Review Article

Intervention for Prevention of Type 2 Diabetes Mellitus Among Prediabetes: A Review of the Literature

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Sopida Thipsawat, MNS[1]

Abstract

Introduction: In recent decades, the prevalence and incidence of type 2 diabetes mellitus (T2DM) have increased rapidly and represent a significant public health problem worldwide. Long-term T2DM is associated with microvascular complications such as retinopathy, nephropathy, and neuropathy. Prediabetes is a state of hyperglycemia with blood glucose levels higher than normal but lower than the diabetes threshold. Several studies have demonstrated the effectiveness of lifestyle interventions that resulted in a 40% to 70% reduction in diabetes mellitus in adults with prediabetes. These interventions focused on increased physical activity and dietary changes that were able to prevent or delay the onset of T2DM in prediabetes. However, most review studies focused on interventions to prevent T2DM in high-risk groups such as obesity. There was a limitation of reports related to prediabetes. Nevertheless, it remains a high-risk condition for the development of T2DM with a conversion rate of 5% to 10% per year. Therefore, the aim of this study was to review the current evidence on intervention studies aimed at reducing the incidence of type 2 diabetes in prediabetes.

Method: The researcher conducted a literature search of common online databases such as Medline, Google Scholar, and Cochrane Library between January 2011 and December 2021.

Result: The intervention for the prevention of T2DM in prediabetes consisted of a lifestyle intervention, a nutritional supplementation intervention, and a pharmacological intervention

Conclusion: Several studies suggest that T2DM in prediabetes can be prevented by lifestyle modification and pharmacological interventions, or a combined intervention. However, further interventions may be needed to confirm this.

Keywords

prediabetes, prevention, incidence, type 2 diabetes mellitus, impaired glucose tolerance, impaired fasting glucose

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Introduction

In recent decades, the prevalence and incidence of type 2 diabetes mellitus (T2DM) have increased rapidly and represent a significant public health problem worldwide. Moreover, it is estimated that the global prevalence of T2DM will increase from 382 million to 592 million by 2035 (Guariguata et al., 2014). Long-term T2DM is associated with microvascular complications such as retinopathy, nephropathy, and neuropathy (Beckman & Creager, 2016). Several studies have shown that lifestyle modification and drug treatment help prevent or delay the onset of T2DM in individuals at risk for developing T2DM, especially prediabetes (Choudhary et al., 2012; Schellenberg et al., 2013). In addition, prediabetes has an increased risk of cardiovascular disease and mortality (Rao Kondapally Seshasai et al., 2011).

"Prediabetes" is defined as a condition in which abnormal glucose levels do not meet the criteria for a diagnosis of diabetes mellitus but are too high to be considered normal (Selvin, 2016; Selvin et al., 2013). Currently, there are definitions of prediabetes issued by several organizations, including the American Diabetes Association (ADA) (Sims et al., 2021) and the World Health Organization (Tabák et al., 2012). These definitions cite several tests for hyperglycemia,

[1]Excellence Center of Community Health Promotion, School of Nursing, Walailak University, Nakhon Si Thammarat, Thailand

Corresponding Author:
Sopida Thipsawat, Excellence Center of Community Health Promotion, School of Nursing, Walailak University, Nakhon Si Thammarat, Thailand.
Email: alizabeththarn@outlook.com

namely impaired glucose tolerance (IGT), defined as after consumption of 75 g of oral glucose load based on a 2-h oral glucose tolerance test (OGTT), impaired fasting glucose (IFG), defined as fasting plasma glucose (FPG), and glycated hemoglobin (HbA1C). According to ADA, diagnostic criteria for prediabetes are defined as IGT 140 mg/dl (7.8 mmol/L) to 199 mg/dl (11.0 mmol/L) and/or IFG 100 mg/dl (5.6 mmol/L) to 125 mg/dl (6.9 mmol/L) and/or HbA1C 5.7% (39 mmol/mol) to 6.4% (47 mmol/mol) (Sims et al., 2021). WHO has defined prediabetes using two specific parameters: IFG 110 mg/dl (6.1 mmol/L) to 125 mg/dl (6.9 mmol/L) and/or IGT 140 mg/dl (7.8 mmol/L) to 199 mg/dl (11.0 mmol/L) (Tabák et al., 2012). They have the same cut-off value for IGT (140–199 mg/dl) but a different cut-off value for IFG (100–125 mg/dl). However, IFG defined with the FBG cut-point of 100 mg/dl has been shown to have a lower risk of developing T2DM than IFG based on the FBG cut-point of 110 mg/dl. Because of this lower risk profile and the much higher prevalence of IFG based on the 100 to 125 mg/dl range, the WHO proposed that the cut-point for IFG remain at 110 mg/dl (Echouffo-Tcheugui & Selvin, 2021). These are high-risk levels that convert to T2DM at a rate of 5% to 10% per year (Tabák et al., 2012). Long-term elevated glucose levels can damage endothelial cells, leading to microvascular complications (Grundy, 2012).

