

# Physical Activity: An Under-utilized Tool in Managing Type 2 Diabetes in Older Adults: A Narrative Review

Iqbal Akhtar Khan<sup>1,\*</sup>, Mujtaba Hasan Siddiqui<sup>2</sup>, Mehnaz Liaqat Sheikh<sup>3</sup>

<sup>1</sup>Independent Scholar, Lahore 54792, Pakistan

<sup>2</sup>Consultant Endocrinologist and Diabetologist, Akhtar Saeed Medical College, Lahore, Pakistan

<sup>3</sup>Physical Therapist, Hameed Latif Teaching Hospital, Lahore, Pakistan

## ABSTRACT

Diabetes mellitus, a chronic metabolic disorder, is currently the 8th leading cause of disease burden globally and estimated to become the second leading cause by 2050. Its prevalence increases with age. In 2024 the older adult population (65-99 years) was 667.8 million with 158.3 million cases of diabetes (23.7%). Type 2 diabetes (T2DM) accounts for over 90% of all diabetes, with around half of all people affected unaware that they have the condition. Sedentary lifestyle, late adulthood, and comorbidities constitute a “Worrisome Triad” for those with T2DM. Evidence proves that the right dose physical activity, in addition to its preventive and rehabilitative role and a safe adjunct to pharmacotherapy, plays a pivotal role in optimizing glycemic control, reduction of symptoms of depression and improve health-related quality of life (HRQoL). Moreover, the combination of exercise training with multicomponent exercise and oral Metformin were more rewarding than either of the two alone, in the overall management of T2DM.

The distinct options of physical activity for older adults with T2DM include aerobic, resistance, stretching and balance. Multi-component exercises like tai chi chuan and yoga combine flexibility, balance, and resistance activities and have significant impact on health outcomes. While regulatory bodies have made their recommendations available, FITT Principle (Frequency: Intensity, Timing, Type) should be followed in developing exercise prescription which should be individualized because the “one size fits all” does not suit every case. Whereas “Role of Physical Therapists in Fighting the T2DM Epidemic” has been defined, it is hoped that they will be accepted to play a central role in the multidisciplinary health care team.

**Keywords:** Type 2 Diabetes, Physical therapy, FITT Principle, Role of Physical Therapist, Therapeutic Adherence.

## Vol No: 03, Issue: 01

Received Date: April 21, 2025

Published Date: July 02, 2025

## \*Corresponding Author

**Prof. Iqbal Akhtar Khan**

MBBS, DTM, FACTM, PhD, Independent Scholar, Lahore 54792, Pakistan, E-mail: profiakhan@gmail.com

**Citation:** Khan IA, et al. (2025). Physical Activity: An Under-utilized Tool in Managing Type 2 Diabetes in Older Adults: A Narrative Review. Mathews J Diabetes Obes. 8(1):22.

**Copyright:** Khan IA, et al. © (2025). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## INTRODUCTION

*"Diabetes is not a burden, but a lesson in perseverance and self-care".*

Peter M. House

Diabetes, the shortened version of the full name diabetes mellitus, has a long and venerable history affecting all ages and all cultures. It is characterized by systemic inflammation and insulin resistance resulting in chronic hyperinsulinemia and hyperglycemia. Left untreated, hyperglycemia can lead to micro and macro-vascular disease resulting in an increased mortality risk. It is currently the 8th leading cause of disease burden globally [1] and estimated to become the second leading cause by 2050 [2]. Its prevalence increases with age, the highest estimated figure being in people over 65 who are highly vulnerable to diabetes because of age related bodily changes, sedentary lifestyle, and comorbidities. Its global prevalence is projected to rise sharply over the forthcoming decades.

In 2024, the older adult population (65-99 years) was 667.8 million with 158.3 million cases of diabetes. In 2050, the population of this age group is projected to be 1.1 billion with 278 million cases of diabetes [3]. According to the estimates of International Diabetes Federation (IDF), type 2 diabetes (T2DM) accounts for over 90% of all diabetes, with around half of all people affected unaware that they have the condition [3].

Those in late adulthood may have long-standing diabetes (with onset in middle age or earlier) or they may have incident disease (diagnosed after 65 years) [4]. They do have higher risk of developing diabetes complications, due to the combination of both modifiable (higher body mass index, physical inactivity, hypertension, smoking, and alcohol use), and non-modifiable risk factors (age, gender, ethnicity) [5]. Within this population, T2DM has been linked to increased brain atrophy [6], impaired cognitive function [7], increased risk of depression [8] and dementia (vascular dementia and Alzheimer's disease) [9]. The prospective studies show that the metabolic syndrome, regardless of how it is defined, is a significant predictor of incident diabetes in different populations [10].

The most vital component of lifestyle intervention of diabetic management is physical activity with its preventative, therapeutic and rehabilitative roles. Centers for Disease Control and Prevention (CDC) have defined physical activity as: *"any bodily movement that is produced by the contraction of skeletal muscle and that substantially increases energy*

*expenditure"* [11]. Regular physical activity is proven to help, prevent and manage chronic diseases including T2DM [12]. Physical Exercise, a subset of physical activity, has been defined as: *"a type of physical activity that involves planned, structured, and repetitive bodily movement done to maintain or improve one or more components of physical fitness"* [11]. It is a cornerstone of diabetes management and the prevention of incident diabetes [13].

**Objective:** To highlight the perspectives of physical activity as a powerful tool for managing T2DM in older adults.

## A WORRISOME TRIAD

Sedentary behavior (used interchangeably with physical inactivity), late adulthood, and comorbidities constitute a "Worrisome Triad" for those with T2DM. Physical inactivity, which Blair has termed as the "biggest" public health problem of the 21st century [14], is a principal contributor to the global burden of chronic diseases including T2DM. A meta-analysis of 10 studies suggests that there is a 112% greater relative risk associated with a large duration of sedentary behavior for T2DM [15]. Relatively prolonged sedentary time (daily/weekly sitting time) have been associated with significantly greater risk for T2DM and metabolic syndrome in two meta-analyses [15]. Watching TV and working on computer are obviously just two of the more common reasons why people sit for long periods of time with inactive muscles. Obviously, the disease risks are associated with many hours per day of sitting idle, averaging ~10 hours/day or 70 hours each week. In a randomized controlled trial registered with the Australian New Zealand Clinical Trials Registry, aimed to examine whether reductions in sitting time through alternating 30-min bouts of sitting and standing can reduce postprandial glucose, insulin, and triglyceride responses, alternating standing and sitting in 30-minutes bouts, resulted in modest beneficial effects on postprandial glucose responses in study population [16]. There is another issue necessitating attention of the diabetologists. Dempsey has argued that sedentary behavior-too much sitting as distinct from too little physical activity-contributes adversely to cardiometabolic health outcomes and premature mortality [17]. In a systematic review and meta-analysis, aimed to quantify the size, consistency, and manner of association between sedentary time and outcomes independent of physical activity, prolonged sedentary time was independently associated with deleterious health outcomes regardless of physical activity [18].

