A Narrow Window of Opportunity:

Diagnosis and Management of Rheumatoid Arthritis in Underserved Populations

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General Objective:

To improve the knowledge, confidence, and performance of primary care physicians and other healthcare clinicians in the care of rheumatoid arthritis (RA) among diverse populations.

Specific Objectives:

At the end of this activity learners will be able to:

- Recognize signs and symptoms suggestive of RA
- Determine when to refer patients with RA to a rheumatologist
- Develop a comfort level in prescribing disease-modifying antirheumatic drugs (DMARDs)
- Help patients understand their disease and engage in shared decision making
- Use motivational interviewing to recognize patients' concerns
- Recognize and mitigate implicit bias to build a culture of equity in their practice

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INTRODUCTION:

The Impact of Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disorder that is typically characterized by pain and inflammation in the small joints. If untreated, RA may introduce complications that impact the lungs, eyes, bones, and heart. Affecting an estimated 1.3 million US adults,[1,2] RA represents the most common type of autoimmune arthritis.[3] Although onset commonly occurs between the ages of 30 and 50, RA can manifest at any age. Women account for approximately 75% of diagnosed RA cases, and The American College of Rheumatology (ACR) estimates that 1-3% of women may be afflicted in their lifetimes.[3] Furthermore, analysis of self-reported National Health and Nutrition Examination Survey (NHANES) data from 2005-2018 indicates a significant difference in RA prevalence among people from different races, educational levels, and poverty-income ratio groups.[1] Independent of gender, non-Hispanic African Americans, individuals with an educational level of less than high school, and those with low family income had a significantly higher RA risk than age-adjusted comparator cohorts.[1]

Although it is difficult to obtain exact totals, RA exerts a formidable economic impact. Based on 2010 data, the total annual health costs for the US RA population were estimated to be $19.3 billion dollars.[4] Given various advances in treatment, the economic burden has shifted from inpatient costs to indirect costs (e.g., disability, work absenteeism).[5]

Proactively treating RA will promote tight management and improve the quality of life for patients with the disorder, and many patients who experience symptoms of RA will visit their primary care clinician for treatment. To address the management of RA in primary care, the New Jersey Academy of Family Physicians (NJAFP) assembled a panel of experts to improve patient outcomes by increasing primary care clinicians' knowledge, comprehension, and performance in managing RA, especially when treating underserved populations. To help clinicians understand issues related to RA management, this publication reviews current literature and guidelines and provides recommendations for using pharmacologic and non-pharmacologic modalities to develop successful, personalized management plans for patients who report symptoms of RA.

At-A-Glance

- Primary care clinicians play critical roles in identifying patients who have or are at risk for rheumatoid arthritis (RA) and ensuring that they receive prompt and effective care and appropriate referrals.
- Signs and symptoms of RA may include the bilateral presentation of tender, warm, and swollen joints; joint stiffness that is more notable in the morning or following a period of inactivity; and fatigue, fever, and loss of appetite.
- RA treatment should aim to achieve remission or low disease activity, thus limiting signs and symptoms of disease while enhancing physical function and maintaining quality of life.
- Disease-modifying anti-rheumatic agents (DMARDs) are highly effective pharmacologic options to manage RA and will improve pain symptoms and prevent joint damage.
- Disparities exist in the diagnosis and treatment of RA among various patient populations.
- Clinicians and patients must become partners in ongoing shared decision-making regarding RA management.
- Care pathways that include evidence-based therapies, patient education, support, and collaborations with an informed care team will improve outcomes for all patients, including those that represent underserved groups.

Signs and Symptoms of Rheumatoid Arthritis

RA is a chronic autoimmune inflammatory disease in which the body's immune system attacks the lining of the joints, causing pain, swelling, stiffness, and loss of function.[6,7] RA damages the synovial tissue that envelops the ends of the bones within a joint, which differentiates it from the cartilage degeneration (or "wear and tear") that characterizes osteoarthritis. The inflammation associated with RA eventually causes localized damage (e.g., bone erosion and joint deformity), with more systemic effects reported in approximately 40% of RA patients.[8] Untreated RA may cause irreversible joint damage within the first year of onset.[7] Symptoms vary in severity across individuals and may oscillate between intensive surges known as "flares" and periods of relative remission. A flare may be tied to a likely stressor, such as an environmental factor or viral infection, or have no clearly associated cause.

Signs and symptoms of RA may include tender, warm, and swollen joints; joint stiffness that is more notable in the morning or following a period of inactivity; and fatigue, fever, and loss of appetite.[8] RA can affect joints in the wrists, hands, elbows, shoulders, feet, spine, knees, and jaw,[7] and RA-associated pain usually presents bilaterally. Patients with RA may report discomfort in both hands, both knees, and so forth.[9] "Morning stiffness" associated with RA usually lasts for at least 30 minutes but may lessen as the day's activity commences. The inflammation with RA can notably interfere with numerous daily activities, from buttoning a shirt to combing one's hair to sitting down/standing up. Individuals with RA may exhibit depression or anxiety, possibly resulting from physical symptoms and/or chronic inflammation.

The specific causes of RA are not known, although it has been postulated that RA-related autoimmunity may begin in the oral, lung, or gastrointestinal mucosa years before the onset of joint symptoms.[10] However, certain genetic and environmental factors are associated with the risk of developing RA.[9] The Centers for Disease Control and Prevention (CDC) notes that the likelihood of RA onset increases with age, peaking for individuals in their sixties. Furthermore, women are 2-3 times more likely to develop RA than men. RA risk and severity have been linked with smoking, obesity, and human leukocyte antigen (HLA) Class II genes. Early life exposure to secondhand smoke may also increase the risk of developing RA as an adult. The CDC also notes that women who have never given birth may be at greater risk of developing RA, while women who breastfeed their infants may have a *decreased* risk of RA.

The Role of the Primary Care Clinician

Primary care clinicians play critical roles in identifying patients who have or are at risk for RA and ensuring that they receive prompt and effective care.

The primary care clinician should communicate with patients who have signs of RA and support those who require additional assessment and ongoing services. Additional roles of the clinician include:

- Identifying patients at risk for RA or other connective tissue or autoimmune disorders
- Assessing and determining referral needs
- Understanding cultural factors and patient preferences for treatment
- Discussing treatment options and adjunctive interventions
- Coordinating efforts with an RA care team (e.g., rheumatologist, physical therapist, gynecologist, pulmonologist, dietitian, social worker)
- Keeping the patient actively engaged in disease management

Given that many patients may be uncomfortable when receiving a diagnosis of RA, the primary care clinician must recognize that he or she provides key support to help the individual receive proper treatment. In some cases, the clinician may represent the patient's sole resource when seeking help.

Diagnosing RA

RA is a chronic disorder, and early diagnosis and prompt treatment are critical to retard disease progression, minimize potential disability, and improve the patient's outcome and quality of life. There is no single blood test or physical finding that confirms a diagnosis of RA unequivocally, and early symptoms can resemble those of other forms of arthritis. The clinician must therefore use a combination of physical examination/medical history, imaging, and laboratory tests to rule out other conditions. The American College of Rheumatology (ACR) notes that RA symptoms usually need to be present for more than three months to consider a diagnosis of RA, although some patients are diagnosed sooner.[3]

Medical History and Physical Exam. When a patient presents with symptoms that suggest RA, the first step is to collect a full medical history and conduct a thorough medical exam. Communicating with the patient about their symptoms and history will provide insight into symptom duration, comorbidities, risk factors, and potential exacerbating factors. The physical examination should assess the severity of the inflammation and potential complications. Suggestions regarding what to ask and observe in a patient who presents with symptoms of RA are listed in Table 1.

TABLE 1. What to Ask a Patient Who Presents with RA Signs and Symptoms

- A review of joint symptoms—anatomic location, when and how the patient noted their presence, how they have changed over time
- Limitations that symptoms have imposed on the patient's activities
- Other symptoms that could indicate chronic inflammation (e.g., weight loss, fever, fatigue, weakness, difficulty breathing)
- Other medical conditions (e.g., depression/anxiety)
- Family history of RA or family members with similar symptoms
- Medication history
- Diet and activity
- Smoking history
- Vaccination status
- Relevant cancer screenings

Although the physical exam should assess joint swelling and stiffness, the inflammation associated with RA can also affect the lungs, skin, eyes, and digestive and cardiovascular systems. Interstitial lung disease (ILD) is a common complication of RA, and it has been estimated that approximately one-third of patients with RA may have subclinical disease with possible functional impairment.[14] A complete physical examination should assess the lungs for inflammation. Skin nodules should be noted along with signs of cardiovascular disease or diabetes.

