Pediatric Rheumatology Year in Review-2019

PRES PAEDIATRIC RHEUMATOLOGY EUROPEAN ASSOCIATION

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Pediatric Rheumatology breaking borders Cooperation in Research

Cooperation in Research

- SHARE Project
- EULAR-PRES-ACR papers
- Guidelines- Classifications
- Based on literature EBM
- Large patient registries

- JIA- SLE- Auto inflammatory- ARF-

Single Hub and Access point for pediatric Rheumatology in Europe

Treatment approaches in Europe: from best practices to treat-to-target

SHARE

mission of SHARE

Single **H**ub and **A**cces point to pediatric **R**heumatology in **E**urope

Improve the quality of care for PRD by:

- resolving existing barriers between networks / research groups
- facilitating exchange of data, ideas and best practices
- improving access to relevant patient information
- facilitating implementation of results into training programs

SHARE

SHARE Methods

Literature review

- **Systematic literature search**
- Selection of papers (fellows+PI's)
- **Validity scoring** by 2 independent experts

Survey

- **Formulation** of recommendations
- Web-based survey
- **Reformulation** if <80% agreement or major comments

Consensus

- **Consensus meeting**
- Nominal Group Technique
- **Recommendations** accepted when >80% agreement

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Methods : literature review

- Focussed on diagnosis and treatment
- English literature, from 1970 onwards*
- No case reports, case series ≥ 3 pediatric patients
- Experienced librarians involved
  - Search strings, using MESH terms, clearly defined

((((("Arthritis, Juvenile Rheumatoid"[Mesh])) OR (jia[tiab] OR jra[tiab])) OR ((((juvenile*[tiab] OR child*[tiab] OR pediatric*[tiab] OR paediatric*[tiab])) AND (rheumatoid[tiab] OR rheumatic[tiab] OR idiopathic[tiab] OR chronic[tiab] OR systemic[tiab])) AND (arthritis[tiab] OR arthritides[tiab] OR polyarthritis[tiab] OR oligoarthritis[tiab])))) OR ((("still's disease"[tiab] OR "still disease"[tiab] OR "stills disease"[tiab])) AND (juvenile*[tiab] OR child*[tiab] OR pediatric*[tiab] OR paediatric*[tiab]))

SHARE

Paper selection on predefined criteria

-JIA: 172 papers
- JDM: 108
- SLE/APS: 128 / 15
- Scleroderma: 52 / 37

Periodic fevers:
- MKD: 28
- CAPS: 25
- TRAPS: 22
- FMF: 25
- Blau: 34

- All papers scored by 2 experts independently on validity and level of evidence. In case of disagreement: 3rd expert

- Results grouped and developed into recommendations

- Web-based survey to pre-test recommendations

Evidence based Vs. Consensus based

- Level of evidence
- Expert opinion based

European evidence-based recommendations for diagnosis and treatment of childhood-onset systemic lupus erythematosus: the SHARE initiative

Noortje Groot,[1,2] Nienke de Graeff,[1] Tadej Avcin,[3] Brigitte Bader-Meunier,[4] Paul Brogan,[5] Pavla Dolezalova,[6] Brian Feldman,[7] Isabelle Kone-Paut,[8] Pekka Lahdenne,[9] Stephen D Marks,[5] Liza McCann,[10] Seza Ozen,[11] Clarissa Pilkington,[5] Angelo Ravelli,[12] Annet van Royen-Kerkhof,[1] Yosef Uziel,[13] Bas Vastert,[1] Nico Wulffraat,[1] Sylvia Kamphuis,[2] Michael W Beresford[10,14]

Ann Rheum Dis. 2017 Nov;76(11):1788-1796

Recommendation

European evidence-based recommendations for the diagnosis and treatment of childhood-onset lupus nephritis: the SHARE initiative

Noortje Groot,[1,2] Nienke de Graeff,[1] Stephen D Marks,[3] Paul Brogan,[3] Tadej Avcin,[4] Brigitte Bader-Meunier,[5] Pavla Dolezalova,[6] Brian M Feldman,[7] Isabelle Kone-Paut,[8] Pekka Lahdenne,[9] Liza McCann,[10] Seza Özen,[11] Clarissa A Pilkington,[3] Angelo Ravelli,[12] Annet van Royen-Kerkhof,[1] Yosef Uziel,[13] Bas J Vastert,[1] Nico M Wulffraat,[1] Michael W Beresford,[10,14] Sylvia Kamphuis[2]

Ann Rheum Dis. 2017 Dec;76(12):1965-1973

Examples - General diagnostic recommendations

	%LOE
Based on the **current evidence (mainly in adults) on the SLICC-criteria, the SLICC criteria can be used as classification criteria in cSLE**	100
In the presence of a **positive ANA combined with at least two clinical SLICC criteria, or** in the presence of a positive ANA combined with **at least one clinical and one immunological SLICC** criterion, referral to a paediatric rheumatologist should be warranted	100
When considering a diagnosis of cSLE, **anti-Sm, anti-RNP-a, anti-Ro/SS-A and anti-La/SS-B should be included routinely at baseline to come a positive ANA without an closer to a definite diagnosis**	100
In a clinical context, when a patient is **ANA positive, but anti-dsDNA and ENA negative, a diagnosis of cSLE can still be made**	100

SHARE

European evidence-based recommendations for diagnosis and treatment of paediatric antiphospholipid syndrome: the SHARE initiative

Noortje Groot,[1,2] Nienke de Graeff,[1] Tadej Avcin,[3] Brigitte Bader-Meunier,[4] Pavla Dolezalova,[5] Brian Feldman,[6] Gili Kenet,[7] Isabelle Koné-Paut,[8] Pekka Lahdenne,[9] Stephen D Marks,[10] Liza McCann,[11,12] Clarissa A Pilkington,[10] Angelo Ravelli,[13] Annet van Royen-Kerkhof,[1] Yosef Uziel,[14] Sebastiaan J Vastert,[1] Nico M Wulffraat,[1] Seza Ozen,[15] Paul Brogan,[10] Sylvia Kamphuis,[2] Michael W Beresford[11,12]

European consensus-based recommendations for the diagnosis and treatment of rare paediatric vasculitides - the SHARE initiative.

de Graeff N, Groot N, Brogan P, Ozen S, Avcin T, Bader-Meunier B, Dolezalova P, Feldman BM, Kone-Paut I, Lahdenne P, Marks SD, McCann L, Pilkington C, Ravelli A, van Royen A, Uziel Y, Vastert B, Wulffraat N, Kamphuis S, Beresford MW.

Rheumatology (Oxford). 2019, 58:656-671

Rheumatology (Oxford). 2019

RHEUMATOLOGY

Original article

doi:10.1093/rheumatology/kez041

European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative

Seza Ozen[1], Stephen D. Marks[2], Paul Brogan[2], Noortje Groot[3,4,5], Nienke de Graeff[3], Tadej Avcin[6], Brigitte Bader-Meunier[7], Pavla Dolezalova[8], Brian M. Feldman[9], Isabelle Kone-Paut[10], Pekka Lahdenne[11], Liza McCann[5], Clarissa Pilkington[2], Angelo Ravelli[12], Annet van Royen[3], Yosef Uziel[13], Bas Vastert[3], Nico Wulffraat[3], Sylvia Kamphuis[4] and Michael W. Beresford[5,14]

RHEUMATOLOGY

Original article

doi:10.1093/rheumatology/key344

European consensus-based recommendations for the diagnosis and treatment of Kawasaki disease – the SHARE initiative

Nienke de Graeff[1,*], Noortje Groot [1,2,3,*], Seza Ozen[4], Despina Eleftheriou[5], Tadej Avcin[6], Brigitte Bader-Meunier[7], Pavla Dolezalova[8], Brian M. Feldman[9], Isabelle Kone-Paut[10], Pekka Lahdenne[11], Liza McCann[3], Clarissa Pilkington[5], Angelo Ravelli[12], Annet van Royen-Kerkhof[1], Yosef Uziel[13], Bas Vastert[1], Nico Wulffraat[1], Sylvia Kamphuis[2], Paul Brogan[5,†] and Michael W. Beresford [3,14,†]

ARD 2018- **uveitis**

Consensus-based recommendations for the management of uveitis associated with juvenile idiopathic arthritis: the SHARE initiative

Tamas Constantin,[1] Ivan Foeldvari,[2] Jordi Anton,[3] Joke de Boer,[4] Severine Czitrom -Guillaume,[5] Clive Edelsten,[6] Raz Gepstein,[7] Arnd Heiligenhaus,[8,9] Clarissa A Pilkington,[10] Gabriele Simonini,[11] Yosef Uziel,[12] Sebastian J Vastert,[13] Nico M Wulffraat,[13] Anne-Mieke Haasnoot,[4] Karoline Walscheid,[8] Annamária Pálinkás,[1] Reshma Pattani,[6] Zoltán Györgyi,[1] Richárd Kozma,[1] Victor Boom,[14] Andrea Ponyi,[1] Angelo Ravelli,[15] Athimalaipet V Ramanan[16]

Arthritis Care & Research
Vol. 71, No. 6, June 2019, pp 703–716
DOI 10.1002/acr.23871

American College of Rheumatology
Empowering Rheumatology Professionals

SPECIAL ARTICLE

2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis–Associated Uveitis

Sheila T. Angeles-Han,[1] Sarah Ringold,[2] Timothy Beukelman,[3] Daniel Lovell,[1] Carlos A. Cuello,[4] Mara L. Becker,[5] Robert A. Colbert,[6] Brian M. Feldman,[7] Gary N. Holland,[8] Polly J. Ferguson,[9] Harry Gewanter,[10] Jaime Guzman,[11] Jennifer Horonjeff,[12] Peter A. Nigrovic,[13] Michael J. Ombrello,[6] Murray H. Passo,[14] Matthew L. Stoll,[3] C. Egla Rabinovich,[15] H. Nida Sen,[16] Rayfel Schneider,[7] Olha Halyabar,[17] Kimberly Hays,[14] Amit Aakash Shah,[18] Nancy Sullivan,[19] Ann Marie Szymanski,[6] Marat Turgunbaev,[18] Amy Turner,[18] and James Reston[19]

Due to the lack of controlled trial data, most recommendations relied on **expert opinion**

The ultimate goal is to –

maintain optimal vision and ocular health

limiting the duration of ocular inflammation

minimizing exposure to long-term topical glucocorticoids

expedited use of systemic medications,

preventing secondary ocular sequelae

Recommendations

1. In children and adolescents with JIA at high risk of developing uveitis, ophthalmic ***screening every 3 months*** *is conditionally recommended over screening at a different frequency*

2. In children and adolescents with JIA and controlled uveitis who are tapering or discontinuing topical glucocorticoids, ophthalmic monitoring within 1 month after each change of topical glucocorticoids is ***strongly*** *recommended over monitoring less frequently*

Recommendations

8. In children and adolescents with JIA and CAU still requiring 1–2 drops/day of prednisolone acetate 1% (or equivalent) for uveitis control, and not on systemic therapy, adding systemic therapy in order to taper topical glucocorticoids is conditionally recommended over not adding systemic therapy and maintaining on topical glucocorticoids only

Recommendations

9. In children and adolescents with JIA and CAU still requiring 1–2 drops/day of prednisolone acetate 1% (or equivalent) for at least 3 months and on systemic therapy for uveitis control, changing or escalating systemic therapy is conditionally recommended over maintaining current systemic therapy

Recommendations

11. In children and adolescents with JIA with severe active CAU and sight-threating complications, starting **methotrexate and a monoclonal antibody TNFi immediately** *is conditionally recommended over methotrexate as monotherapy*

Recommendations

15. In children and adolescents with JIA and active CAU who have failed methotrexate and 2 monoclonal antibody TNFi at above-standard dose and/or frequency,

the use of abatacept or tocilizumab as biologic DMARD options, and mycophenolate, leflunomide, or cyclosporine as alternative nonbiologic DMARD options is conditionally recommended

Recommendations

19. In children and adolescents with uveitis that is well controlled on DMARD and biologic systemic therapy only, conditionally recommend that there be at least 2 years of well-controlled disease before tapering therapy

EXTENDED REPORT

Consensus-based recommendations for the management of juvenile dermatomyositis

Felicitas Bellutti Enders,[1,2] Brigitte Bader-Meunier,[3] Eileen Baildam,[4] Tamas Constantin,[5] Pavla Dolezalova,[6] Brian M Feldman,[7] Pekka Lahdenne,[8] Bo Magnusson,[9] Kiran Nistala,[10] Seza Ozen,[11] Clarissa Pilkington,[10] Angelo Ravelli,[12] Ricardo Russo,[13] Yosef Uziel,[14] Marco van Brussel,[15] Janjaap van der Net,[15] Sebastiaan Vastert,[1] Lucy R Wedderburn,[10] Nicolaas Wulffraat,[1] Liza J McCann,[4] Annet van Royen-Kerkhof[1]

JDM

The importance- the yield of capilaroscopy

AMERICAN COLLEGE OF RHEUMATOLOGY
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Arthritis Care & Research
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DOI 10.1002/acr.23687

BRIEF REPORT

Association Between Nailfold Capillary Density and Pulmonary and Cardiac Involvement in Medium to Longstanding Juvenile Dermatomyositis

Zoltan Barth,[1] Thomas Schwartz,[2] Berit Flatø,[3] Trond M. Aaløkken,[4] Akos Koller,[5] May B. Lund,[6] Ivar Sjaastad,[2] and Helga Sanner[7]

Objective. To explore the associations between microvascular abnormalities as assessed by nailfold capillaroscopy (NFC) and pulmonary and cardiac involvement in patients with juvenile dermatomyositis (DM) who are assessed after medium- to long-term follow-up.

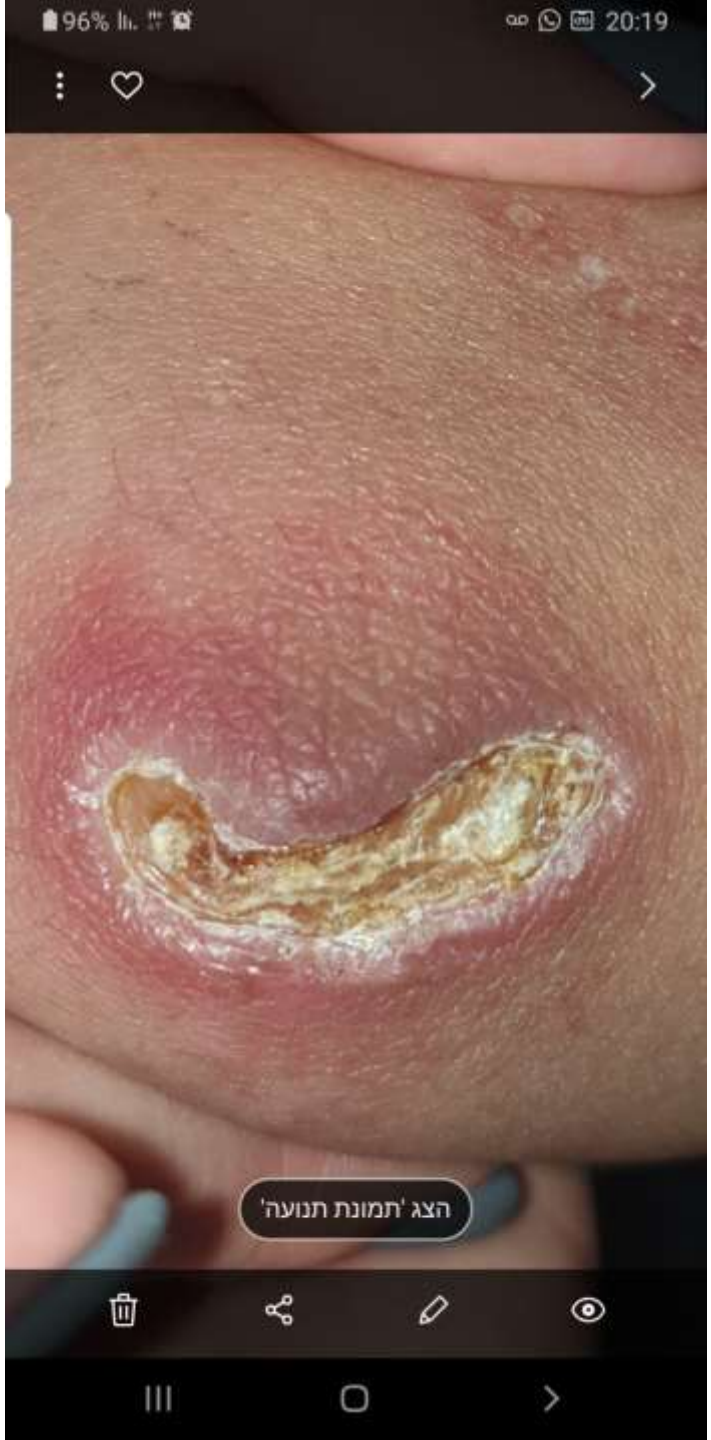
Methods. Fifty-eight patients with juvenile DM were examined a mean ± SD of 17.0 ± 10.6 years after symptom onset. Nailfold capillary density (NCD) and a neovascular pattern (defined as an active or late scleroderma pattern) were analyzed, with blinding to clinical data. Pulmonary involvement was assessed by pulmonary function tests including spirometry, diffusing capacity for carbon monoxide (DLco), and body plethysmography. High-resolution computed tomography (HRCT) was also performed. Cardiac involvement was assessed by electrocardiography, Holter monitoring (heart rate variability), and echocardiography.