Several studies have established the efficacy of lifestyle interventions to reduce T2DM by 40% to 70% in adults with prediabetes. These interventions focused on increased physical activity and dietary changes (Bansal, 2015). The ADA reported that large randomized controlled trials of intensive lifestyle intervention reduced the risk of T2DM occurrence by 58% over a 3-year period (Sims et al., 2021). Three large lifestyle intervention studies for diabetes prevention have shown a 39% reduction in T2DM at 30 years in the Da Qing Diabetes Prevention Study Group (Gong et al., 2019), a 43% reduction at 7 years in the Finnish Diabetes Prevention Study Group by (ADA, 2022), a 34% reduction at 10 years in the Diabetes Prevention Program Research Group (ADA, 2022), and a 27% reduction at 15 years in the U.S. Diabetes Prevention Program Outcomes Study (Diabetes Prevention Program Research Group, 2015). In addition, some interventions suggested that dietary intervention by reducing total dietary fat and calories may prevent the development of T2DM in an overweight or obese body mass index (BMI) (ADA, 2022). Other intervention studies suggested that Mediterranean and low-carbohydrate diet plans may also be useful for preventing T2DM (Bloomfield et al., 2016; Correia, 2018; Salas-Salvadó et al., 2015). However, there is no ideal percentage of calories from protein, carbohydrate, and fat for all individuals to prevent T2DM. In addition, a physical activity intervention was conducted to reduce T2DM. Moderate-intensity physical activity of 150 min per week, such as brisk walking, has been shown to have a positive effect on people with prediabetes (ADA, 2022). It has been demonstrated to improve insulin sensitivity and decrease abdominal fat in children and young adults (Davis et al., 2012; Rynders et al., 2014) Although lifestyle interventions, nutritional interventions, and physical activity have been shown to reduce T2DM. For long-term treatment, however, they have been difficult (ADA, 2022). A number of pharmacological agents used to treat T2DM have been approved for diabetes prevention. Metformin therapy should be recommended for the prevention of T2DM in individuals with prediabetes (Aroda & Ratner, 2018), particularly those aged < 60 years and those with a BMI ≥ 35 kg/m^2. They have the strongest evidence base (ADA, 2022) and have demonstrated long-term safety as pharmacologic therapy for diabetes prevention (ADA, 2022). However, most review studies focused on interventions to prevent T2DM in high-risk groups such as obesity. There were few reports that addressed prediabetes. Nevertheless, it remains a high-risk condition for the development of T2DM with a conversion rate of 5% to 10% per year (Tabák et al., 2012). Therefore, the aim of this study was to review the current evidence on intervention studies aimed at reducing the incidence of T2DM in prediabetes.

Materials and Methods

The researcher performed a literature search of common online databases such as Medline, Google Scholar, and Cochrane Library. The databases were searched for English-language articles and human studies between January 2011 and December 2021. The researcher used the following search terms: "Intervention" "Program" "type 2 diabetes mellitus," "Prediabetes" "Protection" "Prevention" "impaired glucose tolerance," "impaired fasting blood glucose." Keywords were searched alone or in combination with other keywords. Other relevant publications were hand-searched in the reference lists for additional papers of interest. Studies were included if they (1) were full-text randomized controlled trials of an intervention to prevent or delay T2DM in prediabetes, (2) examined in the prediabetes group which parameter of blood glucose level (IGT, IFG, or HbA1C), (3) reported the incidence of T2DM after the intervention, and (4) were reported in English. Studies were excluded if they were conducted among T2DM patients. Our search yielded a total of 8 studies published to date (see Figure 1).

Results

Several interventions have been found to be associated with a reduction in the incidence of T2DM, including the following (Table 1).