Whereas the patients with T2DM are more likely to develop multiple morbidities compared with those without diabetes

[19], the disease related effects on microvasculature, microvasculature, and immune response lead to an approximate doubling of risk for myocardial infarction, a 5-fold increased risk of renal failure, and more than a 10-fold increased risk of amputation and blindness [20]. Epidemiological studies have shown that poorly controlled diabetes dramatically increases various complications, including retinopathies, nephropathies, neuropathies, and diabetic foot [21]. Hypertension is a common comorbidity affecting more than 60% of individuals with T2DM [22]. The risk of vascular complications in hypertensive individuals with T2DM is 66–100% higher than with either condition alone [23]. The incidence of T2DM in people with COPD is markedly elevated compared to the general population. Epidemiological studies demonstrate that those with COPD possess an increased risk of acquiring T2DM as a result of chronic inflammation, oxidative stress, and physical inactivity [24]. Moreover, T2DM may accelerate the course of COPD by compromising lung function, amplifying vulnerability to infections, and deteriorating overall prognosis.

The issue of the “aging population” is also of serious concern. It will result in substantial increase in the numbers and proportion of older adults. Aging is characterized by loss of function and older adults are among the most sedentary segment of society [25]. According to the estimates of WHO, the pace of population aging is much faster than in the past and by 2050, the world’s population of people aged 60 years and older will double (2.1 billion). The number of people aged 80 years or older is expected to triple between 2020 and 2050 to reach 426 million [26]. They are prone to the emergence of several complex health states commonly called geriatric syndromes, often the consequence of multiple underlying factors. Musculoskeletal impairments associated with joint mobility limitation and tissue changes may go undetected and impact the ability to participate in physical activity program [27].

The phrase “add insult to injury”, with its origin in ancient Roman law, becomes significant when the Triad is complicated by Frailty, a multifactorial geriatric condition characterized by the reduction of physiological reserve such that the ability to cope with every day or acute stressors. Diagnostic criteria include involuntary loss of weight and muscle mass, exhaustion, low physical activity, slowness, and reduced grip strength. The presence of three or more criteria indicates frailty while the presence of less than three is known as pre-frailty [28].

## PREVENTATIVE ROLE OF PHYSICAL ACTIVITY IN PRE-DIABETES

It has been estimated that up to 80% of patients referred to outpatient physical therapy have diabetes, pre-diabetes, or diabetes risk factors [29]. American Diabetes Association (ADA) defines Pre-diabetes as: “*having blood glucose (sugar) levels that are higher than normal, but not yet at the point that defines diabetes*”. It refers to an intermediate stage of dysglycemia along the continuum from normoglycemia to diabetes [30]. It is the same as Impaired Glucose Tolerance (IGT) or Impaired Fasting Glucose (IFG). As estimated by US Institute of Aging, millions of older adults have pre-diabetes. Although they have a greater chance of developing T2DM, there are ways to help prevent or delay the disease. According to the Joint Position Statement of the American College of Sports Medicine and the American Diabetes Association, participation in regular physical activity improves blood glucose control and can prevent or delay onset of T2DM [31]. Their Evidence Statement adds: “*At least 150 minutes/ week of moderate to vigorous physical activity should be undertaken as part of lifestyle changes to prevent type 2 diabetes onset in high-risk adults. ACSM evidence category A. ADA A level recommendation*” [31].

The findings of meta-analysis of 10 cohort studies show that adherence to physical activities of moderate intensity such as brisk walking can substantially reduce the risk of T2DM [32]. A population-based cohort Chinese study provided compelling evidence that engagement in physical activity holds a pivotal role in mitigating the occurrence of T2DM among individuals classified as pre-diabetes, based on fasting blood glucose criteria [33]. In a systemic review with meta-analysis on the effects of physical activity on pre-diabetes, it was inferred that physical activity helps to slow down the progression of disease by a favorable effect on improving oral glucose tolerance, fasting blood sugar, HbA1C, maximum oxygen uptake (VO<sub>2</sub> max), and body composition [34]. Exercise training, whether aerobic or resistance training or a combination, facilitates improved glucose regulation [35]. Daly argues the efficacy of targeted multi-modal programs incorporating traditional and high-velocity traditional progressive resistance training (PRT), weight-bearing impact exercises and challenging balance/mobility activities for optimizing musculoskeletal function in those with ‘sarco-osteoporosis’ (osteoporosis and sarcopenia co-existing) [36].

## THERAPEUTIC ROLE OF PHYSICAL ACTIVITY IN T2DM

Gabriel and Zierath, while ratifying “The Limits of Exercise Physiology: From Performance to Health” inferred that the acute effects of exercise include enhanced glucose metabolism and improved insulin sensitivity. Such an activity regulates blood glucose levels in those with insulin resistance [37].

Duration of physical activity counts but not so much, even one minute will pay. There is evidence that sedentary people will benefit from regular short activity periods of as little as 1 min [38] or 10 min bouts [39] to break-up periods of sitting or lying.

Prospective cohort studies show that regular aerobic activity and short-term exercise programs confer a reduced risk of functional limitations and disability in older age [25]. Walking 5–7 days per week was associated with 50–80 % lower risk of mobility impairments [40]. It increases longevity by around 4 years and disability-free life expectancy by around two years [41]. In a 16 -year UK longitudinal study on associations of changes in exercise level with subsequent disability among seniors, the results suggested a beneficial effect of exercise, even when begun later in life, on postponement of disability [42]. Exercise has psychological benefits for persons with T2DM. “Increased physical activity and physical fitness can reduce symptoms of depression and improve health-related QoL in those with type 2 diabetes. *ACSM evidence category B.*”

In the systematic review by Savvakis et al, underlining the role of physical-activity interventions on FoF (fear of fall) reduction in frail and pre-frail older adults, the interventions focusing on muscle strengthening with the combination of balance or mobility exercises were found most effective in reducing FoF [43]. In a Portuguese cohort study, to analyze the effect of three types of treatment (sole or in combination), the combination of exercise training with multicomponent exercise and oral Metformin were the most effective long-term therapies to improve mood states and HRQoL in older adults with T2DM [44].

