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Decreased HOMA-IR levels after physical exercise as a therapy to reduce insulin resistance: A systematic review

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ABSTRACT

A sedentary lifestyle can increase metabolic diseases such as diabetes mellitus. The aim of this study was to determine how physical activity reduces insulin resistance by reducing HOMA-IR levels. This study also provides a theoretical basis for physical exercise in preventing insulin resistance in humans. For our systematic review, we searched several literature databases (PubMed, Web of Science, and ScienceDirect) for articles published in the past five years that examined physical activity and HOMA-IR. A total of 422 published papers were located using the Web of Science, Pubmed, and Science Direct databases. Ten papers that satisfied the inclusion criteria were chosen and examined for this systematic review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used in this study to assess standard operating procedures. It has been demonstrated that regular exercise lowers insulin resistance by lowering HOMA-IR values. It has been proven that physical exercise is the best therapy for people with metabolic diseases, especially insulin resistance. Physical exercise has been shown to significantly reduce insulin resistance by decreasing HOMA-IR levels. Therefore, regular physical exercise is highly recommended as the best therapy for insulin resistance in humans.

KEYWORDS

Insulin Resistance; Physical Exercise; Physical Fitness; HOMA-IR

1. INTRODUCTION

Diabetes mellitus is a deadly disease that has impacted over 463 million individuals worldwide aged 20-79 years with a prevalence rate of 9.3%. The prevalence rate is expected to increase to 10.9% by 2025 and there will be around 700 million patients with diabetes mellitus by that year (Li et al., 2024). Approximately 40% of patients with type 2 diabetes already have diabetic nephropathy, and by 2025, that number is predicted to rise to 50% (Wheeler et al., 2020). Diabetes mellitus is among the world's ten leading causes of mortality and disability according to the World Health Organization, 2021. Diabetes mellitus is characterized by hyperglycemia that causes various metabolic dysfunctions and increases inflammation that will worsen a person's condition. The decline in people's physical activity levels and unhealthy lifestyles such as overeating make this disease significantly increase in prevalence (Balakrishnan & Thurmond, 2022).

Non-physiologically elevated blood sugar levels, appearing before insulin resistance is the main clinical sign in patients with diabetes mellitus. In people with pre diabetes mellitus, insulin levels are increased to meet the general insulin demand, which ultimately results in the disease-enhancing conditions of T2DM, hyperglycemia, and persistent hyperinsulinemia (Lee et al., 2022).

Clinical signs of insulin resistance include the metabolic effects of insulin resistance, which are categorized as insulin resistance disorders and metabolic syndrome (Nellaiappan et al., 2021). Insulin sensitivity is decreased in controlling blood sugar which is the initial trigger for insulin resistance which will result in an increase in metabolic syndrome diseases that will worsen a person's condition (Lee et al., 2022). Insulin resistance is indeed an early sign of clinical symptoms preceded by hyperglycemia conditions that will trigger an increase in T2DM. In the pancreas, there are β cells that have the task of secreting the hormone insulin. In prediabetes conditions that make the insulin hormone increase, it will trigger hyperinsulinemia which makes β cells fail to do their job (Lee et al., 2022). Research based on observation has demonstrated that insulin resistance plays a role in the onset of diabetes mellitus (Khalili et al., 2023).

Insulin resistance (IR) and β-cell function are assessed using basal glucose and insulin concentrations in the homeostasis model assessment of insulin resistance (HOMA-IR), which was first presented in 1985. The effects of a physiological feedback loop brought on by lessened insulin suppression during hepatic glucose synthesis are measured by HOMA-IR (Matthews et al., 1985; Yu et al., 2025). Previous studies have shown that high levels of HOMA-IR are significantly associated with type 2 diabetes mellitus (Lee et al., 2023). Thus, HOMA-IR levels have become a biomarker

that has been observed in determining increased insulin resistance in patients with metabolic diseases such as diabetes mellitus.

Nowadays, everyone agrees that physical activity is essential to preserving both adults' and children's metabolic health. Body motions brought on by skeletal muscle contractions that require more energy to perform than when at rest are referred to as physical activity. Numerous daily, recreational, and professional activities can be considered forms of physical activity (Moffa et al., 2024). As the recommendation states American Diabetes Association, 2024, physical activity is also a well-known therapeutic strategy for managing a number of chronic illnesses, and it is especially recommended for type 2 diabetes. Regular exercise has been demonstrated in earlier research to lower HOMA-IR levels, which in turn reduces insulin resistance (Mezghani et al., 2022). However, the reasons for physical exercise and its mechanism in reducing HOMA-IR levels are still not fully understood. Therefore, this systematic review will discuss in depth the mechanism of physical exercise in reducing HOMA-IR levels as a biomarker of insulin resistance in humans.