The ACR endorses five RA disease activity measures and three RA functional status assessment measures for use in routine clinical practice.[11,12] These tools, which can be used in telehealth visits,[13] help clinicians rapidly assess the severity of a patient's RA. ACR Guidelines for the Treatment of RA can be found here. Disease Activity and Functional Status Assessments can also be found on the ACR website.

Imaging. Several imaging modalities, including X-rays, MRI, and ultrasound, can be considered when diagnosing or monitoring RA disease progression. Although X-rays are often normal during the early stages of RA, they can sometimes rule out other conditions. MRI of symptomatic areas such as the hand or wrist may also support a diagnosis of RA or inflammatory arthritis. Early-stage RA is associated with periarticular osteoporosis (osteopenia),[15] and measurement of bone mineral density (of the hand) using imaging can predict the severity and progression of the joint destruction. Ultrasound can indicate synovitis, synovial hypertrophy, and/or power Doppler signal (increased circulation associated with inflammation).

Blood Tests. As noted earlier, no single test confirms a diagnosis of RA. However, many blood-based biomarkers, including rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP) antibodies (ACPA), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and antinuclear antibodies (ANA), can indicate inflammatory processes and aid with differential diagnoses.

Most patients with RA will present serologic evidence of disease by the time symptoms are evident. RF and ACPA are serologic markers that can serve as diagnostic and prognostic indicators of autoimmune disease. The presence of high-titer RF indicates increased risk for extra-articular involvement, and the presence of ACPA points to aggressive disease with risk for erosive disease. However, both tests are negative on presentation in up to 25% of patients with RA and can remain negative during follow-up in 20% of these individuals.[16] A positive result on both tests increases the specificity compared to either test alone. However, it is possible for a patient with RA to be seronegative (to have low RF and ACPA levels) and for a patient's classification to change from seronegative to seropositive over time.

ESR and CRP are acute-phase reactants, markers that undergo significant serum concentration changes in response to inflammation. Both are typically elevated in RA and can be used to monitor systemic inflammation following initial evaluation and/or diagnosis.[16] When

patients are monitored serially, changes in ESR and CRP levels can also be used to assess treatment response.

Antinuclear antibody (ANA) panel testing using immunofluorescence assays (IFA) will identify the presence of antinuclear antibodies that are associated with autoimmune rheumatic diseases, including RA, systemic lupus erythematosus (SLE), systemic sclerosis (scleroderma), and mixed connective tissue disease as well as some viral infections (e.g., Epstein-Barr, HIV, hepatitis C, parvovirus). A positive ANA test indicates an autoimmune reaction process, although up to 15% of healthy people have positive ANA test results.[17] The ANA may be positive in up to one-third of patients with RA.[16] However, ANA testing has limited value in patients who present solely with nonspecific symptoms, such as malaise and fatigue.[18]

ANA test results are usually reported in titers (levels) and patterns. The titer of the antibodies refers to the highest dilution of serum that produces visible fluorescence. It is reported as a ratio that reflects the number of serial 1:1 saline dilutions of the plasma; commonly reported titers include 1:40, 1:80, 1:160, 1:320, and 1:640. Although a titer of 1:160 is a common standard to define a positive ANA, laboratories vary in their qualification standards. Moreover, ANA titers may change during the course of the disease, and fluctuations do not necessarily correlate with disease activity.[19] ANA tests are also reported in patterns (e.g., homogeneous, speckled, centromere) that refer to the distribution of staining observed when ANA reacts with antigens in the human HEp-2 cell line commonly used as a substrate in the indirect immunofluorescence assays. ANA stain patterns can be nuclear, cell cycle-associated, or cytoplasmic and can inform about the type of autoimmune disease present and the appropriate treatment program.

For all cases of suspected RA, the Expert Panel recommends immunofluorescent ANA testing. Additional comprehensive ANA panels, which include antibodies that are highly specific for SLE and mixed connective tissue diseases, will not assist further with diagnosing RA.

Other Diagnostic Tests. Other tests that may provide insight include a complete blood count, which may indicate inflammation-associated anemia or thrombocytosis. A Comprehensive Metabolic Panel is useful to assess renal and hepatic function, which can inform therapy choices and/or dosing.

Assembling the Data for Diagnosis. In 2010, the ACR and the European League Against Rheumatism (EULAR) issued classification criteria for RA to help confirm a diagnosis in patients who have at least one swollen joint that cannot be better explained by another disease (Table 2).[20]

TABLE 2. 2010 ACR / EULAR Classification Criteria for RA[20]

Category	Value	Score*
Joint Involvement ‡	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	>10 joints (at least one small joint)	5
Serology *(at least 1 result needed)*	Negative RF **and** negative ACPA	0
	Low-positive RF **or** low-positive ACPA	2
	High-positive RF **or** high-positive ACPA	3
Acute-phase Reactants *(at least 1 result needed)*	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
Duration of Symptoms *(self-reported)*	Less than 6 weeks	0
	Six weeks or longer	1

***A cumulative score of >6 classifies a patient as having definite RA.** Although scores less than 6 are not classifiable as RA, values can be reassessed and diagnostic criteria fulfilled over time.

‡Any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are excluded from assessment. "Large joints" refers to shoulders, elbows, hips, knees, and ankles. "Small joints" include the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

Legend: RF—rheumatoid factor; ACPA—anti-citrullinated protein antibody; CRP—C-reactive protein; ESR—erythrocyte sedimentation rate.

Differential Diagnosis

It is reasonable to suspect RA in any adult who presents with inflammation in multiple joints (inflammatory polyarthritis).[16] However, joint pain and swelling can also indicate other inflammatory and/or autoimmune disorders, and some patients who are ultimately diagnosed with RA will present with "non-canonical" symptoms. This section will highlight several common differential diagnoses that should be investigated when RA is suspected.

Post-viral Arthritis. Several common viruses, including parvovirus B19, hepatitis B and C, HIV, alphaviruses,[21] and COVID-19[22] can cause an acute polyarthritis syndrome that could be mistaken for RA. However, virally-induced polyarthritis rarely lasts more than six weeks, in contrast to RA's chronic and persistent symptoms. Patients who report experiencing symptoms for fewer than six weeks should be considered for RA but may possibly have post-viral arthritis. Clinicians should monitor these patients closely and ask them about recent acute infections and travel.

Osteoarthritis (OA). RA-associated inflammation manifests in the joints rather than at other sites where patients commonly report pain, such as the lower back. OA results from a gradual breakdown in the cartilage between heavily used joints, and as such, it presents with different characteristics than RA. Table 3 summarizes characteristics of RA and OA that can help to distinguish the two conditions upon presentation.[23]

Psoriatic Arthritis. Psoriatic arthritis is an immune-mediated condition

TABLE 3. Distinguishing Characteristics of Rheumatoid Arthritis and Osteoarthritis[23]

Characteristic	Rheumatoid Arthritis	Osteoarthritis
Age of onset	Any time in life	Later in life
Speed of onset	Relatively rapid (weeks to months)	Slowly, over a period of years
Joint-related symptoms	Pain, swelling, stiffness	Tenderness and pain, but little or no swelling
Pattern of affected joints	Symmetric/bilateral; can affect small and large joints	• Often begins unilaterally with gradual onset • May be limited to one set of joints, usually the finger joints closest to the fingernails or thumbs, large weight-bearing joints (hips, knees), or spine
Duration of morning stiffness	At least 30 minutes; can be greater than one hour	More transient (a few minutes); may not be present
Associated systemic symptoms	Frequent fatigue; feeling "ill"; fever	Not associated with whole-body symptoms

of unknown etiology that may be triggered by genetic or environmental factors.[24] Symptoms vary among individuals, although most people with psoriatic arthritis will also have the scaly, inflamed rash that characterizes psoriasis. Like RA, psoriatic arthritis presents with joint stiffness, pain, and swelling that is often worse in the morning. Symptoms that may distinguish psoriatic arthritis from RA include tenderness in the entheses, or areas where ligaments or tendons attach to bones; a "sausage-like" swelling of an entire finger or toe; or changes to the nail beds.[16] It should be noted that the two conditions are initially managed similarly, and an absolute distinction between them is unnecessary to initiate therapy.

