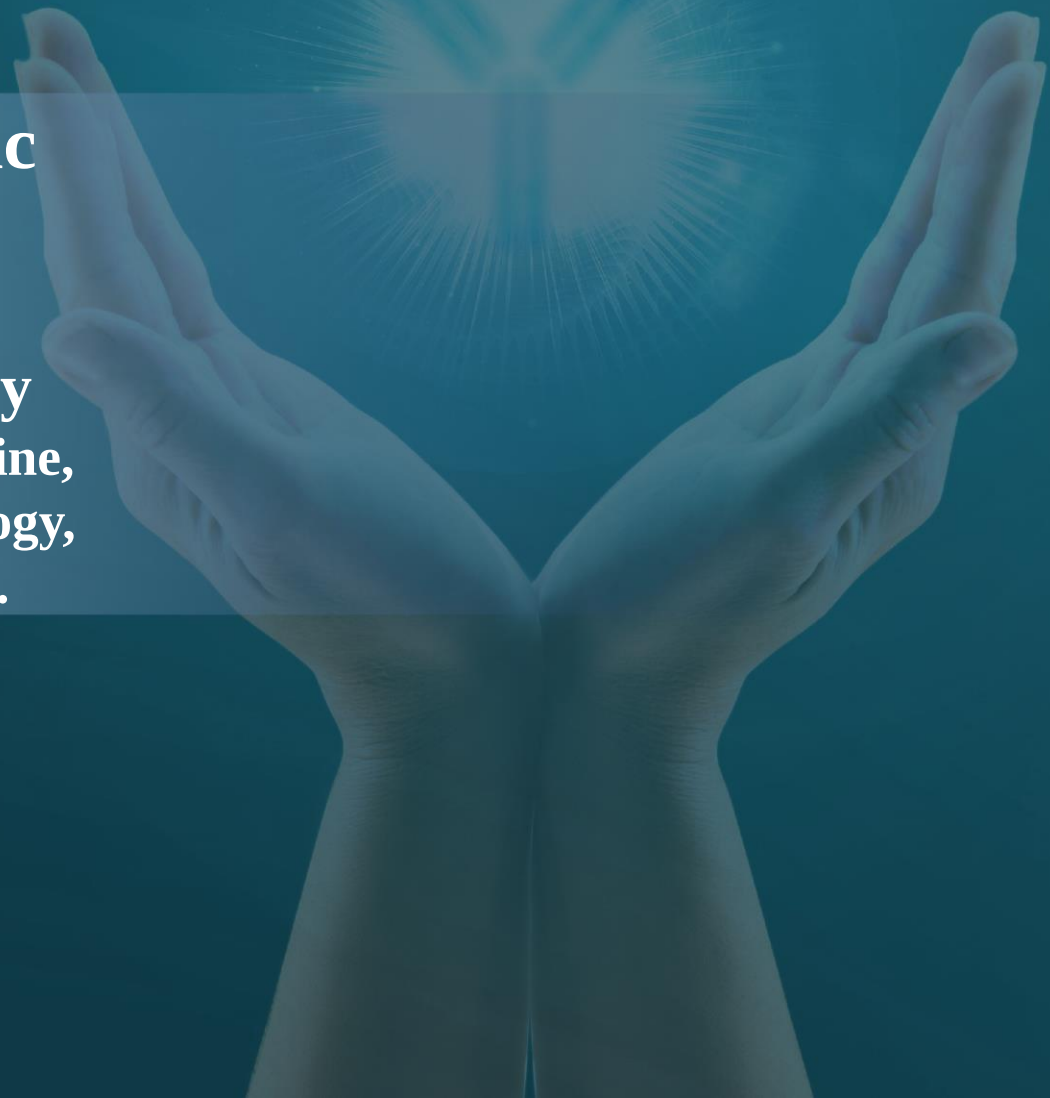
JIA & Updates on Pediatric Autoimmune Disorders

By: Mohamed Tharwat Hegazy
Associate Professor of Internal Medicine,
Rheumatology and Clinical Immunology,
Faculty of Medicine, Cairo University.



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Cases: How will you manage?

Case 1

- A 55-year- Female patient presented with a 6 months history of bilateral symmetrical arthritis affecting both hands, wrists and elbows with morning stiffness for 1 hour.
- ESR: 80 mm/hr
- With negative RF and Anti CCP
- Ultrasound= Synovitis

Case 2

- A 12-year- female patient presented with a 6 months history of bilateral symmetrical arthritis affecting both hands, wrists and elbows with morning stiffness for 1 hour.
- ESR: 80 mm/hr
- With negative RF and Anti CCP
- Ultrasound= Synovitis

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Juvenile idiopathic arthritis

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of idiopathic inflammatory arthritis affecting children younger than 16 years of age and lasting six weeks or longer.

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Petty RE et al., International League of Associations for Rheumatology. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004 Feb;31(2):390-2

Classification of juvenile idiopathic arthritis

1. Systemic
2. Oligoarthritis
   a. Persistent
   b. Extended
3. Polyarthritis (rheumatoid factor negative)
4. Polyarthritis (rheumatoid factor positive)
5. Psoriatic arthritis
6. Enthesitis-related arthritis
7. Undifferentiated arthritis

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2021 American College of Rheumatology Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Oligoarthritis, Temporomandibular Joint Arthritis, and Systemic Juvenile Idiopathic Arthritis

Karen B. Onel,[1] Daniel B. Horton,[2] Daniel J. Lovell,[3] Susan Shenoi,[4] Carlos A. Cuello,[5] Sheila T. Angeles-Han,[3] Mara L. Becker,[6] Randy Q. Cron,[7] Brian M. Feldman,[8] Polly J. Ferguson,[9] Harry Gewanter,[10] Jaime Guzman,[11] Yukiko Kimura,[12] Tzielan Lee,[13] Katherine Murphy,[14] Peter A. Nigrovic,[15] Michael J. Ombrello,[16] C. Egla Rabinovich,[6] Melissa Tesher,[17] Marinka Twilt,[18] Marisa Klein-Gitelman,[19] Fatima Barbar-Smiley,[20] Ashley M. Cooper,[21] Barbara Edelheit,[22] Miriah Gillispie-Taylor,[23] Kimberly Hays,[24] Melissa L. Mannion,[7] Rosemary Peterson,[25] Elaine Flanagan,[26] Nadine Saad,[27] Nancy Sullivan,[28] Ann Marie Szymanski,[29] Rebecca Trachtman,[30] Marat Turgunbaev,[31] Keila Veiga,[32] Amy S. Turner,[31] and James T. Reston[28]

