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Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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THE IMPACT OF PHYSICAL ACTIVITY ON AUTOIMMUNE DISEASES: A NARRATIVE REVIEW OF MECHANISMS, OUTCOMES AND PRACTICAL IMPLICATIONS

Karolina Błądzińska *(Corresponding Author, Email: bladzinska.karolina@gmail.com)*
Clinical Provincial Hospital No. 2 named after St. Queen Jadwiga in Rzeszów, St. Lwowska 60, 35-301 Rzeszów, Poland
ORCID ID: 0009-0008-4510-3982

Maciej Błądziński
Clinical Provincial Hospital No. 2 named after St. Queen Jadwiga in Rzeszów, St. Lwowska 60, 35-301 Rzeszów, Poland
ORCID ID: 0000-0001-9615-0959

Małgorzata Zach
University Clinical Hospital named after Fryderyk Chopin in Rzeszów, St. Szopena 2, 35-055 Rzeszów, Poland
ORCID ID: 0009-0006-8061-9613

Kacper Szeląg
City Hospital of John Paul II in Rzeszów, St. Rycerska 4, 35-241 Rzeszów, Poland
ORCID ID: 0009-0004-0591-735X

Barbara Wołoszyn
Independent Public Health Care Facility – A Complex of Facilities in Maków Mazowiecki, Witosa 2, 06-200 Maków Mazowiecki, Poland
ORCID ID: 0009-0009-0386-1205

ABSTRACT

Autoimmune diseases are chronic, heterogeneous disorders characterized by immune-mediated tissue damage, systemic inflammation, and reduced quality of life. Pharmacological treatments often alleviate symptoms but rarely address functional limitations such as fatigue, deconditioning, and psychosocial distress. Physical activity (PA) is increasingly recognized as a safe and effective adjunctive therapy. This narrative review synthesizes biological mechanisms, disease-specific outcomes, and practical applications of PA across major autoimmune conditions including rheumatoid arthritis (RA), multiple sclerosis (MS), systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), and type 1 diabetes (T1D). Evidence shows that PA functions as a multimodal immunomodulator, reducing pro-inflammatory cytokines, enhancing regulatory T-cell activity, rebalancing adipokines, recalibrating neuroendocrine pathways, and supporting microbiome diversity. Clinically, PA improves fatigue, functional capacity, mood, and cardiometabolic risk, without increasing relapse or flare frequency. The FITT framework (Frequency, Intensity, Time, Type) offers a practical model for prescribing exercise, with disease-specific adaptations ensuring safety and adherence. Despite strong evidence, implementation remains limited due to patient fears, clinician knowledge gaps, and systemic barriers. Digital health and tele-exercise hold promise for precision exercise medicine. In conclusion, physical activity is a safe, effective, and indispensable adjunct in autoimmune disease management, warranting integration into standard care pathways.

KEYWORDS

Autoimmune Diseases, Physical Activity, Exercise Prescription, Inflammation, Fatigue, Quality of Life

CITATION

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1. Introduction

Autoimmune diseases are chronic, often lifelong conditions in which the immune system loses tolerance to self-antigens, leading to tissue injury and organ dysfunction. More than 80 autoimmune conditions have been identified, ranging from organ-specific diseases such as type 1 diabetes mellitus (T1D) to systemic disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and multiple sclerosis (MS) [1]. Collectively, these diseases affect 3–8% of the population worldwide and disproportionately impact women of reproductive age [2].

Pharmacologic treatments—including disease-modifying antirheumatic drugs (DMARDs), biologics, and small-molecule immunosuppressants—have revolutionized care. However, these therapies are not curative, carry risks of infection or toxicity, and fail to address common residual symptoms such as fatigue, pain, and decreased physical function [3]. Furthermore, many autoimmune diseases are associated with increased risk of cardiovascular disease, osteoporosis, and metabolic syndrome, which are only partly mitigated by pharmacotherapy [4].

