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# Role of Regular Physical Exercise Training on the Prediabetes among Adults

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## Abstract

**Background:** People with pre-diabetes are at increased risk to develop type 2 Diabetes Mellitus (DM) and cardiovascular diseases. Behavioral lifestyle intervention may play an important role in slowing down, stop or even reverse the progression to type 2 DM. The purpose of this study is exploring the epidemiological characteristics of prediabetes and assess the available knowledge about the role of PE intervention on prediabetic adults.

**Methodology:** Narrative review was done through using academic database search. Fifty-one English online articles about the effect of exercises on prediabetic adults have been included in the study.

**Findings:** Most studies agreed on positive effects of PE on glycemic status in prediabetic patients. However, some studies find slight or even no effects of lifestyle modifications including PE on developing type 2 DM and other complications. Studies agreed that, PE on both aerobic and resistance exercise adjusts cellular glucose uptake, improve insulin sensitivity, muscular and hepatic glucose metabolism resulting in more glycemic control, which reverses many pathological factors related to the usual glycemic & metabolic control and cardiopulmonary function. Substantial inconsistency in some studies could be explained by race, existing comorbidities, individual physiological status and PE prescription.

**Conclusion:** This review suggests that PE may express a positive influence among prediabetic patients. However more population-based studies with clinical trial design are needed taking into consideration many confounders including race, gender, genetics, physiological status and PE training prescription.

**Keywords:** Prediabetes; Impaired glucose tolerance test; Impaired fasting glucose; Physical exercise; Type 2 diabetes mellitus

**Abbreviations:** ADA: American Diabetes Association; CVD: Cardiovascular Disease; DM: Diabetes Mellitus; HIIT: High Intensity Intermittent Training; IDF: International Diabetes Federation; IEC: International Expert Committee; IFG: Impaired Fasting Glucose; IGT: Impaired Glucose Tolerance; NDDG: National Diabetes Data Group; NICE: National Institute for Health Care Excellence; WHO: World Health Organization

## Introduction

Recognition and effective management of prediabetes become a target for many health care authorities exponentially. The ultimate purpose is not to slow the progression of pathological sequelae but to have cost-effective management that ensures good quality of life.

The importance of prediabetes is not limited to a precondition for one of the most prevalent chronic diseases worldwide but as a preventable condition. Nevertheless, unrecognized conditions will eventually progress to type 2 Diabetes Mellitus (DM) in one-quarter of the patients in the presence of other risk factors. While a majority of them may live the rest of their lives as prediabetics [1].

Spectrum for the management of prediabetes is between pharmacological intervention and lifestyle modification, including Physical Exercise (PE). The use of PE is becoming now days a promising option from a clinical and cost-effectiveness perspective.

### Aim and Objective

This article attempts to explore the epidemiological characteristics of prediabetes and assess the available knowledge and evidence about the role of regular PE on prediabetes.

### Methodology

This is a narrative review study to highlight the role of PE on prediabetes. The searching was through using the following searching engine; google scholar, PubMed, Cochrane library, and TRIP database. The following keywords were used. The related articles; "effect," "impact," "influence," "physical exercise," physical exercise training," "prediabetes," and "impaired glucose tolerance test." A total of (51) English online published articles were identified and assessed accordingly with no date limit for publication time.

## Epidemiology of Prediabetes

### Definition and Diagnosis

Historically, the National Diabetes Data Group (NDDG) was the first to address the concept of a metabolic state between normal glucose homeostasis and diabetes. Later on, during (1979), it was called Impaired Glucose Tolerance (IGT), which represents the transitional phase prior to (DM) [2]. After two decades, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus introduced in (1997) the terminology of Impaired Fasting Glucose (IFG) in addition to (IGT) [3]. The definition of prediabetes basically refers to IGT and IFG. The terms of non-diabetic hyperglycemia and intermediate hyperglycemia are also used interchangeably as synonyms for prediabetes [4-7].

Overall, from an epidemiologic framework perspective, both IGT and IFG are standardized terms describing the prevalence of intermediate hyperglycemia in different populations at any one time or in the same population over time. This further reflects hyperglycemia with glucose levels above the normal state but below the diagnostic level of type 2 DM [8].

