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EXERCISE IS MEDICINE AND WELL-BEING: A SYSTEMATIC REVIEW AND META-ANALYSIS[p.p.1-17]

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ABSTRACT

Regular exercise is an important aspect of maintaining good health and well-being, as recognized by various scientific and regulatory organizations. Exercise is Medicine (EiM) is a global health initiative that was established in 2007 by the American College of Sports Medicine (ACSM) in collaboration with the American Medical Association (AMA). This initiative was founded upon the overwhelming evidence that physical activity plays an essential therapeutic role in both preventing and managing a range of chronic health conditions. The vision of EIM is to promote physical activity assessment and make it a standard practice in clinical care. This will connect healthcare with evidence-based resources for people of all abilities, regardless of their location. It is a proven fact that there is a direct relationship between one's activity level and their health status. More than half of one's health status can be attributed to unhealthy behaviors, and smoking, poor diet, and physical inactivity are the main culprits. Exercise has been proven to help treat and prevent a variety of chronic conditions like heart disease, pulmonary disease, diabetes, and obesity.

Keywords: Exercise, Health, Well-being, Vitals & Behaviors.

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INTRODUCTION

Exercise is a very powerful tool for both the treatment and prevention of chronic disease, for mitigating the harmful effects of obesity, and for lowering mortality rates. There is a linear relationship between activity level and health status. People who maintain an active and fit way of life live longer, healthier lives. Exercise is widely recognized as a critical component of a healthy lifestyle by multiple scientific and regulatory bodies.

"Exercise is Medicine" (EiM) is a United States-based health initiative that was co-launched by the American College of Sports Medicine (ACSM) and the American Medical Association (AMA) in 2007. Public health and research institutions in several countries and regions have embraced this philosophy, and over 40 countries have embraced EiM as a health initiative. EiM focuses on making exercise in the promotion of health care (ACSM, 2020). Undoubtedly, without strong epidemiological and medical evidence, the promotion of physical activity will limit motivation (WHO, 2018). However, there are many views on the nature and purpose of exercise. The increase in the population of the elderly and the prevalence of chronic diseases has resulted in a growing number of people living with disabilities (Cieza et al., 2021). In such cases, mortality and morbidity cannot adequately describe the clinical outcomes of most health conditions. Hence, in 2016, the World Health Organization (WHO) proposed functioning as the third clinical outcome indicator (Stucki and Bickenbach, 2017). Exercise is an important modality for improving functioning and health conditions. The American College of Sports Medicine and the American Medical Association have suggested that "exercise is medicine" (Lobelo et al., 2014), and this marks a new direction in healthcare. Scientific research eventually followed through, and the role of regular physical activity in influencing health grew in importance so much as to be proffered as a possible therapy (Shephard R.J., et al. 1999), at the end of the nineties, being subsequently considered an official treatment ten years later when the scientific community launched the slogan "exercise is medicine", and is considered today a sustainable tool both for individual health and community and a real tool to foster health and well-being in the general

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population and not only in patients affected by chronic diseases Sjøgaard G., et al. 2016).Exercise plays an important role in the prevention, treatment, and rehabilitation of diseases, and is the basis of active and universal health. This article discusses this statement from the perspective of the proposal of "exercise is medicine" - initiative, consequences of exercise in health, considerations of exercise, and the exercise prescription.

Exercise is Medicine - initiative:

Lack of exercise (A global problem): Lack of exercise is a health concern worldwide. According to WHO, 31% of the world's population does not attain the minimum required level of physical activity (Kohl et al., 2012). This unhealthy lifestyle is the fourth leading cause of death worldwide with approximately 3.2 million deaths annually (Hall et al., 2021). This situation is continuously worsening and poses a substantial burden on health systems and societies.A considerable portion of health conditions can be attributed to physical inactivity. Sedentary behavior and physical inactivity are the leading risk factors for cardiovascular disease and all-cause mortality (Lavie et al., 2019). Compared with people who have previously been physically active, those who are inactive have a higher risk of developing neurological diseases (Kim et al., 2019). A systematic review revealed that the incidence of osteoarthritis among people who engaged in running exercisers was lower than the incidence in those who did not exercise; furthermore, lack of exercise is associated with a high risk of sports injuries and musculoskeletal diseases (Alentorn-Geli et al., 2017). Increasing evidence suggests that exercise can play an important role in cancer prevention; physically inactive people have a higher cancer morbidity than those who exercise regularly (Wang and Zhou, 2021). In addition, lack of exercise can accelerate aging, resulting in a rapid decline in functioning (Angulo et al., 2020).

