Lifestyle Factors and Their Impact on Rheumatoid Arthritis: A Literature Review

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterized by joint inflammation and systemic manifestations. Increasing attention has been directed towards the role of modifiable lifestyle factors in influencing RA susceptibility, disease progression, and therapeutic response.

Objective: This review aims to systematically evaluate the associations between lifestyle factor including tobacco use, dietary patterns, obesity, physical activity, educational attainment, and socioeconomic status and the risk, clinical course, and treatment outcomes of RA.

Methods: A comprehensive search of the PubMed database was conducted to identify epidemiological and prospective studies examining the impact of lifestyle behaviors on RA onset and management. Studies were selected based on relevance, methodological rigor, and focus on both disease incidence and treatment efficacy.

Results: Consistent evidence implicates smoking, poor dietary quality, excess adiposity, lower educational levels, and socioeconomic deprivation as significant contributors to increased RA incidence. Furthermore, smoking, obesity, and physical inactivity are associated with attenuated responses to disease-modifying antirheumatic therapies.

However, heterogeneity in study designs and residual confounding limit definitive causal conclusions.

Conclusions: Despite inherent methodological challenges, current data underscore the importance of lifestyle modification—specifically smoking cessation, adherence to a nutritious diet, maintenance of healthy body weight, and regular exercise—as critical strategies to mitigate RA risk and enhance therapeutic outcomes. Future longitudinal and mechanistic studies are warranted to further elucidate these relationships and inform personalized interventions.

***Keywords**: Mediterranean diet, cigarette smoking, socioeconomic status, physical activity, obesity, disease progression, rheumatoid arthritis, lifestyle factors*

Introduction

Individuals afflicted with inflammatory rheumatic diseases (IRDs) often seek to enhance therapeutic efficacy or reduce pharmacologic dependency through lifestyle modifications. This interest is partly driven by widespread media narratives emphasizing the role of nutrition, body mass regulation, physical activity, and psychosocial stressors in health outcomes and longevity. Meanwhile, commercial entities target this population with dietary supplements and wellness products claiming to offer prophylactic or therapeutic benefits for rheumatic diseases.

Despite these claims, evidence-based medicine identifies a limited set of lifestyle factors that clearly influence disease risk or progression in IRDs. Most research focuses on rheumatoid arthritis (RA), where epidemiological and mechanistic studies have highlighted lifestyle determinants as key modulators of disease susceptibility. Notably, longitudinal analyses within large cohorts have examined modifiable behavior including smoking, obesity, sedentary lifestyle, diet quality, and alcohol consumption and their relationship to RA risk. Researchers developed composite indices, such as the Healthy Lifestyle Index Score (HLIS), to quantify these factors, finding that adherence to healthier lifestyle practices correlates with a significantly reduced risk of RA, particularly among women and in seropositive subtypes.

This review aims to synthesize the current evidence on lifestyle influences in RA, critically evaluating the literature and addressing its limitations.

Nutritional Determinants in the Etiology and Progression of Rheumatoid Arthritis (RA)

Understanding the role of nutrition in the onset and progression of rheumatoid arthritis (RA) is complex due to the diverse nature of diet and its interactions with systemic inflammation. Diet significantly influences the gut microbiome, which is a key factor in inflammatory rheumatic diseases. For instance, high-fiber diets are linked to lower levels of inflammatory cytokines, while omega-3 polyunsaturated fatty acids demonstrate anti-inflammatory effects and are associated with reduced autoantibody levels in individuals at risk of RA [5, 6, 8].

Large cohort studies such as the Nurses' Health Study (NHS) have shown that healthier dietary patterns, reflected by scores like the Alternative Healthy Eating Index (AHEI), correlate with a decreased risk of RA. Diets rich in fruits, vegetables, nuts, unsaturated fats, and whole grains tend to be protective, whereas high consumption of sugar-sweetened beverages is associated with increased RA risk. Moderate alcohol intake and lower red meat consumption also appear beneficial .

The Empirical Dietary Inflammatory Index (EDII) further identifies pro-inflammatory diets, characterized by high intake of red and processed meats and refined grains, which correspond with elevated inflammatory markers and increased RA risk. Conversely, components like wine, coffee, and leafy greens are linked to anti-inflammatory effects [11, 12].

While evidence on the Mediterranean diet (MD) is mixed, some studies report a protective effect against seropositive RA, particularly among men, although other large cohorts have not found a definitive association [14, 15].