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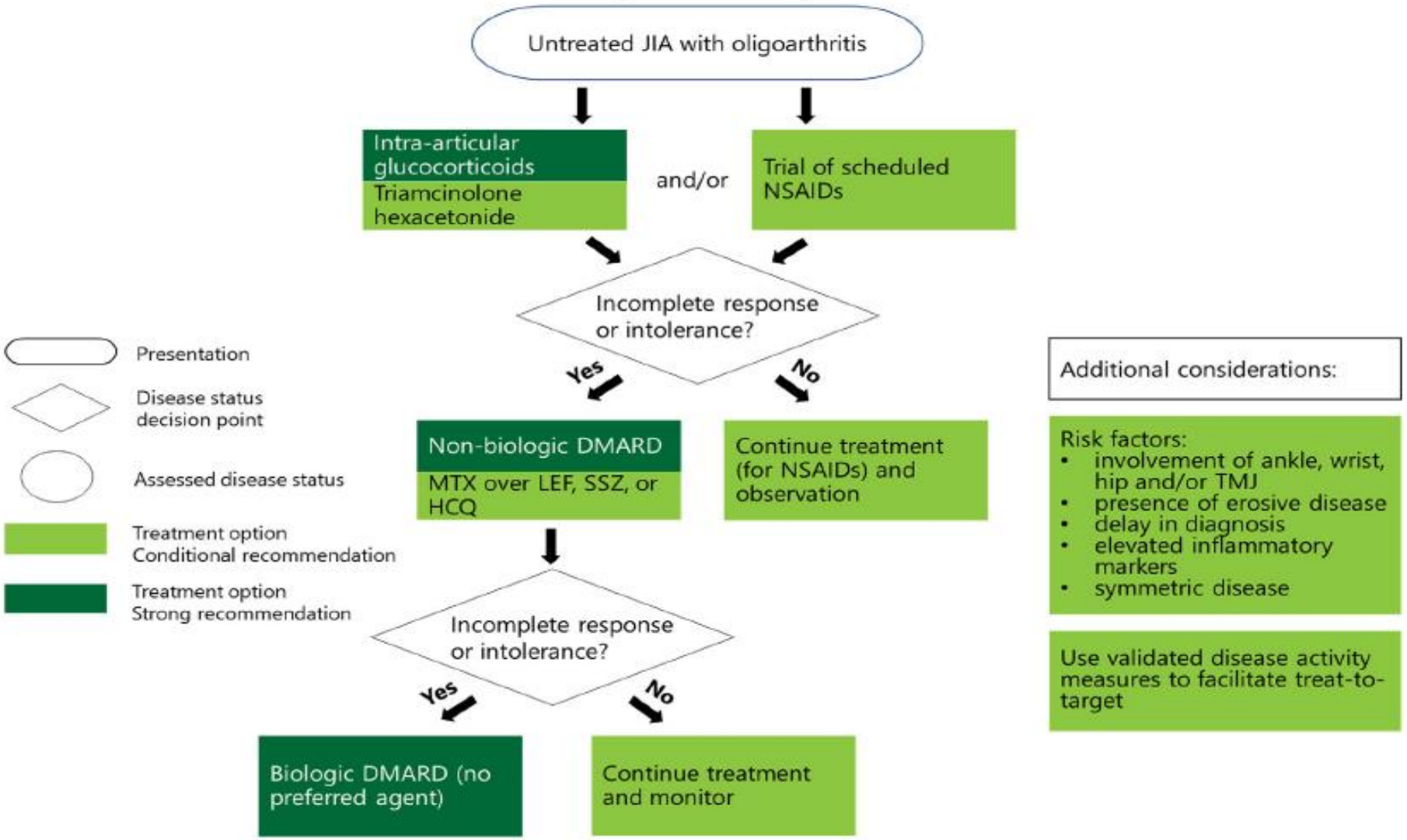
Treatment algorithm for oligoarthritis



DMARD = disease-modifying antirheumatic drug, HCQ = hydroxychloroquine, JIA = juvenile idiopathic arthritis, LEF = leflunomide, MTX = methotrexate, NSAIDs = nonsteroidal antiinflammatory drugs, SSZ = sulfasalazine, TMJ = temporomandibular joint

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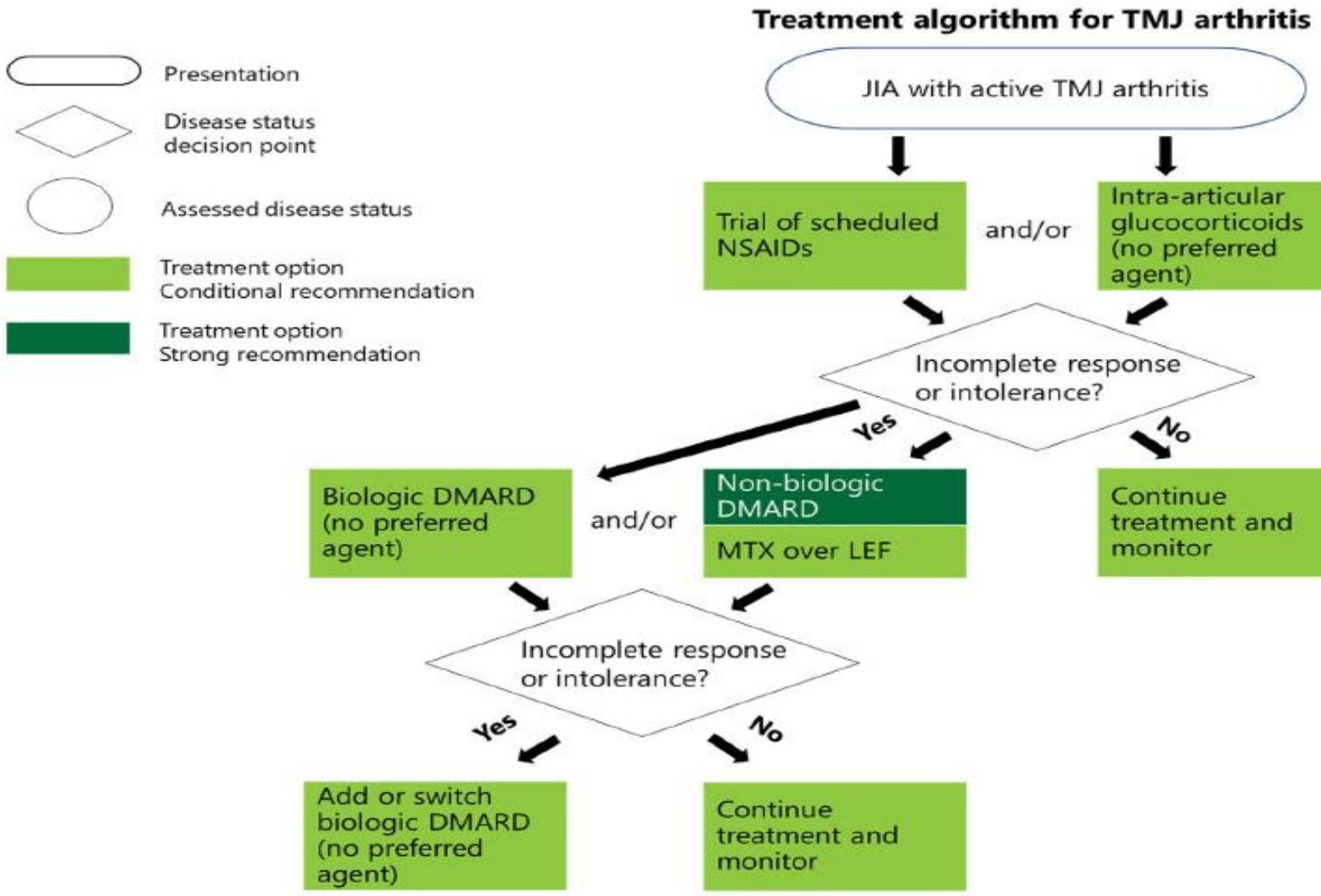