2. METHODS

2.1. Design

The researchers conducted a thorough search through journal databases (Science Direct, Web of Science, and Pubmed) for this kind of systematic review investigation. These databases collect papers with significant impact and strong scientific foundation. This initial search technique eliminated duplicate articles. The search results were further filtered using pre-defined inclusion and exclusion criteria.

2.2. Eligibility Criteria

The inclusion criteria for this study were established by looking at publications within the previous five years that addressed physical exercise and HOMA-IR. In addition, journals that did not adhere to scientific validity guidelines or were not listed in reliable search indices, such as Web of Science, Pubmed, or Science Direct, were excluded from our study.

2.3. Procedures

Full text, abstracts, and paper titles were added to the Mendeley database after verification and review. In the first stage, 422 publications were found using Science Direct, Pubmed, and Web of Science databases. For the second screening stage after screening for title suitability, 343 eligible papers were selected. In the third stage after reading the title, abstract, and keywords, 105 papers

were selected. At this last stage we read all the articles and determined that based on suitability, the sample should be human, the study should be original, the parameter should be the insulin resistance biomarker HOMA-IR, and the intervention should be physical exercise of any kind. At this point, we organized the items based on their overall suitability. Ten papers that met the inclusion criteria were selected for analysis after a thorough review and observation process. The operational criteria in this investigation were to fulfill the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Figure 1).