Association Between Nailfold Capillary Density and Pulmonary and Cardiac Involvement in Medium to Longstanding Juvenile Dermatomyositis

Results. Patients with low NCD (<6 capillaries/mm) (n = 21), compared to patients with normal NCD (≥6 capillaries/mm) (n = 37) had lower forced vital capacity (89.7% versus 98.5% predicted), total lung capacity (87.8% versus 94.5% predicted), and more often had low DLco values (15 [71%] of 21 patients versus 14 [38%] of 37 controls) (all $P < 0.05$). Use of HRCT to assess airway disease was more frequent in the group with low NCD (6 [30%] of 20 patients versus 3 [8%] of 36 patients in the normal NCD group; $P = 0.034$). No associations between NCD and cardiac parameters or between neovascular pattern and pulmonary or cardiac parameters were observed.

Conclusion. In patients with juvenile DM, low NCD was associated with lung involvement, which was mostly subclinical. No significant associations with cardiac involvement were observed. These results shed light on possible mechanisms underlying organ involvement, but further and preferably larger studies are needed to identify NCD as a potential biomarker for lung and cardiac involvement in juvenile DM.

Severe JDM- new options?


96%
20:19
הצג 'תמונת תנועה'

Arthritis & Rheumatology
Vol. 71, No. 6, June 2019, pp 1011–1021
DOI 10.1002/art.40800

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Empowering Rheumatology Professionals

Muscle Expression of Type I and Type II Interferons Is Increased in Juvenile Dermatomyositis and Related to Clinical and Histologic Features

Gian Marco Moneta,[1] Denise Pires Marafon,[1] Emiliano Marasco,[1] Silvia Rosina,[2] Margherita Verardo,[1] Chiara Fiorillo,[2] Carlo Minetti,[3] Luisa Bracci-Laudiero,[4] Angelo Ravelli,[3] Fabrizio De Benedetti,[1] and Rebecca Nicolai[1]

BRAIN
A JOURNAL OF NEUROLOGY

JAK inhibitor improves type I interferon induced damage: proof of concept in dermatomyositis

Leandro Ladislau,[1,2,*] Xavier Suárez-Calvet,[1,3,*] Ségolène Toquet,[1,4] Océane Landon-Cardinal,[1,5] Damien Amelin,[1] Marine Depp,[1] Mathieu P. Rodero,[1] Denisa Hathazi,[6] Darragh Duffy,[7] Vincent Bondet,[7] Corinna Preuße,[8] Boris Bienvenu,[9] Flore Rozenberg,[10] Andreas Roos,[8,11] Claudia F. Benjamim,[1] Edzard Gallardo,[3,4] Isabel Illa,[3,4] Vincent Mouly,[1] Werner Stenzel,[8] Gillian Butler-Browne,[1] Olivier Benveniste[1] and Yves Allenbach[1]

BRAIN
A JOURNAL OF NEUROLOGY

LETTER TO THE EDITOR

A child with severe juvenile dermatomyositis treated with ruxolitinib

Florence A. Aeschlimann,[1,*] Marie-Louise Frémond,[1,2,3,*] Darragh Duffy,[4,5,6] Gillian I. Rice,[7] Jean-Luc Charuel,[8] Vincent Bondet,[4,5,6] Elsa Saire,[1] Bénédicte Neven,[1,2] Christine Bodemer,[2,9] Laurent Balu,[10] Cyril Gitiaux,[11,12] Yanick J. Crow[2,3,13,#] and Brigitte Bader-Meunier[1,2,14,#]

BRAIN
A JOURNAL OF NEUROLOGY

LETTER TO THE EDITOR

Janus kinase 1/2 inhibition with baricitinib in the treatment of juvenile dermatomyositis

Charalampia Papadopoulou,[1] Ying Hong,[1] Ebun Omoyinmi,[1] Paul A Brogan[1] and Despina Eleftheriou[1,2]

BRAIN
A JOURNAL OF NEUROLOGY

LETTER TO THE EDITOR

Reply: Janus kinase 1/2 inhibition with baricitinib in the treatment of juvenile dermatomyositis

Yves Allenbach,[1] Lois Bolko,[1] Ségolène Toquet,[2] Océane Landon-Cardinal[1,3] and Olivier Benveniste[1]

Localized Scleroderma

Consensus-based recommendations for the management of juvenile localised scleroderma

Francesco Zulian,[1] Roberta Culpo,[1] Francesca Sperotto,[1] Jordi Anton,[2] Tadej Avcin,[3] Eileen M Baildam,[4] Christina Boros,[5] Jeffrey Chaitow,[6] Tamàs Constantin,[7] Ozgur Kasapcopur,[8] Sheila Knupp Feitosa de Oliveira,[9] Clarissa A Pilkington,[10] Ricardo Russo,[11] Natasa Toplak,[3] Annet van Royen,[12] Claudia Saad Magalhães,[13] Sebastiaan J Vastert,[12] Nico M Wulffraat,[12] Ivan Foeldvari[14]

Ann Rheum Dis 2019;78:1019–1024

Table 1 Recommendations regarding diagnosis and assessment

		L	S	Agreement (%)
	Overarching principle			
	All children with suspected localised scleroderma should be referred to a specialised paediatric rheumatology centre.	4	D	100
1	LoSSI, which is part of LoSCAT, is a good clinical instrument to assess activity and severity in JLS lesions and is highly recommended in clinical practice.	3	C	90
2	LoSDI, which is part of LoSCAT, is a good clinical instrument to assess damage in JLS and is highly recommended in clinical practice.	3	C	90
3	Infrared thermography can be used to assess activity of the lesions in JLS, but skin atrophy can give false-positive results.	4	D	90
4	A specialised US imaging, using standardised assessment and colour Doppler, may be a useful tool for assessing disease activity, extent of JLS and response to treatment.	4	D	100
5	All patients with JLS at diagnosis and during follow-up should be carefully evaluated with a complete joint examination, including the temporomandibular joint.	2a	C	100
6	MRI can be considered a useful tool to assess musculoskeletal involvement in JLS, especially when the lesion crosses the joint.	3	C	100
7	It is highly recommended that all patients with JLS involving face and head, with or without signs of neurological involvement, have an MRI of the head at the time of the diagnosis.	3	C	90
8	All patients with JLS involving face and head should undergo an orthodontic and maxillofacial evaluation at diagnosis and during follow-up.	2b	B	90
9	Ophthalmological assessment, including screening for uveitis, is recommended at diagnosis for every patient with JLS, especially in those with skin lesions on the face and scalp.	2a	C	100
10	Ophthalmological follow-up, including screening for uveitis, should be considered for every patient with JLS, especially in those with skin lesions on the face and scalp.	3	C	100

JLS, juvenile localised scleroderma; L, level of evidence; LoSCAT, Localized Scleroderma Cutaneous Assessment Tool; LoSDI, Localized Scleroderma Skin Damage Index; LoSSI, Localized Scleroderma Skin Severity Index; S, strength of recommendation; US, ultrasound.

Table 2 Recommendations regarding treatment

	L	S	Agreement (%)
Systemic corticosteroids may be useful in the active inflammatory phase of JLS. At the same time as starting systemic corticosteroids, MTX or an alternative DMARD should be started.	2b	C	100
All patients with active, potentially disfiguring or disabling forms of JLS should be treated with oral or subcutaneous methotrexate at 15 mg/m²/week.	1b	A	100
If acceptable clinical improvement is achieved, methotrexate should be maintained for at least 12 months before tapering.	3	C	100
Mycophenolate mofetil may be used to treat severe JLS or MTX-refractory or MTX-intolerant patients.	2a	B	100
Medium-dose UVA1 phototherapy may be used to improve skin softness in isolated (circumscribed) morphoea lesions.	1b	A	100
Topical imiquimod may be used to decrease skin thickening of circumscribed morphoea.	3	C	100

DMARD, disease-modifying antirheumatic drug; JLS, juvenile localised scleroderma; L, level of evidence; MTX, methotrexate; S, strength of recommendation; UVA1, ultraviolet A1.

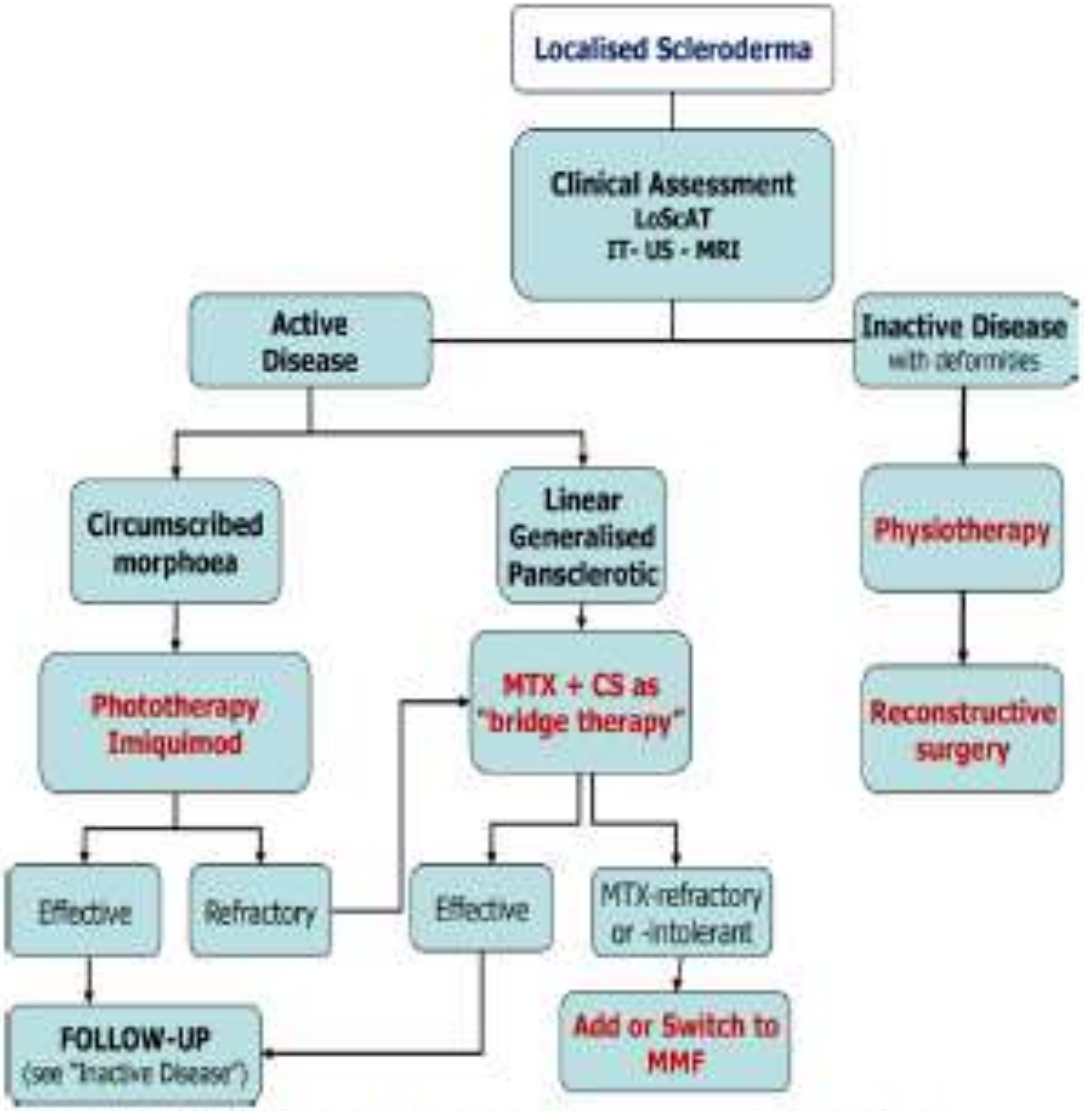

Figure 1 Flow chart for the treatment of newly diagnosed or refractory patients with juvenile localised scleroderma according to the clinical subtype. CS, corticosteroid; IT, infrared thermography; LoSCAT, Localized Scleroderma Cutaneous Assessment Tool; MMF, mycophenolate mofetil; MTX, methotrexate; US, ultrasound.

Recommendations for the management of autoinflammatory diseases

Nienke M ter Haar,[1,2] Marlen Oswald,[3] Jerold Jeyaratnam,[4] Jordi Anton,[5] Karyl S Barron,[6] Paul A Brogan,[7] Luca Cantarini,[8] Caroline Galeotti,[9] Gilles Grateau,[10] Veronique Hentgen,[11] Michael Hofer,[12] Tilmann Kallinich,[13] Isabelle Kone-Paut,[14] Helen J Lachmann,[15] Huri Ozdogan,[16] Seza Ozen,[17] Ricardo Russo,[18] Anna Simon,[19] Yosef Uziel,[20] Carine Wouters,[21] Brian M Feldman,[22] Sebastiaan J Vastert,[2] Nico M Wulffraat,[2] Susanne M Benseler,[23] Joost Frenkel,[4] Marco Gattorno,[24] Jasmin B Kuemmerle-Deschner[3]

Evidence-based recommendations for genetic diagnosis of familial Mediterranean fever

Gabriella Giancane,[1] Nienke M Ter Haar,[2] Nico Wulffraat,[1] Sebastiaan J Vastert,[1] Karyl Barron,[3] Veronique Hentgen,[4] Tilmann Kallinich,[5] Huri Ozdogan,[6] Jordi Anton,[7] Paul Brogan,[8] Luca Cantarini,[9] Joost Frenkel,[10] Caroline Galeotti,[11] Marco Gattorno,[12] Gilles Grateau,[13] Michael Hofer,[14] Isabelle Kone-Paut,[15] Jasmin Kuemmerle-Deschner,[16] Helen J Lachmann,[17] Anna Simon,[18] Erkan Demirkaya,[19] Brian Feldman,[20] Yosef Uziel,[21] Seza Ozen[22]

ARD Online First, published on October 11, 2017 as 10.1136/annrheumdis-2017-211904

Recommendations for collaborative paediatric research including biobanking in Europe: a Single Hub and Access point for paediatric Rheumatology in Europe (SHARE) initiative

Jasmin B Kuemmerle-Deschner,[1] Sandra Hansmann,[1] Nico M Wulffraat,[2] Sebastiaan J Vastert,[3] Kristien Hens,[4] Jordi Anton,[5] Tadej Avcin,[6] Alberto Martini,[7] Isabelle Koné-Paut,[8] Yosef Uziel,[9,10] Angelo Ravelli,[7] Carine Wouters,[11] David Shaw,[12,13] Seza Özen,[14] Andreas Eikelberg,[1] Berent J Prakken,[15] Nicolino Ruperto,[7] Gerd Horneff,[16] Tamas Constantin,[17] Michael W Beresford,[18] Marijn Sikken,[19] Helen E Foster,[20] Iris Haug,[1] Sabrina Schuller,[1] Christine Jägle,[1] Susanne M Benseler[1,21]

Vision - Future almost here

One centralized ethic comittee

Easy samples across the borders to central research lab

SHARE

11 October 2019

Concern: Letter to Health Care Authorities

Dear Health Care Authority, ERN- European Reference Network

The Pediatric Rheumatology European Society (PReS) is working to advance the goal of improving education and knowledge, not only among pediatric rheumatologists, but also for primary healthcare providers across Europe and across the globe.

