Rheumatoid Arthritis Treatments and Guidelines

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Disclosures

Relevant relationships with commercial entities

- American College of Rheumatology
- Royalties from UpToDate

Potential for conflicts of interest within this presentation

- RCT site investigator: Bristol Myers Squibb, Roche, Boehringer Ingelheim

Steps taken to review and mitigate potential bias

- I gave up these relationships 1 year prior to the development of the guidelines, and will continue to do so for at least 1 year after publication

Learning Objectives

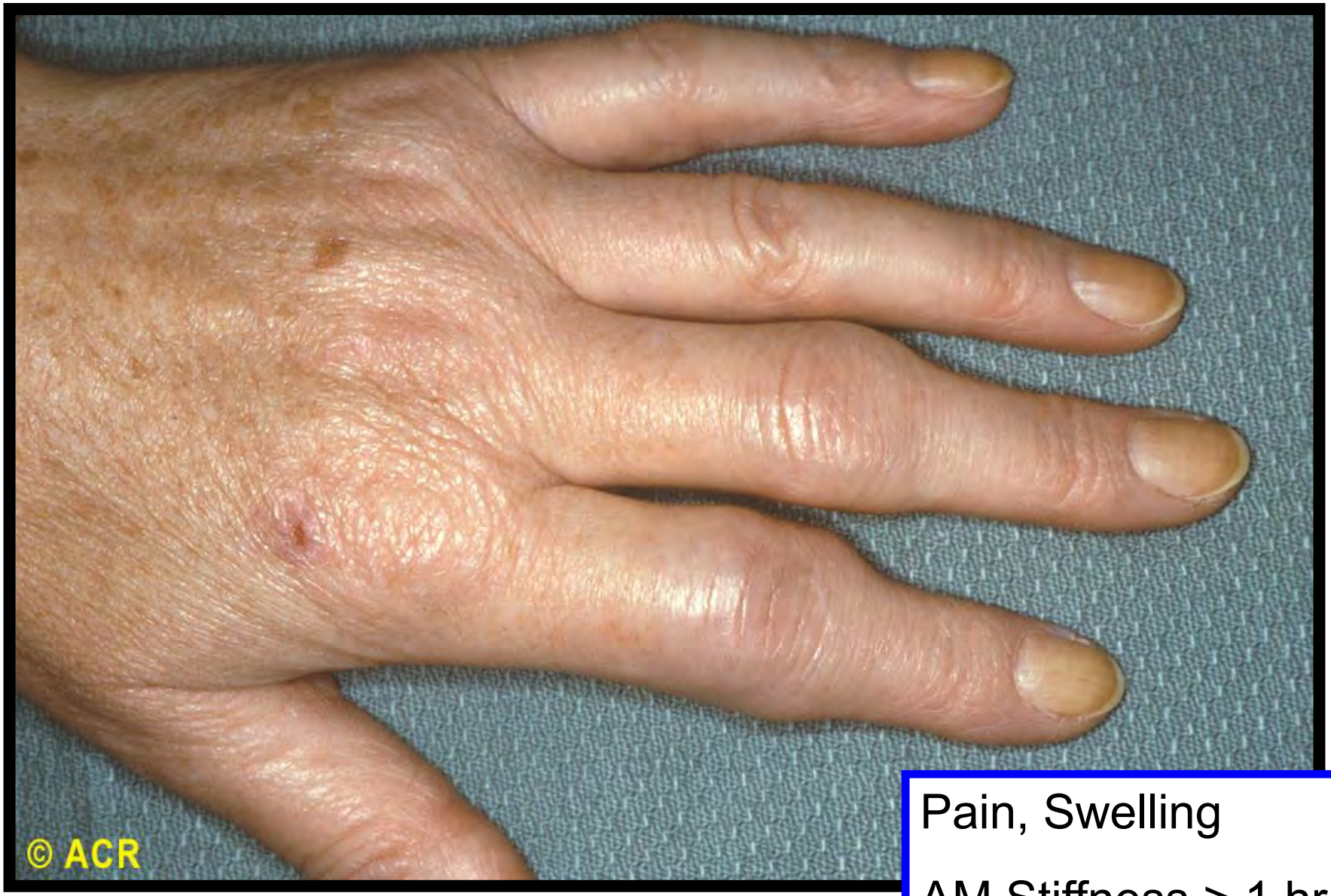
In this session, we will discuss use of the American College of Rheumatology (ACR) guidelines for rheumatoid arthritis patient care.

At the end of this session, participants will be able to:

1) Explain the ACR guideline process.

2) Describe how a clinician may use multiple guidelines for RA management (RA pharm, RA non-pharm, vaccination, reproductive, etc.),

3) Discuss how RA guidelines have been evolving to cover more systemic aspects of the disease over time (e.g., ILD, osteoporosis)

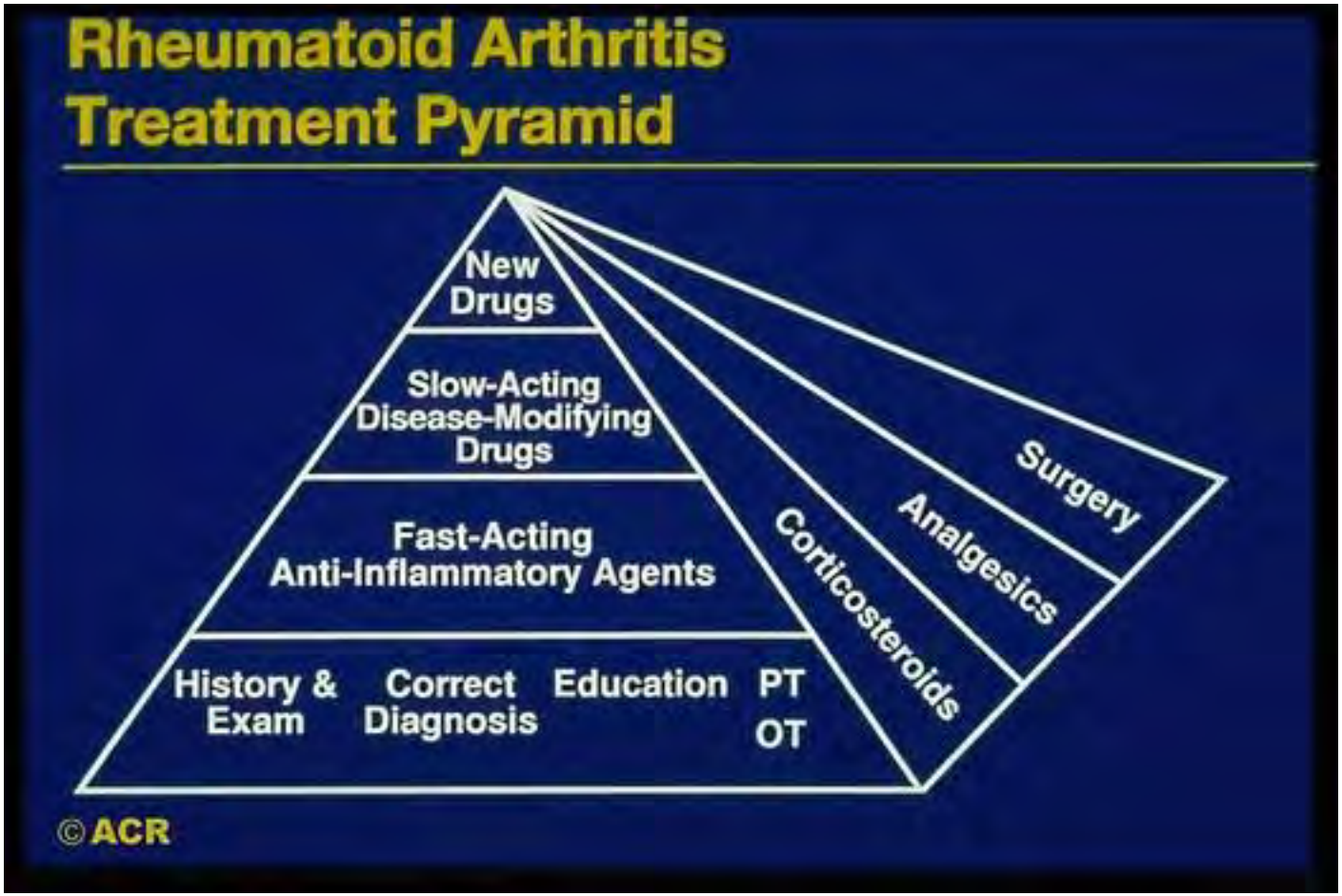


Pain, Swelling

AM Stiffness > 1 hr

> 6 weeks duration

Old Pyramid of Treatment



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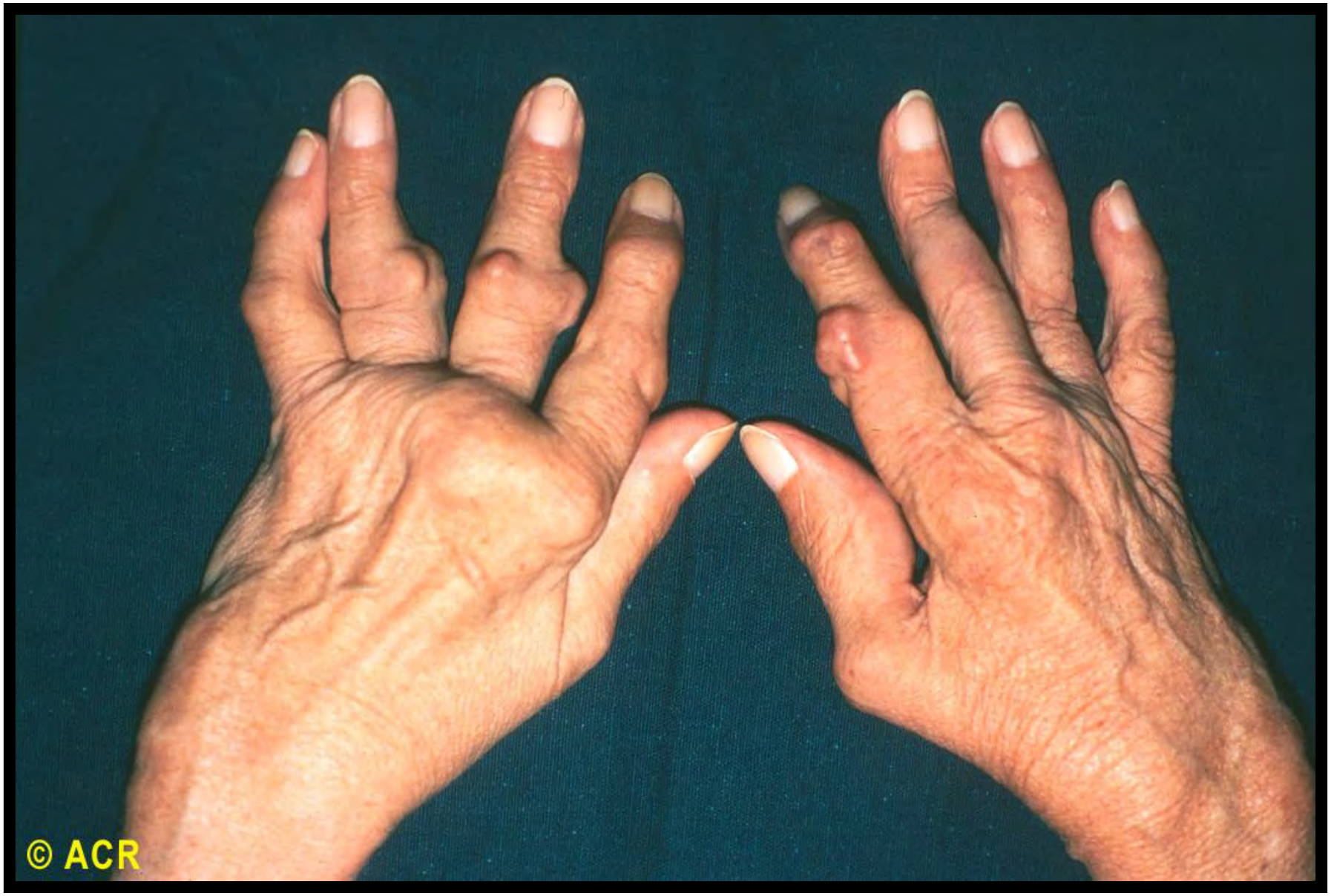
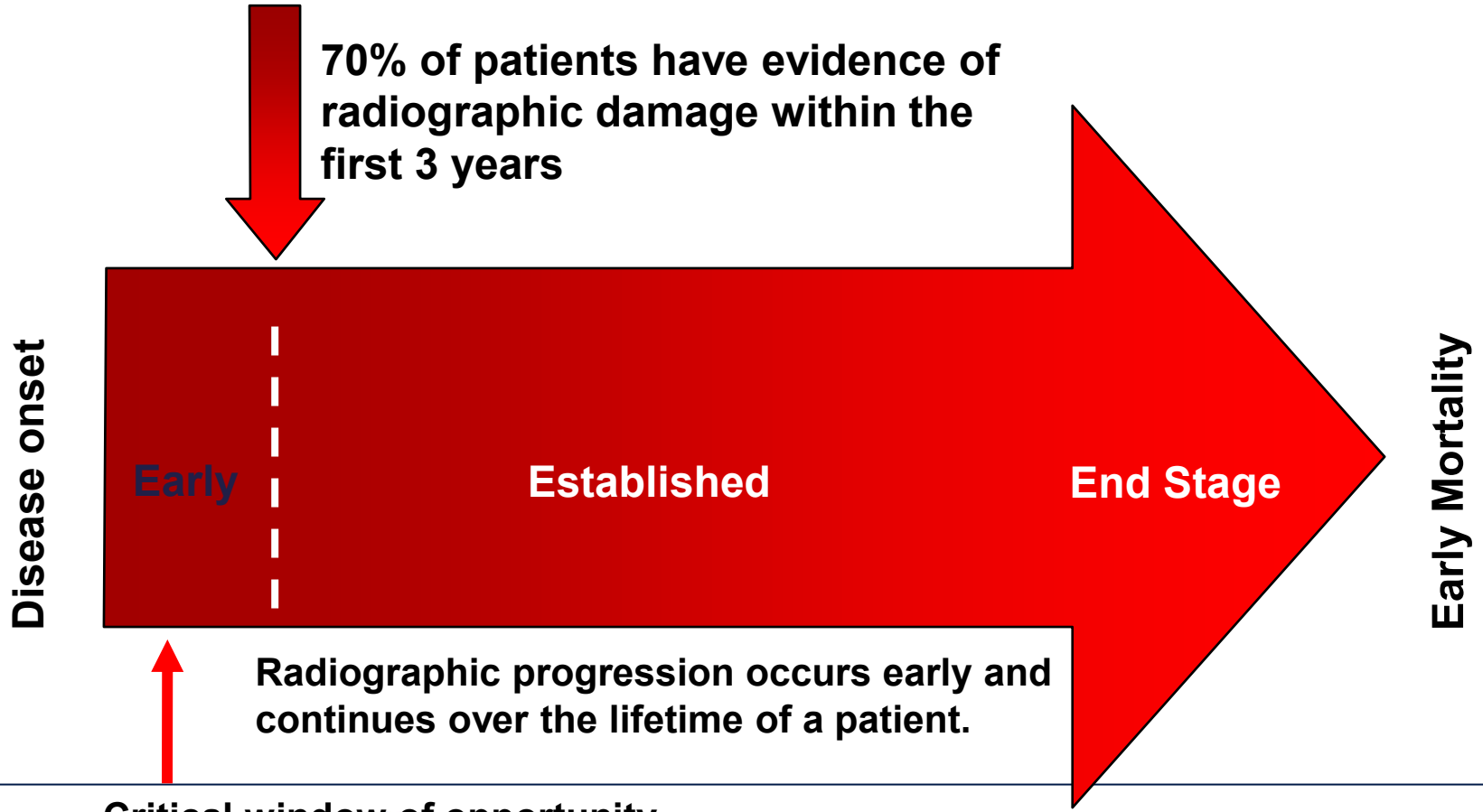
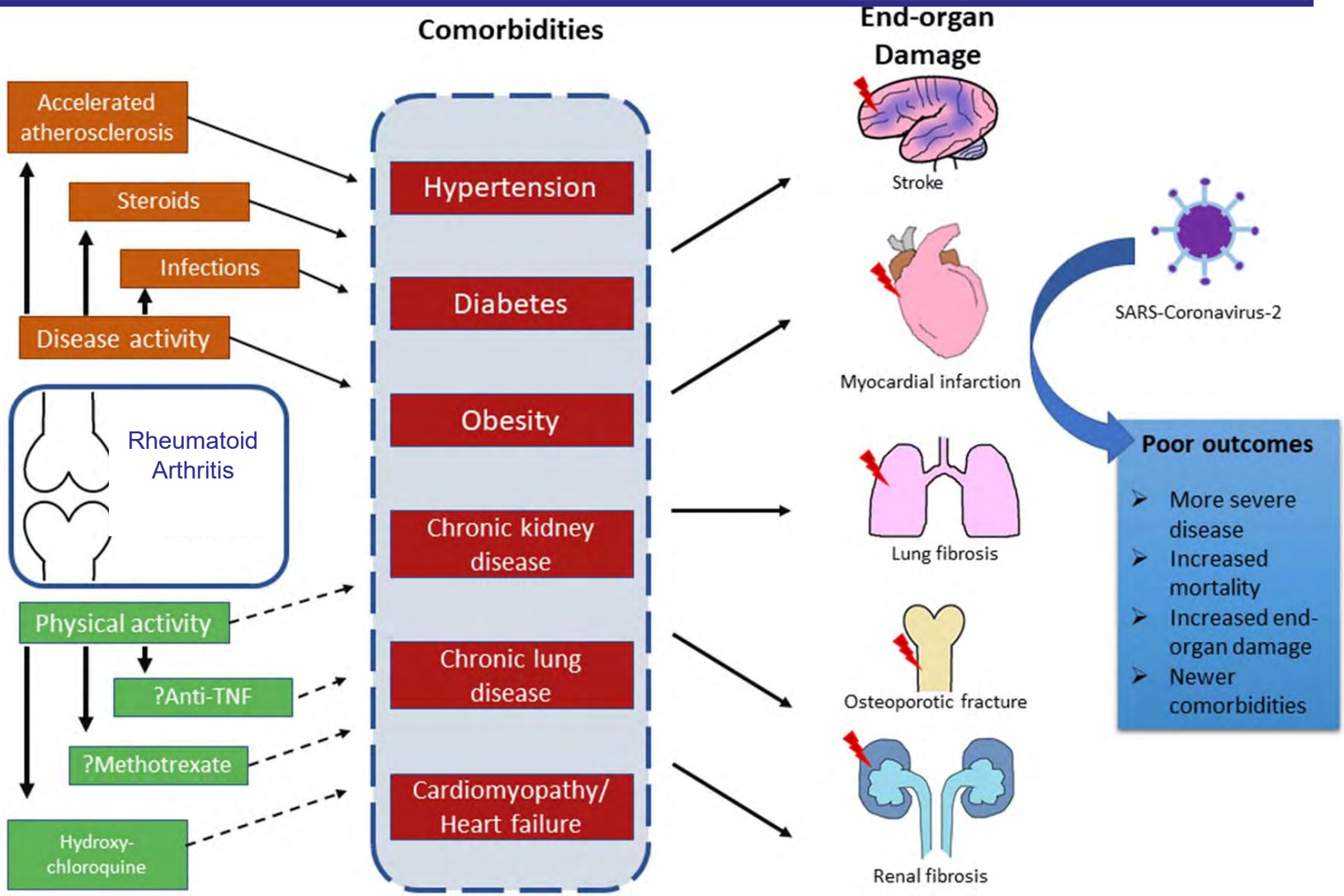