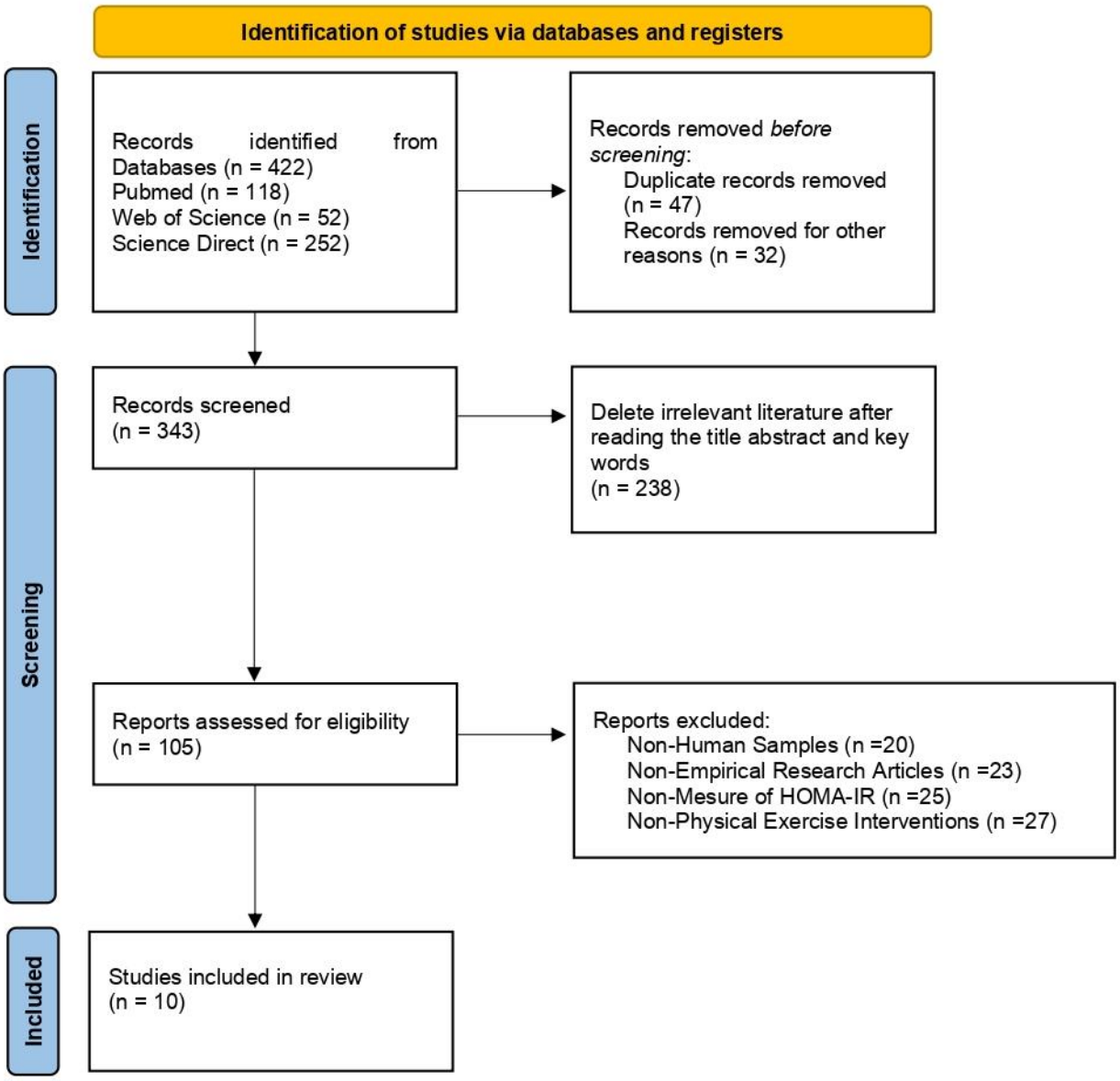

Figure 1. PRISMA flowchart of the article selection process

3. RESULTS

Table 1 presents a summary of randomized controlled trials (RCTs) that examined the effects of different exercise interventions on insulin resistance (HOMA-IR) and insulin levels across various populations.

Table 1. Summary of the studies

Author	Design	Participants	Participants Age	Intervention	Outcome
Ha et al. (2024)	Randomized controlled trials	Thirty-three elementary school students	11-12 years	Exercise Program 1. The training program is conducted 3x a week for 16 weeks. 2. Each session has a duration of 60 minutes consisting of a five-minute warm-up. Five minutes of cooling down after fifty minutes of core workouts. 3. The intensity of the exercise increases gradually. 4. Weeks 1-4 exercise intensity 50%-60% HRR. 5. Week 5-13 training intensity 60%-70% HRR. 6. Week 14-16 training intensity 70%-80% HRR.	1. HOMA-IR levels decreased significantly after the intervention. 2. Insulin hormone also decreased significantly after the exercise intervention.
Meng et al. (2022)	Randomized controlled trials	Forty-five adolescent boys with obesity	11 years	HIIT and MICT Workout Program 1. Workouts are done 3x a week for 12 weeks. 2. For MICT participants ran for 30 minutes at 60% HRR in the first 4 weeks. 3. For weeks 5-8 increase to 65% HRR. And for weeks 9-12 increase to 70% HRR. 4. For the HIIT protocol participants ran at 90% intensity in the first 4 weeks, 95% for weeks 5-8. And finally 100% for weeks 9-12.	1. HOMA-IR levels in the HIIT and MICT groups decreased significantly after the intervention. 2. Insulin hormone also decreased significantly in both the HIIT group and the MICT group.
Ghahfarrokhi et al. (2024)	Randomized controlled trials	Forty-eight elderly T2D patients	67 years	HIFT and LIFT Exercise Program 1. The exercise program consists of high-intensity low-volume and low-intensity high-volume. 2. Functional training is done 3x a week for 6 weeks. 3. Exercises consisted of resistance training, posture and balance training, upper extremity and lower extremity strength training, pelvic control training and core stability training. 4. In the HIFT group, weeks one and two the exercise intensity was 75% HRR, weeks three and four 80% HRR, and weeks five and six 85% HRR. 5. In the LIFT group weeks one and two the exercise intensity was 35% HRR, weeks three and four the exercise intensity was 40% HRR, and weeks five and six the exercise intensity	1. HOMA-IR levels in both HIFT and LIFT groups decreased significantly after the intervention. 2. Insulin hormone also decreased significantly after the intervention in both HIFT and LIFT groups.