Lifestyle Intervention: Physical Activity and Dietary Intervention

Several studies in the past have shown that the progression of T2DM can be prevented or delayed by lifestyle modification

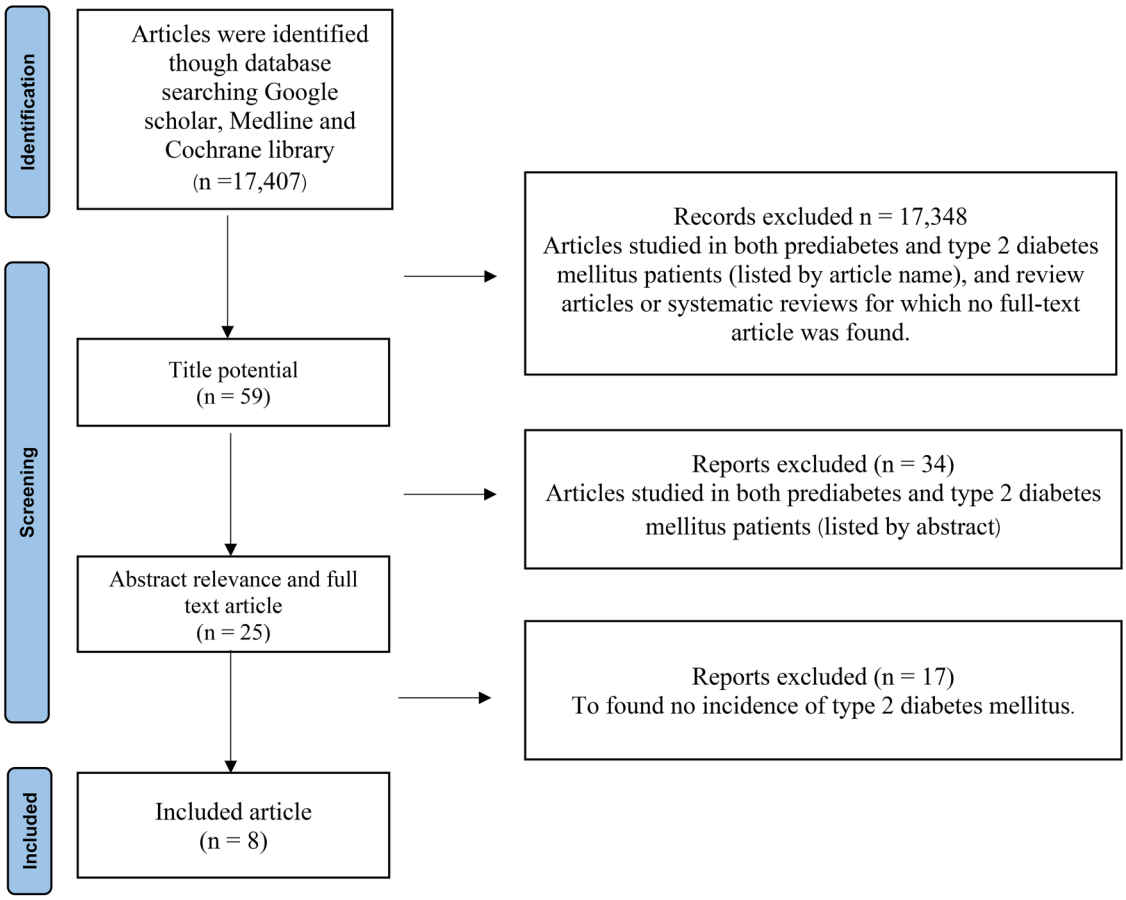

Figure 1. The literature search flow diagram.

or medication (Choudhary et al., 2012; Schellenberg et al., 2013). Most interventions to prevent T2DM have been aimed at reducing body weight in combination with a controlled diet and physical activity. One study reported that lifestyle changes could prevent T2DM in prediabetes with IFG levels. Subjects were divided into two groups. The intervention group received individualized instructions consisting of dietary measures and physical activity and was followed up nine times at baseline, 1, 3, 6, 12, 18, 24, 30, and 36 months. The control group received similar individualized instructions four times at baseline, 12, 24, and 36 months later. Results showed that the incidence of T2DM was 12.2% in the intervention group and 16.6% in the control group. In addition, the average weight reduced by 2.5 kg in the intervention group and 1.1 kg in the control group, and the difference between the groups was statistically significant ($P < .001$). They demonstrated that three years of individual lifestyle intervention can prevent T2DM in Japanese with prediabetes (Saito et al., 2011). In another randomized control trial, subjects were divided into two groups. The intervention group received a concentration program, such as diabetes education materials, group sessions with slides, videotapes, and a pamphlet, individual sessions to set goals for each subject, telephone or in-person follow-up with recommendations on dietary intake and physical activity. The control group received only one group session on healthy living and diabetes prevention at the beginning of the study. At the end of the study, the incidence of T2DM tended to be lower in the intervention group (14.8% vs. 8.2%, log-rank test: $P = .097$). This study suggests that lifestyle intervention may prevent or delay the development of T2DM in middle-aged Japanese with IGT (Sakane et al., 2011). Another study reported that in participants who received intensive lifestyle modification counseling (total fat intake of less than 30% of energy consumed, fiber intake of 15 g per 1.000 kcal, frequent consumption of whole grains, vegetables and fruits, low-fat dairy, meat products, and vegetable oils high in monounsaturated fatty acids) and engaged in at least 30 min of moderate exercise per day were diagnosed with less T2DM (2.5 cases per 1,000 person-months) than the control group (8.6 cases per 1,000 person-months). However, this study showed that participants who received intensive lifestyle modification counseling and 500 mg of metformin twice daily were also diagnosed with T2DM (2.3 cases per 1,000 person-months), less than in the control group (8.6 cases per 1,000 person-months).