Lifestyle interventions—including nutrition, stress management, sleep, and physical activity—are increasingly recognized as modulators of immune function. Of these, **physical activity (PA)** and structured exercise stand out for their systemic benefits. Epidemiologic evidence suggests that physically active individuals have lower incidence of autoimmune disease, while interventional studies consistently show improvements in physical and psychological outcomes among patients already diagnosed [5,6].

Mechanistically, exercise exerts profound immunomodulatory effects. Skeletal muscle functions as an endocrine organ, releasing myokines (e.g., interleukin-6 in its acute, anti-inflammatory role) that reduce tumor necrosis factor-α (TNF-α) signaling and stimulate anti-inflammatory mediators [7]. Exercise also enhances regulatory T-cell (Treg) function, improves adipokine balance, modulates neuroendocrine responses, and shapes gut microbiota composition [8–10]. Importantly, these adaptations are **dose-dependent**: moderate activity induces tolerance-promoting pathways, whereas excessive high-intensity training without adequate recovery can transiently impair immune competence and gastrointestinal integrity [11].

Despite mounting evidence, structured exercise is underutilized in clinical management of autoimmune diseases. Many patients report insufficient guidance, while clinicians remain uncertain about disease-specific prescriptions or concerned about exacerbations [12]. This narrative review aims to:

1. Summarize biological mechanisms linking exercise to immune regulation;
2. Evaluate clinical outcomes across major autoimmune diseases (RA, MS, SLE, IBD, T1D);
3. Provide practical prescriptions using the FITT framework;
4. Discuss safety considerations, implementation challenges, and future research directions.

2. Biological Mechanisms Linking Exercise and Autoimmunity

The therapeutic rationale for physical activity in autoimmune diseases rests on a diverse set of molecular and systemic mechanisms. Exercise acts not only on musculoskeletal and cardiovascular systems but also directly modulates the immune network. These mechanisms can be grouped into six domains: (i) myokine and cytokine signaling, (ii) T-cell and B-cell regulation, (iii) neuroendocrine pathways, (iv) adipose tissue and metabolic effects, (v) gut microbiota and barrier integrity, and (vi) mitochondrial and epigenetic reprogramming.

2.1 Myokines and Cytokine Signaling

Skeletal muscle, once considered only a mechanical tissue, is now recognized as an endocrine organ that secretes *myokines* during contraction [13]. Among these, **interleukin-6 (IL-6)** is central. While chronically elevated IL-6 in obesity or RA promotes inflammation, acute IL-6 release during exercise induces anti-inflammatory cascades: it stimulates production of interleukin-10 (IL-10) and interleukin-1 receptor

antagonist (IL-1ra) and concurrently suppresses TNF-α [14]. This phenomenon—often termed the *IL-6 paradox*—illustrates the context-dependent nature of cytokine signaling.

Other relevant myokines include:

- **Interleukin-15 (IL-15):** Supports muscle–fat crosstalk and enhances natural killer (NK) and CD8+ T-cell survival [15].
- **Irisin:** Induces browning of white adipose tissue and improves metabolic health [16].
- **Secreted protein acidic and rich in cysteine (SPARC):** Involved in extracellular matrix remodeling, potentially relevant in fibrotic processes [17].
- **Brain-derived neurotrophic factor (BDNF):** Facilitates neuroplasticity and exerts immunomodulatory effects [18].

Repeated exercise bouts result in chronically reduced baseline inflammation, with lower circulating C-reactive protein (CRP), TNF-α, and IL-6, and elevated anti-inflammatory cytokines [19].

2.2 T Cells, B Cells, and Regulatory Balance

Autoimmune pathology frequently involves dysregulation of T helper subsets and loss of immune tolerance. Exercise influences this balance:

- **Regulatory T cells (Tregs):** Moderate-intensity exercise increases both number and suppressive function of Tregs, restoring immune tolerance and dampening autoreactive responses [20].
- **Th17/Treg ratio:** Exercise decreases Th17 cells, reducing production of IL-17 and associated tissue inflammation [21].
- **B cells and autoantibodies:** Data suggest exercise decreases autoantibody production by reducing B-cell hyperactivity, though evidence remains limited [22].
- **Innate immunity:** Exercise mobilizes NK cells and promotes M2 macrophage polarization, which supports tissue repair [23].