Fish and Polyunsaturated Fatty Acids (PUFAs) in Rheumatoid Arthritis (RA)

Polyunsaturated fatty acids (PUFAs), including fish oil and plant-derived oils, are well-recognized for their anti-inflammatory properties. Several studies suggest a protective effect of oily fish consumption on RA development, although the statistical strength varies [16,19]. Data from the UK Biobank (n > 500,000) reported an inverse relationship between RA risk and intake of oily fish, breakfast cereals, and moderate alcohol consumption . Moreover, a cohort of over 30,000 elderly women showed a dose-response effect, where PUFA intake above 0.21 grams/day was associated with a 52% reduction in RA incidence . Higher erythrocyte levels of n-6 PUFAs were linked to lower RA risk (OR 0.29, highest vs. lowest tertile) . Similarly, n-3 PUFA concentrations negatively correlated with rheumatoid factor and anti-CCP antibodies in genetically susceptible individuals .

Adiposity and Rheumatoid Arthritis Risk

The association between a pro-inflammatory diet (high EDII) and RA risk diminished after adjusting for body mass index (BMI) [1]. Obesity stands out as a major modifiable risk factor for RA, as highlighted in the Nurses' Health Study (NHS) cohort . After BMI adjustment, dietary quality (AHEI score) showed no independent effect on RA risk . Longitudinal data from approximately 108,000 women (1989–2017) indicated that weight gain over 20 kg was linked to a significantly higher risk of seropositive RA (RR 3.8) [2]. These results align with previous findings showing a positive relationship between BMI and RA risk, despite some variability among studies . Notably, combined obesity and smoking synergistically increase RA risk beyond their individual effects [3]. Central adiposity, often measured by waist circumference, has been implicated as a significant RA risk factor in some cohorts , although other studies found no independent effect beyond overall adiposity [4].

Alcohol Consumption and Rheumatoid Arthritis

Moderate alcohol intake appears to reduce the risk of rheumatoid arthritis (RA). The Malmö Diet and Cancer Study (n=30,447) reported that consuming 3.5 to 15.2 grams of alcohol per day was associated with a 52% lower odds of RA compared to lower intake, even after adjusting for smoking and education . A meta-analysis of eight prospective cohorts (over 195,000 participants) confirmed this protective effect, showing a relative risk (RR) of 0.86 for low-to-moderate drinkers versus abstainers, with a non-linear dose-response peaking at around 9 grams daily. Higher intake (~30 grams) may negate this benefit . Beverage type did not significantly influence RA risk.

Nutritional Interventions in the Management of Rheumatoid Arthritis

The efficacy of dietary interventions as adjunctive treatments for rheumatoid arthritis (RA) remains a subject of considerable debate, with existing evidence characterized by heterogeneity and limited conclusiveness. A Cochrane systematic review published in 2009, encompassing 14 clinical trials with a cumulative sample of 837 patients, concluded that the impact of dietary modifications on RA outcomes was uncertain, primarily due to methodological limitations including small sample sizes and a high risk of bias . Subsequent systematic reviews have reinforced this uncertainty, underscoring the current lack of robust evidence to definitively support dietary interventions as effective modalities in RA management .

Although certain studies have observed trends suggesting amelioration of pain and inflammatory markers following specific dietary regimens, the extant data are insufficient to endorse any dietary protocol as a viable substitute for conventional disease-modifying antirheumatic drugs (DMARDs). Diets such as the Mediterranean diet (MD) and other anti-inflammatory dietary patterns have demonstrated potential in attenuating systemic inflammation and improving cardiovascular risk profiles among RA patients, yet consistent evidence demonstrating a reduction in disease activity remains elusive [35,37–39].

Notably, nutritional interventions incorporating the Mediterranean diet have been associated with modest improvements in disease activity indices, including reductions in the Disease Activity Score in 28 joints (DAS28), which are partially attributed to enhanced intake of omega-3 polyunsaturated fatty acids (PUFAs). Nonetheless, such interventions are unlikely to supplant DMARD therapy or forestall the progression of joint damage in the long term . Furthermore, dietary approaches involving vegan or Mediterranean patterns may yield improvements in patient-reported outcomes such as pain; however, these benefits do not extend to the prevention of structural joint damage or the control of highly active disease states.

