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REVIEW ARTICLE

Pediatric Society of the African League Against Rheumatism juvenile idiopathic arthritis recommendations for enthesitis-related arthritis and juvenile psoriatic arthritis

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Abstract

The objective of this study is to develop evidence-based recommendations for the diagnosis and management of enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) in the African context. The recommendations for ERA and JPsA were combined into a single document. The steering committee and task force identified 15 key questions and formulated 35 research questions. A comprehensive literature review, utilizing Medline and a manual search for African local data, was conducted to gather evidence. Following this synthesis, the task force developed draft recommendations and engaged in a Delphi process with an expert panel, including 17 African and three international experts, to reach a consensus and ensure alignment with global standards. The final recommendations were assigned a level of evidence and subsequently approved by the task force members, the expert panel, and the PAFLAR Board. Fifteen recommendations on the diagnosis and management of ERA and JPsA were developed, covering the role of the pediatric rheumatologist in multiple aspects of disease management, including diagnosis, monitoring of disease and extra-articular manifestations, determining treatment strategies, and guiding interventions. The level of evidence supporting these recommendations was variable, leading to the identification of a research agenda to address African particularities and answer pending questions. The final recommendations achieved a high level of agreement, with consensus ranging from 90 to 100%. These recommendations represent an important achievement for pediatric rheumatology in Africa, being the first of their kind, tailored specifically to the region. Developed through a rigorous methodology and collaboration between international and African experts, they aim to standardize care and address the unique challenges faced in African setting.

Innovation

What is known in this area?

- Existing guidelines for ERA and JPsA are typically based on data from non-African populations and may not fully address the unique challenges faced in African settings.

What is new?

- For the first time, evidence-based recommendations specifically tailored to the African context for the diagnosis and management of ERA and JPsA have been developed.
- The recommendations are the result of a comprehensive, regionally focused literature review, combining both global standards and local data to ensure relevance and applicability in Africa.
- A collaborative Delphi process, involving both African and international experts, was employed to achieve consensus, reflecting a balance between global expertise and local insights.

What is the clinical implication?

- These tailored recommendations aim to standardize the care of ERA and JPsA across Africa, addressing specific regional challenges and potentially improving patient outcomes in these settings.

Keywords Africa · Enthesitis-related arthritis · Juvenile idiopathic arthritis · Juvenile psoriatic arthritis · PAFLAR · Recommendations

Introduction

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) represent a spectrum of diseases characterized by a shared genetic background and a range of musculoskeletal manifestations involving the axial and appendicular skeleton, along with non-musculoskeletal symptoms like inflammatory bowel disease, uveitis, and, specifically in JPsA, the skin, and nails [1, 2]. The phenotype of these diseases can vary widely in severity, and active disease can significantly affect patients' quality of life and lead to disability [3]. ERA and JPsA epidemiology in Africa is underexplored, with limited studies suggesting low occurrence, particularly in Sub-Saharan Africa, although rates in North Africa align with Caucasian populations [4, 5]. Comprehensive prevalence data are urgently needed to inform healthcare policies and strategies [6].

Managing ERA and JPsA involves both non-pharmacological and pharmacological approaches. In the past two decades, the arsenal of disease-modifying antirheumatic drugs (DMARDs) has greatly expanded for adult spondyloarthritis, offering new treatment options for children. This includes conventional synthetic DMARDs (csDMARDs) such as methotrexate and sulfasalazine, biological agents (bDMARDs) particularly tumor necrosis factor inhibitors (TNFi), and other interleukin (IL)−12/23 and IL-17A inhibitors [7]. Additionally, targeted synthetic DMARDs (tsDMARDs) inhibiting Janus kinases (JAKs) have been recently introduced. Despite their effectiveness in adults, these newer treatments are less studied in children, highlighting the need for clinical guidance [8].

In response, PAFLAR initiated a task force to develop practical recommendations for diagnosing and treating JPsA and ERA. This marks the first collaborative effort among African physicians to establish a consensus on managing a musculoskeletal disease and set a unified research agenda. Furthermore, PAFLAR plans to focus on implementing the recommendations in African countries as the next step in its future agenda.

Method

Design

The PAFLAR board established a steering committee to develop guidelines for the main subtypes of JIA. Following the model of the adult guidelines and to align the new JIA classification PRINTO, it was decided to combine the ERA and PsoA guidelines into one document to better inform practical recommendations. The steering committee issued a call for participation, and a working group for ERA and PsoA subtypes was formed. The steering committee identified 15 key questions that the guidelines should address (Table 1). The working group then formulated 37 PICO (population, intervention, comparator, and outcome) questions, averaging 1 to 4 PICO questions per key question (supplementary material 1).

Literature search & review

The working group conducted a literature review using keywords based on the PICO questions through Medline, supplemented with manual searches for local data. This review included a synthesis of scientific evidence and a consensus process that combined existing scientific evidence with clinical experience (supplementary material 2). The literature review was updated in February 2024, just before the guidelines underwent the third Delphi round.

Steering committee, expert panel, and working group

The steering committee consisted of three experienced rheumatologists (two pediatric and one adult), all with expertise in the field of international collaboration and guidelines methodology. The working group included five university rheumatologists, each tasked with preparing the draft of three recommendations responding to three key questions randomly assigned to them (Version 0). Subsequent Zoom meetings allowed the working group to review and discuss the draft recommendations and supporting arguments, ultimately reaching a consensus on the recommendations and producing the first version of the guidelines (version 1). The expert panel consisted of three international specialists with extensive experience in spondyloarthritis and 17 African experts from different regions across the continent. This panel engaged in three rounds of Delphi voting to refine and finalize the recommendations.

Target of the recommendations

All healthcare professionals involved in the care of children with JIA in Africa, including pediatric rheumatologists, adult rheumatologists, pediatricians, general practitioners, family physicians, physical medicine specialists, clinical immunologists, orthopedic surgeons, and paramedical professionals, particularly physiotherapists, and nurses, as well as policymakers and healthcare providers, including departments of health and hospital administrations.

Table 1 Research agenda and perspectives

QD1 and 2	A referral strategy should be developed and evaluated in Africa to accommodate available resources and address local challenges
QD3	The revised ILAR criteria, as updated by PRINTO in 2019, need to be evaluated for their applicability, sensitivity, and specificity in assessing children with JIA in Africa
QD4	A strategic approach needs to be established and evaluated regarding the hierarchy of investigations to rule out alternative diagnoses, adapted to the African context
QD5	Epidemiological studies assessing the frequency of ERA and JPsA, as well as their comorbidities and extra-musculoskeletal manifestations, should be conducted in Africa
QT6	Feasibility and impact of the treat-to-target strategy should be assessed in African children with ERA and JPsA
QT7	Real-life data from registries and large clinical hospital-based studies on the efficacy and tolerance of csDMARDs in the African context are needed
QT8	Real-life data from registries and large clinical hospital-based studies on the efficacy and tolerance of bDMARDs and tsDMARDs in the African context are needed
QT9	High risk of disability In African children with ERA/PsoA should be identified
QT10	The short- and long-term impact and tolerance of steroid use should be assessed among African children
QT11	Different therapeutic strategies should be assessed in the African context to determine whether a step-down strategy and early aggressive treatment would be more effective than conventional therapeutic regimens, which are based on treatment escalation
QT12	Safety and cost-effectiveness studies are needed for biologic (originator and biosimilar) and targeted therapies in children with ERA and JPsA in Africa. Head-to-head studies are needed to establish a preferred order of use of biologic/targeted therapy in children with JIA
QT13	Disease activity scores and cut-offs should be validated in children with ERA and JPsA in Africa. Feasibility and impact of treat-to-target strategy should be assessed in African children with ERA and PsoA
QT14	Treatment availability and tapering strategies should be assessed in children with ERA and JPsA in the African context
QT15	The availability of non-pharmacological treatments such as physical therapy, occupational therapy, psychological support, and transitional care should be assessed in the African context to determine the best implementation strategies

QD key question for diagnosis, *QT* key question for treatment

Delphi process

The Delphi method, a structured iterative process, was used to achieve consensus among African practitioners and international experts. This involved three rounds of questionnaires sent via Google Forms, ensuring alignment with global standards and up-to-date management recommendations and reaching a consensus on the guidelines. Experts rated each recommendation on a 5-point Likert scale (1, totally disagree; 2, disagree; 3, neutral; 4, agree; 5, totally agree) and provided comments during the initial two rounds of Delphi questionnaires. All voting results from Delphi surveys are included in the supplementary material 1. For the final vote, the process was binary, with experts voting to either validate or not validate the final version without providing additional comments.