© ACR

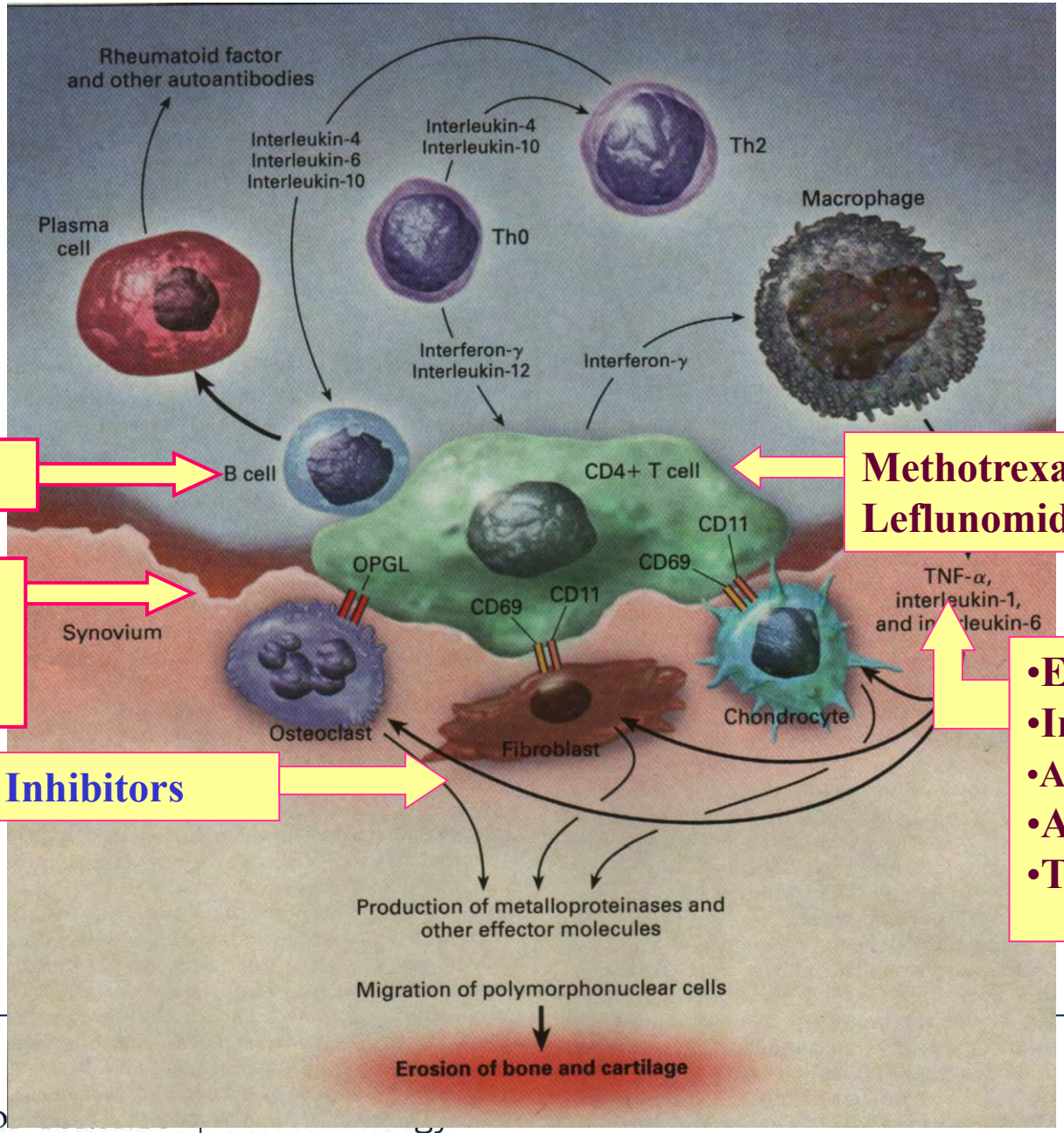
Importance of Early Treatment



Multi-morbidity in rheumatoid arthritis



Nat Rev Dis Primers **4**, 18001 (2018).
Rheumatol Int **41**, 243–256 (2021)



Rituximab

Abatacept

(Blocks activation of T cell)

JAK Inhibitors

Methotrexate
Leflunomide

- **Etanercept** (TNFα)
- **Infliximab** (TNFα)
- **Adalimumab** (TNFα)
- **Anakinra** (IL1)
- **Tocilizumab** (IL6)

Clinical Practice Guidelines

Guide health care professionals

How the American College of Rheumatology Develops Guidelines

Sindhu R. Johnson, MD, PhD[a,*], Amy S. Turner[b], Susan M. Goodman, MD[c]

KEYWORDS

• Guidelines • Clinical practice • Evidence

KEY POINTS

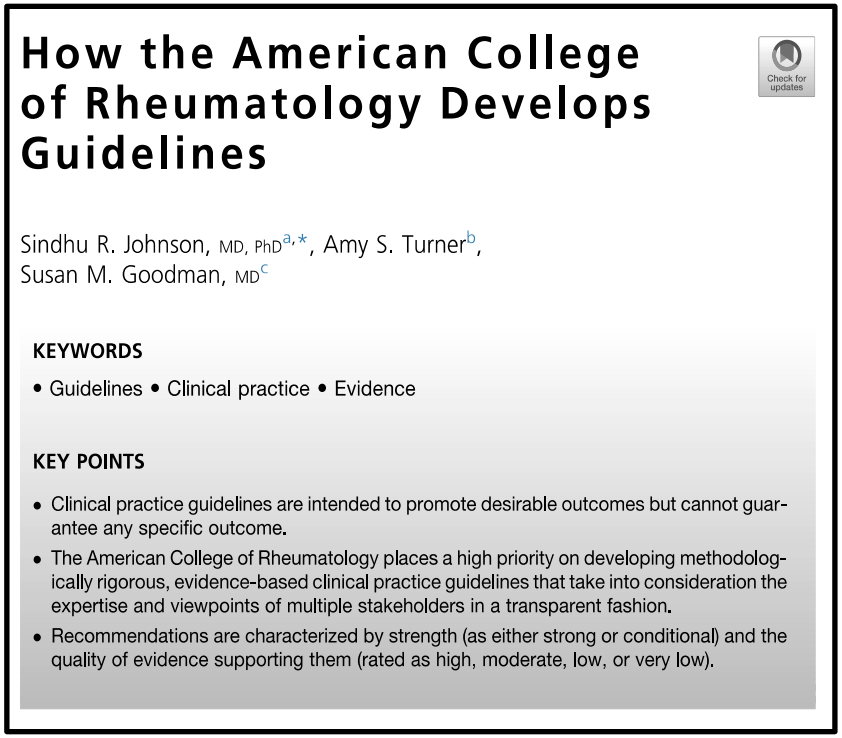
- Clinical practice guidelines are intended to promote desirable outcomes but cannot guarantee any specific outcome.
- The American College of Rheumatology places a high priority on developing methodologically rigorous, evidence-based clinical practice guidelines that take into consideration the expertise and viewpoints of multiple stakeholders in a transparent fashion.
- Recommendations are characterized by strength (as either strong or conditional) and the quality of evidence supporting them (rated as high, moderate, low, or very low).

Johnson et al. Rheum Dis Clin N Am 2022;579-588

Clinical Practice Guidelines

Guide health care professionals

Reduce geographic practice variation



How the American College of Rheumatology Develops Guidelines

Sindhu R. Johnson, MD, PhD[a,*], Amy S. Turner[b], Susan M. Goodman, MD[c]

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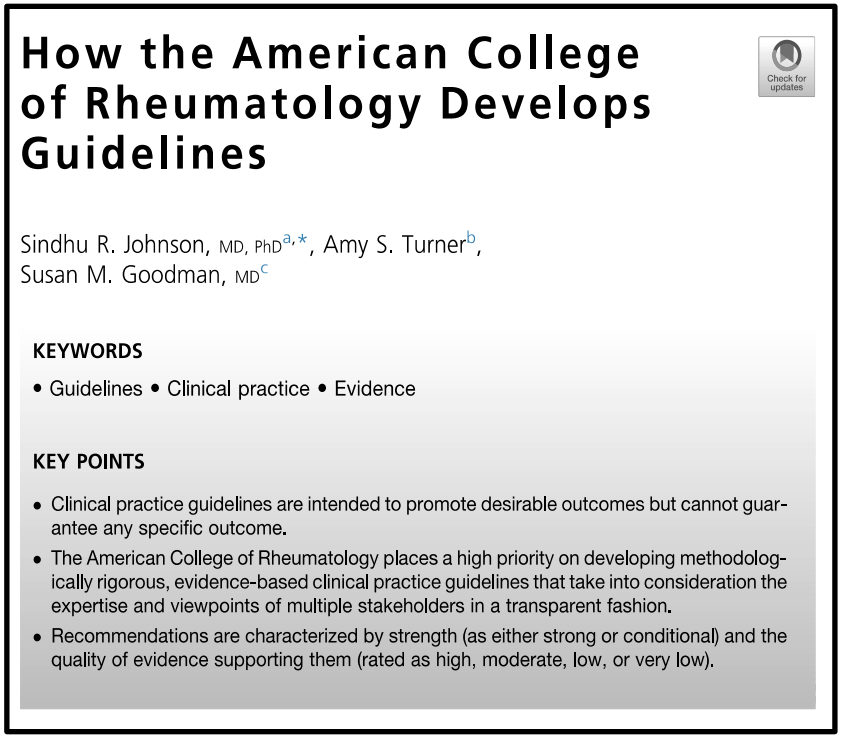
Johnson et al. Rheum Dis Clin N Am 2022;579-588

Clinical Practice Guidelines

Guide health care professionals

Reduce geographic practice variation

Advocacy & Awareness



How the American College of Rheumatology Develops Guidelines

Sindhu R. Johnson, MD, PhD[a,*], Amy S. Turner[b], Susan M. Goodman, MD[c]

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Johnson et al. Rheum Dis Clin N Am 2022;579-588

Guideline Development Process

Johnson et al.
Rheum Dis Clin N Am 2022;579-588

Guideline Development Process

The ACR needs you!

Johnson et al.
Rheum Dis Clin N Am 2022;579-588

Guideline Development Process

The ACR needs you!

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Grading of Recommendations Assessment, Development & Evaluation (GRADE)

Certainty of evidence

Grade	Definition
High	Very confident that the true effect lies close to that of the estimate of the effect
Moderate RCTs	Moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low Observational	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect

Factors that Downgrade Certainty of Evidence	Consequence
Limitations in study design or execution (risk of bias)	↓ 1 or 2 levels
Inconsistency of results	↓ 1 or 2 levels
Indirectness of evidence	↓ 1 or 2 levels
Imprecision	↓ 1 or 2 levels
Publication bias	↓ 1 or 2 levels

Adapted from the GRADE Handbook

Some points about rheumatology trials

- In the world of clinical trials, rheumatology clinical trials are relatively small

Trial	N
SLS 1	158
SLS 2	142
SENSCIS	576
TRAIL1	123

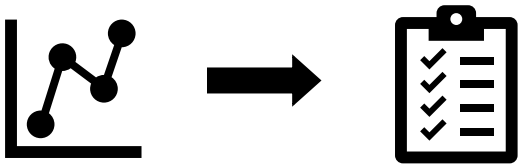
Trial	N
ALLHAT	33,357
JUPITER	17,802
CANTOS	10,061
TWILIGHT	9,006

- Primary outcome in SARD-ILD clinical trials is usually forced vital capacity, which is a surrogate outcome
- Surrogate outcomes are 1 step removed from what patients care about – they care about living longer and how they feel & function
- Consequence: Even in a well-designed SARD-ILD clinical trial, the certainty of evidence is low or very low

Tashkin DP, et al. N Engl J Med 2006. Tashkin DP, et al. Lancet Respir Med 2016. Distler O, et al. N Engl J Med 2019. Solomon JJ, et al. Lancet Respir Med 2023. ALLHAT Officers. JAMA 2002. Ridker PM, et al. N Engl J Med 2008. Ridker PM, et al. N Engl J Med 2017. Mehran R, et al. N Engl J Med 2019.

Moving from Evidence to Recommendations

- Voting Panel members cast 2 votes for each PICO
  - Direction of recommendation
  - Strength of recommendation
- 70% agreement on direction & strength required to achieve consensus
- Four possible outcomes for each recommendation
  - Strongly for
  - Conditionally for
  - Conditionally against
  - Strongly against
- The ACR is transparent about instances in which Voting Panel could not achieve consensus



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Vol. 0, No. 0, Month 2021, pp 1–16
DOI 10.1002/acr.24596

American College of Rheumatology
Empowering Rheumatology Professionals

2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

Liana Fraenkel,[1] Joan M. Bathon,[2] Bryant R. England,[3] E. William St.Clair,[4] Thurayya Arayssi,[5] Kristine Carandang,[6] Kevin D. Deane,[7] Mark Genovese,[8] Kent Kwas Huston,[9] Gail Kerr,[10] Joel Kremer,[11] Mary C. Nakamura,[12] Linda A. Russell,[13] Jasvinder A. Singh,[14] Benjamin J. Smith,[15] Jeffrey A. Sparks,[16] Shilpa Venkatachalam,[17] Michael E. Weinblatt,[16] Mounir Al-Gibbawi,[18] Joshua F. Baker,[19] Kamil E. Barbour,[20] Jennifer L. Barton,[21] Laura Cappelli,[22] Fatimah Chamseddine,[18] Michael George,[23] Sindhu R. Johnson,[24] Lara Kahale,[18] Basil S. Karam,[18] Assem M. Khamis,[18] Iris Navarro-Millán,[25] Reza Mirza,[26] Pascale Schwab,[21] Namrata Singh,[27] Marat Turgunbaev,[28] Amy S. Turner,[28] Sally Yaacoub,[18] and Elie A. Akl[18]

Table 1 | **Key differences between the 2021 ACR guideline and the 2019 EULAR recommendations for RA treatment**

Clinical scenario	2021 ACR guideline[2]	2019 EULAR recommendations[3]
First-line therapy	Low disease activity: hydroxychloroquine	Methotrexate (in the absence of contraindications)
	Moderate-to-high disease activity: methotrexate	
Use of glucocorticoids	Conditional recommendation against glucocorticoids when starting csDMARDs	Consider short-term glucocorticoids when starting or switching csDMARDs
Insufficient response to methotrexate	Add bDMARDs or tsDMARDs	Poor prognostic factors absent: consider other csDMARDs
		Poor prognostic factors present: add bDMARDs or tsDMARDs
Drug tapering in persistent remission	Continue all DMARDs	Taper glucocorticoids first, then consider tapering bDMARDs or tsDMARDs, then csDMARDs
	If tapering is considered, taper methotrexate, not bDMARDs or tsDMARDs	

bDMARDs; biologic DMARDs; csDMARDs, conventional synthetic DMARDs; RA, rheumatoid arthritis; tsDMARDs, targeted synthetic DMARDs.

Alten, R., Mischkewitz, M. 2021 ACR guideline reflects changes in RA treatment. *Nat Rev Rheumatol* **17**, 513–514 (2021).

Guidelines for Other Aspects of Rheumatoid Arthritis Care

Arthritis Care & Research
Vol. 75, No. 8, August 2023, pp 1603–1615
DOI 10.1002/acr.25117

American College of Rheumatology
Empowering Rheumatology Professionals

2022 American College of Rheumatology Guideline for Exercise, Rehabilitation, Diet, and Additional Integrative Interventions for Rheumatoid Arthritis

Bryant R. England,[1*] Benjamin J Smith,[2*] Nancy A. Baker,[3] Jennifer L. Barton,[4] Carol A. Oatis,[5] Gordon Guyatt,[6] Allen Anandarajah,[7] Kristine Carandang,[8] Karmela Kim Chan,[9] Deb Constien,[10] Eileen Davidson,[11] Carole V. Dodge,[12] Anita Bemis-Dougherty,[13] Sotiria Everett,[14] Nadine Fisher,[15] Liana Fraenkel,[16] Susan M. Goodman,[9] Janet Lewis,[17] Victoria Menzies,[18] Larry W. Moreland,[19] Iris Navarro-Millan,[20] Sarah Patterson,[21] Lawrence "Rick" Phillips,[22] Neha Shah,[23] Namrata Singh,[24] Daniel White,[25] Rawan AlHeresh,[26] Kamil E. Barbour,[27] Thomas Bye,[25] Dana Guglielmo,[28] Rebecca Haberman,[29] Tate Johnson,[1] Anatole Kleiner,[7] Chris Y. Lane,[30] Linda C. Li,[31] Hiral Master,[32] Daniel Pinto,[33] Janet L. Poole,[34] Kimberly Steinbarger,[35] Daniel Sztubinski,[36] Louise Thoma,[30] Vlad Tsaltskan,[37] Marat Turgunbaev,[38] Courtney Wells,[39] Amy S. Turner,[38] and Jonathan R. Treadwell[36]

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Table 1. Recommendations on integrative interventions for the management of rheumatoid arthritis (RA)

Exercise	Rehabilitation	Diet	Additional
Consistent engagement in exercise (++)	Comprehensive occupational therapy (+)	Mediterranean-style diet (+)	Standardized self-management program (+)
Aerobic exercise (+)	Comprehensive physical therapy (+)	Against formally defined diet other than Mediterranean-style (-)	Cognitive behavioral therapy and/or mind-body approaches (+)
Aquatic exercise (+)	Hand therapy exercises (+)	Against dietary supplements (-)	Acupuncture (+)
Resistance exercise (+)	Splinting, orthoses, compression, bracing, and/or taping (+)		Massage therapy (+)
Mind-body exercise (+)	Joint protection techniques (+)		Thermal modalities (+)
	Activity pacing, activity modification, energy conservation, and/or fatigue management (+)		Against electrotherapy (-)
	Assistive devices, adaptive equipment, and/or environmental adaptations (+)		Against chiropractic therapy (-)
	Vocational rehabilitation, work site evaluations and/or modifications (+)		

Strong recommendations **for** an intervention are shown in dark green and ++.
Conditional recommendations **for** an intervention are shown in light green and +.
Conditional recommendations **against** an intervention are shown in light red and -.

Arthritis & Rheumatology
Vol. 75, No. 3, March 2023, pp 333–348
DOI 10.1002/art.42386

American College of Rheumatology
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]

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

* 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.

Arthritis Rheumatol. 2023 Mar;75(3):333-348.

Table 5. Immunosuppressive medication management at the time of live attenuated virus vaccine administration*

	Hold before live attenuated virus vaccine administration	Hold after live attenuated virus vaccine administration
Glucocorticoids†	4 weeks	4 weeks
Methotrexate, azathioprine‡	4 weeks	4 weeks
Leflunomide, mycophenolate mofetil, calcineurin inhibitors, oral cyclophosphamide	4 weeks	4 weeks
JAK inhibitors	1 week	4 weeks
TNF, IL-17, IL-12/23, IL-23, BAFF/BLyS inhibitors	1 dosing interval§	4 weeks
IL-6 pathway inhibitors	1 dosing interval¶	4 weeks
IL-1 inhibitors		
Anakinra	1 dosing interval¶	4 weeks
Rilonacept	1 dosing interval¶	4 weeks
Canakinumab	1 dosing interval¶	4 weeks
Abatacept	1 dosing interval§	4 weeks
Anifrolumab	1 dosing interval§	4 weeks
Cyclophosphamide, intravenous	1 dosing interval§	4 weeks
Rituximab	6 months	4 weeks
IVIG#		
300–400 mg/kg	8 months	4 weeks
1 gm/kg	10 months	4 weeks
2 gm/kg	11 months	4 weeks

Arthritis Rheumatol. 2023 Mar;75(3):333-348.