				was 45% HRR.	
Tambuwa et al. (2024)	Randomized controlled trials	54 Nigerians with pre-diabetes	20-60 years	Exercise Program 1. Exercise is performed for 12 weeks of intervention. 2. The intervention was a morning walk with a total of 10,000 steps per day. 3. A pedometer (SW-200; Yamax, Tokyo, Japan) was provided to the study participants in this group, and they were instructed to take a certain number of steps each day. 4. The pedometer, which has a memory capacity of up to one month, was worn by participants in this group every day, and their walking activity was tracked and recorded.	1. There was a significant decrease in HOMA-IR levels after 12 weeks of intervention. 2. Insulin levels also decreased significantly after 12 weeks of intervention.
Garg et al. (2025)	Randomized controlled trials	70 participants	30-60 years	Exercise Program 1. Exercises are carried out with a duration of 30 minutes with details of 5 minutes of warm-up, 20 minutes of core exercises and 5 minutes of cooling down. 2. Exercise is done by walking on a treadmill. 3. Moderate intensity was maintained at 64%-76% of maximum heart rate. 4. The speed and incline of the treadmill were adjusted to keep it at a moderate intensity.	1. There was a significant decrease in HOMA-IR levels in both diabetes mellitus and non-diabetes mellitus groups. 2. Insulin levels also decreased significantly after physical exercise intervention in both diabetes mellitus and non-diabetes mellitus groups.
Moffa et al. (2024)	Randomized controlled trials	32 participants	20-35 years	Exercise Program 1. Aerobic exercise with a duration of 30 minutes. 2. Exercise consists of light jogging. 3. Aerobic exercise intensity between 60%-65% was maintained. 4. Exercise was supervised by a sample supervisor.	1. There was a significant decrease in HOMA-IR levels after physical exercise intervention. 2. Insulin levels also decreased significantly after physical exercise intervention.
Mezghani et al. (2022)	Randomized controlled trials	Forty-three obese young women	26 years	Exercise Program 1. Participants from the G50, G75, and G50/G75 groups participated in the training, which was conducted 5 sessions per week for 12 weeks. 2. Training was conducted over 60 sessions. 3. Exercises were conducted for a duration of 20-60 minutes. 4. Exercise intensity was moderate running in the G50 group with 50% HRR. 5. High exercise intensity running in group G75 with 75% HRR. 6. And alternating between medium and high for the G50/G75 group.	1. There was a significant decrease in HOMA-IR levels after the physical exercise intervention in the three groups given the physical exercise intervention. 2. Insulin levels also decreased significantly

					after the physical exercise intervention in all three groups given the exercise intervention.
Wang et al. (2025)	Randomized controlled trials	46 participants	22-36 years	Exercise Program 1. The workout begins with a 5-minute warm-up. 2. Core exercises are performed for 50 minutes and end with a 5-minute cool down. 3. The aerobic exercise group completed moderate intensity exercise (40%-59% VO2peak) on a treadmill, elliptical, stationary bike, rower, and/or stair equipment. 4. The aerobic combined resistance training group (aerobic + resistance) performed half of the aerobic regimen and half of the resistance regimen over five cycles, each of which lasted 4.5 to 5 minutes. 5. For resistance training, participants used seated machines, dumbbells, resistance bands/dumbbells, exercise balls, benches, and/or MATS. 6. Training was conducted for 20 weeks.	1. HOMA-IR levels in the aerobic group and the aerobic + resistance combination group were shown to decrease significantly. 2. Insulin levels in both the aerobic group and the aerobic + resistance combination group decreased significantly.
Li et al. (2024)	Randomized controlled trials	60 obese patients with type 2 diabetic nephropathy	20-50 years	Exercise Program 1. Participants carry out exercises according to the group both aerobic exercise and resistance exercise groups. 2. Before exercising, participants warm up for five minutes. 3. After 30 minutes of brisk running, participants took a 5-minute break. 4. Training takes place five times a week and lasts forty minutes per session. 5. After walking slowly for five minutes to warm up, the observation group used portable resistance bands for the following exercises: squat with the band and perform back neck flexion and extension with the band, 15–25 times for women and 20–25 times for men. 6. Exercise lasts roughly 40 minutes each time, and if done weekly, it can be done five times. During that period, the goal heart rate, which is 60% to 80% of the maximal heart rate, is maintained for 20 to 40 minutes. 7. Exercise is performed for 12 weeks.	1. HOMA-IR levels were shown to decrease significantly in both groups that had been given a 12-week physical exercise intervention.
Amanat et al. (2020)	Randomized controlled trials	60 participants	46-60 years	Exercise Program 1. The workout begins with a 10-minute warm-up and ends with a	1. There was a significant decrease in

