International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

Physical Activity and Depression in Rheumatoid Arthritis

Rana Hossam Salah Eldein Mohamd, Heba Abdelwahab Selim, Shereen Eissa Mohamad and Youmna Ahmed Amer

Rheumatology, Rehabilitation and Physical medicine Department, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Rana Hossam Salah Eldein Mohamed

Email: ranazhossam@gmail.com

Abstract:

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory systemic disease that primarily affects synovial joints, functional impairment, and a lower quality of life. In addition to its physical burden, RA is commonly linked with major psychological comorbidities, particularly depression, which affects a large proportion of patients and correlates to poorer clinical outcomes, increased disease activity, and lower treatment adherence. The coexistence of RA and depression is caused by complicated bidirectional connections between inflammatory pathways, neuroendocrine abnormalities, and psychosocial stresses. Physical activity (PA), which is defined as any physiological action that requires energy expenditure, is becoming more acknowledged as an important therapeutic and preventive strategy in chronic diseases. PA is essential for patients with RA because it reduces inflammation, improves joint function, improves cardiovascular and metabolic health, and relieves fatigue. Furthermore, physical activity has significant psychological advantages by alleviating depressed symptoms via neurobiological, behavioral, and social pathways. Understanding the significance of PA in the setting of RA and its accompanying depression is critical for improving patient outcomes and devising comprehensive management plans.

Keywords: Rheumatoid arthritis, Physical activity, Depression, Exercise therapy, Inflammation, Quality of life

Introduction:

The synovial membrane of joints is the primary target of rheumatoid arthritis (RA), a chronic autoimmune inflammatory systemic illness. It is a complicated ailment that varies greatly from case to case as the condition worsens. Significant joint injury and deformity result in reduced functional ability and a lower quality of life if treatment is not received (1).

RA affects a patient's life in a number of ways, including potential negative effects on psychological well-being in addition to physical limits. For instance, RA patients frequently suffer from sadness and significant levels of exhaustion (2).

Any skeletal muscle-driven movement that requires energy is referred to as physical activity (PA) (3). For people with RA, PA is essential for reducing inflammation, maintaining joint function, and enhancing general quality of life (4).

Classification of physical activity:

The WHO guidelines on physical activity and sedentary behaviour (5) classify PA into dual classification — by type and by domain — By type includes; aerobic, muscle-strengthening, balance, and flexibility — By domain includes:

- Leisure (exercise, sports, recreational activity, dancing)
- Work/occupational (job-related physical effort)

• Transport-related (walking, cycling for work),

• Household/domestic (housework, caregiving, gardening, lifting)

1. Aerobic Exercise

Walking, cycling, swimming, and jogging are examples of continuous, rhythmic exercises that use broad muscle groups. It can improve functional capacity, lessen fatigue, increase cardiovascular fitness, and alleviate pain without exacerbating RA disease activity (4).

Current recommendations place a strong emphasis on moderate-to-intense aerobic exercise for managing chronic illnesses as well as maintaining overall health. According to the WHO 2020 Physical Activity Guidelines, all adults, including those with long-term conditions like RA, should engage in at least 150–300 minutes of moderate-intensity Should engage weekly in at least, 75–150 minutes of vigorous-intensity activity, or a combination of both, with modifications for flare-ups. When inflammation is active, care must be taken to avoid high-impact activities (6).

2. Resistance (Strength) Training:

Resistance training increases muscle power, strength, and endurance by using body weight or external loads. It has been demonstrated that progressive resistance training (PRT) can improve joint stability, increase function, and combat RA-related sarcopenia. Research conducted over the past five years has shown that it can lower disability without raising inflammatory indicators **(7).**

3. Flexibility and Range-of-Motion Exercises:

Work on flexibility, such as joint range-of-motion exercises and mild dynamic stretching, helps preserve independence and lessen stiffness. For improved joint function, recent research suggests combining mobility workouts with low-load strengthening. During flare-ups, overstretching could exacerbate symptoms**(8).**

4.Balance and Stability Training:

