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A DETAILED REVIEW ON RHEMATOID ARTHRITIS

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease characterized by synovitis, pain, stiffness, progressive joint damage and functional impairment. The supplied literature consistently presents early recognition and disease-modifying treatment as central to preventing irreversible structural damage and disability.

Symptomatic medicines such as analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) may reduce pain, while glucocorticoids can provide rapid control during active disease or while slower disease-modifying antirheumatic drugs (DMARDs) take effect. Conventional synthetic DMARDs, particularly methotrexate (MTX), form the core of pharmacological management, with biologic DMARDs and targeted synthetic DMARDs providing additional options when response is inadequate or treatment is not tolerated.

RA management extends beyond inflammation. Pain may persist despite good inflammatory control because mechanical pain, fibromyalgia, neuropathic mechanisms and psychosocial factors can contribute. RA is additionally associated with generalized and local bone loss and increased fracture risk. Obesity may worsen disease activity and treatment response, while weight reduction has been associated with lower disease activity in patients with obesity. Patient perceptions of DMARD efficacy and adverse effects can influence treatment experience and adherence, and pharmacoeconomic analysis further highlights the importance of rational medicine selection and resource use.

Overall, the evidence assembled supports a multidimensional, treat-to-target approach in which early diagnosis, appropriate DMARD therapy, monitoring, management of pain and comorbidities, and attention to patient preferences are combined to improve long-term outcomes.

KEYWORDS: Rheumatoid arthritis; pharmacotherapy; DMARDs; methotrexate; NSAIDs; glucocorticoids; biologic DMARDs; JAK inhibitors; pain; osteoporosis; obesity; adherence.

1. INTRODUCTION

Rheumatoid arthritis is described across the supplied sources as a chronic inflammatory autoimmune disease that primarily involves synovial joints but may have systemic manifestations. The disease commonly presents with joint swelling, tenderness, pain and prolonged morning stiffness, particularly involving the small joints of the hands and feet. Persistent inflammation can produce synovial proliferation, cartilage destruction, bone erosion, deformity and loss of function. The condition therefore has consequences extending beyond symptoms to work capacity, quality of life and long-term disability.

The epidemiological descriptions in the sources place adult prevalence broadly around 0.5–1.0%, with women affected more often than men. One source reports a female-to-male ratio of approximately 3:1 and emphasizes the importance of RA among middle-aged women; another estimates worldwide prevalence at approximately 0.8%. These figures vary according to population and diagnostic criteria, but together indicate that RA is a common chronic inflammatory disorder with substantial societal impact.

The clinical importance of early intervention is repeatedly emphasized. The early-diagnosis review states that modern management should involve disease-modifying treatment within the first three months, continuous assessment of disease activity, remission as a treatment goal and multidisciplinary care. The treatment landscape has changed substantially: earlier strategies relied heavily on symptom control and gradual escalation, whereas modern approaches seek to suppress disease activity rapidly and prevent structural damage through DMARD-based treatment, including conventional synthetic, biologic and targeted synthetic agents [3,6,8,9].

Project Aim

To consolidate the supplied literature into a structured academic review of RA pharmacotherapy and comprehensive disease management, with emphasis on diagnosis, treatment classes, methotrexate, advanced therapies, pain, bone health, obesity, pharmacoeconomics and patient-centered care [1–13].

Project Objectives

- Describe the clinical and pathological basis of rheumatoid arthritis.
- Summarize approaches to early diagnosis and disease monitoring.
- Review symptomatic drugs and disease-modifying therapies.
- Explain the pharmacological mechanisms and clinical role of methotrexate.
- Discuss biologic and targeted synthetic DMARDs.
- Integrate management of pain, osteoporosis, obesity and patient concerns.

2. Etiology and Pathophysiology

The supplied literature describes RA as the result of a complex interaction between genetic susceptibility, immune dysregulation and environmental influences. Genetic factors include

susceptibility associated with major histocompatibility complex regions, while environmental exposures such as cigarette smoking are discussed as contributors. The disease process involves both innate and adaptive immunity.