Table 1. Intervention for Prevention of T2DM Among Prediabetes.

Author, Year of publication, reference	Study design	Sample	Sample size	Method	Intervention	Result
Saito et al., 2011	Randomized controlled trial	1. Subjects aged 30–60 years. 2. Prediabetes: FPG of 100–125 mg/dl.	640	Life style modification	Subjects were divided into two groups: 1. **Intervention group**: They received individualized lifestyle modification instructions and support from medical staff 9 times at baseline and at 1, 3, 6, 12, 18, 24, 30, and 36 months. 2. **Control group**: They received similar individual instructions four times at 12-month intervals during the same period at baseline and at 12, 24, and 36 months. **Instruction** • Individual equipment: all participants in both groups received pedometers and brochures with general information about diabetes and lifestyle changes. • Dietary intervention: limiting excessive intake of fat or carbohydrate by limiting fat intake to 20%–25% of total energy intake and carbohydrate intake to 55%–60% of total energy intake. Additional intake of dietary fiber, reasonable alcohol consumption (23 g/day) (if needed) • Physical activity: increase physical activity to 200 kcal/day by walking more, walking faster, or walking from 1 bus stop before destination. Nurses, nutritionists, physiotherapists and doctors were involved to help all subjects.	The incidence of T2DM was 12.2% in the intervention group and 16.6% in the control group.
DeFronzo et al., 2011	Randomized, double-blind, placebo-controlled study	1. Subjects aged 18 years of age or older. 2. Prediabetes: IGT defined as a 2 h glucose level of 140 to 199 mg/dl. FPG between 95 and 125 mg/dl.	602	Medicine	Comparison between the pioglitazone-treated group and the placebo group 1. **The intervention group**: Subjects received 30 mg of pioglitazone per day. One month after the study, the pioglitazone dose was increased to 45 mg/day. Participants were followed up at 2, 4, 6, 8, 10, and 12 months in the first year of the study and every 3 months thereafter. 2. **The control group**: Subjects received 30 mg placebo per day and were then followed up similarly to the intervention	The incidence rate for T2DM was 2.1% per year in the intervention group and 7.6% per year in the control group, and the hazard ratio for conversion to diabetes in the pioglitazone group was 0.28 (95% confidence interval, 0.16–0.49; $P < .001$).

(continued)

Table 1. Continued.

Author, Year of publication, reference	Study design	Sample	Sample size	Method	Intervention	Result
					group. The median follow-up time was 2.4 years.	
Sakane et al., 2011	Randomized controlled trial	1. Subjects aged 30–60 years. 2. Prediabetes: • FPG ≥ 5.6 mmol/L but < 7.0 mmol/L, • Casual plasma glucose (CPG) concentration ≥7.8 mmol/L but < 11.1 mmol/L when blood is drawn within 2 h after a meal, or CPG concentration ≥6.1 mmol/L but < 7.8 mmol/L when blood is drawn 2 h or more after meal. • IGT as indicated by a previous 75 g OGTT.	304	Lifestyle intervention: Physical activity and dietary intervention	**1. The intervention group**: Subjects received guide, curriculum, and educational materials "Change your lifestyle to prevent diabetes" • Group sessions were conducted using slides, videotapes, and a brochure, with each session lasting 2–3 h. An initial 6-month trial was scheduled. • Individual meetings were held to set a goal of walking moderately for at least 20 min each day. This goal was set every 6 months for 20–40 min during each of the 3 years. • Contact them by phone number or in person for the first year. • Dietary intake: Subjects were given some advice, such as to consume the correct amount of calories, to reduce the average percentage of energy from dietary fat to <25%, to limit daily alcohol consumption to <160 kcal, to eat three meals a day, and to avoid eating late at night. • Physical activity questionnaire: Aerobic exercise such as walking was recommended to the subjects. **2. The control group**: Subjects received only one group session on healthy lifestyle and prevention of diabetes at the beginning of the study. The trial was performed for 3 years by public health nurses.	Incidence at the end of the study tended to be lower in the intervention group (14.8% vs. 8.2%, log-rank test: $P = .097$).
Chuengsamarn et al., 2012	Randomized, double-blinded, placebo- controlled trial	1. Subjects aged ≥ 35 years. 2. Prediabetes: -FPG between 100 and 124 mg/dl. -OGGT plasma glucose at 2 h post glucose 140–199 mg/dl. ○ HbA1C 5.7%–6.4%.	240	Medicine	Comparison between the curcumin-treated group and the placebo group over 9 months. **1. The intervention group**: Subjects received three capsules of curcumin twice daily for 9 months continuously with blinded labels. **2. The control group**: Subjects received three capsules twice daily with a blinded	In the control group, 16.4% were diagnosed with T2DM while no T2DM was diagnosed in the intervention group.