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases

Lisa R. Sammaritano,[1] Bonnie L. Bermas,[2] Eliza E. Chakravarty,[3] Christina Chambers,[4] Megan E. B. Clowse,[5] Michael D. Lockshin,[1] Wendy Marder,[6] Gordon Guyatt,[7] D. Ware Branch,[8] Jill Buyon,[9] Lisa Christopher-Stine,[10] Rachelle Crow-Hercher,[11] John Cush,[12] Maurice Druzin,[13] Arthur Kavanaugh,[4] Carl A. Laskin,[14] Lauren Plante,[15] Jane Salmon,[1] Julia Simard,[13] Emily C. Somers,[6] Virginia Steen,[16] Sara K. Tedeschi,[17] Evelyne Vinet,[18] C. Whitney White,[19] Jinoos Yazdany,[20] Medha Barbhaiya,[1] Brittany Bettendorf,[21] Amanda Eudy,[5] Arundathi Jayatilleke,[15] Amit Aakash Shah,[22] Nancy Sullivan,[23] Laura L. Tarter,[17] Mehret Birru Talabi,[24] Marat Turgunbaev,[22] Amy Turner,[22] and Kristen E. D'Anci[23]

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Arthritis Rheumatol. 2020 Apr;72(4):529-556..

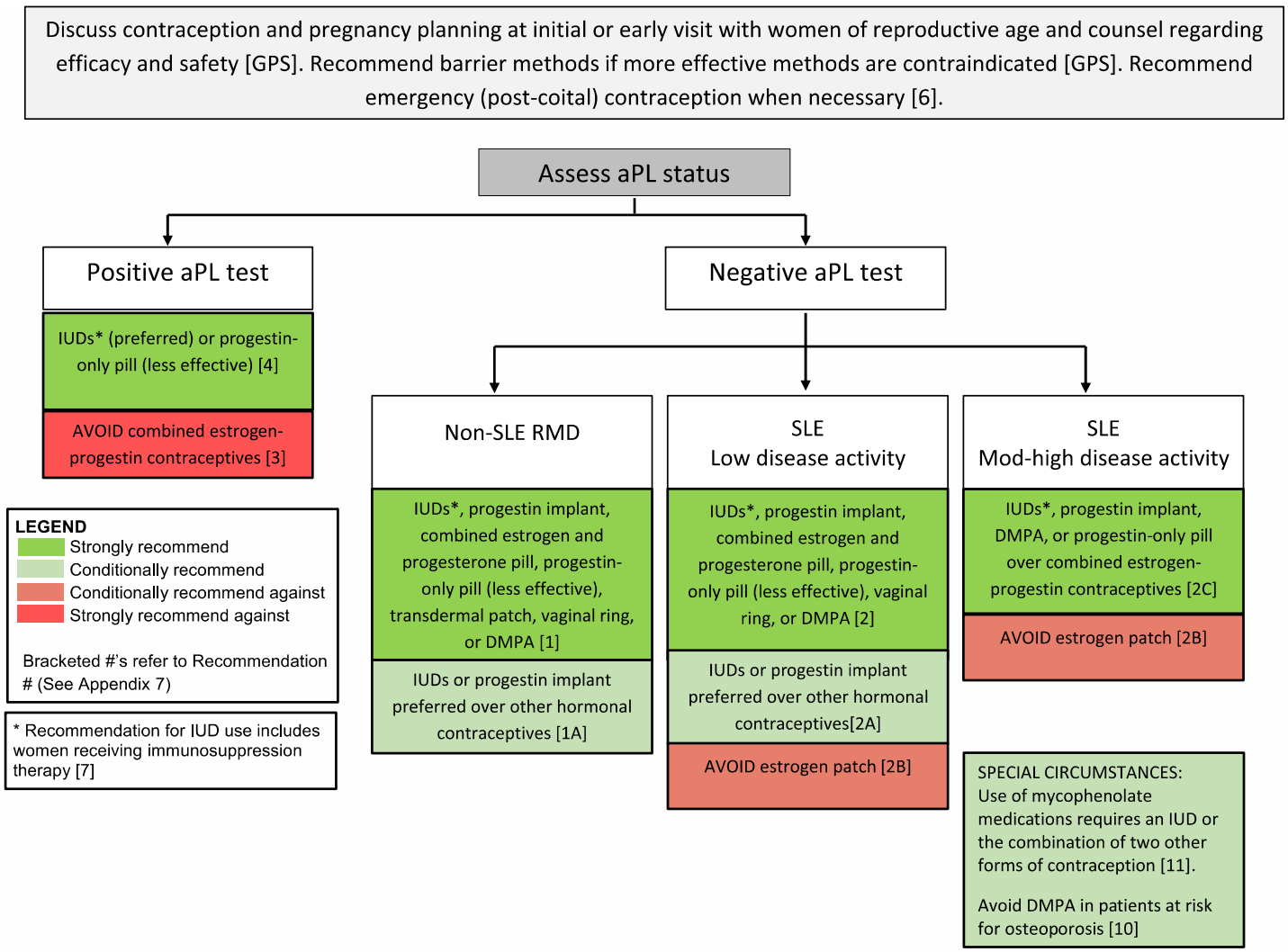

Figure 1. Recommendations and good practice statements (GPS) for use of contraception in women with rheumatic and musculoskeletal disease (RMD). aPL = antiphospholipid antibody (persistent moderate [Mod]–to-high–titer anticardiolipin or anti–β_2-glycoprotein I antibody or persistent positive lupus anticoagulant); IUDs = intrauterine devices (copper or progestin); SLE = systemic lupus erythematosus; DMPA = depot medroxyprogesterone acetate.

Arthritis Rheumatol. 2020 Apr;72(4):529-556..

2022 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

Susan M. Goodman,[1] Bryan D. Springer,[2] Antonia F. Chen,[3] Marshall Davis,[4] David R. Fernandez,[1] Mark Figgie,[1] Heather Finlayson,[5] Michael D. George,[6] Jon T. Giles,[7] Jeremy Gilliland,[8] Brian Klatt,[9] Ronald MacKenzie,[1] Kaleb Michaud,[10] Andy Miller,[1] Linda Russell,[1] Alexander Sah,[11] Matthew P. Abdel,[12] Beverly Johnson,[13] Lisa A. Mandl,[1] Peter Sculco,[1] Marat Turgunbaev,[14] Amy S. Turner,[14] Adolph Yates Jr.,[9] and Jasvinder A. Singh[15]

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Arthritis Rheumatol. 2022 Sep;74(9):1464-1473.

MEDICATIONS TO CONTINUE THROUGH SURGERY		
DMARDs: CONTINUE these medications through surgery. (All patients)	**Dosing Interval**	**Recommended timing of surgery since last medication dose**
Methotrexate	Weekly	Anytime
Sulfasalazine	Once or twice daily	Anytime
Hydroxychloroquine	Once or twice daily	Anytime
Leflunomide (Arava)	Daily	Anytime
Doxycycline	Daily	Anytime
Apremilast (Otezla)	***Twice daily***	***Anytime***
SEVERE SLE-SPECIFIC MEDICATIONS††: CONTINUE these medications in the perioperative period in consultation with the treating rheumatologist.	**Dosing Interval**	**Recommended timing of surgery since last medication dose**
Mycophenolate mofetil	Twice daily	Anytime
Azathioprine	Daily or twice daily	Anytime
Cyclosporine	Twice daily	Anytime
Tacrolimus	Twice daily (IV and PO)	Anytime
Rituximab (Rituxan)	***IV Every 4-6 months***	***Month 4-6***
Belimumab (Benlysta)	***Weekly SQ***	***Anytime***
Belimumab (Benlysta)	***Monthly IV***	***Week 4***
Anifrolumab (Saphnelo)†	***IV Every 4 weeks***	***Week 4***
Voclosporin (Lupkynis)†	***Twice daily***	***Continue***

Arthritis Rheumatol. 2022 Sep;74(9):1464-1473.

MEDICATIONS TO WITHHOLD PRIOR TO SURGERY***		
BIOLOGICS: WITHHOLD these medications through surgery		**Recommended timing of surgery since last medication dose**
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Adalimumab (Humira)	Every 2 weeks	Week 3
Etanercept (Enbrel)	Every week	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5 Week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4-6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2 Week 5
Anakinra (Kineret)	Daily	Day 2
IL-17-Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
Ixekizumab (Taltz)†	***Every 4 weeks***	***Week 5***
IL-23 Guselkumab (Tremfya)†	***Every 8 weeks***	***Week 9***
JAK inhibitors WITHHOLD this medication 3 days prior to surgery*		
Tofacitinib (Xeljanz):	***Daily or twice daily***	***Day 4***
Baricitinib (Olumiant)†	***Daily***	***Day 4***
Upadacitinib (Rinvoq)†	***Daily***	***Day 4***
NOT-SEVERE SLE: WITHHOLD these medications 1 week prior to surgery	**Dosing Interval**	**1 week after last dose**
Mycophenolate mofetil	Twice daily	**1 week after last dose**
Azathioprine	Daily or twice daily	1 week after last dose
Cyclosporine	Twice daily	**1 week after last dose**
Tacrolimus	Twice daily (IV and PO)	**1 week after last dose**
Rituximab (Rituxan)	Every 4-6 months	Month 7
Belimumab IV (Benlysta)	***Monthly***	***Week 5***
Belimumab SQ (Benlysta)	***Weekly***	***Week 2***

Arthritis Rheumatol. 2022 Sep;74(9):1464-1473.

Guidelines for Systemic Aspects of Rheumatoid Arthritis

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Arthritis Care & Research
Vol. 75, No. 12, December 2023, pp 2405–2419
DOI 10.1002/acr.25240

American College of Rheumatology
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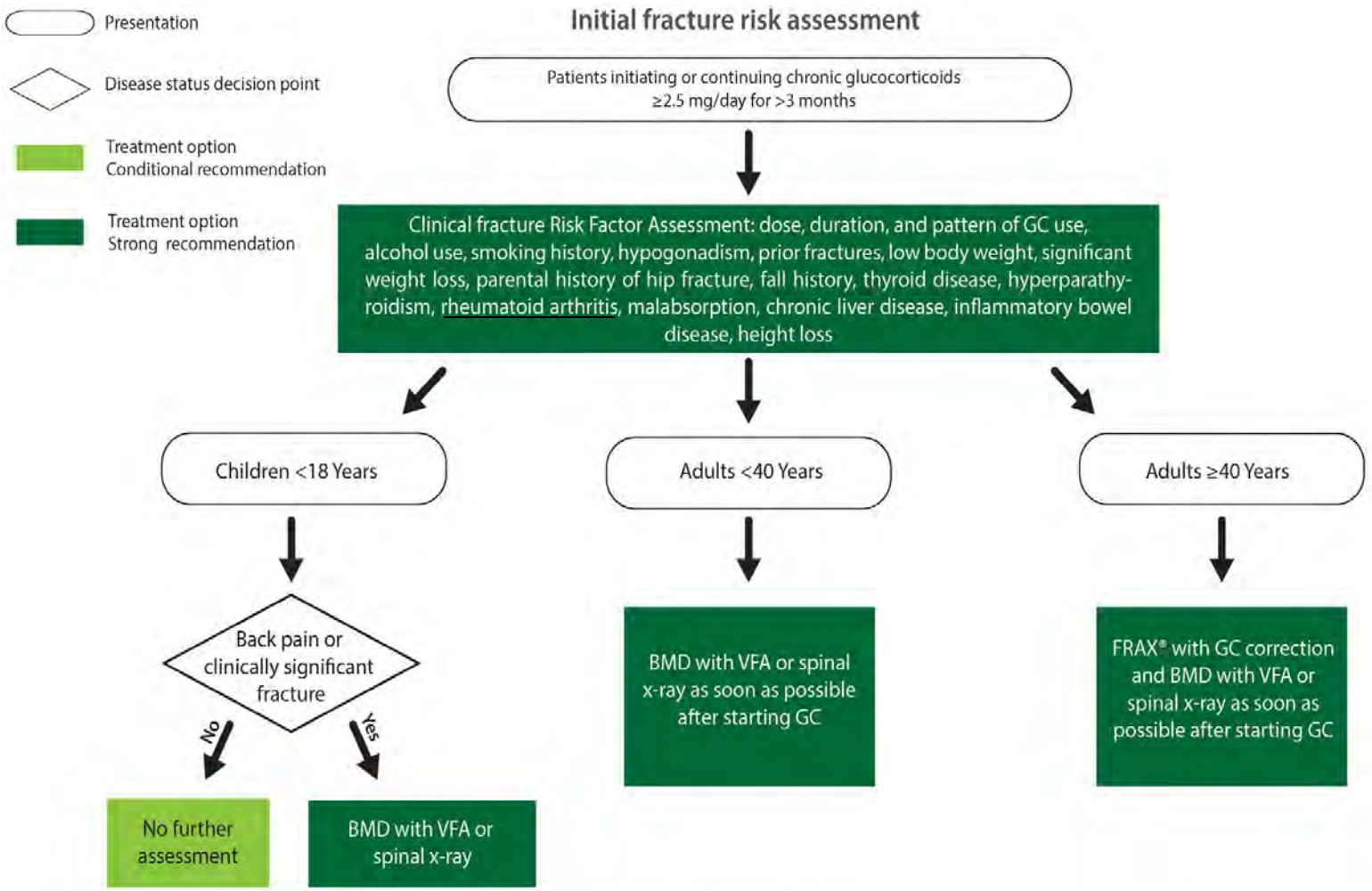
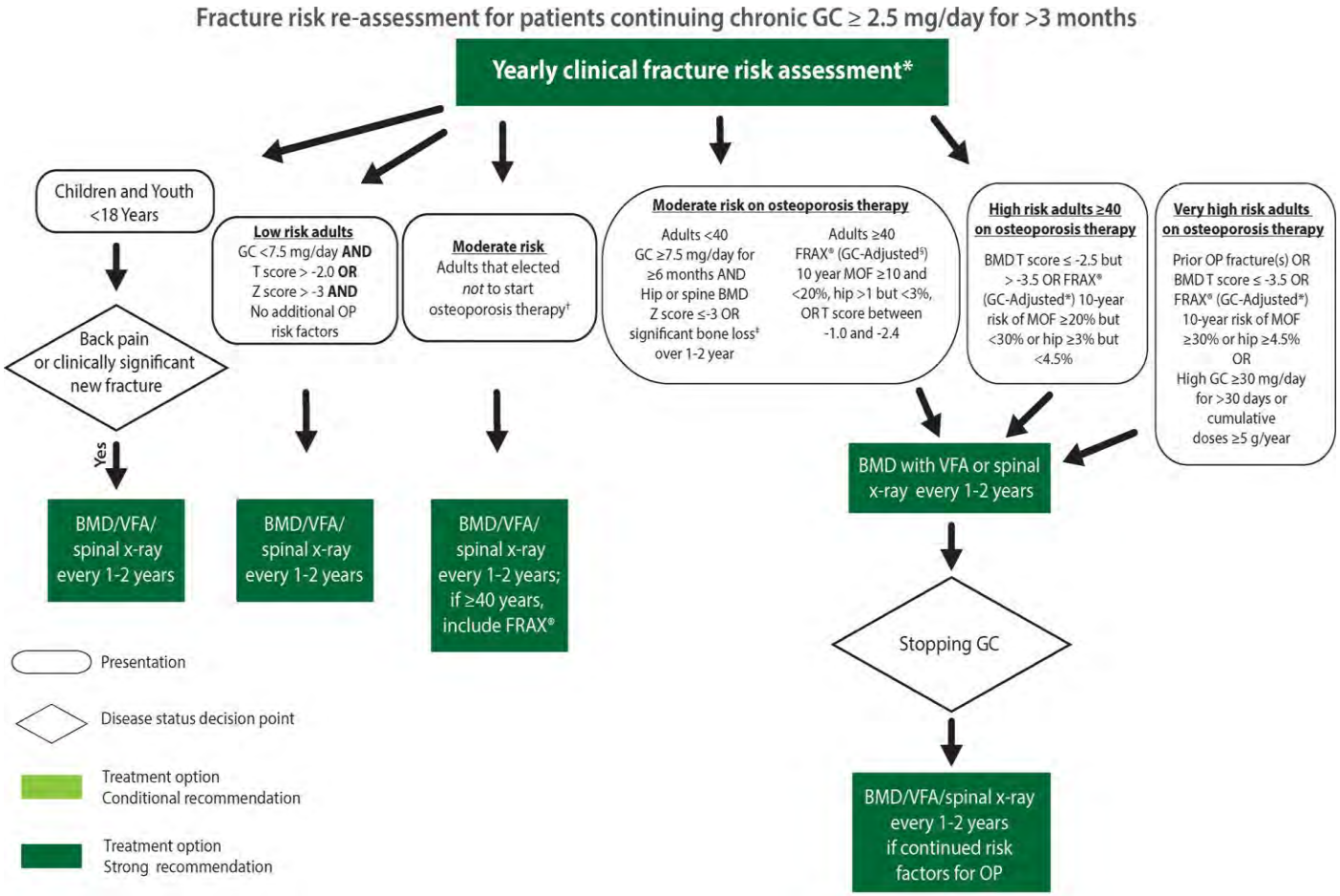
2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis

Mary Beth Humphrey,[1*] Linda Russell,[2*] Maria I. Danila,[3] Howard A. Fink,[4] Gordon Guyatt,[5] Michael Cannon,[6] Liron Caplan,[7] Sara Gore,[8] Jennifer Grossman,[9] Karen E. Hansen,[10] Nancy E. Lane,[11] Nina S. Ma,[12] Marina Magrey,[13] Tim McAlindon,[14] Angela Byun Robinson,[15] Sumona Saha,[10] Charles Womack,[8] Basma Abdulhadi,[3] Julia F. Charles,[16] Jonathan T. L. Cheah,[17] Sharon Chou,[16] Itivrita Goyal,[1] Katherine Haseltine,[2] Lesley Jackson,[3] Reza Mirza,[5] Iram Moledina,[3] Emma Punni,[1] Tim Rinden,[18] Marat Turgunbaev,[19] Katherine Wysham,[20] Amy S. Turner,[19] and Stacey Uhl[21]



OP = osteoporosis; FRAX® = Fracture risk assessment tool, validated for adults ≥40 Years, https//www.shef.ac.uk/FRAX/Tool.jsp; FRAX® with GC correction = If GC dose is >7.5 mg/day, increase the MOF risk by multiplying 1.15 times and hip fracture risk by multiplying 1.2 times (e.g., if hip fracture risk is 2.0% multiply by 1.2 for adjusted risk =2.4%); BMD = bone mineral density testing

Arthritis & Rheumatology, Volume: 75, Issue: 12, Pages: 2088-2102, First published: 16 October 2023