These changes are particularly relevant in diseases such as RA, MS, and psoriasis, where Th17/Treg imbalance drives pathology.

2.3 Neuroendocrine Modulation

Exercise stimulates the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system, increasing cortisol, adrenaline, and noradrenaline [24]. In acute bouts, these hormones suppress NF-κB activation, reduce pro-inflammatory cytokine release, and promote apoptosis of autoreactive lymphocytes [25]. Chronic training lowers resting cortisol levels, improves heart rate variability, and enhances resilience to psychological stress [26]. Because psychosocial stress is a known trigger of autoimmune flares, this neuroendocrine adaptation represents an indirect but clinically significant protective effect.

2.4 Adipose Tissue and Metabolic Effects

Obesity is both a risk factor and a disease modifier for several autoimmune conditions. Adipose tissue secretes **adipokines** such as leptin and resistin (pro-inflammatory) and adiponectin (anti-inflammatory) [27]. Excess visceral fat skews immune balance toward Th1 and Th17 activation while impairing Treg activity.

Exercise reduces visceral adiposity, improves insulin sensitivity, and increases adiponectin secretion, thereby restoring a healthier immunometabolic profile [28]. Notably, even in the absence of significant weight loss, exercise improves inflammatory biomarkers, indicating benefits extend beyond caloric expenditure [29].

2.5 Gut Microbiota and Intestinal Barrier Integrity

The gut microbiome exerts systemic influence through metabolite production, immune priming, and epithelial barrier regulation. Dysbiosis has been linked to RA, IBD, and MS [30]. Exercise promotes greater microbial diversity and abundance of short-chain fatty acid (SCFA)-producing bacteria such as *Faecalibacterium prausnitzii* [31]. SCFAs, including butyrate, enhance Treg differentiation and intestinal barrier integrity.

Moderate-intensity activity strengthens gut barrier function and reduces circulating endotoxin levels (lipopolysaccharide, LPS) [32]. In contrast, excessive high-intensity or endurance exercise, especially in heat or dehydration, can transiently increase intestinal permeability, leading to systemic endotoxemia [33]. This "J-shaped" relationship underscores the importance of individualized exercise dosing in autoimmune populations.

2.6 Mitochondrial and Epigenetic Adaptations

Mitochondrial dysfunction contributes to chronic inflammation and autoimmunity, particularly via oxidative stress and metabolic reprogramming of immune cells [34]. Exercise induces mitochondrial biogenesis, enhances oxidative phosphorylation, and improves redox homeostasis in muscle and immune cells [35].

In parallel, exercise exerts **epigenetic effects** on immune regulation. These include:

- DNA methylation changes in cytokine promoter regions,
- Histone modifications that suppress pro-inflammatory gene expression,
- Alterations in microRNA profiles associated with T-cell differentiation [36].

Such adaptations may provide long-term "immune training," supporting tolerance beyond acute exercise sessions.

2.7 Integrated Conceptual Model

Together, these mechanisms establish exercise as a **multilevel immunomodulator**:

- **Acute phase (minutes–hours):** Mobilization of leukocytes, transient cytokine shifts, neuroendocrine activation.
- **Chronic adaptations (weeks–months):** Lower systemic inflammation, improved Treg activity, healthier adipokine balance, resilient stress response, optimized microbiome.
- **Clinical outcomes:** Reduced fatigue, lower flare frequency, enhanced physical function, and protection against comorbidities.

This integrative model provides biological plausibility for the consistent clinical benefits observed across autoimmune diseases.

3. Clinical Outcomes by Disease

3.1 Rheumatoid Arthritis (RA)

RA is a systemic autoimmune disease characterized by chronic synovial inflammation, cartilage damage, and progressive joint deformity. Beyond articular manifestations, RA is associated with sarcopenia, fatigue, and increased cardiovascular risk [37].