Lyme Arthritis. Lyme arthritis results when the *Borrelia burgdorferi,* bacterium that causes Lyme disease, enters joint tissue and causes inflammation.[25] Most commonly presenting in the knees, inflammation from Lyme arthritis can also affect the shoulders, ankle, elbow, jaw, wrist, or hip. Swelling may move between joints and vary in intensity. Antibody-based Lyme tests are highly sensitive in individuals with Lyme arthritis, who should be treated with an oral antibiotic regimen.

Systemic Lupus Erythematosus (SLE). SLE is a chronic autoimmune disorder that may present with symptoms observed with RA, including joint pain/swelling/stiffness, fever, and fatigue.[26] Patients who have lupus may also report that their symptoms "flare" in a manner analogous to those of RA. More common in women than men, lupus affects various organs. Symptoms vary widely among affected individuals but can include rashes, chest pain, hair loss, sun/light sensitivity, mouth sores, anemia, renal issues (e.g.chronic kidney disease), and ocular sequelae. Several types of lupus have been characterized, including the systemic condition, SLE (the most common type), and the skin-specific condition, cutaneous lupus erythematosus. Although approximately 98% of individuals with lupus test positive for ANA,[19] a positive ANA test does not confirm a diagnosis. ANAs are present in 5-10% of healthy individuals as well as those with RA and scleroderma. Moreover, approximately 20% of women will have a weakly positive ANA, most of whom never develop signs of lupus. Evidence to support a diagnosis of SLE includes the presence of additional symptoms and results from a complete ANA panel (e.g., anti-double-stranded DNA, anti-Smith, anti-U1RNP, anti-Ro/SSA, and anti-La/SSB).

Gout. A form of inflammatory arthritis, gout results from the buildup of uric acid crystals in the joints and other tissues.[27] Although gout symptoms in the joints are non-specific (pain, swelling, redness, heat), they usually occur in only one joint at a time, often the big toe, although any joint can be affected. Gout is diagnosed during a flare and supported by synovial fluid or blood tests for urate crystals or uric acid, respectively.

Inflammatory Bowel Disease (IBD). IBD encompasses two conditions, Crohn's disease and ulcerative colitis, which are caused by chronic gastrointestinal tract inflammation. This inflammation can lead to arthritis in approximately 30% of IBD patients, most commonly peripheral arthritis of the arms and legs and axial arthritis of the spine and hip.[28] Unlike RA, Crohn's-related arthritis typically does not cause joint deformity or breakdown, and swelling may be sudden and severe, move among joints, and affect larger joints. IBD-associated arthritis is RF-negative.[28] However, a recent meta-analysis of eight observational studies suggests that patients with IBD have a significantly higher risk of RA than those without IBD (RR=2.59; 95% CI: 1.93–3.48).[29] Symptoms commonly associated with IBD include diarrhea, abdominal pain, loss of appetite, unintended weight loss, fatigue, and bloody stools.[30,31] To aid with differential diagnosis, the clinician should assess for abdominal tenderness or pain and inquire about family history of GI conditions in patients who present with joint pain.

Cancer. Although the relationship between cancer and inflammation continues to emerge, inflammation is considered an enabling characteristic of cancer—innate inflammatory responses inadvertently support multiple cancer hallmark capabilities and promote tumor development.[32] Types of cancer that originate in or metastasize to the bones (e.g., lung, prostate, and breast cancers; multiple myeloma) may cause joint pain.

Treating RA

The joint damage associated with RA is irreversible, making early diagnosis and prompt treatment the cornerstones of successful management. RA treatment should aim to achieve remission or low disease activity, thus limiting signs and symptoms of disease while enhancing physical function and maintaining quality of life.[7,33] Early

diagnosis and proactive treatment can slow progressive joint damage in up to 90% of patients with RA.[34] The ACR recommends treating to target—i.e., aiming toward a clearly defined goal—regardless of disease activity level.[33] Because of the progressive nature of RA, patients should be monitored regularly. Optimal management incorporates a holistic approach that combines medical, social, and emotional support. This section will review treatment modalities for RA that can be implemented in primary care, including pharmacotherapy, physical activity/therapy, and dietary considerations.

Pharmacotherapy. Pharmacotherapies for RA fall within three general categories: 1) non-steroidal anti-inflammatory agents (NSAIDs), 2) corticosteroids, and 3) disease-modifying anti-rheumatic drugs (DMARDs).

NSAIDs. NSAIDs, which inhibit prostaglandin formation by blocking the active site of the cyclooxygenase enzymes COX-1 and COX-2, have long been used to treat various forms of arthritis.[35] Prostaglandins play a role in mediating inflammation and pain, and NSAIDs have independent anti-inflammatory effects and mild-to-moderate analgesic properties. However, despite improving pain and stiffness, these agents alone do not modify RA progression or prevent joint destruction.[35, 36] Individual agents are comparably efficacious when used to treat RA symptoms, but are associated with gastrointestinal and cardiovascular risks and the risk of bleeding.[36,37] Moreover, long-term use of NSAIDs can lead to chronic kidney disease, and caution should be taken in patients with renal disease. The Expert Panel notes that some patients with RA may require a relatively high NSAID dose to experience symptom relief and that responsiveness to NSAIDs does not correlate with changes in serologic marker levels.

Corticosteroids / Glucocorticoids. Corticosteroids (e.g., cortisone, prednisone, and methylprednisolone) are hormones that reduce inflammation and regulate immune response. These agents can be administered orally, intravenously, intramuscularly, or by direct injection into the affected joint(s). Low-dose corticosteroids have been shown to slow radiographic progression of articular disease in early RA.[38] However, long-term use has been associated with increased mortality, cardiovascular events, and bone fractures, and there is no consensus about the optimal procedure for tapering these drugs.[39] As such, corticosteroids are not used as monotherapy to control RA—they are most appropriate as a temporary "bridge" therapy while awaiting DMARDs to take effect or as chronic adjunctive therapy in patients with severe disease that is poorly controlled with NSAIDs and DMARDs.[36] To this end, ACR and EULAR recommend using low-dose glucocorticoids (≤10 mg daily of a prednisone equivalent) when starting a new DMARD or for no longer than three months when treating a flare.[40,41] The ACR also strongly recommends initiating a conventional DMARD without longer-term (≥3 months) glucocorticoids over initiating the agent with longer-term glucocorticoids.[33]

Disease-modifying Antirheumatic Drugs (DMARDs). Although the concept of disease-modifying anti-rheumatic drugs has been around for nearly 100 years (beginning with gold injections in the 1930s), the contemporary era of DMARD treatment for RA began with the 1988 FDA approval of methotrexate. DMARDs improve symptoms, alter the disease course, and improve radiographic outcomes in patients with RA.[36] Although DMARDs generally act more slowly on RA than do NSAIDs or glucocorticoids, their introduction effectively shifted the goal of therapy from symptom relief to sustained remission.[42,43]

Table 4 provides a summary of DMARDs that are currently FDA-approved for RA indications. DMARD agents should generally be initiated when a diagnosis of RA is confirmed.[36] In 2021, the ACR updated its 2015 comprehensive RA treatment guidelines[40] to focus on aspects of treating RA using DMARDs, with numerous strong and conditional recommendations based on various scenarios.[33] ACR's strong recommendations and general principles of DMARD treatment are summarized here. In general, the ACR recommends that DMARD treatment decisions should:[33]

- Follow a shared decision-making process
- Be reevaluated within three months based on efficacy and tolerability of the chosen agent(s)
- Follow a systematic, treat-to-target approach that involves frequent monitoring of disease activity using validated instruments and modifying treatment to reach a pre-defined target of low disease activity or remission
- Consider tapering only when patients have been at target (low disease activity or remission) for at least six months.