(continued)

Table 1. Continued.

Author, Year of publication, reference	Study design	Sample	Sample size	Method	Intervention	Result
					placebo for a period of 9 months. All groups were followed up three times at 3, 6, and 9 months.	
Iqbal Hydrie et al., 2012	Randomized controlled trial	1. Subjects aged > 30 years. 2. Prediabetes: -2 h glucose levels between 140 and 199 mg/dl.	273	Lifestyle modification, Lifestyle modification + medicine	Subjects were divided into three groups: 1. **The control group**: Subjects received standard medical advice at the beginning of the study, such as general information about diet and exercise. 2. **Lifestyle modification group**: Subjects received intensive lifestyle change counseling, such as information on foods consumed (total fat intake of less than 30% of energy consumed, fiber intake of 15 g/1,000 kcal, frequent consumption of whole grains, vegetables and fruits, low-fat milk, meat products, and vegetable oils rich in monounsaturated fatty acids), and engaged in at least 30 min of moderate exercise per day. 3. **Lifestyle modification + medicine group**: Subjects received intensive lifestyle counseling similar to the **lifestyle modification** group in combination with metformin 500 mg twice daily. They were also examined by a physician every 2 months. Reinforcement and counseling were performed in all groups every 2 months. All groups were followed-up for 18 months.	A total of 47 subjects were diagnosed with T2DM (8.6 cases in the control group, 2.5 cases in the lifestyle modification group, and 2.3 cases per 1,000 person-months in the lifestyle modification and medication group)
Gaddam et al., 2015	Randomized controlled parallel study	1. Subjects aged 30–70 years. 2. Prediabetes: FPG 100–125 mg/dl Post 75 g oral glucose load, plasma glucose OGTT at 140–199 mg/dl	140	Dietary supplement intervention	1. **The intervention group:** Subjects were given 5 g of fenugreek powder twice daily along with 200 ml of water half an hour before meals. They took the same dose continuously until the end of the study. • Subjects received instructions on physical activity and diet (modification of usual lifestyle, adjustment of diet to weight and activity, weight reduction if necessary, and physical activity of at least 30 min/day for at least 5 days per week).	At the end of the study, the incidence rate of T2DM decreased significantly in the intervention group compared with the control group (chi-square = 13.4; $P < .01$)

(continued)

Table 1. Continued.

Author, Year of publication, reference	Study design	Sample	Sample size	Method	Intervention	Result
					• Subjects were counseled once every 3 months with recommendations on appropriate lifestyle and dietary habits. **2. The control group:** Subjects received similar instructions on physical activity, diet, and counseling as the intervention group. The trial was carried out for a period of 3 years	
Pittas et al., 2019	Randomized, double-blind, placebo-controlled clinical trial	1. Subjects aged > 30 years or older (25 years or older for American Indians, Alaska Natives, or Native Hawaiians or other Pacific Islanders) 2. Prediabetes: FPG 100–125 mg/dl. Plasma glucose level 2 h after a 75-g oral glucose load, 140–199 mg/dl. HbA1C 5.7%–6.4%**.**	2,423	Medicine	**1. The intervention group**: Subjects received a single tablet of vitamin D3 (cholecalciferol) in the form of soft gels containing 4,000 IU/day. • Subjects were asked not to take diabetes-specific or weight-loss medications during the study and to limit intake of vitamin D, including multivitamin supplements, outside the study. To limit intake of calcium supplements to 600 mg/day. • They received information about diabetes prevention through information sheets. • Participants were followed up at month 3, month 6, and twice per year thereafter through group meetings. **2. The control group**: Subjects received placebo drugs. • They received a similar recommendation as the intervention group. The trial was performed for 24 months.	T2DM occurred in 293 participants in the intervention group and 323 in the control group (9.39 and 10.66 events per 100 person-years, respectively) Vitamin D3 supplementation at a dose of 4,000 IU/day did not result in a significantly lower risk of T2DM than placebo.
Cea-Soriano et al., 2021	Randomized controlled trials	1. Subjects aged between 30 and 74 years. 2. Prediabetes: FPG 100–125 mg/dl (5.6–6.9 mmol/L) and/or HbA1c 5.7%–6.4% (39–47 mmol/mol)	1,184	Mediterranean diet	**1. The intervention group:** Subjects received diet information from simplified 20-item food frequency questionnaire**.** Adherence to the Mediterranean diet was estimated using an adaptation of the score used by Panagiotakos in the ATTICA study.	Incidence rate of T2DM with high versus low/medium adherence to Mediterranean diet was 2.9 versus 4.8 per 100 person-years

These studies suggest that lifestyle intervention has a major impact and is very effective in preventing T2DM in individuals with IGT (Iqbal Hydrie et al., 2012).