Single-leg stands, wobble board work, and tai chi are examples of balance exercises that have been demonstrated to enhance postural stability, proprioception, and lower the risk of falls, particularly in older persons or those with long-term musculoskeletal conditions like RA. When there is significant joint swelling, safety precautions must be taken, such as avoiding unstable surfaces. For a bigger impact, current recommendations combine functional strength training with balance exercises(**9).**

Physiological effects of physical activity on RA (figure 1):

1.Cardiovascular Effects:

PA decreases blood pressure, increases cardiac efficiency, improves endothelial function, and minimizes the risk of atherosclerosis and hypertension. Because systemic inflammation and decreased exercise increase cardiovascular risk in RA patients, these effects are advantageous**(10).**

2.Metabolic Effects:

PA reduces the incidence of type 2 diabetes and dyslipidemia by increasing insulin sensitivity, improving skeletal muscle glucose absorption, and regulating lipid metabolism (11).
Due in part to systemic inflammation and long-term glucocorticoid usage, patients with RA often have insulin resistance and a higher risk of metabolic syndrome. Additionally, increased pro-inflammatory cytokines disrupt insulin signaling, worsening endocrine dysfunction and increasing the risk of cardiovascular disease**(12).**

3.Musculoskeletal Effects:

PA improves bone density, joint stability, and muscle strength. Resistance and aerobic training prevent sarcopenia, lessen fatigue, and maintain mobility in RA patients**(4).**

4.Immune and Inflammatory Effects:

Frequent PA reduces circulating cytokines (TNF-α, IL-6), enhances immune surveillance, and has anti-inflammatory effects. Exercise reduces chronic inflammation in RA, which is a benefit of medication therapy**(13).**

5.Psychological and Cognitive Effects:

Through both neurochemical (endorphins, monoamines) and psychosocial routes, regular PA lowers stress, eases anxiety and sadness, and elevates mood **(14).** With long-term advantages for brain health and defense against cognitive decline, PA improves executive function and memory **(15).** Additionally, PA is linked to a lower risk of neurodegenerative diseases and a slower rate of brain aging **(16).** For RA patients, who frequently experience despair, anxiety, and exhaustion, this is crucial**(17).**

6.Respiratory Effects:

By increasing lung capacity, maximal oxygen absorption (VO_2max), and general cardiorespiratory fitness, PA improves respiratory efficiency. Aerobic exercise improves gas exchange, builds stronger respiratory muscles, and postpones the start of ventilatory fatigue during exertion (18). In RA, when respiratory problems such interstitial lung disease, decreased pulmonary function, and weakened respiratory muscles are frequent, these adaptations are essential**(19).**