At the joint level, inflammatory cells and synovial cells infiltrate and proliferate. Proliferation of synovial macrophages and fibroblasts, lymphocytic infiltration, endothelial proliferation and neovascularization are described, and the inflamed synovium can form invasive pannus tissue that progressively damages cartilage and bone.

Molecular detail is added by the 2026 pharmacotherapy review: autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) are associated with the autoimmune response, while macrophages and dendritic cells produce inflammatory cytokines including tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and interleukin-1. CD4+ T cells and B cells contribute to adaptive immune activation. The combined inflammatory response produces synovitis, swelling, pain, stiffness, deformity and functional impairment.

Consequences of persistent inflammation include joint destruction, disability and extra-articular complications. Local and generalized bone loss are important complications, while pain can persist through mechanisms not directly proportional to inflammatory disease activity. RA should therefore be considered a systemic and multidimensional disorder rather than only a disease of swollen joints [4,9,13].

Major Clinical Manifestations

- Symmetrical inflammatory joint pain, swelling and prolonged stiffness.
- Progressive cartilage and bone destruction with possible deformity.
- Fatigue and reduced physical function.
- Possible systemic and extra-articular involvement.
- Increased risk of osteoporosis and fragility fractures.
- Persistent pain from inflammatory and non-inflammatory mechanisms.

Pathophysiological Implication for Therapy

Because inflammatory immune pathways drive structural damage, treatment must not rely only on analgesia. Symptom-relieving medicines have an important supportive role, but DMARDs are required to alter disease activity and reduce progression — a recurring theme across the supplied pharmacotherapy sources [1,2,3,13].

3. Early Diagnosis and Disease Monitoring

RA is primarily a clinical diagnosis supported by laboratory investigations and imaging; no single laboratory test is diagnostic. The supplied diagnostic review emphasizes joint examination, acute-phase responses, serology and symptom duration. RF and ACPA are important serological markers, while ESR and CRP help assess inflammatory activity.

The 2010 ACR/EULAR classification approach gives substantial weight to joint involvement and antibody results. Radiographically detectable erosions can support classification, while positive RF or ACPA can help identify patients likely to require disease-modifying therapy. Importantly, patients who do not initially meet classification criteria may still require close follow-up, particularly in early or seronegative disease.

A practical evaluation therefore includes history and examination of swollen joints, duration and pattern of symptoms, ESR/CRP, RF and ACPA, blood count and relevant clinical chemistry, with radiography or other imaging when indicated. Alternative explanations for joint swelling — trauma, infection and osteoarthritis — must be considered.

Early treatment is a major determinant of outcome. Early remission-oriented DMARD treatment under a treat-to-target strategy can produce several years of normal bodily function without disability in a substantial proportion of patients, with the strongest emphasis on intervention within the first three months and continuous monitoring. Monitoring should evaluate both disease control and treatment safety: disease activity assessment, functional status, laboratory monitoring and structural progression are used to determine whether treatment should be continued, intensified, combined or changed [3,4,8].

Treatment Principle

Early diagnosis → early DMARD therapy → regular disease-activity assessment → adjustment toward remission / low disease activity → prevention of structural and functional damage.

4. Pharmacological Management: Overview

The supplied pharmacotherapy literature divides treatment broadly into symptomatic therapies and disease-modifying therapies. Analgesics and NSAIDs are mainly used to relieve pain and inflammation, while glucocorticoids provide rapid anti-inflammatory effects. DMARDs are the core disease-modifying treatment because they act on the underlying inflammatory process and aim to prevent structural progression.

Therapy	Main Purpose	Important Points
Analgesics	Pain relief	Supportive symptom control; does not modify RA disease [1,2,3,9,13]
NSAIDs	Pain and inflammation	Useful for symptoms; gastrointestinal, bleeding and cardiovascular risks require attention
Glucocorticoids	Rapid suppression of inflammation	Often short-term / bridging therapy; long-term exposure increases adverse effects
csDMARDs	Control disease activity and prevent damage	Methotrexate, sulfasalazine, leflunomide and hydroxychloroquine are key agents
bDMARDs	Target specific immune	Includes TNF inhibitors and other biologic

Therapy	Main Purpose	Important Points
	pathways	mechanisms
tsDMARDs	Target intracellular signalling	JAK inhibitors such as tofacitinib and baricitinib act on intracellular pathways

NSAIDs

NSAIDs inhibit cyclooxygenase pathways and reduce prostaglandin-mediated symptoms. The supplied sources stress that they do not alter the underlying disease course and therefore should not be used as the sole treatment. Long-term use can be associated with dyspepsia, peptic ulcer disease, gastrointestinal bleeding and cardiovascular concerns.