A recent review notes that a treat-to-target strategy aimed at reducing disease activity by at least 50% within three months and achieving remission or low disease activity within six months, with sequential drug treatment if needed, can improve outcomes and prevent RA-related disability.[34] For DMARD-naïve patients with symptomatic early RA, the ACR recommends using DMARD monotherapy (preferably methotrexate) over combination DMARD therapy.[40] For DMARD-naïve patients with moderate to high disease activity, ACR strongly recommends methotrexate monotherapy over hydroxychloroquine or sulfasalazine.[33] ACR also strongly recommends methotrexate monotherapy over biologic DMARD (bDMARD) or targeted synthetic DMARD (tsDMARD) monotherapy and over methotrexate plus a non tumor necrosis factor (TNF) inhibitor, bDMARD, or tsDMARD.[33] ACR conditionally recommends methotrexate monotherapy over methotrexate plus a tumor necrosis factor (TNF) inhibitor as some patients, especially those with a poor prognosis, may experience a greater chance of improvement associated with combination therapy.[33] Furthermore, the ACR conditionally recommends oral methotrexate over subcutaneous methotrexate for those patients initiating methotrexate therapy. Treatment should be titrated to a weekly dose of 15 mg within 4 - 6 weeks of treatment.[33]

DMARDs at therapeutic doses may require up to six weeks to exert their full effects - hence, the practice of using glucocorticoids as temporary bridging agents. The ACR recommends moving to combined therapy if moderate or high disease activity persists despite DMARD monotherapy (with or without glucocorticoids).[40] In this situation, the ACR strongly recommends adding another DMARD, a TNF inhibitor, or a non-TNF biologic agent (all choices with or without methotrexate and in no order of preference) rather than continuing with DMARD monotherapy. Similarly, the ACR strongly recommends adding one or two DMARDs to TNF inhibitor therapy if disease activity remains moderate or high despite TNF inhibitor monotherapy in a DMARD-naïve patient. These recommendations follow the treat-to-target paradigm—to slow joint degradation, adding another agent is preferable to continuing with monotherapy or stopping treatment altogether.

The ACR strongly recommends these approaches for patients with established RA, with several additional caveats.[40] If disease activity is low, the patient should continue extant DMARD, bDMARD,

TABLE 4. DMARDs Approved by the US FDA to Treat RA

Characteristic	MOA-based Subcategory	Approved Agents (Alphabetical by Subcategory	RA Indication	FDA Pregnancy Category
Conventional DMARDs		Hydroxychloroquine	• Acute and chronic RA in Adults	Not assigned [44]
		Leflunomide	• Active RA	X[45]
		Methotrexate	• Adults with severe, active RA • Children with active polyarticular-course juvenile RA • Insufficient therapeutic response or intolerance to NSAIDs	X[46]
		Sulfasalazine	• RA in children and adults • Inadequate response with salicyclates or other non-steroidal anti-inflammatory drug	B[47]
‡Biologic DMARDs (bDMARD)	TNF Inhibitors	Adalimumab	• Moderately to severely active RA	Not assigned [48]
		Certolizumab pegol	• Moderately to severely active RA	Not assigned [49]
		Etanercept	• Moderately to severely active RA	Not assigned [50]
		Golimumab	• Moderately to severely active RA • In combination with methotrexate	Not assigned [51]
		Infliximab	• Moderately to severely active RA • In combination with methotrexate	Not assigned [52]
	IL-6 Receptor Inhibitors	Sarilumab	• Moderately to severely active RA • Inadequate response or intolerance to one or more DMARDs	Not assigned [53]
		Tocilizumab	• Moderately to severely active RA • Inadequate response or intolerance to one or more DMARDs	Not assigned [54]
	Anti-CD20 Antibody / B Cell Depleting Agent	Rituximab	• Moderately to severly active RA • In combination with methotrexate • Inadequate response to one or more TNF antagonist therapies	Not assigned [55]
	T-Cell Costimulatory Inhibitor	Abatacept	• Moderately to severely active RA	Not assigned [56]
	IL-1 Receptor Antagonist	Anakinra*	• Moderately to severely active RA • Inadequate response or intolerance to one or more DMARDs	Not assigned [57]
Targeted Synthetic DMARDs (tsDMARD)	JAK Inhibitors	Baricitinib	• Moderately to severely active RA • Inadequate response to one or more TNF blockers	Not assigned [58]
		Tofacitinib	• Moderately to severely active RA • Inadequate response or intolerance to methotrexate	Not assigned [59]
		Upadacitinib	• Moderately to severely active RA • Inadequate response or intolerance to methotrexate	Not assigned [60]

‡ Biosimilars are considered equivalent to FDA-approved originator bDMARDs.
* Infrequently used for RA.

Legend: TNF = tumor necrosis factor; IL-6 = Interleukin-6; JAK = Janus kinase.

or tsDMARD therapy rather than discontinuing medication. If the patient's disease is in remission, clinicians should not discontinue all RA therapies, as stopping all DMARDs increases the potential for irreversible long-term damage. Furthermore, patients in remission for less than six months should not routinely be considered for dose reduction or withdrawal.[33]

DMARDs, Pregnancy, and Family Planning. Two FDA-approved DMARDs, methotrexate and leflunomide, are considered teratogens and carry the FDA Pregnancy Category X (Table 4). As such, the ACR strongly recommends against prescribing these medications to women with RA at pre-conception, during pregnancy, or while breastfeeding.[61] The College also conditionally recommends discontinuing anakinra, abatacept, rituximab, and tocilizumab during pregnancy. Agents that are strongly recommended to be continued pre-conception, during pregnancy, and during breastfeeding include hydroxychloroquine, sulfasalazine, and certolizumab. The other TNF inhibitors are conditionally recommended in pre-conception and during the first and second trimesters but strongly recommended during breastfeeding. Rituximab is strongly recommended during breastfeeding.

As noted in Table 4, the US FDA has not assigned the majority of approved DMARDs to a pregnancy category. The conditional nature of many of the ACR recommendations regarding these agents' use in reproductive contexts reflects minimal data. Guidelines should therefore be used to inform shared decision-making between the clinician and patient. The Expert Panel recommends pre-pregnancy counseling with any patient who is suspected of having rheumatic or musculoskeletal disease.

Initiating Methotrexate. Common side effects of methotrexate include gastrointestinal distress, oral ulcers, and mild alopecia, which can be safely improved with folic acid supplementation.[36] Routinely co-administered, folic acid (1 mg daily) does not diminish methotrexate's efficacy. Biotin supplementation can also be considered for patients who experience hair loss and thinning. Methotrexate is also commonly co-administered with NSAIDs, and the combination is considered safe with adequate monitoring of liver function tests and blood counts. Serious complications of methotrexate therapy (e.g., hepatic cirrhosis, interstitial pneumonitis, and severe myelosuppression) are rare and should be monitored. Patients who are initiating methotrexate should be evaluated for bone marrow, liver, lung, and kidney toxicities.[46] As noted in Table 4, methotrexate is considered a teratogen and is contraindicated for women of childbearing potential unless there is clear medical evidence that the benefits can be expected to outweigh the considered risks.[46] The clinician should discuss the need for birth control with women of childbearing potential or men with partners of childbearing potential, and methotrexate should be discontinued before attempting conception. Alcohol use is contraindicated with methotrexate use due to increased risk of hepatotoxicity.