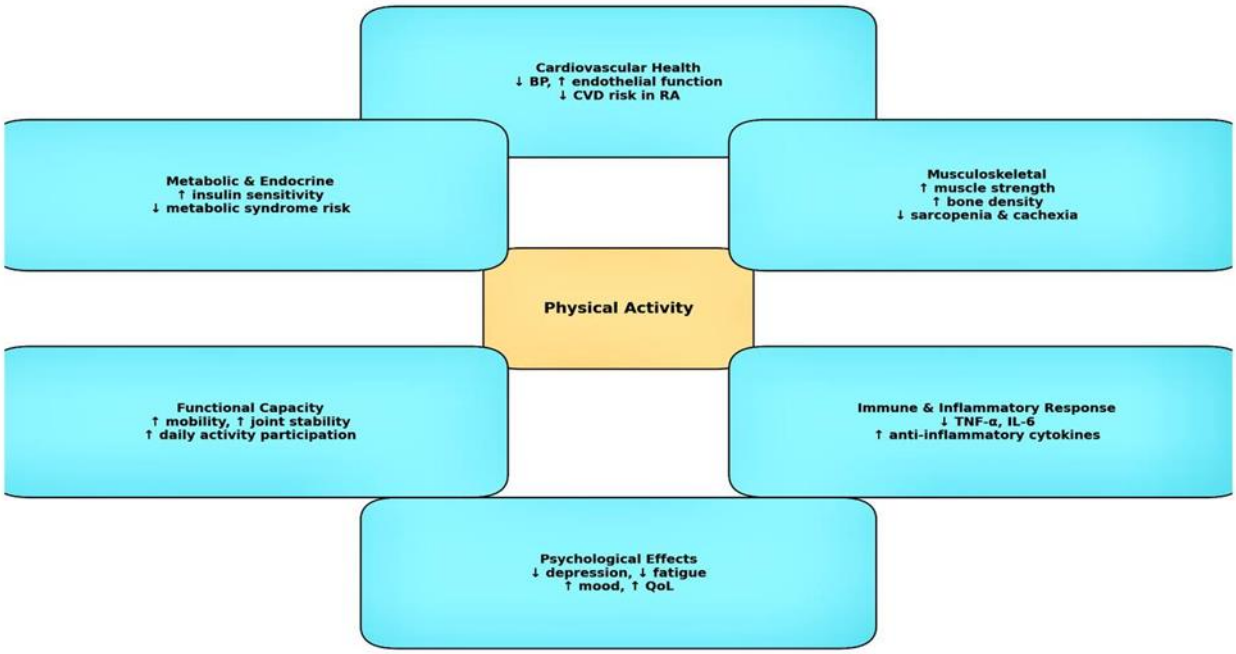

Figure 1. Physiological Effects of Physical Activity in Rheumatoid Arthritis **(**Adapted from **20, 21)**. TNF; tumor necrosis factor, QoL; quality of life.

Motivators and Barriers to Physical Activity

Personal, social, environmental, and clinical aspects are the categories of motivators and obstacles to physical activity that have been extensively researched. These factors are crucial in determining whether or not people choose to lead physically active lifestyles. In populations with chronic illnesses like RA, where obstacles may exceed motivators, it is especially crucial to comprehend these elements**(22).**

1. Personal Factors

The desire to manage weight, lower stress levels, improve general fitness, and improve health are all personal motivators for PA. These incentives frequently serve as powerful catalysts for regular activity and behavior modification (23). However, common obstacles include time constraints, exhaustion, low motivation, pain, or fear of damage, which are especially pertinent for older adults and people with musculoskeletal disorders (24).

2. Social Factors

Activity levels are significantly influenced by social variables. Opportunities for group exercise, encouragement from medical specialists, and support from friends and family are examples of motivators. It has been demonstrated that social support improves participation in activity programs (25). On the other hand, obstacles can include caregiving obligations, cultural or gender conventions, and a lack of social support, all of which can restrict possibilities for consistent engagement**(26).**

3. Environmental Factors

Activity levels are significantly influenced by the physical surroundings. Access to green spaces, recreational amenities, and safe communities that promote outdoor activities and walking are examples of facilitators. However, hazardous surroundings, bad weather, and limited access to amenities have all been repeatedly noted as obstacles **(22).**

4. Clinical Factors

Pain alleviation, higher vitality, and improved mobility are clinical motivators for physical activity in those with chronic illnesses like arthritis. However, participation may be hampered by clinical obstacles like joint stiffness, physical restrictions, and adverse drug reactions. These difficulties emphasize how crucial customized exercise regimens and expert monitoring are in clinical settings**(24).**

Guidelines & Recommendations of PA in RA patients:

Adults with RA should adhere to the general public health PA guidelines (aerobic, muscle-strengthening, flexibility, and neuromotor/balance), customized to their disease status and preferences, according to the EULAR recommendations for physical activity (27).

As part of integrative therapy with DMARDs, regular exercise is strongly advised by the American College of Rheumatology (ACR) 2022 guidelines (29).

(Recommendations Adapted from EULAR, (29))

• **Aerobic activity**: patients should perform ≥150 min/week moderate intensity, but exercise should be tailored to disease activity, joint health, and fatigue.

• **Strength training**: At least 2 days/week, progressive resistance exercise is safe and improves muscle strength and function (important due to RA-associated sarcopenia and cachexia).

• **Flexibility**: Joint range of motion and stretching exercises recommended daily.

• **Balance training**: Especially emphasized in RA due to fall risk from impaired mobility.

Precautions:

patients with RA should: **(29)**

• Avoid high-impact exercise during active flares.

• Monitor joint integrity and cardiovascular comorbidities (higher in RA).

• Have individualized exercise prescription with supervision (e.g. physiotherapist).