DMARD = disease-modifying antirheumatic drug, JIA = juvenile idiopathic arthritis, LEF = leflunomide, MTX = methotrexate, NSAIDs = nonsteroidal antiinflammatory drugs, TMJ = temporomandibular joint

Figure 2. Treatment algorithm for temporomandibular joint arthritis.

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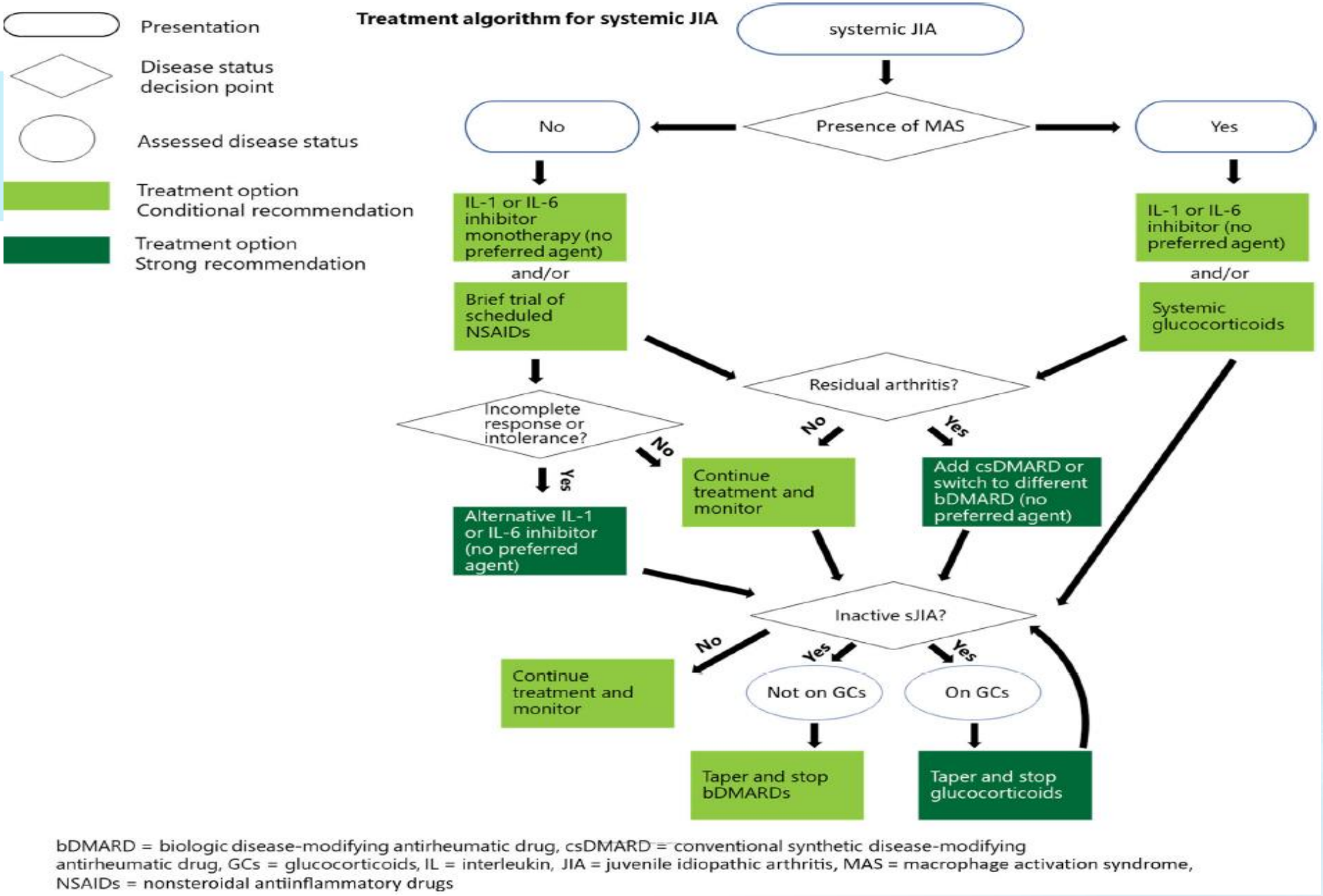
Treatment algorithm for systemic JIA



bDMARD = biologic disease-modifying antirheumatic drug, csDMARD = conventional synthetic disease-modifying antirheumatic drug, GCs = glucocorticoids, IL = interleukin, JIA = juvenile idiopathic arthritis, MAS = macrophage activation syndrome, NSAIDs = nonsteroidal antiinflammatory drugs

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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]