## PHYSICAL ACTIVITIES FOR OLDER ADULTS WITH T2DM: VARIOUS OPTIONS

### Aerobic/ Endurance/Cardio activities

Aerobic/ Endurance/Cardio activities are physical activities in which people move their large muscles in a rhythmic manner for a sustained period of time, normally lasting for at least 10 minutes at a time. Moderate-intensity aerobic activities range from 3–6 metabolic equivalents (METs) and include brisk walking, dancing, light cycling, gardening

and domestic chores. Vigorous-intensity activities (>6 METs) include running, climbing stairs or hill walking, fast cycling or swimming, aerobics and most competitive sports and games [45]. Moderate to high-intensity exercises are more effective for glycemic control and, unlike previously thought, are generally safe for the elderly population [46]. The expected benefits include improved blood sugar control, enhanced insulin sensitivity, reduced cardiovascular risk, and improved overall well-being.

The results of a meta-analysis of the effect of walking exercise on lower limb muscle endurance, whole body endurance and upper body flexibility in elders indicate that walking exercise, doable at any time and at any place, improves physical function in older adults [40]. Another meta-analysis showed that regular physical activity has a statistically and clinically significant effect on VO<sub>2</sub>max in T2DM suggesting that those already exercising at a moderate intensity should consider undertaking some vigorous activity to obtain additional glycated hemoglobin (HbA1c) and cardiovascular benefits [47].

### Resistance Training/Strength Training/Weight Training:

Resistance exercise is any type of exercise where the muscles work against an external force to make muscles contract, aiming to increase strength, endurance, and size. It can be done with weights (using dumbbells, barbells, or kettlebells), weight machines (using gym equipment with adjustable weights or hydraulics) and resistance bands (using elastic bands to create resistance). It can even be done by using one's own weight by exercises like squats, lunges, push-ups and seated knee lift exercise can be done at home or in a gym. Resistance Band Training is safe and effective way to build strength and flexibility. The expected benefits include increased muscle mass, strength and endurance, improved cardiovascular health, enhanced bone density and weight management. In an Australian study, high-intensity progressive resistance training, in combination with moderate weight loss, was effective in significant reduction of HbA1c with additional benefits of improved muscular strength [48].

### Stretching Exercises

These are physical activities designed to improve the body's ability to move and bend through a full range of motion, enhancing muscle length and joint mobility. In diabetes, there is glycation of collagen, where sugar binds to collagen in the muscles and joints making the tissues stiffer and requires muscle stretching. These exercises focus on



stretching muscles and improving the range of motion at joints. Static Stretching is holding a stretch for a period of time without moving. It includes neck side stretch, seated calf stretch (chair supported), seated hamstring stretch, quadriceps stretch (seated or chair assisted), ankle and foot flexion. Dynamic Stretching incorporates movement while stretching, like arm circles or leg swings. The expected benefits include improved range of motion and flexibility, reduced risk of injury during exercise and daily activities, increased muscle strength and tone, improved posture and balance and enhanced athletic performance. Important examples include Yoga and Tai Chi Chuan.

### **Balance Exercises**

Balance exercises are exercises that focus on improving one's ability to stay upright (Static Balance) and maintain control of body's position in motion like walking or playing sports (Dynamic Balance) by strengthening muscles and enhancing coordination. Balance training can be defined as a training aimed at improving postural control. The examples of balance exercises include: One-leg stand, Heel-toe walking, Balance board exercises, Squats and Reaching exercises (when standing, reach for objects or try to touch your toes, while maintaining balance). The expected benefits include improved coordination, improved posture, reduced risks of fall and enhanced stability for routine tasks like walking and climbing stairs. Moreover, balance training improves peripheral neuropathy as in diabetes there is reduced sensation in feet. It keeps the body and brain to cope with limited sensations.

### **Multi-component Exercises**

Some activities, such as yoga, tai chi, gardening, and many sports, include more than one type of physical activity. Activities like tai chi and yoga combine flexibility, balance, and resistance activities. Doing activities of all three types is important for improving physical function and decreasing the risk of falls [11].

### ***Tai Chi Chuan / Chinese Boxing***

This mind-body practice, which originated in ancient China as a martial art, is often described as "meditation in motion." However, it may be preferable to call it "meditation in motion." As exercise, it is designed to provide relaxation in the process of body-conditioning exercise. Depending on school and master, the number of prescribed exercise forms varies from 24 to 108 or more. All starts from one of three stances, weight forward, weight on rear foot, and horse riding, or oblique exercises. It could be easily adapted for anyone, from

the most fit to people confined to wheelchairs or recovering from surgery. It is of special benefit for those in late adulthood to help maintain strength, flexibility, and balance, and could be the perfect activity for improving the quality of life [49,50]. There is growing evidence of the impact of Tai Chi in those with T2DM. In 3 randomized controlled trials and 5 systematic reviews and meta-analyses, aimed to investigate the effectiveness of Tai Chi on various health outcomes in those with T2DM, Tai Chi demonstrated a significant effect in enhancing glycemic control, lowering blood pressure, improving serum lipid profiles, reducing insulin resistance, positively influencing obesity-related indices, and improving overall HRQoL in individuals with T2DM [51].