Glucocorticoids

Glucocorticoids can rapidly reduce inflammation and are commonly used as short-term or bridging therapy while DMARDs take effect. Cumulative exposure should be minimized because chronic treatment is associated with osteoporosis, metabolic effects, infection risk and other complications [2,3,13].

5. Conventional Synthetic DMARDs

Conventional synthetic DMARDs are the foundation of disease-modifying treatment in the supplied literature. The principal agents discussed are methotrexate, sulfasalazine, leflunomide and hydroxychloroquine. Selection depends on disease severity, comorbidities, previous response, tolerability and the overall treatment strategy [1,2,9,13].

Methotrexate (MTX)

MTX is repeatedly identified as the anchor or first-line DMARD. It may be used alone or in combination. Its clinical benefit develops more slowly than that of symptomatic therapies, and regular laboratory monitoring is important because of potential hepatic and hematological toxicity. Folic-acid supplementation is discussed as a strategy to reduce adverse effects [2,5,13].

Sulfasalazine

Sulfasalazine is one of the established conventional DMARDs used for RA. The supplied social-media study found that patients discussed both efficacy and adverse effects when describing this medication, illustrating the importance of treatment experience in addition to pharmacological effectiveness [2,9].

Leflunomide

Leflunomide is included among commonly used conventional DMARDs and may be used when MTX is unsuitable or when additional disease control is needed. It requires appropriate safety monitoring and individualized treatment decisions [2,9,13].

Hydroxychloroquine

Hydroxychloroquine is another conventional DMARD discussed in the supplied sources. Notably, the guideline-consistency study found that recommendations for hydroxychloroquine were the one area in which direction itself was inconsistent across the examined guidelines, whereas many other recommendations were directionally consistent but differed in strength [9,12].

Combination Treatment and Escalation

When disease control is inadequate, conventional DMARDs may be combined or treatment may be escalated to biologic or targeted synthetic agents. The older treatment algorithm illustrates increasing MTX dosage, switching or adding another conventional DMARD, or adding a biologic when pain and swelling remain inadequately controlled [2,3,12,13].

Safety and Monitoring

Treatment requires monitoring tailored to the medicine. The supplied material specifically describes complete blood count, platelets, liver-related tests, albumin and creatinine monitoring around MTX therapy, together with folic-acid supplementation [4,5].

6. Methotrexate: Pharmacology and Clinical Role

Methotrexate has been used in RA for decades and remains a central component of standard treatment. The dedicated MTX review explains that its efficacy results from multiple pharmacological mechanisms rather than a single action, including folate antagonism, promotion of adenosine accumulation, modulation of inflammatory signalling, effects on bone and maintenance of immune-system balance [5,13].

Folate-Pathway Effects

MTX enters cells and can be converted to polyglutamated forms. It interferes with enzymes involved in folate-dependent nucleotide metabolism, including dihydrofolate reductase and thymidylate synthase, and also affects ATIC in purine metabolism. These actions reduce the availability of substrates needed for DNA and RNA synthesis and help suppress proliferation of inflammatory cells [5].

Adenosine-Mediated Anti-Inflammatory Effects

An important non-folate mechanism is increased adenosine accumulation. Inhibition of ATIC promotes AICAR accumulation, which contributes to increased extracellular adenosine. Adenosine then interacts with receptors on immune cells and contributes to anti-inflammatory signalling, with A2A and A3 receptor pathways highlighted as relevant to MTX-mediated effects [5].