Role of exercise in healthcare: As incurable chronic diseases have become a major health concern, an increasing number of people experience a decline in functioning. It is widely accepted that functioning is the basis of health, and exercise is crucial for maintaining and improving function. This situation drives the demand for

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rehabilitation services. Rehabilitation is to take specific interventions against patients' disabilities to restore their functioning, re-establish their health, and reintegrate them into society. These interventions are predominantly exercise training and relevant physical activity. However, exercise is rarely used as medical advice in other clinical settings. The role of exercise in healthcare should be highlighted.

The logic of exercise health promotion is self-limiting: The logic behind EiM recognizes that non-communicable diseases (such as diabetes, cardiovascular diseases, obesity, etc.) are closely related to sedentary lifestyles (Segar et al., 2016). Exercise intervention is an extension and derivative of medical treatment and health care. Several studies confirm that acute exercise improves cognitive ability, reduces anxiety, and increases well-being; long-term regular exercise can control weight, reduce the risk of cardiovascular diseases, delay the onset of type 2 diabetes, enhance bone and muscle mass, prevent falls and prolong life in the elderly (Lobelo et al., 2014). Thus, as for people at high risk of non-communicable chronic diseases, exercise can be used as a "vaccine" to reduce the risk of disease and improve the quality of life. The purpose of medicine is "to seek common ground", and the essence of sports is "to chase the threshold".The goal of all medical treatments is to cure abnormal physical and mental conditions and to restore physiological indicators to normal or near-normal values. In contrast, exercise applies an optimal stimulus to the body to promote better health and well-being.

Medicine restores health, exercise promotes health: EiM requires health-related physiological indicators (such as weight, blood pressure, blood sugar, blood lipids, etc.) to maintain exercise compliance. However, changes in physiological indicators often require a period of adaptation and accumulation, and there are individual differences due to some non-motor factors such as ethnicity, genetics, gender, and physical activity levels (Rawlins et al., 2010). Moreover, EiM weakens or ignores the role of exercise in promoting physical and mental health. Exercise is a manifestation of our inherent survival instincts, increasing our prowess in the hunter-gatherer environment by improving our agility and strength.

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Consequences of exercise in health: Exercise acts as a form of medicine in multiple ways. First, exercise changes sedentary behaviour, reduces risk factors, and enhances immunity, thus functioning as a form of prophylaxis. Second, appropriate exercise can prevent or alleviate dysfunction after the onset of disease and prevent disease recurrence. That is, exercise plays an important role in primary, secondary, and tertiary prevention of different health conditions. Many studies show that sedentary behavior is an important cardio-metabolic risk factor and physical activity may attenuate the detrimental effects of sedentary behaviour.

Table 1: Exercise is Medicine (EiM): Fundamentals and Operational Terms

Sr. No.	Fundamentals	Operational Terms
1	EXERCISE	A subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness.
2	PHYSICAL ACTIVITY	Any bodily movement produced by skeletal muscles those results in energy expenditure.
3	PHYSICAL FITNESS	Set of attributes that are either health- or skill-related that people have or achieve. It is a multidimensional concept. The health-related components of physical fitness are; cardio respiratory endurance, muscular endurance and strength, body composition, and flexibility.
4	SPORT	An activity involving physical exertion and skill in which an individual or team competes against another or others for entertainment.
5	SEDENTARINESS	Activities that typically are in the energy expenditure range of 1.0–1.5 METs, such as sitting during commuting, in the workplace, in the domestic environment, and during leisure time.
6	LIFESTYLE	A set of habits and customs that is influenced by the life-long process of socialization, including social use of substances such as alcohol and tobacco, dietary habits, and exercise, all of which have important implications for health.
7	PREVENTION	Efforts aimed at avoiding a clinical event/disease. Secondary prevention: efforts aimed at preventing the recurrence of clinical events in patients who have manifest clinical disease. Primary prevention: efforts focus on preventing the first occurrence of a clinical event among individuals who are at risk.