Fasting and Rheumatoid Arthritis Disease Activity

Short-term fasting interventions have demonstrated potential benefits in alleviating symptoms associated with rheumatoid arthritis (RA), although evidence supporting their sustained efficacy, particularly in the context of structural joint preservation, remains lacking. A meta-analysis synthesizing available clinical trials on fasting in RA patients concluded that controlled fasting protocols, typically not exceeding 12 weeks in duration, may result in transient reductions in pain and inflammatory symptoms [5]. Nevertheless, these symptomatic improvements appear to be temporary, and current data are insufficient to endorse fasting as a viable long-term therapeutic strategy for RA management.

Exclusion Diets in Rheumatoid Arthritis

Various exclusion diets have been investigated for their potential therapeutic effects in rheumatoid arthritis (RA), primarily targeting the removal of suspected dietary allergens such as gluten and dairy. One study evaluating the elimination of milk allergens and azo dyes failed to demonstrate any definitive clinical benefit among RA patients, although it remains plausible that specific food allergies may influence disease activity in certain subpopulations. A 2001 investigation employing a vegan, gluten-free diet reported modest

improvements in inflammatory markers, including reductions in C-reactive protein (CRP) levels; however, adherence was notably poor, with over 40% of participants discontinuing the regimen due to its restrictive nature . Despite some encouraging outcomes in limited studies, exclusion diets are generally not recommended for RA management owing to challenges related to tolerability, potential nutritional deficiencies, and inconsistent evidence regarding their efficacy.

Weight Reduction Interventions in Rheumatoid Arthritis

Weight management constitutes a critical component of rheumatoid arthritis (RA) care, given the contributory role of excess adiposity in amplifying systemic inflammation and disease activity. Multiple studies have evaluated the efficacy of weight reduction interventions among RA patients, with bariatric surgery and hypocaloric dietary regimens demonstrating favorable outcomes. A retrospective cohort analysis of RA patients undergoing bariatric surgery revealed significant decreases in inflammatory biomarkers alongside notable improvements in clinical disease activity following the surgical intervention [7]. Correspondingly, a randomized controlled trial investigating a 12-week hypocaloric diet (ranging from 1000 to 1500 kcal/day) in RA patients reported an average weight loss of 9.5 kilograms, which was concomitant with statistically significant reductions in disease activity scores (DAS28) and enhancements in functional status, as assessed by the Health Assessment Questionnaire (HAQ) Disability Index [8].

Nutritional Supplements in the Management of Rheumatoid Arthritis

Nutritional supplementation has been investigated as a potential adjunctive strategy in the management of rheumatoid arthritis (RA), with varying degrees of efficacy and quality of evidence. Among the most extensively studied are omega-3 polyunsaturated fatty acids (PUFAs), which have demonstrated beneficial effects in reducing joint pain intensity, morning stiffness, and the requirement for nonsteroidal anti-inflammatory drugs (NSAIDs) in several clinical trials [12].

Other supplements, including curcumin, garlic, and saffron, have shown anti-inflammatory and antioxidative properties in preclinical models; however, the clinical literature supporting their use in RA remains limited and is frequently characterized by small sample sizes, methodological weaknesses, and substantial risk of bias . Similarly, probiotic supplementation has been explored for its potential to modulate immune and inflammatory responses, yet existing studies are heterogeneous and underpowered, providing insufficient evidence to support their routine use in RA management [23-24-25].

Although omega-3 PUFA supplementation appears to offer modest clinical benefits, there is no robust evidence to support the efficacy of trace element supplementation such as zinc, copper, magnesium, or selenium in altering disease activity or progression in RA patients [27-28-29-30-31-32-33]. Furthermore, while vitamin E was initially proposed as a therapeutic antioxidant, subsequent studies have failed to demonstrate significant clinical benefit, and excessive intake has been associated with increased all-cause mortality, raising concerns about its safety in long-term use .

Consequently, supplementation with vitamins, trace elements, and other micronutrients should be approached with caution. Nutritional interventions in RA should be guided by laboratory-confirmed deficiencies particularly of vitamin D and iron which may warrant correction within the broader framework of disease management.

Nutrition and Rheumatoid Arthritis: Current Recommendations

Current clinical guidelines acknowledge the role of nutrition as a supportive element in the comprehensive management of rheumatoid arthritis (RA). The European League Against Rheumatism (EULAR) recommends the adoption of a balanced diet and the maintenance of a healthy body weight for individuals with rheumatic and musculoskeletal diseases, including RA, as part of a broader strategy to improve health outcomes and reduce comorbid risk factors .