	10-minute cool-down. 2. The aerobic group underwent running training on a treadmill 3x a week for 12 weeks. 3. Total exercise was performed for 60 minutes consisting of running on a treadmill and stationary bike with 75% HRmax. 4. Resistance training was done 3 sessions per week for 12 weeks. 5. Forty minutes of strength training consisted of 2 sets of 10 different exercises, including bench press, seated row, shoulder press, chest press, lateral pull-down, abdominal crunches, leg press, leg extension, triceps pushdown, and seated bicep curls, for the upper and lower body. 6. This combination group participated in a group-based training session, so they performed AE and RE simultaneously in one session. 7. The combination group performed the exercises two sessions a week for the first 2 weeks and three sessions for the rest of the intervention period. 8. Each session consisted of 20 minutes of walking on a treadmill, followed by 5 minutes of rest and a set of strength training, consisting of 10 different exercises similar to the RE exercise program. 9. The intensity of aerobic and strength training was gradually increased according to the AE and RE protocols.	HOMA-IR levels in the group with physical exercise intervention for 12 weeks. 2. Insulin levels also decreased significantly in the group with physical exercise intervention for 12 weeks.

4. DISCUSSION

Based on the results of this study, it has been proven that physical exercise can significantly reduce HOMA-IR levels. Research conducted by Ha et al. (2024) has proven that physical exercise interventions carried out with a duration of 60 minutes per session and carried out 3x a week for 16 weeks have been shown to significantly reduce HOMA-IR and insulin levels. So that indeed consistent and continuous exercise has a good impact on reducing the risk of insulin resistance. The type of exercise both high intensity and moderate intensity both have an effect in reducing HOMA-IR levels after physical exercise intervention (Meng et al., 2022). However, in the future, further exploration is needed to find out whether there are differences with various types of exercise on reducing HOMA-IR levels.

In patients with diabetes mellitus, physical exercise both high intensity and low intensity is highly recommended as one of the therapies. Getting older for people with diabetes mellitus can

indeed worsen health conditions if there is no effort to reduce these effects through therapy. In accordance with the results of research conducted by Ghahfarrokhi et al. (2024) that functional exercise performed 3x a week for 6 weeks was significantly shown to reduce HOMA-IR levels. This is an amazing discovery that exercise is indeed a medicine in every sense. For sick people, especially metabolic diseases, this is the best therapy in keeping the body healthy. And maintain body balance. In addition to medical treatment, exercise is highly recommended to be done regularly for people with diabetes mellitus. Another study also proved that routine morning walks of 10,000 steps per day for 12 weeks of treatment were significantly shown to reduce HOMA-IR levels in people with pre diabetes mellitus (Tambuwal et al., 2024).

Another study conducted by walking on a treadmill with moderate intensity for 30 minutes was significantly shown to reduce HOMA-IR levels (Garg et al., 2025). In addition, training with moderate intensity light jogging also has a significant impact on reducing HOMA-IR levels (Moffa et al., 2024). So even moderate intensity exercise does have a beneficial impact as therapy in insulin resistance. So there is no reason whatsoever for people not to exercise because of the good and long-term effects it has in an effort to keep the body healthy and fit, especially keeping insulin sensitive and not experiencing insulin resistance which will adversely affect several metabolic diseases such as diabetes mellitus. The combination of aerobic and resistance training is not a problem for people to exercise. The results of the study prove that a combination of aerobic and resistance training is significantly proven to reduce HOMA-IR levels (Wang et al., 2025). Research conducted by proving also that chronic exercise with various intensities of physical exercise interventions conducted 60 minutes per session 5 sessions per week for 16 weeks is significantly proven to reduce HOMA-IR levels (Mezghani et al., 2022). So it can be concluded that regular exercise is proven to significantly reduce HOMA-IR levels as a biomarker of insulin resistance. However, the underlying mechanism in reducing this biomarker needs to be discussed further.

4.1. Physiological Mechanism of Physical Exercise in Reducing HOMA-IR Levels

It is known that regular physical exercise can reduce HOMA-IR levels as a biomarker of insulin resistance. In addition, we must learn how the mechanism of exercise can reduce HOMA-IR levels (Figure 2). Further, we will discuss step by step that occurs when doing physical exercise.