OP = osteoporosis; GC = glucocorticoids; FRAX® = Fracture risk assessment tool can only be used in adults ≥40 years; BMD = bone mineral density testing; *Clinical fracture risk assessment: dose duration and pattern of GC use, alcohol use, smoking history, hypogonadism, prior fractures, low body weight, significant weight loss, parental history of hip fracture, fall history, thyroid disease, hyperparathyroidism, rheumatoid arthritis, malabsorption, chronic liver disease, inflammatory bowel disease, height; †Moderate risk adults should be offered therapy but may choose not to be treated; ‡ > least significant decline according to DXA machine (typically 3-5%); §FRAX® GC correction for GC ≥7.5 mg/day example: if hip fracture risk is 2.0% multiply by 1.2 for adjusted risk = 2.4%

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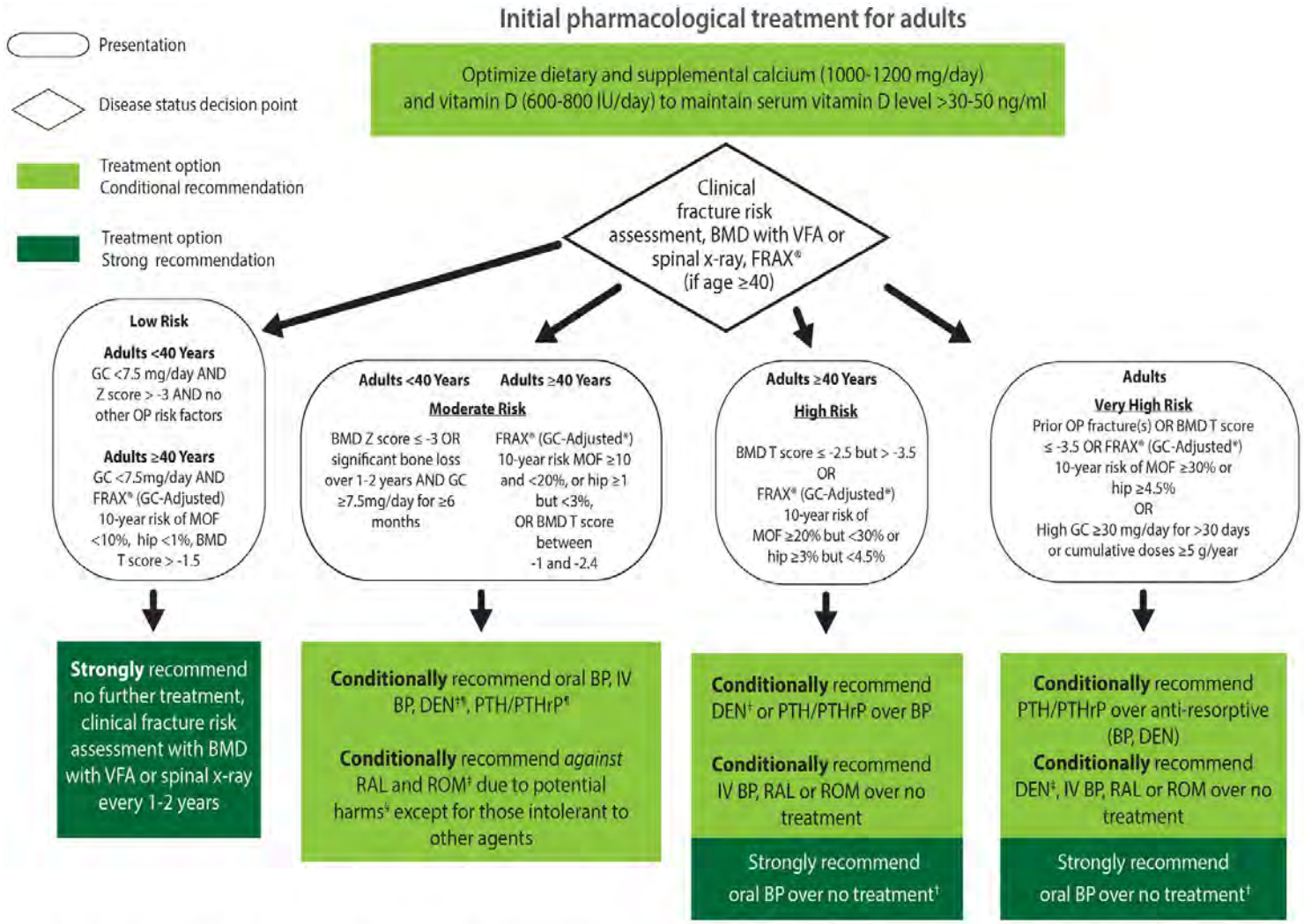

FRAX® = https//www.shef.ac.uk/FRAX/Tool.jsp; MOF= major osteoporotic fracture; *FRAX® GC correction for GC ≥7.5 mg/day example: if hip fracture risk is 2.0% multiply by 1.2 for adjusted risk = 2.4%, BP = bisphosphonate, IV = intravenous, PO = oral, PTH/PTHrP = parathyroid hormone/ parathyroid hormone related protein, DEN = denosumab, RAL = raloxifene, ROM = romosozumab, †Based on fracture data in GIOP, ‡Women who may become pregnant need birth control and avoid pregnancy until >5 months after last dose; §RAL(PE, DVT, fatal stroke); ROM (myocardial infarction, stroke and death; conditionally recommend RAL/ROM use in the highest risk patients unable to tolerate other agents; ¶Use with caution in persons with open growth plates

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ACR Convergence
Where Rheumatology Meets
#ACR23

2023 ACR/CHEST Guidelines for the screening, monitoring and treatment of ILD in the systemic autoimmune rheumatic diseases

Who should be screened?

Rheumatoid arthritis
confer an increased risk of developing ILD compared to the general population.

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Disease	Risk Factors
Rheumatoid arthritis	• High titer RF, anti-CCP • Smoking, older age at RA onset, high disease activity • Male sex, higher BMI

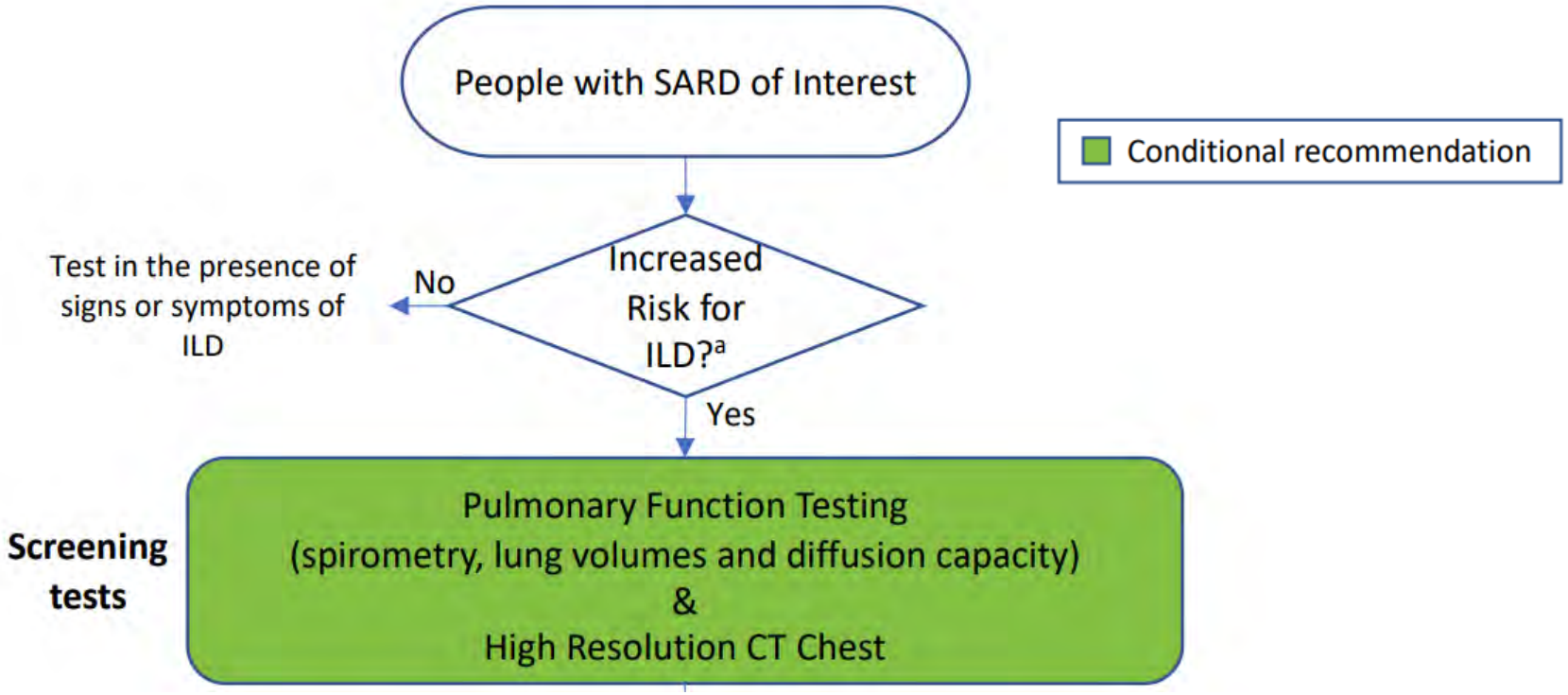
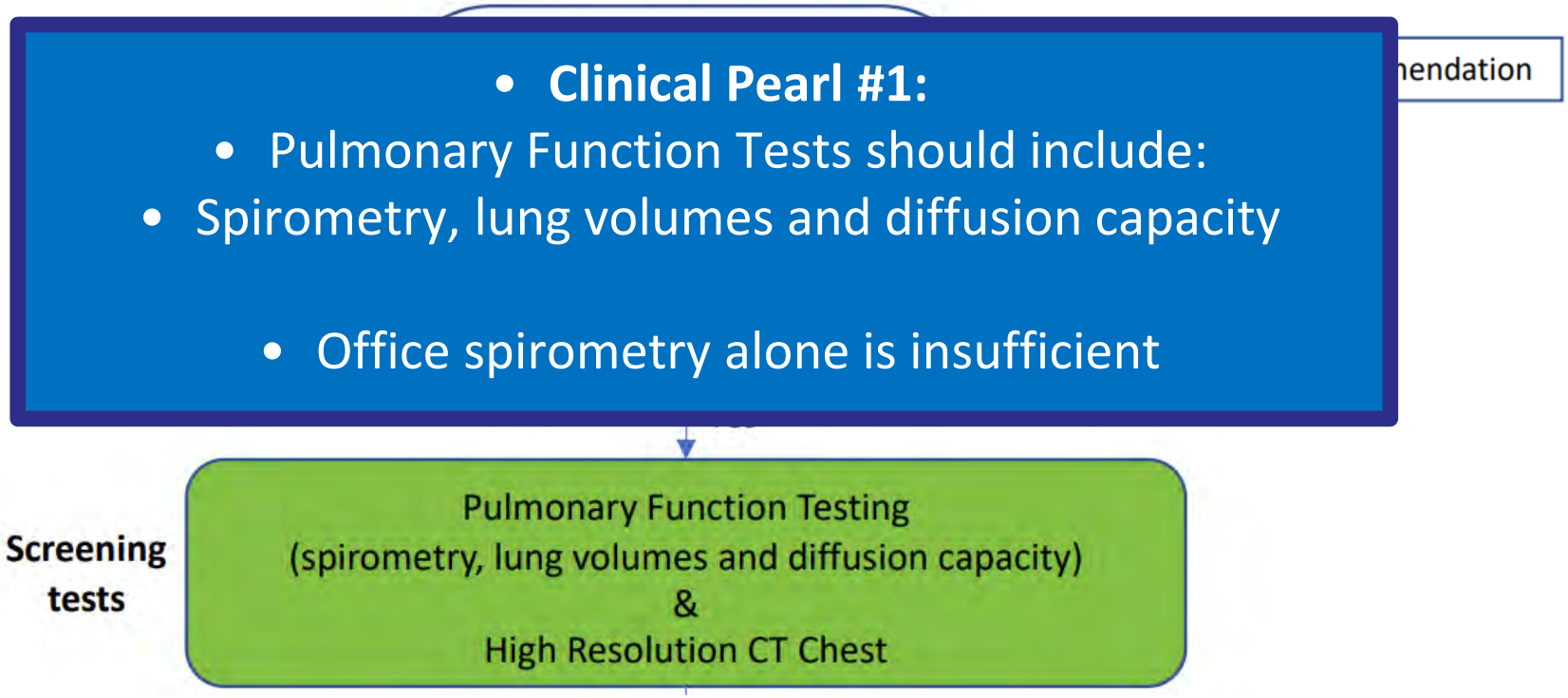


Figure 1: Recommendations for ILD Screening and Monitoring

[a] See Table 1 for risk factors for interstitial lung disease

SARD = systemic autoimmune rheumatic disease; ILD = interstitial lung disease; CT = computed tomography



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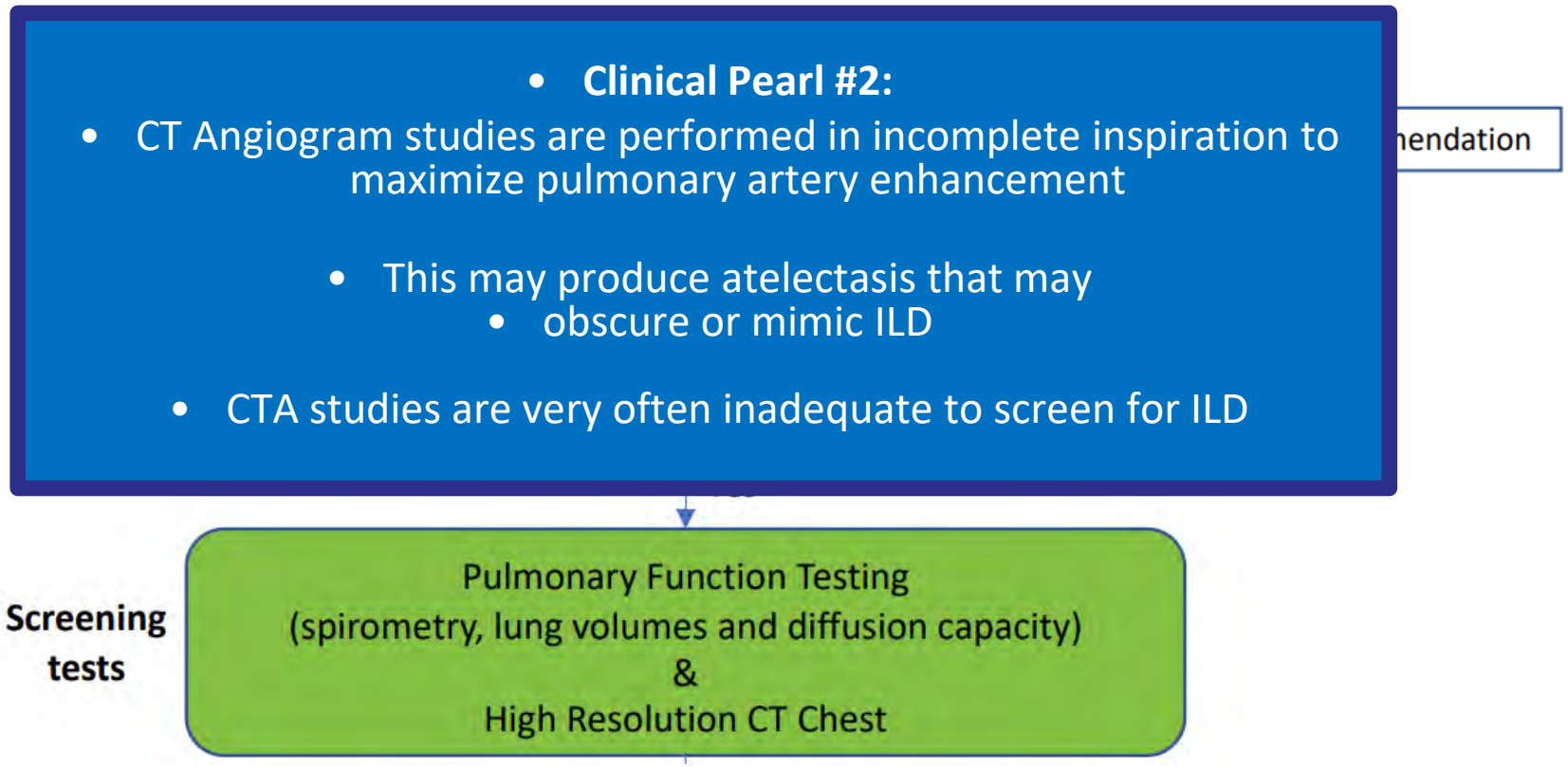