### **Yoga**

According to Harvard Publishing, Harvard Medical School, Yoga is a combination of four components: postures (like tree pose), breathing practices, deep relaxation and meditation that can transform one's health on many different levels. It improves strength, balance, flexibility and well-being. Gordon argues that, in patients with T2DM, yoga therapy increases the number of insulin receptors and the proportion of receptors binding in patients with diabetes [52]. It improves insulin kinetics by reducing fasting insulin levels, shifting the peak insulin level to the left, and by normalizing the insulin-to-glucose ratio [53]. Yoga also reduces levels of free fatty acids, indirectly indicating improved insulin sensitivity or reduced insulin resistance [54]. Moreover, it improves cell-mediated immunity, as demonstrated by improvements in the lymphocyte migration test [55]. Sahay, while comparing the efficacy of breathing exercises in diabetics, inferred that yoga leads to improvements on lung function tests [56]. Chair yoga, a practical option for those with mobility challenges, is a gentle, accessible form of yoga practiced while seated or using a chair for support, offering benefits like improved flexibility, balance, and strength. The beauty of yoga is that it can be tailored to all age groups and fitness levels.

### **Hot tub therapy / Chronic passive heat therapy**

It offers new hope for those with T2DM. It is a new study investigating the effect of repeated hot water immersion (HWI) on insulin sensitivity, inflammatory status, and substrate utilization in individuals with T2DM. The main findings of the University of Portsmouth study were that HWI improved fasting insulin sensitivity and lowered fasting plasma insulin but did not change postprandial measures or plasma glucose [57]. The promising results from this study warrant further investigation over a longer period of time.

### Objective Monitoring of Physical Activity

While evaluating the levels of fitness in their clients, the physical therapists are expected to advise them to self-monitor their physical activity with a pedometer or accelerometer. A pedometer is a wearable device that detects and counts each step a person takes. An accelerometer is a device that measures non-gravitational acceleration. They are well suited to measuring walking or jogging but not cycling or swimming. Pedometers measure steps but not speed, whereas accelerometers can measure both steps and speed. Smart watches have almost replaced these instruments in the modern era.

### Supervised Exercise Program

Whereas the exercise intervention studies showing the greatest effect on blood glucose control have all involved supervision of exercise sessions by qualified exercise trainers, the most direct test of the incremental benefits of supervised training was the Italian Diabetes and Exercise Study (IDES) [58]. In an Australian systematic review of 20 resistance training studies on T2DM, the supervised training of varying volume, frequency, and intensity improved blood glucose control and insulin sensitivity, but it was observed that when supervision was removed, compliance and blood glucose control both deteriorated [59]. It showed that the supervision had an important impact on significant improvement. It seems justifiable to recommend that individuals with long term complications of T2DM, such as vascular diseases, peripheral neuropathy, autonomic neuropathy, retinopathy and nephropathy, classified as moderate or high risk, should take a supervised exercise program, at least initially. A Supervised Physical Exercise Program (SPEP) has given promising results in those with such problems, as noted in a Brazilian study [60]. The guidelines of Clinical Exercise Physiology Association (CEP) could be incorporated in SPEP [61].

### Risks of Exercising

Whereas the right dose physical therapy offers many benefits to diabetic older adults, the potential risks including cardiovascular events, hypoglycemia, hyperglycemia and foot problems should not be underscored.

Post-exercise hypoglycemia has been identified as the greatest barrier to exercise in older adults with T2DM, more so for insulin and secretagogue-dependent individuals. In low-intensity activity, the risk is certainly low but during moderate exercise, blood glucose utilization by muscles

usually rises more than hepatic glucose production with resultant hypoglycemia [62]. Conversely, during brief intense aerobic exercise, plasma catecholamine levels rise markedly, driving a major increase in glucose production. Since the raised catecholamine levels do not return to normal immediately with cessation of the activity, the resultant hyperglycemia persists for up to 1–2 hours [63].

In older adults, particular care must be taken, for the presence of contraindications, for the practice of different types of exercise, possible pharmacological interactions and concomitant morbidities which could adversely affect the individualized exercise program. Of note, heat stress is associated with a reduction in exercise capacity and an increase in disease-related symptoms [64]. As already emphasized, a tailored exercise plan, under medical supervision, is essential to mitigate these risks and maximize the benefits of physical activity. There are certain practical tips for incorporating physical activity into a successful intervention program:

- Take an “Accurate Exercise History” to sort out the barriers preventing the individual from being active.
- Assess the physical activity level of the individual.
- Safety Screening prior to intervention.
- Follow the FITT Principle (Frequency: Intensity, Timing, Type) in developing exercise prescription which should be individualized because the “one size fits all” does not suit every case.
- Set Realistic Goals: achievable, enjoyable, sustainable.
- Start slowly and gradually increase intensity and duration. Remember that some physical activity is better than none at all.
- Monitor blood sugar levels, before, during, and after exercise.
- Stay hydrated before, during, and after exercise.

The quote “Listen to your patient; he is telling you the diagnosis” is famously attributed to Sir William Osler (1849-1919), the Father of Modern Medicine. This highlights his belief that patient interaction is crucial for accurate diagnosis. While he emphasized observation and examination, the quote reflects his view that patients often possess valuable insights into their own conditions. Same is applicable in the executing the prescription of physical activity in older adults with T2DM. They deserve to be given adequate hearing and their reservations and apprehensions be properly dealt with.

## RECOMMENDED DOSAGE OF PHYSICAL ACTIVITY FOR OLDER ADULTS

According to Guidelines of CDC, the Goal is:

- (i) Aerobic physical activity that includes:
  - At least **150 minutes** at moderate intensity. This could be 30 minutes a day, 5 days a week.
  - **Or** 75 minutes at vigorous intensity.
  - **Or** an equivalent combination of moderate and vigorous intensity.
- (ii) At least **2 days** of activities that strengthen muscles.
- (iii) Balance activities such as walking heel-to-toe or standing from a sitting position.
- (iv) Muscle-strengthening activities.

A repetition is one complete movement of an activity, like lifting a weight or doing one sit-up. It is highly advisable to do 8 to 12 repetitions per activity, which counts as one **set**. Start from one such set and to increase gradually [65].

According to “Physical Activity Guidelines for Americans”, the goal is:

At least 150 to 300 minutes of moderate-intensity physical activity a week, or an equivalent amount (75 to 150 minutes) of vigorous-intensity activity. They can also perform an equivalent amount of activity by doing both moderate and vigorous-intensity activity [66].

In a Brazilian study, it was inferred that the structured exercise training (consisting of aerobic exercise, resistance training or both) of more than 150 minutes per week is associated with greater HbA1c declines than that of 150 minutes or less per week [67]. However, adequate care should be taken in opting “More the Better”, in view of the anticipated adverse effects.