Consensus process

After each Delphi round, comments were discussed in Zoom meetings, and the recommendations were reformulated accordingly. The process was drafted in line with the EULAR standard operating procedures (SOPs) for developing recommendations and the AGREE II document. Three Delphi rounds were conducted to establish consensus, which allows sufficient consideration of group responses and is considered an effective method for reaching consensus.

Patient perspective assessment

After finalizing the recommendations, the validated version was reviewed by three patients to gain their perspectives: an adult female with juvenile-onset spondyloarthritis from North Africa, a 17-year-old adolescent with JPsA from North Africa, and a guardian of a child with a similar condition from Sub-Saharan Africa. The selection of patients was based on their willingness to voluntarily participate in the review process and their ability to engage in the process independently.

Recommendation rating, level of agreement, level of evidence

Following the meeting, the levels of evidence (LoE) and grades of recommendation (GoR) were assigned to each recommendation by the working group, based on the standards of the Oxford Centre for Evidence-Based Medicine [9]. A research agenda was developed to address identified evidence gaps and to guide the formulation of an educational agenda for future PAFLAR initiatives. The draft manuscript was subsequently sent to all working groups and expert panel

members for review. The final manuscript was approved by all authors and the PAFLAR Board.

Result

Recommendations

The recommendations for diagnosis and treatment, along with the corresponding levels of evidence and agreement, are presented in Tables 2 and 3, respectively. Figure 1 illustrate the Enthesitis-related arthritis and Juvenile Psoriatic arthritis Treatment algorithm.

Diagnosis

Recommendation n°1

- The diagnosis of enthesitis-related arthritis (ERA) should be suspected in a child with inflammatory arthralgia or arthritis, especially if it is asymmetrical, involves the lower limb (particularly the hip), and is associated with enthesitis. It is recommended to refer the patient to a pediatric rheumatologist. (LoE, IIb)
- The diagnosis of juvenile psoriatic arthritis (JPsA) should be suspected in a child with inflammatory arthralgia, arthritis, or enthesitis associated with psoriasis, or a family history of psoriasis, psoriatic nail involvement, or dactylitis. Referring the patient to a pediatric rheumatologist is recommended. (LoE, IIb)

Contrary to adult spondyloarthritis, no studies have identified early signs indicating the risk of developing ERA. However, several studies highlight the clinical symptoms at onset and their differences from the adult form [10, 11]. Ethnic variations exist, but male predominance in ERA is well-documented, suggesting that boys with chronic arthritis should be evaluated for ERA. Peripheral arthritis and enthesitis are typical features, while axial arthritis usually develops after about 5 years [10–14]. Lower limb asymmetrical oligoarthritis is the most common presentation, seen in 60–75% of cases [10, 11]. Monoarticular and polyarticular arthritis are rare at onset, occurring in 5–20% of cases. Hip involvement, affecting one-third of patients, may be the initial presentation of the disease, as documented by studies from Tunisia and Morocco [15, 16]. Male gender, ERA, and North African origin are associated with a higher prevalence of hip arthritis [17, 18].

Observational studies show that JPsA involves arthritis along with either psoriasis or a family history of psoriasis [19, 20]. Unlike adult psoriatic arthritis, where psoriasis typically precedes arthritis, in JPsA, arthritis often appears first, with psoriasis emerging up to a decade later. Initially, JPsA is often oligoarticular but progresses to polyarthritis in 60–80% of cases [21]. Distal interphalangeal joint involvement, dactylitis, and enthesitis occur in about one-third of patients at onset. These signs should prompt consideration of JPsA and referral to a pediatric rheumatologist [21].

Recommendation no. 2

- HLA B27 antigen should be tested if clinical and/or radiological signs are insufficient for the diagnosis of ERA (LoE, IIb).
- Ultrasound should be considered to assess clinical or subclinical enthesitis and arthritis. (LoE, IIb).
- Conventional radiography (CR) of the affected joints may be performed, to assess structural damage*(LoE, IIIc).
- MRI should be performed (if available) in case of sacroiliac joint and/or spinal symptoms** (LoE, IVc).

* The risk of pelvic radiation should be considered. CR exhibits low sensitivity for detecting arthritis or enthesitis in the early stages.

** MRI interpretation should be performed by an experienced radiologist in musculoskeletal imaging in children.

JIA is primarily a clinical diagnosis, with no specific tests to identify ERA or JPsA, as these can mimic other JIA forms. First-line assessments help rule out other diagnoses. Laboratory investigations such as CBC, ESR, CRP, ANA, RF, HLA-B27, and musculoskeletal imaging contribute to diagnosis [22]. HLA-B27 is highly prevalent in ERA and is included in the ILAR classification exclusion criteria for other categories [1]. The prevalence of HLA-B27 in ERA varies, with reports showing 66% positivity in Egyptian studies, and seems less frequent in Sub-Saharan Africa [23, 24]. HLA-B27 is associated with sacroiliitis, higher disease activity, and male gender [1, 24–26]. ANA is typically negative in ERA but can be positive in psoriatic arthritis and is a biomarker for JIA-related uveitis [26].

Conventional radiography (CR) has low sensitivity for early detection of arthritis and enthesitis and should be used to assess chronic damage or exclude other diagnoses [25, 27]. The risk of pelvic radiation should be considered and evaluated according to the expected benefit of the X-ray for diagnosis [28]. CR is recommended for focal bone pain to rule out infection or malignancy. In cases of acute monoarthritis, CR of the affected joint is advised [27, 28]. For hip involvement, MRI is preferred over CR due to lower radiation exposure [29].

Recent advancements in JIA imaging, including ultrasound and MRI, aid in diagnosis, monitoring, and treatment evaluation [30–32]. MRI and ultrasound can detect joint effusion and synovitis, with MRI also identifying bone oedema [32]. These methods are recommended as first-line

Table 2 PAFLAR JIA recommendation for ERA and JPsA for diagnosis

N	Recommendations	LOE	LOA
1	- The diagnosis of enthesitis-related arthritis (ERA) should be suspected in a child with inflammatory arthralgia or arthritis, especially if it is asymmetrical, involves the lower limb (particularly the hip), and is associated with enthesitis. It is recommended to refer the patient to a pediatric rheumatologist	IIb	100%
	- The diagnosis of juvenile psoriatic arthritis (JPsA) should be suspected in a child with inflammatory arthralgia, arthritis, or enthesitis associated with psoriasis, or a family history of psoriasis, psoriatic nail involvement, or dactylitis. Referring the patient to a pediatric rheumatologist is recommended	IIb	
2	- HLA B27 antigen should be tested if clinical and/or radiological signs are insufficient for the diagnosis of ERA	IIb	100%
	- Ultrasound should be considered to assess clinical or subclinical enthesitis and arthritis	IIb	
	- A conventional radiography (CR) of the affected joints should be performed, to assess structural damage*	IIIc	
	- An MRI should be performed (if available) in case of sacroiliac and/or spinal joint symptoms**	IVc	
	* The risk of pelvic radiation should be considered. CR exhibits low sensitivity for detecting arthritis or enthesitis in the early stages ** MRI interpretation should be performed by an experienced radiologist in musculoskeletal imaging in children		
3	- The ILAR 2001 classification criteria should be used to assist in the diagnosis of ERA and JPsA	IIb	90%
	• When there is clinical suspicion of ERA in a patient who does not meet the ILAR criteria, clinicians may refer to the ASAS criteria for adult Spondylarthritis in case of early axial involvement	IIIb	
	• When there is clinical suspicion of JPsA in a patient who does not fulfill the ILAR criteria, clinicians may refer to the CASPAR criteria for adult PsoA or the Vancouver Criteria	IIIb	
4	Alternative diagnoses should be considered based on the clinical presentation before concluding a diagnosis of ERA or JPsA	IV	100%
	• In case of enthesitis, consider orthopedic conditions* or mechanical enthesopathy		
	• In case of low back pain and/or sacroiliitis**, consider infectious, tumoral, traumatic, and other inflammatory and mechanical causes		
	• In case of articular involvement***, consider infection-related arthritis, post-infectious arthritis, inflammatory, metabolic, vasculitis, tumoral, and mechanical causes		
	• In case of articular and cutaneous involvement, consider viral infections, post-infectious disease, inflammatory, vasculitis, and granulomatosis ¥		
	• In case of dactylitis, consider infectious causes, sickle-cell disease, and tumor§		
	• In case of acute or chronic (JPsA, ERA) uveitis, consider infectious conditions, post-infectious conditions, and non-infectious conditions) Ω		
	*Osteochondrosis and apophysitis: Sever disease, Osgood-Schlatter disease, Sinding-Larsen–Johansson syndrome…		
	**Behçet disease, Familial Mediterranean Fever (FMF), inflammatory bowel disease, chronic recurrent multifocal osteomyelitis or juvenile fibromyalgia, Scheurman disease…		
	*** Reactive arthritis, Juvenile systemic lupus erythematosus, inflammatory bowel disease, FMF, polyarticular and oligoarticular JIA, hemophilic arthropathy, Vasculitis (Henoch–Schönlein purpura), osteoid osteoma, synovial osteochondroma, Freiberg disease, Primary Hypertrophic Osteoarthropathy, Neuropathic Arthropathy, benign joint hypermobility syndrome, Pachydermodactyl, idiopathic hip chondrolysis…		
	¥ Reactive arthritis, systemic JIA, Juvenile dermatomyositis, IBD, Behçet disease, Kawasaki disease, granulomatous dermatitis, sarcoidosis…		
	§ Tuberculosis, *Staphylococcus*, *Streptococcus*, osteoid osteoma		
	Ω Viral anterior uveitis, tuberculosis, brucellosis, post-streptococcal syndrome and post-viral or post-vaccination uveitis, Blau syndrome, sarcoidosis, tubulointerstitial nephritis and uveitis syndrome, Fuchs uveitis, Kawasaki syndrome, hereditary autoinflammatory syndromes, leukemia, juvenile xanthogranuloma, and intraocular foreign body…		
	This list is not exhaustive but for information only		
5	In children and adolescents diagnosed with ERA or JPsA, extra-musculoskeletal manifestations, complications, and comorbidities should be actively assessed, including screening for:	IVb	100%
	VI. Uveitis: For children with ERA and JPsA, regular ophthalmic screening for uveitis is recommended • In high-risk JPsA patients (ANA positive, age of onset < 7 years, disease duration ≤ 4 years), screening should be performed every 3 months • In low-risk JPsA patients (ANA negative, age of onset ≥ 7 years, disease duration > 4 years), as well as in ERA patients, screening should be conducted every 6–12 months		
	II. Skin manifestations (e.g., oral ulcers, erythema nodosum, pyoderma gangrenosum, psoriasis, and nail involvement)		
	III. Inflammatory bowel diseases (in case of poor linear growth, poor weight gain, anemia, hypoalbuminemia, abdominal pain, diarrhea, and bloody stools)	IIb	
	IV. Cardiovascular complications, particularly aortic regurgitation, should be conducted using echocardiography, ideally performed by a pediatric cardiologist if clinical suspicion arises	IVb	
	V. Risk factors of atherosclerosis, including obesity and metabolic syndrome, by assessing body mass index and lipid profile	Ib	

