inman RD, Lambert RG. Validation of the spondyloarthritis research consortium of Canada magnetic resonance imaging spinal inflammation index: is it necessary to score the entire spine? *Arthritis Rheum* 2007;57:501-7.
14. van der Heijde D, Landewé R, Hermann KG, Rudwaleit M, Østergaard M, Oostveen A, et al. Is there a preferred method for scoring activity of the spine by magnetic resonance imaging in ankylosing spondylitis? *J Rheumatol* 2007;34:871-3.
15. Rudwaleit M, Landewé R, van der Heijde D, Listing J, Brandt J, Braun J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis* 2009;68:770-6.
16. Rudwaleit M, van der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777-83.
17. Rudwaleit M, van der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis* 2011;70:25-31.
18. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H ; CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 2006;54:2665-73.
19. Bykerk VP, Akhavan P, Hazlewood GS, Schieir O, Dooley A, Haraoui B, et al. Canadian rheumatology association recommendations for pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs. *J Rheumatol* 2012;39:1559-82.

20. Scottish Intercollegiate Guidelines Network (SIGN). SIGN 50: A guideline developer's handbook [Internet. Accessed January 9, 2015.] Available from: [www.sign.ac.uk/guidelines/fulltext/50/index.html](http://www.sign.ac.uk/guidelines/fulltext/50/index.html)
21. Smolen JS, Braun J, Dougados M, Emery P, Fitzgerald O, Helliwell P, et al. Treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target: recommendations of an international task force. *Ann Rheum Dis* 2014;73:6-16.
22. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. *Ann Rheum Dis* 2010;69:48-53.
23. Coates LC, Helliwell PS. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. *Arthritis Care Res* 2010;62:965-9.
24. Sudre A, Figueiredo IT, Lukas C, Combe B, Morel J. On the impact of a dedicated educational program for ankylosing spondylitis: effect on patient satisfaction, disease knowledge and spinal mobility, a pilot study. *Joint Bone Spine* 2012;79:99-100.
25. Masiero S, Bonaldo L, Pigatto M, Lo Nigro A, Ramonda R, Punzi L. Rehabilitation treatment in patients with ankylosing spondylitis stabilized with tumor necrosis factor inhibitor therapy: a randomized controlled trial. *J Rheumatol* 2011;38:1335-42.
26. Grønning K, Skomsvoll JF, Rannestad T, Steinsbekk A. The effect of an educational programme consisting of group and individual arthritis education for patients with polyarthritis—a randomised controlled trial. *Patient Educ Couns* 2012;88:113-20.
27. Ozgocmen S, Khan MA. Current concept of spondyloarthritis: special emphasis on early referral and diagnosis. *Curr Rheumatol Rep* 2012;14:409-14.
28. Haroon M, Gallagher P, Fitzgerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2014 Feb 27 (E-pub ahead of print).
29. Carneiro S, Bortoluzzo A, Gonçalves C, Silva JA, Ximenes AC, Bértolo M, et al. Effect of enthesitis on 1505 Brazilian patients with spondyloarthritis. *J Rheumatol* 2013;40:1719-25.
30. Turan Y, Duruöz MT, Cerrahoglu L. Quality of life in patients with ankylosing spondylitis: a pilot study. *Rheumatol Int* 2007;27:895-9.
31. Haywood KL, M Garratt A, Jordan K, Dziedzic K, Dawes PT. Disease-specific, patient-assessed measures of health outcome in ankylosing spondylitis: reliability, validity and responsiveness. *Rheumatology* 2002;41:1295-302.
32. Calin A, Nakache JP, Gueguen A, Zeidler H, Mielants H, Dougados M. Defining disease activity in ankylosing spondylitis: is a combination of variables (Bath Ankylosing Spondylitis Disease Activity Index) an appropriate instrument? *Rheumatology* 1999;38:878-82.
33. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994;21:2286-91.
34. Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis* 2009;68 Suppl 2:ii1-44.
35. Benhamou M, Gossec L, Dougados M. Clinical relevance of C-reactive protein in ankylosing spondylitis and evaluation of the NSAIDs/coxibs' treatment effect on C-reactive protein. *Rheumatology* 2010;49:536-41.
36. Fagerli KM, Lie E, van der Heijde D, Heiberg MS, Kaufmann C, Rodevand E, et al. Selecting patients with ankylosing spondylitis for TNF inhibitor therapy: comparison of ASDAS and BASDAI eligibility criteria. *Rheumatology* 2012;51:1479-83.