The French Society for Rheumatology has issued more specific dietary guidance, advocating for adherence to a Mediterranean diet rich in fruits, vegetables, legumes, whole grains, and healthy fats, alongside supplementation with polyunsaturated fatty acids. Importantly, the society discourages restrictive dietary patterns such as vegan or gluten-free diets and the unnecessary elimination of dairy products, citing a lack of consistent evidence supporting their efficacy in RA management. In addition, these guidelines emphasize the importance of cardiovascular risk reduction, given the well-documented association between RA and increased cardiovascular morbidity and mortality [6].

In summary, while evidence supports the role of balanced nutrition, weight control, and Mediterranean dietary patterns in modulating inflammation and improving comorbid outcomes, dietary interventions should be viewed as adjunctive strategies rather than standalone therapies. Disease-modifying antirheumatic drugs (DMARDs) remain the cornerstone of RA treatment. Continued research is warranted to further elucidate the role of specific nutritional interventions and to inform evidence-based dietary recommendations for RA patients.

Smoking and the Development of Rheumatoid Arthritis (RA)

Tobacco smoke exposure is among the most well-established environmental risk factors for the development of rheumatoid arthritis (RA), particularly in seropositive disease forms. Epidemiological studies estimate that smoking accounts for approximately 20% of all RA cases and up to 35% of anti-citrullinated protein antibody (ACPA)-positive RA cases [70,71]. The causal link between smoking and RA has been substantiated through robust longitudinal and genetic studies. A landmark twin study conducted in 1996, involving 79 monozygotic and 71 dizygotic twin pairs discordant for RA, demonstrated that smoking was associated with a fourfold increase in RA risk among smoking twins, with the odds ratio (OR) rising to 5.5 among monozygotic pairs underscoring a gene environment interaction in RA pathogenesis [16].

Further evidence arises from a large Swedish case-control study involving 858 incident RA cases and 1,048 controls, which investigated the combined effects of smoking and genetic susceptibility conferred by the shared epitope (SE) alleles of the HLA-DRB1 gene. The study revealed a striking synergistic interaction between smoking and SE alleles in promoting seropositive RA. Specifically, individuals with one SE allele who smoked had a relative risk (RR) of 7.5, which increased to 15.7 in those with two SE alleles. Notably, smoking did not elevate the risk of seronegative RA regardless of SE status, highlighting a distinct pathogenic mechanism in ACPA-positive disease .

These findings were further supported by data from the Swedish Epidemiological Investigation of RA (EIRA), which demonstrated a dose-dependent relationship between smoking intensity and the risk of developing ACPA-positive RA. Among individuals with one or two copies of the SE allele, smoking increased the risk by 6.5-fold and 21-fold, respectively. No such association was observed for ACPA-negative RA, reinforcing the specificity of the smoking–genotype interaction in driving seropositive disease .

The biological mechanisms by which smoking contributes to RA pathogenesis are multifaceted. Tobacco smoke promotes systemic inflammation through its impact on pulmonary and periodontal inflammation two conditions frequently linked to RA onset. Nicotine, a key component of tobacco smoke, has been shown to promote autoimmunity through multiple pathways. One of the principal mechanisms involves the activation of peptidyl-arginine deaminase (PAD) enzymes in the lung, leading to protein citrullination. This process generates neoantigens that are central to ACPA formation, particularly in genetically susceptible individuals carrying HLA-DRB1 SE alleles.

Moreover, nicotine has been implicated in the induction of neutrophil extracellular trap (NET) formation, or NETosis, a mechanism through which neutrophils release citrullinated proteins into the extracellular space, thereby enhancing autoantigen exposure and promoting autoreactive B and T cell activation [17]. Experimental models have shown that nicotine administration exacerbates disease activity and NET formation, even in the absence of other tobacco smoke components. This suggests that nicotine alone, such as through e-cigarette use, may contribute to RA pathogenesis in genetically predisposed individuals [17].

A large cohort study involving 6,239 Japanese RA patients corroborated these findings, identifying a positive correlation between nicotine exposure and the presence of both ACPA and rheumatoid factor (RF). Interestingly, nicotine use showed a stronger association with RF formation than with ACPA, though the development of ACPA was confined to individuals carrying the SE allele. Furthermore, elevated ACPA levels were detectable up to 20 years after smoking cessation, indicating the long-term immunological consequences of nicotine exposure .