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		Primordial prevention: to prevent the development of risk factors in the first place.
8	HEALTH	State of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.
9	WELLNESS	The state of being in good health, especially as an actively pursued goal. It is an active process of becoming aware of and making choices toward a healthy and fulfilling life. It is more than being free from illness, it is a dynamic process of change and growth.
10	WELL-BEING	Positive outcomes that are meaningful for people and many sectors of society, state that people perceive that their lives are going well.

Considerations of exercise: Exercise is known as a form of medicine owing to its numerous health benefits. There are three major principles for exercise, individualization, gradualness, and persistence. Individualization means that people should choose the intensity and time of exercise according to their situation. For gradualness, the intensity and time of exercise should be increased step by step. The principle of persistence refers to that people should take exercise as a part of life and develop regular habits. Choosing the modality and the intensity of exercise is a complex task. However, it is worth saying that regular exercise, regardless of type, duration, or intensity, is beneficial. Here we recommend running or brisk walking, which is the simplest form of exercise, 3–5 days a week, once a day, 45–60 min each time, in combination with appropriate resistance training.

The exercise prescription: The simplest way to administer an exercise prescription is by using the FITT formula. "F" stands for frequency, and the ideal frequency of exercise is most days of the week (5 or more). "I" stands for intensity, and the recommended intensity of exercise is at the moderate level, which can be gauged by a heart rate that is roughly 50% to 70% of the maximum. Maximum heart rate can be estimated by subtracting the patient's age from 220. The first "T" stands for the type of exercise, although the type is not too important, just as long as the exercise works for large muscle groups and is something that the patient enjoys and is likely to do over and over again. The second "T" stands for time, and the time spent exercising should be 30 minutes

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minimum. International Guidelines define the optimal dose of exercise to obtain health benefits, to promote and maintain health, all healthy adults aged 18 to 65 years need moderate-intensity aerobic physical activity for a minimum of 30 min on five days each week or vigorous-intensity aerobic physical activity a minimum of 20 min on three days each week (Piercy K.L., et al. 2018). Children and adolescents require a higher exercise dose corresponding to at least an average of 60 min/day of moderate to vigorous intensity physical activity including muscle-strengthening and bone-loading activities, performed at least 3 days a week. (Steinberger J., et al. 2016).The prescription of exercise programs is strongly recommended in all exercise guidelines and requires the clear definition of modality, intensity, frequency, duration and progression of exercise.

Exercise Modality: It may be important to define exercise modality in the context of physiological and biomechanical demands/types (Fletcher G.F., et al. 2013):Endurance activity entails rhythmic motion of large muscle groups in aerobic activities (walking, jogging, swimming, etc.) Endurance aerobic activities are primarily prescribed to improve cardiorespiratory fitness, reduce cardio-metabolic-oncologic risk, reduce fat mass, improve wellness, and maintain health.Resistance or strength exercise involves activities that use low- or moderate-repetition movements against resistance, it is primarily prescribed to increase strength muscle mass, and physical independence. Flexibility and muscle stretching exercises are focused on improving joint range of motion (flexibility), and on decreasing muscle tension (Nakamura K., et al. 2014). Balance exercises are aimed at improving the ability to maintain the body's centre of gravity within its base of support and it is primarily prescribed to reduce the risk of falls and injury (DiStefano L.J., et al. 2009).

Exercise Intensity: Endurance aerobic exercise: Ideally, to define the intensity of an aerobic endurance exercise, a cardiopulmonary exercise test (CPX) would be required to establish cardio respiratory fitness (VO2max) and subsequently define the exercise intensity as percent of it. From a practical point of view, the exercise intensity is usually indicated by training heart rate, based on the approximate linear relationship between the increase of O2 consumption and the increase of heart rate (HR). Training heart rate may

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be calculated employing the heart rate reserve (HRR) formula starting from resting heart rate and actual maximal heart rate measured by a conventional maximal exercise stress test (Vanhees L., et al. 2012). General physical activity promotion tools are given in Table 2.