There are five major international health authorities directed the definition of prediabetes in the literature; The American Diabetes Association (ADA), World Health Organization (WHO) with International Diabetes Federation (IDF), National Institute for Health Care Excellence (NICE) and International Expert Committee (IEC). The authorities agree for the diagnosis of prediabetes to obtain IGT, IFG or HbA1c%. Table 1 illustrates the differences between them based on diagnosis and definition [9-12]. There is agreement between WHO/IDF, NICE and IEC on the cut off values of the diagnostic biomarkers in comparison with ADA cutoffs which are lower in IFG and $HbA_1c$%.

| Criterion | ADA | WHO and IDF | NICE | IEC |
|---|---|---|---|---|
| **Terminology** | Prediabetes | Intermediate hyperglycemia Impaired glucose tolerance | Prediabetes | Prediabetes |
| **IGT (2-h PG 75g OGTT)**<br>mmol/L<br>mg/dL | <br>7.8-11.0<br>140-199 | <br>7.8-11.0<br>140-199 | <br>7.8-11.0<br>140-199 | <br>-<br>- |
| **IFG (using FPG)**<br>mmol/L<br>mg/dL | <br>5.6-6.9<br>100-125 | <br>6.1-6.9<br>110-125 | <br>6.1-6.9<br>110-125 | <br>6.1-6.9<br>110-125 |
| **$HbA_1c$**<br>%<br>mmol/mol | <br>5.7-6.4<br>39-47 | Not recommended | <br>6.0-6.4<br>42-47 | <br>6.0-6.4<br>42-47 |
| ADA: American Diabetes Association; WHO: World Health Organization; IDF: International Diabetes Federation; IGT: Impaired Glucose Tolerance; PG: Plasma Glucose; OGTT: Oral Glucose Tolerance Test; IFG: Impaired Fasting Glucose; FPG: Fasting Plasma Glucose; NICE: National Institute for Health and Care Excellence; IEC: International Expert Committee. | | | | |

**Table 1:** Major criteria of diagnosis and definition of prediabetes.

### Burden

Prediabetes is proportionally recognized as an essential metabolic abnormality [13]. There is a wide variety in the prevalence of prediabetes worldwide, properly due to the biomarkers' variable definition and diagnostic cut-off values. It was reported to be as high as (36%) in a large meta-analysis of studies among Caucasian and Asian cohorts using IFG cut-off points of WHO/IDF. While it was (53.1%) using ADA guideline, which uses a lower biomarkers threshold. The same study defined similar prevalence rates for patients who have both IGT and IFG; (15.8%) for WHO and (20.2%) for ADA guideline [14].

However, using $HbA_1c$% as a diagnostic tool is still debatable but is recognized by many authors as a more valid test of impaired glucose homeostasis. A study of (1542) normal Swiss adults identified prediabetes in (30.9%) of the population; of these (79.9%) were identified using $HbA_1c$ %, while only (9.9%) based on FPG, and (10.3%) based on both ADA guideline criteria [15].

There is an accumulative data to expect the progressive surge of prediabetes globally from (7.3%) of the adult population during (2017) which is equivalent to (352.1) million individuals to (8.3%) by (2045) which is an estimate for (587) million individuals [16].

**Complications**

Prediabetes will progress to overt type 2 DM in approximately (25%) of subjects within (3-5) years if no tangible behavioral and lifestyle intervention is done [17]. Furthermore, prediabetes is well recognized with a cause-effect relationship to Cardiovascular Diseases (CVD) and all-cause mortality. Based on multiple studies, vascular complications are placed on top of prediabetes complications at micro and macrovascular levels. The macrovascular complications of prediabetes are; myocardial infarction, stroke, and peripheral vascular disease. The microvascular complications are; retinopathy, neuropathy, and nephropathy [18,19].

The pathological explanation for the connection between prediabetes and related CVD complications is still not fully explored. Nevertheless, many authors believe that; associated atherosclerosis, coexisting metabolic syndrome, overweight or obesity, and lipid profile disturbances explain the atheroma development and subsequent CVD complications [20]. Moreover, others added the effect of an increase in fibrinogen, high-sensitivity C-reactive protein, and other inflammatory markers contribute to the pathophysiology of CVD complications among prediabetics [21-23].

**Risk factors**

The common risk factors attributed to prediabetes development are remarkably similar to those in prevalent non-communicable disease. Table 2 summarizes the risk percentage for each risk factor. Hypertension is the leading risk factor for prediabetes, far from the second common risk factor, i.e., obesity. While the age illustrates normal distribution curve, with less risk on the younger age group of (30-49) by (16%), peaks at middle age category of (50-64) to (50%), and then curves down on elderly group to (33%) [24]. There is no gender base statistically significant relation to be anticipated as a related risk factor [21].

| Risk Factor | Risk Percentage (%) |
|---|---|
| Hypertension | 72% |
| Obesity | 59% |
| Family history of diabetes | 56% |
| Age (50-64) years | 50% |
| Physical inactivity | 38% |
| Alcohol consumption (Risky drinker) | 34% |
| Smoking habit | 19% |

**Table 2:** Prediabetes risk factors.

Knowledge about the related risk factors for prediabetes makes the intervention on the modifiable risk factors area of interest for many authors. One of the currently, raising modality for management of prediabetes is using (PE) training.