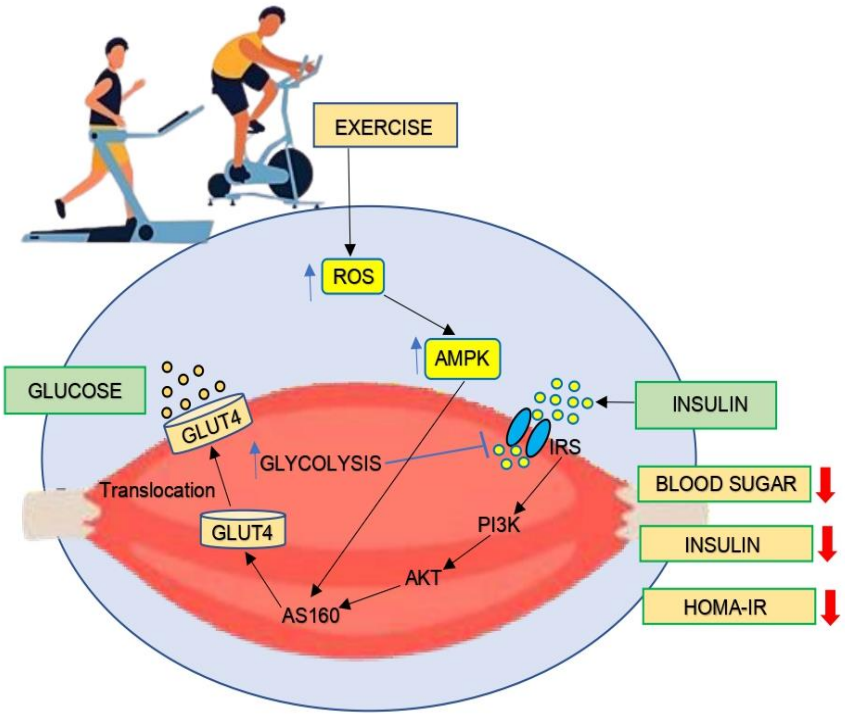

Figure 2. Mechanism of physical exercise in reducing HOMA-IR levels

When blood glucose levels spike, the hormone insulin is secreted and enters through the insulin receptor as a physiological response to control blood sugar levels (Takahashi et al., 2025). Its metabolic effects, such as increased lipid synthesis and glucose uptake, are mainly controlled by the phosphoinositide 3-kinase (PI3K)/AKT pathway (Yunn et al., 2023). GLUT4 is a major glucose transporter that facilitates glucose uptake in the musculoskeletal system (Bradley et al., 2015). In muscle and adipose tissue, insulin receptor signaling causes GLUT4 translocation, which increases blood glucose uptake into these tissues (Yunn et al., 2023). Insulin causes AS160 to become phosphorylated at several Akt consensus sequences, which inhibits its GAP function and causes GLUT4 to go to the plasma membrane (Sakamoto & Holman, 2008). Mutations in one or more of these phosphorylation sites will result in decreased insulin-stimulated GLUT4 translocation, demonstrating the functional significance of phosphorylated AS160 (Thong et al., 2007).

On the other hand, the key mechanism of reducing HOMA-IR levels lies in the mechanism of increasing GLUT4 during physical exercise. In addition, we must also know that physical exercise can make GLUT4 increase without using insulin. The results of a previous research systematic review conducted by Ayubi et al. (2024) shows GLUT4 translocation increases in response to

physical activity. Physical activity causes the body to absorb glucose more readily in the muscles, which lowers blood glucose levels (Asfaw & Dagne, 2022). Exercise also raises the demand for ATP (Sorriento et al., 2021). Because exercise reduces ATP, it can enhance AMPK phosphorylation. Muscle contraction energy consumption will raise AMP and decrease intracellular ATP levels, which will cause AMPK phosphorylation and activation (Kartinah et al., 2024). The sarcoplasmic reticulum Ca2+ release channel opens in response to the stimulation of muscle contraction by the propagation of action potentials throughout the t-tubules once the muscle contracts and ROS levels rise. Ca2+ ions enter the cytoplasm passively, increasing the amount of Ca2+ in the cytosol by ten to twenty times (Gejl et al., 2020). Increased intracellular Ca2+ concentration triggers CaMKK activation (Tokumitsu & Sakagami, 2022). Research indicates that exercise can amplify these benefits by enhancing muscle function through AMPK regulation. CaMKK activation will raise AMPK activity, which is equally crucial and required for physical fitness (Chen et al., 2023). GLUT4 exocytosis is increased by AMPK activation. GLUT4 translocation to the cell surface membrane results from the phosphorylation of TBC1 domain family members 1 (TBC1D1) and 4 (TBC1D4) upon AMPK activation (Okabe et al., 2019). Additionally, AMPK levels rose following physical activity (Kartinah et al., 2024). GLUT4, a protein involved in glucose transport, will therefore be produced at a higher rate due to the rise in phosphorylated AMPK (Kartinah et al., 2024).