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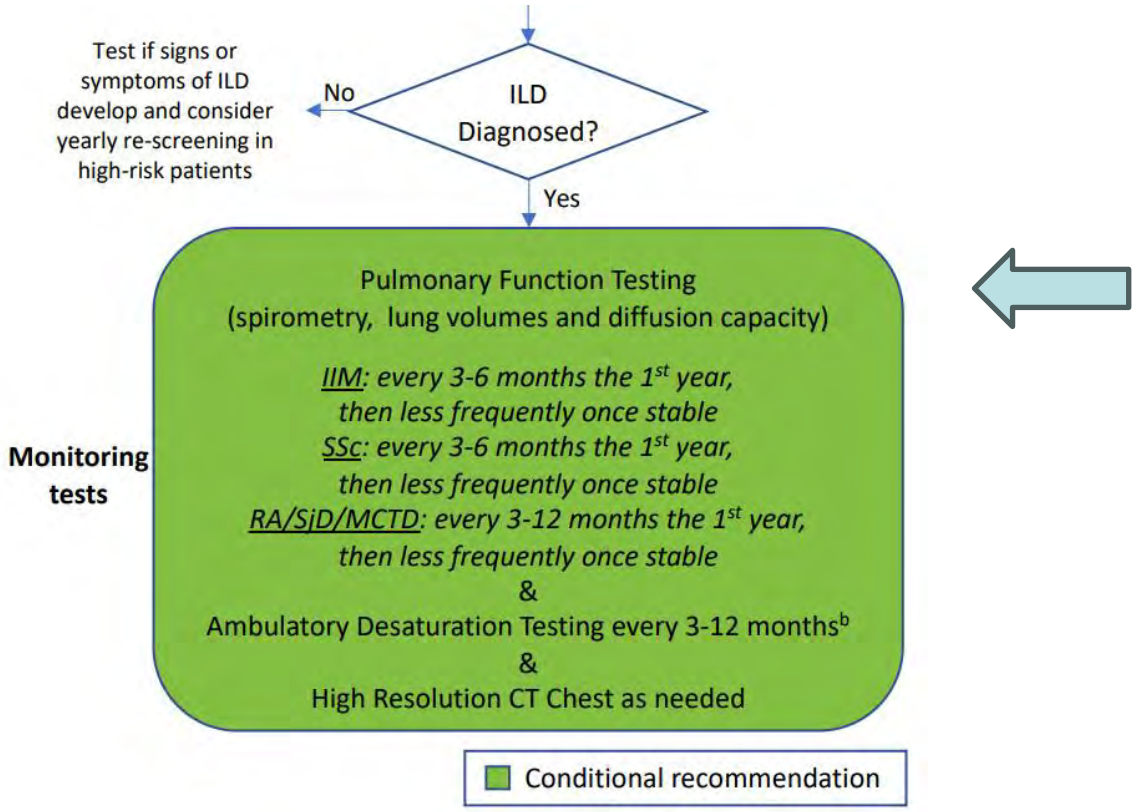
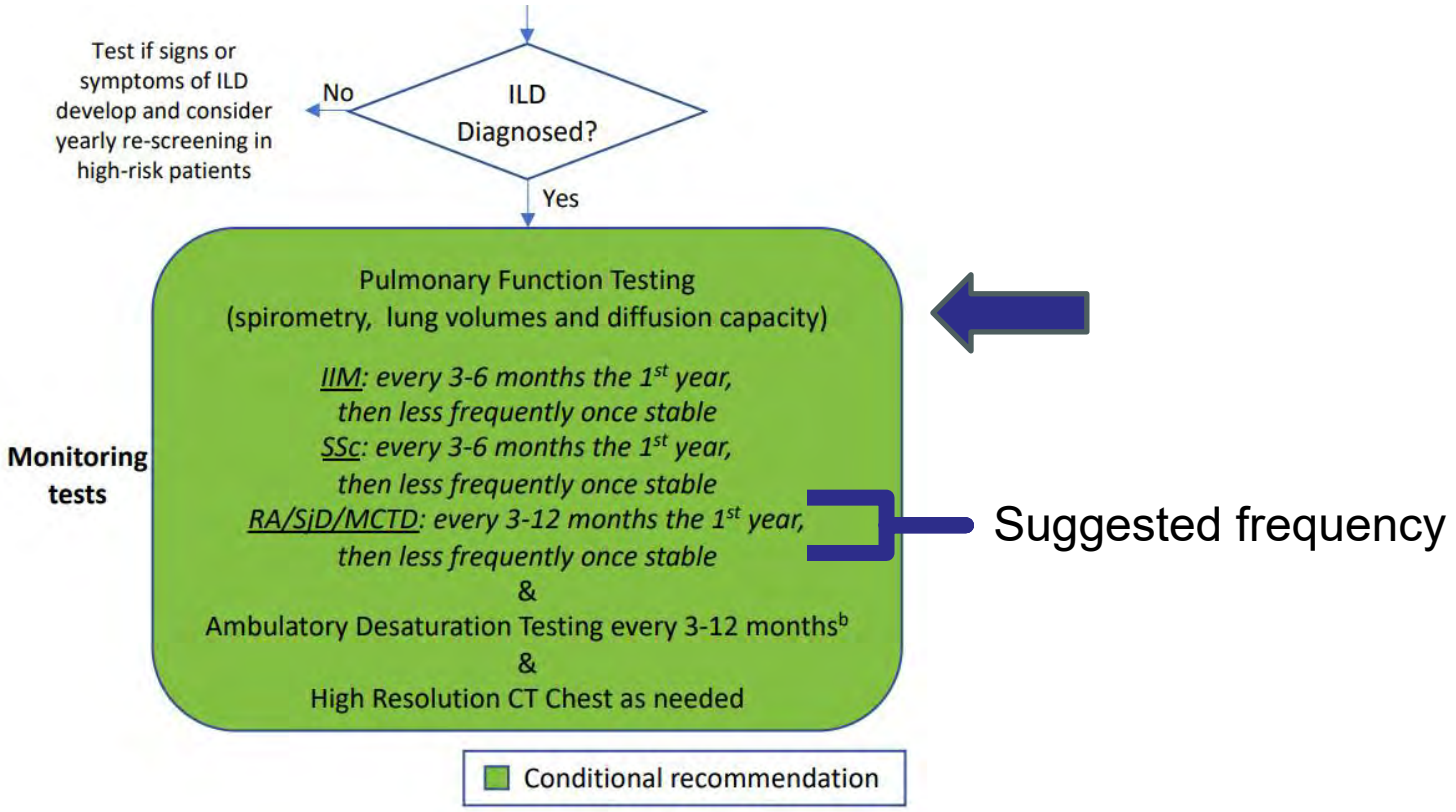


Figure 1 (continued): Recommendations for ILD Screening and Monitoring

[b] Ambulatory desaturation can be done during a routine office visit or as part of 6-minute walk testing

ILD = interstitial lung disease; CT = computed tomography; IIM = idiopathic inflammatory myopathy; SSc = systemic sclerosis; RA = rheumatoid arthritis; SjS = Sjogren's disease, MCTD = mixed connective tissue disease



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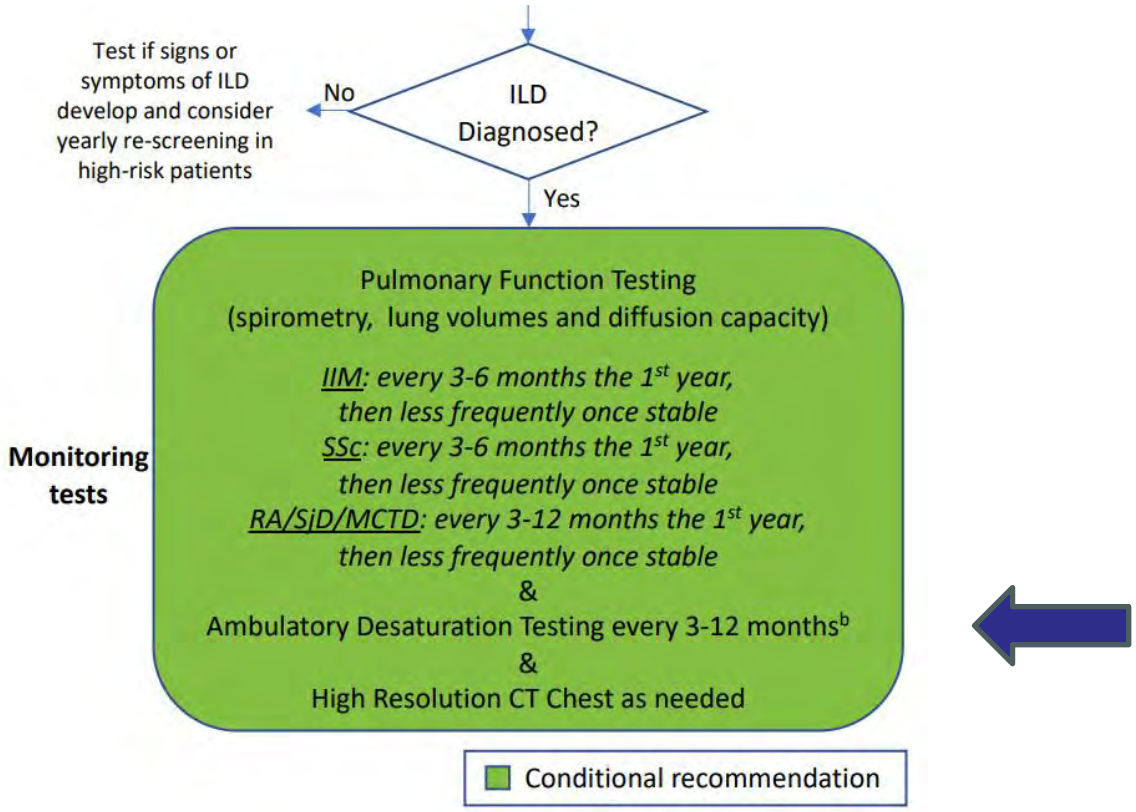

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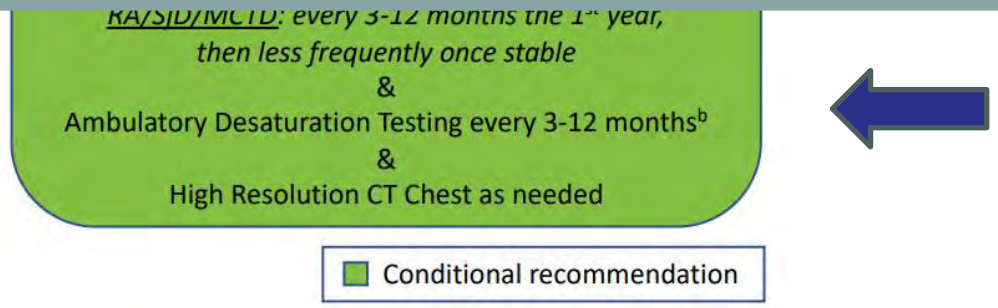
Clinical Pearl #3:
A 6MWT with continuous oximetry is insufficient.

Ambulatory desaturation testing includes up titration of oxygen.



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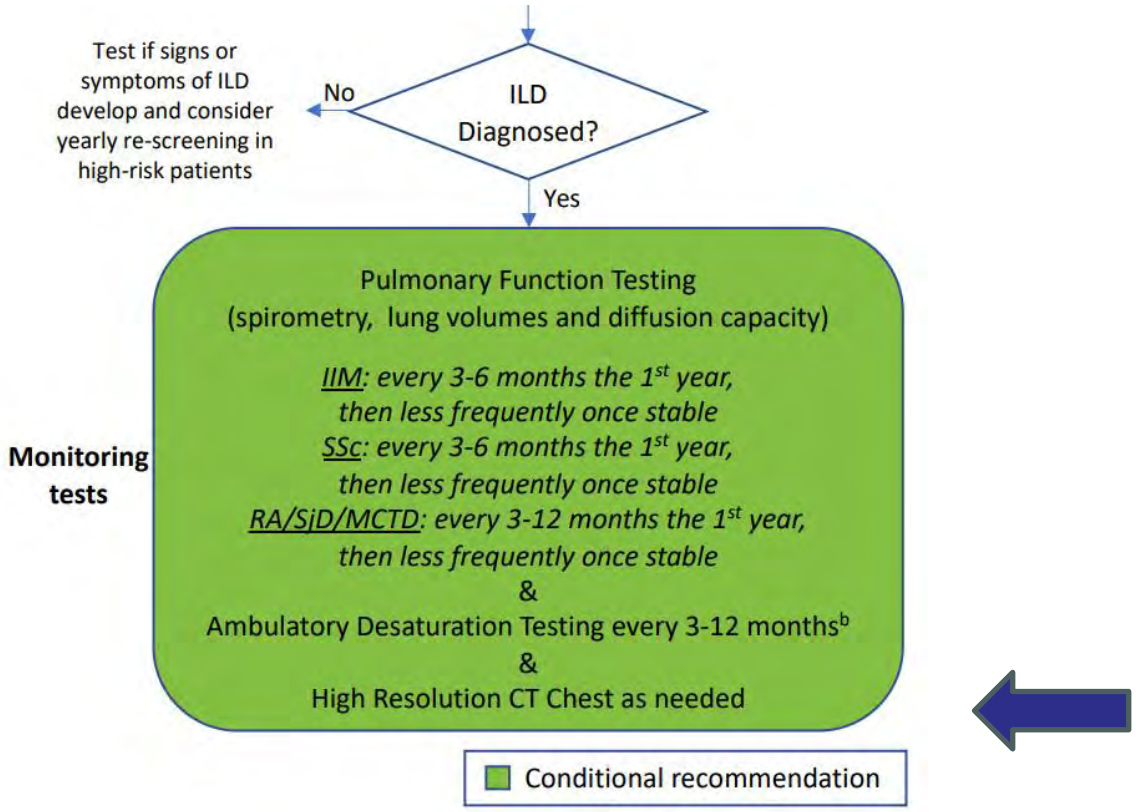

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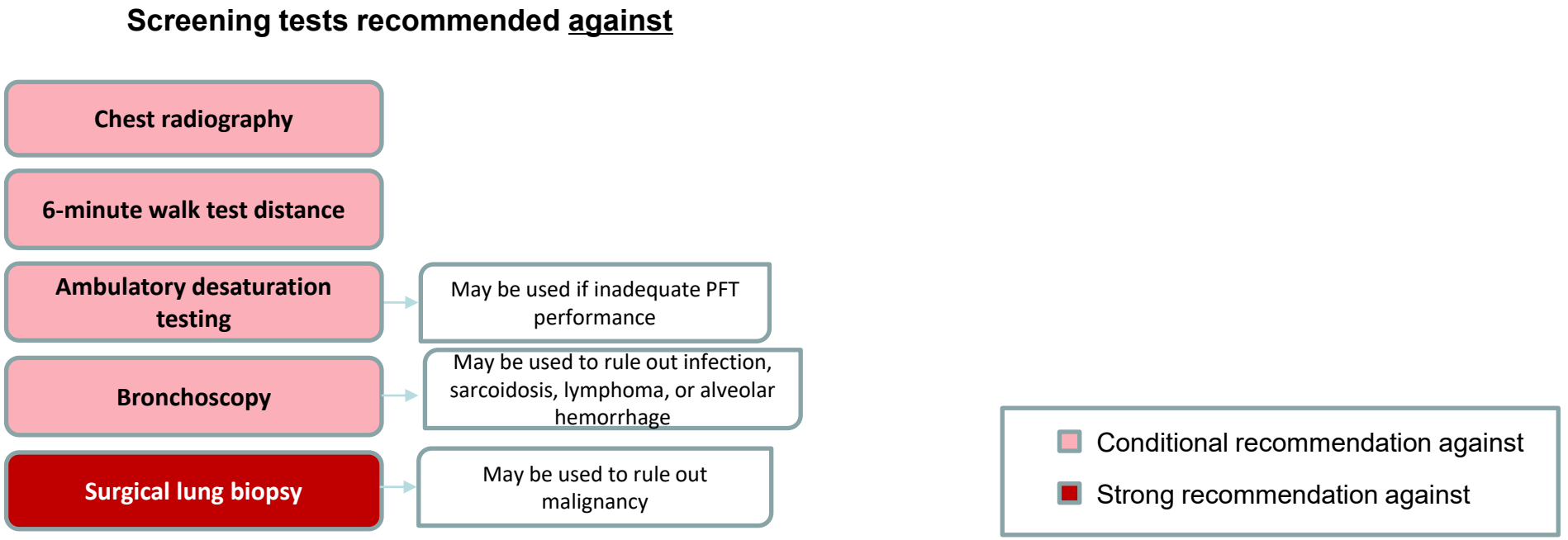
Screening tests recommended <u>against</u>

Figure 2. Interstitial lung disease screening and monitoring tests recommended <u>against</u>. Tests shown are recommended agains
for routine use although examples are provided when these tests may have utility for assessing patients or ruling out other conditions
PFT = pulmonary function test



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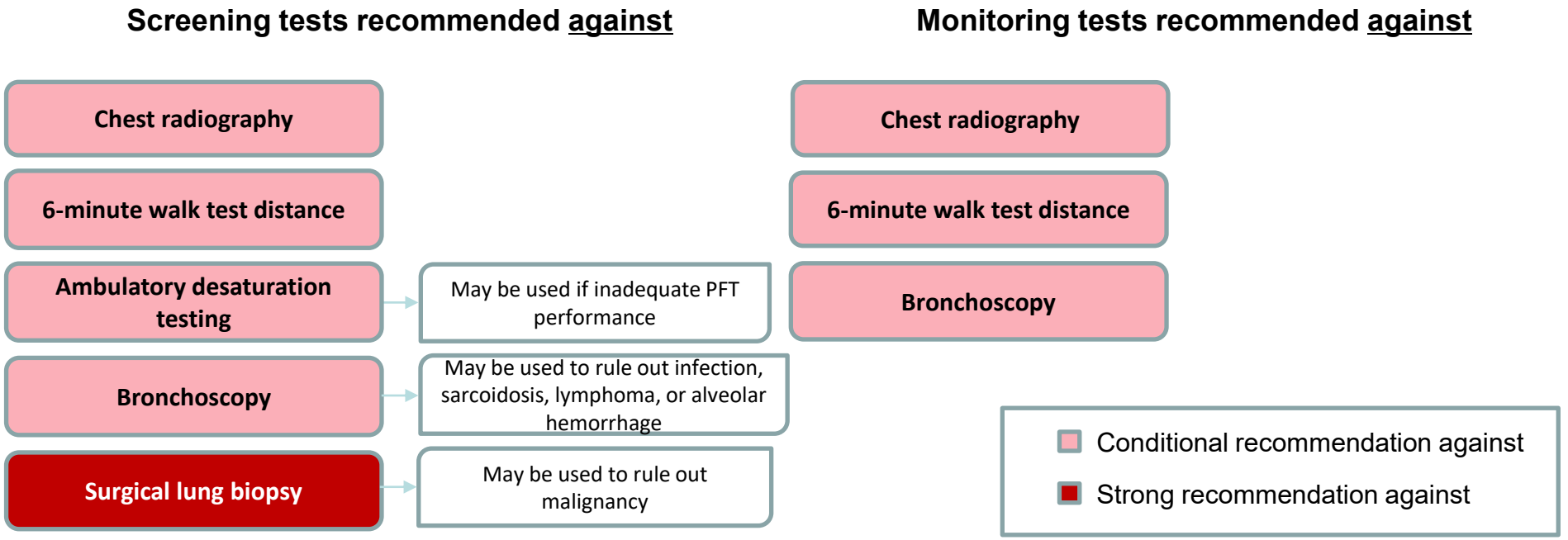

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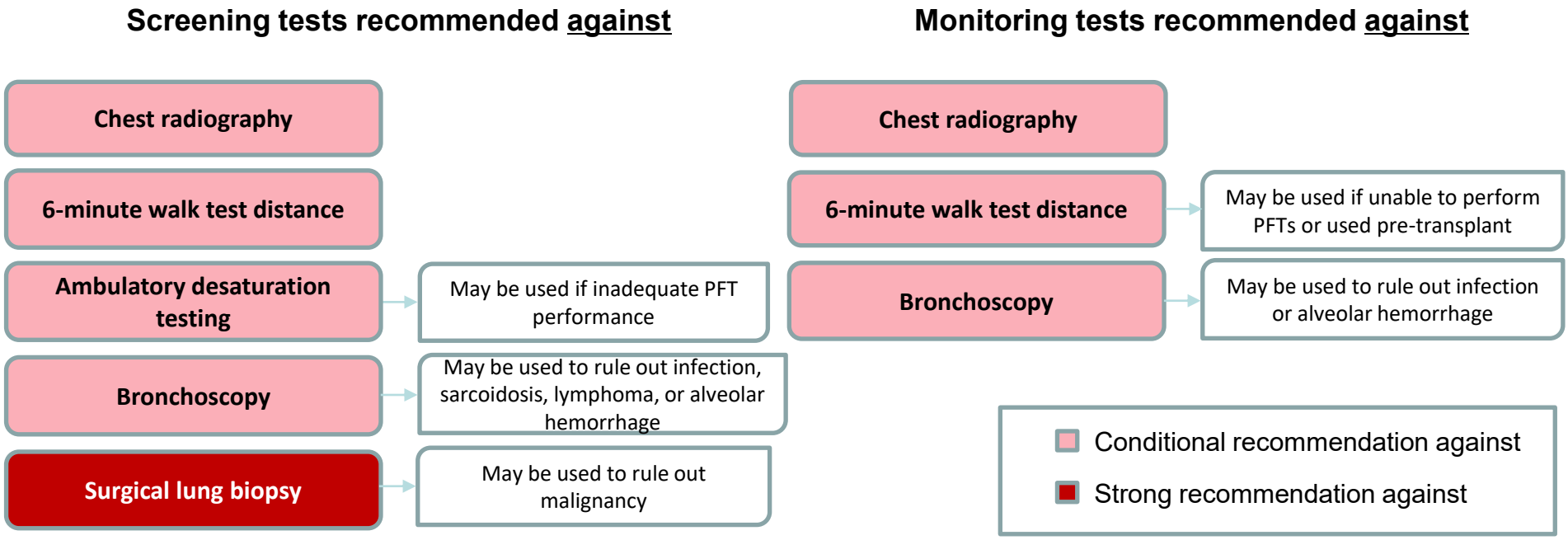