ERA enthesitis-related arthritis, *JPsA* juvenile psoriatic arthritis, *LOA* level of agreement, *LOE* level of evidence, *CR* conventional radiography, *ILAR* international league against rheumatism, *ANA* antinuclear antibody, *HLA* human leucocyte antigen

Table 3 PAFLAR JIA recommendation for ERA and JPsA for treatment

N	Recommendations	LOE	LOA
6	The primary treatment target in ERA and JPsA should be to achieve remission, defined as the complete absence of disease symptoms and signs without ongoing treatment. In cases where remission is not feasible, maintaining low disease activity may be considered as an alternative target	IIb	100%
7	• Treatment with NSAIDs should be recommended as the first-line therapy for children with ERA and JPsA	IIIb	90%
	• Continuous NSAID therapy may be preferred over on-demand treatment	IIb	
	• csDMARDs should be considered as part of the first-line treatment for JPsA and ERA with polyarthritis	IIb	
8	• The use of intraarticular glucocorticoids (IAGC) may be recommended for children with ERA and JPsA as an adjunct treatment when persistent inflammation is present in one or a few joints, prior to considering treatment escalation	IIb	100%
	• In children with active sacroiliitis despite ongoing treatment with NSAIDs, IAGC may be recommended if radiological guidance equipment is available	IV	
	• Triamcinolone hexacetonide (THA), if available, should be recommended as the drug preparation of choice for intra-articular injections	IIa	
	• More soluble corticosteroid preparations may be recommended in small or superficial joints (betamethasone or methylprednisolone) to avoid subcutaneous atrophy or hypopigmentation	V	
	• The use of ultrasound guidance for injections may be recommended, especially in small, deformed, or clinically challenging joints, when performed by skilled practitioners	IIIb	
	• In patients with sacroiliitis, enthesitis, or polyarthritis in a high or moderate disease activity despite treatment with NSAIDs and/or DMARDs, bridging therapy with a limited course of oral glucocorticoid (< 3 months) during initiation or escalation of therapy may be recommended	IIIb	
	• In patients with sacroiliitis, enthesitis, or polyarthritis with a low disease activity, it is conditionally recommended against bridging therapy with oral glucocorticoid and in a chronic setting regardless of the disease activity	IIIb	
	• The use of the minimal effective dose of corticosteroids for the briefest duration possible should be recommended to achieve/maintain the target of remission or low disease activity and to mitigate the risk of adverse events, especially concerning growth and bone health	IIb	
	• Children undergoing corticosteroid therapy may benefit from receiving supplementation with calcium, vitamin D, and gastroprotective measures	IIIb	
9	In children with ERA or JPsA with a high risk of disability (high disease activity, active sacroiliitis, involvement of high-risk joints: hips, wrists, ankles, cervical spine, and limited spinal mobility) the prompt initiation of a second-line therapy should be recommended	V	95%
10	• In children with active enthesitis who have failed first-line treatment (NSAIDs), using a TNFi* should be recommended over csDMARDs	Ia	100%
	• In the case of mild enthesitis or concomitant arthritis csDMARDs should be considered before the initiation of biologics	IIb	
	• In case of active oligoarthritis, who have failed first-line treatment (NSAIDs and IAGC), csDMARDs should be recommended	Ib	
	• In case of active sacroiliitis despite NSAIDs (two families of NSAIDs for at least 2 weeks each) adding a TNFi should be recommended over continued NSAIDs monotherapy	IVa	
	• In children with acute anterior uveitis, topical glucocorticoid therapy or systemic glucocorticoid should be recommended, according to the severity of uveitis	IIIb	
	• In ERA or JPsA-associated chronic uveitis, csDMARDs, preferably MTX, may be recommended before escalating to monoclonal therapy TNFi	IIIa	
	• In severe and extensive psoriasis, bDMARDs should be considered over csDMARDs	IIIa	
	*If available and in the absence of contraindication		
11	For children experiencing active enthesitis and/or active sacroiliitis who have not responded to initial treatment with a first TNFi, or have a contraindication to TNFi, another targeted therapy (biologic or synthetic) should be recommended as a third-line treatment following careful analysis of the clinical features and reasons for treatment failure	IVc	90%
12	• Selecting biologic therapy for children with ERA and PsoA should consider various criteria such as cost, availability, and safety in the African context. Involving experts is crucial for making well-informed decisions regarding the most appropriate treatment option	IV	90%
	• For patients eligible for targeted therapy, starting with TNFi as the initial targeted treatment may be recommended	Ib	
	• The choice of the TNFi molecule (monoclonal or receptor, originator or biosimilar) depends mainly on the clinical features and availability	IV	
	• In case of TNFi therapy failure, a second TNFi or anti-IL17 or IL 23i or JAKi should be considered in no preferred order but depending on clinical features, extra-articular manifestation, cause of the failure of the first TNFi, the availability and the approval of the treatment	IV	
	• Adding Methotrexate to the biologic treatment may be recommended during initiation of the bDMARD	IIa	

Table 3 (continued)

N	Recommendations	LOE	LOA
13	• Children with ERA or JPsA should undergo assessment for symptoms related to spinal, peripheral joints, and entheses symptoms as well as extra-articular manifestations and comorbidities in each clinical visit	IV	100%
	• Adapted and validated specific scores (ex: JADAS, JSpADAS) should be used to monitor disease activity and adjust treatment strategy	IIb	
	• Children diagnosed with ERA and PsoA stand to gain from regular clinical evaluations at 3-month intervals. The frequency may be adjusted to shorter intervals during flare-ups and extended during periods of remission. The repetition of comprehensive assessments, including workup, imaging, and specialized examinations (ophthalmologist, dermatologist….), should be tailored based on the severity of symptoms and the disease's activity	IV	
14	• Considering tapering medication in ERA and JPsA may be recommended only after at least 6 months of disease inactivity while on treatment	IV	100%
	• The minimal duration of remission before medication tapering should be prolonged in the presence of predictive factors of flares*	V	
	• Medication withdrawal in ERA and JPsA may be considered only after progressive tapering in patients with longstanding remission	V	
	• The decision of tapering should be individualized and based on shared decision-making**	V	
	• The choice of the tapering strategy should be guided by the recommendation of the treating physician	V	
	*Predictive factors of flares: long time interval between disease onset and csDMARDs initiation, late bDMARDs initiation since diagnoses (more than 2 years), treatment with bDMARDs, and the presence of uveitis (V)		
	** Factors to take into consideration include disease duration, early inactive disease, efforts made to achieve inactive disease, and the safety of the treatment		
15	• Physical therapy and occupational therapy should be recommended in JIA patients including ERA and JPsA	IV	100%
	• Patients with ERA and JPsA should receive the necessary support for transitioning to adult care	IV	
	• The use of a specific diet should not be recommended without first discussing it with the treating physician	V	
	• We strongly recommend against using traditional medicine before discussing it with the treating physician	V	
	• The vaccination schedule should be updated for children with ERA and JPsA prior to initiating immunosuppressive therapy**.** Inactivated vaccines* are strongly advised**;** however, live attenuated vaccines are strongly discouraged during immunosuppressive treatment, and specific precautions should be considered. Discussions regarding vaccine administration are recommended during periods of remission, with careful planning for immunosuppressor withdrawal and reintroduction based on the specific vaccine type	IV	
	*Inactivated pneumococcal vaccines, influenza virus, and those scheduled according to the country vaccine calendar		