Depression

Anybody can be affected by depression, often known as major depressive disorder (MDD). Long-term lack of enjoyment or interest in activities or a depressed mood are its hallmarks. Regular mood swings and sentiments about daily living are not the same as this. For at least two weeks, depressive episodes usually last the majority of the day, almost every day (30).

Additionally, it is defined as follows: According to the International Classification of Diseases, 11th Revision (ICD-11), depressive episodes lasting at least two weeks are defined by a depressed mood, loss of interest or pleasure, and decreased energy. These symptoms are frequently accompanied by other symptoms like diminished concentration, low self-esteem, guilt, disturbed sleep, and changes in appetite (30).

Classification and types of depression:

Depression is a heterogeneous disorder with multiple subtypes that vary in presentation, severity, and course. According to the DSM-5 **(31)** and ICD-11 **(30)**, depressive disorders are classified into several major categories:

1. Major Depressive Disorder (MDD)

The most prevalent type of depression is major depressive disorder. It is typified by at least one severe depressive episode that lasts for at least two weeks and is marked by persistent melancholy, anhedonia, feelings of worthlessness, hunger changes, sleep disturbances, exhaustion, and impaired attention. MDD is linked to a high risk of suicide and substantially inhibits day-to-day functioning (32).

2. Persistent Depressive Disorder (Dysthymia)

Chronic low mood lasting at least two years in adults (or one year in children/adolescents) is referred to as persistent depressive disorder, formerly known as dysthymia. The chronicity makes it extremely incapacitating and raises the chance of having superimposed major depressive episodes, or "double depression," even though the symptoms are frequently less severe than those of MDD (30).

3. Bipolar-related Depressions

Depressive episodes are a fundamental feature of both bipolar I and bipolar II, despite the fact that bipolar disorder is a separate diagnosis. Atypical characteristics like hypersomnia, psychomotor slowness, and an increased risk of psychosis are common in bipolar depression, but symptoms may overlap with MDD. When bipolar depression is mistakenly diagnosed as unipolar MDD, antidepressant monotherapy may be administered inappropriately, which may result in manic episodes (33).

4. Psychotic Depression

Delusions or hallucinations accompany mood symptoms in this severe subtype of depression. Compared to non-psychotic depression, psychotic depression is linked to a worse prognosis, higher relapse rates, and a higher chance of suicide. Antidepressants and antipsychotic drugs, or electroconvulsive therapy (ECT) in certain situations, are typically needed for treatment (34).

5. Perinatal and Postpartum Depression

Depression that develops during pregnancy and in the first year after giving birth is referred to as perinatal depression. It is one of the most frequent complications of childbirth, affecting 10–20% of moms. Hormonal fluctuations, psychological pressures, and a lack of social support are risk factors. The development of infants and the well-being of families are adversely affected by postpartum depression in addition to mothers (35).

6. Seasonal Affective Disorder (SAD)

A recurrent depression pattern associated with seasonal variations, especially in autumn and winter when daylight hours are shorter, is known as seasonal affective disorder. Hypersomnia, increased hunger (particularly for carbs), low energy, and social disengagement are some of the symptoms. Effective therapeutic approaches include circadian rhythm control and bright light therapy (36).

7. Atypical Depression

Mood reactivity (mood improves in response to pleasant occurrences), hypersomnia, hyperphagia (increased eating), leaden paralysis, and rejection sensitivity are characteristics of atypical depression. It is more prevalent in women and younger populations, and it is frequently linked to a chronic course, an earlier onset, and higher rates of comorbidity with anxiety disorders (37).

8. Disruptive Mood Dysregulation Disorder (DMDD)

DMDD was first identified in the DSM-5 and is diagnosed in children and teenagers up to the age of eighteen. It is characterized by violent, frequent outbursts of rage, impatience, and a persistently angry mood that lasts for at least a year. Concerns over the overdiagnosis of bipolar illness in children are addressed by the diagnosis (38).