Aerobic exercise. Randomized controlled trials (RCTs) demonstrate that moderate-intensity aerobic programs (walking, cycling, swimming) improve cardiorespiratory fitness, fatigue, and quality of life without increasing disease activity measured by DAS28 [38].

Resistance training. RA often leads to rheumatoid cachexia, with loss of muscle mass despite stable or increased fat mass. Progressive resistance training (PRT) increases muscle strength and lean mass, improving functional independence and reducing disability scores [39].

High-intensity interval training (HIIT). Preliminary studies show HIIT is feasible and safe in stable RA, providing comparable cardiovascular benefits to moderate-intensity continuous training [40].

Guidelines. The 2018 EULAR recommendations endorse structured physical activity for RA patients, with general population targets (≥150 minutes/week of moderate aerobic activity plus resistance training) adapted to individual capacity [41].

Summary. Exercise in RA is safe, reduces fatigue, improves function, and counteracts cachexia, while lowering cardiovascular risk.

3.2 Multiple Sclerosis (MS)

MS is an autoimmune demyelinating disease of the central nervous system, affecting ~2.8 million people worldwide. Major symptoms include mobility impairment, fatigue, and depression [42].

Aerobic training. Moderate aerobic exercise (cycling, treadmill walking) enhances VO_2peak, walking capacity, and quality of life [43].

Resistance and balance training. Resistance training improves strength and daily function, while balance programs (yoga, tai chi) reduce fall risk [44].

Fatigue and mood. Meta-analyses confirm exercise reduces fatigue and depressive symptoms, outcomes that are inadequately managed with pharmacotherapy [45].

Safety. No evidence supports concerns that exercise increases relapse risk. Uhthoff's phenomenon (heat-induced symptom exacerbation) is transient and mitigated by cooling strategies [46].

Summary. Exercise is disease-modifying in terms of function, alleviating fatigue, mood, and mobility without worsening disease activity.

3.3 Systemic Lupus Erythematosus (SLE)

SLE is a systemic autoimmune disorder with multisystem involvement. Fatigue, reduced physical capacity, and cardiovascular risk are prominent concerns [47].

Fatigue and quality of life. Controlled trials demonstrate exercise reduces fatigue and improves vitality and mental health scores on SF-36 [48].

Aerobic and resistance training. Combined programs improve muscle strength, aerobic fitness, and quality of life without worsening SLE Disease Activity Index (SLEDAI) [49].

Safety. Exercise is safe; flare rates are not increased. However, programs should be adapted for organ involvement (e.g., nephritis, cardiac disease) and sun protection is essential for photosensitive patients [50].

Summary. Exercise in SLE reduces fatigue and improves overall well-being, countering a major unmet need.

3.4 Inflammatory Bowel Disease (IBD)

IBD (Crohn's disease and ulcerative colitis) is characterized by relapsing intestinal inflammation, extraintestinal manifestations, and reduced quality of life [51].

Aerobic training. Moderate-intensity activity improves disease activity indices, reduces fatigue, and enhances quality of life [52].

Resistance and bone health. Resistance exercise counters corticosteroid-induced osteoporosis and supports muscle function [53].

Safety. Exercise is safe during remission and mild activity, but vigorous endurance training under heat stress can exacerbate gastrointestinal permeability and symptoms [54]. During flares, light activity such as walking and stretching is preferable [55].

Summary. Exercise improves fatigue, bone health, and psychosocial outcomes in IBD, with adaptations required during flares.

3.5 Type 1 Diabetes Mellitus (T1D)

T1D is caused by autoimmune destruction of pancreatic β-cells, resulting in lifelong insulin dependence. Exercise is beneficial but requires careful glucose management [56].

Aerobic training. Improves insulin sensitivity, cardiovascular fitness, and psychosocial health. However, it carries higher risk of hypoglycemia, particularly with prolonged or evening sessions [57].

Resistance training. Provides metabolic and strength benefits and may reduce risk of hypoglycemia compared with aerobic exercise alone [58].