Effects on Inflammatory Signalling

MTX is connected with reduced inflammatory-cell activity and lower levels of pro-inflammatory cytokines, helping explain why MTX can reduce synovitis and disease activity despite its original classification as an antifolate drug [5].

Clinical Advantages

- Established role as an anchor DMARD.
- Can be used as monotherapy or in combination.
- Relatively flexible dosing and broad clinical experience.
- Can support treat-to-target strategies when monitored appropriately.

Important Limitations

- Slow onset compared with symptomatic medicines.
- Requires regular safety monitoring.
- Potential hepatic and bone-marrow toxicity.
- Folic-acid supplementation is used to reduce adverse effects in the supplied sources.

Overall, MTX occupies a central position because it combines disease-modifying efficacy, extensive clinical experience and suitability for combination strategies.

7. Biologic and Targeted Synthetic DMARDs

Biologic DMARDs were developed to target specific components of the immune response. The supplied pharmacotherapy sources describe TNF inhibitors such as infliximab and etanercept, along with agents such as abatacept, rituximab and tocilizumab. These therapies broaden treatment options for patients who have inadequate response or intolerance to conventional DMARDs [2,13].

TNF Inhibition

Infliximab is described as an intravenously administered antibody generally used with MTX, while etanercept is a fusion protein that acts as a decoy receptor for TNF signalling and can be used alone or with MTX. Clinical trials show meaningful improvement with these agents, although response and treatment strategy depend on the patient and clinical context [2,13].

IL-6 Receptor Blockade

Tocilizumab targets the IL-6 receptor and may be administered intravenously or subcutaneously. It is useful in patients who have not responded to DMARDs and has a potential role as monotherapy when MTX is not tolerated; infection risk is an important safety consideration [2,13].

Targeted Synthetic DMARDs and JAK Inhibition

Targeted synthetic DMARDs are small molecules that act on intracellular signalling pathways, particularly the JAK-STAT pathway. Tofacitinib inhibits JAK enzymes and may be used alone or with MTX, while baricitinib targets JAK1 and JAK2. Selective JAK1 inhibitors such as upadacitinib and filgotinib are also discussed [1,13].

Evidence and Guideline Consistency

The guideline-consistency study found that most pharmacotherapy recommendations across the examined clinical practice guidelines were consistent in direction, but many differed in strength: seven PICs were consistent in both direction and strength, ten were consistent in direction but

inconsistent in strength, and one was inconsistent in direction. This highlights why clinical decisions require interpretation of evidence, patient factors and the strength of recommendations rather than reliance on a single rule.

Patient experience is also important — social-media analysis of 54,742 DMARD-related posts found overall positive sentiment toward both conventional and biologic/targeted classes, with efficacy the leading positive theme and lack of efficacy followed by side effects among negative themes [12].

8. Pain Management and Psychosocial Dimensions

Pain is one of the most important symptoms in RA, but the supplied literature stresses that pain should not automatically be equated with active inflammation. Pain may arise from inflammatory activity, secondary joint damage, osteoarthritis, fibromyalgia, neuropathic mechanisms, treatment effects and psychosocial factors [4,6,10].

Non-Inflammatory Pain

The review focused on women with RA identifies mechanical pain and fibromyalgia as important contributors, alongside anxiety, depression, sleep disturbance, sexual dysfunction and disability. These factors can reinforce pain and reduce quality of life even when conventional anti-inflammatory treatment has controlled disease activity, supporting a broader, multimodal assessment of pain rather than simply increasing anti-inflammatory medication [6].

Analgesics and NSAIDs

Analgesics and NSAIDs can be useful for temporary symptom relief, particularly during flares or while DMARDs take effect. However, NSAIDs do not modify the underlying disease and should be reduced or withdrawn when adequate DMARD response is achieved, when clinically appropriate [1,2,3,13].

Opioid Analgesics

The supplied opioid-focused editorial questions the role of opioid pharmacotherapy in RA. Earlier evidence indicates that weak opioids may sometimes provide short-term pain relief, but adverse effects can outweigh benefits; other analgesic and non-pharmacological options should generally be considered first [10].