ERA enthesitis-related arthritis, *JPsA* juvenile psoriatic arthritis, *LOA* level of agreement, *LOE* level of evidence, *csDMARD* conventional synthetic disease-modifying anti-rheumatic drug, *bDMARD* biologic disease-modifying anti-rheumatic drug, *JAK* Janus kinase, *TNF* tumor necrosis factor, *IL* interleukin, *JADAS* juvenile arthritis disease activity score, *JSpADAS* juvenile spondylarthritis disease activity score, *THA* triamcinolone hexacetonide, *NSAID* non-steroid ant-inflammatory drugs, *IAGC* intraarticular glucocorticoids

imaging techniques, with the US being useful for affected joints and enthesis and differential diagnosis [30, 31]. MRI is ideal for evaluating hard-to-assess joints and soft tissue inflammation [32].

Recommendation 3 The ILAR 2001 classification criteria should be used to assist in the diagnosis of ERA and JPsA. (LoE, IIb).

- When there is clinical suspicion of ERA in a patient who does not meet the ILAR criteria, clinicians may refer to the ASAS criteria for adult Spondylarthritis in case of early axial involvement. (LoE, IIIb)
- When there is clinical suspicion of JPsA in a patient who does not fulfill the ILAR criteria, clinicians may refer to the CASPAR criteria for adult PsoA or the Vancouver Criteria. (LoE, IIIb)

Numerous classification criteria have been proposed since the 1970s, but none have been universally adopted as diagnostics standards or achieved consensus approval [33]. This lack of consensus stems from the substantial heterogeneity among patients with ERA and JPsA and the inconsistent performance of these criteria for diagnosis [33]. International guidelines focus on therapeutic management for JIA rather than diagnosis, often relying on the ILAR classification criteria [34, 35]. Some studies indicate that the ASAS criteria for peripheral SpA show high sensitivity, while the ILAR and PRINTO criteria demonstrate higher specificity for ERA patients [36]. ASAS criteria for peripheral SpA are particularly sensitive for classifying ERA, and ASAS axial SpA criteria can detect early axial involvement [36, 37]. Furthermore, it has been observed that the ILAR criteria are less sensitive than the ASAS criteria in classifying patients with childhood-onset spondyloarthropathies [33]. PRINTO

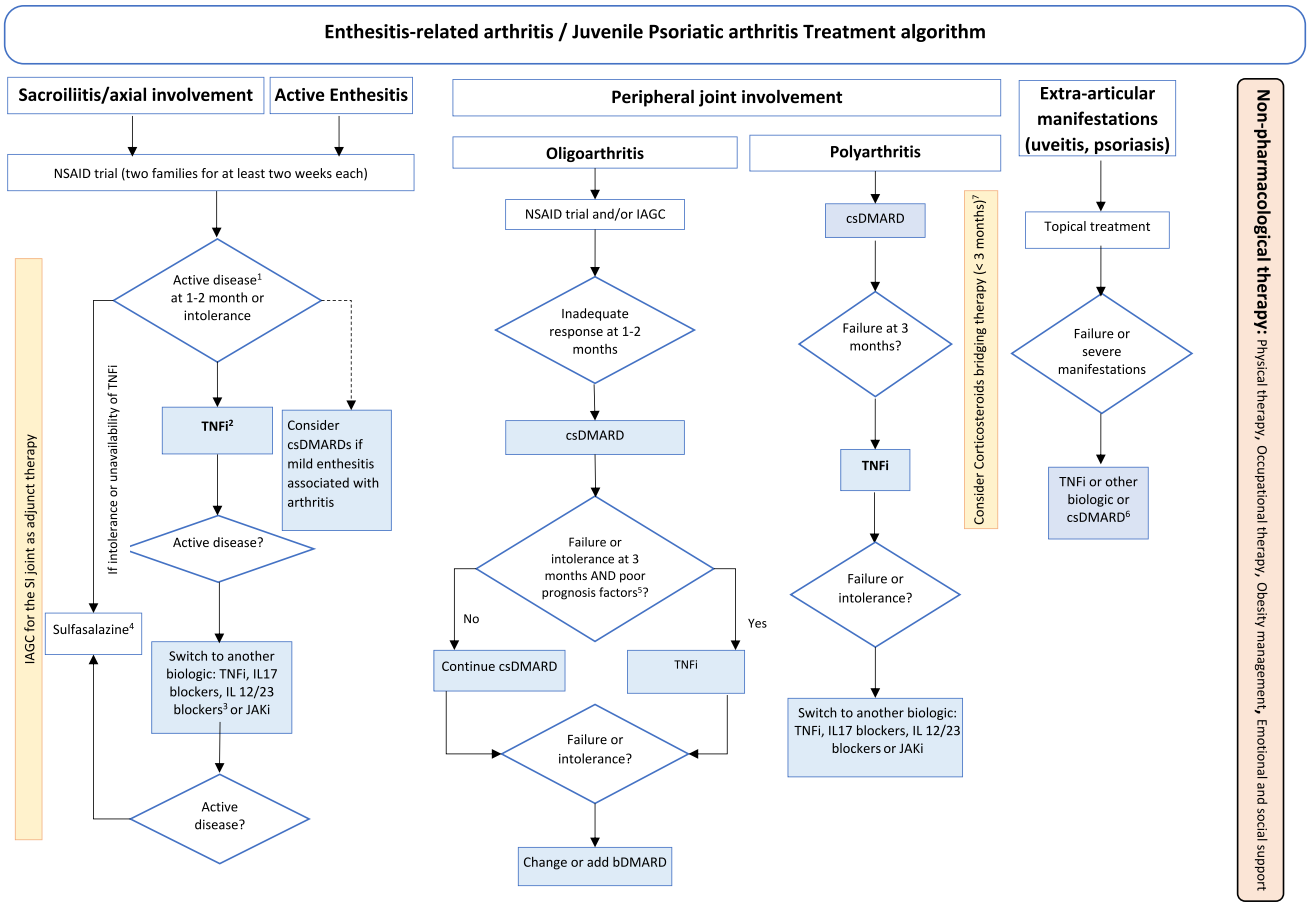

Fig. 1 Enthesitis-related arthritis and Juvenile Psoriatic arthritis Treatment algorithm. 1: active enthesitis is defined as tenderness and/or swelling of the entheses determined to require medical treatment. Active sacroiliitis is defined as Prior or current magnetic resonance imaging findings consistent with sacroiliitis along with clinical examination findings consistent with sacroiliitis (e.g., pain with direct palpation of the sacroiliac joints) and/or patient-reported symptoms of inflammatory back pain. 2: TNFi associated with low dose methotrexate. 3: secukinumab or ustekinumab, in case of enthesitis or peripheral arthritis. 4: sulfasalazine is not efficacious in axial manifestations. 5: Features of poor prognosis: involvement of ankle, wrist, hip, presence of erosive disease or enthesitis, delay in diagnosis, elevated levels of inflammation markers, symmetric disease. 6: chose a TNFi monoclonal antibody in case of uveitis. 7: consider systemic corticosteroids in case of failure of first line treatment as bridging therapy for a short course

criteria were introduced to address ILAR limitations but currently apply to only a minority of JIA patients. They do not necessarily align better with clinic-biologic subtypes or adult arthritis compared to ILAR [38].

For psoriatic arthritis, ILAR criteria are insufficient to identify all patients. Data support dividing JPsA into subgroups based on age at onset. Pediatric rheumatologists may not diagnose JPsA in all children meeting CASPAR criteria, suggesting a need to unify adult and pediatric psoriatic arthritis criteria [21].

Stoll et al. [39] confirmed that ILAR definitions significantly restrict the diagnosis of childhood psoriatic arthritis with the Vancouver criteria showing higher sensitivity but lower specificity.