The SHARE initiative, which stands for 'Single Hub and Access Point to Pediatric Rheumatology in Europe' aims to provide optimal treatment for pediatric rheumatologic diseases by combining patient- and family-centered approaches. It provides recommendations for diagnosing and therapy of the range of rare rheumatic diseases of childhood aiming for facilitating, and improving care throughout Europe.

It is the task of health care authorities to enable optimal health care based on scientific evidence.

We therefore would like to ask you to acknowledge these guidelines and recommendation papers in your country, with the aim of giving the best standard of care to all children in Europe.

The formulation and endorsement of existing clinical treatment protocols is one of the key tasks of the European reference Networks (ERN). ERNs were created under an EU initiative and are supervised by the national health care authorities of all EU member states. https://europa.eu/european-union/about-eu/countries_en

The autoinflammatory condition specified below is included in the scope of the ERN-RITA.

We will also be submitting these recommendations to the members of this ERN. There is close interaction between ERN RITA and PReS, also to ensure there are no discrepancies of approach.

Enclosed is a short summary (see Appendix) of the PReS / SHARE Recommendation manuscripts that have been published in the recent years.

The full list of recommendations for each paper are in the enclosed papers.

Sincerely yours

M.W. Beresford

Prof. Michael Beresford
Secretary- PReS Council

Prof. Nico Wulffraat
Chair- SHARE

Prof Yosef Uziel
Chair of Clinical Affairs,
PReS

JIA

Pediatrician Beliefs about Juvenile Idiopathic Arthritis May Result in Referral Delays: A Spanish National Survey

Maria Rosa Pavo, MD, and Jaime de Inocencio, MD, PhD

J Peds 2019

Pediatrician Beliefs about Juvenile Idiopathic Arthritis May Result in Referral Delays: A Spanish National Survey

A national survey -831 pediatricians participated.

Approximately one half of the respondents underestimated the incidence of the disease and

thought wrongly that pain was the leading symptom of oligoarticular forms.

Misconceptions that can be interfere with early recognition and referral of patients with JIA.

Juvenile Idiopathic Arthritis—Education, Knowledge, and Patient Outcomes

THE JOURNAL OF PEDIATRICS • www.jpeds.com EDITORIALS

Persistent, undiagnosed JIA with high disease activity interferes with daily life and carries a risk of irreversible Physical and psychosocial damage.

Pediatrician Beliefs about Juvenile Idiopathic Arthritis May Result in Referral Delays: A Spanish National Survey

Another national survey?

What is the situation in other European countries?

In adults RA?

In JIA?

Arthritis Care & Research
Vol. 71, No. 4, April 2019, pp 471–481
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EDUCATION • TREATMENT • RESEARCH

Time of Disease-Modifying Antirheumatic Drug Start in Juvenile Idiopathic Arthritis and the Likelihood of a Drug-Free Remission in Young Adulthood

Kirsten Minden,[1] Gerd Horneff,[2] Martina Niewerth,[3] Eva Seipelt,[4] Martin Aringer,[5] Peer Aries,[6] Ivan Foeldvari,[7] Johannes-Peter Haas,[8] Ariane Klein,[9] Stefanie Tatsis,[10] Klaus Tenbrock,[11] Angela Zink,[1] and Jens Klotsche[1]

Objective. To study juvenile idiopathic arthritis (JIA) long-term outcomes in relation to the time of initiation of biologic disease-modifying antirheumatic drug (bDMARD).

Methods. Outcomes of JIA patients prospectively followed by the Biologika in der Kinderrheumatologie (BiKeR) and Juvenile Arthritis Methotrexate/Biologics Long-Term Observation (JuMBO) registers were analyzed with regard to drug-free remission and inactive disease, functional status and quality of life, and surgery. To analyze the influence of early bDMARD therapy on outcomes, patients were assigned to 3 groups based on the time from symptom onset to bDMARD start (G1: ≤2 years, G2: >2 to ≤5 years, and G3: >5 years). Propensity score–adjusted outcome differences were analyzed by multinomial logistic regression analyses among the groups.

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Results. A total of 701 JIA patients were observed for mean ± SD 9.1 ± 3.7 years. At the last follow-up (disease duration mean ± SD 14.3 ± 6.1 years), 11.7% of patients were in drug-free remission, and 40.0% had inactive disease. More than half of the patients reported no functional limitation, while 5% had undergone arthroplasty, and 3% had eye surgery. At the 10-year time point, patients in G1 (n = 108) were significantly more likely to be in drug-free remission than those patients who began treatment later (G2, n = 199; G3, n = 259), with 18.5%, 10.1%, and 4.9%, respectively. Patients in G1 had significantly lower disease activity (clinical Juvenile Arthritis Disease Activity Score in 10 joints = 4.9), a better overall well-being (18.2% patient global assessment score = 0), and higher functional status (59.2% Health Assessment Questionnaire score = 0), compared to patients in G3 (7.1, 8.4%, and 43.7%, respectively). G1 patients required arthroplasty significantly less frequently than G3 patients and had significantly lower disease activity over time than patients in both G2 and G3.

Conclusion. Early DMARD treatment is associated with better disease control and outcomes, which supports the concept of a "window of opportunity" for JIA.

Treat to Target TTT Approach

- ACR- 20- 30%!!??

- For ACR 70- 90%!!
- **Remission or low disease activity!!**

Ravelli A, Consolaro A, Horneff G, et al (30 international)
Treating juvenile idiopathic arthritis to target: recommendations of an International task force

Ann Rheum Dis. 2018 Apr

Treating juvenile idiopathic arthritis to target: recommendations of an international task force

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- Daniel J Lovell,5 Nico M Wulffraat,6 Jonathan D Akikusa,7 Sulaiman M Al-Mayouf,8
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- Ruben Burgos-Vargas,13 Rolando Cimaz,14 Fabrizio De Benedetti,15 Erkan Demirkaya,11
- Dirk Foell,16 Yasuhiko Itoh,17 Pekka Lahdenne,18 Esi M Morgan,5 Pierre Quartier,19
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- Christiaan Scott,24 Susan Shenoi,25 Joost F Swart,6 Yosef Uziel,26,27
- Sebastiaan J Vastert,6 **Josef S Smolen28**

- Ravelli A, et al. Ann Rheum Dis 2018;77:819–828

Table 1 Instruments and criteria used for the definition of clinical inactive disease and low (minimal) disease activity in JIA

	Items included							
	PhGA	Pa/ChGA	AJC	ESR/CRP	Systemic features	Uveitis	Morning stiffness	Requirements for classification as CID or LDA
Criteria for CID								
Wallace's preliminary criteria[4]	X		X	X	X	X*		Normal ESR/CRP and all other items at 0 or not present
ACR preliminary criteria[5]	X		X	X	X	X†	X	Normal ESR/CRP, morning stiffness ≤15 min, and all other items at 0 or not present
JADAS criteria[3]	X	X	X	X				JADAS≤1
cJADAS criteria[11]	X	X	X					cJADAS≤1
Criteria for LDA								
Magni-Manzoni criteria—Oligo[6]	X		X					PGA≤2.5, AJC=0
Magni-Manzoni criteria—Poly[6]	X	X	X					PGA≤3.4, Pa/PtGA≤2.1, AJC≤1‡
JADAS criteria[3]	X	X	X	X				Oligoarticular course: JADAS≤2.0 Polyarticular course: JADAS≤3.8
cJADAS criteria[11]	X	X	X					Oligoarticular course: cJADAS≤1.5 Polyarticular course: cJADAS≤2.5

*Inactive uveitis was not defined.
†Inactive uveitis as defined by the Standardization of Uveitis Nomenclature Working Group.
‡In systemic arthritis, absence of systemic features is required.
ACR, American College of Rheumatology; AJC, active joint count; CID, clinical inactive disease; cJADAS, clinical JADAS; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; JADAS, Juvenile Arthritis Disease Activity Score; JIA, juvenile idiopathic arthritis; LDA, low disease activity; Oligo, persistent oligoarthritis; Pa/ChGA, parent's/child's global assessment of child's overall well-being; PhGA, physician's global assessment of overall disease activity; Poly, extended oligoarthritis, polyarthritis and systemic arthritis.

Table 2 Recommendations to treat juvenile idiopathic arthritis (JIA) to target

	Percentage of positive votes at consensus conference	Level of evidence	Strength of recommendation	Mean±SD level of agreement
Overarching principles				
A. The treatment targets and the therapeutic strategy should be based on shared decisions between the parents/patient and the paediatric rheumatology healthcare team.	90			9.8±0.5
B. JIA is a heterogeneous group of diseases that requires distinct treatment approaches.	100			10
C. The goals of treating patients with JIA are to control signs and symptoms; to prevent structural damage; to avoid comorbid conditions and drug toxicities; and to optimise function, growth and development, quality of life, and social participation.	100			10
D. Abrogation of inflammation is essential to achieve these goals.	100			9.8±0.5
E. Long-term use of systemic glucocorticoids to maintain the target should be avoided.	100			9.8±0.5
F. Treatment to target by regularly assessing disease activity and adapting therapy accordingly is important to achieve these goals.	100			10
Recommendations				
1. The primary target for treatment of patients with JIA is clinical remission, which means the absence of signs and symptoms of inflammatory disease activity, including extra-articular manifestations.	85	2b	C	9.7±0.5
2. Minimal (or low) disease activity may be an alternative target, particularly in patients with long-standing disease.	97	2c	B	9.7±0.6
3. Setting the target, selecting the tools and the therapeutic decisions should be based on individual patients' characteristics and agreed on with the parents/patient.	100	5	D	9.7±0.6
4. Disease activity should be assessed and documented regularly using a validated composite instrument.	100	2c	C	9.8±0.5
5. The frequency of assessments depends on the category of JIA, level of disease activity and presence of extra-articular manifestations. This may require weekly assessments, such as in systemic JIA with active systemic manifestations; monthly to every 3 months evaluations for patients who have high/moderate disease activity; and less frequent assessments, in states of persistent clinical remission.	93	5	C	9.6±0.7
6. In all patients, at least a 50% improvement in disease activity should be reached within 3 months and the target within 6 months. In patients with systemic JIA with active systemic manifestations, resolution of fever should be attained within 1 week.	93	2b	B	9.2±0.9
7. Treatment should be adjusted until the target is achieved.	100	2b	C	9.7±1.0
8. Once the treatment target has been achieved, it should be sustained. Ongoing monitoring should occur to ensure maintenance of the target.	100	2b	C	9.9±0.3

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Tocilizumab in Systemic Juvenile Idiopathic Arthritis

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The NEW ENGLAND JOURNAL of MEDICINE

New ERA

EDITORIALS

A New Era in the Treatment of Systemic Juvenile Idiopathic Arthritis

Christy Sandborg, M.D., and Elizabeth D. Mellins, M.D.

Arthritis & Rheumatology
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American College of Rheumatology
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Treatment to Target Using Recombinant Interleukin-1 Receptor Antagonist as First-Line Monotherapy in New-Onset Systemic Juvenile Idiopathic Arthritis: Results From a Five-Year Follow-Up Study

Nienke M. ter Haar,[1] E. H. Pieter van Dijkhuizen,[1] Joost F. Swart,[1] Annet van Royen-Kerkhof,[1] Ayman el Idrissi,[2] Arjen P. Leek,[2] Wilco de Jager,[1] Mark C. H. de Groot,[1] Saskia Haitjema,[1] Dirk Holzinger,[3] Dirk Foell,[4] Jorg van Loosdregt,[1] Nico M. Wulffraat,[1] Sytze de Roock,[1] and Sebastiaan J. Vastert[1]

Objective. Systemic juvenile idiopathic arthritis (JIA) is a multifactorial autoinflammatory disease with a historically poor prognosis. With current treatment regimens, approximately half of patients still experience active disease after 1 year of therapy. This study was undertaken to evaluate a treat-to-target approach using recombinant interleukin-1 receptor antagonist (rIL-1Ra; anakinra) as first-line monotherapy to achieve early inactive disease and prevent damage.

Methods. In this single-center, prospective study, patients with new-onset systemic JIA with an unsatisfactory response to nonsteroidal antiinflammatory drugs received rIL-1Ra monotherapy according to a treat-to-target strategy. Patients with an incomplete response to 2 mg/kg rIL-1Ra subsequently received 4 mg/kg rIL-1Ra or additional prednisolone, or switched to alternative therapy. For patients in whom inactive disease was achieved, rIL-1Ra was tapered after 3 months and subsequently stopped.

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Results. Forty-two patients, including 12 who had no arthritis at disease onset, were followed up for a median of 5.8 years. The median time to achieve inactive disease was 33 days. At 1 year, 76% had inactive disease, and 52% had inactive disease while not receiving medication. High neutrophil counts at baseline and a complete response after 1 month of rIL-1Ra were highly associated with inactive disease at 1 year. After 5 years of follow-up, 96% of the patients included had inactive disease, and 75% had inactive disease while not receiving medication. Articular or extraarticular damage was reported in <5%, and only 33% of the patients received glucocorticoids. Treatment with rIL-1Ra was equally effective in systemic JIA patients without arthritis at disease onset.

Conclusion. Treatment to target, starting with first-line, short-course monotherapy with rIL-1Ra, is a highly efficacious strategy to induce and sustain inactive disease and to prevent disease- and glucocorticoid-related damage in systemic JIA.