Patient-Centered Pain Management

- Determine whether pain reflects active inflammation or another mechanism.
- Assess function, sleep, mood and other contributors to symptom burden.
- Use disease-modifying therapy to control inflammatory activity.
- Use symptomatic medicines judiciously and reassess their continued need.
- Consider non-pharmacological and multidisciplinary interventions.

The key message is that successful RA management requires control of both disease activity and the broader experience of pain and disability [4,6,10].

9. Osteoporosis and Bone Health in RA

The osteoporosis review identifies local and generalized bone loss as major extra-articular complications of RA. Increased bone resorption in active disease contributes to loss of bone mass and increased risk of vertebral and non-vertebral fragility fractures, which can further reduce function, quality of life and independence.

Risk is multifactorial. Disease activity itself contributes to bone loss, while general factors such as low body mass, fall risk, reduced physical activity and other fracture risks may add to the burden. Glucocorticoid exposure is particularly important, as chronic corticosteroid treatment is associated with osteoporosis and skeletal fractures [7].

Assessment and Prevention

- Evaluate fracture risk in patients with RA, especially those with additional risk factors.
- Assess bone mineral density when clinically indicated.
- Address modifiable fall and lifestyle risks.
- Optimize calcium and vitamin D status where appropriate.
- Minimize unnecessary long-term glucocorticoid exposure.
- Use pharmacological osteoporosis treatment when fracture risk warrants it.

The supplied osteoporosis literature discusses antiresorptive options including bisphosphonates and newer agents, as well as osteoanabolic treatment such as teriparatide, including evidence for alendronate in RA patients receiving chronic low-dose prednisone and studies of teriparatide in glucocorticoid-induced osteoporosis [7].

Interaction with RA Pharmacotherapy

Bone protection is an important part of comprehensive treatment because RA disease activity and its therapies can influence skeletal health. Effective control of inflammation may help reduce disease-related bone loss, while excessive glucocorticoid exposure may increase fracture risk. RA treatment decisions should therefore consider both inflammatory control and long-term skeletal safety — identifying fracture risk early, managing modifiable factors and treating osteoporosis appropriately rather than waiting for a fragility fracture to occur [7,11].

10. Obesity, Pharmacoeconomics and Patient Perspectives

Obesity and RA

The prospective cohort study supplied with the project examined patients with RA and obesity and reported that weight loss following bariatric surgery was associated with lower disease activity. At 12

months, ACR20, ACR50 and ACR70 response rates were higher in the surgery group than in the pharmacotherapy-only group, and disease-activity scores were lower, although medication tapering was not superior in the surgery group. The same study notes that overweight and obesity can aggravate RA disease activity and clinical outcomes, and that RA patients with obesity may have worse responses to several conventional, biologic and targeted DMARDs. These findings support routine attention to weight indicators as part of comprehensive RA care [8].

Pharmacoeconomic Considerations

The pharmacoeconomic source applies ABC/VEN analysis to RA pharmacotherapy. It reports that a large share of analyzed medicines belonged to the ATC L category of antineoplastic and immunomodulatory agents and identifies methotrexate, sulfasalazine, hydroxychloroquine and several other agents within the vital category used in its analysis. The authors argue that pharmacoeconomic information can support appropriate organization of medicine purchasing, prescribing, storage, accounting and quality control [12].

Patient Perceptions and Adherence

The social-media study analyzed 54,742 posts about DMARDs. Both conventional and biologic/targeted groups had overall positive sentiment, although the positive-to-negative ratio was higher for biologic/targeted agents. Efficacy was the most common positive theme, while lack of efficacy and side effects were the main negative themes. Medication selection should therefore consider not only expected efficacy but also tolerability, patient concerns, treatment burden and communication — patient-generated information may complement conventional methods and support shared decision-making and adherence [9].

Integrated Care Model

- Control inflammation early with appropriate DMARD therapy.
- Monitor efficacy and safety continuously.
- Address pain mechanisms beyond inflammation.
- Protect bone health and reduce fracture risk.
- Manage obesity and other comorbidities.
- Consider cost, access, patient experience and adherence.