Technology. Continuous glucose monitoring (CGM) and hybrid closed-loop insulin pumps improve exercise safety by allowing real-time glucose tracking and insulin adjustments [59].

Guidelines. The American Diabetes Association recommends ≥150 minutes/week of moderate-to-vigorous aerobic activity and 2–3 resistance sessions per week, with individualized strategies for insulin and carbohydrate adjustment [60].

Summary. Exercise is indispensable in T1D management but must be paired with proactive glucose monitoring and patient education.

3.6 Other Autoimmune Conditions

- **Psoriasis and psoriatic arthritis (PsA):** Exercise reduces systemic inflammation, supports weight reduction (improving skin and joint outcomes), and alleviates fatigue [61].
- **Ankylosing spondylitis (AS):** Flexibility and postural exercises maintain spinal mobility; guidelines recommend lifelong exercise as standard care [62].
- **Autoimmune thyroid disease:** Limited evidence suggests benefits for fatigue and metabolic health, though more research is needed [63].
- **Idiopathic inflammatory myopathies:** Supervised low-intensity training improves strength and endurance without worsening disease activity [64].

Summary of Section

Evidence across autoimmune diseases consistently supports exercise as:

1. **Safe** – no increase in relapse or flare risk when appropriately prescribed.
2. **Effective** – improves fatigue, quality of life, mobility, and cardiometabolic risk.
3. **Condition-specific** – requires tailored modifications (joint protection in RA, cooling in MS, glucose monitoring in T1D, flare awareness in IBD).

4. Practical Applications: Exercise Prescription in Autoimmune Diseases

Physical activity should be considered a therapeutic adjunct for autoimmune diseases, not merely a lifestyle option. The **FITT framework** (Frequency, Intensity, Time, Type) provides a structured approach for tailoring exercise prescriptions to disease-specific needs. While international guidelines recommend at least 150–300 minutes per week of moderate-intensity aerobic activity plus two or more resistance sessions [65], adaptations are necessary for safety, symptom management, and long-term adherence in autoimmune populations.

4.1 General FITT Principles

Frequency. Aerobic training should occur 3–5 times per week, and resistance sessions 2–3 times per week. Flexibility and balance exercises, particularly beneficial in MS and RA, should be included at least 2 days weekly [66].

Intensity. Moderate-intensity activity (40–60% VO_2max; 11–13 on Borg's RPE scale) is safe and effective. Vigorous activity (≥70% VO_2max) may be tolerated in stable patients but requires careful adaptation, especially in MS (heat intolerance), IBD (gut sensitivity), and T1D (glucose management) [67].

Time. Aerobic sessions should last 20–60 minutes. Resistance exercise typically involves 1–3 sets of 8–12 repetitions targeting major muscle groups. For patients with fatigue, shorter bouts (10–15 minutes) accumulated throughout the day are effective [68].

Type. Aerobic activities may include walking, cycling, swimming, or elliptical training. Resistance exercise can involve free weights, resistance bands, or bodyweight movements. Flexibility and balance activities such as yoga and tai chi are beneficial, particularly in MS and AS [69].

Progression. Programs should follow a "start low, go slow" principle, with 5–10% increases in volume or intensity weekly depending on tolerance [70].

4.2 Safety Considerations

- **Disease activity.** During flares (e.g., RA or IBD), intensity should be reduced to gentle activity such as stretching or walking [71].
- **Joint protection.** Low-impact modalities and aquatic therapy minimize stress on inflamed joints in RA and PsA [72].
- **Heat sensitivity.** MS patients benefit from cooling strategies (air-conditioned rooms, fans, cool pools) to prevent Uhthoff's phenomenon [73].
- **Metabolic risks.** T1D requires structured glucose monitoring and adjustment of insulin and carbohydrate intake before and after activity [74].
- **Medication considerations.** Corticosteroid-treated patients should emphasize bone-loading activities to counter osteoporosis [75].
- **Comorbidities.** Cardiovascular screening is recommended prior to vigorous activity, especially in RA and SLE with elevated CV risk [76].