In conclusion, smoking is a significant and modifiable environmental risk factor for RA, particularly in individuals with genetic susceptibility defined by the presence of shared epitope alleles. The cumulative evidence supports a gene–environment interaction in the pathogenesis of ACPA-positive RA, with mechanisms involving citrullination and NET formation. These insights underscore the critical importance of smoking cessation—both as a primary prevention strategy and as a means of reducing disease risk and severity in predisposed populations.

Smoking and the Outcome of Rheumatoid Arthritis (RA)

Beyond its well-established role in the pathogenesis of rheumatoid arthritis (RA), smoking also significantly influences disease progression, treatment response, and the development of comorbidities. Numerous studies have demonstrated that smoking is associated with a poorer prognosis in RA patients, including reduced responsiveness to both conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and biologic agents, particularly tumor necrosis factor-alpha (TNF-α) inhibitors . Smokers are less likely to achieve sustained remission and are at greater risk for disease flare-ups compared to non-smokers. These adverse outcomes are believed to be mediated by smoking's pro-inflammatory effects, which intensify synovial inflammation and alter immune system dynamics.

Importantly, the negative impact of smoking on disease activity persists even after RA is established. Retrospective cohort analyses have indicated that smoking

cessation following RA diagnosis does not significantly alter the disease course. Patients who discontinued smoking after diagnosis continued to experience similar levels of disease activity and joint damage compared to those who remained active smokers . These findings suggest that the pathogenic effects of smoking may induce irreversible immunologic and structural changes in established RA.

The role of passive smoking has also been investigated. The Swedish BARFOT (Better Anti-Rheumatic PharmacOTherapy) study reported a high prevalence (68%) of secondhand smoke exposure among RA patients who identified as non-smokers—a figure notably higher than in the general population. While passive smoke exposure was not directly associated with increased disease activity, the data imply that environmental tobacco exposure may contribute to RA pathogenesis, particularly in genetically predisposed individuals, by amplifying early immune dysregulation .

Smoking is further linked to an increased risk of comorbid conditions in RA, notably interstitial lung disease (ILD), which affects approximately 10% of RA patients. The risk of developing RA-associated ILD is significantly elevated among smokers, especially in those with high titers of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) . The underlying mechanism involves nicotine-induced citrullination of lung proteins, which promotes ACPA production. These autoantibodies not only play a central role in RA pathogenesis but are also implicated in the development of ILD, indicating a shared immunopathogenic mechanism .

In summary, smoking exerts a multifactorial detrimental influence on RA, compromising treatment efficacy, accelerating disease progression, and increasing the likelihood of comorbid complications such as ILD. Although smoking cessation is universally recommended, current evidence suggests that its benefits may be more pronounced in disease prevention than in modifying established disease. Passive smoking, though less directly associated with disease activity, may still contribute to RA onset and severity in genetically susceptible individuals. These findings underscore the critical importance of early smoking cessation and public health measures aimed at minimizing tobacco exposure to reduce both the incidence and burden of RA.

Fine Particulate Matter and Rheumatoid Arthritis (RA)

Fine particulate matter (PM), especially particles with aerodynamic diameters of 10 micrometers or less (PM_{10}) and 2.5 micrometers or less ($PM_{2.5}$), has garnered increasing attention as a potential environmental contributor to the development of rheumatoid arthritis (RA) and its pulmonary comorbidities, particularly interstitial lung disease (ILD). Among these environmental exposures, silica

dust often encountered in occupational setting has been most robustly linked to increased RA risk.

One of the earliest recognized associations is between silica exposure and the dual manifestation of pulmonary fibrosis and RA, a clinical presentation known as Caplan's syndrome, commonly observed among coal miners . In the Swedish Epidemiological Investigation of Rheumatoid Arthritis (EIRA) study, occupational exposure to stone dust among men was associated with a twofold increased risk of developing RA . Subsequent analyses reinforced this finding, revealing that silica exposure was significantly associated with an increased risk of ACPA-positive RA (odds ratio [OR]: 1.7), while no corresponding association was observed for ACPA-negative RA. This distinction highlights the relevance of autoimmune mechanisms in the development of RA in the context of particulate exposure.

Moreover, a synergistic effect has been observed between smoking and silica exposure. In individuals who both smoked and were exposed to silica, the risk of developing ACPA-positive RA increased substantially, with an OR of 7.4 compared to unexposed non-smokers . These findings suggest that environmental triggers can interact with one another and with genetic susceptibility to enhance autoimmune responses, potentially through mechanisms involving lung inflammation and citrullination of self-proteins.