Several studies of systemic JIA have indicated that, especially in the early phase of this disease, activation of the innate immune system, including activation of the IL- 1 pathway, is most prominent

IL- 1 blocking therapy specifically would be favorable during this so- called "window of opportunity"

In 2008 we initiated a prospective trial of recombinant IL- 1 receptor antagonist (rIL- 1Ra) as first- line monotherapy for patients with new- onset systemic JIA, in which inactive disease was achieved in 85% of the patients within 1 year

In the present study, we investigated the long- term efficacy of our treat- to- target approach using rIL- 1Ra as first- line monotherapy

Unsatisfactory response (persistence of fever and arthritis after 7 days of treatment) to indomethacin (or NSAID), **rIL-1Ra** was initiated at a dosage of **2 mg/kg/day (with a maximum of 100 mg/day in patients weighing ≥50 kg) SC**

If **fever persisted after 3 days**, the rIL- 1Ra dosage was increased to **4 mg/kg/day (maximum of 200 mg/day)**

In patients who had **persistent disease activity** while receiving rIL- 1Ra monotherapy, **prednisolone 0.5–1 mg/kg/day** was added and/**or** patients were **switched to alter-native biologic agents**, such as **canakinumab 4 mg/kg or tocilizumab 8 mg/kg (for patients >30 kg) or 12 mg/kg** (for patients <30 kg)

If patients had **inactive disease at 3 months** while receiving rIL- 1Ra only, **rIL- 1Ra was tapered for a month** (alternate day regimen) and subsequently stopped

When a disease flare occurred, rIL- 1Ra was restarted

When multiple attempts at tapering failed, canakinumab was offered in order to avoid daily injections

Clinical information	All JIA patients (n = 42)	JIA patients with arthritis (n = 30)	JIA patients without arthritis (n = 12)
Age at start of rIL-1Ra treatment, years	7.1 (3.9, 11.8)	7.9 (4.1, 12.2)	5.2 (3.7, 10.9)
Sex, no. male/female	25/17	17/13	8/4
Duration between first symptom and start of rIL-1Ra treatment, days	30 (19, 61)	31 (21, 65)	25 (16, 49)
Fever, %	100	100	100
Rash, %	88.1	93.3	75
Lymphadenopathy, %	57.1	50	75
Hepatomegaly, %	38.1	33.3	50
Splenomegaly, %	19.0	16.7	25
Serositis, %	9.5	10	8.3
No. of joints with active disease	2 (0, 4)	3 (2, 4)	0 (0, 0)†
Physician's global assessment	40 (30, 49)	40 (30, 50)	40 (28, 40)
ESR, mm/hour	106 (83, 131)	107 (87, 135)	101 (81, 109)
CRP, mg/liter	138 (93, 225)	156 (103, 233)	116 (78, 207)
Ferritin, μg/liter	656 (284, 2,354)	672 (284, 2,354)	648 (250, 3,385)
Hemoglobin, mmoles/liter	6.1 (5.7, 6.5)	6.1 (5.4, 6.6)	6.2 (5.8, 6.5)
Leukocytes, $\times 10^9$/liter	18.8 (12.5, 26.2)	18.0 (12.3, 25.4)	20.90 (12.85, 30.18)
Neutrophils, $\times 10^9$/liter	14.61 (8.51, 22.07)	13.60 (8.20, 21.34)	18.32 (9.89, 26.03)
Lymphocytes, $\times 10^9$/liter	2.54 (1.83, 23.20)	2.60 (2.07, 3.33)	2.13 (1.52, 2.81)
Monocytes, $\times 10^9$/liter	0.67 (0.52, 0.83)	0.66 (0.47, 0.81)	0.79 (0.52, 0.93)
Platelets, $\times 10^9$/liter	603 (375, 707)	576 (376, 688)	623 (286, 805)

Results

After 1 mo 55% had completely inactive disease
After 3 mo 83% had inactive disease
After 1 year 76% had inactive disease
After 5 years 96% had inactive disease

Median period of tapering was 3.7 months

Median total duration of treatment was 6 months

60% after stopping therapy remained free of flares and have remission without therapy for years

30% more than usual therapy

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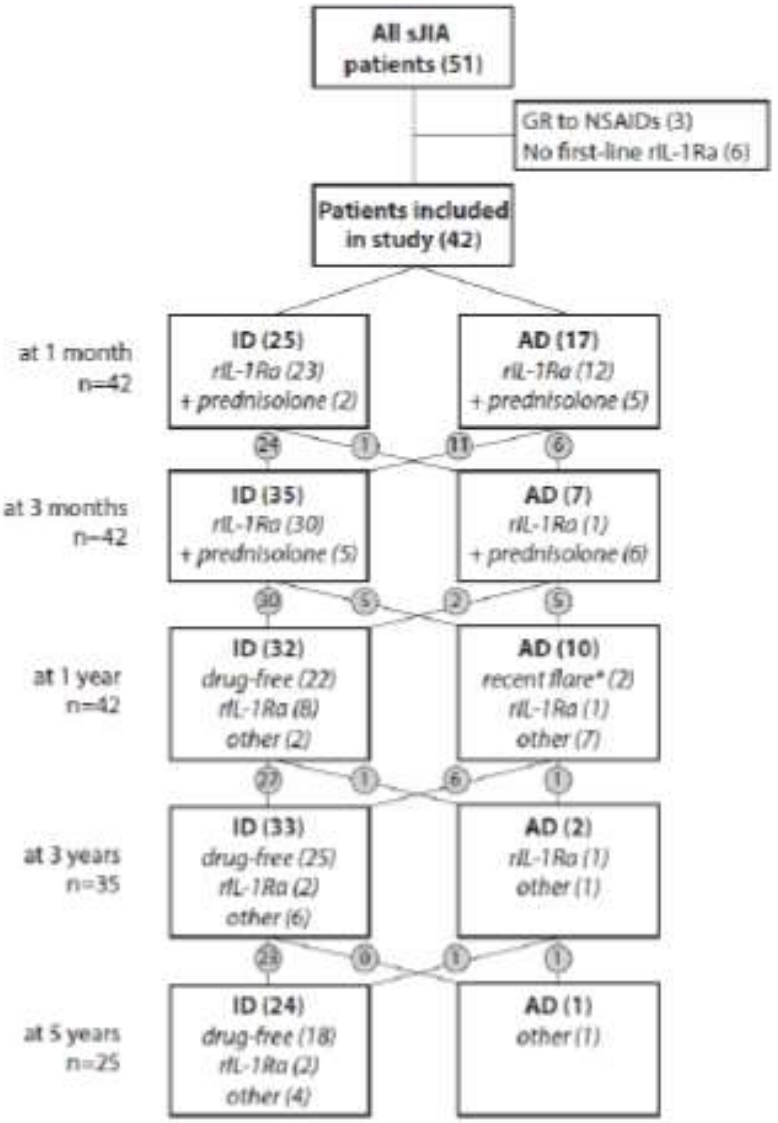
High neutrophil counts at baseline and a complete response after 1 month of rIL-1Ra were highly associated with inactive disease at 1 year



Results

Median time to flare was 5 weeks after stopping

Flares often subsided after therapy reinitiation

Non develop growth failure

Severe disease-

1/3 received systemic GC to achieve or sustain inactive disease

More than 50% needed only rIL1a and NSAIDs to achieve inactive disease

33% switched to other biologic or MTXcombined with steroids

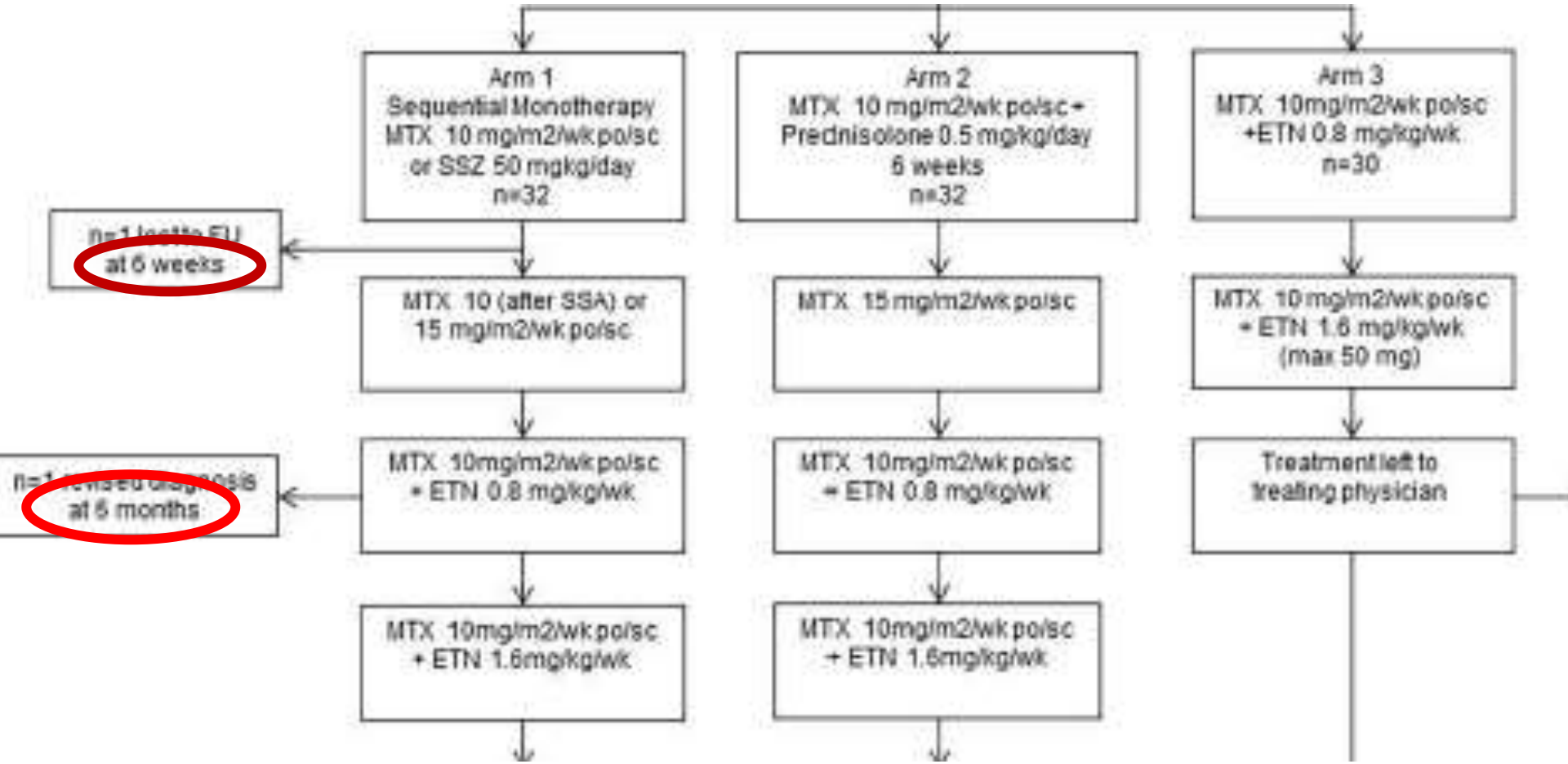
Best for kids study

CLINICAL SCIENCE

Treat to target (drug-free) inactive disease in DMARD-naive juvenile idiopathic arthritis: 24-month clinical outcomes of a three-armed randomised trial

Petra Hissink Muller,[1,2] Danielle M C Brinkman,[1,3] Dieneke Schonenberg-Meinema,[4] Wytse Bastiaan van den Bosch,[1] Yvonne Koopman-Keemink,[5] Isabel C J Brederije,[1] Peter W Bekkering,[6] Taco W Kuijpers,[4] Marion Van Rossum,[7,8] Lisette WA van Suijlekom-Smit,[2] J Merlijn van den Berg,[4] Stefan Boehringer,[9] Cornelia F Allaart,[10] R ten Cate[1]

Hissink Muller P, et al. Ann Rheum Dis 2019;78:51


Arm 1
Sequential Monotherapy
MTX 10 mg/m2/wk po/sc
or SSZ 50 mg/kg/day
n=32
Arm 2
MTX 10 mg/m2/wk po/sc +
Prednisolone 0.5 mg/kg/day
6 weeks
n=32
Arm 3
MTX 10mg/m2/wk po/sc
+ETN 0.8 mg/kg/wk
n=30
at 6 weeks
MTX 10 (after SSA) or
15 mg/m2/wk po/sc
MTX 15 mg/m2/wk po/sc
MTX 10 mg/m2/wk po/sc
+ ETN 1.6 mg/kg/wk
(max 50 mg)
at 6 months
MTX 10mg/m2/wk po/sc
+ ETN 0.8 mg/kg/wk
MTX 10mg/m2/wk po/sc
+ ETN 0.8 mg/kg/wk
Treatment left to
treating physician
MTX 10mg/m2/wk po/sc
+ ETN 1.6mg/kg/wk
MTX 10mg/m2/wk po/sc
+ ETN 1.6mg/kg/wk

	Arm 1 Sequential monotherapy n=31	Arm 2 Combination MTX + 6 weeks prednisolone n=32	Arm 3 Combination MTX + etanercept n=29
	Events (no. patients)		
Common adverse events			
Nausea or abdominal pain	18 (12)	26 (16)	28 (13)
URTI	9 (9)	20 (13)	23 (14)
Gastroenteritis	4 (4)	4 (4)	6 (6)
Other infections	8 (7)	12 (9)	12 (8)
General malaise	11 (8)	12 (8)	7 (7)
New onset CAU*	1 (1)	0	0
Liver enzyme abnormalities	9 (5)	11 (8)	4 (3)
Other adverse events			
Headache and psychosomatic complaints*	10 (9)	12 (8)	4 (3)
Anemia	1 (1)	2 (2)	0
Leucopenia other	8 (6) 25	2 (2) 31	1 (1) 30
Severe adverse events			
Hospital admissions†	4 (3)	3 (3)	5 (5)

TTT- (pediatric BeSt study)

- In 2 years- >70%- inactive disease
- 59%- drug free inactive disease
- Faster response in MTX and Etanrecept
- Time to inactive disease was similar- TTT approach
- After stopping medication-3mos in oligo, 6 mos on poly- 26% flare

Conclusion Regardless of initial specific treatments, after 24 months of treatment-to-target aimed at drug-free inactive disease, 71% of recent-onset patients with JIA had inactive disease (median onset 9 months) and 39% were drug free. Tightly controlled treatment-to-target is feasible.

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AMERICAN COLLEGE of RHEUMATOLOGY
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SPECIAL ARTICLE

2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis

Sarah Ringold,[1] Sheila T. Angeles-Han,[2] Timothy Beukelman,[3] Daniel Lovell,[2] Carlos A. Cuello,[4] Mara L. Becker,[5] Robert A. Colbert,[6] Brian M. Feldman,[7] Polly J. Ferguson,[8] Harry Gewanter,[9] Jaime Guzman,[10] Jennifer Horonjeff,[11] Peter A. Nigrovic,[12] Michael J. Ombrello,[6] Murray H. Passo,[13] Matthew L. Stoll,[3] C. Egla Rabinovich,[14] Rayfel Schneider,[7] Olha Halyabar,[15] Kimberly Hays,[13] Amit Aakash Shah,[16] Nancy Sullivan,[17] Ann Marie Szymanski,[6] Marat Turgunbaev,[16] Amy Turner,[16] and James Reston[17]

DISCUSSION

This guideline includes **39 recommendations** for the treatment of children with JIA and non-systemic **polyarthritis, sacroiliitis, and enthesitis**

The quality of most of the **available evidence was low or very low** in relation to the relevant clinical PICO questions, resulting in 31 of the **recommendations being conditional**

Equivalent data for safety and efficacy between the biologics and lack of head-to-head comparisons

The exceptions were that TNFi are specifically recommended for sacroiliitis, and rituximab is considered only after TNFi, abatacept, and tocilizumab have been tried

This guideline considered parent and patient preferences assessed by a separate Parent and Patient Panel

Primary themes that emerged from that discussion were:

1) the importance of **shared decision-making**

2) the importance of **parents and patients receiving information** regarding not only the preferred medication or intervention but also the alternatives

3) parent/patient support of earlier consideration of biologics given their experiences with decreased adverse effects and improved quality of life with the use of these medications relative to their experiences with MTX

Studies in pediatrics are underway or planned for a number of new medications, including JAK inhibitors and IL-17 and IL-12/23 inhibitors, and these medications may become useful additions as treatment options for JIA, particularly in patients with sacroiliitis for whom limited options exist

Treatment should be escalated in patients with even 1 active joint

The management of inactive disease and the tapering and withdrawal of medications for patients with inactive disease are not addressed in this guideline but will be important for future guidelines

Because the quality of evidence was overall low and most recommendations were conditional, clinicians, caregivers, and patients should use a shared decision-making process when considering these recommendations

This guideline considered parent and patient preferences assessed by a separate Parent and Patient Panel

Primary themes that emerged from that discussion were:

the importance of **shared decision-making**

2) the importance of parents and patients receiving information regarding not only the preferred medication or intervention but also the alternatives

3) parent/patient support of earlier consideration of biologics given their experiences with decreased adverse effects and improved quality of life with the use of these medications relative to their experiences with MTX

The Journal of Rheumatology

Establishing an Updated Core Domain Set for Studies in Juvenile Idiopathic Arthritis: A Report from the OMERACT 2018 JIA Workshop

Esi M. Morgan, Jane E. Munro, Jennifer Horonjeff, Ben Horgan, Beverley Shea, Brian M. Feldman, Hayyah Clairman, Clifton O. Bingham III, Susan Thornhill, Vibeke Strand, Alessandra Alongi, Silvia Magni-Manzoni, Marion A.J. van Rossum, Richard Vesely, Jelena Vojinovic, Hermine I. Brunner, Julia G. Harris, Daniel B. Horton, Daniel J. Lovell, Melissa Mannion, Homaira Rahimi, Angelo Ravelli, Sarah Ringold, Nicolino Ruperto, M. Suzanne Schrandt, Susan Shenoi, Natalie J. Shiff, Karine Toupin-April, Nikolay Tzaribachev, Pamela Weiss and Alessandro Consolaro

Outcome Measures- patients Role

Establishing an Updated Core Domain Set for Studies in Juvenile Idiopathic Arthritis Physicians and patients/parents together!!