4.3 Disease-Specific FITT Applications

Rheumatoid Arthritis (RA)

- **Frequency:** Aerobic 3–5 days/week; resistance 2–3 days/week.
- **Intensity:** Moderate; HIIT cautiously in stable disease.
- **Time:** Aerobic 20–40 min; resistance 1–3 sets, 8–12 reps.
- **Type:** Walking, cycling, swimming, resistance bands/weights.
- **Special notes:** Prioritize joint protection; aquatic therapy for painful joints [77].

Multiple Sclerosis (MS)

- **Frequency:** Aerobic 2–3 days/week; resistance 2 days/week; balance/flexibility 2–3 days/week.
- **Intensity:** Moderate; vigorous possible with cooling adaptations.
- **Time:** 10–40 minutes, split into shorter bouts if fatigue limits tolerance.
- **Type:** Cycling, treadmill, aquatic therapy, yoga, tai chi.
- **Special notes:** Manage heat sensitivity; prioritize fall prevention [78].

Systemic Lupus Erythematosus (SLE)

- **Frequency:** Aerobic 2–3 days/week; resistance 2 days/week; flexibility 2–3 days/week.
- **Intensity:** Light-to-moderate.
- **Time:** 20–40 minutes.
- **Type:** Walking, cycling, yoga, swimming.
- **Special notes:** Sun protection for photosensitive patients; slow progression with severe organ involvement [79].

Inflammatory Bowel Disease (IBD)

- **Frequency:** Aerobic 3–5 days/week; resistance 2–3 days/week.
- **Intensity:** Moderate; avoid prolonged endurance in heat or dehydration.
- **Time:** Aerobic 30–45 minutes; resistance 1–3 sets of 8–12 reps.
- **Type:** Walking, cycling, resistance bands/weights.
- **Special notes:** Light activity during flares; emphasize hydration and symptom monitoring [80].

Type 1 Diabetes Mellitus (T1D)

- **Frequency:** Aerobic 3–5 days/week; resistance 2–3 days/week.
- **Intensity:** Moderate to vigorous depending on glucose control.
- **Time:** 20–60 minutes per session.
- **Type:** Aerobic and resistance of patient's preference.
- **Special notes:** Pre/during/post glucose checks, carbohydrate supplementation, CGM and hybrid closed-loop pumps recommended [81].

4.4 Special Populations

- **Children/adolescents:** With increasing incidence of pediatric autoimmune disease, exercise prescriptions should emphasize fun, variety, and family participation [82].
- **Older adults:** Focus on balance, flexibility, and resistance to reduce fall and fracture risk [83].
- **Pregnancy:** Light-to-moderate activity is generally safe in RA and SLE, with supervision recommended in high-risk pregnancies [84].

4.5 Tele-Exercise and Digital Health

Remote exercise delivery has expanded rapidly. Tele-exercise interventions in RA, MS, and SLE show similar adherence and effectiveness compared with in-person programs [85]. Wearables and apps can monitor heart rate, steps, and glucose (in T1D), enhancing safety and motivation [86]. Integration of digital health with clinical care enables **precision exercise medicine**, tailoring activity to individual needs and real-time physiological responses [87].

Summary of Section

The FITT framework provides a structured, flexible model for prescribing exercise in autoimmune diseases. Emphasis on **moderate-intensity aerobic and resistance training**, complemented by flexibility and balance, ensures safety and efficacy across diverse conditions. Disease-specific adaptations—such as joint protection in RA, cooling strategies in MS, flare monitoring in IBD, and glucose regulation in T1D—are essential for optimizing outcomes. Exercise should be formally integrated into standard care pathways, supported by clinician guidance and digital health innovations.