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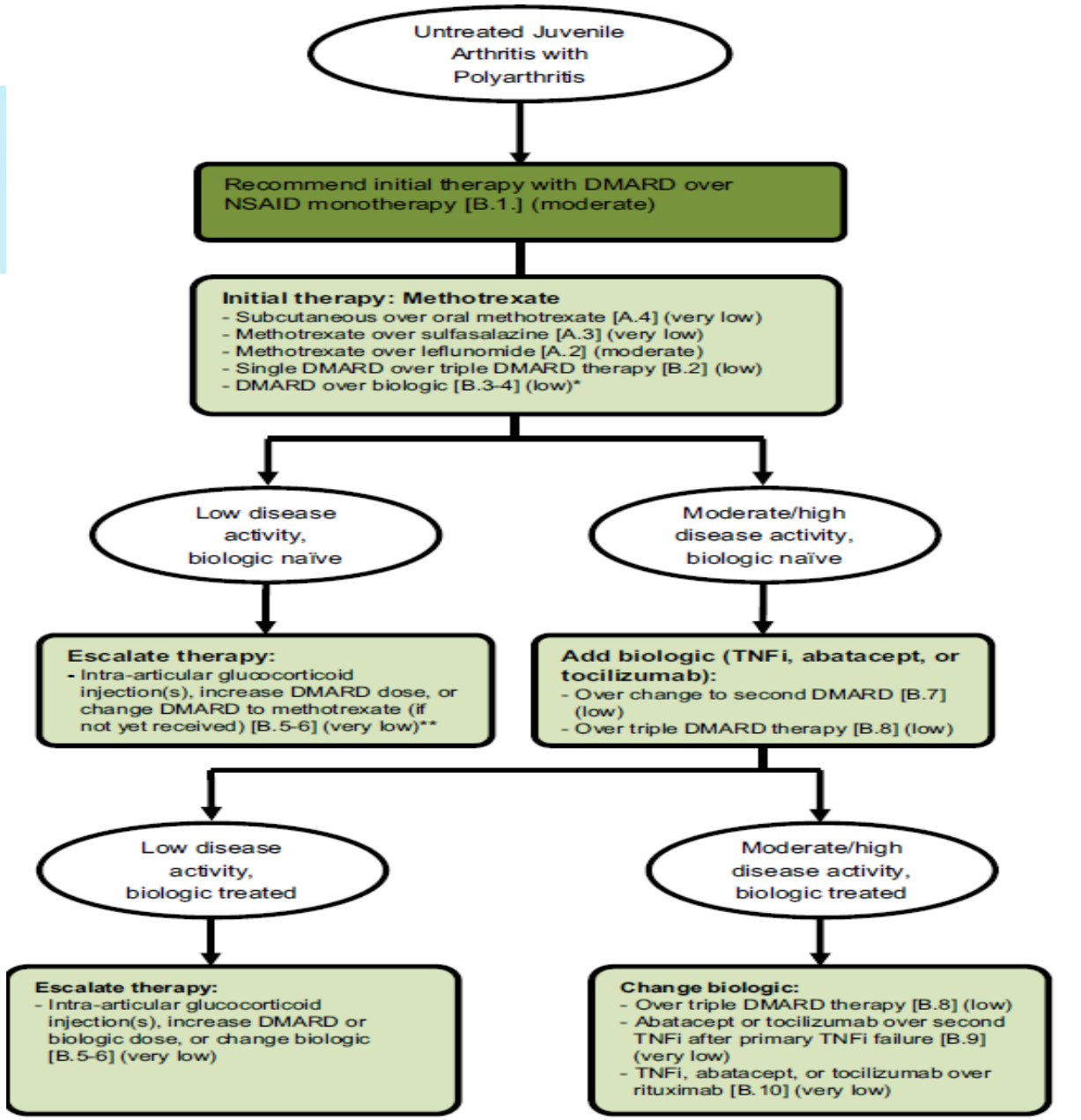

Adjunctive Therapy:

NSAIDs [A.1] (very low)

Intra-articular glucocorticoids* [A.5] (very low)

PT and/or OT for those with or at risk for functional limitations [A.16, A.17] (low and very low)

Bridging therapy with **limited course of oral glucocorticoids** (< 3 months) during initiation/escalation of therapy in patients with high or moderate disease activity [A.6] (very low)

Recommend triamcinolone hexacetonide over triamcinolone acetonide for intraarticular glucocorticoid injections [A.6] (moderate)

Recommend against bridging with glucocorticoids in patients with low disease activity [A.7] (very low)

Recommend against use of chronic low dose glucocorticoids [A.9] (very low)

LEGEND

- Strongly recommend
- Conditionally recommend
- Conditionally recommend against
- Strongly recommend against

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Ringold, S. et al., (2019). 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis care & research*, *71*(6), 717–734.

Table 5. Recommendations for the initial and subsequent treatment of children and adolescents with JIA and sacroiliitis*

Recommendation
In children and adolescents with active sacroiliitis, treatment with an NSAID is ***strongly*** recommended over no treatment with an NSAID (PICO C.1). In children and adolescents with active sacroiliitis despite treatment with NSAIDs: • Adding TNFi is ***strongly*** recommended over continued NSAID monotherapy (PICO C.2). • Using sulfasalazine for patients who have contraindications to TNFi or have failed more than one TNFi is conditionally recommended (PICO C.3). • ***Strongly*** recommend *against* using methotrexate monotherapy (PICO C.4).
Glucocorticoids In children and adolescents with active sacroiliitis despite treatment with NSAIDs: • Bridging therapy with a limited course of oral glucocorticoids (<3 months) during initiation or escalation of therapy is conditionally recommended (PICO C.5).† Bridging therapy may be of most utility in the setting of high disease activity, limited mobility, and/or significant symptoms. • Intraarticular glucocorticoid injection of the sacroiliac joints as adjunct therapy is conditionally recommended (PICO C.6).
Physical therapy • In children and adolescents with sacroiliitis who have or are at risk for functional limitations, using physical therapy is conditionally recommended (PICO C.7).

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Ringold, S. et al., (2019). 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis care & research*, *71*(6), 717–734.

Table 6. Recommendations for the initial and subsequent treatment of children and adolescents with JIA and enthesitis

Recommendation
In children and adolescents with active enthesitis, NSAID treatment is ***strongly*** recommended over no treatment with an NSAID (PICO D.1). In children and adolescents with active enthesitis despite treatment with NSAIDs: • Using a TNFi is conditionally recommended over methotrexate or sulfasalazine (PICO D.2, D.3). • Bridging therapy with a limited course of oral glucocorticoids (<3 months) during initiation or escalation of therapy is conditionally recommended (PICO D.4).† Bridging therapy may be of most utility in the setting of high disease activity, limited mobility, and/or significant symptoms.
Physical therapy • In children and adolescents with enthesitis who have or are at risk for functional limitations, using physical therapy is conditionally recommended (PICO D.5).

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Ringold, S. et al., (2019). 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis care & research*, *71*(6), 717–734.

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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]

Angeles-Han, S. T. et al., (2019). 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis. *Arthritis care & research*, *71*(6), 703–716.

- Children with juvenile idiopathic arthritis (JIA) are at increased risk for developing uveitis and sight-threatening complications.
- Regular ophthalmology screening in children with JIA is important for early uveitis detection, and timely and appropriate treatment.
- Regular ophthalmology monitoring of children with an established diagnosis of uveitis is needed.
- Appropriate use of topical glucocorticoids, non-biological disease modifying anti-rheumatic drugs, and biologic systemic therapy can improve vision outcomes.