A Report from the OMERACT 2018 JIA Workshop

53 patients with JIA (ages 15-24 yrs)

55 parents

The Journal of Rheumatology August 2019, 46 1006-1013

OMERACT ???

- *OMERACT = Outcome Measures in Rheumatology.*
- *An international health outcomes measurement group.*
- *Has been funded by unrestricted support from more than 12 pharmaceutical & clinical research organizations in the last 2 years.*

1997- Outcome Measures- international patients role

1) MD evaluation of disease activity (10cm VAS)
2) Parent evaluation of overall well-being (10cm VAS)
3) Functional ability (Childhood Health Assessment Questionnaire)
4) Number of joints with active arthritis
5) Number of joints with limited range of motion
6) Erythrocyte sedimentation rate

Results - *Domain definitions used for Delphi Survey voting reference*

Domain	Example Items that May Be Included in this Domain
Activity limitation	Effect on physical function/physical disability, effect on activities of daily life
Coping with illness	Coping with medication administration, effect on family, adherence to therapy
Eye inflammation	Uveitis, iritis, related vision loss
Fatigue	Tiredness, lack of energy, lack of vitality
Growth and maturation	Height, weight, Tanner stage (puberty), fertility
Health care use	Costs of care, frequency of medical visits
Imaging signs of inflammation	MRI, ultrasound, radiographs
Effect on emotional function, mood or cognition	Depressive symptoms, anxiety, need for psychologic/psychiatric support, cognition, ability to think
Effect on social relationships	Effect on relationships with friends, family, etc.
Inflammatory signs outside of joints and eyes	Fever, systemic rash, psoriasis, enthesitis, back pain, etc.
Joint damage	Permanent deformity, fixed contracture, erosions, etc.
Joint inflammatory signs	Redness, swelling, warmth, tenderness, "active joint," limitation in joint ROM
Laboratory signs of inflammation	Acute-phase reactants (ESR, CRP, etc.)

Mandatory domains are

- **pain**,
- joint inflammatory signs,
- activity limitation/physical function,
- patient's perception of disease activity (overall well-being),
- adverse events.
- (MTX)

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Early Self-Reported Pain in Juvenile Idiopathic Arthritis as Related to Long-Term Outcomes: Results From the Nordic Juvenile Idiopathic Arthritis Cohort Study

Ellen Dalen Arnstad,[1] Veronika Rypdal,[2] Suvi Peltoniemi,[3] Troels Herlin,[4] Lillemor Berntson,[5] Anders Fasth,[6] Susan Nielsen,[7] Mia Glerup,[4] Maria Ekelund,[8] Marek Zak,[7] Kristiina Aalto,[3] Ellen Nordal,[2] Pål Richard Romundstad,[9] and Marite Rygg,[10] on behalf of the Nordic Study Group of Pediatric Rheumatology

Objective. To study self-reported pain early in the disease course of juvenile idiopathic arthritis (JIA) as a predictor of long-term disease outcomes.

Methods. Consecutive cases of JIA with disease onset from 1997 to 2000 from defined geographical areas of Norway, Sweden, Finland, and Denmark were prospectively enrolled in this population-based cohort study. Self-reported, disease-related pain was measured on a 10-cm visual analog scale (VAS pain). Inclusion criteria were a baseline visit with a pain score 6 months after disease onset, followed by an 8-year study visit. Remission was defined according to Wallace et al (2004) preliminary criteria. Functional disability was measured by the Childhood Health Assessment Questionnaire and the Child Health Questionnaire Parent Form if the child was age <18 years and by the Health Assessment Questionnaire if age ≥18 years. Damage was scored using the Juvenile Arthritis Damage Index.

Early Self-Reported Pain in Juvenile Idiopathic Arthritis as Related to Long-Term Outcomes: Results From the Nordic Juvenile Idiopathic Arthritis Cohort Study

Results. The final study cohort consisted of 243 participants, and 120 participants (49%) had oligoarticular onset. At baseline, 76% reported a VAS pain score >0 compared to 57% reporting at 8 years. Half of those who reported baseline pain also reported pain at 8 years but at a lower intensity. Compared to no pain, higher pain intensity at baseline predicted more pain at 8 years, more functional disability, more damage, and less remission without medication. Baseline pain predicted more use of disease-modifying antirheumatic drugs/biologics during the disease course. Participants with oligoarticular JIA reporting pain at baseline were more likely to develop extended oligoarticular JIA or other JIA categories with an unfavorable prognosis.

Conclusion. Early self-reported, disease-related pain among children and adolescents with JIA is common and seems to predict persistent pain and unfavorable long-term disease outcomes.

PAIN-Conclusions

Patients reporting pain at baseline were not in remission without medication

Patients that not reported pain at baseline rarely reported pain and functional disability at 8 years, 74% were in remission without medication

Pain and functional disability at baseline was associated with the use of DMARRDs and biologics during the 8 year disease course

Psychosocial health assessed summary score did not show an association with the baseline pain score

PAIN-Conclusions

Oligo JIA reporting VAS pain score > 0 at baseline, 48% developed extended oligoJIA or other JIA compared to 30% of those reporting no pain

Higher proportion of patients with VAS score > 0 at baseline was not in remission without medication 65% and reported pain in 61% at 8 years

70% of those reported no pain at baseline remained in the persistent oligoJIA at the 8 year follow up

Look for PAIN

Rheumatology team

Rheumatologist

Primary Physician

Physical therapist - Occupational therapist, Medical clown, Social worker, Psychologist, Secretary, Rehabilitation expert

Patient and family (working parties of PRES)

The Journal of Rheumatology

Research Article | Pediatric Rheumatology

Toward New Classification Criteria for Juvenile Idiopathic Arthritis: First Steps, Pediatric Rheumatology International Trials Organization International Consensus

Alberto Martini, Angelo Ravelli, Tadej Avcin, Michael W. Beresford, Ruben Burgos-Vargas, Ruben Cuttica, Norman T. Ilowite, Raju Khubchandani, Ronald M. Laxer, Daniel J. Lovell, Ross E. Petty, Carol A. Wallace, Nico M. Wulffraat, Angela Pistorio, Nicolino Ruperto and for the Pediatric Rheumatology International Trials Organization (PRINTO)

The Journal of Rheumatology February 2019, 46 (2) 190-197; DOI: https://doi-org.meir-ez.medlcp.tau.ac.il/10.3899/jrheum.180168

New proposed Classification of JIA

Some of these categories appear to be quite **homogeneou**s and **present both in children as well as in adults**, others are **heterogeneous** and may be better defined

1. **Systemic JIA** is characterized by an autoinflammatory phenotype with its adult equivalent named **adult-onset Still disease (AOSD**)

2. **RF-positive polyarthritis** represents the childhood equivalent of RF-positive adult rheumatoid arthritis **(RA)**

3. **Enthesitis-related arthritis ERA** is a form of undifferentiated spondyloarthritis **(SpA)**

New proposed Classification of JIA

2 categories: **RF-negative polyarthritis and PsA**, have been shown to be heterogeneous

Both were characterized by **early onset** and antinuclear antibody **(ANA) positivity**, a more homogeneous entity observed **only in childhood**, representing the majority of patients with oligoarticular JIA in the Western world

Therefore, that the **number of joints** involved and the **presence of psoriasis may not represent reliable criteria** for JIA classification

Outlook and outstanding future work

In Step **3**: it is foreseen that a **prospective cohort of 1000 patients with JIA at onset will be collected**, with a longitudinal **follow up for 1–5** years

In Step **4**: once the prospective data collection is finished and analyzed, a **final consensus conference** will be organized to discuss the results and to finalize the new, validated PRINTO JIA classification criteria

SAFETY ISSUES

Cooperation

Pharma child data-ARD supp 2019

- SERIOUS/AT LEAST MODERATE INFECTIONS IN
- PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ON SYNTHETIC AND BIOLOGIC DRUGS FROM THE PHARMACHILD REGISTRY.

- Gabriella Giancane, Joost F. Swart, Nikolay Tzaribachev, Nadina Rubio,
- Ruben Cuttica, Ingrida Rumba-Rozenfelde, Wafaa Mohammed Saad Suwairi,
- Calin Lazar, Yosef Uziel, Albena Telcharova, Tadej Avcin, Angela Minaici,
- Claudio Len, Stella Maris Garay, Alina Boteanu, Angela Pistorio, Nico Wulffraat,
- Nicolino Ruperto.

- **9000 patients- MTX and biologics- safe!!**

Swart et al. Arthritis Research & Therapy (2018) 20:285
https://doi.org/10.1186/s13075-018-1780-z

Arthritis Research & Therapy

RESEARCH ARTICLE Open Access

Pharmacovigilance in juvenile idiopathic arthritis patients treated with biologic or synthetic drugs: combined data of more than 15,000 patients from Pharmachild and national registries

Joost Swart[1†], Gabriella Giancane[2†], Gerd Horneff[3†], Bo Magnusson[5], Michael Hofer[6,7], Ekaterina Alexeeva[8,9], Violeta Panaviene[10], Brigitte Bader-Meunier[11], Jordi Anton[12], Susan Nielsen[13], Fabrizio De Benedetti[14], Sylvia Kamphuis[15,16], Valda Stanevičiūtė[17], Maria Tzioufas[18], Laura Marinella Alloisio[19], Elena Tsitsami[20], Ariane Klein[3], Kirsten Minden[21,22], Ivan Foeldvari[23], Johannes Peter Haas[24], Jens Klotsche[21,22], Anna Carin Horne[5], Alessandro Consolaro[25,26], Francesca Bovis[2], Francesca Bagnasco[2], Angela Pistorio[27], Alberto Martini[28], Nico Wulffraat[1], Nicolino Ruperto[2*] and for the Paediatric Rheumatology International Trials Organisation (PRINTO), BIKeR and the board of the Swedish Registry

Table 1 Demographic and clinical characteristics of the juvenile idiopathic arthritis patients from different registrie

	Pharmachild *N* = 8274	BiKeR *N* = 3990
Number of countries	32	2#
Number of centers	86	72
Number of patients per center	55.5 (17–124)	10.5 (3–39.8)
Age at onset	5.4 (2.4–10.0)	7.6 (3.2–11.7)
Age at JIA diagnosis	6.2 (2.8–10.9)	–
Disease duration at last visit	5.3 (2.7–8.8)	6.1 (3.5–9.5)
Female	5584 (67.5%)	2670 (66.9%)
Antinuclear antibodies (ANA)*	1767 (21.4%)	1900 (47.6%)
ILAR JIA category		4
Systemic	911 (11.0%)	267 (6.7%)
Oligo	3071 (37.1%)	1215 (30.5%)
Oligo persistent	2011 (24.3%)	494 (12.4%)
Oligo extended	1060 (12.8%)	721 (18.1%)
Polyarticular RF^-	2183 (26.4%)	1192 (29.9%)
Polyarticular RF^+	322 (3.9%)	243 (6.1%)
Psoriatic arthritis	285 (3.4%)	296 (7.4%)
Enthesitis-related arthritis	924 (11.2%)	649 (16.3%)
Undifferentiated arthritis	578 (7.0%)	127 (3.2%)

Etanercept	3600 (43.5%); 719 (300–1338)	2467 (61.8%); 489 (184–934)	726 (24%); 827 (341–1666)
Adalimumab	1778 (21.5%); 442 (174–927)	810 (20.3%); 350 (117–755)	657 (21.8%); 701 (292–1604)
Infliximab	705 (8.5%); 425 (160–951)	68 (1.7%); 213 (129–717)	189 (6.3%); 825 (328–1738)
Tocilizumab	633 (7.7%); 351 (126–742)	281 (7%); 377 (127–730)	122 (4%); 660 (193–1353)
Abatacept	420 (5.1%); 342 (156–715)	101 (2.5%); 190 (83–582)	80 (2.6%); 378 (164–1125
Anakinra	339 (4.1%); 299 (94–837)	50 (1.3%); 304 (9–806)	48 (1.6%); 422 (144–836)
Golimumab	161 (1.9%); 270 (106–623)	63 (1.6%); 344 (88–783)	93 (3.1%); 796 (370–1743)
Canakinumab	145 (1.8%); 351 (133–1032)	39 (1%); 364 (214–733)	7 (0.2%); 654 (604–1654)
Rituximab	103 (1.2%); 42 (24–87)	4 (0.1%); 15 (0–108)	20 (0.7%); 129 (15–1550)
Certolizumab	33 (0.4%); 166 (106–309)	4 (0.1%); 49 (0–110)	8 (0.3%); 984 (714–1538)
Other biologic agents	14 (0.2%); 217 (54–432)	4 (0.1%); 77 (25–149)	2 (0.1%); 325 (223–426)

Table 3 Total number of adverse events by MedDRA system organ class ordered by decreasing frequencies

	Pharmachild $N = 5173$	BiKeR $N = 5013$
Infections and infestations	1523 (29.4%)	1509 (30.1%
Gastrointestinal disorders	595 (11.5%)	984 (19.6%
Injury, poisoning and procedural complications	325 (6.3%)	152 (3.1%)
Blood and lymphatic system disorders	291 (5.6%)	99 (2%)
Investigations	285 (5.5%)	377 (7.5%)
Eye disorders	270 (5.2%)	309 (6.2%)
Skin and subcutaneous tissue disorders	256 (4.9%)	217 (4.3%)
General disorders and administration site conditions	245 (4.7%)	410 (8.2%)
Hepatobiliary disorders	233 (4.5%)	24 (0.5%)
Surgical and medical procedures	209 (4.1%)	98 (2%)
Nervous system disorders	151 (2.9%)	227 (4.5%)
Musculoskeletal and connective tissue disorders	147 (2.8%)	138 (2.7%)
Respiratory, thoracic, and mediastinal disorders	112 (2.2%)	50 (1%)

Psychiatric disorders	105 (2.1%)	157 (3.1%)
Endocrine disorders	104 (2.0%)	6 (0.1%)
Metabolism and nutrition disorders	77 (1.5%)	34 (0.7%)
Renal and urinary disorders	66 (1.3%)	21 (0.4%)
Immune system disorders	33 (0.6%)	77 (1.5%)
Vascular disorders	30 (0.6%)	46 (0.9%)
Reproductive system and breast disorders	26 (0.5%)	13 (0.3%)
Congenital, familial, and genetic disorders	22 (0.4%)	9 (0.2%)
Cardiac disorders	19 (0.4%)	13 (0.3%)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	16 (0.3%)	29 (0.6%)
Ear and labyrinth disorders	13 (0.3%)	7 (0.1%)
Social circumstances	11 (0.2%)	0
Pregnancy, puerperium and perinatal conditions	9 (0.2%)	7 (0.1%)

Conclusion

- First attempt to present very large national and international data
- 15284 patients-
- 8274- pharmachild
- 3990- German
- 3020- Swedish
- Most powerful tool for analyzing efficacy and safety

SAFETY ISSUES

Original article •

Efficacy, immunogenicity and safety • of vaccination in adult patients with • autoimmune inflammatory rheumatic • diseases: a systematic literature • review for the 2019 update of • EULAR recommendations •

Christien Rondaan, 1,2 Victoria Furer,3,4 Marloes W Heijstek,5
Nancy Agmon-Levin,4,6 Marc Bijl,7 Ferdinand C Breedveld,8 Raffaele D'Amelio,9
Maxime Dougados,10,11 Meliha C Kapetanovic,12 Jacob M van Laar,13
Annette Ladefoged de Thurah,14 Robert Landewe,15,16 Anna Molto, 10
Ulf Muller-Ladner,17 Karen Schreiber,18,19 Leo Smolar,20 Jim Walker,21
rmdopen-2019-001035Klaus Warnatz,22 Nico M Wulffraat,23 Sander van Assen,24 Ori Elkayam3,4

RMD Open
2019;5:/

MTX, Biological drugs

- Patients should not receive live attenuated vaccines while on these drugs. **??**
- **Measles outbreak**

Breaking borders
Cooperation is powerful

Live Attenuated MMR/V booster Vaccines in Pediatric Rheumatic Diseases **are Safe:**
Multicenter, retrospective data collection

Patient Therapy – 234 patients

- 124 while on MTX, of whom 3 reported local mild side-effects.
- 71 on MTX + biologics, 9 reported mild, transient local skin reaction, fever or URTI.
- 39 on biologics, 1 reported fever.