5. Discussion

This narrative review demonstrates that physical activity (PA) exerts clinically meaningful benefits across a wide range of autoimmune diseases. Mechanistically, PA modulates immune function through myokine release, T-cell regulation, neuroendocrine recalibration, favorable adipokine shifts, microbiome diversity enhancement, and mitochondrial adaptations. Clinically, structured exercise improves fatigue, mobility, quality of life, and cardiometabolic risk factors without exacerbating disease activity. Despite this growing body of evidence, exercise remains underutilized in autoimmune disease management.

5.1 Exercise as a Multimodal Immunomodulator

Unlike pharmacologic immunosuppression, which suppresses immune responses broadly, exercise functions as a **multimodal immunomodulator**. It reduces pathological inflammation while preserving host defense. The IL-6 paradox exemplifies this duality: exercise-induced IL-6 promotes anti-inflammatory cascades, whereas chronically elevated IL-6 in obesity and RA is deleterious [88]. Similarly, exercise-induced expansion of regulatory T cells (Tregs) and reduction in Th17 cells restore immune tolerance, which is impaired in conditions such as RA, MS, and psoriasis [89]. These findings suggest that PA can serve as a natural adjunctive therapy targeting core immunopathogenic pathways.

5.2 Clinical Outcomes and Disease-Specific Nuances

The evidence base confirms that exercise is beneficial across autoimmune diseases, though condition-specific nuances are critical:

- **RA:** Exercise reduces fatigue and counters rheumatoid cachexia, while lowering cardiovascular risk [90].
- **MS:** Exercise improves fatigue, mobility, and depression, with no evidence of increased relapse risk. Heat sensitivity requires individualized cooling adaptations [91].
- **SLE:** Exercise primarily reduces fatigue and enhances vitality. Concerns regarding flare induction are unsupported by evidence [92].
- **IBD:** Moderate exercise improves quality of life and bone health, while high-intensity endurance under heat or dehydration may worsen gut permeability [93].
- **T1D:** Exercise improves insulin sensitivity but requires vigilant glucose management. Modern technologies, such as continuous glucose monitoring (CGM) and hybrid closed-loop pumps, enhance safety [94].

The consistency of benefit across such diverse conditions reinforces the systemic, not disease-specific, nature of exercise-mediated immune modulation.

5.3 Safety and Patient Concerns

A major barrier to implementation is **patient and clinician concern about safety**. Fears include joint damage in RA, relapse in MS, flares in SLE and IBD, and hypoglycemia in T1D. However, systematic reviews consistently report that exercise is safe when prescriptions are individualized [95]. The primary determinant of risk is **dose**: moderate-intensity exercise is universally safe, while prolonged high-intensity training may require adaptations.

Patient-centered counseling and supervised initiation increase adherence and reassurance. Importantly, the perception of risk often outweighs actual risk, underscoring the need for clinician education and clear communication [96].

5.4 Barriers to Implementation

Several barriers limit exercise integration into autoimmune care pathways:

1. **Clinician knowledge gaps.** Many physicians lack training in exercise prescription [97].
2. **Patient fears.** Patients often self-limit due to pain, fatigue, or fear of exacerbation [98].
3. **Systemic barriers.** Access to physiotherapists or safe facilities may be limited, especially in low-resource settings [99].
4. **Disease-related limitations.** Severe fatigue, mobility impairment, or organ involvement can reduce adherence to conventional programs [100].

Addressing these barriers requires interdisciplinary collaboration, patient education, and scalable models such as tele-exercise.

5.5 Digital Health and Precision Exercise Medicine

Digital health tools, including wearables and tele-exercise programs, offer promising solutions. Remote interventions have demonstrated feasibility and adherence comparable to in-person training in RA, MS, and SLE [101]. Wearables allow continuous monitoring of heart rate, step count, and energy expenditure, while CGM provides real-time glucose feedback in T1D [102]. Integration of such tools enables **precision exercise medicine**, tailoring prescriptions to individual physiology, disease activity, and patient preferences [103].