Table 2: Classification of physical activity intensity

	Effort	Light	Average	Moderate	Hard	Very Hard	Maximal
Relative intensity	VO2max (%)	<25	25–44	45–59	60–84	≥85	100
	Maximal HR	<30	30–49	50–69	70–89	≥90	100
	RPE	<9	9–10	11–12	13–16	>16	20
Absolute intensity	INTENSITY	Sedentary	Light	Moderate	Vigorous	Very Hard	Maximal
	METs	1–1.5	1.6–2.9	3.0–5.9	6–9	≥9	15
Training zone ***		Aerobic	Aerobic	Aerobic	Aerobic + Lactate	Aerobic + Lactate + Anaerobic	Anaerobic
Example		sitting, reclining or lying, watching TV, using a PC, driving a car	walking slowly, light work while standing, playing an instrument	brisk walking (5–6 Km/h), slow cycling (15 Km/h), ballroom dancing, recreational swimming	jogging, running, biking > 15 km/h, swimming laps, single tennis	straining or competing in most competitive sports, racing, or any all-out activity	-

Note: VO2 max = maximal aerobic capacity; HRR = Heart rate reserve = Maximal heart rate — resting HR; METs indicate metabolic equivalents. 1 MET = 3.5 mL O2 kg−1 min−1. * % Heart rate reserve (HRR) = calculate HRR target by (HRR × %value) + resting HR; RPE, rating of perceived exertion, using training zones related to aerobic and anaerobic thresholds. Low-intensity exercise is below the aerobic threshold; moderate is above the aerobic threshold but not reaching the anaerobic zone; high intensity is close to the anaerobic zone; and very intense exercise is above the anaerobic threshold.

Strength exercise: To define the intensity of strength exercise is quite difficult. It depends on many factors, such as the resistance (generally represented by a weight to lift) that the

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muscle must win, the speed of movement, and number of repetitions. A lower repetition range with a heavier weight (anaerobic) may better optimize muscular strength and power, whereas a higher repetition range with a lighter weight may better enhance muscular endurance. Using weight loads that permit 8 to 15 repetitions will generally facilitate improvements in muscular strength and endurance (Williams M.A., et al. 2007).

Exercise Duration: This parameter is particularly important for endurance exercise and the session length required to improve health is 30 min every day if the intensity is moderate. In unfit subjects who cannot exercise for 30 min consecutively, even shorter duration at moderate intensity may grant some benefits when compared with individuals who were inactive particularly if the shorter period is repeated during the day (Wen C.P., et al. 2011).

Exercise Frequency: Endurance aerobic exercise needs to be performed ideally every day, at least 5 days/week, particularly if the intensity of exercise is light or moderate. Subjects who are fit and can exercise at aerobic vigorous intensity may also exercise 3 days/week. Strength exercise requires exercise of the same muscular group two to three days/week, non-consecutive days to permit muscular recovery (Piepoli M.F., et al. (2016).

Exercise Progression: Progression consists of modulating intensity, frequency, and duration of exercise considering the subject's training level, preference, and personal characteristics. For instance, for an obese, unfit patient 30 min of endurance aerobic moderate exercise performed every day may be a very difficult goal to reach. Starting with a less demanding protocol, and subsequently improving it, could be a better solution (Zubin Maslov P., et al. (2017).

Exercise Execution: Execution of exercise may occur in different places considering subjects' preferences/needs. The presence of a health professional, such as an exercise physiologist or physiotherapist, capable of transforming into concrete actions the prescribed program, will tremendously improve the program and the results (Gates A.B., et al. 2016).

Discussion on Review and Mata-Analysis:

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Previous reviews and meta-analyses have shown that exercise is an important way to improve health and functioning. However, the findings have been mixed. In contrast, this meta-analysis includes a larger number of studies and focuses on specific objectives, providing more clear and consistent results. The findings show that regular physical activity leads to higher levels of habitual physical activity, which supports the idea that "exercise is medicine". In Table 3, we present evidence of significant findings in the literature on this topic.