Recommendation 4 Alternative diagnoses should be considered based on the clinical presentation before concluding a diagnosis of ERA or JPsA. (LoE, IV).

- In case of enthesitis, consider orthopedic conditions* or mechanical enthesopathy.
- In case of low back pain and/or sacroiliitis**, consider infectious, tumoral, traumatic, and other inflammatory and mechanical causes.
- In case of articular involvement ***, consider infection-related arthritis, post-infectious arthritis, inflammatory, metabolic, vasculitis, tumoral, and mechanical causes.
- In case of articular and cutaneous involvement, consider viral infections, post-infectious disease, inflammatory, vasculitis, and granulomatosis ¥

- In case of dactylitis, consider infectious causes, sickle-cell disease, and tumor §
- In case of acute or chronic (JPsA, ERA) uveitis, consider infectious conditions, post-infectious conditions, and non-infectious conditions Ω (LoE: IV)

*Osteochondrosis and apophysitis: Sever disease, Osgood–Schlatter disease, Sinding-Larsen–Johansson syndrome…

**Behçet disease, familial Mediterranean fever (FMF), inflammatory bowel disease, chronic recurrent multifocal osteomyelitis or juvenile fibromyalgia, Scheurman disease…

*** Reactive arthritis, juvenile systemic lupus erythematosus, inflammatory bowel disease, FMF, polyarticular and oligoarticular JIA, hemophilic arthropathy, vasculitis (Henoch–Schönlein purpura), osteoid osteoma, synovial osteochondroma, Freiberg disease, primary hypertrophic osteoarthropathy, neuropathic arthropathy, benign joint hypermobility syndrome, pachydermodactyly, idiopathic hip chondrolysis…

¥ Reactive arthritis, systemic JIA, Juvenile dermatomyositis, IBD, Behçet disease, Kawasaki disease, granulomatous dermatitis, sarcoidosis…

§ Tuberculosis, *Staphylococcus*, *Streptococcus*, osteoid osteoma.

Ω Viral anterior uveitis, tuberculosis, brucellosis, post-streptococcal syndrome and post-viral or post-vaccination uveitis, Blau syndrome, sarcoidosis, tubulointerstitial nephritis and uveitis syndrome, Fuchs uveitis, Kawasaki syndrome, hereditary autoinflammatory syndromes, leukemia, juvenile xanthogranuloma, and intraocular foreign body…

This list is not exhaustive but is for information only.

Diagnosing ERA or JPsA requires a careful and thorough approach due to significant symptom overlap with various other conditions [40–43]. Several differential diagnoses share clinical features with ERA/JPsA, making it essential to consider a broad range of possibilities [43]. The literature primarily reports these differential diagnoses in case-based reviews or case reports, making it challenging to establish a strategic approach for prioritizing them due to the low level of evidence. Differential diagnoses should be based on the clinical presentation of ERA/JPsA rather than the specific JIA subtype [44, 45]. A thorough evaluation of the disease presentation is crucial to rule out malignancies and infections before confirming a diagnosis of ERA/JPsA [43].

Recommendation 5 In children and adolescents diagnosed with ERA or JPsA, extra-musculoskeletal manifestations, complications, and comorbidities should be actively assessed, including screening for:

I. Uveitis: For children with ERA and JPsA, regular ophthalmic screening for uveitis is recommended.
   - In high-risk JPsA patients (ANA positive, age of onset < 7 years, disease duration ≤ 4 years), screening should be performed every 3 months.
   - In low-risk JPsA patients (ANA negative, age of onset ≥ 7 years, disease duration > 4 years), as well as in ERA patients, screening should be conducted every 6–12 months.

II. Skin manifestations (e.g., oral ulcers, erythema nodosum, pyoderma gangrenosum, psoriasis, and nail involvement).

III. Inflammatory bowel diseases (in case of poor linear growth, poor weight gain, anemia, hypoalbuminemia, abdominal pain, diarrhea, and Bloody stools) (LoE, IIb).

IV. Cardiovascular complications, particularly aortic regurgitation, should be conducted using echocardiography, ideally performed by a pediatric cardiologist if clinical suspicion arises (LoE, IVb).

V. Risk factors of atherosclerosis, including obesity and metabolic syndrome, by assessing body mass index and lipid profile (LoE, Ia).

More than one-third of adult SpA patients develop ocular inflammation, often manifesting as acute uveitis. In Marino et al.'s [46] cross-sectional study of 223 patients, ERA patients had the highest uveitis prevalence (ERA-U) (13%) with similar prevalences in UA, JPsA, and IBD-A (7% each). The 2019 ACR/Arthritis Foundation Guidelines for Screening, Monitoring, and Treatment of JIA-Associated Uveitis recommends regular ophthalmic screening based on individual risk factors. The high-risk groups include children with psoriatic or undifferentiated arthritis who are ANA positive, younger than 7 years at JIA onset, and have a JIA duration of 4 years or less [47].

More than one-third of patients with JIA report chronic gastrointestinal (GI) symptoms, indicating an increased risk of inflammatory bowel disease (IBD) [48–50]. IBD incidence in JIA patients ranges from 20 to over 40 times higher than in the general pediatric population [48–50]. Data from the German Biologics' registry (2001–2013) involving 3071 patients found that IBD was more prevalent in those with ERA, extended oligoarthritis, JPsA, and RF-negative polyarthritis [51]. Lamot et al. [52] measured fecal calprotectin levels in 71 ERA patients, and found higher levels in patients with active disease and MRI signs of sacroiliitis, indicating parallel inflammation in the gut and musculoskeletal system in children with ERA.

Given the prevalence of skin and mucocutaneous manifestations in SpA types like reactive arthritis, IBD-associated arthritis, and JPsA, we recommend screening for these manifestations in patients with ERA and JPsA [21, 53].

Cardiovascular disease is prevalent among juvenile spondyloarthropathy patients and adults with ankylosing

spondylitis [54]. Patients with ERA and JPsA should be screened for cardiac complications, particularly aortic regurgitation. The study of Yildiz et al. [55] found early signs of right ventricular diastolic dysfunction and a possible link between MRI-confirmed enthesitis and reduced left ventricular systolic function. Early detection of cardiac dysfunction can help prevent long-term cardiovascular complications.

Patients with JIA face a significantly increased risk of atherosclerosis [56, 57]. In fact, dyslipidemia in JIA may result from chronic inflammation, cytokine release, and antirheumatic drugs. A 2023 meta-analysis revealed common lipid abnormalities in JIA patients compared to healthy controls [58]. An Egyptian study in 2021 found significant lipid profile abnormalities correlated with active disease in JIA patients, emphasizing the need for regular monitoring [59]. Adult PsA patients are more prone to obesity and metabolic issues, and similar risks are observed in pediatric psoriasis patients. Thus, BMI assessment and screening for obesity and metabolic syndrome components are crucial for ERA and JPsA patients [60].

Treatment

Recommendation no 6 The primary treatment target in ERA and JPsA should be to achieve remission, defined as the complete absence of disease symptoms and signs without ongoing treatment. In cases where remission is not feasible, maintaining low disease activity may be considered as an alternative target (LoE, II).

The treatment goals for patients with JIA are to control symptoms, prevent structural damage, avoid comorbidities, and optimize function, growth, and quality of life. The primary target, according to treat-to-target recommendations, is clinical remission—the absence of inflammatory disease signs and symptoms, including extra-articular manifestations [61]. Low disease activity can be an alternative target. Treat-to-target is a recognized strategy with positive effects on chronic inflammatory disease prognosis, but its feasibility and impact on African children with JIA need further assessment. Since remission definition is not yet standardized, the expert panel recommends using JADAS criteria to assess remission in children with ERA and PsA [61].

Recommendation no 7

- Treatment with NSAIDs should be recommended as the first-line therapy for children with ERA and JPsA (LoE, IIIb).
- Continuous NSAID therapy may be preferred over on-demand treatment (LoE, IIb).
- csDMARDs should be considered as part of the first-line treatment for JPsA and ERA with polyarthritis (LoE, IIb).

For patients with ERA, NSAIDs are the most frequently used treatment according to multiple case series [11–13, 16, 22]. This preference is largely attributable to the extensive experience with NSAIDs in treating children with JIA. However, the available studies provide limited evidence, and no clinical trials have definitively established the efficacy of NSAIDs specifically for children with ERA [10, 13, 17].

While direct evidence supporting the continuous use of NSAIDs in children is lacking, the ACR recommends continuous use for patients with active disease and CRP levels, extrapolating from adult spondyloarthritis treatment [62]. Moreover, studies from Africa indicate that children with ERA frequently exhibit higher rates of hip involvement and more severe disease outcomes [15, 16]. Based on these findings, continuous NSAID treatment is conditionally recommended over on-demand use.