5.6 Research Gaps

Despite progress, several gaps remain:

- **Dose–response relationships.** The optimal frequency, intensity, and duration of exercise for specific autoimmune diseases remain unclear [104].
- **Mechanistic human studies.** Most evidence comes from animal models; more trials linking immunological biomarkers with clinical outcomes are needed [105].
- **Long-term outcomes.** Few studies exceed 6–12 months; effects on disease progression and cardiovascular mortality are underexplored [106].
- **Pediatric populations.** With rising incidence of juvenile autoimmune diseases, research in children is critically needed [107].
- **Implementation science.** Trials must address how best to integrate exercise into routine care across diverse healthcare systems [108].

5.7 Clinical and Public Health Implications

For clinicians, the implications are clear: exercise should be prescribed as part of standard care for autoimmune diseases. Structured prescriptions within the FITT framework improve adherence and outcomes. Multidisciplinary teams—including rheumatologists, neurologists, gastroenterologists, endocrinologists, and exercise specialists—are best positioned to deliver effective programs [109].

From a public health perspective, integrating exercise can reduce disability, healthcare utilization, and comorbid burden in populations with autoimmune disease [110]. As a low-cost and broadly accessible intervention, PA represents a highly scalable tool for improving outcomes globally.

Summary of Discussion

Exercise is a safe, effective, and underutilized therapeutic strategy in autoimmune diseases. It acts as a multimodal immunomodulator, addressing fatigue, mobility, and quality of life across conditions without increasing flare risk. Implementation barriers—including safety concerns, lack of clinician training, and systemic resource limitations—must be addressed to realize its potential. Future research should define optimal exercise prescriptions, investigate mechanistic pathways in humans, and integrate digital health to advance precision exercise medicine.

6. Conclusions

This review underscores that physical activity is a powerful, evidence-based adjunctive therapy for autoimmune diseases. Across diverse conditions—including rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, inflammatory bowel disease, and type 1 diabetes—exercise consistently demonstrates benefits for fatigue reduction, physical function, psychosocial health, and cardiometabolic risk [111]. Importantly, these outcomes are achieved without increasing relapse or flare frequency when exercise is prescribed appropriately.

Mechanistically, exercise functions as a **multilevel immunomodulator**: it promotes anti-inflammatory cytokine release, enhances regulatory T-cell activity, rebalances adipokines, recalibrates neuroendocrine stress pathways, improves mitochondrial function, and fosters a more diverse and resilient gut microbiome [112]. These adaptations address core pathophysiological processes of autoimmunity and provide a biological basis for observed clinical benefits.

The **FITT framework** offers a practical structure for integrating exercise into clinical care. Moderate-intensity aerobic and resistance training should form the foundation of programs, complemented by balance and flexibility exercises where relevant. Disease-specific adaptations—joint protection in RA, cooling strategies in MS, flare-aware pacing in IBD, and glucose monitoring in T1D—are crucial to ensuring safety and adherence [113].

Despite robust evidence, implementation remains limited. Barriers include clinician uncertainty, patient fears, resource limitations, and lack of structured referral pathways. Addressing these requires **interdisciplinary collaboration**, clinician education, and use of **digital health tools** to expand access and personalization. Tele-exercise programs, wearables, and continuous monitoring technologies represent promising enablers of **precision exercise medicine** in autoimmune populations [114].

Future research should focus on defining dose–response relationships, conducting mechanistic human trials, evaluating long-term outcomes, and expanding investigations into pediatric and underrepresented

populations [115]. By addressing these gaps, exercise prescriptions can evolve from generic recommendations to tailored, evidence-based interventions integrated seamlessly into autoimmune disease management.

In conclusion, physical activity is safe, effective, and indispensable in the care of patients with autoimmune diseases. Clinicians should move beyond encouragement and toward structured prescription, embedding exercise as a standard component of therapeutic strategy.

Author's contribution:

Conceptualization: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Methodology: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Check: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Formal analysis: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Investigation: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Resources: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Data curation: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Writing - rough preparation: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Writing - review and editing: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Supervision: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

Project administration: Małgorzata Zach; Karolina Błądzińska; Maciej Błądziński; Kacper Szeląg; Barbara Wołoszyn

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