**Management**

All patients with prediabetes should be provided with comprehensive lifestyle behavioral modifications that include; diet advice, regular PE prescription, smoking cessation, stress management, and healthy sleep hygiene. The ultimate goal for such intervention is to obtain (5-10%) weight reduction, which eventually improves insulin resistance and glycemic hemostasis [25,26]. According to the ADA the prediabetes is reversible in (58%) of the high-risk subjects once there is (5-10%) weight loss. Also, evidence for decelerating the progression to type 2 DM is growing by (150 minutes) of weekly PE [27].

Pharmacological intervention is a widely used option by prescribing Metformin with or without a lifestyle intervention. The combined therapy of lifestyle intervention and Metformin looks attractive for further assessment as no sufficient data support a significant effect of one on the other [28-30].

**Evidence on the Role of Regular Physical Exercise Training on the Pre-Diabetes among Adults**

The term physical exercise is interchangeably used with physical activity in the literature. Physical exercise is the repetitive and designed movements of muscles or groups of muscles that lead to either health or skill-related benefits. The health-related benefits are alteration in; body composition, cardiopulmonary fitness, muscle endurance & strength, and flexibility. In contrast, the skill related benefits are agility, coordination, balance, power, reaction time, and speed. Physical exercise is under the umbrella of physical activity, which comprises all the daily movements of an individual [31].

There is building up evidence on the impact of PE on almost all the body systems, including the influence of preconditions metabolism and long-term complications of a wide variety of chronic diseases especially type 2 DM [32-35].

Lifestyle intervention, including PE training, was superior to the control group across a couple of intervention studies. The influence of PE was demonstrated by a variable reduction in the accumulative incidence of type 2 DM (11-46%) in comparison with the control group (16.6-67.7%). With a variable sample size of prediabetics (522- 3234) subjects, with age average (45-55) years and variable study duration of (3-6) years [28,36-38].

Xia D, et al. determined from his clinical trial in (2019), after two years of follow up of adult prediabetics on supervised PE training, that aerobic PE could reduce the incidence of type 2

DM by (74%) in comparison with resistance PE training which could do by (65%). Close to the aerobic results were the combined aerobic and resistance by (72.5%) reduction in the occurrence of type 2 DM [39]. Similar but with less proportion, Wani K and his team confirmed on (2020) the normalization of (46.5%) of the Saudi with prediabetes on adults following a randomized clinical trial of (12) months healthy lifestyle intervention which included PE program [40]. Relatively, consistent findings were reported by König D and his colleagues after (12) months of healthy lifestyle intervention. Around (38%) of the adult participants showed no longer the criteria of prediabetes post-intervention [41].

Furthermore, Jaana Lindström et al. documented similar results from the Finnish Diabetes Prevention Study upon the use of both dietary and PE intervention in (2003) as well as Costa B and his team who reported the reduction in the incidence of type 2 DM on around (4) years follow up of adults with impaired glucose metabolism [42,43]. Additionally, collected data documented by Preethi Srikanthan and his working group. The increase in muscle mass improved insulin sensitivity and lower risk of type 2 DM observed on the National Health and Nutrition Examination Survey III data analysis [44].

Beyond exclusive Connolly PE, et al. in (2018), also concluded through (15) weeks interventional study that High Intensity Intermittent Training (HIIT) of swimming of low volume is an effective training strategy for improving insulin, glucose control, and biomarkers of (62) inactive middle-aged hypertensive premenopausal women [45]. Comparable findings were also determined by Zadeh MAM and his colleagues (2018) through an interventional study on (33) middle-aged non-active obesity with type 2 DM. The participants received HIIT along with low carbohydrate regimes [46].

Eijnde BO, et al. in (2017) concluded from a small-scale sample size of (10) obese participants with insulin resistance, equivalent results. The interventional study carried out using (12) week exercise training program improved metabolic profile and other body composition [47]. T. Vepsäläinen and his team in (2013) confirmed after (18) years following on prospective population-based of (1059) patients consistent results of the clear preventive influence of PE on CVD mortality in patients with type 2 DM [48].

Other authors reported no statistically detected influence of the regular PE on the prediabetic subjects, or at least the PE is not favoring the biochemical change of the glucose intolerance.

Newton RL team reported in (2020) through community-based clinical control trail of exercise training intervention the not favoring effect. When (113) middle age African Americans underwent aerobic and resistance training program comparing to the controlled group for (5) months follow up. In this study, despite improvement in some health-related parameters, there was no statistically effect of PE on glycemic status of the participants following comparison of control to aerobic & resistance exercise training group [49].

Idowu drew the same conclusion among young (55) overweight and obese pregnant ladies. After the observational cohort study, participants were self-reporting the level of regular PE at early and late gestation while glucose tolerance was correlated. Idowu concluded that there was moderate to no correlation between self-reported PE levels and 2-hour plasma glucose in late pregnancy [50].