37. Arends S, Brouwer E, van der Veer E, Groen H, Leijnsma MK, Houtman PM, et al. Baseline predictors of response and discontinuation of tumor necrosis factor-alpha blocking therapy in ankylosing spondylitis: a prospective longitudinal observational cohort study. *Arthritis Res Ther* 2011;13:R94.
38. Arends S, van der Veer E, Kallenberg CG, Brouwer E, Spoorenberg A. Baseline predictors of response to TNF- $\alpha$  blocking therapy in ankylosing spondylitis. *Curr Opin Rheumatol* 2012;24:290-8.
39. Vastesaeger N, van der Heijde D, Inman RD, Wang Y, Deodhar A, Hsu B, et al. Predicting the outcome of ankylosing spondylitis therapy. *Ann Rheum Dis* 2011;70:973-81.
40. Poddubnyy D, Rudwaleit M, Haibel H, Listing J, Marker-Hermann E, Zeidler H, et al. Rates and predictors of radiographic sacroiliitis progression over 2 years in patients with axial spondyloarthritis. *Ann Rheum Dis* 2011;70:1369-74.
41. Rudwaleit M, Haibel H, Baraliakos X, Listing J, Märker-Hermann E, Zeidler H, et al. The early disease stage in axial spondylarthritis: results from the German Spondylarthritis Inception Cohort. *Arthritis Rheum* 2009;60:717-27.
42. Poddubnyy D, Haibel H, Listing J, Märker-Hermann E, Zeidler H, Braun J, et al. Baseline radiographic damage, elevated acute-phase reactant levels, and cigarette smoking status predict spinal radiographic progression in early axial spondylarthritis. *Arthritis Rheum* 2012;64:1388-98.
43. Gladman DD, Mease PJ, Choy EH, Ritchlin CT, Perdok RJ, Sasso EH. Risk factors for radiographic progression in psoriatic arthritis: subanalysis of the randomized controlled trial ADEPT. *Arthritis Res Ther* 2010;12:R113.
44. Coates LC, Cook R, Lee KA, Chandran V, Gladman DD. Frequency, predictors, and prognosis of sustained minimal disease activity in an observational psoriatic arthritis cohort. *Arthritis Care Res* 2010;62:970-6.
45. Iervolino S, Di Minno MN, Peluso R, Lofrano M, Russolillo A, Di Minno G, et al. Predictors of early minimal disease activity in patients with psoriatic arthritis treated with tumor necrosis factor- $\alpha$  blockers. *J Rheumatol* 2012;39:568-73.
46. Chandran V, Cook RJ, Edwin J, Shen H, Pellett FJ, Shanmugarajah S, et al. Soluble biomarkers differentiate patients with psoriatic arthritis from those with psoriasis without arthritis. *Rheumatology* 2010;49:1399-405.
47. Arnbak B, Leboeuf-Yde C, Jensen TS. A systematic critical review on MRI in spondyloarthritis. *Arthritis Res Ther* 2012;14:R55.
48. Weber U, Lambert RG, Østergaard M, Hodler J, Pedersen SJ, Maksymowych WP. The diagnostic utility of magnetic resonance imaging in spondylarthritis: an international multicenter evaluation of one hundred eighty-seven subjects. *Arthritis Rheum* 2010;62:3048-58.
49. Weber U, Hodler J, Kubik RA, Rufibach K, Lambert RG, Kissling RO, et al. Sensitivity and specificity of spinal inflammatory lesions assessed by whole-body magnetic resonance imaging in patients with ankylosing spondylitis or recent-onset inflammatory back pain. *Arthritis Rheum* 2009;61:900-8.
50. Maksymowych WP, Morency N, Conner-Spady B, Lambert RG. Suppression of inflammation and effects on new bone formation in ankylosing spondylitis: evidence for a window of opportunity in disease modification. *Ann Rheum Dis* 2013;72:23-8.
51. Coates LC, Hodgson R, Conaghan PG, Freeston JE. MRI and ultrasonography for diagnosis and monitoring of psoriatic arthritis. *Best Pract Res Clin Rheumatol* 2012;26:805-22.
52. Østergaard M, McQueen F, Wiell C, Bird P, Bøyesen P, Ejbjerg B, et al. The OMERACT psoriatic arthritis magnetic resonance imaging scoring system (PsAMRIS): definitions of key pathologies, suggested MRI sequences, and preliminary scoring system for PsA hands. *J Rheumatol* 2009;36:1816-24.