Vaccines and RA. The ACR recommends that all patients who are initiating or already taking DMARD therapy receive all recommended pneumococcal, influenza, hepatitis B, and HPV vaccines.[40] These vaccines are killed or recombinant and should pose no inherent concerns for individuals who take DMARDs. The CDC recommends that adults 50 years and older and immunocompromised adults ages 19 and older who have RA receive the recombinant zoster vaccine for shingles.[62] For patients with hepatitis B infection, the ACR strongly recommends prophylactic antiviral therapy over frequent monitoring alone for patients who are initiating any bDMARD or tsDMARD.[33]

Additionally, patients should also be tested for tuberculosis (TB) before initiating bDMARDs and tsDMARDs. In particular, treatment with TNF inhibitors is associated with an increased relative risk for TB of up to 25 times, depending on clinical setting and the agent used.[63]

Physical Activity. RA is associated with a constellation of sequelae ("rheumatoid cachexia") that includes decreased joint health, fatigue, increased incidence and progression of cardiovascular disease, and accelerated loss of muscle mass.[64] A physical activity regimen, whether structured (e.g., physical or occupational therapy) or individually administered, can help to maintain or regain strength and improve overall function. Physical activity provides numerous health benefits (e.g., cardiovascular fitness, muscle strength, improved insulin sensitivity, increased mobility in overweight persons) that extend beyond preserving joint mobility.[65] Exercise training can reverse cachexia and substantially improve function without exacerbating disease activity.[64] Exercise promotes muscle strength, helps to maintain a healthy body weight, improves sleep, and promotes flexibility. The EULAR recommends exercise and the maintenance of a healthy body weight for people with rheumatic and musculoskeletal diseases.[66]

The Expert Panel recommends encouraging patients with RA to be active within appropriate contexts. Patients should be encouraged to move but not to undertake exercise that actively causes pain. Many non-traditional exercises can be considered. For example, a patient with a great deal of inflammation may be able to strengthen intrinsic muscles by squeezing putty or picking up coins. A successful activity regimen will be tailored to the patient's needs and should utilize available resources—a recommendation for water exercise classes does not benefit the patient who lacks access to a facility in which these classes are conducted. Physical activity/exercise for RA management is optimally provided through an exercise or rehabilitation specialist, such as a physical therapist.

Diet and Supplements. A recent meta-analysis of dietary exposures and RA notes that definitive recommendations are hampered by small numbers of controlled studies and/or small sample sizes, and exposures with moderate quality evidence (probiotics, vitamin D, fish oil/omega-3 fatty acids) showed either no effect or effect sizes that may not be clinically significant.[67] These studies generally used improvement in RA symptoms (e.g., joint pain and swelling, morning stiffness) as endpoints. The Expert Panel notes that mineral supplements have no proven benefit for RA, and any dietary additive that promotes liver toxicity should be avoided. However, vitamin D optimization is warranted for RA patients, who have an increased risk for osteoporosis.

While there is no practice recommendation for a specific diet that RA patients should follow, certain foods may naturally help to control inflammation. Many patients will ask about an "Anti-Inflammatory" or "Mediterranean" diet, which is frequently linked to longevity and health in popular information sources. These diets are rich in whole foods (fruits, vegetables, fish, nuts, beans, olive oil) but low in processed foods and saturated fats. Foods commonly included in a Mediterranean diet can lower blood pressure, protect against chronic conditions, reduce inflammation, and support weight loss regimens. While detailed dietary recommendations are beyond the scope of this monograph, general guidelines are available online.[68] Given that obesity is a strong predictor of worse clinical outcomes and treatment

responses in patients with early RA,[69] the Expert Panel endorses anti-inflammatory diets as part of a healthy lifestyle that may positively impact RA. When possible, the Panel suggests partnering with a clinical nutritionist or dietitian to work with the patient to tailor a healthy diet.

Talking with Your Patient about RA

Primary care clinicians are often the initial medical points of contact for individuals who present with signs of RA. Diagnosis and management of this chronic disorder mandate an ongoing conversation between patient and clinician. Many patients will be worried about RA based on family history or anecdotal experiences; others will harbor misperceptions about the disease and treatment options. It is not uncommon for patients to associate RA with disability, premature death, or a diminished quality of life. Given the advances in effective treatments, however, RA can usually be managed proactively in the context of daily life.

TABLE 5: Suggestions for Talking About RA with a Patient

Remind the patient that they are not at fault. RA pathogenesis may be genetic or triggered by an environmental factor but does not arise from "doing something wrong."

Stress that many effective pharmacologic options can treat RA. Treatments have advanced significantly from those of previous eras, such as gold infusions, and toxicities can be managed effectively.

Stress that approved treatments will improve pain symptoms and prevent joint damage. RA management is supported by evidence-based guidelines and methods.

Discuss medication side effects and onset of efficacy. Patients should know that side effects are to be expected but are relatively mild in most patients and that a DMARD will not begin to work immediately.

Discourage the use of non-evidence-based practices and agents. Mineral supplements and "panaceas" such as CBD oil have no proven benefit for RA, and any agent that is associated with liver toxicity should be avoided.

Recognize that managing RA is a journey. A patient will have a certain willingness to embark on this journey, and it may be appropriate to ask certain patients what they would ideally like to do.

Reiterate that, with proper management, the patient can continue to live a meaningful life with RA. While RA presents a disease burden, it does not automatically equate to an inability to work, travel, or live an otherwise engaged life.

Initiate a conversation (if appropriate) about how the patient can favorably affect RA management through lifestyle changes. Obesity and smoking lower the efficacy of biologics, and initiating lifestyle changes can favorably affect RA outcomes.

Discuss reproductive issues and family planning in the context of RA management with appropriate patients. Reproductive considerations will affect the selection of appropriate pharmacotherapy regimens.

Discuss the patient's role in adherence and changes to treatment plans. Patients should be provided with available medications and reasonable expectations, but they should also recognize that their management plan will be unique. If the patient feels that they cannot continue with a medication, encourage them to contact you before stopping.

Encourage the patient to use the practice's patient portal. This resource, which the patient can use to ask/answer questions as they arise, lets them know that the clinician is accessible.

The primary care clinician can set the stage for effective management by framing these early conversations so that the patient feels empowered to participate in their treatment. An informed, activated patient understands the RA disease process and realizes their role in daily management—evidence-based treatments only work when the patient adheres to them. To optimize health outcomes and promote a high quality of life, the healthcare team must work to foster the patient's sense of control and responsibility. A prepared practice team will have relevant information, decision support materials, staff, equipment, and time required to deliver evidence-based clinical management and self-management support at the time of the patient visit.

Effective management requires honest conversations, and the clinician is encouraged to educate and inform the patient about what to expect. Patients will likely have gathered information (and misinformation) from various sources and will arrive at the office with a combination of accurate knowledge and misperceptions. As such, each patient is unique in their needs, and initial visits should aim to build a relationship of trust that will promote effective management over the long term. The patient's concerns must be factored into the management plan, and these concerns will evolve over time. However, simply providing directives may encourage suboptimal adherence and, ultimately, adversely affect the patient's quality of life. For follow-up visits, the Expert Panel suggests that the patient write down their questions before coming to the office so that no concern is overlooked. Table 5 provides some suggestions for framing discussions with patients who may have RA.

When to Refer to a Rheumatologist

In general, it is prudent to involve a rheumatologist as soon as feasible when a patient presents with symptoms of RA. Rheumatologists bring expertise in diagnosing and treating systemic autoimmune diseases and are represent integral components of a chronic inflammatory disease care team. However, some patients may need to receive care from the primary care clinician for various reasons, such as insurance coverage or access to specialist care. Although patients with mild symptoms and normal markers of inflammation can usually be monitored in the primary care setting, it is likely that a rheumatologist will need to be involved at some point in the continuum of treatment. The Expert Panel recommends referring any patient for whom you are confident of an RA diagnosis. Other situations that warrant referral include:

- Patients who present with canonical RA symptoms but have a normal serology
- Patients with a family history or RA or autoimmune disease;
- Patients who have other organ involvement, especially lung nodules
- Patients who have high CCP levels or other markers of systemic inflammation
- Clinician discomfort with prescribing and managing DMARDs;
- Patients who require medications beyond DMARDs.

The American College of Rheumatology provides a searchable directory of rheumatologists at https://my.rheumatology.org/rheumatology-provider-directory

Addressing Health Disparities in RA Care

Racial and ethnic minorities are face disparities with regard to RA care,[70] thus increasing the negative impact for the individual (e.g.,

long-term disability, increased mortality) and society (e.g., higher levels of unemployment, decreased work productivity).[71] African Americans receive an estimated 30% fewer DMARD prescriptions than Caucasians, and this disparity is even greater if they are seeing a non-rheumatologist.[72] A study of patients who used bDMARDs and filed for disability benefits before retirement age showed that 49.3% of African Americans and 53.3% of Caucasians received bDMARDs after controlling for social determinants of health.[73] In a study of 93,143 Medicare patients with RA, researchers found a significant correlation between DMARD use and socioeconomic factors, with low personal income, male gender, and African American race designation associated with a decreased likelihood of receiving a prescription for a DMARD.[74] Mitigating disease effects of RA requires early diagnosis and treatment, thereby creating a narrow window of opportunity for minority patients who are disproportionality affected by disability.[75]

Hispanics with RA also face disparities in care. A recent study reported a delay for a rheumatology evaluation of 23 months in this cohort, compared to 6-8 months for other groups in the study.[76] This study identified disparities in referral patterns, with white and African American patients being referred for treatment versus self-referral for Hispanics, possibly reflecting cultural differences.