Table 3: Characteristics of Literature with Different Significance Levels

Sr. No.	Author/year	Title	DOI
1	Sallis R.E. (2019)	Exercise is medicine and physicians need to prescribe it	10.1136/bjsm.2008.054825.
2	Piercy K.L., et al. (2018)	The physical activity guidelines for Americans.	10.1001/jama.2018.14854
3	Schmitz K.H., et al. (2019)	Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer.	10.3322/caac.21579.
4	Neville, R. (2013)	"Exercise is Medicine: Some Cautionary Remarks in Principle as Well as in Practice."	10.1007/s11019-012-9383-y
5	Diniz-Sousa, F., et al. (2022)	The Effect of Exercise for the Prevention of Bone Mass After Bariatric Surgery: a Systematic Review and Meta--	10.1007/s11695-021-05873-1
6	Carretero-Ruiz A, et al. (2019)	Effects of exercise training on weight loss in patients who have undergone bariatric surgery:	10.1007/s11695-019-04096-9
7	M. Halle, W. et al.	Exercise and sports after COVID-19—guidance from a clinical perspective	10.1002/tsm2.247
8	Hongjuan Li, et	Exercise is medicine: the best evidence-based	10.19582/j.cnki.11-
9	Osadzki, P., et al. (2020).	Exercise/physical activity and health outcomes: an overview of Cochrane systematic reviews.	10.1186/s12889-020-09855-3
10	Rodrigues, I.B., et al. (2021).	The Effect of Impact Exercise on Health-Related Outcomes in Individuals at Risk of Fractures: A Systematic Review and Meta-analysis	10.1007/s40279-021-01432-x

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Additionally, evidence from systematic reviews and meta-analyses supports the notion that "exercise is medicine" interventions have a positive impact on overall health and well-being. Furthermore, this discussion included large-scale studies from various authors.

According to research from the office of Disease Prevention and Health Promotion (2018), exercise can prevent and treat chronic diseases. Those who incorporate exercise into their lives tend to live longer and enjoy a higher quality of life. In 2018, the Physical Activity Guidelines Advisory Committee released a Scientific Report that would be the foundation for the second edition of the Physical Activity Guidelines for Americans issued by the US Office of Disease Prevention and Health, Centers for Disease Control and Prevention, the National Institutes of Health, and the President's Council on Sports, Fitness, and Nutrition. Naci H and Ioannidis JP (2015) highlighted the profound impact of physical activity and exercise on overall health, quality of life, and disease prevention and treatment. A meta-analysis of studies evaluating the relative effectiveness of pharmaceutical versus physical activity interventions found that regular exercise was just as effective as commonly prescribed medications in the secondary prevention of coronary heart disease, treatment of heart failure, prevention of diabetes, and even more effective than medication in the rehabilitation of patients after a stroke. Blair SN (2009) discovered that physical activity is effective in preventing and treating various chronic diseases and health conditions, including heart disease, hypertension, obesity, type 2 diabetes, osteoarthritis, dementia, and many types of cancer. Despite the many benefits, levels of inactivity are alarming and have tremendous costs. The benefits of physical activity extend across a variety of medical conditions and populations. The following sampling of research findings illustrates the breadth of the impact of regular physical activity. Yang, G. et al.(2023)studies have shown that physical activity plays a crucial role in facilitating the recovery of exercise capacity and pulmonary function in COVID-19 patients, helping to expedite the restoration of overall physical health. COVID-19 patients must undergo an accurate assessment of their physical condition before engaging in any physical activity. According to Posadzki et al. (2020), a sedentary lifestyle is a

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major risk factor for non-communicable diseases like cardiovascular diseases, cancer, and diabetes. It has been estimated that approximately 3.2 million deaths each year are attributable to insufficient levels of physical activity and the available evidence from Cochrane systematic reviews (CSRs) on the effectiveness of exercise/physical activity for various health outcomes.