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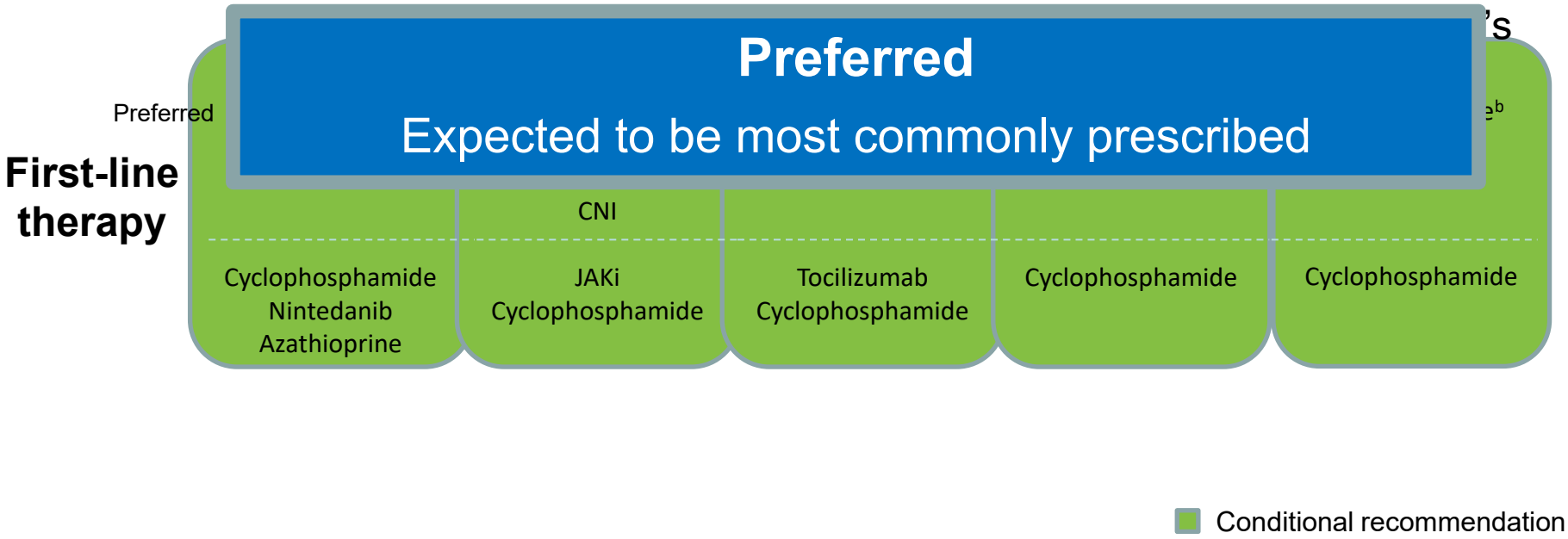
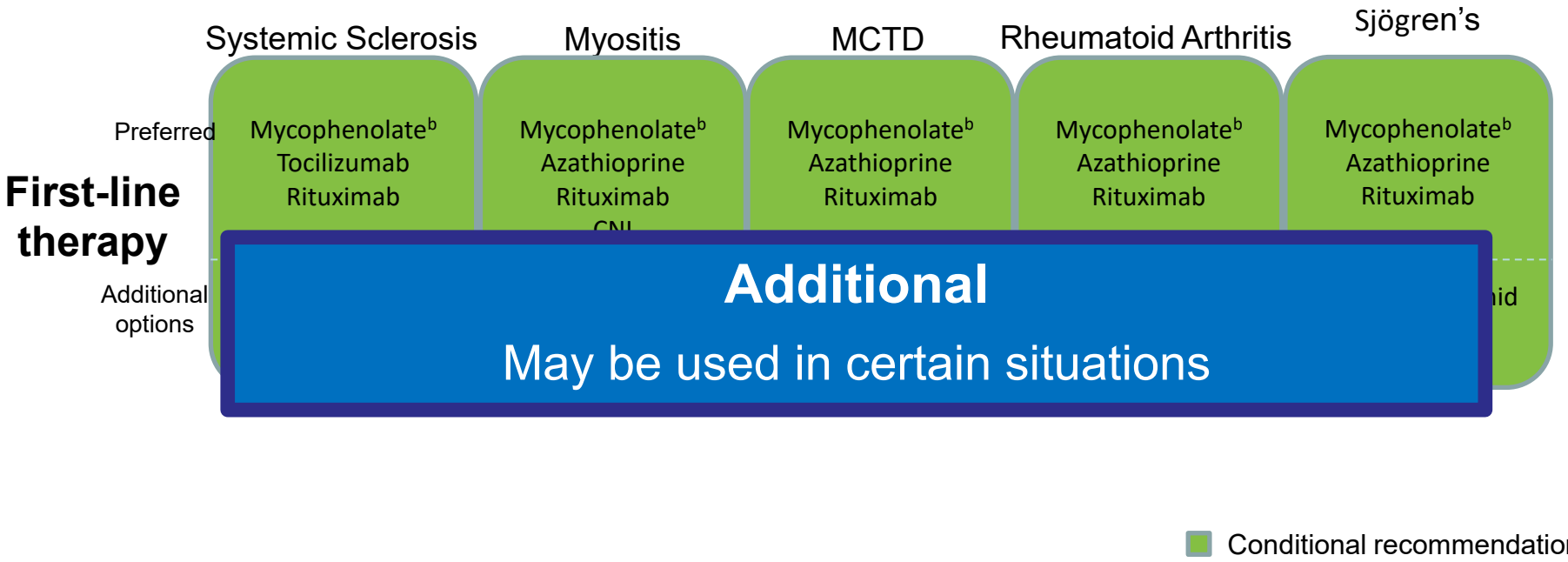


Figure 1: Initial treatment options for the treatment of interstitial lung disease associated with systemic autoimmune rheumatic diseases of interest.

[a] Decisions on GC dose and use of oral versus intravenous therapy depend on severity of disease. GCs should be used cautiously in patients with MCTD with a systemic sclerosis phenotype who may be at increased risk of renal crisis.

[b] Treatments are listed in order based on a hierarchy established by head-to-head votes, although the panel noted that decisions on which first-line therapy to use were dependent on specific situations and patient factors. In all diseases mycophenolate was conditionally recommended over the other listed therapies. Therapies here are divided into “preferred” options and “additional options” based on the rank-order hierarchy.

MCTD = mixed connective tissue disease; GCs = glucocorticoids; CNI = calcineurin inhibitor; JAKi = janus kinase inhibitor



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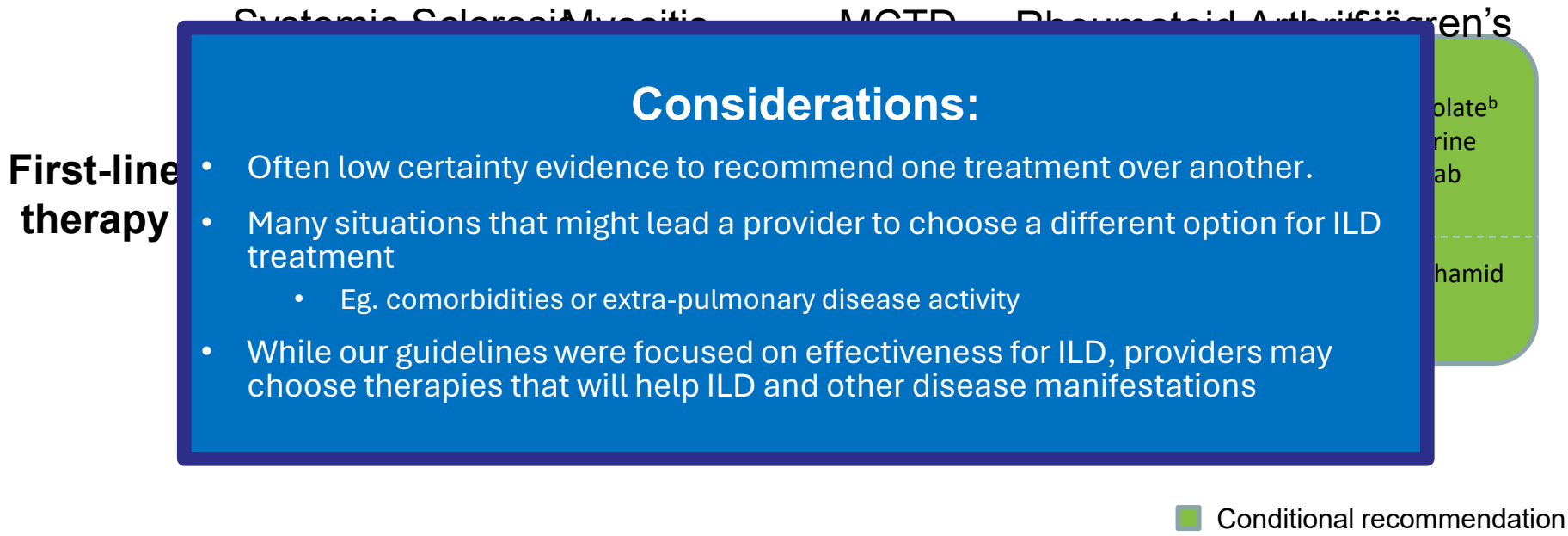

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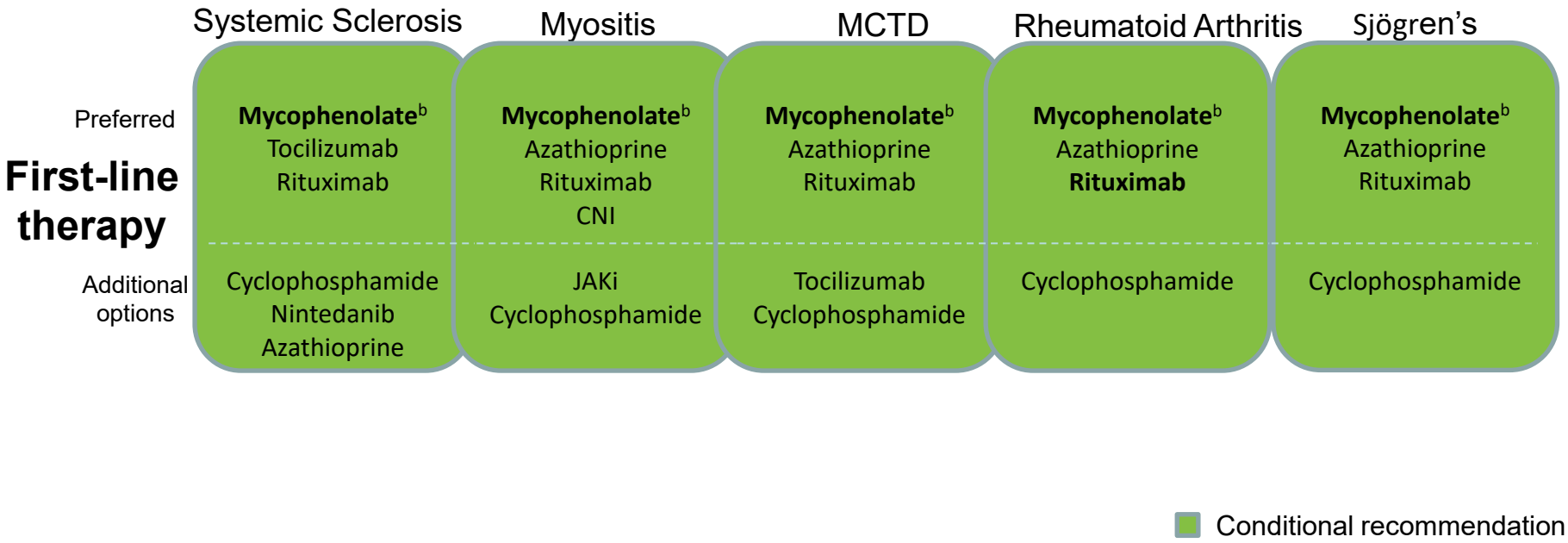

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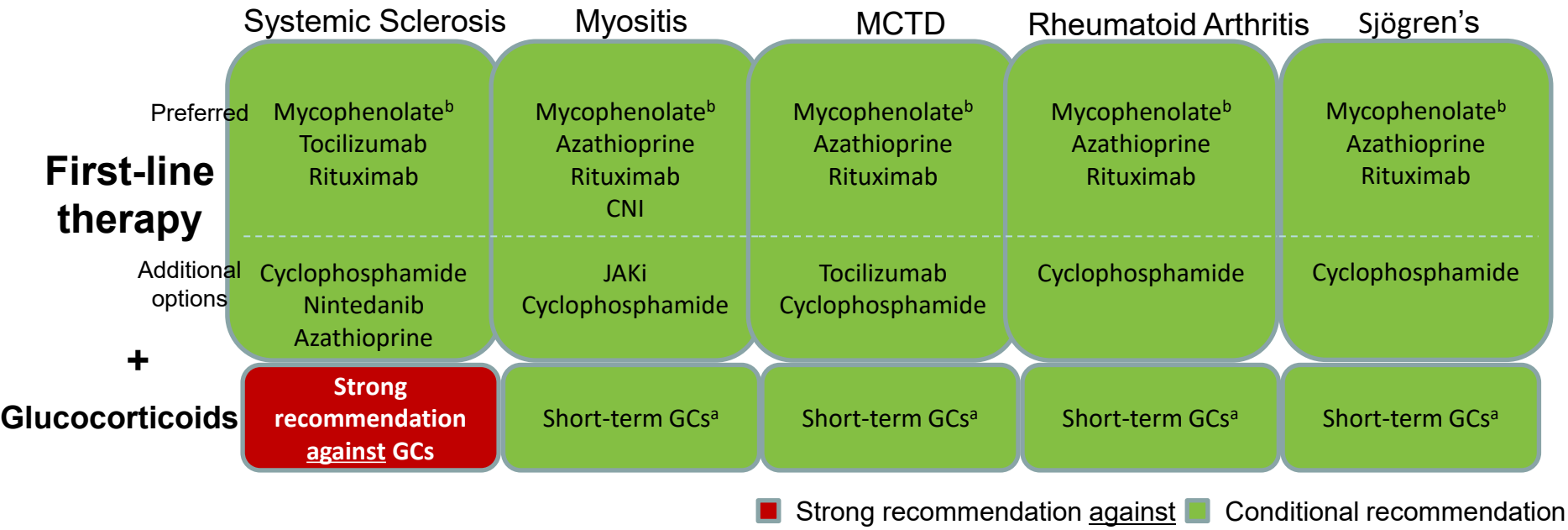

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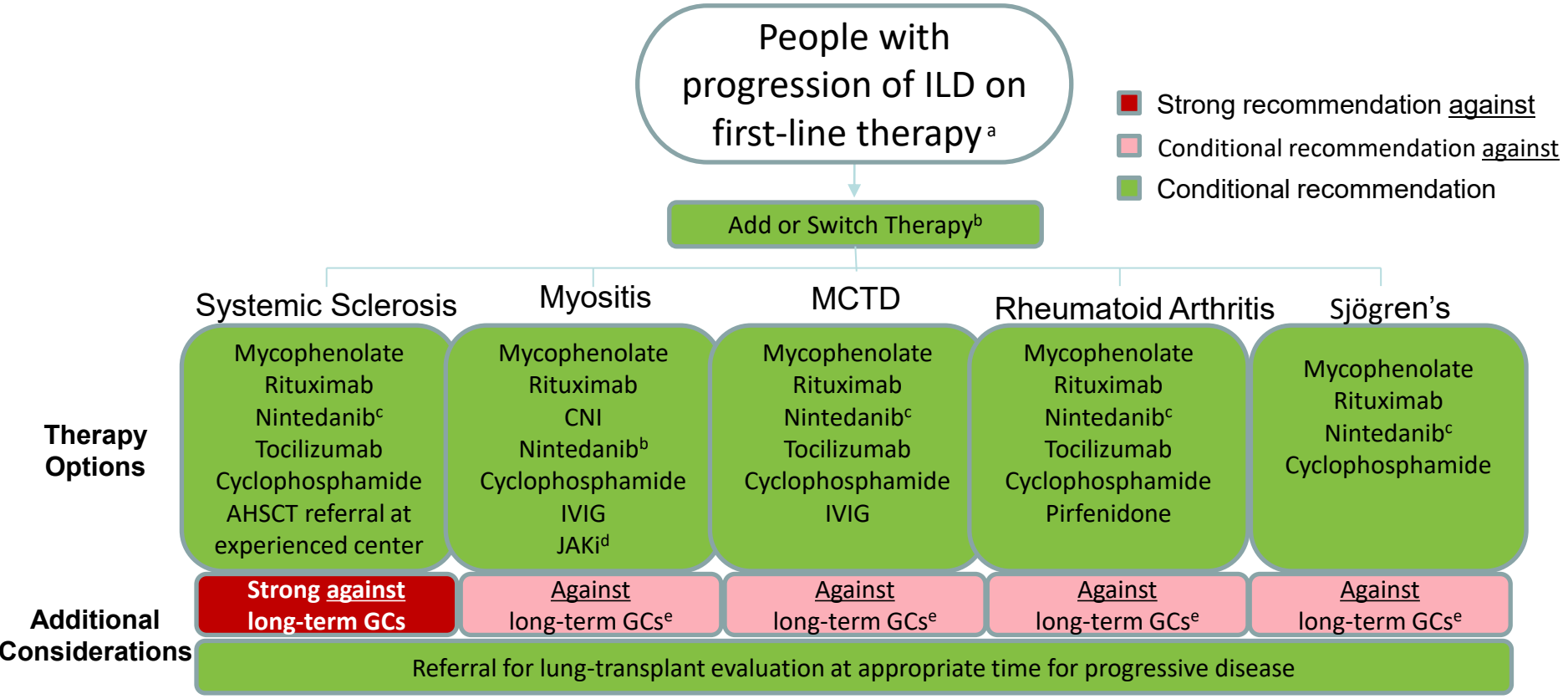
Progression of ILD

Progression was defined using the INBUILD trial criteria

- ✓ a relative decline in the FVC of at least 10% of the predicted value,
- ✓ a relative decline in the FVC of 5% to <10% of the predicted value and worsening of respiratory symptoms, or an increased extent of fibrosis on high-resolution CT
- ✓ worsening of respiratory symptoms and an increased extent of fibrosis

all within 24 months.

Flaherty KR et al. *N Engl J Med.* 2019;381(18):1718-1727.



[a] If intolerance leads to suboptimal dosing of first-line therapy consider switch to an alternative first-line therapy

[b] Therapies are generally listed in order based on a hierarchy established by head-to-head votes, but decisions depend on specific clinical situations. Decision on whether to switch therapy or add to current therapy depends on current therapy and on which therapy is being initiated. Cyclophosphamide is not typically used in combination with other therapies, while others may be used individually or in combination

[c] Decision on use of nintedanib vs immunosuppression depends on pace of progression and amount of fibrotic disease or presence of a usual interstitial pneumonia pattern on CT chest.