Involvement of the Physical Therapist in the Care of the Diabetic Patient: Expectations versus Reality

Harris-Hayes et al, while defining “Role of Physical Therapists in Fighting the Type 2 Diabetes Epidemic”, proposed that the physical therapist should intervene in three important ways and play a central role in the multidisciplinary health care team:

1. Provide guidance on safe and rewarding physical activity participation for patients who have or are at risk for diabetes.
2. Regularly assessing risk factors for diabetes and diabetes-related complications that modify traditional

musculoskeletal exercise prescription.

3. Advocate regular physical activity as a key component of the treatment of chronic diseases in all patient interactions. Harris-Hayes et al, further expect that modifiable risk factors such as physical inactivity, obesity, and hypertension can be directly addressed by physical therapists, by assisting the patient in developing and implementing programs to increase physical activity [29]. “The 2018 Physical Activity Guidelines for Americans” has also advocated that the “Physical therapists should advocate for regular physical activity as a key component of the treatment of chronic diseases in all patient interactions” [29].

To accomplish the proposed task, it is imperative that the physical therapists are accepted as a part of the multidisciplinary team and they should be the front-line providers in diabetes prevention and management. This could be an expectation but unfortunately not reality.

Here is a thought-provoking example. There is a study on 52,667 patients, identified from the Centricity Electronic Medical Records Database United States, during the period of December 13, 1995, to June 30, 2007, referred for physical therapy. Although majority of them were referred for a musculoskeletal-related condition, approximately 80% of the total study population had diabetes, pre-diabetes, or risk factors associated with diabetes. Ideally, physical therapist-led intervention, including guidance on safe physical activity, should have been a key component in the above scenario, only 2% of referrals to outpatient physical therapy were for diabetes as the primary health condition to be treated [68].

How could expectations be met when there is such a disparity between Expectation and Reality!

## DISCUSSION

*“Physical activity can replace many drugs, but no drug can ever replace physical activity”.*

Ibn Sina (980-1037AD): Author of the First Textbook of Medicine on Earth

According to “ADA’s Standards of Care in Diabetes—2025”, both the physical activity and medication management are crucial for effective blood sugar control and preventing complications in those with T2DM. Physical activity is, undoubtedly, a powerful adjunct to medications in management of T2DM. It can improve drug efficacy, reduce medications needed, and can lead to better overall health outcomes [69,70,71]. It plays a critical role in enhancing

pancreatic  $\beta$ -cell function, which is vital for insulin secretion and glucose homeostasis. Different forms of exercise— aerobic, resistance, and high-intensity interval training (HIIT)—exert their effects through a combination of molecular signaling pathways, myokines/exerkines, and epigenetic modifications [72]. In a Danish four-armed randomized trial, adding an exercise intervention to diet-induced weight loss improved glucose-stimulated beta-cell function in people with newly diagnosed T2DM (<7 years) in an exercise dose-dependent manner [73].

There are different types, or classes, of medications that work in different ways to exhibit anti-hyperglycemic effect. Some options are taken orally while others are injectable. Some of the commonly used classes of non-insulin medications include:

- Metformin
- Dipeptidyl peptidase 4 (DPP-4) inhibitors
- Glucagon-like peptide 1 (GLP-1) and dual GLP-1/gastric inhibitory peptide (GIP) receptor agonists
- Sodium-glucose cotransporter 2 (SGLT2) inhibitors
- Sulfonylureas
- Thiazolidinediones (TZDs)

Many of these medications are safe to use during physical activity, but some require caution or adjustments. Metformin is generally considered safe although the rare risk of lactic acidosis does exist. Insulin and sulfonylureas may require careful monitoring to prevent hypoglycemia during prolonged and strenuous physical activity. SGLT2 inhibitors (e.g., empagliflozin, dapagliflozin etc) reduce glucose reabsorption in the kidneys, cause glycosuria and control diabetes in a fashion independent of pancreas. Physical activity is generally safe with this group of drugs. However, there is a small risk of dehydration or ketoacidosis, especially if physical activity is quite intense or prolonged. GLP-1 receptor agonists (e.g., semaglutide, liraglutide etc) help control diabetes with increased insulin and decreased glucagon secretion from pancreas, decrease appetite and increase satiety. Physical activity is usually safe with these and can amplify their positive effects on weight loss and glucose control with minimal risk of hypoglycemia [74-79].

Whereas many effective anti-hyperglycemic medications are available, those with clinically meaningful effect on weight management should be prioritized to achieve both glycemic and weight management goals. Such agents include glucagon-like peptide 1 (GLP-1) receptor agonists (RAs) and

a dual glucose- dependent insulinotropic polypeptide (GIP) and GLP-1 RA (tirzepatide) [69,70].

One of the major causes of sub-optimal control of T2DM is the patient's inadequate adherence to therapeutic regime. Adherence has been defined, by WHO, as *"the extent to which a person's behavior taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider"* [80]. It would be appropriate to phrase it "Therapeutic Adherence", instead of 'Medication Adherence', as the former covers both pharmacological and non-pharmacological interventions.

Therapeutic non-adherence in diabetics is a serious clinical problem worldwide. A meta- analysis of 569 studies of medication adherence revealed an average non-adherence rate of 25% [81]. In a study, conducted by Siddiqui et al in Pakistan, the adherence rate to medication alone was 42% while to medication plus lifestyle recommendations 27% [82]. It is of interest to refer to an identical study by Khattab et al in Jordan where the medication adherence rate was 91.9%. However, 81.4% did not follow the diabetic meal plans while 67.9% did not participate in physical exercise program [83].

It would not be out of context to refer to the cost considerations for medications -taking behaviors. The cost of diabetes medications and devices is an ongoing barrier to achieving glycemic goals. Based on a US National Survey, conducted in 2021, 15.8% of those with insulin-treated T2DM reported rationing (i.e., skipping, taking less, and/or delaying) their insulin to save money [84].