Some authors demonstrated no further effect of the lifestyle, including PE training, on developing type 2 DM and CVD complications in high-risk populations, as seen in the meta-epidemiological study by Huseyin Naci (2013). The metanalysis study compared the PE intervention and the medication on the secondary prevention of prediabetes and CVD. Huseyin's study revealed no statistical differences between PE and pharmacological interventions in preventing CVD and prediabetes [51].

Relatively, same results seen with David M. Nathan (2019) where no impressive effect detected and the need of longer follow us is recommended [52].

Although all available studies with inconsistent data, many of them agreed on the positive effect of the PE even though incorporated with healthy lifestyle intervention. The varying knowledge about the effect of PE is quite explanatory by many epidemiological and metabolic factors.

**Mechanism of the Regular Physical Exercise on Prediabetes**

Regular PE reverses many pathological factors related to the usual glycemic & metabolic control and cardiopulmonary function. Physical exercise on both aerobic and resistance exercise improves glycemic control & metabolism, cardiopulmonary function, and inflammatory biomarkers to an extent equivalent to some pharmacological intervention. The effect is comprehensive, simultaneous, and in a synergistic manner.

Physical exercise improves fasting glucose levels through many means. Insulin sensitivity looks to be the most positively associated mechanism. Physical exercise adjusts cellular glucose uptake, muscular and hepatic glucose metabolism resulting in more glycemic control. A regular PE is a unique option for patients who choose not to take any medication or wish to obtain additional glycemic control [53].

On an attempt for additional explanation glycemic control due to PE was further categorized into immediate and long-term effect. Where, the immediate effect is properly by [54]:

- Acceleration in the uptake of glucose into the active skeletal muscles by non-insulin-dependent mechanism.

- Activation of the gluconeogenesis in the liver to meet the energy need.
- Improvement of the instant action of insulin that could be lasts (2-3) days post-exercise session.
- Improvement in the intracellular and molecular glucose pathway.

Further to the acute effect of the PE on glucose metabolism, the following are observed on the long-term:

- Reduction in the probability of progression to type 2 DM.
- Decreasing in all cause of mortality including hypertension, which is leading risk factor for prediabetes, dyslipidemia, and other CVD.
- Growing in overall muscle mass, with reduce in total body fat mass and weight which was contributed greatly as core factor in pathogenesis of prediabetes.
- Reduction in the overall DM related inflammatory markers, which is also detected in prediabetes.
- Improvement of mitochondrial functions with a substantial increase in the mitochondrial capacity and energy utilization [55].
- Modifying positively the oxidative homeostasis of tissues, through diminishing the basal levels of oxidative damage and increasing resistance to oxidative stress. Thus, protecting body tissues from the effects of oxidative stress, and preventing cellular damage associated with type 2 DM [56].
- Reduction in the pathogenic pathway of Polyol in both animal models and human trials. This was critically linked to the prediabetes and progression to type 2 DM neuropathy [57].

Furthermore, the regular physical exercisers will obtain the other health benefits on cardiopulmonary, mental, and musculoskeletal systems which results in overall improvement of the quality of life [58].

## Discussion

Many authors addressed the inconsistent results of regular PE on the prediabetes, which could be explained by many factors like race and genetic. There was high normalization in the Chinese population that has been reported by Xia Dai Compared to (46.5%) in the Saudi population as determined by Wani K. On the contrary, Newton RL team reported opposite findings among African Americans in community-based clinical trial of exercise training intervention.

There was no marked statistical significance from gender perspectives, as repeatedly concluded form many studies. Other factors could be attributed to the physiological status, like in pregnancy, when Idowu showed this among obese pregnant ladies through his observational cohort study.

Another crucial factor is the presence of associated obesity that could give a logical rationale for the favorite effect of the PE on the metabolic hemostasis in prediabetes. Reducing the (2-5%) weight is an approved influencer by most scientists to normalize glycemic status and possibly reverse prediabetes.

Also, PE prescription variation could be hypothesized as the explanatory factor for the inconsistent outcomes, as illustrated by Xia Dai et al. and Connolly et al., where aerobic exercise is more effective than resistant or companied PE.

Additional studies at the design of the clinical trial on the population-based sample are required to explore any unknown confounders that might contribute to the effect of the regular PE on the prediabetes. Population-based screening programs must be developed in addition to PE prescription type research suitable for prediabetes for early detection and cost-effective management of prediabetes as well as long-term sustainability of the prevention. The cost-effectiveness of prediabetes management was not addressed in any of the previous studies. Therefore, cost-effective studies must be conducted to determine the superiority of pharmacological management versus PE and healthy lifestyle intervention.

## Conclusions

The area for reversing prediabetes by using PE as exclusive non-pharmacological intervention, is still in need for further evaluation. Nevertheless, the available considerable evidence of the influence on the glucose tolerance should be practiced as part of prevention management plan for any patient with prediabetes.

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