12. Extended Topics: Comorbidities, Risk Factors and Emerging Considerations

Beyond the core pharmacotherapy literature summarized above, a broader body of recent research addresses additional dimensions of RA care — cardiovascular and pulmonary comorbidity, genetic and environmental risk, lifestyle interventions, treatment economics, reproductive health, and patient-reported outcomes. These findings reinforce and extend the treat-to-target, patient-centered model described earlier.

Cardiovascular Risk

RA is now recognized as an independent risk factor for cardiovascular disease, with overall cardiovascular risk in RA patients estimated at roughly twice that of the general population. A 2024 systematic review notes that the European League Against Rheumatism (EULAR) has proposed multiplying standard cardiovascular risk scores by 1.5 in patients with disease duration over ten years, seropositivity for RF or anti-CCP antibodies, and extra-articular manifestations, although this adjustment has been shown to underestimate risk in some cohorts. The review concludes that an optimal, validated approach to cardiovascular prevention specific to RA remains undefined, underscoring the need for individualized cardiovascular screening alongside disease-activity control [14].

Genetic Susceptibility: HLA-DRB1 and the Shared Epitope

Variants of the HLA-DRB1 gene that share a common amino-acid sequence — the so-called shared epitope (SE) alleles — remain the strongest known genetic risk factor for RA, particularly for antibody-positive (ACPA-positive) disease. Genetic studies have also explored interactions between SE alleles and other genes, such as CIITA, to determine whether additional loci modify RA risk. One such analysis found no significant interaction between CIITA variants and SE alleles, suggesting that much of the genetic risk beyond HLA-DRB1 remains unexplained and that gene–gene and gene–environment interactions are an active area of investigation [15].

Smoking and Environmental Risk

Cigarette smoking is the best-established modifiable environmental risk factor for RA, particularly in genetically susceptible individuals carrying HLA-DRB1 shared-epitope alleles. A 2025 review describes how tobacco exposure may generate neoantigens through cellular damage, disrupt respiratory and intestinal microbiota, and thereby trigger or amplify autoimmune responses years before clinical joint symptoms appear. Smoking has also been linked to higher disease activity and elevated inflammatory markers in patients who already have RA, reinforcing smoking cessation as a preventive and disease-modifying lifestyle measure [16].

Exercise, Rehabilitation and Physical Function

Contrary to older assumptions that rest protects inflamed joints, structured physical activity is now considered safe and broadly beneficial in RA. A 2025 systematic review of rehabilitation therapy combined with DMARD treatment found consistent improvements in physical function (reflected by reductions in Health Assessment Questionnaire scores) and modest reductions in composite disease-activity scores compared with DMARD therapy alone. Exercise-related benefits reported across the literature include reduced fatigue and pain, improved cardiovascular fitness, and better psychological well-being, supporting the integration of individualized exercise programs into routine RA management [17].

Diet and Nutritional Approaches

Dietary pattern is increasingly recognized as a modifiable, complementary factor in RA management. A 2026 narrative review concludes that omega-3 fatty acid supplementation and Mediterranean-style dietary patterns have the most consistent supporting evidence, showing modest but clinically meaningful reductions in inflammatory markers and disease-activity scores. Marine-derived omega-3s and olive oil were specifically highlighted for anti-inflammatory effects, supporting the inclusion of dietary counseling as an adjunct — rather than a replacement — for standard pharmacotherapy [18].

Pulmonary Involvement: Interstitial Lung Disease

Interstitial lung disease (RA-ILD) is among the most serious extra-articular complications of RA and a leading cause of RA-related mortality after cardiovascular disease. A 2024 review describes usual interstitial pneumonia and nonspecific interstitial pneumonia as the most common histopathological patterns, with risk increased by smoking, high rheumatoid factor titers, and elevated ACPA levels. Because pharmacological options remain limited and evidence specific to RA-ILD is sparse, the review emphasizes early screening with high-resolution CT and multidisciplinary management combining immunosuppression with, where indicated, antifibrotic therapy [19].