There is well proven evidence that the right dose physical activity, in addition to its preventive and rehabilitative role and a safe adjunct to pharmacotherapy, contributes significantly to optimizing glycemic control and production of positive health outcomes. Unfortunately, older adults with diabetes may not be able to get optimal benefit from the physical therapy program. It could be due to a combination of factors, including physical limitations (age-related declines, comorbidities, functional impairments), psychological (fear of new injuries or worsening of already existing ones, low self-efficacy), lack of social support (inadequate motivation, sub-optimal family buck-up), medical challenges (fear of hypoglycemia, cardiac attack, musculoskeletal injury). Identification of these barriers during patient assessment may be important in order to adopt appropriate management strategies which could help to counteract their effects and improve treatment outcome. Addressing such barriers is of paramount importance for encouraging older adults with



diabetes to become more physically active. Individualized exercise programs, providing support groups, and health education sessions on diabetes management would certainly overcome these barriers and promote a more active lifestyle.

#### The Flame of Hope

The Flame of Hope is an eternal flame that honours Sir Frederick Banting's discovery of insulin, as well as all those who have been affected by diabetes located in London, Ontario, Canada. Simultaneously, it serves as a reminder that insulin controls diabetes but does not cure it; ultimately, it stands for the hope that a cure will soon be found. The Flame of Hope was kindled before 4,000 spectators by Her Majesty Queen Elizabeth the Queen Mother on July 7, 1989. The Flame will only be extinguished when a cure for diabetes is developed. The team responsible for finding the cure will be flown in to do so.

#### CONCLUSION

*"Diabetes is not curable. It's sustainable".*

#### Alvin Leung

Engagements in physical activity have been found to play a pivotal role in the management of T2DM, in addition to preventing or delaying the onset of full-blown clinical picture in pre-diabetics. Right-dose physical exercise should be prescribed to older adult diabetics as part of management of glycemic control and overall, well-being. Recommendations need to be tailored to meet the specific needs of the individual.

Given that the older adults are among the most sedentary segment of society, they should be motivated to decrease the total amount of daily sedentary time and to break up sitting time with frequent bouts of activity. The fitting closing sentence is that **"managing diabetes requires significant self-discipline"**.

#### AUTHORS' CONTRIBUTION

All the authors made substantial contributions to the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article, revising it critically for important intellectual content, and final approval of the version to be submitted.

#### ETHICAL APPROVAL

The authors declare that the conducted research is not related to either human or animals use.

#### FUNDING STATEMENT

The authors declare that they did not receive any financial

support, from any quarter, for the research, authorship, and/or publication of this paper.

#### DUALITY OF INTEREST

All the authors declare that there is no duality of interest related to the present study.

#### ACKNOWLEDGEMENT

The authors are highly grateful to Dr. Murad Ahmad Khan for his suggestions to improve the quality of the manuscript, throughout the conduct of the study.

#### REFERENCES

1. GBD Compare. (2024). Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington.
2. Institute for Health Metrics and Evaluation (IHME). (2024). GBD Foresight Visualization. Seattle, WA: IHME, University of Washington. Available at: <https://vizhub.healthdata.org/gbd-foresight>
3. IDF-Diabetes Atlas. (2025). 11th edition. Available at: [https://diabetesatlas.org/media/uploads/sites/3/2025/04/IDF\\_Atlas\\_11th\\_Edition\\_2025.pdf](https://diabetesatlas.org/media/uploads/sites/3/2025/04/IDF_Atlas_11th_Edition_2025.pdf)
4. Kirkman MS, Briscoe VJ, Clark N, Florez H, Haas LB, Halter JB, et al. (2012). Diabetes in older adults. *Diabetes Care*. 35(12):2650-2664.
5. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. (2014). Diabetes: a 21st century challenge. *Lancet Diabetes Endocrinol*. 2(1):56-64.
6. Novak V, Zhao P, Manor B, Sejdic E, Alsop D, Abduljalil A, et al. (2011). Adhesion molecules, altered vasoreactivity, and brain atrophy in type 2 diabetes. *Diabetes Care*. 34(11):2438-2441.
7. Reijmer YD, van den Berg E, de Bresser J, Kessels RP, Kappelle LJ, Algra A, Biessels GJ; Utrecht Diabetic Encephalopathy Study Group. (2011). Accelerated cognitive decline in patients with type 2 diabetes: MRI correlates and risk factors. *Diabetes Metab Res Rev*. 27(2):195-202.
8. Anderson DN. (2001). Treating depression in old age: the reasons to be positive. *Age Ageing*. 30(1):13-17.
9. Cheng G, Huang C, Deng H, Wang H. (2012). Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. *Intern Med J*. 42(5):484-491.

10. Ford ES, Li C, Sattar N. (2008). Metabolic syndrome and incident diabetes: current state of the evidence. *Diabetes Care*. 31(9):1898-1904.
11. CDC-Physical Activity. Available at: <https://www.cdc.gov/physical-activity/php/about/index.html>
12. WHO— Physical activity. Available at: <https://www.who.int/health-topics/physical-activity>
13. Chudyk A, Petrella RJ. (2011). Effects of exercise on cardiovascular risk factors in type 2 diabetes: a meta-analysis. *Diabetes Care*. 34(5):1228-1237.
14. Blair SN. (2009). Physical inactivity: the biggest public health problem of the 21st century. *Br J Sports Med*. 43(1):1-2.
15. Hamilton MT, Hamilton DG, Zderic TW. (2014). Sedentary behavior as a mediator of type 2 diabetes. *Med Sport Sci*. 60:11-26.
16. Thorp AA, Kingwell BA, Sethi P, Hammond L, Owen N, Dunstan DW. (2014). Alternating bouts of sitting and standing attenuate postprandial glucose responses. *Med Sci Sports Exerc*. 46(11):2053-2061.
17. Dempsey PC, Owen N, Biddle SJ, Dunstan DW. (2014). Managing sedentary behavior to reduce the risk of diabetes and cardiovascular disease. *Curr Diab Rep*. 14(9):522.
18. Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS, et al. (2015). Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med*. 162(2):123-132.
19. Piette JD, Kerr EA. (2006). The impact of comorbid chronic conditions on diabetes care. *Diabetes Care*. 29(3):725-731.
20. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, et al. (2014). Changes in diabetes-related complications in the United States, 1990-2010. *N Engl J Med*. 370(16):1514-1523.
21. Deshpande AD, Harris-Hayes M, Schootman M. (2008). Epidemiology of diabetes and diabetes-related complications. *Phys Ther*. 88(11):1254-1264.
22. Stewart KJ. (2004). Role of exercise training on cardiovascular disease in persons who have type 2 diabetes and hypertension. *Cardiol Clin*. 22(4):569-586.
23. Grossman E, Messerli FH, Goldbourt U. (2000). High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal? *Arch Intern Med*. 160(16):2447-2452.
24. Park SS, Perez Perez JL, Perez Gandara B, Agudelo CW, Rodriguez Ortega R, Ahmed H, et al. (2022). Mechanisms Linking COPD to Type 1 and 2 Diabetes Mellitus: Is There a Relationship between Diabetes and COPD? *Medicina (Kaunas)*. 58(8):1030.
25. Paterson DH, Warburton DE. (2010). Physical activity and functional limitations in older adults: a systematic review related to Canada's Physical Activity Guidelines. *Int J Behav Nutr Phys Act*. 7:38.
26. WHO. Ageing and health. Available at: <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>
27. Shah KM, Clark BR, McGill JB, Mueller MJ. (2015). Upper extremity impairments, pain and disability in patients with diabetes mellitus. *Physiotherapy*. 101(2):147-154.
28. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. (2001). Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 56(3):M146-M156.
29. Harris-Hayes M, Schootman M, Schootman JC, Hastings MK. (2020). The Role of Physical Therapists in Fighting the Type 2 Diabetes Epidemic. *J Orthop Sports Phys Ther*. 50(1):5-16.
30. ADA-definition of pre-diabetics by American Diabetes Association. Available at: <https://www.google.com/search?q=definition+of+pre-diabetics+by+ADA&ie=UTF-8&oe=UTF-8&hl=en-us&client=safari>
31. Colberg SR, Sigal RJ, Fernhall B, Regensteiner JG, Blissmer BJ, Rubin RR, et al. (2010). Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care*. 33(12):e147-e167.
32. Jeon CY, Lokken RP, Hu FB, van Dam RM. (2007). Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care*. 30(3):744-752.
33. Yang W, Wu Y, Chen Y, Chen S, Gao X, Wu S, Sun L. (2024). Different levels of physical activity and risk of developing type 2 diabetes among adults with prediabetes: a population-based cohort study. *Nutr J*. 23(1):107.