Rheumatoid Arthritis and Depression:

One of the most prevalent psychiatric comorbidities in RA is depression, which is becoming more well acknowledged as a significant factor affecting the burden of the disease. A complex interaction of biological, psychological, and social factors is shown in the co-occurrence of depression and RA. **(39).**

Prevalence of depression in RA

According to meta-analyses, depression is a prevalent comorbidity in RA, with a global prevalence ranging from 17% to 48%, depending on demographic features and evaluation techniques (17). Research indicates that individuals with higher levels of pain, disability, and disease activity are more likely to experience depression, which is associated with lower quality of life and treatment adherence **(40).**

Shared Biological Mechanisms

Both RA and depression share overlapping biological pathways:

- **Chronic inflammation**: Proinflammatory cytokines (e.g., TNF-α, IL-6) contribute to both RA

disease activity and depressive symptoms **(41).**

- **Neuroendocrine dysfunction**: Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has been implicated in the pathophysiology of both conditions **(41).**

- Immune activation: Depression may increase systemic inflammation, creating a bidirectional relationship that worsens RA progression **(39).**

Psychosocial factors (Bidirectional relationship):

Emerging studies now suggest a bidirectional relationship (figure 2) between the two conditions beyond just co-morbidity **(42).** While RA can lead to depression - through pain, fatigue, disability, reduced social participation, Loss of independence and employment challenges - depression itself can amplify inflammatory responses, worsening RA progression **(39).** Also depression negatively affects coping strategies and self-management of RA, worsening overall outcomes **(43).**

Impact of Depression on RA Outcomes

Depression in RA is associated with:

- Increased disease activity and perceived pain **(17).**

- Poorer treatment adherence, leading to suboptimal disease control **(17).**

- Greater functional disability and reduced health-related quality of life. **(43).**

- Increased risk of mortality, particularly due to cardiovascular disease **(43).**

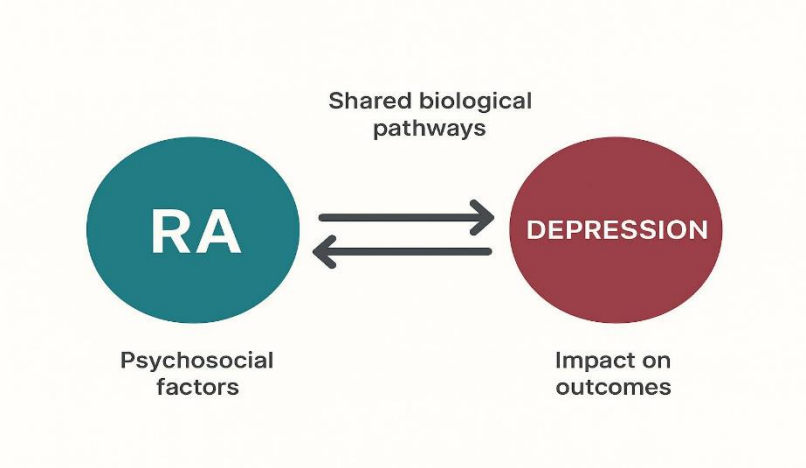

Figure.2 Bidirectional relationship between RA and depression, mediated by shared biological and psychosocial pathways **(39, 41)**

Management Approaches

An integrated approach is essential for addressing RA and depression:

- Pharmacological interventions: Disease-modifying antirheumatic drugs (DMARDs) and biologics reduce inflammation, which may indirectly alleviate depressive symptoms. Antidepressants are effective but should be tailored to individual needs **(41).**

- Psychological therapies: Cognitive-behavioural therapy (CBT), mindfulness, and psychoeducation improve mood, pain perception, and coping **(44).**

- Lifestyle interventions: Exercise, sleep hygiene, and stress management are effective for both RA and depression management **(45).**

Eventually, depression is highly prevalent among patients with RA and significantly worsens disease outcomes. The shared biological and psychosocial mechanisms highlight the bidirectional relationship between the two conditions. Early identification and integrated management of depression in RA are critical to improving both mental health and physical outcomes **(39).**

Physical Activity and Depression

Introduction

Depression is one of the leading causes of disability worldwide, and lifestyle factors, particularly PA, have emerged as important modifiable risk and protective factors. Evidence from observational and intervention studies suggests that PA can play both a preventive and a therapeutic role in depression **(45).**