Dietary Supplement Intervention

Fenugreek. Fenugreek is a traditional plant with bitter taste and pungent odor. From some reports, fenugreek seeds have medicinal properties such as hypocholesterolemia, antibacterial, gastric stimulant, and antidiabetic effects (Wani & Kumar, 2018). Previous studies showed that fenugreek had hypoglycemic and hypolipidemic effects in animal and human models of T1DM and T2DM (Pandey et al., 2011). In a recent study, the effect of fenugreek on prediabetes was investigated by dividing subjects into two groups. The intervention group received 5 g of fenugreek powder twice daily along with 200 ml of water half an hour before meals in combination with instructions on physical activity and diet. The control group received similar instructions on physical activity, diet and guidance. At the end of the study, it was found that the incidence rate of T2DM significantly decreased in the intervention group compared with the control group (chi-square = 13.4; $P < .01$). In addition, FPG and postprandial plasma glucose (PPPG) were significantly reduced in the intervention group, while serum insulin significantly increased (Gaddam et al., 2015). The study suggests that 10 g of fenugreek per day in the prediabetes group was associated with less conversion to T2DM without adverse effects.

Mediterranean Diet. The Mediterranean diet is a nutritional model characterized by high consumption of olive oil, whole grain cereals, legumes, vegetables, and fruits, moderate consumption of wine, fish, and dairy products and low consumption of poultry, red meat, highly processed foods, refined grains, and sugars (Filippatos et al., 2016). In a randomized controlled trial, subjects were informed about their diet using a simplified 20-item food frequency questionnaire. Adherence to the Mediterranean diet was estimated using an adaptation of the score used by Panagiotakos in the ATTICA study. The Mediterranean diet was divided into three categories: low (0–53 points), medium (54–59 points), and high (60–80 points). Results have shown that incidence rate of T2DM with high versus low/medium adherence to Mediterranean diet was 2.9 versus 4.8 per 100 person-years (Cea-Soriano et al., 2021). Their results show the importance of focusing on the Mediterranean diet to prevent the T2DM.

Pharmacological Intervention

Curcumin. Curcumin is a famous spice in Asian cuisine and is widely considered to be beneficial for health (Marchiani et al., 2014). Curcumin extract from rhizomes has been shown to possess antidiabetic and anti-inflammatory properties (Shao et al., 2012). In one study, a randomized, double-blind, placebo-controlled trial was conducted in which all subjects were blinded and took three capsules of either curcumin or placebo twice daily for a period of 9 months. In the placebo group, 16.4% (11 subjects (9.5%) were diagnosed with T2DM at 6 months, 18 (15.5%) at 9 months, and 19 (16.4%) at 12 months, whereas no T2DM was diagnosed in the curcumin-treated group. HbA1C, FPG, and OGTT at 2 h were significantly lower in the curcumin-treated group compared with the placebo group at 3, 6, and 9 months ($P = .01$). In addition, the curcumin-treated group showed an increasing increase in homeostatic model score for β-cell function at all follow-ups. It was higher compared with the placebo group (61.58 vs. 48.72; $P = .01$). Blood levels of C-peptide were significantly lower in the curcumin-treated group than in the placebo group (1.7 vs. 2.17; $P = .05$). Homeostatic model assessment of insulin resistance values was lower in the curcumin-treated group than in the placebo group (3.22 vs. 4.04; $P = .001$), and adiponectin was higher in the curcumin-treated group than in the placebo group (22.46 vs. 18.45; $P = .05$). The study suggests that curcumin may be beneficial in prediabetes prone to develop T2DM and may improve B-cell functions, as indicated by increased Homeostatic Model Assessment of B-cell functions and decreased C-peptide. In addition, curcumin extract can be used for at least 9 months without serious adverse effect (Chuengsamarn et al., 2012).