53. Boyesen P, McQueen FM, Gandjbakhch F, Lillegraven S, Coates L, Wiell C, et al. The OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS) is reliable and sensitive to

- change: results from an OMERACT workshop. *J Rheumatol* 2011;38:2034-8.
54. Rosen CF, Mussani F, Chandran V, Eder L, Thavaneswaran A, Gladman DD. Patients with psoriatic arthritis have worse quality of life than those with psoriasis alone. *Rheumatology* 2012;51:571-6.
  55. Borman P, Toy GG, Babaoğlu S, Bodur H, Ciliz D, Alli N. A comparative evaluation of quality of life and life satisfaction in patients with psoriatic and rheumatoid arthritis. *Clin Rheumatol* 2007;26:330-4.
  56. Husted JA, Gladman DD, Farewell VT, Cook RJ. Health-related quality of life of patients with psoriatic arthritis: a comparison with patients with rheumatoid arthritis. *Arthritis Rheum* 2001;45:151-8.
  57. Ovayolu N, Ovayolu O, Karadag G. Health-related quality of life in ankylosing spondylitis, fibromyalgia syndrome, and rheumatoid arthritis: a comparison with a selected sample of healthy individuals. *Clin Rheumatol* 2011;30:655-64.
  58. Ward MM. Health-related quality of life in ankylosing spondylitis: a survey of 175 patients. *Arthritis Care Res* 1999;12:247-55.
  59. Bodur H, Ataman S, Rezvani A, Buğdaycı DS, Cevik R, Birtane M, et al. Quality of life and related variables in patients with ankylosing spondylitis. *Qual Life Res* 2011;20:543-9.
  60. Ozdemir O. Quality of life in patients with ankylosing spondylitis: relationships with spinal mobility, disease activity and functional status. *Rheumatol Int* 2011;31:605-10.
  61. Vesović-Potić V, Mustur D, Stanisavljević D, Ille T, Ille M. Relationship between spinal mobility measures and quality of life in patients with ankylosing spondylitis. *Rheumatol Int* 2009;29:879-84.
  62. Ward MM. Predictors of the progression of functional disability in patients with ankylosing spondylitis. *J Rheumatol* 2002;29:1420-5.
  63. Guillemin F, Briancón S, Pourel J, Gaucher A. Long-term disability and prolonged sick leaves as outcome measurements in ankylosing spondylitis. Possible predictive factors. *Arthritis Rheum* 1990;33:1001-6.
  64. van der Horst-Bruinsma IE, Zack DJ, Szumski A, Koenig AS. Female patients with ankylosing spondylitis: analysis of the impact of gender across treatment studies. *Ann Rheum Dis* 2013; 72:1221-4.
  65. Vander Cruyssen B, Muñoz-Gomariz E, Font P, Mulero J, de Vlam K, Boonen A, et al. Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery. *Rheumatology* 2010;49:73-81.
  66. Doran MF, Brophy S, MacKay K, Taylor G, Calin A. Predictors of longterm outcome in ankylosing spondylitis. *J Rheumatol* 2003;30:316-20.
  67. Brophy S, Mackay K, Al-Saidi A, Taylor G, Calin A. The natural history of ankylosing spondylitis as defined by radiological progression. *J Rheumatol* 2002;29:1236-43.
  68. Healey EL, Haywood KL, Jordan KP, Garratt AM, Packham JC. Patients with well-established ankylosing spondylitis show limited deterioration in a ten-year prospective cohort study. *Clin Rheumatol* 2013;32:67-72.
  69. Stafford L, Kane D, Murphy E, Duffy T, Lassere M, Youssef PP, et al. Psoriasis predicts a poor short-term outcome in patients with spondylarthropathy. *Arthritis Rheum* 2001;45:485-93.
  70. di Minno MN, Peluso R, Iervolino S, Lupoli R, Russolillo A, Scarpa R, et al. Obesity and the prediction of minimal disease activity: a prospective study in psoriatic arthritis. *Arthritis Care Res* 2013;65:141-7.
  71. Tse SM, Burgos-Vargas R, Colbert RA. Juvenile spondyloarthritis treatment recommendations. *Am J Med Sci* 2012;343:367-70.
  72. Rachlis AC, Babyn PS, Lobo-Mueller E, Benseler SM, Stimec J, Anderson M, et al. Whole body magnetic resonance imaging in juvenile spondyloarthritis: will it provide vital information compared to clinical exam alone? *Arthritis Rheum* 2011;63 Suppl 10:749.