Further, Bennasar-Veny M, et al. (2023) studies have demonstrated the beneficial effects of exercise on glycaemia control in people with pre-diabetes. However, the most effective exercise modality for improving glycolic control remains unclear. We aimed to assess which exercise training modality is most effective in improving glycaemia control in a population with pre-diabetes. Resistance training and IT had demonstrated benefits on glycaemia indices, especially on FPG, in a population with pre-diabetes. Chen et al. (2013) found that exercise can improve pre-existing conditions and quality of life. To overcome the epidemic of inactivity and the associated chronic diseases, a paradigm change is required for the public, clinicians, medical education, healthcare delivery model, and public health policies. Every clinician has a unique role to inform and empower. Through educating patients and the public, clinicians can help patients make the right choice for their health. Equally important, they have a role to act as advocates of an active lifestyle for the community, to influence health at the policy level, and to help bring awareness that an active lifestyle and exercise is every bit as vital as medicine. Goodhew, R.E., Edwards, B.A (2023) studies that literatures search of 10 sources was performed in June 2022 to identify eligible studies for synthesis. Meta-analysis was performed using a random-effects model with inverse variance and 95% confidence intervals. Forest plots were constructed to present pooled data. Exercise interventions have no positive impact on the quality of life of patients with multiple myeloma. The analysis is limited by a high risk of bias across included studies and low certainty evidence. Further high-quality trials are needed to assess the role of exercise in patients with multiple myeloma.

Furthermore, Lin Y, et al. (2023) conducted RCTs on post-breast cancer surgery patients of any type of exercise. The meta-analysis was conducted with CMA2.0

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software. Aerobic exercise reduced the intensity of the pain (MD = −1.043), improved shoulder flexion (MD = 3.398) and internal rotation range (MD = 3.868), lessened upper limb dysfunction (MD = −5.231), and improved muscle strength during flexion (MD = 1.076) and abduction (MD = 0.991). Shoulder elbow movement improved the range of shoulder external rotation (MD = 2.691) and reduced the incidence of arm lymphedema (RR = 0.343). Anti-resistance exercise also lessened upper limb dysfunction (MD = −4.094).This review and meta-analysis confirm that the benefits of exercise after breast cancer surgery depend on the type of exercise and the particular medical complication. Shivgulam et al. (2023) aimed to determine the impact of exercise training on flow-mediated dilation in healthy adults and those with chronic disease. Dysfunction of the endothelium is a key precursor of cardiovascular disease. In addition, adults with type 2 diabetes benefitted most from low-intensity resistance or aerobic exercise training, whereas those with cardiovascular conditions should consider engaging in high-intensity aerobic training to improve endothelial function. The study by Bogataj et al. (2019) aimed to determine the impact of various exercise types on functional capacity (measured through the 6-minute walk test), oxygen consumption (VO2max and peakVO2), lower limb muscle strength endurance (assessed by the 10-repetition sit-to-stand test), and inflammation levels indicated by CRP. The summary of the results of our analysis indicates that all selected outcomes improved with exercise training. The aim of the study conducted by Zhang, Fan MD, et al. (2020) was to determine the effectiveness of exercise interventions on fatigue and health-related quality of life (HRQoL) in patients undergoing hemodialysis (HD). The study provided more practical and targeted results and identified the main limitations of previous studies. The meta-analysis presented recent evidence for evaluating the therapeutic efficacy of exercise interventions for patients undergoing HD on fatigue and HRQoL.

CONCLUSION

Exercise is not just a way to improve physical fitness, but it is also a form of medicine that can and should be included in health plans. It is crucial not only in rehabilitation but also in promoting overall health and well-being. Exercise is Medicine

(EiM) is a program that recognizes the importance of physical activity and actively promotes its health benefits while counteracting the health risks of a sedentary lifestyle. However, despite its benefits, EiM may overlook important aspects of exercise science. Therefore, it is crucial to acknowledge that exercise is a vital component of maintaining and promoting physical and mental health and well-being. By incorporating exercise into our daily routines, we can improve our quality of life and reduce the risk of many chronic diseases.

Ethical Approval: Ethical approval is not required as our study will not include confidential participant data and intervention.

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