In cases of NSAID failure or polyarthritis, DMARDs should be considered [22]. The Voting Panel acknowledged that csDMARDs are appropriate as first-line therapy for children with ERA and JPsA with polyarthritis in the African context, given the known risks of active disease and joint damage. In alignment with other JIA categories, methotrexate is considered the cornerstone of this treatment strategy [19].

Recommendation 8

- The use of intraarticular glucocorticoids (IAGC) may be recommended for children with ERA and JPsA as an adjunct treatment when persistent inflammation is present in one or a few joints, prior to considering treatment escalation (LoE, IIb).
- In children with active sacroiliitis despite ongoing treatment with NSAIDs, IAGC may be recommended if radiological guidance equipment is available (LoE, IV).
- Triamcinolone hexacetonide (THA), if available, should be recommended as the drug preparation of choice for intra-articular injections (LoE, IIa).
- More soluble corticosteroid preparations may be recommended in small or superficial joints (betamethasone or methylprednisolone) to avoid subcutaneous atrophy or hypopigmentation (LoE, V).
- The use of ultrasound guidance for injections may be recommended, especially in small, deformed, or clinically challenging joints, when performed by skilled practitioners (LoE, IIIb).
- In patients with sacroiliitis, enthesitis, or polyarthritis in a high or moderate disease activity despite treatment

with NSAIDs and/or DMARDs, bridging therapy with a limited course of oral glucocorticoid (< 3 months) during initiation or escalation of therapy may be recommended (LoE, IIIb).
- In patients with sacroiliitis, enthesitis, or polyarthritis in a low disease activity, it is conditionally recommended against bridging therapy with oral glucocorticoid and in a chronic setting regardless of the disease activity (LoE, IIIb).
- The use of the minimal effective dose of corticosteroids for the briefest duration possible should be recommended to achieve/maintain the target of remission or low disease activity and to mitigate the risk of adverse events, especially concerning growth and bone health (LoE, IIb).
- Children undergoing corticosteroid therapy may benefit from receiving supplementation with calcium, vitamin D, and gastroprotective measures (LoE, IIIb).

The primary goal of administering potent anti-inflammatory treatment directly into an inflamed joint is to achieve rapid resolution of synovitis. However, specific studies examining the role of IAG in ERA or JPsA are lacking. Thus, current recommendations are based on studies involving oligoarticular and polyarticular arthritis [27, 35]. According to the ACR clinical guidelines, IAGs are recommended as first-line treatment for JIA with the involvement of a few joints [27]. For active polyarthritis and active sacroiliitis, IAGs are suggested as an adjunctive therapy rather than a first-line treatment [35]. This conditional recommendation stems from the very low-quality evidence available, which primarily pertains to children with oligoarthritis. Additionally, IAG injections may not be suitable for a large number of joints or joints that have undergone multiple injections; in such cases, escalation to systemic therapy may be preferable [63, 64]. Triamcinolone hexacetonide (THA) is strongly recommended for intra-articular injections due to its effectiveness and duration of effect. For smaller or harder-to-access joints, more soluble forms like methylprednisolone acetate are preferred to avoid local side effects from extravasation of THA [65]. Research by Zulian et al. [66, 67] demonstrated that THA provides longer-lasting remission compared to triamcinolone acetonide (TA), even at higher doses of TA.

While ultrasound (US) is an ideal imaging technique for the pediatric population and can guide needle placement during IAG, its use is conditionally recommended only in expert hands, particularly for small, complicated, or clinically inaccessible joints like the hip. The current scientific evidence is insufficient to recommend US guidance for all IAG procedures in children. Although various descriptions of its use are reported by several teams, they do not compare the efficacy of operations performed with or without US guidance [68, 69]. Literature indicates that MSUS-guided injections are effective for clinically inaccessible joints, suggesting that MSUS shows great promise for evaluating and managing JIA in children, warranting further study [70].

Recommendation No 9 In children with ERA or JPsA with a high risk of disability (high disease activity, active sacroiliitis, involvement of high-risk joints: hips, wrists, ankles, cervical spine, and limited spinal mobility) the prompt initiation of a second-line therapy should be recommended. (LoE, V).

There have been no clinical trials specifically investigating the initial use of biologics or early aggressive treatment with combined biologics and DMARDs in ERA or JPsA patients. Thus, our recommendations are based on studies conducted with polyarticular JIA patients [71, 72]. The ACR advises that the initial use of biologics in polyarticular JIA be limited to high-risk patients, defined by expert opinion and parent preferences [35]. High-risk patients include those with high disease activity and involvement of critical joints like hips, wrists, and the cervical spine [35, 71, 72]. A study from the CARRA registry reported polyarticular involvement in 57% of ERA children and 72% of JPsA children, with significantly worse disease activity scores in those with active sacroiliitis [22]. Therefore, we recommend reserving initial biologic treatment for high-risk patients who need a rapid response, as both DMARDs and biologics are effective in inducing remission. Treating physicians should identify these patients based on their disease activity and risk of disability.

Recommendation No 10

- In children with active enthesitis who have failed first-line treatment (NSAIDs), using a TNFi* should be recommended over csDMARDs (LoE, Ia).
- In the case of mild enthesitis or concomitant arthritis csDMARDs should be considered before the initiation of biologics (LoE, IIb).
- In case of active oligoarthritis, who have failed first-line treatment (NSAIDs and IAGC), csDMARDs should be recommended (LoE, Ib).
- In case of active sacroiliitis despite NSAIDs (two families of NSAIDs for at least 2 weeks each) adding a TNFi should be recommended over continued NSAIDs monotherapy (LoE, IVa).
- In children with acute anterior uveitis, topical glucocorticoid therapy or systemic glucocorticoid should be recommended, according to the severity of uveitis (LoE, IIIb).
- In ERA or JPsA-associated chronic uveitis, csDMARDs, preferably MTX, may be recommended before escalating to monoclonal TNFi (LoA: IIIa)
- In severe and extensive psoriasis, bDMARDs should be considered over csDMARDs (LoA: IIIa).

*If available and in the absence of contraindication.

The introduction of biologics and their role in subsequent therapy for ERA depends on osteoarticular manifestations, disease activity, control by previous treatments, and severity of extra-articular manifestations [35]. For active enthesitis, NSAIDs are the recommended first-line treatment due to their established analgesic effects in adults [73]. If NSAIDs are ineffective or not tolerated, TNFi is preferred over csDMARDs [27, 35]. In cases of active oligoarthritis unresponsive to NSAIDs and IAGC, csDMARDs are recommended [3]. If there is no adequate response, biologic DMARDs are strongly preferred over switching csDMARDs [27].

For sacroiliitis, we recommend NSAIDs as first-line treatment, with csDMARDs not preferred if NSAIDs are ineffective or not tolerated. This is based on the established efficacy of NSAIDs in adult spondyloarthritis and their positive effect in children. Active sacroiliitis is defined by MRI results, clinical signs (pain on palpation), and/or symptoms of inflammatory lower back pain [35]. The 2019 ACR guidelines strongly recommend adding a TNFi if NSAIDs are ineffective [35]. We advise trying two NSAIDs for at least two weeks each, considering the risk of kidney damage and long-term joint damage [74, 75]. Extrapolating from adult ASAS/EULAR recommendations is questionable [34, 75, 76].

NSAIDs alone may suffice for 20–30% of patients with axial diseases and 20–40% with peripheral diseases [75]. However, data on the structural effect of NSAIDs in ERA are lacking [77, 78]. Without sacroiliitis or axial involvement, peripheral arthritis in ERA is managed similarly to other non-systemic JIA forms per the 2011 and 2019 ACR guidelines [34, 35], though this lacks sufficient evidence. Further research is needed to determine csDMARD duration in ERA to avoid delaying biologics. Early treatment with TNFi shows slight benefits. The 2011 ACR recommends a 3-month csDMARD trial for high/moderate activity [34].

In ERA, the risk of uveitis is 5–20%, with cases often being acute and symptomatic [47, 79]. Initial treatment should involve topical glucocorticoids to control inflammation, with systemic corticosteroids used if there is no response or if the condition is severe. However, frequent recurrent episodes of acute anterior uveitis (AAU) despite csDMARD (MTX) treatment may necessitate escalating therapy by introducing a monoclonal TNFi to prevent ocular complications from prolonged glucocorticoid use [47, 80, 81].

Childhood psoriasis is seen as a potential multisystem disorder requiring optimized management to prevent disease progression, reduce psychological burden, and address metabolic syndrome. Psoriasis vulgaris is the most common type in children, followed by guttate psoriasis [82]. MTX is the first-line option for moderate to severe plaque psoriasis, with biologics considered if systemic treatments are ineffective, contraindicated, or not tolerated [82, 83].