While the role of silica exposure is well established, the evidence regarding ambient exposure to fine particulate matter, such as PM_{10} and $PM_{2.5}$, is more nuanced. Early investigations, including those conducted within the EIRA and the Nurses' Health Study (NHS) cohorts, did not demonstrate a statistically significant association between general PM exposure and RA risk . However, more recent evidence has suggested a broader environmental impact. A large Italian retrospective cohort study involving 81,363 individuals reported a dose-dependent relationship between PM exposure and the development of autoimmune diseases, including RA . Specifically, higher concentrations of $PM_{2.5}$ were more strongly associated with increased RA incidence compared to PM_{10}, suggesting that smaller particulate size may facilitate deeper penetration into lung tissue, thereby enhancing immune activation and systemic inflammatory responses.

In summary, while occupational exposure to silica is a well-documented risk factor for ACPA-positive RA, particularly in smokers, the relationship between general fine particulate matter and RA is still evolving. Emerging data suggest that $PM_{2.5}$, in particular, may play a role in triggering autoimmune processes through chronic pulmonary inflammation, potentially leading to ACPA production and RA onset in genetically predisposed individuals. These findings underscore the importance of considering both occupational and environmental air quality in RA risk assessment and prevention strategies.

Socioeconomic Status and Rheumatoid Arthritis (RA)

The relationship between socioeconomic status (SES) and health outcomes is well established, with individuals of higher SES generally experiencing more favorable health outcomes than those of lower SES . In rheumatoid arthritis (RA), SES influences not only disease onset but also progression and prognosis. Several SES-related factors such as smoking behavior, nutritional status, obesity, and marital status contribute to disease activity and functional impairment. Importantly, evidence suggests that SES itself may independently affect the severity and course of RA.

Multiple observational studies have demonstrated that lower SES correlates with more severe disease activity and greater functional limitations in RA patients. A cohort study conducted in England involving 869 RA patients found that lower SES, as measured by educational attainment, was associated with higher disease activity both at baseline and longitudinally. Patients from lower SES backgrounds exhibited worse functional outcomes, including elevated Health Assessment Questionnaire (HAQ) scores, reduced grip strength, and increased joint involvement. However, these disparities were not reflected in radiographic progression or inflammatory markers such as erythrocyte sedimentation rate (ESR) .

Educational level, often employed as a proxy for SES, has also been linked to disease severity. A U.S. study with 385 RA patients reported that individuals with lower educational attainment had higher disease activity, as indicated by ESR, grip strength, and joint counts . Similarly, a prospective study of 814 RA patients in England and Scotland observed that residence in socioeconomically deprived areas was associated with greater functional impairment, evidenced by elevated HAQ scores, although no significant differences were found in inflammatory markers such as ESR or C-reactive protein (CRP) . A recent review of 30 studies examining social status and RA disease activity concluded that 25 studies demonstrated a clear association between lower SES and increased disease severity. However, heterogeneity in the operationalization of SES and disease activity limited cross-study comparability, underscoring the need for standardized measures in future research .

While the impact of SES on RA progression and severity is well documented, its role as a risk factor for RA development is less clear. The Swedish Epidemiological Investigation of Rheumatoid Arthritis (EIRA) case-control study, which included 930 incident RA cases and 1,126 controls, assessed the relationship between SES indicators (education and occupation) and RA risk. After adjustment for confounders including age, smoking, and residential area, individuals without a

university degree had a relative risk (RR) of 1.4 for developing RA, with a stronger effect observed for seropositive RA (RR = 1.6). Moreover, individuals employed in high-ranking non-manual occupations had a 20% lower risk of RA compared to those in other non-manual jobs .

In summary, socioeconomic status significantly influences RA disease activity and progression. Lower SES is consistently associated with greater disease severity and functional impairment. Although the evidence is less definitive, lower SES may also increase the risk of developing RA, particularly seropositive RA. Future research employing standardized definitions of SES and disease metrics is essential to clarify these relationships and to guide targeted public health interventions aimed at reducing socioeconomic disparities in RA outcomes.