Pioglitazone. Pioglitazone is an oral antihyperglycemic agent used for the treatment of T2DM. It is a highly selective agonist for the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR-gamma), which is found in tissues such as adipose tissue, skeletal muscle, and liver that are critical for insulin action (Satheeshkumar et al., 2014). One study reported that participants who received 30 mg of pioglitazone per day and were switched to 45 mg/day after 1 month of the study had an annual incidence rate of 2.1% for T2DM, compared with 7.6% for placebo participants. In addition, treatment with pioglitazone was associated with a significant decrease in fasting blood glucose levels compared with the placebo group (a decrease of 11.7 mg/dl vs. 8.1 mg/dl [0.7 mmol/L vs. 0.5 mmol/L], $P < .001$). During this study, the 2-h glucose level and HbA1C were significantly lower in the pioglitazone group than in the placebo group. However, pioglitazone was associated with significant weight gain and edema, which continue to be observed (DeFronzo et al., 2011).

Vitamin D Supplement. In the last decade, vitamin D supplementation has been reported as a potential intervention to reduce the risk of T2DM (Lu et al., 2018). One study found an association between low blood 25-hydroxyvitamin D levels and risk of T2DM. A linear trend analysis showed that each 10 nmol/L increase in 25-hydroxyvitamin D level was associated with a 4% lower risk of T2DM (95% CI 3–6; P for linear trend, .0001) (Song et al., 2013). In addition,

both impaired pancreatic beta-cell function and insulin resistance have been demonstrated with low blood 25-hydroxyvitamin D levels (Kayaniyil et al., 2011). In contrast, a randomized, double-blind, placebo-controlled clinical trial reported that vitamin D3 supplementation in a single dose of 4,000 IU/day did not result in a significantly lower risk of T2DM than placebo. Therefore, the use of vitamin D3 supplementation to prevent T2DM in the prediabetes group is still unclear (Pittas et al., 2019)

Discussion

The objective of this study was to review the current evidence on intervention trials aimed at reducing the incidence of T2DM in prediabetes. Our literature review found that lifestyle interventions, dietary supplement intervention, and pharmacologic interventions are effective in preventing or reducing the incidence of T2DM.

Lifestyle intervention: Our study found that lifestyle intervention consists of two main types: physical activity and dietary intervention. Three studies showed that these interventions can reduce the incidence of T2DM. One study reported that lifestyle changes could prevent T2DM in prediabetes with IFG levels. Results showed that the incidence of T2DM was 12.2% in the intervention group and 16.6% in the control group. They demonstrated that three years of individual lifestyle intervention can prevent T2DM in Japanese with prediabetes. These interventions focused on physical activity by increasing physical activity to 200 kcal/d, walking more, walking faster, or walking away from a bus stop before destination. In addition, they focused on dietary measures such as limiting excessive fat or carbohydrate intake by limiting fat intake to 20% to 25% of total energy intake and carbohydrate intake to 55% to 60% of total energy intake. Additional intake of dietary fiber, adequate alcohol consumption (23 g/day) (if needed) (Saito et al., 2011). However, both groups received similar intervention but different frequency of follow-up support. Therefore, follow-up support can help patients to be consistent with the intervention. In another randomized control trial, the intervention group received a concentration program with recommendations on diet and physical activity. At the end of the study, the incidence of T2DM tended to be lower in the intervention group (14.8% vs. 8.2%, log-rank test: $P = .097$) (Sakane et al., 2011). Another study reported that participants who received intensive lifestyle modification counseling and food consumption recommendations were diagnosed with less T2DM (2.5 cases per 1,000 person-months) than the control group (8.6 cases per 1,000 person-months). Thus, physical activity and dietary interventions are most effective in reducing T2DM in the prediabetes group.

Dietary supplement: In a recent study, the effect of fenugreek was investigated by taking 5 g of fenugreek powder twice daily before meals in combination with instructions on physical activity and diet. At the end of the study, it was found that the incidence rate of T2DM significantly decreased in the intervention group compared with the control group (chi-square = 13.4; $P < .01$). The study suggests that 10 g of fenugreek per day in the prediabetes group was associated with less conversion to T2DM without adverse effects (Gaddam et al., 2015). However, this study included a lifestyle intervention and a dietary intervention, so the results of this study may be influenced by those interventions. Thus, taking fenugreek may be a way to reduce the incidence of T2DM, but more studies are needed. In addition, consumption of a Mediterranean diet has been shown to have an incidence rate of T2DM of 2.9 versus 4.8 per 100 person-years with high versus low/medium adherence to the Mediterranean diet (Cea-Soriano et al., 2022). Future efforts should focus on the Mediterranean diet to prevent T2DM.

Pharmacological: Previous studies focused on curcumin, pioglitazone, vitamin D supplement.