Individual-, clinician-, and system-level barriers contribute to unequal care among patients with RA.[75] Primary care clinicians are humans; they carry implicit biases that contribute to disparities despite their best intentions to the contrary.[77] Bias can impact clinical judgement and promote clinical inertia, which occurs when clinicians do not act even when they know a patient needs treatment or more intensive therapy. Educational and quality improvement interventions directed at clinicians can increase DMARD use in RA and move toward eliminating disparities based on socioeconomic status, demographics, and geography.[74]

Disparities also are apparent in medication adherence, regardless of patient socioeconomic status, further impeding care. Physicians and their care teams should acknowledge implicit bias and implement interventions to counter clinical inertia and nonadherence to mitigate health disparities for at-risk populations. Modern health care delivery usually involves several individuals in clinical decision-making, and team-based care and linkages to the medical neighborhood mean that interventions must address the racial bias of care teams. Improving patient-physician communication skills, practicing evidence-based medicine, improving adherence to therapy, recognizing comorbidities such as depression, and raising awareness of racial and ethnic disparities are steps that physicians and their care teams can take to eliminate the racial and ethnic disparities experienced by patients with RA.[70]

Communication Can Remove Barriers to Adherence. Despite the availability of many approved DMARD agents, poor adherence to medications remains a significant barrier to successful RA management.[78] However, physicians and practice teams can influence certain contributing factors, including support, community services, and the physician-patient relationship. Research has suggested that interventions that lack direct patient contact are less effective for ethnic populations.[79] Further, patient education alone, particularly when used only once and/or briefly, does not improve adherence.[79]

Successful management of RA requires patients to have a basic knowledge of the disease, the available treatment options, and the safety and efficacy of those treatments. A patient with a language barrier or low literacy can be overwhelmed when trying to make decisions with their physician, thus contributing to poor medication adherence.[78,80] Prioritizing health literacy can have a powerful impact on medication adherence. Additionally, a strong patient-clinician relationship is critical to uncovering a patient's beliefs and fears about medications that lead to intentional nonadherence, such as the need to "take a break from medications every once in a while" or a concern that all medicines are addictive.

Current educational interventions have limited effect on improving adherence to RA therapy, perhaps due to an overemphasis on biomedical information.[78] To improve medication adherence in patients with RA, the Expert Panel supports practical, evidence-based, patient-centered interventions. Care teams require training and support in how to communicate risks and incorporate patient beliefs into their conversations with patients.

Patients may have difficulty adhering to a pharmacotherapy regimen or be anxious about taking pharmacotherapy for a variety of reasons. Concerns may be culturally informed or anecdotal. The clinician should inform the patient that managing RA is an ongoing *process*. The patient and clinician are *partners* in this journey to attain a beneficial outcome. The clinician must communicate realistic expectations about the steps in the journey; otherwise, some patients may conclude that the medications are not working before the effective dose is established. The clinician should be aware that titration schedules reflect clinical judgment; tolerability will vary among individuals and agents.

Providing Culturally Informed Care to the Minority Patient

Why Being Culturally Informed Is Important. Being culturally informed extends beyond simply being thoughtful or politically correct; it has become a necessary component of contemporary medical practice in the U.S. According to 2022 estimates from the U.S. Census Bureau, people of color (Latinos, African-Americans, Asians, Pacific Islanders, and American Indian /Alaskan Natives) make up nearly one-third of the U.S. population.[81] Data from 2017-2021 indicate that 21.7% of the U.S. population speaks a language other than English at home, and an estimated 13.6% of the U.S. population is foreign-born.[81] Because of the increasing need for medical personnel to interact with persons from diverse cultural backgrounds, governing bodies of medical schools (e.g., the Liaison Committee on Medical Education) and residency programs (e.g., the Accreditation Council for Graduate Medical Education) require that cultural competence be included in medical school and residency curricula. In addition, several states have enacted laws or mandates requiring practicing physicians to have continuing medical education in cultural competency to maintain licensure.

Cultural Beliefs and Norms Shape Attitudes Toward Illness and Medical Treatment. Attitudes toward illness and medical treatment are influenced by cultural beliefs and norms. A primary care practice will serve patients whose cultural norms vary widely with respect to disease causation, acceptable forms of treatment, spiritual beliefs, and family structure and member roles— factors that can impact the diagnosis and treatment of RA. While it is impossible to understand the nuances of every cultural *milieu* that will be encountered in primary health care, the clinician must be informed of patterns and trends in cultural beliefs to communicate effectively with minority populations commonly encountered in a culturally diverse practice.

Considerations for delivering culturally appropriate care to African-American and Latino patients are detailed below.

Establishing a Culturally Informed Office Environment. Establishing a culturally informed office environment is the first step toward providing culturally appropriate care. Patients within specific ethnic groups may exhibit substantial differences in the degree of their sensitivities toward prevailing American culture. For example, recent African immigrants may exhibit cultural sensitivities that differ widely from those seen in American-born black patients, and Spanish-speaking patients may represent the diverse cultural backgrounds of their home countries (e.g., Guatemala, Mexico, Nicaragua). Components of a culturallyinformed office include the appropriate physical environment (e.g., language- and topic-appropriate magazines for adults, books and toys appropriate to children, a staff to match the patient population served, and bilingual or language-appropriate wall posters and signs). Reading capacity should be evaluated in cases where language barriers or health literacy barriers may pose communication issues. To facilitate comprehension, it is recommended that written text be geared toward a 6th-grade reading level or below. Interpretation services should also be made available; per Federal law (enforced through the U.S. Office of Civil Rights), the healthcare clinician's office must provide a trained medical interpreter. The "teach-back" approach - asking the patient to explain the plan and instructions back to you - will help ensure that vital information is not misunderstood. Staff should also be trained in a culturally informed manner to overcome assumptions about, or bias against, particular cultural backgrounds.

Partnering With the Minority Patient. Appreciating the value system imposed by cultural heritage is necessary to begin a conversation with a patient who presents with symptoms of rheumatologic disease. Minority patients may respond to a holistic biopsychosocial approach that emphasizes patient care by recognizing biological, psychological, and spiritual components. Such an approach encourages an ongoing, active partnership between the patient and the physician in which treatment is structured to account for the patient's value system. Patients must be given a framework to understand their condition that takes into account the level of disease severity and realistic treatment options. Communicating effectively with a given patient depends to an extent on the individual and his/her relationship with the clinician. Nonetheless, an engaged attitude is central to a successful relationship. Showing the patient that you care promotes trust; invoking a paternalistic approach may create a barrier to providing appropriate care.

Conducting the Cross-Cultural Interview. An interview with a patient from another culture should be carried out carefully and appropriately to establish trust.[82] Key elements of such an interview are listed in Table 6. A list of cross-cultural interview questions that may be adapted to suit a specific patient is provided in Table 7.

TABLE 6. Strategies for a Successful Cross-Cultural Interview[82]

- Establish trust through "small talk"
- Use open body language
- Speak slowly and directly to the patient (rather than to the interpreter)
- Use short sentences and a normal tone of voice
- Avoid use of idioms
- Ask patient what illness means to them and about their current treatments
- Provide treatment instructions in writing
- Have patient repeat instructions in their own words

Considerations for Delivering Culturally Informed Care to Latino Patients.[83] While the assessment of treatment needs of Latinos varies somewhat according to population subgroup, this section will summarize several key considerations and strategies to provide effective, appropriate care to Latino patients.

The Hispanic community tends to wait much longer to seek care, often leading to higher disease activity and severity.[76] Cultural beliefs toward illness shape many aspects of the interaction between the Latino patient and the clinician, and cultural idioms may surface during conversation. For example, illness may be perceived as the result of an imbalance between external and internal sources (e.g., hot and cold, body and soul). The clinician should recognize that some Latinos remain strongly grounded in the folk-healing traditions of their home cultures; patients may have sought the assistance of a *curandero* (folk healer) to alleviate symptoms. Furthermore, the process of acculturation may also lead some Latino patients to define certain diseases using folk idioms (e.g., *empacho* for indigestion) while characterizing others according to Western medical criteria (e.g., measles, asthma).