Mechanisms Linking Physical Activity and Depression

- **Biological Mechanisms**

Exercise promotes neuroplasticity, increases brain-derived neurotrophic factor (BDNF), regulates neurotransmitters such as serotonin and dopamine, and reduces pro-inflammatory cytokines, all of which contribute to improved mood and resilience against depression **(14).**

- **Psychological and Social Mechanisms**

PA enhances self-esteem, provides social interaction, and reduces rumination and negative thought cycles. These factors act synergistically with biological mechanisms to reduce depressive symptoms **(46).**

Physical Activity as a Preventive Strategy

Prospective studies show that individuals who engage in regular PA have a significantly lower risk of developing depression. A systematic review and meta-analysis found that even low levels of activity reduce risk, supporting the role of exercise in public health prevention strategies **(47).**

Physical Activity as a Treatment for Depression

Meta-analyses consistently demonstrate that exercise interventions, particularly aerobic and resistance training, have moderate to large effects in reducing depressive symptoms. Their effectiveness is comparable to pharmacological and psychological treatments in certain populations **(46).**

Eventually, PA plays a dual role in both preventing and treating depression through biological, psychological, and social pathways. Current evidence supports incorporating exercise into routine clinical management and public health recommendations to address the global burden of depression **(45).**

References:

1. Abdelnaser S., Yousef A., Abd El Sattar M. et al., (2023). Level of 14-3-3 (Eta) Protein in Rheumatoid Arthritis Patients. Journal of Advances in Medicine and Medical Research, 35(4), 82-89.
2. Liu, N., Yan, W., Su, R., et al., (2023) Research progress on rheumatold arthritis-associated depression. Front. Behav. Neurosci, 16:992223.
3. World Health Organization (2024) *Physical activity*. Available at: https://www.who.int/news-room/fact-sheets/detail/physical-activity (Accessed: August 2025).
4. Ye, H., Weng, H., Xu, Y., Wang, L., Wang, Q. and Xu, G. (2022) 'Effectiveness and safety of aerobic exercise for rheumatoid arthritis: a systematic review and meta-analysis of randomized controlled trials', *BMC Sports Science, Medicine and Rehabilitation*, 14, Article 17.
5. World Health Organization (2020) WHO guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization.
6. Bull, F.C., Al-Ansari, S.S., Biddle, S., et al. (2020) 'World Health Organization 2020 guidelines on physical activity and sedentary behaviour', British Journal of Sports Medicine, 54(24), pp. 1451–1462.
7. Grgic, J., Schoenfeld, B.J. and Latella, C. (2019) 'Resistance training frequency and skeletal muscle hypertrophy: A review of available evidence', *Journal of Science and Medicine in Sport*, 22(3), pp. 361–370.
8. Verhoeven, F., Tordi, N., Prati, C., Demougeot, C., Mougin, F. and Wendling, D. (2016) 'Physical activity in patients with rheumatoid arthritis', *Joint Bone Spine*, 83(3), pp. 265–270.
9. Sherrington, C., Fairhall, N.J., Wallbank, G.K., Tiedemann, A., Michaleff, Z.A., Howard, K., Clemson, L., Hopewell, S. and Lamb, S.E. (2019) *Exercise for preventing falls in older people living in the community*, Cochrane Database of Systematic Reviews, 2019 Issue 1, Art. No. CD012424.
10. Green, D.J., Hopman, M.T.E., Padilla, J., Laughlin, M.H. and Thijssen, D.H.J. (2017) 'Vascular adaptation to exercise in humans: role of hemodynamic stimuli', *Physiological Reviews*, 97(2), pp. 495–528.
11. Bird, S.R. and Hawley, J.A. (2017) 'Update on the effects of physical activity on insulin sensitivity in humans', *BMJ Open Sport & Exercise Medicine*, 2(1), e000143.
12. Giles, J.T., Danielides, S., Szklo, M., Post, W.S., Blumenthal, R.S., Petri, M., Schreiner, P.J., Budoff, M., Detrano, R. and Bathon, J.M. (2015) 'Insulin resistance in rheumatoid arthritis: disease-related indicators and associations with the presence and progression of subclinical atherosclerosis', *Arthritis & Rheumatology*, 67(3), pp. 626–636.
13. Azeez, M., Clancy, C., O'Dwyer, T., Lahiff, C., Wilson, F. and Cunnane, G. (2020) 'Benefits of exercise in patients with rheumatoid arthritis: a randomized controlled trial of a patient-specific exercise programme', *Clinical Rheumatology*, 39(6), pp. 1783–1792.
14. Schuch, F.B., Vancampfort, D., Richards, J., Rosenbaum, S., Ward, P.B. and Stubbs, B. (2016) 'Exercise for depression in adults: a meta-analysis of randomized controlled trials', *British Journal of Sports Medicine*, 50(4), pp. 260–266.