Curcumin: In one study, a randomized was conducted in which all subjects were blinded and took three capsules of either curcumin or placebo twice daily for a period of 9 months. In the placebo group, 16.4% (11 subjects (9.5%) were diagnosed with T2DM at 6 months, 18 (15.5%) at 9 months, and 19 (16.4%) at 12 months, whereas no T2DM was diagnosed in the curcumin-treated group. The study suggests that curcumin may be beneficial in prediabetes prone to develop T2DM and may improve B-cell functions. In addition, curcumin extract can be used for at least 9 months without serious adverse effect (Chuengsamarn et al., 2012). However, few studies on curcumin were found, although this study is in favor of its effectiveness. But if you want to use it officially, more studies are needed.

Pioglitazone: One study reported that participants who received 30 mg of pioglitazone per day and were switched to 45 mg/day after 1 month of the study had an annual incidence rate of 2.1% for T2DM, compared with 7.6% for placebo participants (DeFronzo et al., 2011). In addition, the safety of pioglitazone has been studied and found that long-term pioglitazone treatment is safe and effective in patients with prediabetes or T2DM and nonalcoholic steatohepatitis (Cusi et al., 2016). Thus, pioglitazone is therefore an attractive alternative to be used in conjunction with prevention of T2DM in patients with prediabetes and in combination with other interventions.

Vitamin D supplementation: One study showed that each 10 nmol/L increase in 25-hydroxyvitamin D level was associated with a 4% lower risk of T2DM (95% CI 3–6; *P* for linear trend, .0001) (Song, 2013). In contrast, a randomized, double-blind, placebo-controlled clinical trial reported that vitamin D3 supplementation in a single dose of 4,000 IU/day did not result in a significantly lower risk of T2DM than placebo. Thus, the use of vitamin D3 supplementation to prevent T2DM in the prediabetes group is still unclear (Pittas et al., 2019) Therefore, the efficacy of vitamin D in reducing T2DM incidence is needed to resolve this contradiction and confirm its effectiveness in reducing T2DM in prediabetes patients.

Our literature review has limitations. First, the studies included in this literature review were small. In addition, each study used different definitions and criteria for diagnosing prediabetes. Further studies are needed to examine a larger number of studies using the same criteria for prediabetes studies. Because when other criteria are used, the onset rate for T2DM is different.

Implications for Practice

According to the ADA, it has been proposed to monitor the development of type 2 diabetes in the prediabetes group (Sims et al., 2021). Including prediabetes, approximately 5% to 10% develop into T2DM each year (Tabák et al., 2012). In addition, prediabetes has been associated with an increased risk of cardiovascular disease. One of the preventive measures against T2DM is a multidisciplinary team, especially nurses. They are one of the largest health care groups in the world, working at various levels of health care. Improving patient care and health services is one of the most important challenges for nurses. Registered nurses were performed in three general contexts consisting of episodic and preventive care, chronic disease management, and practice procedures (Smolowitz et al., 2015). Therefore, prevention of T2DM is one of the nurses' responsibilities. Our study will provide nurses with a guide for implementing and managing hyperglycemia in prediabetes patients. In the future, professional nurses will need to increase their knowledge of prediabetes and develop tools to rapidly screen and treat this patient population before T2DM develops. This includes a program of appropriate lifestyle intervention to lower blood glucose levels. It can also campaign through educational activities. Use of brochures or technology media helps to improve the knowledge of the population and recognize the importance of prevention of T2DM in this group of patients.

Conclusion

Nowadays, we are facing a worldwide epidemic of T2DM. Several studies suggest that T2DM in prediabetes can be prevented by lifestyle modification and pharmacological interventions. Various interventions have been performed, be it a physical intervention, a dietary intervention, a drug intervention, or a combined intervention. Most studies have shown that physical and dietary interventions have a strong impact on the prevention of T2DM. In addition, dietary interventions such as fenugreek, a traditional herb, also had benefits in reducing T2DM, consumption of Mediterranean diet to reduce T2DM incidence. Nevertheless, pharmacological intervention remains important in prediabetes. A clinical trial reported that pioglitazone reduced the incidence rate of T2DM by 2.1% and also significantly reduced fasting glucose levels. Curcumin improved B-cell function and had a positive effect on prediabetes. Finally, vitamin D3 has been demonstrated in some studies. In our study, vitamin D3 supplementation did not result in a significantly lower risk of T2DM. Further interventions may be needed to confirm this.

In summary, multidisciplinary health systems need to recognize "prediabetes" as a serious condition and use this condition to promote interventions for these patients. Further research is needed to find other interventions in combination with standard interventions that can be implemented in the initial phase and to sustain the program in prediabetes.

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ORCID iD

Sopida Thipsawat https://orcid.org/0000-0002-7666-7384

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