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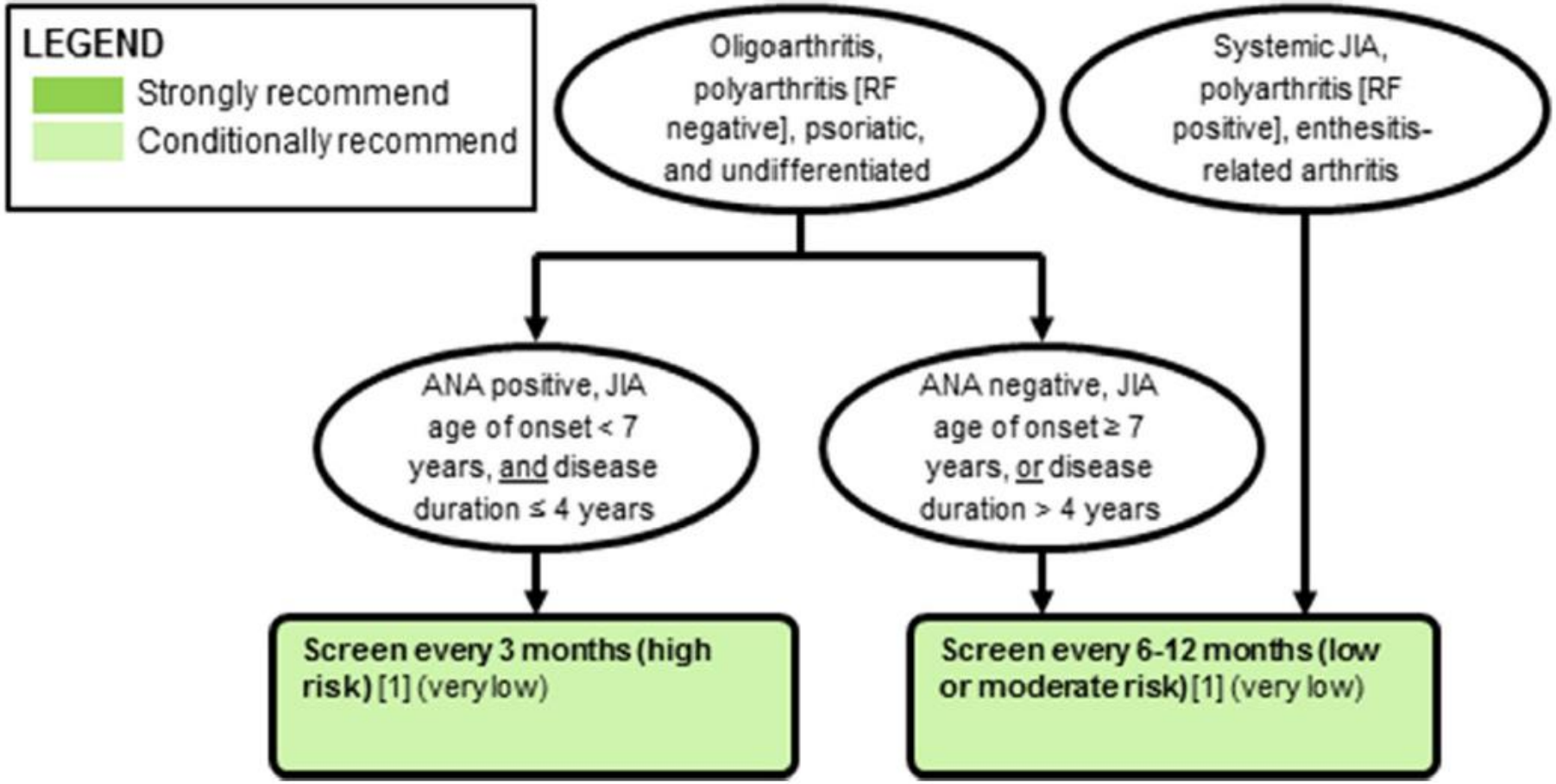

Figure 1a: Ophthalmologic screening examinations

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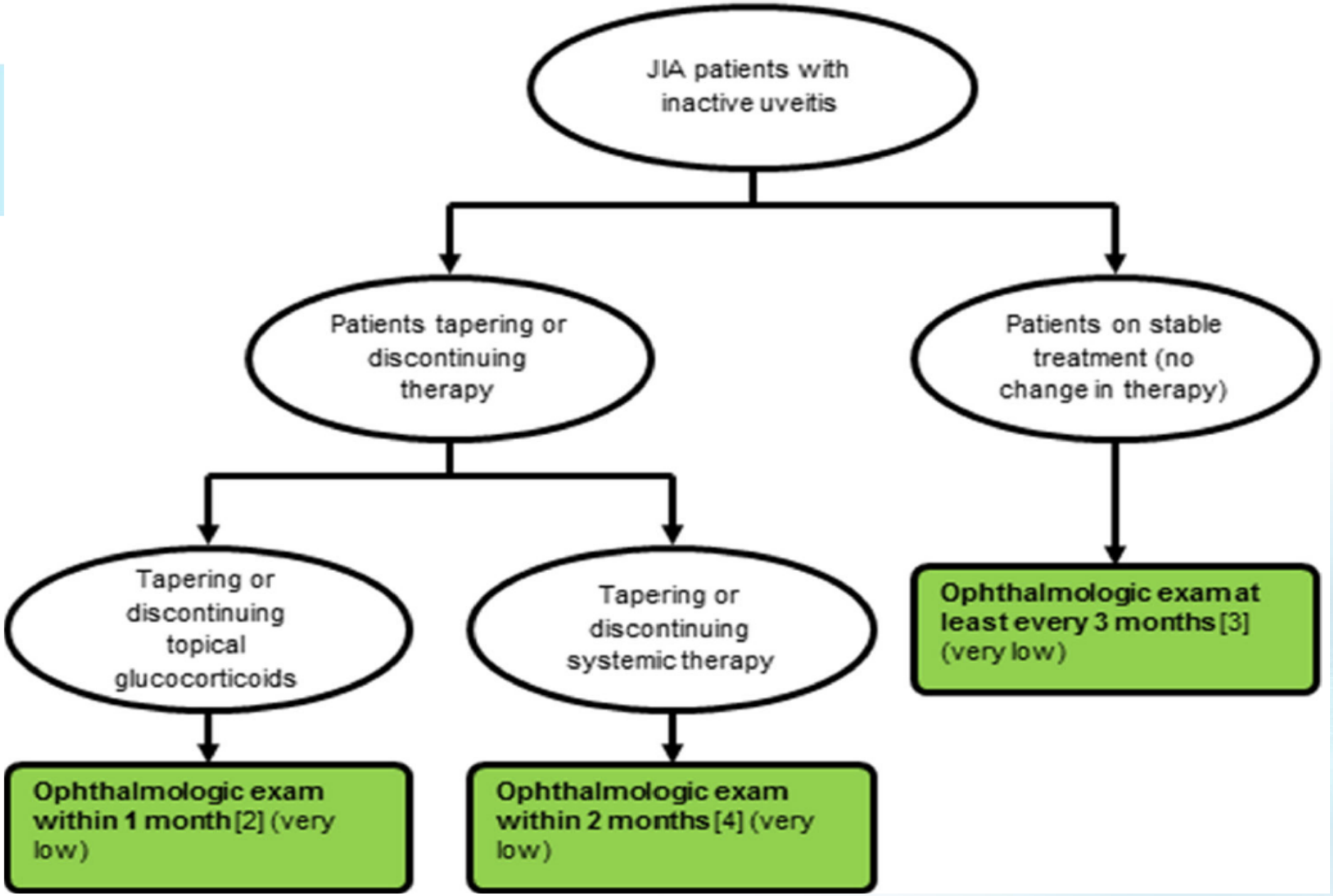