- No vaccinal infection-MMRV was reported.
- None of the patients experienced disease flare.
- We hope that the current recommendation will be updated!

The article is available on Pubmed

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Live attenuated MMR/V booster vaccines in children with rheumatic diseases on immunosuppressive therapy are safe: Multicenter, retrospective data collection

Yosef Uziel[a,*], Veronica Moshe[a], Beata Onozo[b], Andrea Kulcsár[c], Diána Tróbert-Sipos[d], Jonathan D. Akikusa[e], Gecilmara Salviato Pileggi[f], Despoina Maritsi[g], Ozgur Kasapcopur[h], Mariana Rodrigues[i], Roubini Smerla[j], Donato Rigante[k], Balahan Makay[l], Erato Atsali[m], Nico Wulffraat[n], Nataša Toplak[o], for the PReS working party of Vaccination Study Group

https://www.ncbi.nlm.nih.gov/pubmed/3198

From pediatric to adult care

- Cooperation

recommendations for the transitional care of young people with juvenile-onset rheumatic diseases

- Foster H. E et al
- Ann Rheum Dis 2017;76:639-646

Transition paper

EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases

Helen E Foster,[1] Kirsten Minden,[2,3] Daniel Clemente,[4] Leticia Leon,[5,6] Janet E McDonagh,[7] Sylvia Kamphuis,[8] Karin Berggren,[9] Philomine van Pelt,[10] Carine Wouters,[11] Jennifer Waite-Jones,[12] Rachel Tattersall,[13] Ruth Wyllie,[14] Simon R Stones,[15] Alberto Martini,[16] Tamas Constantin,[17] Susanne Schalm,[18] Berna Fidanci,[19] Burak Erer,[20] Erkan Dermikaya,[21] Seza Ozen,[22] Loreto Carmona[23]

Foster HE, *et al. Ann Rheum Dis* 2017;**76**:639–646. c

Box 2 Aspects considered as part of holistic care

Medical aspects:

- identification of medical needs, addressing any issues
- ensuring continuity of provision of high-quality care
- providing generic and disease-specific information
- health promotion, anticipatory guidance
- health behaviour (eg, health literacy, experimentation and risk behaviour), negotiating most appropriate ways to ensure adherence to treatment
- knowledge and skills in areas listed above

Psychosocial aspects:

- identifying individual needs, risk and protective factors (eg, Home, Education, Activities, Drugs, Sex, Suicide (HEADSS))[61 62]
- providing support or referring young people to specific agencies
- ensuring a social life that is equivalent to those of peers
- ensuring support to cope with disease/treatment
- providing advice and/or additional sources of support
- promoting skills in assertiveness, resilience, self-care, self-determination and self-advocacy

Educational and vocational aspects:

- addressing future career prospects
- developing skills in disclosure
- support in preparing for work readiness
- informing about where to get information (recommend: career advisors, appropriate agencies, charity websites)
- addressing work experience and encouraging young people to gain relevant experience
- offer appropriate information, support and advice (support groups, volunteer services)
- liaisons with educational institutions
- informing about rights and obligations, benefits and

Transition Timeline for Children and Adolescents with Special Health Care Needs:

Chronic Illnesses / Physical Disabilities

Parent and Child Interactions that Encourage Independence

Birth to 3-5, or according to your child's developmental ability

- Assure your infant the world is a good place in which to live. The development of a sense of trust is vital to the development of a healthy personality.
- Allow your child to develop at his/her own individual rate
- As a parent it is important to take short breaks from your child to renew energy with which to enjoy him/her.
- Begin keeping a record of your child's educational and medical history, including immunizations.

By ages 3-5, or according to your child's developmental ability

- Assign your child chores appropriate for his/her ability level.
- Encourage decision-making skills by offering choices.
- Teach consequences of your child's behaviors and choices.
- Continue involvement in community and recreational activities that include children with and without special needs.
- Begin asking "What do you want to do when you grow up?"
- Begin teaching your child about his/her special health care need.
- Begin teaching your child self-care skills: normal skills and those related to his/her special health care need.

By ages 6-11, or according to your child's developmental ability

- Begin helping your child interact directly with doctors, nurses, therapists, and teachers.
- Assess your child's perception and basic knowledge of his/her special health care need. Build on their understanding.
- Continue teaching your child normal self-care skills as well as skills related to his/her special health care need.
- Determine whether reasonable accommodations are needed to ensure equal access to school programs; if so, ask if your child qualifies for a 504 plan.
- Encourage hobbies and leisure activities; include exploring community and recreational activities, clubs, 4-H, Scouts, Campfire, YMCA, sports, etc.
- Continue to encourage decision making skills by offering choices.
- Continue assigning your child chores appropriate for his/her ability level.
- Take your child shopping whenever possible so he/she can help in choices.
- Let your child choose how to spend some or all of allowance.
- Teach your child the consequences of his/her behaviors and choices.
- Allow your child to experience the consequences of a poor choice as well as a good choice.
- Begin teaching your child self-advocacy skills.
- Begin asking your child "What will you do when you grow up?"

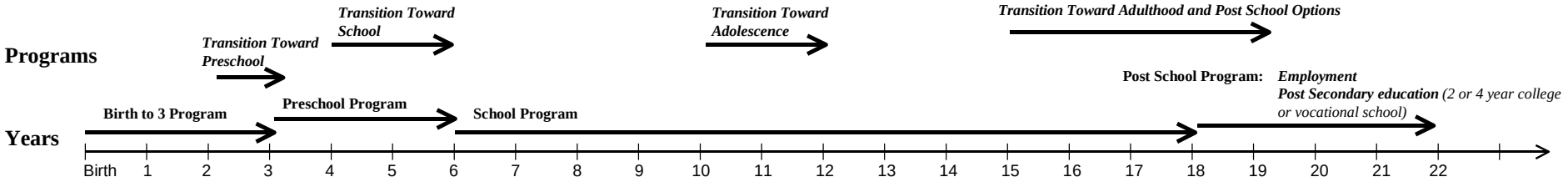
By ages 12-18, or according to your child's developmental ability

- Assess your teen's perception and basic knowledge of his/her special health care need. Fill in gaps in understanding.
- Continue teaching your teen normal self-help skills as well as skills related to special health care need.
- Begin helping your teen keep a record of his/her medical history, including conditions, operations, treatments (dates, doctors, recommendations) and 504 plan if he/she has one.
- If has a 504 plan, encourage teen to participate in any 504 meetings.
- Begin helping your teen take responsibility for making and keeping his/her own medical appointments, ordering their own supplies, etc.
- Begin exploring health care financing for young adult at age 17.
- Discuss sexuality with your teen.
- Help your teen identify and build on his/her strengths.
- Explore support groups, if teen is interested.
- Begin to explore and talk about possible career interests with your teen.
- Help your teen find work and volunteer activities.
- Continue to allow your teen to help with family chores.
- Continue to encourage hobbies and leisure activities.
- Help your teen identify and be involved with adult or older teen role models.
- Begin, with your teen, looking for an adult health care provider.
- Encourage teen to contact campus disabled student services to request accommodations if he/she will be attending college.
- With teen, check eligibility for SSI the month he/she turns 18. At age 18, the teen's financial resources are evaluated, not the parents/guardians'.

By ages 18-21, or according to your child's developmental ability

- Act as a resource and support to young adult.
- Encourage young adult to participate in support groups and/or organizations relevant to his/her special health care need.
- Finalize health care financing with young adult.
- With young adult, finalize transfer of medical care to adult provider.
- For young adult attending college, encourage continued contact with disabled student services as needed for accommodations.
- Encourage young adult to investigate services provided by Department of Vocational Rehabilitation (DVR) if he/she has not already done so.

Supports and Services to Consider (see back for contact information)



From pediatric to adult care

- Cooperation
- Good example in our society- in meetings
- EULAR-PRES combined meeting.

- We need to improve transition and continuity of care!

SLE- LUPUS

Criteria

2019 European League Against Rheumatism/ American College of Rheumatology classification criteria for systemic lupus erythematosus

Martin Aringer,[1] Karen Costenbader,[2] David Daikh,[3] Ralph Brinks,[4] Marta Mosca,[5] Rosalind Ramsey-Goldman,[6] Josef S Smolen,[7] David Wofsy,[8] Dimitrios T Boumpas,[9,10] Diane L Kamen,[11] David Jayne,[12] Ricard Cervera,[13] Nathalie Costedoat-Chalumeau,[14] Betty Diamond,[15] Dafna D Gladman,[16] Bevra Hahn,[17] Falk Hiepe,[18] Søren Jacobsen,[19] Dinesh Khanna,[20] Kirsten Lerstrøm,[21] Elena Massarotti,[22,23] Joseph McCune,[20] Guillermo Ruiz-Irastorza,[24] Jorge Sanchez-Guerrero,[25,26] Matthias Schneider,[27] Murray Urowitz,[28] George Bertsias,[29] Bimba F Hoyer,[18,30] Nicolai Leuchten,[1] Chiara Tani,[31] Sara K Tedeschi,[23,32] Zahi Touma,[33] Gabriela Schmajuk,[3] Branimir Anic,[34] Florence Assan,[35] Tak Mao Chan,[36] Ann Elaine Clarke,[37] Mary K Crow,[38] László Czirják,[39] Andrea Doria,[40] Winfried Graninger,[41] Bernadett Halda-Kiss,[39] Sarfaraz Hasni,[42] Peter M Izmirly,[43] Michelle Jung,[37] Gábor Kumánovics,[39] Xavier Mariette,[44,45] Ivan Padjen,[34] José M Pego-Reigosa,[46] Juanita Romero-Diaz,[47] Íñigo Rúa-Figueroa Fernández,[48] Raphaèle Seror,[35] Georg H Stummvoll,[49] Yoshiya Tanaka,[50] Maria G Tektonidou,[51] Carlos Vasconcelos,[52] Edward M Vital,[53,54] Daniel J Wallace,[55] Sule Yavuz,[56] Pier Luigi Meroni,[57] Marvin J Fritzler,[58] Ray Naden,[59] Thomas Dörner,[18] Sindhu R Johnson[60,61]

Ann Rheum Dis 2019;**78**:1151–1159

The 2019 EULAR/ACR classification criteria for SLE include **positive ANA at least once as obligatory entry criterion**; followed by **additive weighted criteria** grouped in **seven clinical** (constitutional, haematological, neuropsychiatric, mucocutaneous, serosal, musculoskeletal, renal) and **three immunological** (antiphospholipid antibodies, complement proteins, SLE-specific antibodies) **domains**, and **weighted from 2 to 10. Patients accumulating ≥ 10 points are classified.**

In the validation cohort, the new criteria performed better than ARC 1997 and SLICC 2012 criteria

Long-Term Clinical Outcomes in a Cohort of Adults With Childhood-Onset Systemic Lupus Erythematosus

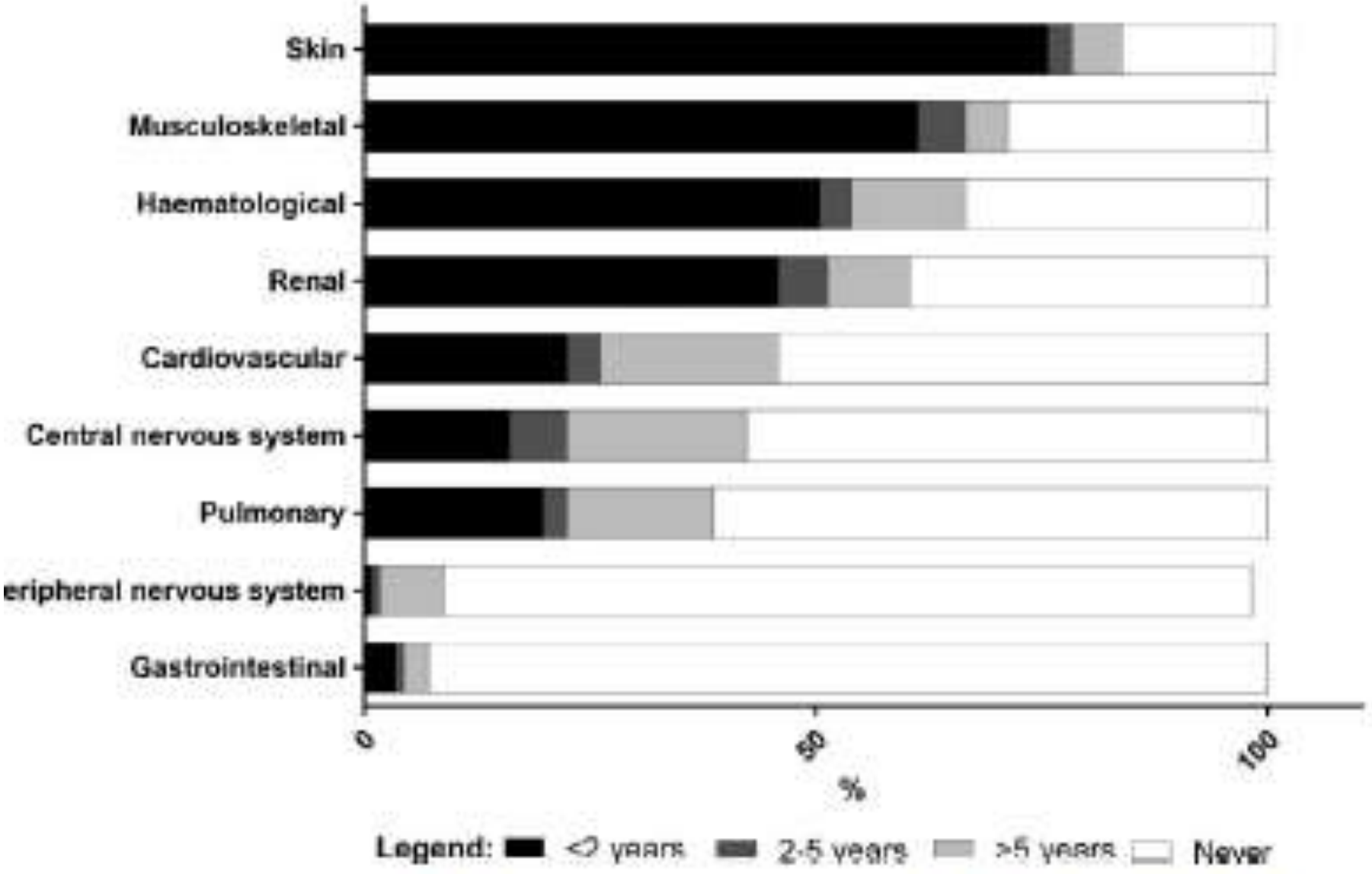
N. Groot,[1] D. Shaikhani,[2] Y. K. O. Teng,[3] K. de Leeuw,[4] M. Bijl,[5] R. J. E. M. Dolhain,[6] E. Zirkzee,[7] R. Fritsch-Sto
I. E. M. Bultink,[8] and S. Kamphuis[2]

Arthritis & Rheumatology
Vol. 71, No. 2, February 2019, pp 290–301

Adult SLE patients – childhood onset

- Single study visit-
- SLEDAI and Damage score
- HRQoL –SF-36- pain, vitality, mental health, ,emotional, social,…