Biosimilar DMARDs and Treatment Economics

Biosimilar versions of TNF inhibitors and other biologics have emerged as lower-cost alternatives with clinically comparable efficacy to their reference products. A 2024 economic evaluation of over 25,000 RA patients found that initiating treatment with a biosimilar after methotrexate failure was more cost-effective — yielding lower lifetime healthcare costs and greater quality-adjusted life-years — than initiating leflunomide, a conventional synthetic DMARD. The authors suggest that treatment guidelines may need updating to reflect the improved affordability and accessibility that biosimilars now offer [20].

Rheumatoid Arthritis and Reproductive Health

Family planning and pregnancy management require special consideration in RA, since several effective DMARDs are contraindicated during conception or gestation. The 2024 update of the EULAR points-to-consider on antirheumatic drugs in reproduction, pregnancy, and lactation confirms that methotrexate and leflunomide are contraindicated in pregnancy, whereas hydroxychloroquine, sulfasalazine, and — based on individualized risk-benefit assessment — TNF-inhibitor biologics may be continued throughout pregnancy when needed to control disease activity. These recommendations aim to balance maternal disease control against fetal safety and reflect an evolving, more permissive stance toward biologic use in pregnancy compared with earlier guidance [21].

Difficult-to-Treat RA

A subset of patients continue to experience symptomatic, active disease despite sequential trials of multiple biologic or targeted synthetic DMARDs. To standardize research and clinical approaches to this group, EULAR published a formal definition of 'difficult-to-treat RA' (D2T RA), requiring failure of at least two b/tsDMARDs with different mechanisms of action after conventional synthetic

DMARD failure, evidence of ongoing active or symptomatic disease, and a shared perception by clinician and patient that management remains problematic. Commentators have noted that the definition, while a useful starting point, does not fully capture the heterogeneous biological, psychological, and social factors that can underlie treatment resistance [22].

Health-Related Quality of Life and Patient-Reported Outcomes

Disease activity and functional status only partly explain how patients experience RA day to day. A cohort study of over 450 patients found that higher cumulative disease activity (DAS28), greater functional disability (HAQ score), and the presence of depression or anxiety were all independently associated with poorer health-related quality of life, measured using the EQ-5D and EQ visual analogue scale. These findings support incorporating validated patient-reported outcome measures — capturing pain, fatigue, mood, and daily function — alongside conventional clinical and laboratory measures when evaluating treatment success [23].

13. CONCLUSION

The supplied literature presents rheumatoid arthritis as a chronic systemic autoimmune disease requiring early, targeted and individualized management. Early diagnosis and prompt DMARD treatment are repeatedly emphasized because uncontrolled inflammation can lead to irreversible joint damage, disability and broader complications.

Symptomatic therapies such as NSAIDs and glucocorticoids remain useful, but they do not replace disease-modifying treatment. Methotrexate is a central anchor therapy with multiple anti-inflammatory mechanisms, while biologic and targeted synthetic DMARDs provide additional options for inadequate response or intolerance.

Comprehensive care must also address persistent non-inflammatory pain, psychosocial burden, osteoporosis, obesity and treatment preferences, together with the broader comorbidity, risk-factor and quality-of-life considerations outlined above. Patient perceptions emphasize efficacy and adverse effects, while pharmacoeconomic analysis highlights the importance of rational medicine selection and resource use. Taken together, these findings support a multidisciplinary, treat-to-target and patient-centered model of RA management [1,2,3,13].

REFERENCES

1. Bullock J, Rizvi SAA, Saleh AM, et al. Rheumatoid Arthritis: A Brief Overview of the Treatment. Med Princ Pract. 2018;27:501–507.
2. Kumar P, Banik S. Pharmacotherapy Options in Rheumatoid Arthritis. Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders. 2013;6:35–43.
3. Schneider M, Krüger K. Rheumatoid arthritis—early diagnosis and disease management. Dtsch Arztebl Int. 2013;110:477–484.