34. Jadhav RA, Hazari A, Monterio A, Kumar S, Maiya AG. (2017). Effect of Physical Activity Intervention in Prediabetes: A Systematic Review With Meta-analysis. *J Phys Act Health*. 14(9):745-755.
35. Kirwan JP, Sacks J, Nieuwoudt S. (2017). The essential role of exercise in the management of type 2 diabetes. *Cleve Clin J Med*. 84(7 Suppl 1):S15-S21.
36. Daly RM. (2017). Exercise and nutritional approaches to prevent frail bones, falls and fractures: an update. *Climacteric*. 20(2):119-124.
37. Gabriel BM, Zierath JR. (2017). The Limits of Exercise Physiology: From Performance to Health. *Cell Metab*. 25(5):1000-1011.
38. Healy GN, Wijndaele K, Dunstan DW, Shaw JE, Salmon J, Zimmet PZ, et al. (2008). Objectively measured sedentary time, physical activity, and metabolic risk: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab). *Diabetes Care*. 31(2):369-371.
39. Powell C, Herring MP, Dowd KP, Donnelly AE, Carson BP. (2018). The cross-sectional associations between objectively measured sedentary time and cardiometabolic health markers in adults - a systematic review with meta-analysis component. *Obes Rev*. 19(3):381-395.
40. Roh KH, Park HA. (2013). [A meta-analysis of the effect of walking exercise on lower limb muscle endurance, whole body endurance and upper body flexibility in elders]. *J Korean Acad Nurs*. 43(4):536-546.
41. Ferrucci L, Izmirlian G, Leveille S, Phillips CL, Corti MC, Brock DB, et al. (1999). Smoking, physical activity, and active life expectancy. *Am J Epidemiol*. 149(7):645-653.
42. Berk DR, Hubert HB, Fries JF. (2006). Associations of changes in exercise level with subsequent disability among seniors: a 16-year longitudinal study. *J Gerontol A Biol Sci Med Sci*. 61(1):97-102.
43. Savvakis I, Adamakidou T, Kleisiaris C. (2024). Physical-activity interventions to reduce fear of falling in frail and pre-frail older adults: a systematic review of randomized controlled trials. *Eur Geriatr Med*. 15(2):333-344.
44. Baptista LC, Machado-Rodrigues AM, Martins RA. (2017). Exercise but not metformin improves health-related quality of life and mood states in older adults with type 2 diabetes. *Eur J Sport Sci*. 17(6):794-804.
45. Diabetes Canada Clinical Practice Guidelines Expert Committee. (2018). Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. *Can J Diabetes*. 42(Suppl 1):S1-S325.
46. Ferrioli E, Pessanha FP, Marchesi JC. (2014). Diabetes and exercise in the elderly. *Med Sport Sci*. 60:122-129.
47. Boulé NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. (2003). Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. *Diabetologia*. 46(8):1071-1081.
48. Dunstan DW, Daly RM, Owen N, Jolley D, De Courten M, Shaw J, et al. (2002). High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care*. 25(10):1729-1736.
49. Encyclopedia Britannica-Tai Chi Chuan - Last Updated: Jan 24, 2025.
50. Harvard Medical School. Harvard Medical Publishing -Health Benefits of Tai Chi-Last Updated: May 24, 2022.
51. Hamasaki H. (2024). Effects of Tai Chi in diabetes patients: Insights from recent research. *World J Diabetes*. 15(1):1-10.
52. Gordon L, Morrison EY, McGrowder D, Penas YF, Zamoraz EM, Garwood D, et al. (2008). Effect of yoga and traditional physical exercise on hormones and percentage insulin binding receptor in patients with type 2 diabetes. *Am J Biochem Biotechnol*. 4:35-42.
53. Sahay BK. (1986). Yoga and diabetes. *J Assoc Physicians India*. 34(9):645-648.
54. Bhaskaracharyulu C, Raju PS, Madhavi S. (1986). The effect of yoga on lipoprotein profile in diabetics. *J Diabet Assoc India*. 26:120-122.
55. Kapur A. (1994). Yoga and diabetes. Bombay: Health Care Communications. Proceedings of novo nordisk diabetes update. pp. 159-167.
56. Sahay BK. (2007). Role of yoga in diabetes. *J Assoc Physicians India*. 55:121-126.
57. James TJ, Corbett J, Cummings M, Allard S, Shute JK, Belcher H, et al. (2023). The effect of repeated hot water immersion on insulin sensitivity, heat shock protein 70, and inflammation in individuals with type 2 diabetes mellitus. *Am J Physiol Endocrinol Metab*. 325(6):E755-E763.