Meanwhile, GLUT4 translocation is mediated by Rab-GTPase activating protein (Richter & Hargreaves, 2013). Physical exercise can activate AMPK, thereby promoting insulin-independent glucose uptake (Loyd et al., 2016). So physical exercise is the best therapy in an effort to reduce HOMA-IR levels because in a physiological response blood sugar levels can experience increased absorption by GLUT4 without insulin. So the sugar in the blood is lower because of the absorption process that occurs during physical exercise. Insulin and blood sugar are low, and HOMA-IR also decreases due to this effect. Based on the results of previous research, it is proven that physical exercise performed 5x a week for 12 weeks can significantly reduce HOMA-IR levels in patients with diabetes mellitus (Li et al., 2024). Glycogen, glucose, and free fatty acids are the three primary substrate types used by skeletal muscle for energy metabolism (Calcaterra et al., 2024). The precise energy source that muscles use is determined by a number of factors, such as food, exercise type, intensity, and duration (Das et al., 2010). Fatty acids are actually the primary energy source at rest, but during exercise, glucose and free fatty acids are necessary for the skeletal muscle's energy metabolism. These findings imply that GLUT4 recruitment, which occurs independently of PI3K at the plasma membrane, mediates the enhanced muscle glucose absorption seen right after exercise

(Iaccarino et al., 2021). Additionally, a strong correlation between glucose absorption and exercise-induced GLUT4 translocation on the cell surface was discovered (Iaccarino et al., 2021).

Blood glucose can be lowered by long-term aerobic exercise because it increases maximum oxygen consumption, increases capillary density and mitochondria, and eventually improves insulin secretion and sensitivity (Strasser & Pesta, 2013). So it can be concluded that the increase in GLUT4 triggered by exercise will reduce insulin secretion. In addition, the increase in glucose absorption will also make blood sugar levels decrease. Michishita et al. (2008) research on overweight individuals with type 2 diabetes mellitus (T2DM) revealed that fasting blood sugar levels dropped by 8.6% following 12 weeks of exercise. Katsuki et al. (2001) reported a significant 25% reduction in fasting blood sugar levels after physical exercise, whereas Misra et al. (2008) found a 28.9% reduction in fasting blood sugar levels among Asian Indians with T2DM after performing physical exercise. In addition, Bacchi et al. (2012) found that the exercise groups significantly reduced their fasting blood sugar levels by 15.2% and 12%, respectively, in a four-month study on the metabolic benefits of aerobic and resistance exercise in T2DM participants. Together, these results demonstrate how well exercise programs work to lower fasting blood sugar levels and enhance glycemic control in people with type 2 diabetes. So that the body can use energy reserves as an energy source to be converted into glucose as the main energy source. Results of research conducted by Amanat et al. (2020) showed that physical exercise performed 3x a week for 12 weeks is proven to significantly reduce HOMA-IR levels. So, based on the analysis of this study, physical exercise has been shown to have a therapeutic effect in people to reduce HOMA-IR levels as a biomarker of insulin resistance.

5. STRENGTHS AND LIMITATIONS

The advantage of this systematic review is that it only looks at randomized controlled trials, which is the most reliable type of scientific evidence because there is no possibility of ambiguous causal relationships. In addition, the samples taken are focused on humans and show homogeneous data and are not mixed with other categories such as samples using animal samples.

The limitation that we found was the lack of discussion and discussion related to how physical exercise can reduce insulin resistance through the mechanism of reducing HOMA-IR levels. Therefore, this study is considered important to be conducted in order to increase insight and knowledge related to how the effect of physical exercise can reduce insulin resistance through reducing HOMA-IR levels. Physical exercise can be a recommendation for people with insulin resistance disorders to reduce the adverse effects it produces. However, regarding which exercise is

effective between moderate intensity, high intensity, or with a combination of exercises is still not known for sure, therefore further research is needed to determine which type and intensity are more effective in reducing insulin resistance through reducing HOMA-IR levels.

6. CONCLUSIONS

Based on the related articles we found, it can be said that regular physical exercise has been proven to significantly reduce HOMA-IR levels as a biomarker for insulin resistance. So physical exercise can be recommended for people with insulin resistance disorders or diabetes mellitus as a therapeutic effort to reduce the adverse effects it causes.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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