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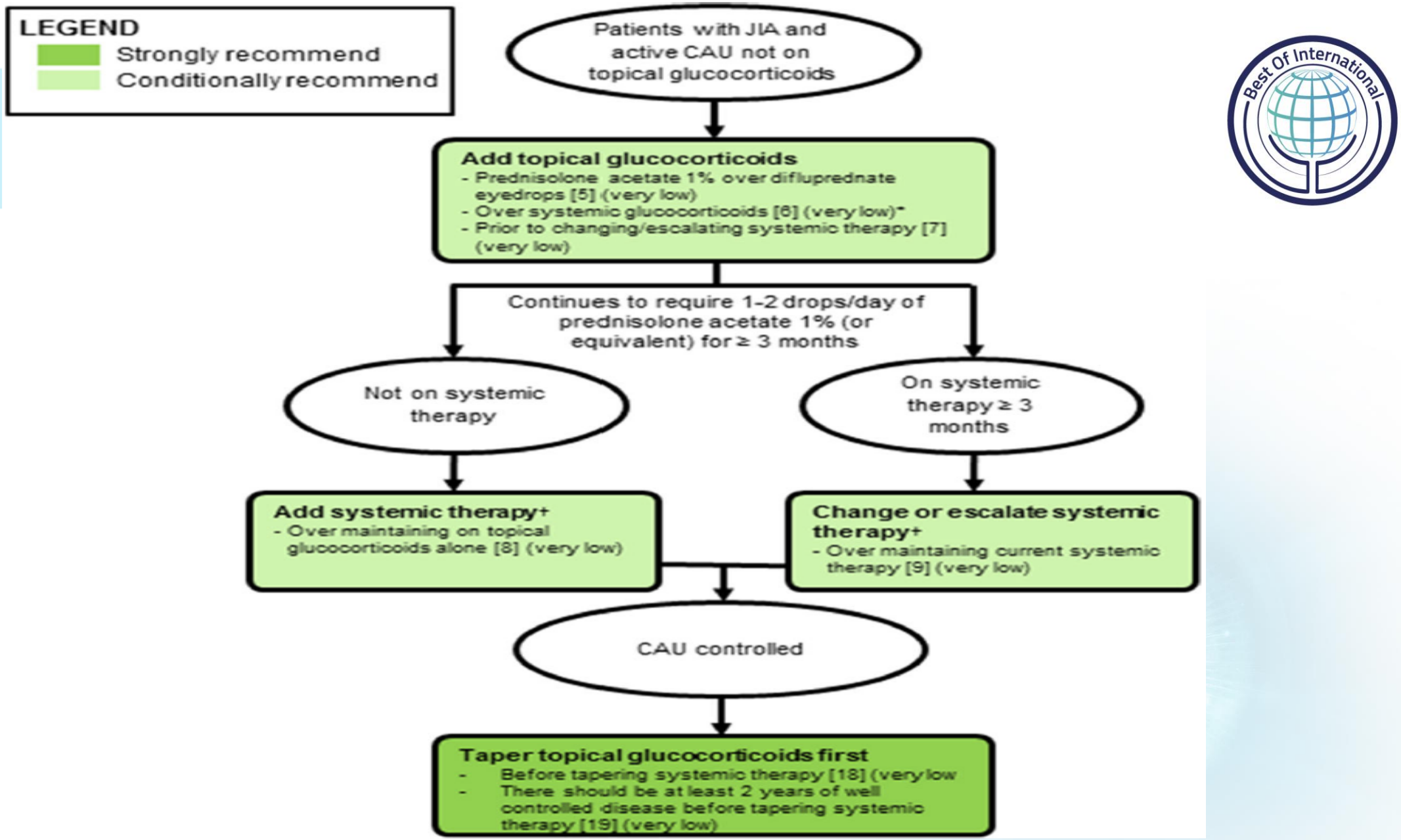

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Transition of Care Concerns in JIA:
how they never lose their 'J'

Rebecca Sadun, MD, PhD
Adult & Pediatric Rheumatology
Duke University

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What's new in ACR 2023?

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The Pediatric Great Debate: Combination Therapy vs Step-up Therapy for Juvenile Idiopathic Arthritis

Moderators:

Daniel B. Horton, MD, MSCE
Rutgers University, NJ, USA

Daniel J. Lovell, MD, MPH
Cincinnati Children's Hospital, OH, USA

Debators:

Petra Hissink Muller, MD, PhD
Leiden University Medical Center, the Netherlands

Yukiko Kimura, MD
Hackensack University Medical Center, NJ, USA

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Lisa Imundo MD
Columbia University Irving Medical Center

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What's new in ACR 2023?

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Safety and Immunogenicity of Vaccines in Pediatric Rheumatology Patients

Kathryn M. Edwards MD
Division of Infectious Diseases
Professor of Pediatrics Emerita
Vanderbilt University School of Medicine
Nashville, TN

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JIA Patients Transfer to Adult Care

- ≥ 50% of young adult JIA patients are lost to care at the time of transfer
  (Hazel 2010, Jensen 2015)
- ~20% of JIA patients not initially transferred may require later referral to adult rheum due to delayed flares
  (Mikola 2022)
- Adults with JIA may experience erosions, contractures, visual loss, and other permanent sequelae

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10 Core Care Features for Adults with JIA

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- **Understanding JIA, the disease:**
  1. JIA **subtypes** guide management
  2. Attention to **uveitis** and **TMJ** arthritis is crucial
  3. **Examination** of all joints is warranted even in asymptomatic patients
  4. Full **remission** is strongly pursued
  5. **Aggressive** management (higher doses, more meds) may be required

- **Understanding the patient who has JIA:**
  1. Physical **exam expectations**: all joints assessed, including TMJ
  2. **De-escalation** of therapy is a double-edged sword
  3. Acknowledge and clarify **differences** between pediatric & adult care
  4. Demonstrate to your patient that you care about him/her as a **whole person**
  5. A careful **social history** is crucial

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JIA is Not One Disease: Subtypes Matter

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JIA Subtype	Adult Counterpart	Key Considerations
Oligo-articular JIA	• No adult counterpart • Most common form of JIA • Arthritis may be *painless*	- History of anterior (painless) uveitis?
RF + polyarticular JIA	= Seropositive RA	- History of TMJ involvement?
RF - polyarticular JIA	≈ Seronegative RA	
Psoriatic JIA	= Adult Psoriatic Arthritis	- Axial involvement?
Enthesitis-related arthritis	≈ Spondlyoarthropathies	
Systemic JIA	= Adult-Onset Stills Disease • Often more aggressive • Poor response to TNFi	- History of lung involvement? - History of MAS? - Recent fevers or rash?
Undifferentiated JIA	• No adult counterpart • Wastebasket term	- Any associated symptoms/extra-articular manifestations?