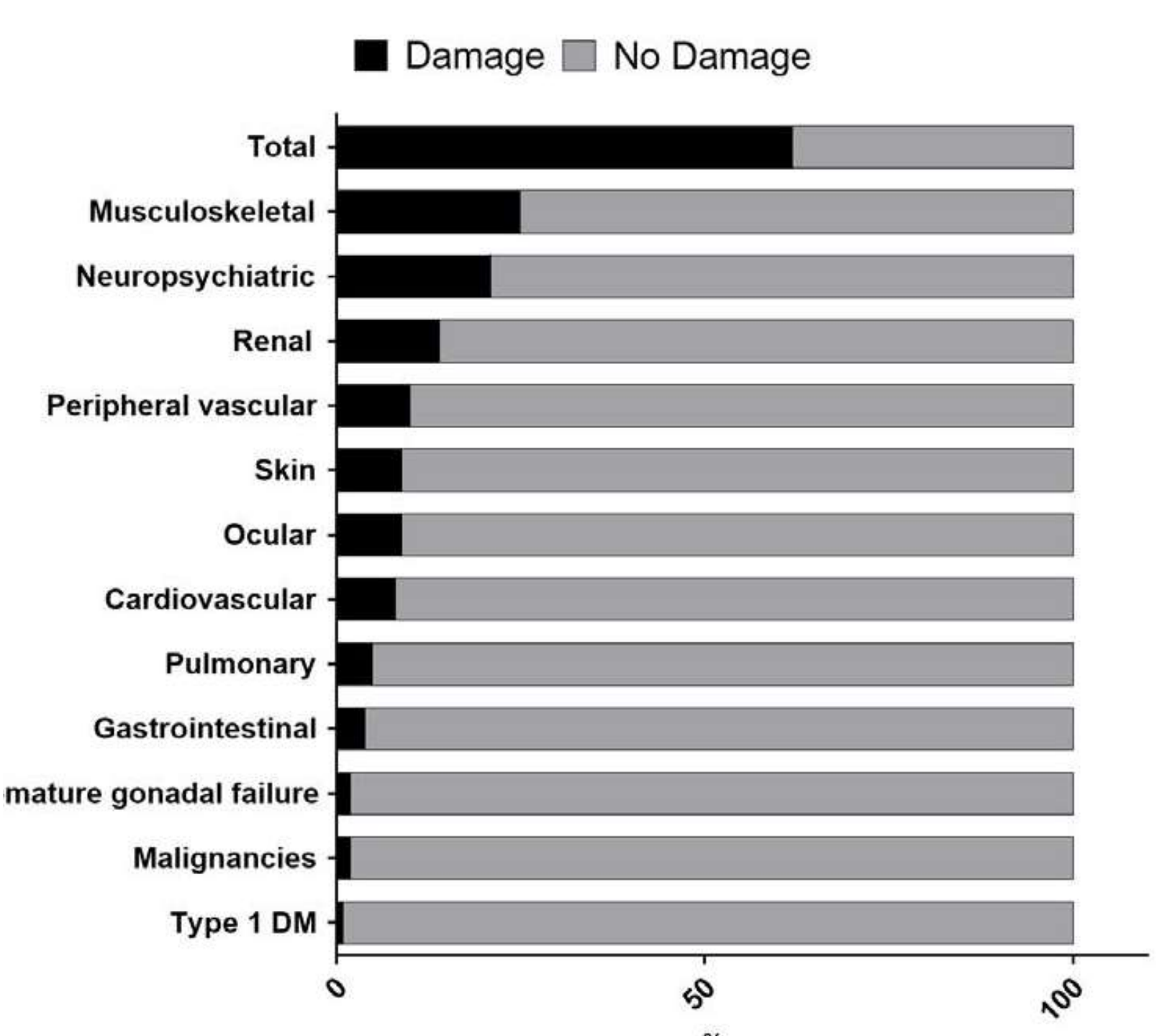
- National data- 136 identified-
- 111 patients included
- Median disease duration- 20 years
- Most manifestations were within first 2 years of onset

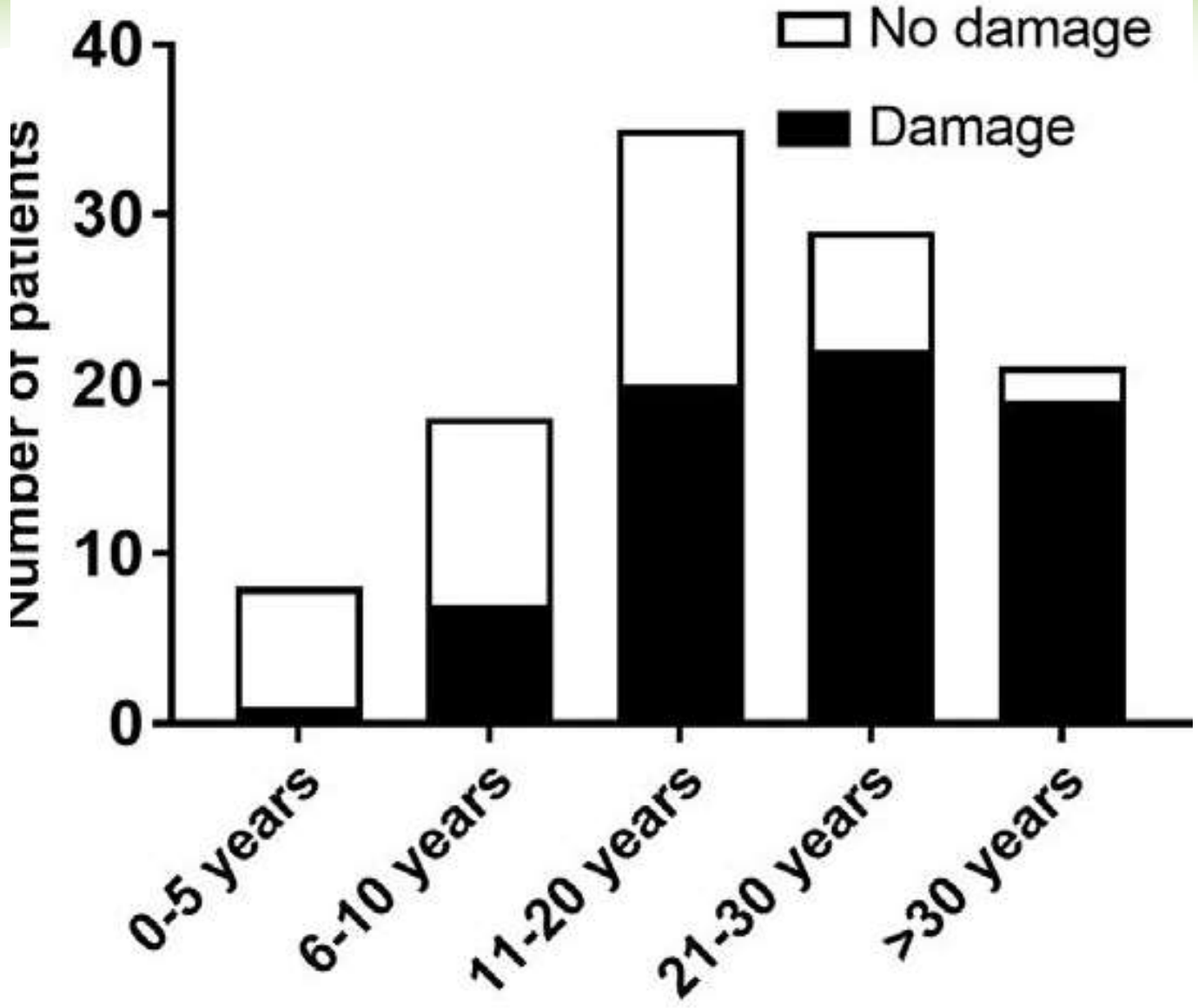


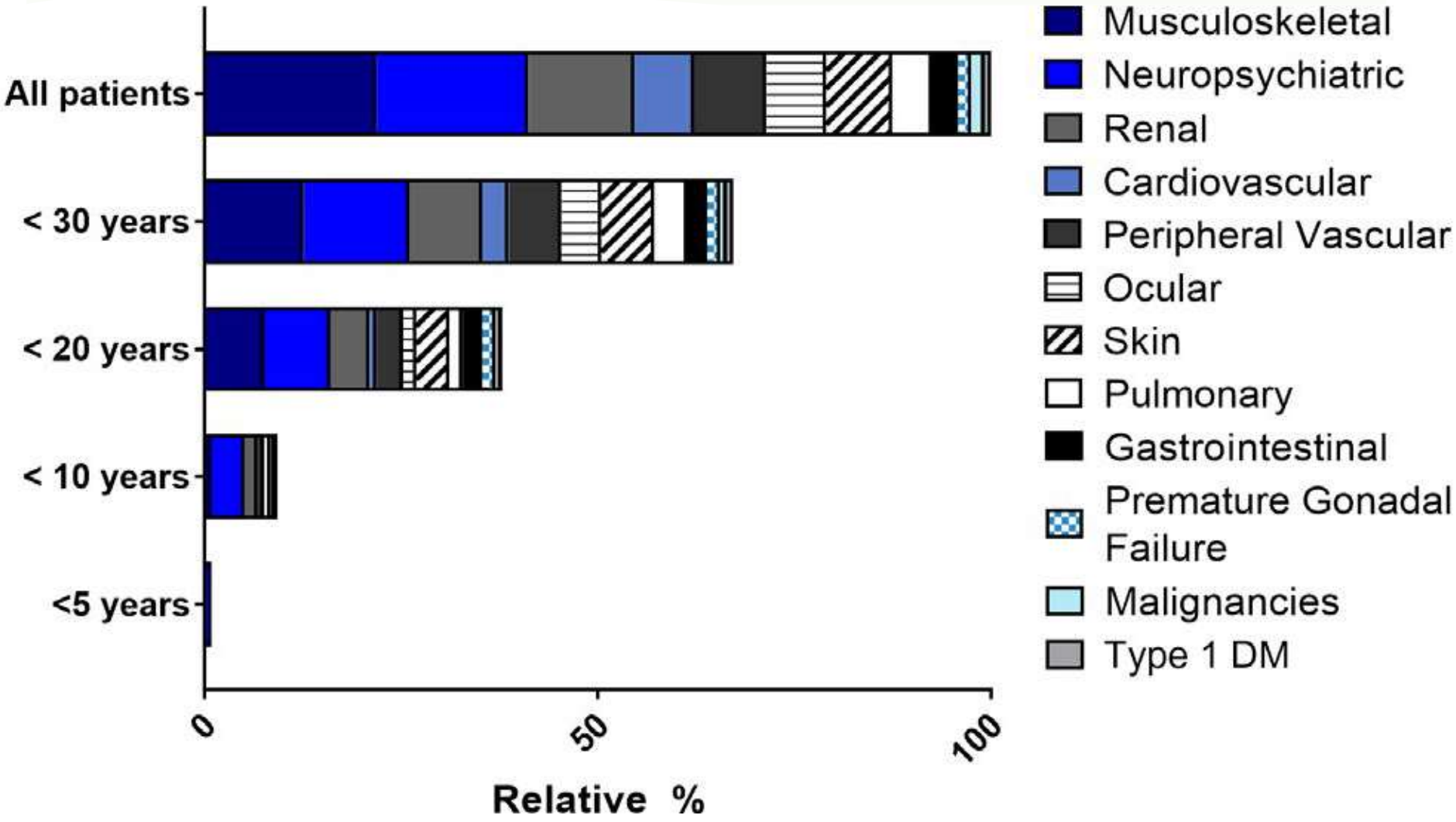
ace of disease manifestations (by organ system) over time since diagnosis of childhood c

- SLEDAI- 4 (relatively low)
- 45%- IV antibiotics in hospital for infections
- Half of them more than once.
- Damage score- depends on disease length

- 62%- damage-
- MSK, CNS, Renal
- Damage accrual-associated with-
- Disease duration, APLA, Hypertension,


Damage
No Damage
Total
Musculoskeletal
Neuropsychiatric
Renal
Peripheral vascular
Skin
Ocular
Cardiovascular
Pulmonary
Gastrointestinal
mature gonadal failure
Malignancies
Type 1 DM
0
50
100


No damage
Damage
Number of patients
40
30
20
10
0
0-5 years
6-10 years
11-20 years
21-30 years
>30 years


All patients
< 30 years
< 20 years
< 10 years
<5 years
0
50
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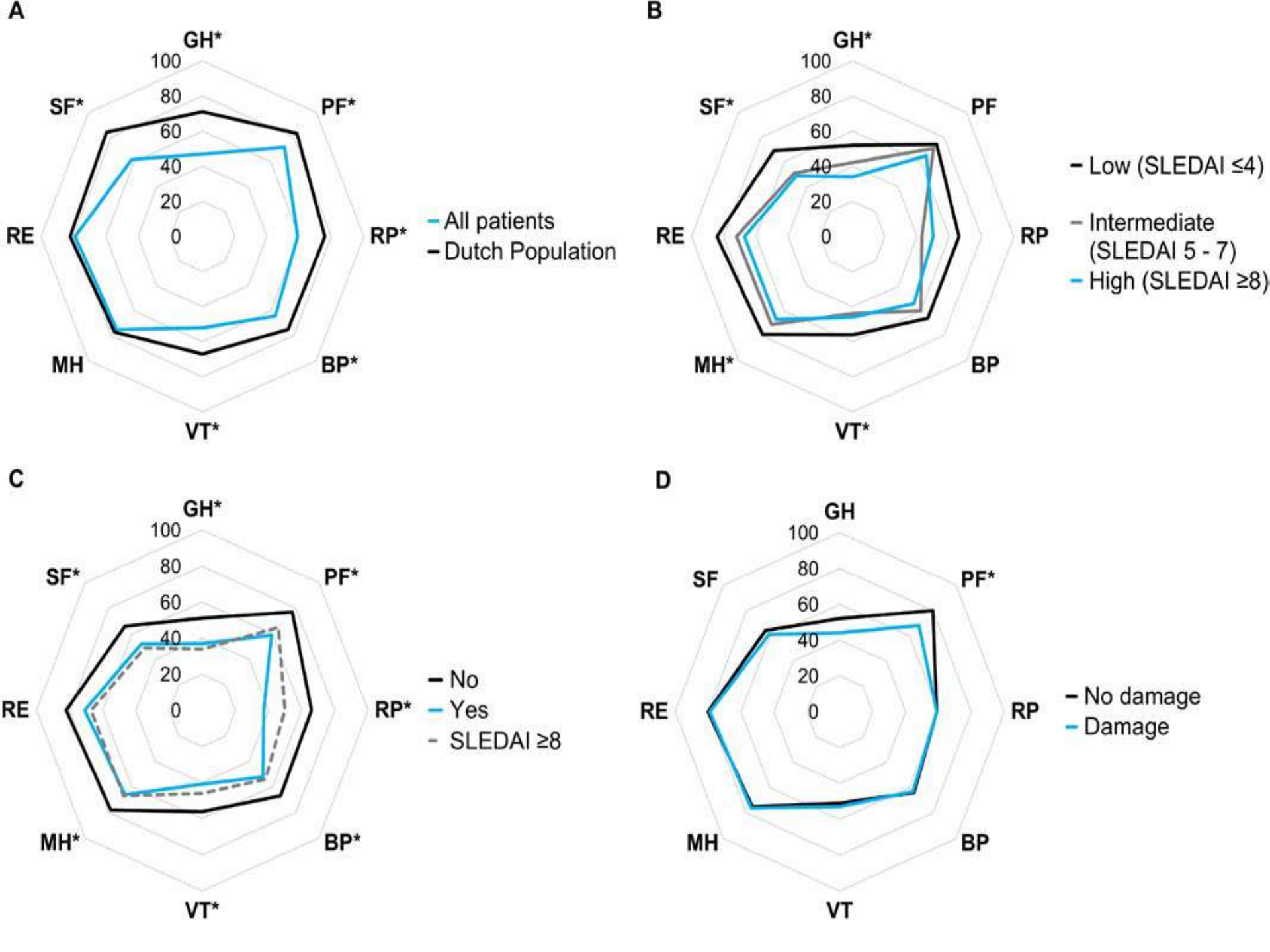
Relative %
Musculoskeletal
Neuropsychiatric
Renal
Cardiovascular
Peripheral Vascular
Ocular
Skin
Pulmonary
Gastrointestinal
Premature Gonadal Failure
Malignancies
Type 1 DM


A
GH*
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100
80
60
40
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All patients
Dutch Population
B
GH*
PF
RP
BP
VT*
MH*
RE
SF*
Low (SLEDAI ≤4)
Intermediate (SLEDAI 5 - 7)
High (SLEDAI ≥8)
C
GH*
PF*
RP*
BP*
VT*
MH*
RE
SF*
No
Yes
SLEDAI ≥8
D
GH
PF*
RP
BP
VT
MH
RE
SF
No damage
Damage

Conclusion-

- Childhood onset SLE- major impact on adult life.- significant damage!
- Lower HRQoL (physical appearance, coping styles)
- Renal transplants, CVA, MI
- Need for optimal control
- Screening measures (cardiovascular) starting before age 30

Auto inflammatory

CLINICAL SCIENCE

Classification criteria for autoinflammatory recurrent fevers

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Classification criteria for autoinflammatory recurrent fevers

Hereditary recurrent fever (HRF) syndromes are genetic disorders secondary to mutations in genes involved in the innate immune response.