15. Northey, J.M., Cherbuin, N., Pumpa, K.L., Smee, D.J. and Rattray, B. (2018) 'Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis', *British Journal of Sports Medicine*, 52(3), pp. 154–160.
16. Ahlskog, J.E., Geda, Y.E., Graff-Radford, N.R. and Petersen, R.C. (2011) Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging. Mayo Clinic Proceedings, 86(9), pp. 876–884.
17. Matcham, F., Rayner, L., Steer, S. and Hotopf, M. (2013) 'The prevalence of depression in rheumatoid arthritis: a systematic review and meta-analysis', Rheumatology, 52(12), pp. 2136–2148.
18. Kodama, S., Saito, K., Tanaka, S., Maki, M., Yachi, Y., Asumi, M., Sugawara, A., Totsuka, K., Shimano, H., Ohashi, Y., Yamada, N. and Sone, H. (2009) 'Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis', *JAMA*, 301(19), pp. 2024–2035.
19. Sparks, J.A. (2019) Rheumatoid arthritis. Annals of Internal Medicine, 170(1), ITC1–ITC16.
20. Baillet, A., Vaillant, M., Guinot, M., Juvin, R. and Gaudin, P. (2012) 'Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials', *Rheumatology International*, 32(2), pp. 287–294.
21. Metsios, G.S., Rausch Osthoff, A.K., Hamer, M. and Kitas, G.D. (2020) 'Cardiovascular effects of physical activity in patients with rheumatoid arthritis: current evidence and future perspectives', *Annals of the Rheumatic Diseases*, 79(1), pp. 4–10.
22. Rhodes, R.E., Janssen, I., Bredin, S.S.D., Warburton, D.E.R. and Bauman, A. (2019) 'Physical activity: health impact, prevalence, correlates and interventions', *Psychology & Health*, 34(1), pp. 1–22.
23. Patel, J.D., Sheth, M. and Jain, A. (2024) 'Barriers and facilitators for physical activity in older adults', *Journal of Integrated Health Sciences*, 12(1), pp. 62–65.
24. McPhail, S.M. and Schippers, M. (2012) 'An evolving perspective on physical activity counselling by medical professionals', BMC Family Practice, 13, p. 31.
25. Bauman, A.E., Reis, R.S., Sallis, J.F., Wells, J.C., Loos, R.J. and Martin, B.W. (2012) 'Correlates of physical activity: why are some people physically active and others not?', The Lancet, 380(9838), pp. 258–271.
26. Rausch Osthoff, A.K., Niedermann, K., Braun, J., Adams, J., Brodin, N., Dagfinrud, H., Duruöz, T., Esbensen, B.A., Günther, K.P., Hurkmans, E., et al. (2018) '2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis', Annals of the Rheumatic Diseases, 77(9), pp. 1251–1260.
27. England, B.R., Smith, B.J., Baker, N.A., Barton, J.L., Oatis, C.A., Guyatt, G., Anandarajah, A., Carandang, K., Chan, K.K. et al., (2023) '2022 American College of Rheumatology guideline for exercise, rehabilitation, diet, and additional integrative interventions for rheumatoid arthritis', *Arthritis & Rheumatology*, 75(8), pp. 1299–1311.
28. American College of Sports Medicine (2021) *ACSM's guidelines for exercise testing and prescription*. 11th edn. Philadelphia: Wolters Kluwer.
29. World Health Organization (2019) International Classification of Diseases 11th Revision (ICD-11): Clinical Descriptions and Diagnostic Guidelines. Geneva: World Health Organization.
30. American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders. 5th edn. Arlington, VA: American Psychiatric Publishing.
31. Hasin, D.S., Sarvet, A.L., Meyers, J.L. et al. (2018) 'Epidemiology of adult DSM-5 major depressive disorder and its specifiers in the United States', *JAMA Psychiatry*, 75(4), pp. 336–346.
32. Grande, I., Berk, M., Birmaher, B. and Vieta, E. (2016) 'Bipolar disorder', The Lancet, 387(10027), pp.1561–1572.
33. Dubovsky, S.L., Ghosh, B.M., Serotte, J.C. and Cranwell, V. (2021) 'Psychotic depression: diagnosis, differential diagnosis, and treatment', *Psychotherapy and Psychosomatics*, 90(3), pp. 160–177.
34. Woody, C.A., Ferrari, A.J., Siskind, D.J. et al. (2017) 'A systematic review and meta-regression of the prevalence and incidence of perinatal depression', Journal of Affective Disorders, 219, pp.86–92.