Recommendation No 11 For children experiencing active enthesitis and/or active sacroiliitis who have not responded to initial treatment with a first TNFi, or have a contraindication to TNFi, another targeted therapy (biologic or synthetic) should be recommended as a third-line treatment following careful analysis of the clinical features and reasons for treatment failure (LoE, IVc).

Recommendation 12

- Selecting biologic therapy for children with ERA and PsoA should consider various criteria such as cost, availability, and safety in the African context. Involving experts is crucial for making well-informed decisions regarding the most appropriate treatment option.
- For patients eligible for targeted therapy, starting with TNFi as the initial targeted treatment may be recommended (LoE, Ib)
- The choice of the TNFi molecule (monoclonal or receptor, originator or biosimilar) depends mainly on the clinical features and availability (LoE, IV)
- In case of TNFi therapy failure, a second TNFi or anti-IL17 or IL 23i or JAKi should be considered in no preferred order but depending on clinical features, extra-articular manifestation, cause of the failure of the first TNFi, the availability and the approval of the treatment (LoE, IV)
- Adding methotrexate to the biologic treatment may be recommended during the initiation of the bDMARD (LoE, IIa)

In the African context, deciding on biologic therapy for children with ERA and JPsA requires careful consideration of cost, availability, and safety [8]. TNFi has demonstrated efficacy in managing ERA through retrospective analyses and multiple RCTs [43, 84–88]. Thus, initiating treatment with an anti-TNF alpha agent is advisable due to its proven long-term efficacy and safety in children. The choice between the original or biosimilar biologic agent should prioritize the patient's clinical characteristics and medication accessibility. Etanercept is commonly used in daily practice, while adalimumab is preferred for patients with concurrent uveitis [8, 43, 89]. Head-to-head comparisons are scarce, so decisions should be based on the patient's clinical profile rather than extra-articular manifestations [90]. If the initial anti-TNF therapy fails, secondary treatment options should be considered, guided by adult treatment experiences [91]. For secondary failure, a second anti-TNF treatment is often preferred, while primary failure may warrant alternative targeted therapy. Recently, the FDA and EMA approved secukinumab, a monoclonal antibody targeting IL-17A, for treating ERA and JPsA in cases unresponsive to conventional therapy [92]. In an

RCT, secukinumab significantly delayed disease relapse and showed a favorable safety profile in 86 children and adolescents with active ERA or JPsA [92]. A recent retrospective study also found that ustekinumab reduced JSpA-DAS and JADAS10 in ERA patients unresponsive to TNFi treatment [93]. Ixekizumab, another anti-IL-17A agent, is approved for adult axial Spondyloarthritis (SpA) and is currently being investigated for ERA and JPsA in children (ClinicalTrials.gov Identifier: NCT04527380). Tofacitinib, an oral JAK inhibitor, demonstrated effectiveness in a pivotal trial for polyarticular course JIA, including 21 ERA patients, and is now FDA-approved for active polyarticular JIA and EMA-approved for both polyarticular JIA and JPsA [94]. Another JAK inhibitor, baricitinib, showed efficacy and safety in a phase-3 trial with 220 JIA patients, including 50 with ERA [95]. The selection of third-line treatment should be based on a thorough assessment of clinical features and the reasons for the failure of the initial TNFi [96]. Adding methotrexate (MTX) to biologic treatment helps prevent anti-drug antibodies (AAA), which are linked to relapse and treatment failure. Although MTX alone may not always be beneficial, its role is crucial in preventing AAA formation, especially in pediatric cases, as studies have shown [97, 98].

Recommendation 13

- Children with ERA or JPsA should undergo assessment for symptoms related to spinal, peripheral joints, and entheses symptoms as well as extra-articular manifestations and comorbidities in each clinical visit (LoE, IV).
- Adapted and validated specific scores (ex, JADAS, JSpA-DAS) should be used to monitor disease activity and adjust treatment strategy (LoE, IIb).
- Children diagnosed with ERA and JPsA stand to gain from regular clinical evaluations at three-month intervals. The frequency may be adjusted to shorter intervals during flare-ups and extended during periods of remission. The repetition of comprehensive assessments, including workup, imaging, and specialized examinations (ophthalmologist, dermatologist….), should be tailored based on the severity of symptoms and the disease's activity (LoE, IV).

Currently, there is no standardized monitoring strategy for patients with ERA and JPsA [99]. Assessing disease activity should evaluate clinical symptoms such as back pain, joints swollen, enthesitis, and morning stiffness, and laboratory tests like ESR and CRP. Composite scores integrate these measurements. The American College of Rheumatology recommends BASDAI or ASDAS for adult SpA monitoring, but these are not well-suited for children with ERA [100]. The JADAS score is reliable for polyarticular and oligoarticular JIA but does not assess spinal involvement or enthesitis [101].

The development of JSpADA is significant as it is the first valid and specific tool for patients with JSpA, recognizing the disease as an independent form of JIA [102]. JSpADA includes specific parameters not covered by JADAS, such as back mobility and extra-articular manifestations like uveitis, making it a more comprehensive tool [102]. However, more data is needed to standardize index levels and assess their therapeutic impact [103]. Accurately defining inactive disease is crucial. While JSpADA effectively identifies high disease activity, further work is needed to identify moderate and low disease activity and establish proper cut-offs for remission. Imaging control frequency depends on disease activity. Establishing standardized remission criteria is also crucial for improving management and prognosis [99].

Recommendation 14

- Considering tapering medication in ERA and JPsA may be recommended only after at least 6 months of disease inactivity while on treatment (LoE, IV).
- The minimal duration of remission before medication tapering should be prolonged in presence of predictive factors of flares* (LoE, V).
- Medication withdrawal in ERA and JPsA may be considered only after progressive tapering in patients with longstanding remission (LoE, V).
- The decision of tapering should be individualized and based on a shared decision-making** (LoE, V).
- The choice of the tapering strategy should be guided by the recommendation of the treating physician (LoE, V).

*Predictive factors of flares: long time interval between disease onset and csDMARDs initiation, late bDMARDs initiation since diagnoses (more than 2 years), treatment with bDMARDs and the presence of uveitis (V).

** Factors to take into consideration include disease duration, early inactive disease, efforts made to achieve inactive disease and the safety of the treatment (V).

Tapering of medication should commence after achieving inactive disease or sustained clinical remission (CR). During tapering and until withdrawal, continuous evaluation is essential, with at least 6 months of remission on medication required. For patients with poor prognosis factors, the remission duration should be extended. The minimal duration of CR before tapering, as reported, is 3 months, but most studies adhere to the Wallace criteria, requiring 6 months of clinically inactive disease (CID) on medication [104, 105]. Some clinicians prefer a one to 2-year interval before withdrawal, influenced by disease duration, prognosis factors, early inactive disease, efforts to achieve inactive disease, and treatment safety [106, 107].

No predictive factors for flares after medication withdrawal, including tapering methods and subtypes, have been identified. Some studies suggest that prolonged CID is associated with variable risks of flares [108]. Tapering may involve decreasing drug dosage, increasing intervals between doses, or a combination of both [108, 109]. Some clinicians may stop csDMARDs or bDMARDs abruptly, while others aim to identify lower-intensity regimens to suppress inflammation. Patients with JPsA or ERA who achieve clinically inactive disease on MTX monotherapy have better flare-free survival compared to those requiring TNFi, indicating milder disease subsets [110]. JPsA patients with at least 12 months of inactive disease before MTX discontinuation had significantly lower uveitis flare rates [108]. Polyarticular JIA is less likely to achieve CID compared to ERA patients [109]. Some studies did not observe a loss of effectiveness after tapering etanercept in JIA populations [109, 111]. Earlier bDMARD initiation has been associated with better disease control and remission [112]. Flares are common in JIA patients with inactive disease on medication, reaching 42.5% within 1 year [110, 112]. Subclinical synovitis and Power Doppler signals were found in up to 84% and 33% of patients in remission, respectively, complicating the distinction between natural disease flares and those due to treatment withdrawal [113]. A clear tapering strategy cannot be universally recommended. From a cost-effectiveness perspective, biologic withdrawal first may be advisable. However, data shows that approximately half of the biologic users experience flare-ups during tapering or post-withdrawal recurrence. In Africa, due to cost considerations, tapering strategy decisions should rely on the expertise of the treating physician.