[d] JAKi conditionally recommended as an option particularly in patients with anti-MDA-5

[e] Short-term glucocorticoids may be of use in some patients with disease flares or as a bridge when switching therapy

~~MCTD = mixed connective tissue disease; CNI = calcineurin inhibitor; AHSCT = autologous hematopoetic stem cell transplant; GCs =~~ glucocorticoids

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Rapidly Progressive ILD (RP-ILD)

A subpopulation of ILD characterized by a

- rapid progression from no oxygen or a patient's baseline oxygen requirement to a high oxygen requirement or intubation
- within days to weeks
- without a documented alternative cause (e.g., infection, heart failure)

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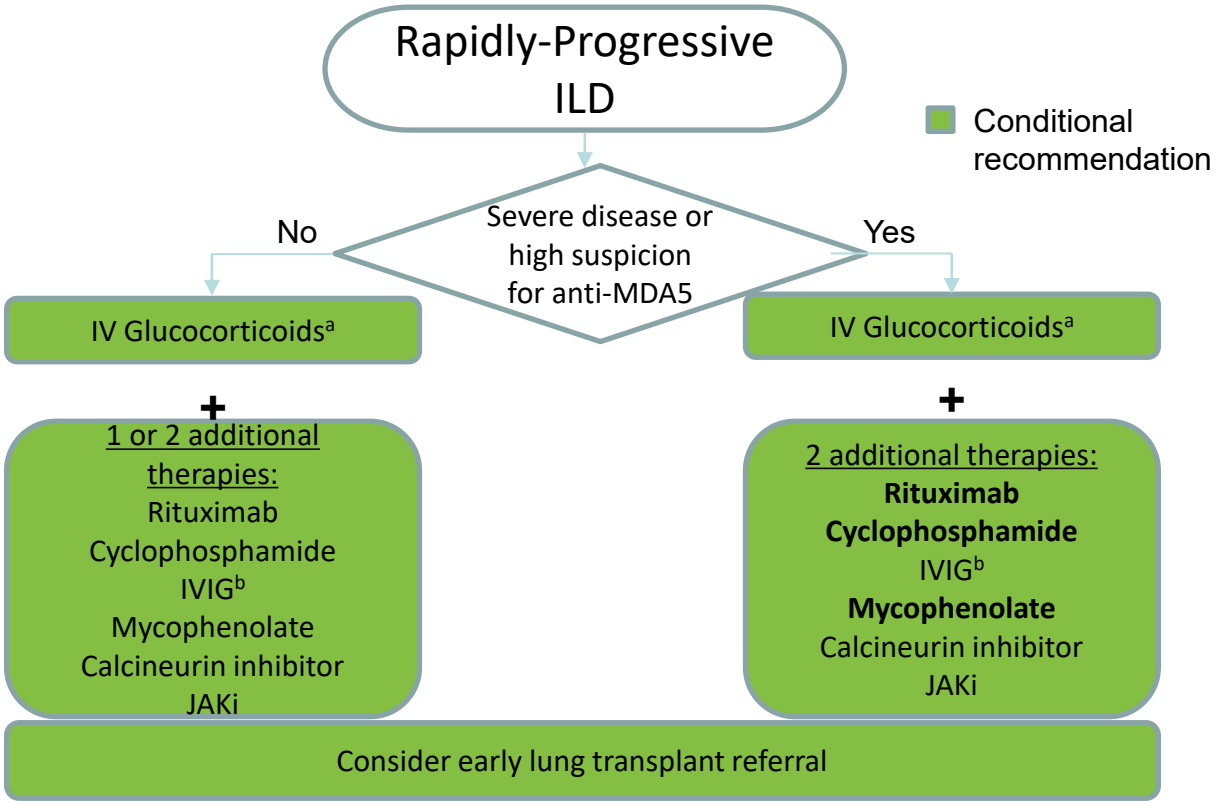

[a] In rare patients with systemic sclerosis with rapidly progressive ILD there was no consensus on whether or not to use glucocorticoids – if used patients should be monitored closely for evidence of renal crisis.
[b] Rituximab and cyclophosphamide recommended over IVIG, but IVIG may be preferred if there is high concern for infection
ILD = interstitial lung disease; IV = intravenous; IVIG = intravenous immune globulin; JAKi = janus kinase inhibitor

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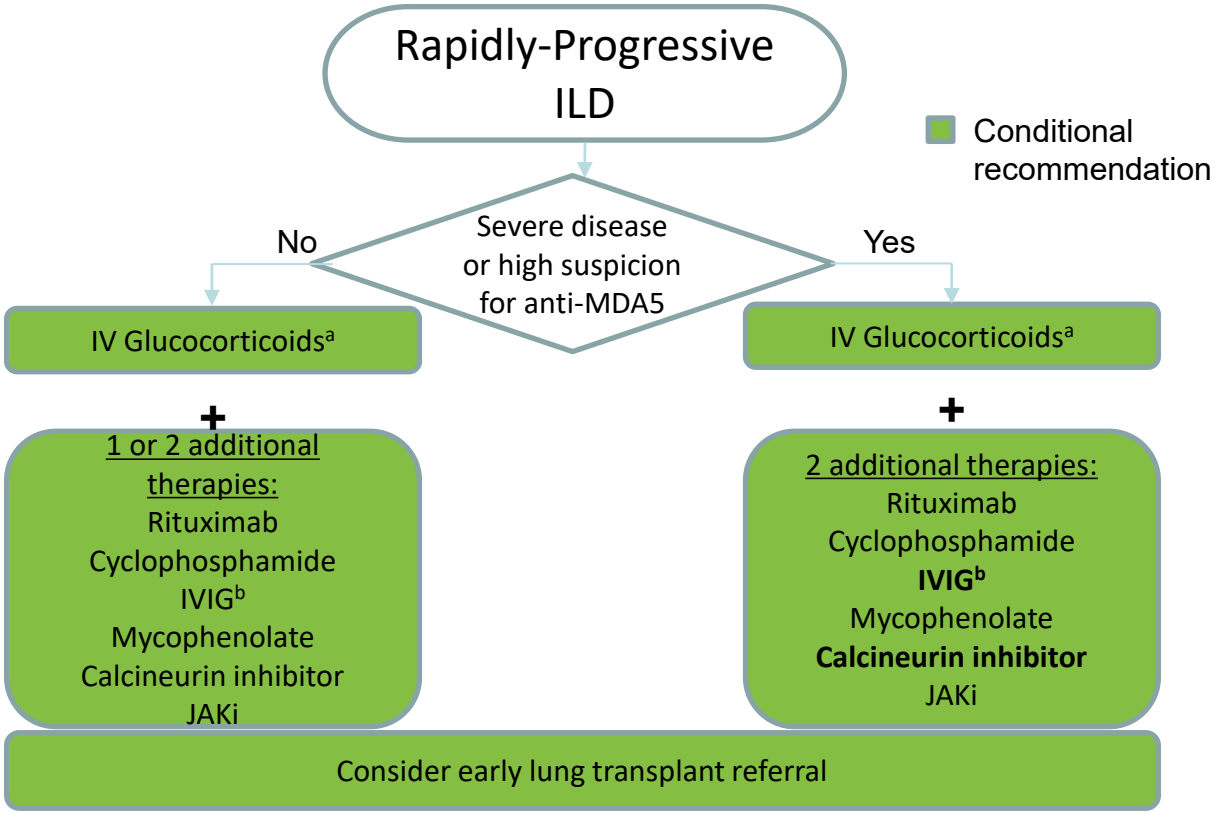

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These guidelines should not be used by insurers to mandate a specific order of prescribing

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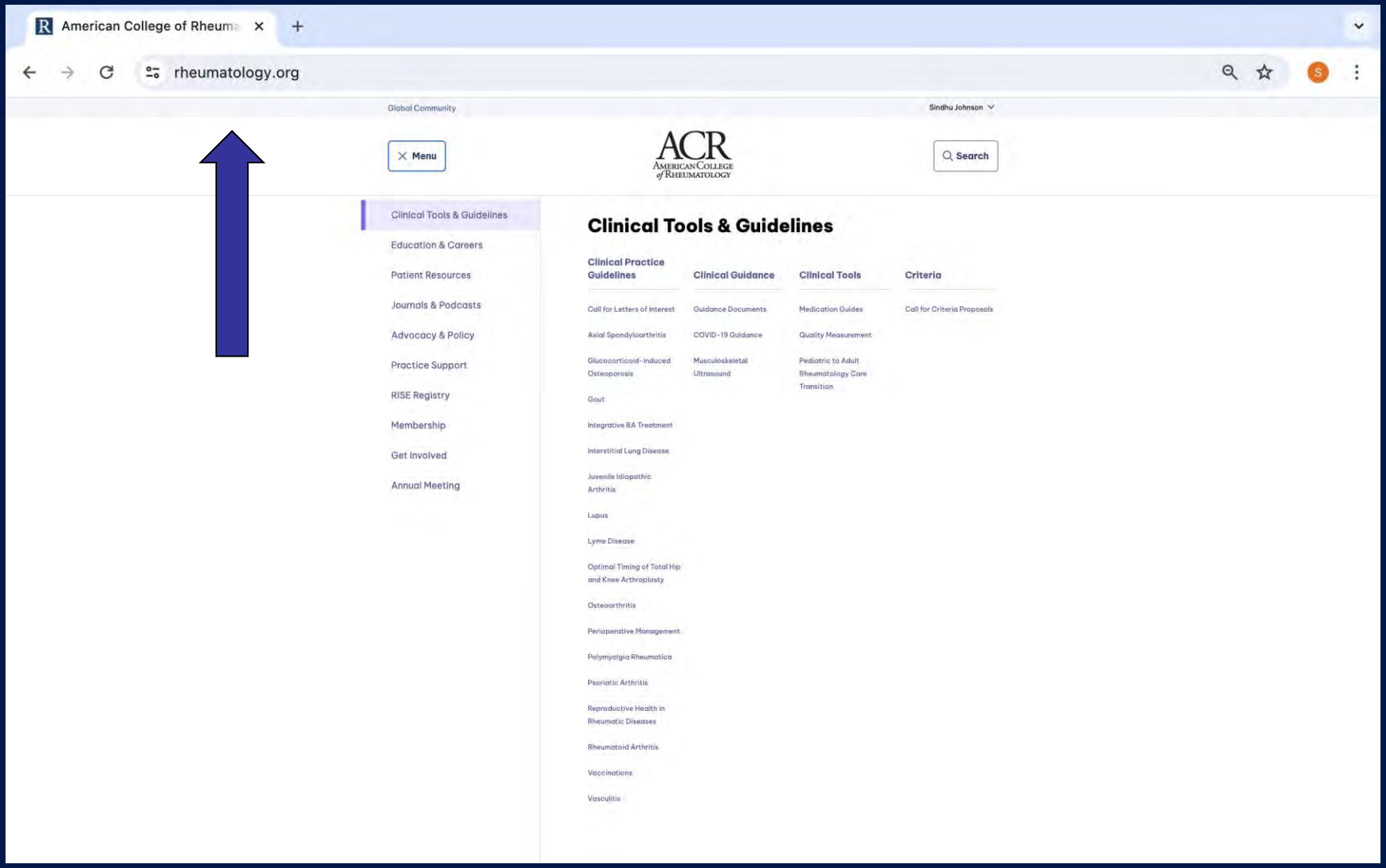
Clinicians must retain the latitude to prescribe medications based on individual patient's factors & preferences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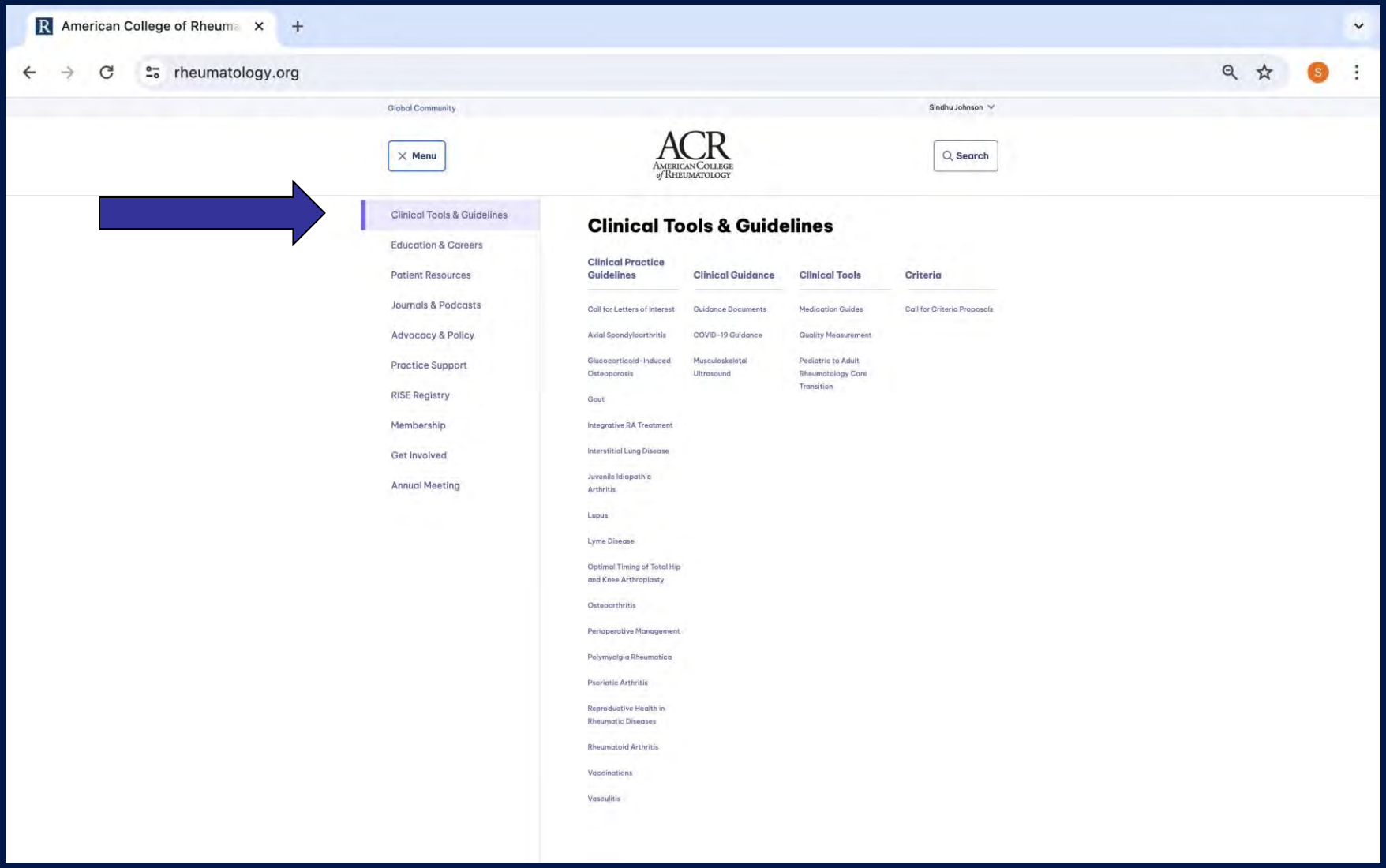
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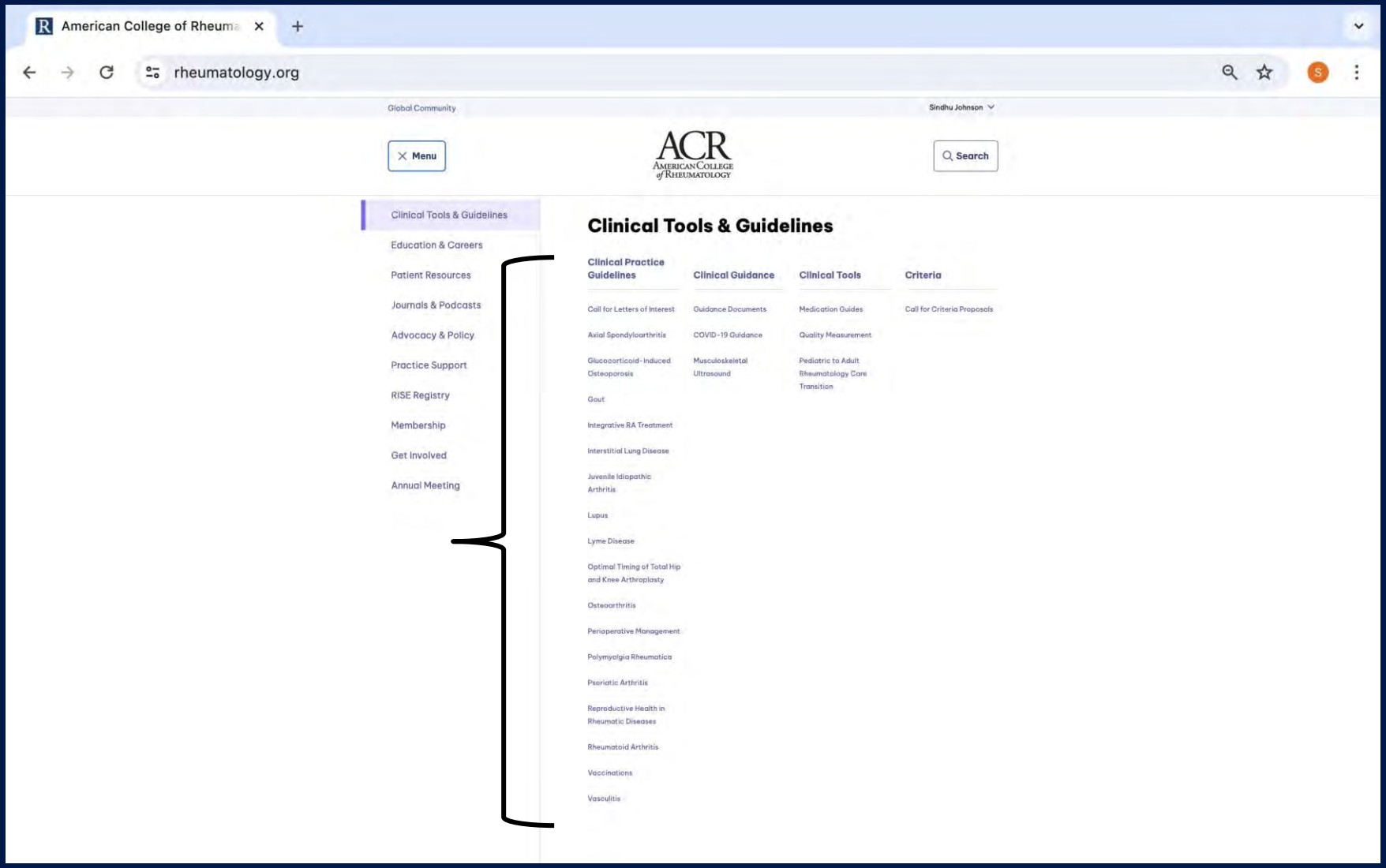
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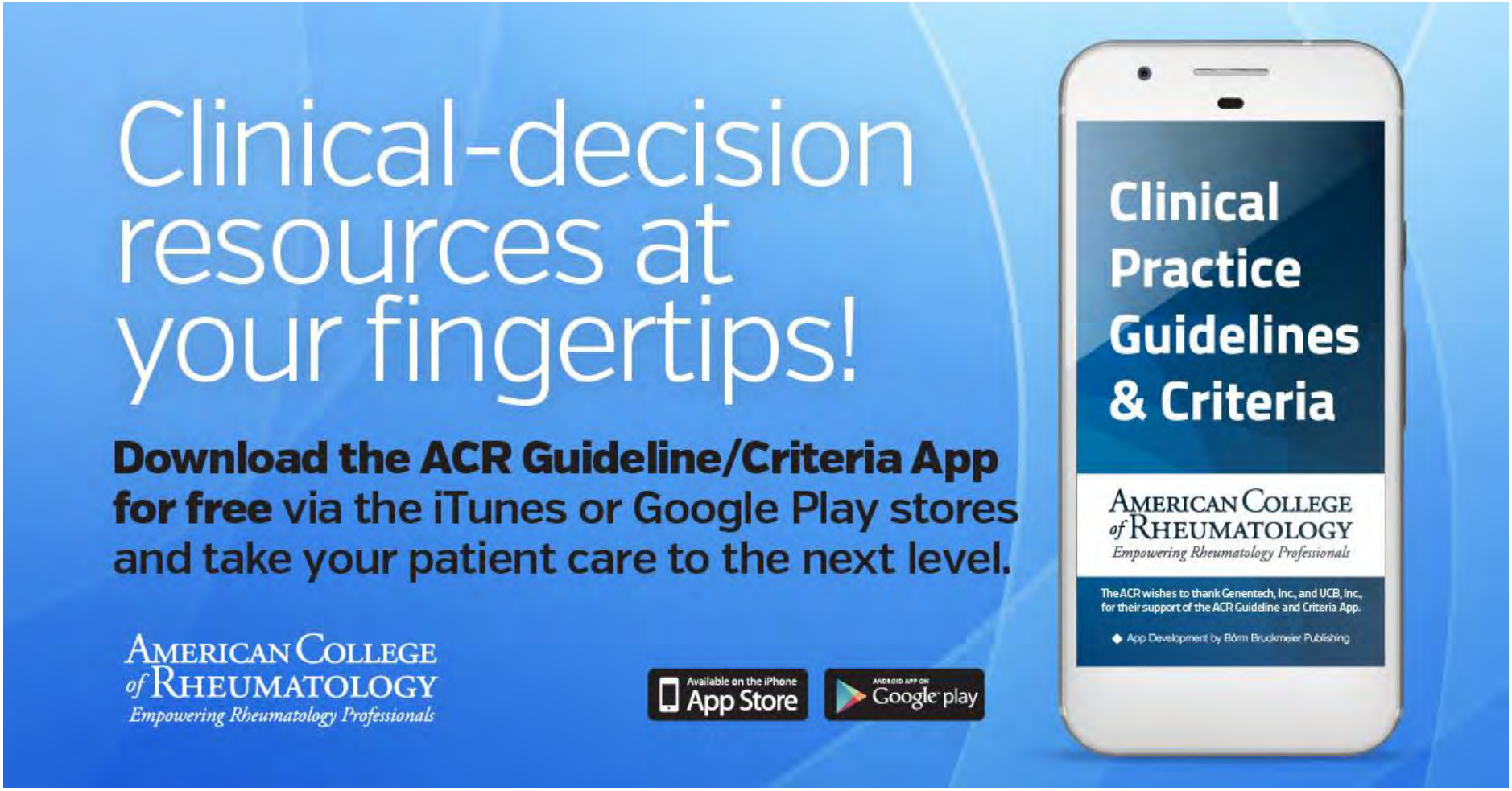
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Clinical Practice Guidelines & Criteria
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The ACR wishes to thank Genentech, Inc., and UCB, Inc., for their support of the ACR Guideline and Criteria App.
App Development by Börm Bruckmeier Publishing