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Major Differences btwn JIA & RA: TMJ

At each visit:	TMJ protocol:
auscultate the TMJ (listening for and documenting crepitus) & measure the maximal incisal opening (MIO)	MRI with contrast & open/closed sequences

Pedersen 2019 (chapter in Contemporary Management of Temporomandibular Disorders) *Stoll 2012; PMID: 22589268*

Treatment Goals & Medication Doses

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Best Of International

- **Pursuit of remission can look different**
  - Risk-benefit calculus differs for an 8-y/o vs an 80-y/o
    - Risk of mild-persistent disease (over *many* years) is greater
    - Risk of infection is much lower in healthy children/young adults
- **Medication metabolism differs by age**
  - Rate of medication metabolization often decreases with age
    - Young adults may need higher doses or more frequent dosing
- **Methotrexate:** 0.5–1 mg/kg (or 15–30 mg/m^2) to a max of 25 mg
- **Infliximab:** 10 mg/kg IV Q4 weeks

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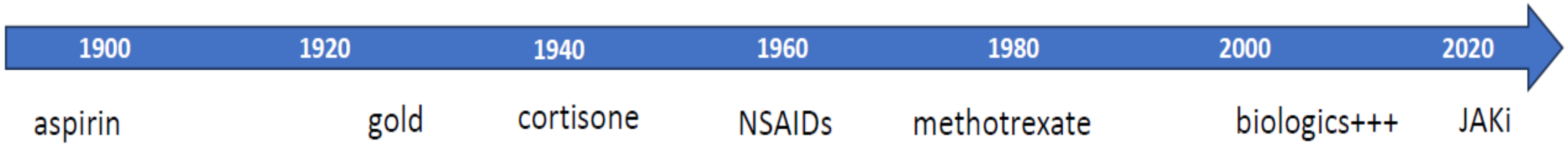

Slide courtesy of Dr. Yukiko Kimura

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The Pediatric Great Depate

Combination Therapy

Start MTx + Biologic

Step up Therapy

Start MTx Then Later biologic if needed

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First: JIA outcomes still need to improve

- How often is inactive disease achieved in JIA?
  - Depends on definition and population
  - Only 40-60% achieve “inactive disease” at 1-2 years
  - 70% CID achieved in one treat to target study (Hissink Muller 2019)
- More difficult:
  - Maintaining inactive disease, and Remission off Medications (ultimate goal)
  - ~25-75% flare after withdrawal of therapy
  - Up to half may not recapture inactive disease after flare (Ringold 2022)

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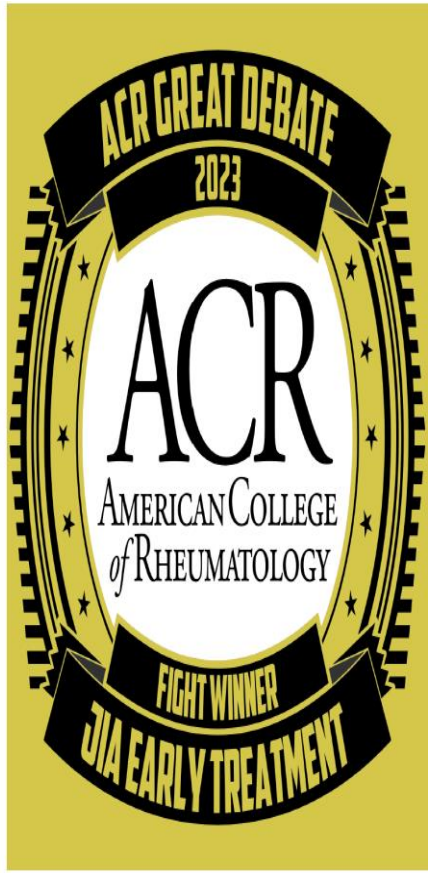

Second:

Use the Window of Opportunity

- There is clearly a window of opportunity in RA (and likely for JIA)
- Mistake to tailor initial treatment for the patient "who may never need biologics"
- Patients who will need biologics may miss the window
- The Big Question is

When does the window close?

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The Window of Opportunity in RA

- Multiple high-quality RCTs show that early treatment initiation results in better radiographic and functional outcomes
  - Lower absolute levels of joint damage and in lower progression rates
  - Less rapid rise over time suggesting true disease modification
- RA Guidelines (ACR, EULAR): Early and targeted treatment is important
- "Early" treatment timeframe getting shorter (as early as 3 or fewer months)
- Key steps in pathogenesis *may even be reversible* early on

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Third: What patients and caregivers want

- They want treatments that:
  - Are effective
  - Work quickly
  - Have lasting impact

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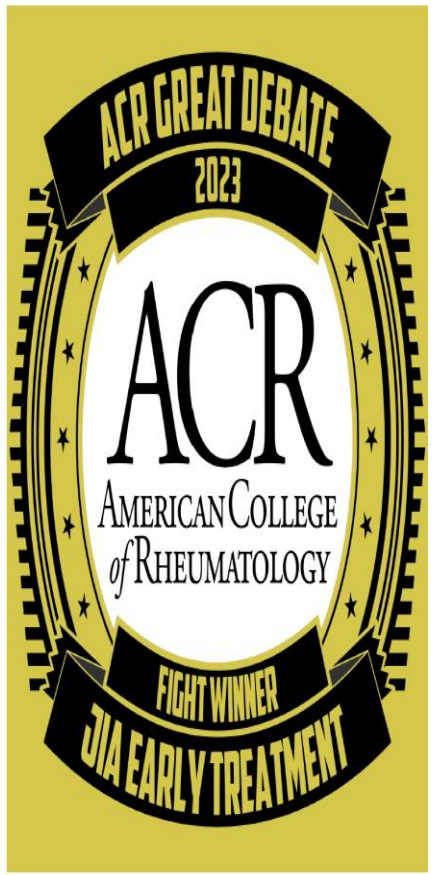

My main argument:
Early Combination "Induction Therapy"

- We all aspire to precision medicine, but until it is a reality:
- Induce inactive disease with **EARLY COMBINATION** (MTX + biologic treatment before 3-6 months) to *take advantage of window of opportunity*

Because every child deserves a chance to attain the best outcomes

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Step up Therapy

Problem: we cannot predict (yet) who needs a biological at the start and who doesn't

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In the meantime:

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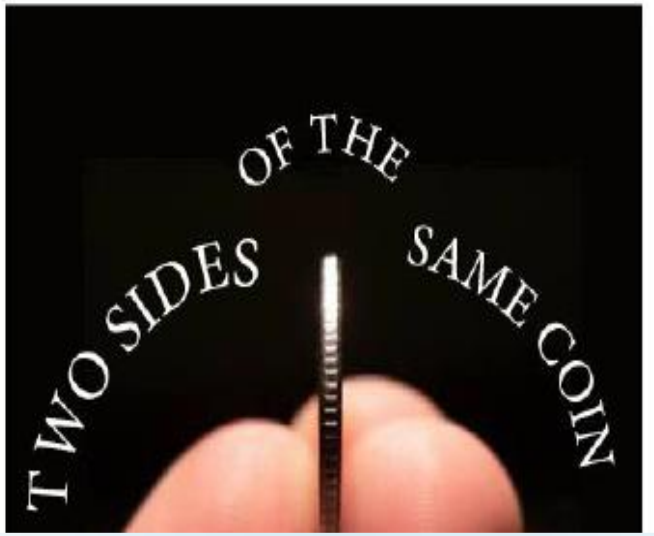