Recommendation 15

- Physical therapy and occupational therapy should be recommended in JIA patients including ERA and JPsA (LoE, IV).
- Patients with ERA and JPsA, should receive the necessary support for transitioning to adult care (LoE, IV).
- The use of a specific diet should not be recommended without first discussing it with the treating physician. (LoE, V).
- We strongly recommend against using traditional medicine before discussing it with the treating physician (LoE, V).
- The vaccination schedule should be updated for children with ERA and JPsA prior to initiating immunosuppressive therapy (LoE, IV). Inactivated vaccines* are strongly advised (LoE, V); however, live attenuated vaccines are strongly discouraged during immunosuppressive treatment, and specific precautions should be considered. Discussions regarding vaccine administration are recommended during periods of remission, with careful planning for immunosuppressor withdrawal and reintroduction based on the specific vaccine type (LoE, IV).

*Inactivated pneumococcal vaccines, influenza virus and those scheduled according to the country vaccine calendar.

Systematic reviews and the latest ACR recommendations highlight the importance of physical therapy in non-pharmacological treatment [27, 114–117]. Key benefits include maintaining range of motion, strength, preventing injuries, and improving aerobic capacity and preventing depression [27, 116]. Exercise therapy also enhances the quality of life for JIA children by building skills, confidence, and social connections. Psychological interventions should focus on pain management, restructuring negative pain-related thoughts, and gradually confronting avoided situations [118]. Cognitive therapy should include stress management, relaxation training, distraction techniques, and optimizing health habits linked to pain and quality of life. Online self-management programs can be beneficial alongside clinical visits. A systematic review showed significant pain reduction through psychological therapies like cognitive-behavioral therapy, relaxation therapy, and biofeedback [119].

An American National Survey of Children's Health reported that only 18% of youth aged 12–17 received comprehensive care transition services [120]. This gap also affects JIA patients, with no data available for African children. Improving transition management includes solo pediatrician visits, skill-building, and counseling for transfer to adult care [121].

Diet in JIA patients aim to promote growth and reduce inflammation [122]. Specific regimens, supplements, or herbal interventions are not recommended for treating JIA. Similarly, there is insufficient evidence on the beneficial effects of vitamin D supplementation on arthritis [123].

Traditional medicine (TM) is widely used in Africa due to its cultural alignment and historical roots, despite lacking safety regulation. Utilization rates of traditional medicine practitioners in Africa range from 1.2% to 67% [124]. It is crucial to highlight the dangers of using TM without clinical evidence. Educating JIA patients and their parents about the potential harms and lack of benefits of certain TM practices is essential.

Regarding vaccination, children with ERA or JPsA should follow the national vaccination program. Among the live vaccines, the tuberculosis vaccine (BCG) is particularly important in the African context. The region accounts for one-third (320,000 children) of all TB cases among children aged 0 to 15 worldwide [125, 126]. Unfortunately, disruptions to the vaccine supply, often due to a lack of resources, can significantly impact BCG distribution [127]. Live

attenuated vaccines are strongly discouraged for children receiving immunosuppressive treatment. These vaccines should be administered before the initiation of immunosuppressive therapy. If necessary, withdrawal of immunosuppressive therapy should be scheduled during remission periods, following a specific timeline tailored to each vaccine's requirements [6].

Patient perspectives: key points and comments

Three patients independently shared their perspectives, with the following key comments:

- Recommendation 1 (Diagnosis): Pain should be emphasized as a major symptom to prompt early referral of patients.
- Recommendation 2 (Diagnosis): Greater emphasis is needed on communicating the cardiovascular risks, which are often overlooked as a potential complication of the disease.
- Recommendation 6 (Treatment): Pain relief should be highlighted as a primary therapeutic goal.
- Recommendation 9 (Treatment): All Joints should be considered as important for defining disease severity.
- Recommendation 15 (Treatment): Physical therapy should be strongly recommended.

All final recommendations were approved by the patients.

Discussion

Managing ERA and JPsA is challenging due to specific clinical specificities, such as the frequency of hip arthritis and limited access to certain imaging, laboratory investigations, and expensive treatments. This paper display recommendations for the management of children with ERA and JPsA, including a treatment algorithm and a research agenda. The working group and steering committee chose to consolidate the two subtypes and formulate recommendations based on clinical presentation rather than separately, aiming to comprehensively address all aspects within a holistic framework. This approach aligns with the ACR and EULAR guidelines, where recommendations are structured according to disease phenotype rather than specific classification criteria [30, 35]. The PAFLAR guideline comprises 5 specific recommendations for diagnosis and 10 for treatment of ERA and JPsA. The level of evidence from the references consulted to address the PICO questions was generally low, resulting in most recommendations being conditional.

Regarding diagnosis, our goal was to emphasize the significance of early identification through prompt referral and the use of appropriate diagnostic tests when necessary. This task is notably challenging in the African context due to a shortage of pediatric rheumatologists [128].

The guidelines advocate for an individualized approach based on disease phenotype, severity, and response to prior treatments. csDMARDs particularly MTX, remain pivotal, serving as first-line therapy for polyarticular involvement, mild enthesitis, chronic uveitis, and moderate to severe plaque psoriasis in children with ERA and JPsA. Biologic therapy selection should consider various factors such as cost, availability, and safety. When considering tapering, a sequential withdrawal starting with csDMARDs rather than biologics is recommended, though applying this in Africa's cost-effectiveness context presents challenges. Therefore, we emphasize that the decision on tapering strategy should be guided by physician expertise and consideration of African context-specific challenges. Our recommendations also cover new ground by addressing medication tapering in inactive disease and defining monitoring intervals, areas previously overlooked. Furthermore, the panel endorsed the use of JAK inhibitors, IL-17 inhibitors, and IL-12/23 inhibitors in cases of TNFi therapy failure.

There is insufficient representation of African patients in clinical trials, posing challenges in applying findings from predominantly Western settings to African contexts [129]. Indeed, implementing research findings into clinical practice in Africa is hindered by inadequate infrastructure, a shortage of healthcare professionals, and limited research funding [129].

These guidelines aim to advance pediatric rheumatology in Africa, marking a significant milestone as the first African recommendations in this field, developed through rigorous process including evidence synthesis and expert opinion [129]. Their primary goal is to standardise care, addressing the specific needs of the region and establish a foundation for future research efforts [129]. A key strength of these guidelines is the collaboration between international and African experts, ensuring they are tailored to the African context while maintaining their universal and current relevance. One of the major limitations of this work was the lack of patient involvement at the beginning of the preparation process. Several factors contributed to this issue. Firstly, this was the first time that patients were involved in such a process in Africa, and there was uncertainty about their potential contributions. To ensure a clear understanding of the recommendations, the decision was made to involve patients only at the review stage of the final version. Secondly, language barriers posed significant challenges. In North Africa, where English is the third language, it was difficult to find patients or guardians fluent in English, which is essential for providing an independent and autonomous opinion on the recommendations. This limitation highlights the need for better strategies to engage patients earlier in the process

and address language barriers in future initiatives. Lastly, the absence of patient associations posed an additional challenge, as such organizations could have provided valuable support in facilitating patient involvement and ensuring their voices were adequately represented throughout the process. This limitation underscores the need to foster the development of patient associations in Africa, which could play a crucial role in future guideline development by offering structured support and advocacy for patient participation.

Significant gaps in evidence still exist, suggesting an agenda for future research. Regarding diagnosis, the new PRINTO classification criteria and disease activity scores and cut-offs need to be evaluated for their applicability in assessing children with JIA in Africa. Similarly, the feasibility and impact of the treat-to-target strategy should be assessed in our population. Another important question is whether a step-down strategy and early aggressive treatment would be more effective in our context than conventional therapeutic regimens, which are based on treatment escalation driven by the treat-to-target approach [130].

The next step will be implementing the guidelines effectively in Africa and that involve a multi-step strategy. This includes first disseminating the guidelines through regional conferences, workshops, and digital platforms to reach healthcare professionals. We will then assess their acceptability and applicability by gathering feedback from practitioners in various settings via surveys and focus groups. Finally, we will monitor adherence and impact through a follow-on implementation study, offering ongoing support and training to ensure successful integration into clinical practice.

Conclusion

The development of the PAFLAR JIA guidelines for ERA and JPsA represents a landmark achievement in pediatric rheumatology in Africa, pioneering its role as the first African recommendation in the field. The ultimate goal is to promote better access to care and personalized management based on shared decision-making within a holistic approach. These guidelines may be updated as more robust evidence emerges, ensuring they remain relevant and effective in addressing the needs of patients and healthcare providers in Africa.

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Data Availability All data are available upon request from the corresponding author and are also provided in the supplementary materials.

Compliance with ethical standards

Conflict of interest Xenophone Baraliakos' COI are Research Grants, Consultant, Scientific Advisory Board: Abbvie, Alphasigma, Amgen, BMS, Cesas, Celltrion, Galapagos, Janssen, Lilly, Moonlake, Novartis, Pfizer, Roche, Sandoz, Springer, Stada, Takeda, UCB, Zuellig. Non-commercial disclosures: ASAS President, EULAR President-Elect, VRA Board Member.
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