Moreover, the clinician must pay careful attention to accommodate the support systems that will likely serve the ailing Latino patient. For example, spiritual belief may play a central role in treatment. A Latino patient may believe that God determines the outcome of the treatment or course of disease; for example, *nervios* (a cultural concept of distress evoked by difficult life circumstances) may result from insufficient prayer or from God failing to hear the patient's supplications. A broad base of potential counseling sources may be appropriate for minority patients; if a Latino patient is amenable to working with clergy or a social worker, this option should be incorporated into the treatment plan. The clinician should also recognize the central role of the family

TABLE 7. Cross-Cultural Interview Questions[82]

- What is your native country?
- How long have you been here?
- What do you think is wrong?
- What do you call the illness?
- What do you think has caused the illness?
- Why do you think that the illness began when it did?
- What problems do you think that the illness causes?
- How severe is your illness?
- What kind of treatment do you think is necessary?
- What are the most important results you hope to receive from treatment?
- What are the main problems that the illness has caused for you?
- What do you fear most about the illness?
- How do you cope with your feelings?
- How do you manage stress?
- What can you change?
- What types of support do you have to help you deal with this illness?

(*familismo*) as a source of emotional support during treatment and recovery processes. Therefore, when possible, the clinician should engage the family in discussions that involve decisions about care, recognizing also that family members may draw upon their own spirituality to cope with a relative's illness. The influence of social and spiritual support suggests that clinicians must access the local world of their patients and their families to provide culturally responsive care to Latino patients.

With Latina patients, the primary care clinician should also recognize an issue with the potential to confound a diagnosis and/or treatment of RA - the central role of male family members (especially among individuals who have recently come to the US). Husbands may make the family's healthcare decisions for their wives and/or serve as the family interpreter, making it difficult for the patient to discuss issues related to illness or stress. Additionally, women may depend upon their husbands to drive them to the appointment. These issues underscore the need for a trained medical interpreter (who is not a member of the patient's family). Nodding of the patient's head may signify that she is listening but not necessarily that she understands.

Considerations for Delivering Culturally Informed Care to African-American Patients. Observed disparities in RA diagnosis and treatment in African-Americans are multifactorial and can include financial barriers, feelings of mistrust, and perceptions of racism or discrimination. Among these are issues with physician communication style, masking of disease by somatic presentation of symptoms or self-medication, and concerns about the stigma of illness. Respectful behavior and a demonstrated willingness to listen and communicate can aid in building trust with African-American patients. To foster communication, the healthcare clinician should:

- Respect the patient's understanding of his/her illness
- Use open-ended questions to ensure that you and the patient have common meaning
- Recognize the medical beliefs of the patient, including folk, home, and herbal-based remedies. This may require cross-cultural negotiation regarding treatment
- Recognize the role of spirituality as a coping mechanism
- Incorporate beneficial or neutral folk remedies into the plan of care
- Recognize that medication cost and complex dosage instructions may promote non-adherence.

Religion, spirituality, and kinship play important roles in the African-American patient's understanding of illness and treatment. The clinician must be willing to accept these contexts and incorporate suggestions and recommendations within their frameworks. For example, treatment barriers such as "God will heal me" may be overcome by using an appropriate explanation, such as "God would want you to feel good so you can care for your family." To assist in adhering to a treatment regimen, the clinician may also recommend support groups or services at the patient's church and should ask about key individuals in the community who may assist in supporting medical recommendations. The clinician should also be aware that the African-American patient may be amenable to, or may be currently using, alternative treatments. The clinician should also consider incorporating a family member in the treatment plan. As with Latino patients, some African-American patients may present symptoms in somatic contexts and according to certain idioms of distress.

RA Resources for Clinicians and Patients

The RA community includes many online communities, support groups, blogs, and resources that may be useful for patients with RA to connect with others. Table 8 lists resources that provide a broad range of RA-related information and can serve as launching points for clinicians and patients who seek information about diagnosing and treating RA.

TABLE 8. RA Resources for Clinicians and Patients

Source	Contact Information	Resources
The American College of Rheumatology (ACR)	www.rheumatology.org	• Medication guides/ apps for physicians • Education center • Patient information resources
The Arthritis Foundation	www.arthritis.org	• Local support group resource finder • Resources for living with arthritis
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)	https://www.niams.nih.gov/health-topics/rheumatoid-arthritis	• Multilingual resources • Patient information • Clinical trials information
The Mayo Clinic	www.mayoclinic.org	• Multilingual resources • Patient information • Continuing medical education and clinician resources
Centers for Disease Control and Prevention	https://www.cdc.gov/arthritis/basics/rheumatoid-arthritis.html	• Patient information materials in multiple languages

CONCLUSION:

Rheumatoid arthritis is a treatable condition that can often be managed in the primary care setting. Because of the degenerative nature of the condition, early diagnosis and prompt treatment are central components of successful management. RA treatment should aim to achieve remission or low disease activity, thus limiting signs and symptoms of disease while enhancing physical function and maintaining quality of life. DMARDs are highly effective pharmacologic options to manage RA and will improve pain symptoms and prevent joint damage. However, RA management extends beyond simply prescribing approved agents. Disparities occur in the diagnosis and treatment of RA, with minority populations being underserved. Informed care is based on a partnership between the patient and the clinician that incorporates biological and psychological aspects within a holistic framework. Care pathways that include evidence-based therapies, patient education, support, and collaborations with an informed care team will improve outcomes for all patients, including those that represent underserved groups. Through diagnosis, treatment, and appropriate referral, the primary care clinician plays a vital role in improving the quality of life for patients who suffer from RA.

SHEILA: *Diagnosing RA*

Sheila is a 30-year-old African-American patient who complains that both hands have hurt off and on for about three months. When the pain is acute, ibuprofen provides temporary relief, but its palliative effect "wears off pretty quickly." She finds some relief in running her hands under hot water. She reports feeling more tired of late and sometimes awakens at night because her hand is asleep or "feels weird." Sometimes, her wrists hurt so badly that she has a hard time lifting objects such as a suitcase, which has become problematic because her job requires frequent travel. She and her partner are planning to start a family, and she is concerned that she will not be able to take care of a baby without pain. Swelling and redness are obvious upon visual inspection of her wrists. Could Sheila have RA?

a. Yes. Sheila shows the hallmark bilateral presentation of swollen joints, which suggests RA. RA often onsets in women of Sheila's age, and RA symptoms commonly flare and may undergo periods of remission.

b. No. RA is unlikely to affect an otherwise young and healthy woman, and the pain associated with RA usually does not remit.

Answer: a. Although there is no single finding that confirms RA definitively, a bilateral presentation of tender, warm, and swollen joints and fatigue are common symptoms of RA, which can onset at any age. Also, the joint pain and swelling associated with RA often flare in intensity.

Sheila's blood pressure is 130/80 mm Hg, and her pulse is 78 beats/minute. Other than her presenting symptoms, her physical exam is normal other than joint symptoms, and her BMI is 28 kg/m2. She does not drink or smoke and does not currently take any prescription medications. What other questions should you ask Sheila to help diagnose RA?

a. Do other joints besides your wrists hurt?

b. At what time of day do you feel the pain most acutely?

c. Can you recall if you first noticed the pain in conjunction with any specific event? (e.g., viral infection, life stress)

d. Do you have a family history of arthritis or similar conditions?

e. All of the above.

Answer: e. At this point, you should inquire more about the "how, when, and where" of the pain, whether it may be tied to a particular stressor, and whether Sheila has other risk factors for RA.

Sheila notes that her knuckles and feet also hurt sometimes, and that the pain is at its worst in the morning. Palpation of her hands indicates tenderness in the second, third, and fourth metacarpophalangeal (MCP) joints, and her proximal interphalangeal (ICP) joints feel warm. You plan to order a CBC and liver/renal function tests, but what other tests will be helpful to proceed?

a. Routine lipid panel

b. Immunofluorescent ANA test

c. Hepatitis panel

d. Serology (RF, ACPA)

e. Acute-phase reactants (ESR, CRP)

f. Thyroid stimulating hormone (TSH)

g. All of the above

Answer: g. Sheila's symptoms are consistent with RA, and each of these tests will aid with differential diagnosis and inform about possible medications.