Psychosocial Stress and Rheumatoid Arthritis (RA)

Chronic psychosocial stress is increasingly recognized as a potential contributor to the development and progression of various chronic diseases, including rheumatoid arthritis (RA). Many RA patients report psychological stress as a possible trigger for disease onset or exacerbation. Psychoneuroendocrinological frameworks propose that chronic psychosocial stress influences immune function via activation of the hypothalamic-pituitary-adrenal (HPA) axis, thereby potentially facilitating autoimmune processes such as those observed in RA .

A recent review examining psychological stress in RA differentiated between types of stress, including role stress, social stress, and work-related stress. The review of 16 studies revealed considerable heterogeneity in stress measurement tools and conceptual definitions. Nonetheless, findings consistently indicated that RA patients experience higher levels of work-related and social stress compared to healthy controls. While the psychological burden of chronic illness and pain on mental health is well documented, research directly addressing the causal role of psychosocial stress in RA development remains sparse.

The Swedish Epidemiological Investigation of RA (EIRA) study provided important insights into work-related psychosocial stress as a risk factor for RA. Using self-reported data and job exposure matrices to assess psychological demand and decision latitude at work, the study found that low decision latitude—reflecting limited control over work tasks—was significantly associated with increased RA risk (odds ratio [OR] = 1.6). Conversely, high psychological job demands showed a nonsignificant trend towards a reduced risk. These associations persisted after adjusting for social class, suggesting an independent role of workplace psychosocial stress in RA pathogenesis .

Furthermore, a Danish population-based survey of 19,890 participants investigated the association between loneliness and RA prevalence. The analysis

revealed a modest positive association (OR = 1.3), although the study design did not allow for causal inference, underscoring the need for further longitudinal research to clarify this relationship .

In summary, although evidence remains limited, current studies suggest that psychosocial stress—particularly in occupational and social contexts—may influence both the onset and course of RA. Future research employing standardized stress measurement and longitudinal designs is essential to elucidate underlying mechanisms and identify effective stress management interventions for RA prevention and treatment.

Psychosocial stress also appears to affect prognosis in established RA. Clinical trial data indicate that psychosocial factors can modulate disease outcomes, particularly in relation to remission maintenance and flare frequency. For instance, the randomized controlled CareRA trial, involving patients with early arthritis, demonstrated that individuals experiencing high psychosocial stress were more likely to relapse from remission, highlighting the negative impact of stress on disease control .

These findings emphasize the complex interplay between psychological and biological factors in RA progression and suggest that integrating psychosocial support and stress management into comprehensive RA care could enhance treatment outcomes. Addressing psychosocial well-being may therefore be vital not only for improving patients' mental health but also for mitigating biological disease activity.

Marital and Family Status in Rheumatoid Arthritis (RA)

While rheumatoid arthritis (RA) does not appear to significantly affect divorce rates compared to the general population, marital status has been shown to influence disease progression and patient well-being. Research indicates that married individuals with RA generally experience slower progression of disability relative to their unmarried counterparts . Moreover, those in stable, non-distressed marriages report lower pain levels and decreased physical disability compared to individuals who are unmarried or in distressed relationships . These observations underscore the potential protective role of social support and emotional security factors commonly associated with stable marital relationships in mitigating both the physical and psychological burdens associated with RA and other inflammatory rheumatic diseases (IRDs).

Sexual dysfunction is notably more prevalent among RA patients than in the general population, although it remains an under-discussed issue in clinical practice . The pathophysiology of sexual dysfunction in RA is multifactorial, involving chronic pain, comorbidities, and psychological factors such as

depression and fatigue . Additionally, disease activity, patient and partner age, and sleep disturbances contribute to the severity and frequency of sexual health problems. Studies report that nearly 50% of female RA patients experience sexual dysfunction, which substantially impairs quality of life .

Regarding parenthood, direct research on the impact of having children on RA disease activity or outcomes is lacking. However, a recent large-scale study investigating parent-child relationships found that offspring born to mothers with RA exhibited an increased incidence of mental health disorders. These included heightened risks of autism spectrum disorders, attention-deficit/hyperactivity disorder (ADHD), bipolar disorder, and major depressive disorder . These findings suggest that the effects of RA may extend beyond the affected individual, potentially influencing the mental health and well-being of offspring, particularly in cases of maternal RA.