A number of classification or diagnostic criteria have been developed in the past.

Overall, these criteria lack accuracy and do not consider the results of genetic analyses, now an essential tool for the accurate diagnosis and classification of HRF.

Classification criteria for autoinflammatory recurrent fevers

- Based on 360 real cases from the Eurofever registry
- * Genetics + clinical
- * Or- only clinical

Table 2 New Eurofever/PRINTO classification criteria for hereditary recurrent fevers and their performance in the 281 patients with consensus

CAPS	FMF	TRAPS	MKD
Presence of a *confirmatory NLRP3 genotype** and *at least one* among the following: ► Urticarial rash. ► Red eye (conjunctivitis, episcleritis, uveitis). ► Neurosensorial hearing loss. OR Presence of *not confirmatory NLRP3 genotype*† and *at least two* among the following: ► Urticarial rash. ► Red eye (conjunctivitis, episcleritis, uveitis). ► Neurosensorial hearing loss.	Presence of *confirmatory MEFV genotype** and *at least* one among the following: ► Duration of episodes 1–3 days. ► Arthritis. ► Chest pain. ► Abdominal pain. OR Presence of *not confirmatory MEFV genotype*† and *at least two* among the following: ► Duration of episodes 1–3 days. ► Arthritis. ► Chest pain. ► Abdominal pain.	Presence of confirmatory *TNFRSF1A* genotype* and at least one among the following: ► Duration of episodes ≥ 7 days. ► Myalgia. ► Migratory rash. ► Periorbital oedema. ► Relatives affected. OR Presence of a not confirmatory *TNFRSF1A* genotype† and *at least two* among the following: ► Duration of episodes ≥ 7 days. ► Myalgia. ► Migratory rash. ► Periorbital oedema. ► Relatives affected.	Presence of a *confirmatory MVK genotype** and *at least one* among the following: ► Gastrointestinal symptoms. ► Cervical lymphadenitis. ► Aphthous stomatitis.
Sensitivity: 1	Sensitivity: 0.94	Sensitivity: 0.95	Sensitivity: 0.98
Specificity: 1	Specificity: 0.95	Specificity: 0.99	Specificity: 1
Accuracy: 1	Accuracy: 0.98	Accuracy: 0.99	Accuracy: 1

Table 3 Eurofever/PRINTO clinical classification criteria for PFAPA and hereditary recurrent fevers and their performance in the 281 for whom consensus was achieved

PFAPA	CAPS	FMF	TRAPS	MKD
At least *seven out of* eight: Presence ► Pharyngotonsillitis. ► Duration of episodes, 3–6 days. ► Cervical lymphadenitis. ► Periodicity. Absence ► Diarrhoea. ► Chest pain. ► Skin rash. ► Arthritis.	Presence of *at least two of five**: ► Urticarial rash. ► Cold/Stress-triggered episodes. ► Sensorineural hearing loss. ► Chronic aseptic meningitis. ► Skeletal abnormalities (epiphysial overgrowth/frontal bossing).	At least *six out of nine*: Presence ► Eastern Mediterranean ethnicity. ► Duration of episodes, 1–3 days. ► Chest pain. ► Abdominal pain. ► Arthritis. Absence ► Aphthous stomatitis. ► Urticarial rash. ► Maculopapular rash. ► Painful lymph nodes.	Score ≥5 points: Presence ► Fever ≥7 days (2 points). ► Fever 5–6 days (1 point). ► Migratory rash (1 point). ► Periorbital oedema (1 point). ► Myalgia (1 point). ► Positive family history (1 point). Absence ► Aphthous stomatitis (1 point). ► Pharyngotonsillitis (1 point).	Presence of *at least three of six*: ► Age at onset <1 years. ► Gastrointestinal symptoms. ► Painful lymph nodes. ► Aphthous stomatitis. ► Triggers. ► Maculopapular rash.
Sensitivity: 0.97	Sensitivity: 0.80	Sensitivity: 0.91	Sensitivity: 0.87	Sensitivity: 0.91
Specificity: 0.93	Specificity: 0.91	Specificity: 0.92	Specificity: 0.92	Specificity: 0.82
Accuracy: 0.99	Accuracy: 0.85	Accuracy: 0.97	Accuracy: 0.96	Accuracy: 0.92

Classification criteria for autoinflammatory recurrent fevers

What does this study add?

We developed and validate new evidence-based classification criteria for HRF and PFAPA, combining international expert consensus, statistical evaluation of real patients from a large data set of patients in the Eurofever Registry.

Classification criteria for autoinflammatory recurrent fevers

The new classification criteria combine for the first time clinical manifestations with genotype.

The use of these classification criteria is recommended for inclusion of patients in translational and clinical studies, but they cannot be used as diagnostic criteria.

CLINICAL SCIENCE

Clinical characteristics and genetic analyses of 187 patients with undefined autoinflammatory diseases

Nienke M Ter Haar,[1,2] Charlotte Eijkelboom,[2,3] Luca Cantarini,[4] Riccardo Papa,[5] Paul A Brogan,[6] Isabelle Kone-Paut,[7] Consuelo Modesto,[8] Michael Hofer,[9] Nicolae Iagaru,[10] Sárka Fingerhutová,[11] Antonella Insalaco,[12] Francesco Licciardi,[13] Yosef Uziel,[14] Marija Jelusic,[15] Irina Nikishina,[16] Susan Nielsen,[17] Efimia Papadopoulou-Alataki,[18] Alma Nunzia Olivieri,[19] Rolando Cimaz,[20] Gordana Susic,[21] Valda Stanevica,[22] Marielle van Gijn,[23] Antonio Vitale,[4] Nicolino Ruperto,[24] Joost Frenkel,[3] Marco Gattorno,[24] Eurofever registry and the Pediatric Rheumatology International Trial Organization (PRINTO)

Ter Haar NM, *et al. Ann Rheum Dis* 2019;**78**:1405–1411

Clinical and genetic data from **187 patients** with undefined systemic autoinflammatory diseases were extracted from the **Eurofever registry**

Patients had a median of **12 episodes per year**, with a median duration of **4 days**

Most commonly reported symptoms were arthralgia, myalgia, abdominal pain, fatigue, malaise and mucocutaneous manifestations

In 15 patients, **genetic variants** were found in autoinflmmatory genes. Patients with genetic variants **more often had affected relatives** compared with patients without genetic variants (p=0.005)

Most patients responded well to NSAIDs, corticosteroids, colchicine and anakinra. Complete remission was rarely achieved with NSAIDs alone.

Patients with **pericarditis** and **intellectual impairment** appeared to comprise distinct subsets

Canakinumab for the Treatment of Autoinflammatory Recurrent Fever Syndromes

- De Benedetti F, Gattorno M, et al.
- N Engl J Med 2018;378:1908-19
- .
- Landmark paper describing the efficacy of canakinumab in TRAPS, HIDS and colchicine resistant FMF.

JAK1/2 inhibition with baricitinib in the treatment of autoinflammatory interferonopathies

- .
- Sanchez GAM, Reinhardt A, Ramsey S, et al.
- J Clin Invest 2018;128:3041-52.

- Elegant prospective study of JAK inhibition in interferonpathies.
- More to come on JAK inhibition other than in RA

Acute Rheumatic fever

- Still a problem?

Acute Rheumatic Fever
J Peds 2018

- Epidemiologic Impact of the New Guidelines for the Diagnosis of Acute Rheumatic Fever

Francesco Licciardi, et al - Italy

Different criteria for-

Low risk Vs. high risk populations

Table I. 2015 revised Jones criteria

The modified Jones criteria (2015)

LR populations

Major criteria	Minor criteria
1. Carditis Clinical and/or subclinical	1. Polyarthalgia
2. Arthritis Polyarthritis only	2. Fever (≥38.5°C)
3. Chorea	3. ESR ≥ 60 mm/h and/or CRP ≥3.0 mg/dL
4. Subcutaneous nodules	4. Prolonged PR interval after accounting for age variability
5. Erythema marginatum	

Moderate risk to HR populations

Major criteria	Minor criteria
1. Carditis Clinical and/or subclinical	1. Monoarthralgia
2. Arthritis Monoarthritis or polyarthritis Polyarthralgia	2. Fever (≥38°C)
3. Chorea	3. ESR ≥30 mm/h and/or CRP ≥3.0 mg/dL
4. Subcutaneous nodules	4. Prolonged PR interval after accounting for age variability
5. Erythema marginatum	

CRP, C-reactive protein; *ESR*, erythrocyte sedimentation rate.
For all patient populations with evidence of preceding Group A streptococcal infection.
Diagnosis of initial ARF: 2 major manifestations or 1 major plus 2 minor manifestations.

- High incidence- middle east, Asia, Australia
- Low incidence- Europe, USA
- Updated criteria- 1992- 2015

- A distinction between high risk and low risk populations
- <2 out of 100,000

pediatric hospital in an area- Turin, Italy (north West)

- 2007-2016
- 2.3 millions people- 203,000 children (5-14)

- Group A-classic- now LR region criteria- 135
- Group B- new HR region criteria- 28

- The use of HR criteria led to a 20.7% increase in the diagnosis of ARF in the entire study period

- Among group B patients, 53.6% had polyarthralgia, 21.4% **monoarthritis**, and 25% both **polyarthralgia** and monoarthritis.

- Our results highlight that the annual incidence of ARF in the Turin metropolitan area was persistently above 2 out of 100 000
- over a 10-year period in children between the age of 5 and 14 years, even using the LR criteria.
- Therefore, according to the latest guidelines, the criteria for HR populations should be used in our region

the incidence of ARF in patients younger than 5 years of age is rare.5,9

Therefore, in this subgroup using HR criteria may lead to significant over diagnosis.

- A crucial question is whether group B patients are really affected by rheumatic fever.

- Our results suggest that they are likely patients with **ARF with a milder phenotype**

AHA Scientific Statement

Revision of the Jones Criteria for the Diagnosis of Acute Rheumatic Fever in the Era of Doppler Echocardiography

A Scientific Statement From the American Heart Association

Endorsed by the World Heart Federation

Michael H. Gewitz, MD, FAHA, Co-Chair; Robert S. Baltimore, MD, Co-Chair; Lloyd Y. Tani, MD, FAHA; Craig A. Sable, MD, FAHA; Stanford T. Shulman, MD; Jonathan Carapetis, MBBS; Bo Remenyi, MBBS; Kathryn A. Taubert, PhD, FAHA; Ann F. Bolger, MD, FAHA; Lee Beerman, MD; Bongani M. Mayosi, MBChB; Andrea Beaton, MD; Natesa G. Pandian, MD; Edward L. Kaplan, MD, FAHA; on behalf of the American Heart Association Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young

Table 3. Doppler Findings in Rheumatic Valvulitis

Pathological mitral regurgitation (all 4 criteria met)
Seen in at least 2 views
Jet length ≥2 cm in at least 1 view
Peak velocity >3 m/s
Pansystolic jet in at least 1 envelope
Pathological aortic regurgitation (all 4 criteria met)
Seen in at least 2 views
Jet length ≥1 cm in at least 1 view
Peak velocity >3 m/s
Pan diastolic jet in at least 1 envelope

Loading conditions should be accounted for at time of echocardiography/Doppler assessment (see the section Differential Diagnosis of ARF for a full discussion). This table reflects an amalgam of the findings from the references listed in Table 5 and other guideline statements[4,5] and also resembles findings described in rheumatic heart disease.[51]

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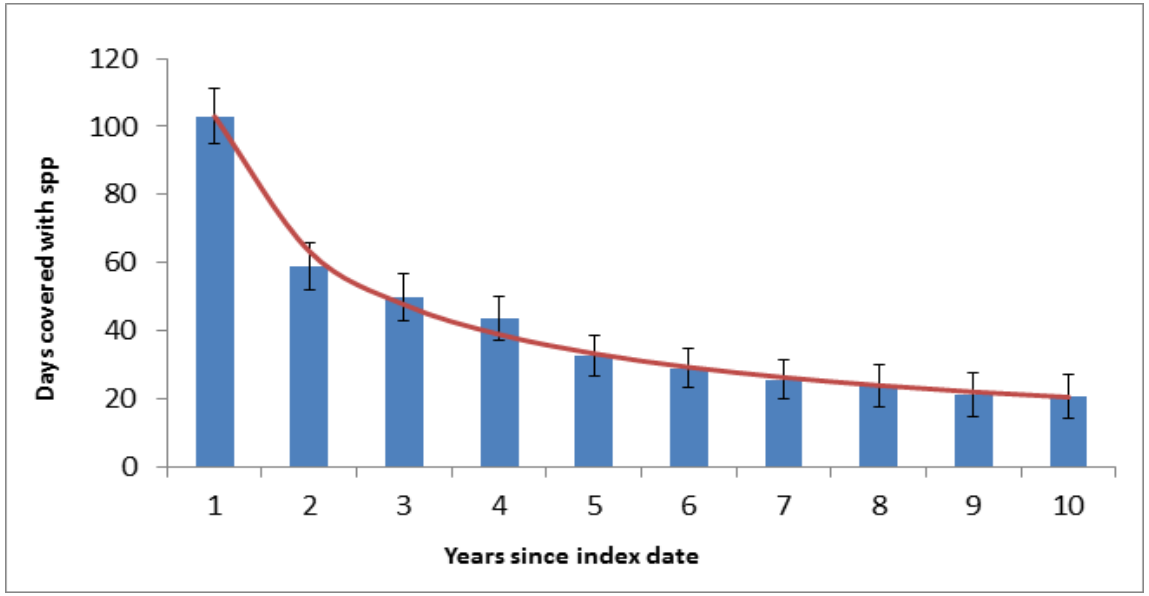
Poor long-term adherence to secondary penicillin prophylaxis in children with history of rheumatic fever

Gil Amarilyo[a,b], Gabriel Chodick[b,c], Jonathan Zalcman[b], Gideon Koren[b,c], Yoel Levinsky[a,b], Ido Somekh[a], Liora Harel[a,b,*]

800 children- Secondary prophylaxis days covered

- From 103 days to 20 days a year in 10 years.



Conclusion

- Poor adherence to secondary penicillin prophylaxis
- PO > IM
- Necessity?
- Are we satisfied?

- Putting all together- important to diagnose- HR population
- Look for cardiac involvement! Important morbidity!
- If only arthritis- is prophylaxis really important?

Dear PReS members and colleagues,

We would like to inform you that PReS has endorsed the initiative described below. All information on IRB and protocol as well as how to enter a case is available on the website of the COVID-19 Global Rheumatology Alliance.

is a large group of academics, clinicians and COVID-19 Global Rheumatology Alliance patients working to establish a global, freely accessible registry where doctors can add details of their patients who either **(1) Have a rheumatic disease, or (2) Are on a drug used in rheumatology who become infected with COVID-19**. The Alliance is interested in all cases, from asymptomatic to severely affected.

It intends to grow a large real dataset in order to update the literature in a frequent and systematic way. Consequently, it will provide a summary of what is and isn't known in relation to rheumatology and COVID-19, including medications and our diseases.

The aim is to be able to provide information back to doctors and patients about how rheumatic disease patients and those treated with rheumatology drugs fare when they get infected with COVID-19. It will potentially provide valuable information going forward to help make decisions about how to treat our patients.

We thank for your cooperation, and wish you all safe and healthy period, in this difficult times. This period also unite us all together, as a big global community!

We all hope and pray that we will all meet in Prague, where most of the epidemic will be behind us.

Kind regards,

Sefi Uziel
Chair of Clinical Affairs
for the PReS council

Corona Era- Education