When you ask Sheila about her vaccination record, she notes that she is up to date on her flu and COVID-19 vaccines but that she contracted COVID about one year ago. Are Sheila's symptoms consistent with common presentations of post-viral arthritis?

a. Yes. Post-viral arthritis is a long-term condition that may last up to one year post-infection.

b. No. Virally induced polyarthritis rarely lasts more than six weeks, in contrast to RA's chronic and persistent symptoms. Patients who report experiencing symptoms for fewer than six weeks should be considered for RA but may possibly have post-viral arthritis.

Answer: b.

Are her symptoms consistent with a diagnosis of osteoarthritis (OA)?

a. Yes.

a. No.

Answer: b. OA usually presents later in life, with symptoms developing over a period of years. Joints affected by OA may be red and tender but are not usually swollen, and initial presentation may be unilateral. OA is also not commonly associated with "whole-body" symptoms, such as Sheila's self-reported fatigue.

It is reasonable to suspect RA in any adult who presents with inflammation in multiple joints, and, based on initial evaluation, Sheila may have RA. Although you are awaiting the lab results to make a formal diagnosis, what are some messages that you should discuss with Sheila at this point?

a. RA is treatable, and safe and effective therapies are available

b. Approved treatments will improve pain symptoms and prevent irreversible joint damage.

c. Successful management of RA is a journey that will involve shared decision-making.

d. Initiating lifestyle changes can favorably affect RA outcomes

e. Family planning will be discussed in the context of RA management and will likely impact the course of treatment.

f. Sheila will play an active role in adhering to treatment and discussing changes to treatment plans.

g. All of the above.

Answer: g. Given the importance of initiating therapy sooner rather than later, it is advisable to begin these conversations now.

Sheila's lab results indicate elevated acute-phase reactants (ESR and CRP) and positive ANA, but she is seronegative (negative values for RF and ACPA). The acute-phase reactants and ANA results are consistent with a diagnosis of RA, but what about the seronegative results?

a. A seronegative result is inconsistent with a diagnosis of RA, and you should consider another diagnosis.

b. A seronegative result is relatively common in patients with RA, so it is consistent with a diagnosis of RA.

c. Serology results may change over time with disease progression, and Sheila has symptoms of early-stage RA.

d. Both b and c are correct.

Answer: d. There is no single test that confirms an RA diagnosis. Up to 25% of patients with RA are seronegative on initial presentation, and 20% of these individuals can remain negative during follow-up.

Based on available information, you diagnose RA in Sheila's case. The next case study will focus on treating RA in primary care.

CONSUELA: *Treating RA*

Consuela is a 55-year-old Latina woman with limited English proficiency who arrives at the office with her 28-year-old bilingual daughter. Consuela presents with multiple swollen and inflamed joints in her hands, wrists, and knees. She grimaces upon palpation and walks with some difficulty. A homemaker, she notes that she feels tired all of the time ("*Tengo nervios*") and that it has become hard to carry out many household activities to provide for her family. With her daughter's help, she reveals that the joint pain has been present for a year or so and that it initially waxed and waned but is now constant. She especially has difficulty getting out of bed in the morning and sometimes needs an hour or two to "feel herself again" and go about daily activity.

She tells you that she was diagnosed with arthritis about a year ago and that she briefly tried "the medicine" but feared that it would cause cancer, so she stopped. She reports that she tries to eat well, has prayed for relief, and was physically active up until about a month ago. She reports taking no medicines other than ibuprofen and herbal tea for pain relief. You have no electronic health record to clarify the arthritis diagnosis.

Her BMI is 29 kg/m2, and her blood pressure is 140/100 mm Hg. She reports no digestive or excretory issues.

Given her presentation, what is the most likely diagnosis for Consuela?

a. Osteoarthritis

b. Rheumatoid arthritis

c. Gout

d. IBD-associated arthritis

Answer: b. The bilateral presentation of pain and swelling across multiple small and large joints supports RA but argues against gout and osteoarthritis. She shows no gastric distress that characterizes IBD.

You order lab tests, including a full ANA panel, to help confirm RA. However, her joint damage makes clear that management should begin immediately. What are some key points to discuss with Consuela and her daughter regarding managing her RA going forward?

a. RA medications have been tested and used successfully in many patients.

b. RA medication will help to reduce joint swelling and pain.

c. You and Consuela will monitor the treatment plan regularly, making necessary adjustments if problems arise.

d. Consuela's input will help to guide the treatment plan.

e. Consuela should let you know if she wishes to stop any prescribed medicine.

f. All of the above.

Answer: f. Treatment adherence will be absolutely necessary to minimize further joint damage and provide relief. Consuela's fears are real to her, but you must be open and frank about the need to proceed with pharmacotherapy (in a stepwise manner) and the consequences of failing to do so. Gaining Consuela's trust will be critical and can be aided by speaking directly and respectfully and letting her know that she will have a voice in this journey.

Which class of agents is the first line of treatment for Consuela?

a. Long-acting glucocorticoid

b. Short-acting glucocorticoid

c. NSAID

d. DMARD

Answer: d. Among these classes, DMARDs are the only option to affect Consuela's joint damage. DMARDs may be taken in conjunction with NSAIDs or short-acting glucocorticoids.

Based on ACR recommendations and FDA indications, which DMARD would be most appropriate to initiate for Consuela?

a. Sulfasalazine
b. Hydroxychloroquine
c. Methotrexate
d. Any TNF inhibitor
e. Any JAK inhibitor

Answer: c. For DMARD-naïve patients with moderate to high disease activity, the ACR strongly recommends methotrexate monotherapy over hydroxychloroquine or sulfasalazine, bDMARD or tsDMARD monotherapy, or the combination of methotrexate plus a non-TNF inhibitor bDMARD or tsDMARD.

You propose initiating methotrexate at 10 mg once weekly with daily folic acid to help with potential side effects such as nausea.

How soon should you see Consuela again?

a. 1 month
b. 3 months
c. 6 months
d. 1 year

Answer: a. Follow-up blood work should be done in one month to compare against baseline values and to assess methotrexate efficacy. Also, it will be important to work with Consuela to address any concerns that she may have with side effects, efficacy, and so forth.

Consuela returns after one month and reports that her symptoms have begun to improve. She no longer wakes at night and reports no nausea or other GI side effects. She is taking her medication regularly. When should you follow up again?

a. 1 month
b. 2 months
c. 3 months
d. 6 months

Answer: b. Going forward, the routine follow-up interval for maintenance should be 3-4 months. A visit 2 months from now will be the three-month interval from initiation of therapy.

At the next visit, Consuela reports less fatigue and notes that she rarely uses ibuprofen. The swelling and inflammation in her joints has been reduced by 60-80%. However, she appears to have reached a maximum response to methotrexate, so you suggest increasing her dose to 20 mg, with another follow-up scheduled in three months. In the meantime, what messages should you convey to Consuela?

a. Suggest that she continue with the DMARD treatment.
b. Reiterate that you are available should she have concerns with the new titration.
c. Encourage her to keep her daughter and other family members involved with her disease management.
d. Recommend lifestyle changes (e.g., Mediterranean diet, physical activity when possible) and refer her to appropriate clinicians as needed.
e. Recommend that she remain up to date on her vaccines.
f. All of the above.

Answer: f. All of these steps are part of a management plan that is tailored to Consuela.

True/False:
Once Consuela's RA is in remission, she will likely be able to discontinue methotrexate with close monitoring.

Answer: False. Stopping all DMARDs increases the potential for irreversible long-term joint damage. Although Consuela's disease activity is low (and hopefully will be lowered more with the new dose), she should continue extant DMARD therapy rather than discontinuing medication.

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The AAFP has reviewed A Narrow Window of Opportunity: Diagnosis and Management of Rheumatoid Arthritis in Underserved Populations and deemed it acceptable for up to 2.00 Enduring Materials, Self-Study AAFP Prescribed credits. Term of Approval is from 07/01/2023 to 07/01/2024. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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