58. Balducci S, Zanuso S, Nicolucci A, De Feo P, Cavallo S, Cardelli P, et al. (2010). Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: a randomized controlled trial: the Italian Diabetes and Exercise Study (IDES). *Arch Intern Med.* 170(20):1794-1803.
59. Gordon BA, Benson AC, Bird SR, Fraser SF. (2009). Resistance training improves metabolic health in type 2 diabetes: a systematic review. *Diabetes Res Clin Pract.* 83(2):157-175.
60. DoReg oAR, Gomes ALM, Veras RP, Junior AED, Alkimin MNR, et al. (2011). Blood Pressure after supervised physical exercise program in elderly women with hypertension. *Rev Bras Med Expor.* 17(5):1-5.
61. CEP. Clinical Exercise Physiology Association. Available at: [https://www.acsm-cepa.org/content.aspx?page\\_id=22&club\\_id=324409&module\\_id=291959](https://www.acsm-cepa.org/content.aspx?page_id=22&club_id=324409&module_id=291959)
62. Minuk HL, Vranic M, Marliss EB, Hanna AK, Albisser AM, Zinman B. (1981). Glucoregulatory and metabolic response to exercise in obese noninsulin-dependent diabetes. *Am J Physiol.* 240(5):E458-E464.
63. Marliss EB, Vranic M. (2002). Intense exercise has unique effects on both insulin release and its roles in glucoregulation: implications for diabetes. *Diabetes.* 51(Suppl 1):S271-S283.
64. Stapleton JM, Poirier MP, Flouris AD, Boulay P, Sigal RJ, Malcolm J, et al. (2015). Aging impairs heat loss, but when does it matter? *J Appl Physiol* (1985). 118(3):299-309
65. CDC. Older Adult Activity: An Overview. Physical Activity Basics. Available at: <https://www.cdc.gov/physical-activity-basics/guidelines/older-adults.html>
66. US Department of Health and Human Services. (2018). Physical Activity Guidelines for Americans. Washington DC. 2nd Edition.
67. Umpierre D, Ribeiro PA, Kramer CK, Leitão CB, Zucatti AT, Azevedo MJ, et al. (2011). Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. *JAMA.* 305(17):1790-1799.
68. Kirkness CS, Marcus RL, Lastayo PC, Asche CV, Fritz JM. (2008). Diabetes and associated risk factors in patients referred for physical therapy in a national primary care electronic medical record database. *Phys Ther.* 88(11):1408-1416.
69. American Diabetes Association Professional Practice Committee. (2025). 1. Improving Care and Promoting Health in Populations: Standards of Care in Diabetes-2025. *Diabetes Care.* 48(1 Suppl 1):S14-S26.
70. American Diabetes Association Professional Practice Committee. (2025). 3. Prevention or delay of diabetes and associated comorbidities: Standards of Care in Diabetes-2025. *Diabetes Care.* 48(Suppl 1):S50-S58.
71. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. (2016). Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care.* Nov;39(11):2065-2079.
72. Almeida FN, Proença AR, Chimin P, Marçal AC, Bessa-Lima F, Carvalho CR. (2012). Physical exercise and pancreatic islets: acute and chronic actions on insulin secretion. *Islets.* 4(4):296-301.
73. Legaard GE, Lyngbæk MPP, Almdal TP, Karstoft K, Bennetsen SL, Feineis CS, et al. (2023). Effects of different doses of exercise and diet-induced weight loss on beta-cell function in type 2 diabetes (DOSE-EX): a randomized clinical trial. *Nat Metab.* 5(5):880-895.
74. Di Murro E, Di Giuseppe G, Soldovieri L, Moffa S, Improta I, Capece U, et al. (2023). Physical Activity and Type 2 Diabetes: In Search of a Personalized Approach to Improving  $\beta$ -Cell Function. *Nutrients.* 15(19):4202.
75. Fujiwara Y, Eguchi S, Murayama H, Takahashi Y, Toda M, Imai K, et al. (2019). Relationship between diet/exercise and pharmacotherapy to enhance the GLP-1 levels in type 2 diabetes. *Endocrinol Diabetes Metab.* 2(3):e00068.
76. Apostolova N, Iannantuoni F, Gruevska A, Muntane J, Rocha M, Victor VM. (2020). Mechanisms of action of metformin in type 2 diabetes: Effects on mitochondria and leukocyte-endothelium interactions. *Redox Biol.* 34:101517.
77. Capuano A, Sportiello L, Maiorino MI, Rossi F, Giugliano D, Esposito K. (2013). Dipeptidyl peptidase-4 inhibitors in type 2 diabetes therapy--focus on alogliptin. *Drug Des Devel Ther.* 7:989-1001.
78. Pathak R, Bridgeman MB. (2010). Dipeptidyl Peptidase-4 (DPP-4) Inhibitors In the Management of Diabetes. *P T.* 35(9):509-513.



79. Gupta V, Kalra S. (2011). Choosing a gliptin. *Indian J Endocrinol Metab.* 15(4):298-308.
80. WHO. (2003). Adherence to long term therapies: Evidence for Action. World Health Organization, Geneva.
81. Hugtenburg JG, Timmers L, Elders PJ, Vervloet M, van Dijk L. (2013). Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. *Patient Prefer Adherence.* 7:675-682.
82. Siddiqui MH, Khan IA, Moyeen F, Chaudhary KA. (2019). Identifying Barriers to Therapeutic Adherence in Type 2-Diabetes: A Complex and Multidimensional Clinical Issue-*Asp Biomed Clin Case Rep.* 2(1):22-28.
83. Khattab M, Khader YS, Al-Khawaldeh A, Ajlouni K. (2010). Factors associated with poor glycemic control among patients with type 2 diabetes. *J Diabetes Complications.* 24(2):84-89.
84. Gaffney A, Himmelstein DU, Woolhandler S. (2022). Prevalence and Correlates of Patient Rationing of Insulin in the United States: A National Survey. *Ann Intern Med.* 175(11):1623-1626.