4. Rindfleisch JA, Muller D. Diagnosis and Management of Rheumatoid Arthritis. American Family Physician. 2005;72:1037–1047.
5. Zhao Z, Hua Z, Luo X, et al. Application and pharmacological mechanism of methotrexate in rheumatoid arthritis. Biomedicine & Pharmacotherapy. 2022;150:113074.
6. Chancay MG, Guendsechadze SN, Blanco I. Types of pain and their psychosocial impact in women with rheumatoid arthritis. Women's Midlife Health. 2019;5:3.
7. Raterman HG, Bultink IE, Lems WF. Osteoporosis in patients with rheumatoid arthritis: an update in epidemiology, pathogenesis, and fracture prevention. Expert Opinion on Pharmacotherapy. 2020;21:1725–1737.
8. Xu F, Yu C, Li DG, et al. The outcomes of bariatric surgery on rheumatoid arthritis disease activity: a prospective cohort study. Scientific Reports. 2020;10:3167.
9. Sharma C, Whittle S, Haghighi PD, et al. Mining social media data to investigate patient perceptions regarding DMARD pharmacotherapy for rheumatoid arthritis. Ann Rheum Dis. 2020;79:1432–1437.
10. Pazmino S, Verschueren P, Westhovens R. Does opioid-based pharmacotherapy have a place in rheumatoid arthritis therapy? Expert Opinion on Pharmacotherapy. 2021;22:1945–1947.
11. Hu Y, Han Y, Ma Y, et al. Consistency of recommendations for pharmacotherapy of rheumatoid arthritis. Frontiers in Pharmacology. 2022;13:967787.
12. Hayduchok IG, Shapovalova VO, Ishcheikin KE, et al. Pharmacoeconomic Approaches for Pharmacotherapy of Rheumatoid Arthritis. 2021.
13. Alhamad YM, Almisbah FH, Alarbash AM, et al. Pharmacotherapy In Rheumatoid Arthritis: A Deep Study. Int. J. Adv. Sig. Img. Sci. 2026;12(5s).
14. Singh T, Laxmiraj B, Chukka RCH, Noor T. Cardiovascular Risk Management In Patients With Rheumatoid Arthritis: A Systematic Review. Cureus. 2024;16(4):e58409.
15. Ronninger M, Seddighzadeh M, Eike MC, et al. Interaction Analysis between HLA-DRB1 Shared Epitope Alleles and MHC Class II Transactivator CIITA Gene with Regard to Risk of Rheumatoid Arthritis. PLoS ONE. 2012;7(3):e32861.
16. Masuko K. Cigarette Smoking: A Modifiable Environmental Factor in the Pathogenesis of Rheumatoid Arthritis. JMA Journal. 2025. doi:10.31662/jmaj.2025-0029.
17. Alapa N, Tafuto B, Mittal R. Impact of Rehabilitation Therapy on Disease Activity, Function, and Quality of Life in Rheumatoid Arthritis: A Systematic Review. Cureus. 2025;17(9):e92627.
18. Deseatnicova E, Covaliov E, Deseatnicova O, Siminiuc R, Rezus E, Groppa L. Impact of Nutritional Diet Therapy on Rheumatoid Arthritis Disease Activity. Nutrients. 2026;18(3):517.
19. Al-Baldawi S, Zúñiga Salazar G, Zúñiga D, Balasubramanian S, Mehmood KT. Interstitial Lung Disease in Rheumatoid Arthritis: A Review. Cureus. 2024;16(2):e53632.
20. Peng K, Chan SCW, Wang Y, et al. Cost-Effectiveness of Biosimilars vs Leflunomide in Patients With Rheumatoid Arthritis. JAMA Netw Open. 2024;7(6):e2418800.

21. Pluma A, Hamroun S, Cecchi I, et al. EULAR recommendations for use of antirheumatic drugs in reproduction, pregnancy, and lactation: 2024 update. Ann Rheum Dis. 2025;84(6):910–926.
22. Roodenrijs NMT, de Hair MJH, van der Goes MC, et al. EULAR definition of difficult-to-treat rheumatoid arthritis. Ann Rheum Dis. 2021;80(1):31–35.
23. Katchamart W, Narongroeknawin P, Chanapai W, Thaweeratthakul P. Health-related quality of life in patients with rheumatoid arthritis. BMC Rheumatol. 2019;3:34.