35. Melrose, S. (2015) 'Seasonal affective disorder: an overview of assessment and treatment approaches', *Depression Research and Treatment*, 2015, Article ID 178256, pp. 1–6.
36. Posternak, M.A. and Zimmerman, M. (2001) 'Symptoms of atypical depression', *Psychiatry Research*, 104(2), pp. 175–181.
37. Copeland, W.E., Angold, A., Costello, E.J. and Egger, H. (2013) 'Prevalence, comorbidity, and correlates of DSM-5 proposed disruptive mood dysregulation disorder', American Journal of Psychiatry, 170(2), pp.173–179
38. Matcham, F., Ali, S., Irving, K., Hotopf, M. and Chalder, T. (2016) 'Are depression and anxiety associated with disease activity in rheumatoid arthritis? A prospective study', *BMC Musculoskeletal Disorders*, 17, p. 155.
39. Zhang, L., Cai, P. and Zhu, W. (2020) 'Depression has an impact on disease activity and health-related quality of life in rheumatoid arthritis: a systematic review and meta-analysis', *International Journal of Rheumatic Diseases*, 23(3), pp. 285–293.
40. Choy, E.H.S. (2012) 'Effects of inflammation on pathways of depression in rheumatoid arthritis', Rheumatology, 51(2), pp. 205–213.
41. Kim, S.Y., Min, C., Oh, D.J., Choi, H.G. *et al.* (2020) 'Association between depression and rheumatoid arthritis: two longitudinal follow-up studies using a national sample cohort', *Rheumatology*, 59(8), pp. 1889–1897.
42. Marrie, R.A., Walld, R., Bolton, J.M., Sareen, J., Patten, S.B., Singer, A., et al. (2018) 'Psychiatric comorbidity increases mortality in immune-mediated inflammatory diseases', *General Hospital Psychiatry*, 53, pp. 65–72.
43. Nerurkar, L., Siebert, S., McInnes, I.B. and Cavanagh, J. (2019) 'Rheumatoid arthritis and depression: an inflammatory perspective', *The Lancet Psychiatry*, 6(2), pp. 164–173.
44. Firth, J., Solmi, M., Wootton, R.E., Vancampfort, D., Schuch, F.B., Hoare, E., Gilbody, S., Torous, J., et al. (2020) 'A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders', World Psychiatry, 19(3), pp. 360–380.
45. Morres, I.D., Hatzigeorgiadis, A., Stathi, A., Comoutos, N., Arpin-Cribbie, C., Krommidas, C. and Theodorakis, Y. (2019) 'Aerobic exercise for adult patients with major depressive disorder in mental health services: A systematic review and meta-analysis', Depression and Anxiety, 36(1), pp. 39–53.
46. Pearce, M., Garcia, L., Abbas, A., Strain, T., Schuch, F.B., Golubic, R., Kelly, P. and Smith, A.D. (2022) 'Association between physical activity and risk of depression: a systematic review and meta-analysis', JAMA Psychiatry, 79(6), pp. 550–559.