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Step up Therapy

1 ‘T2T with Tight Control’

2 ‘Not all patients need a biological’
Methotrexate can induce ID

3 ‘Local factors’
Availability/costs/pain/side effects/future risks

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Safety and Immunogenicity of Vaccines in Pediatric Rheumatology Patients

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Empowering Rheumatology Professionals

2022 American College of Rheumatology Guideline for Vaccinations in Patients With Rheumatic and Musculoskeletal Diseases

Anne R. Bass,[1] Eliza Chakravarty,[2] Elie A. Akl,[3] Clifton O. Bingham,[4] Leonard Calabrese,[5] Laura C. Cappelli,[4] Sindhu R. Johnson,[6] Lisa F. Imundo,[7] Kevin L. Winthrop,[8] Reuben J. Arasaratnam,[9] Lindsey R. Baden,[10] Roberta Berard,[11] S. Louis Bridges Jr.,[1] Jonathan T. L. Cheah,[12] Jeffrey R. Curtis,[13] Polly J. Ferguson,[14] Ida Hakkarinen,[15] Karen B. Onel,[1] Grayson Schultz,[16] Vidya Sivaraman,[17] Benjamin J. Smith,[18] Jeffrey A. Sparks,[10] Tiphanie P. Vogel,[19] Eleanor Anderson Williams,[20] Cassandra Calabrese,[5] Joanne S. Cunha,[21] Joann Fontanarosa,[22] Miriah C. Gillispie-Taylor,[19] Elena Gkrouzman,[12] Priyanka Iyer,[23] Kimberly S. Lakin,[1] Alexandra Legge,[24] Mindy S. Lo,[25] Megan M. Lockwood,[26] Rebecca E. Sadun,[27] Namrata Singh,[28] Nancy Sullivan,[22] Herman Tam,[29] Marat Turgunbaev,[30] Amy S. Turner,[30] and James Reston[22]

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Influenza Vaccine

Influenza vaccine is recommended for all children > 6 months of age

Table 4. Whether to give or defer non–live attenuated vaccinations in patients taking glucocorticoids regardless of disease activity

	Influenza vaccination	Other non–live attenuated vaccinations
Prednisone ≤10 mg daily*	Give	Give
Prednisone >10 mg and <20 mg*	Give	Give
Prednisone ≥20 mg daily*	Give	Defer†

■ = Strong recommendation.
□ = Conditional recommendation.
* Or the equivalent dose of any other glucocorticoid formulation, or the equivalent pediatric dose.
† Defer vaccination until glucocorticoids are tapered to the equivalent of prednisone <20 mg daily.

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Whether to hold immunosuppressive medication at the time of non–live attenuated vaccination to maximize vaccine immunogenicity, although holding medications could be associated with disease flare (Table 3).

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Table 3. Medication management at the time of non–live attenuated vaccine administration

	Influenza vaccination	Other non–live attenuated vaccinations
Methotrexate	Hold methotrexate for 2 weeks *after* vaccination*	Continue methotrexate
Rituximab	Continue rituximab†	Time vaccination for when the next rituximab dose is due, and then hold rituximab for at least 2 weeks after vaccination
Immunosuppressive medications other than methotrexate and rituximab	Continue immunosuppressive medication	Continue immunosuppressive medication

□ = Conditional recommendation.
* Hold only if disease activity allows. Non-rheumatology providers, e.g., general pediatricians and internists, are encouraged to give the influenza vaccination and then consult with the patient's rheumatology provider about holding methotrexate to avoid a missed vaccination opportunity.
† Give influenza vaccination on schedule. Delay any subsequent rituximab dosing for at least 2 weeks after influenza vaccination if disease activity allows.

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Conjugated vaccine

- *PCV 13 (*Prevenar)
- PCV15 (Vaxneuvance) (FDA approved 2022)
- PCV20 (Prevnar 20) (FDA approved 2023)

Pneumococcal polysaccharide vaccine **(PPSV23) (Pneumovax)**

The PPSV23 dose should be given at least 8 weeks after PCV13. When PPSV23 is used, they need another pneumococcal vaccine at least 5 years

Children with Certain Risk

•Received recommended doses of PCV13 or PCV15, but nothing else: These chldren can benefit from the extra protection offered by **PCV20** or **PPSV23**.

•PPSV23 is the only pneumococcal vaccine ever received: **PCV15 or PCV20** can provide these children important protection.

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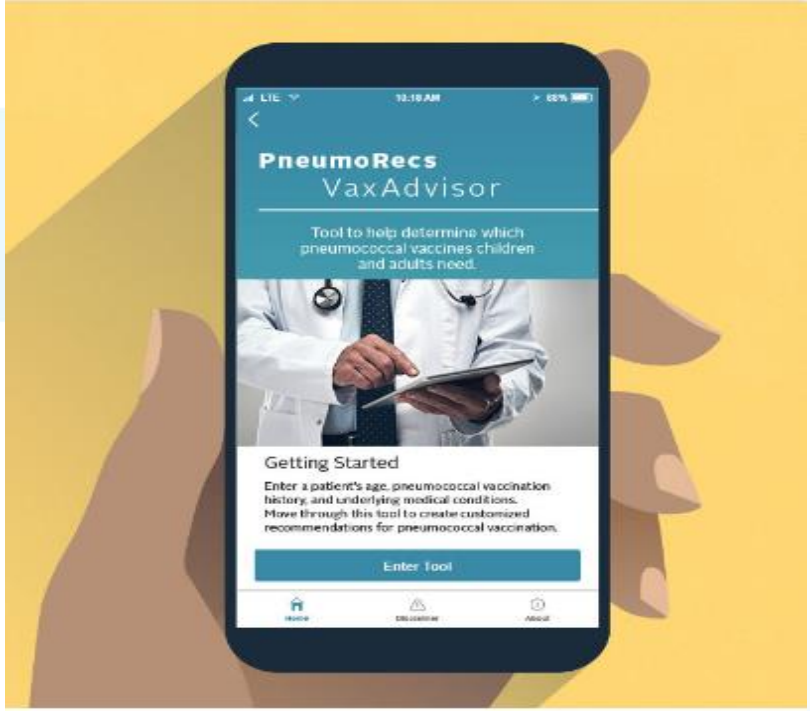

PneumoRecs VaxAdvisor is available for download on iOS and Android mobile devices.

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