Dr Gordon Guyatt
Father of Evidence Based Medicine

Time is a limited resource

Clinicians want:

- Trusted
- Curated

source of information

Summary

In this session, we discussed use of the American College of Rheumatology (ACR) guidelines for rheumatoid arthritis patient care.

At the end of this session, participants will be able to:

1) Explain the ACR guideline process.

2) Describe how a clinician may use multiple guidelines for RA management (RA pharm, RA non-pharm, vaccination, reproductive, etc.),

3) Discuss how RA guidelines have been evolving to cover more systemic aspects of the disease over time (e.g., osteoporosis, ILD)

Rheumatoid Arthritis Treatments and Guidelines

Sindhu Johnson MD PhD
Professor of Medicine
Director, Clinical Epidemiology & Health Care Research
Dalla Lana School of Public Health
University of Toronto

Patient Panel

- People with the disease or at risk of complications
- Provided their values and preferences regarding screening, monitoring, and treatment of SARD-ILD

Assessing Patient Values and Preferences to Inform the American College of Rheumatology Interstitial Lung Disease Guidelines

Patient engagement is critical to clinical practice guideline development. We present our approach to ascertaining patients' values and preferences to inform the American College of Rheumatology Guidelines for Screening, Monitoring, and Treatment of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases.

Themes Identified

Goals of Treatment

"My goal was to survive, then achieve small life goals with my children, go back to work, talk without choking, smell flowers again."

Communication

"My doctor helps me see the big picture of how I could benefit from the medicine, what we are trying to avoid longer term."

Side Effects of Treatment

"...it depends on how sick I am and how badly I need to manage my disease symptoms."

Screening & Monitoring

"With autoimmune diseases, things just come up, and sometimes you don't even think to mention it as a patient. So screening can be important, even just on history, to catch things that may otherwise be overlooked."

"I thought shortness of breath was just fear and dermatomyositis. Early detection is very key and important."

Mirza RD, Bolster MB, Johnson SR, et al. Assessing patient values and preferences to inform the American College of Rheumatology interstitial lung disease guidelines. Arthritis Care Res (Hoboken) 2024.

Arthritis Care & Research

American College of Rheumatology
Empowering Rheumatology Professionals

Medicine
University of Toronto
Rheumatology

Interventions	Examples
Integrative	
Exercise	Aerobic, resistance training, yoga, tai chi
Palliative care	Symptom treatment (cough, pain, air hunger), end of life planning
Physiotherapy	Chest physiotherapy, airway clearance, incentive spirometry
Pulmonary Rehabilitation	Cardiopulmonary rehabilitation, resistance training
Supplemental oxygen	Oxygen administration by nasal prongs

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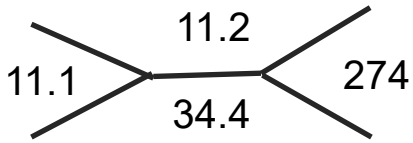
Pharmacologic	
Gastroesophageal reflux management	Proton pump inhibitors, H2 blockers
Pneumocystis jirovecii pneumonia prophylaxis	Trimethoprim sulfamethoxazole
Promotility agents	Domperidone
Vaccines	Measles, mumps, rubella, influenza, Covid-19, pneumococcus, zoster, RSV

APPLY GUIDELINES TO CASES

Case 2: 64-year-old female with rheumatoid arthritis

- Symptoms of inflammatory arthritis- 2014
- RA diagnosis in 2016
- 30-pack-year smoking history
- Current DMARD therapy
  - Anti-TNF therapy
  - Methotrexate 25 mg/ week
- Symptoms
  - SOE on flat ground- 2021
  - Cough 2021
- Examination in 2022
  - SJC 10/28
  - TJC 4/28
  - +Rheumatoid nodules
  - +Subluxations

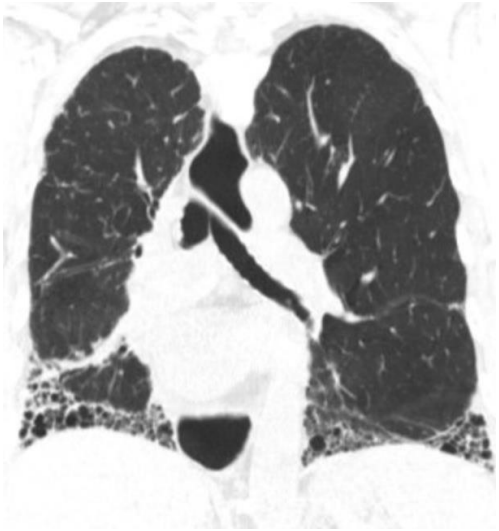


ESR **62** mm/hr (0-20 mm/hr)
CRP **4** mg/dL (< 0.6 mg/dL)
+Anti-CCP
+Rheumatoid Factor

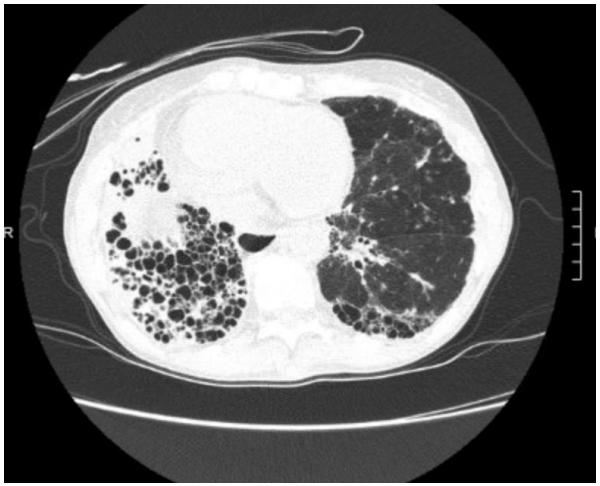
HAQ-DI 1.5

Initial evaluation

	07/2022
FVC, Liter	3.07
FVC, % predicted	66%
TLC, % predicted	68%
Fev1/ FVC	72%
DLCO, % predicted	68%



Coronal View



Axial View

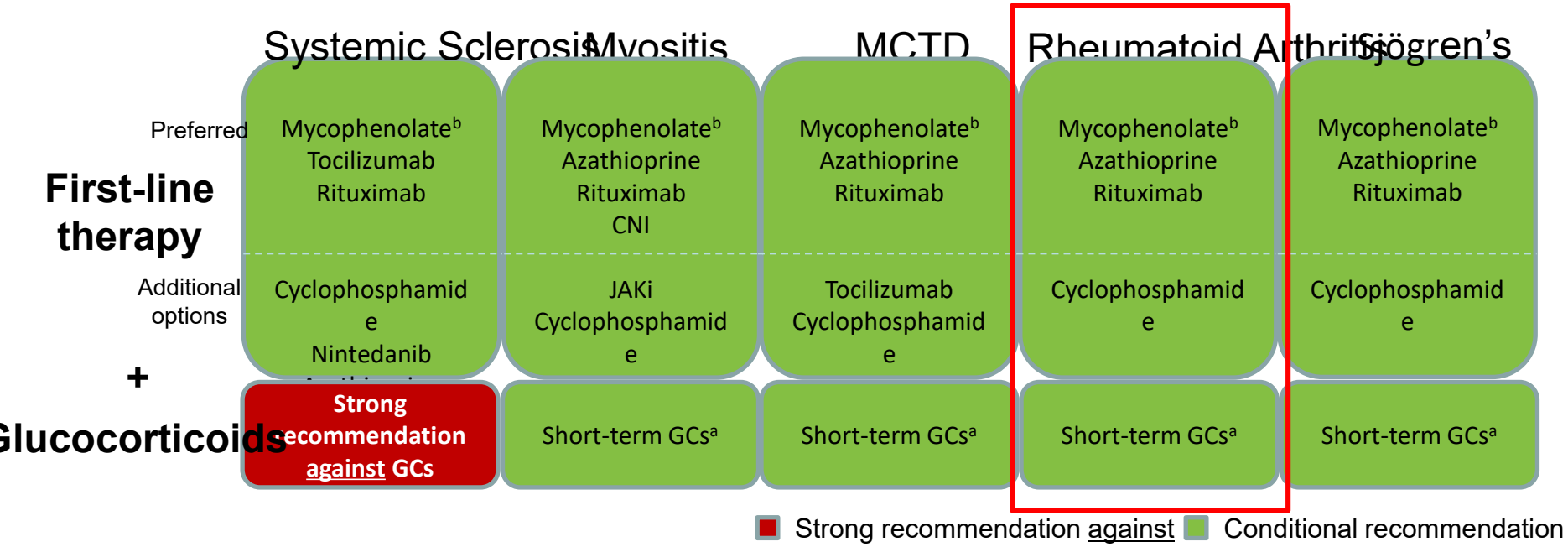


Figure 1: Initial treatment options for the treatment of interstitial lung disease associated with systemic autoimmune rheumatic diseases of interest.

[a] Decisions on GC dose and use of oral versus intravenous therapy depend on severity of disease. GCs should be used cautiously in patients with MCTD with a systemic sclerosis phenotype who may be at increased risk of renal crisis.

[b] Treatments are listed in order based on a hierarchy established by head-to-head votes, although the panel noted that decisions on which first-line therapy to use were dependent on specific situations and patient factors. In all diseases mycophenolate was conditionally recommended over the other listed therapies. Therapies here are divided into "preferred" options and "additional options" based on the rank-order hierarchy.

MCTD = mixed connective tissue disease; GCs = glucocorticoids; CNI = calcineurin inhibitor; JAKi = janus kinase inhibitor

Initial management of ILD

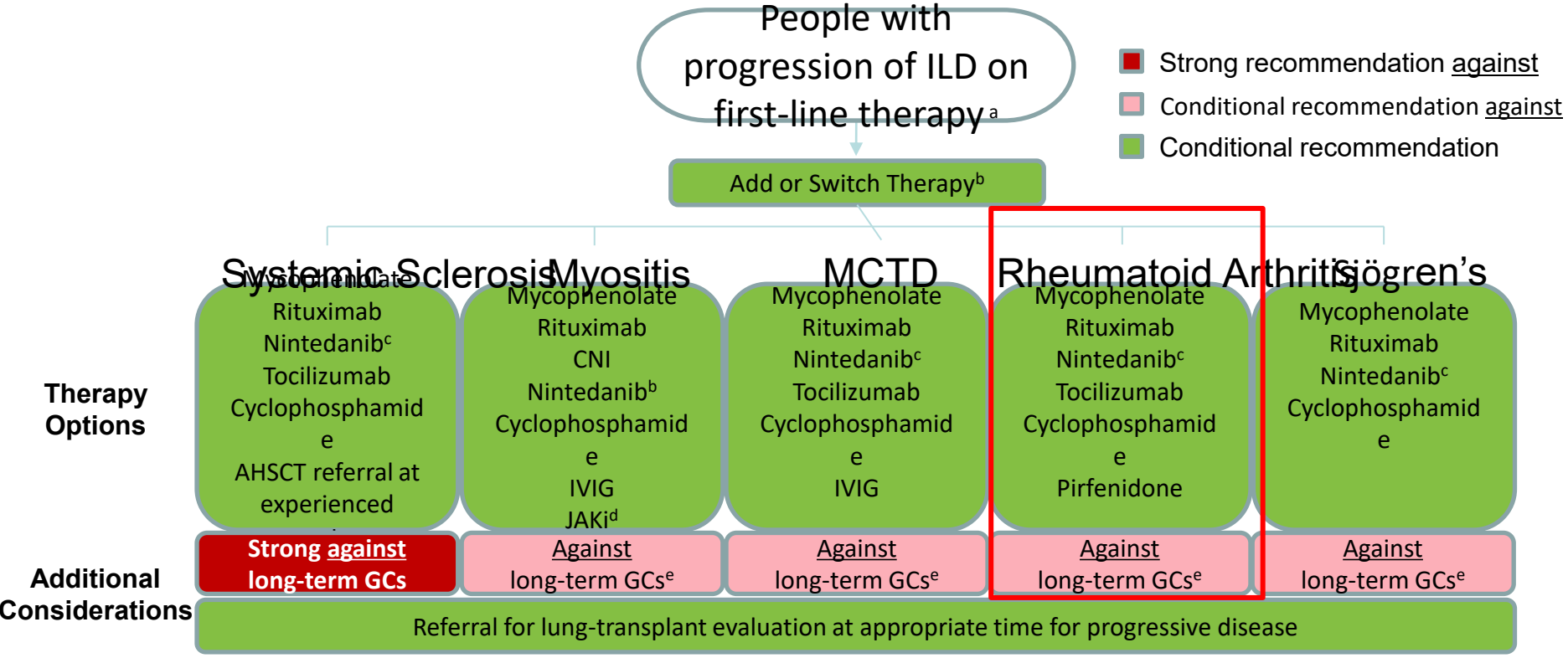
- Changed anti-TNF to rituximab 1000 mg x 2
- Continued MTX at 25 mg/week
  - Presence of articular disease
  - Minimal concern about pneumonitis
- Didn't prescribe short term glucocorticoids- UIP Pattern and fibrotic disease

Serial PFTs

	07/2022	03/2023
FVC, Liter	3.07	3.05
FVC, % predicted	66%	65%
TLC, % predicted	68%	Not Done
Fev1/ FVC	72%	69%
DLCO, % predicted	68%	65%

6 minute walk test

Walked 450 m (66% of predicted)
95% on room air at rest
91% on room air during walk



[a] If intolerance leads to suboptimal dosing of first-line therapy consider switch to an alternative first-line therapy

[b] Therapies are generally listed in order based on a hierarchy established by head-to-head votes, but decisions depend on specific clinical situations. Decision on whether to switch therapy or add to current therapy depends on current therapy and on which therapy is being initiated. Cyclophosphamide is not typically used in combination with other therapies, while others may be used individually or in combination

[c] Decision on use of nintedanib vs immunosuppression depends on pace of progression and amount of fibrotic disease or presence of a usual interstitial pneumonia pattern on CT chest.

[d] JAKi conditionally recommended as an option particularly in patients with anti-MDA-5

[e] Short-term glucocorticoids may be of use in some patients with disease flares or as a bridge when switching therapy

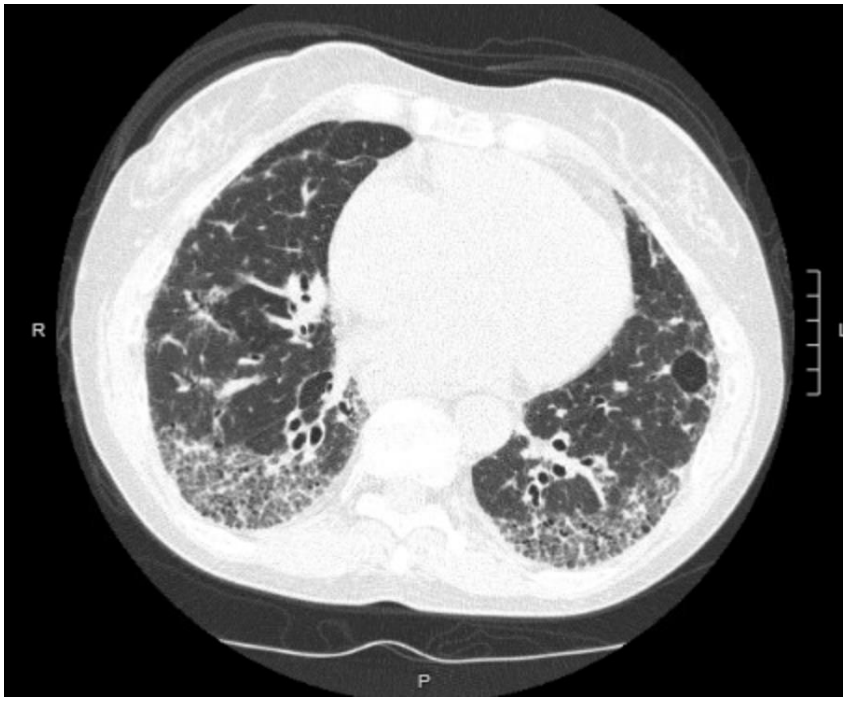
MCTD = mixed connective tissue disease; CNI = calcineurin inhibitor; AHSCT = autologous hematopoetic stem cell transplant; GCs = glucocorticoids

Follow up management of ILD

- Continued on rituximab 1000 mg x 2 q 6 months and MTX at 25 mg/week
- Improvement in joint counts and overall well being
  - SJC 2/28
  - TJC 3/28
  - HAQ-DI 1.0
- Initiated nintedanib 150 mg po BID due to UIP pattern and fibrotic ILD

HRCTs trends

07/ 2020



07/2021