Physical Activity and Rheumatoid Arthritis (RA)

The beneficial effects of regular physical activity on various health parameters, including quality of life, cardiovascular fitness, and muscle strength, in patients with rheumatoid arthritis (RA) are well-established . Reflecting these benefits, the European League Against Rheumatism (EULAR) recommends regular physical exercise as part of the management strategy for RA patients . However, the impact of physical exercise on inflammatory disease activity in established RA remains unclear. While a meta-analysis encompassing ankylosing spondylitis, systemic lupus erythematosus, and RA reported a reduction in inflammatory activity with exercise across these conditions , other meta-analyses focused specifically on RA found no significant effect of cardiovascular or resistance training on disease activity, as measured by the Disease Activity Score 28 (DAS28) .

One study noted progression of joint damage in patients with pre-existing severe joint involvement following high-intensity, weight-bearing exercise . Nevertheless, the consensus from most studies and meta-analyses supports the safety and benefits of resistance and aerobic exercises for RA patients . Accordingly, EULAR guidelines endorse not only aerobic activities but also targeted muscle-strengthening exercises for this population .

Regarding the potential protective role of physical activity against the development of RA, findings are inconsistent. The Nurses' Health Study II, including 113,366 women with 506 incident RA cases, demonstrated a dose-dependent association between recreational physical activity and reduced RA risk. Women engaging in 4 to 7 hours or more than 7 hours per week of physical activity exhibited relative risks (RR) of 0.84 and 0.67, respectively, compared to those with less than 1 hour per week . Similarly, the Swedish Mammography

Cohort, tracking 30,112 women aged 54 to 89 years, found that participants in the highest physical activity category had a significantly lower risk of developing RA (RR: 0.7) relative to the least active group .

In contrast, the Iowa Women's Health Study, involving 31,336 women aged 55 to 69 years, did not identify a significant association between leisure-time physical activity and RA risk, as varying exercise levels (low, medium, high) failed to influence disease development . Furthermore, a meta-analysis of four studies with 255,365 women and 4,213 incident RA cases indicated a negative association between physical activity and RA development (highest activity group RR: 0.8 versus lowest). However, Mendelian randomization analysis from the same authors did not support a causal relationship, suggesting potential limitations in observational studies such as insufficient statistical power or inadequate confounder adjustment .

Major limitations of studies assessing physical activity's role in RA onset include challenges in controlling for confounding lifestyle factors such as diet, smoking, and body mass index. Individuals with higher physical activity levels often engage in generally healthier behaviors, complicating efforts to isolate the independent effect of exercise on RA risk. In conclusion, while physical activity clearly benefits RA patients regarding symptoms and functional status post-diagnosis, current evidence is insufficient to establish a causal preventive role in RA development.

Conclusions

Environmental factors play a critical role in the pathogenesis and progression of rheumatoid arthritis (RA), frequently interacting synergistically with genetic predispositions. A prominent example is the interplay between smoking and the shared epitope (SE), which substantially influences the generation of anti-citrullinated protein antibodies (ACPA), a hallmark of seropositive RA . Modifiable environmental exposures, including diet, physical activity, and tobacco use, are subject to individual behavioral modification, offering opportunities for personalized interventions aimed at reducing disease burden.

Accurately quantifying the individual contribution of environmental factors to RA development remains challenging due to the complex, multifactorial interactions involved. Many such factors—such as lifestyle behaviors (diet, smoking, physical activity) and socioeconomic status—often co-occur and are strongly influenced by educational attainment. Disentangling their independent effects necessitates robust methodological designs, including large-scale cohort studies with multivariate stratification. Furthermore, the onset of RA may itself precipitate changes in lifestyle, engendering a bidirectional relationship between disease activity and socioeconomic determinants.

Epidemiological research on environmental exposures has primarily utilized retrospective cohort designs, with some prospective studies contributing additional insights. Although these investigations demonstrate significant associations, establishing causality remains difficult due to potential confounding variables. The relationship between smoking and RA onset and progression is well-established and underpinned by extensive evidence. In contrast, associations between other factors such as diet, physical activity, and socioeconomic status while consistently linked to improved disease outcomes, are yet to be rigorously defined.

Nonetheless, it is widely accepted that healthy dietary patterns, regular physical exercise, and higher socioeconomic status correlate with more favorable outcomes in RA patients. These factors may also confer protective effects against RA development, although the precise mechanisms remain incompletely understood.

Future research should prioritize elucidating the mechanistic pathways through which environmental factors influence RA initiation and progression. Longitudinal studies integrating genetic and epigenetic analyses will be essential for clarifying causal relationships. Advancing understanding in this domain will facilitate the development of evidence-based preventive strategies and enable more personalized therapeutic approaches for individuals at risk of, or living with, RA.

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