UNIVERSITÀ DEL PIEMONTE ORIENTALE

Department of Sustainable Development and Ecological Transition

Master's degree in Food, Health and Environment

MASTER'S DEGREE THESIS

Eating Behavior, Dietary Pattern and Lifestyle in Patients at The Onset of Type 2 Diabetes Mellitus.

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ABSTRACT

The high incidence of type 2 diabetes mellitus (T2DM) is a raising public health concern at the moment. While it is widely recognized that T2DM onset is heavily dependent on nutrition habits, the relationship with eating behavior and possible deviations from a healthy eating behavior have never been explored. This thesis aimed to explore the eating behavior, dietary patterns, and lifestyle in patients with a recent diagnosis of type 2 diabetes mellitus at their first diabetes visit at the Maggiore della Carità Hospital (Novara, Piedmont, Italy).

This research was conducted with the Department of Endocrinology at the "Maggiore Della Carità" University Hospital in Novara, focusing on the eating habits, lifestyle, and nutrition on38 patients. Three questionnaires that were provided through personal and direct interviews with the patients at their first diabetes visit or had been recently diagnosed with type 2 diabetes within three months. Eating habits and lifestyle were assessed through the use of the INRAN questionnaire, adherence to the Mediterranean Diet was estimated with the PREDIMED questionnaire, and the Dutch Eating Behavior Questionnaire for adults was used for analyzing eating behavior.

Our results showed that patients at their first diabetes visits have a not perfect adherence to the Mediterranean Diet. The intake of vegetables, fruits, fish and nuts was low, while the intake of meat, sweets and processed products was higher compared to recommended intakes. Dysfunctional eating behavior was present, with a restrictive behavior being the major factor influencing diet choices and being correlated with better outcomes. On the contrary emotional eating and external eating behavior were correlated with bad dietary and lifestyle habits.

Despite the Mediterranean Diet's success in managing T2DM, there's limited research on dietary habits at diabetes onset and the link between eating disorders and T2DM. Understanding these patterns could inform early prevention and better management, reducing T2DM complications by addressing both metabolic and psychological factors.

1. INTRODUCTION

Diabetes mellitusis a chronic disease caused by either the pancreas producing insufficient amounts of insulin or the body not being able to use the insulin that is generated, resulting in hyperglycemia (Chen L. et al., 2011). Untreated or poorly managed diabetes is thought to be the cause of 1.5 million deaths every year (World HealthOrganizationWHO,2016).According to the American Diabetes Association, diabetes may be diagnosed in a few different ways (Figure 1.1).

Table 2.2—Criteria for the diagnosis of diabetes
FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).
DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.

Figure1.1ADA 2023 criteria for diabetes diagnosis (El Sayed et al, 2023)

Diagnosis criteria should be done based on clinical objectivity, careful monitoring of typical symptoms and routine blood tests

The American Diabetes Association also proposed the following classifications of diabetes :

1)Type 1 diabetes, which is due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood (LADA)
2) Type 2 diabetes(due to a non-autoimmune progressive loss of adequate b-cell insulin secretion frequently on the background of insulin resistance and metabolic syndrome)
3) Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)
4) Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

In both type 1 and type 2 diabetes, various genetic and environmental factors can result in the progressive loss of b-cell mass and/or function that manifests clinically as hyperglycemia (El Sayed et al, 2023)
Diabetes mellitus can be recognized by several symptoms (Figure 1.2) such as thirst, polyuria, weight loss, and blurred vision (Rutter, G. A.et al.2020)

FIGURE 1.2 Main symptoms of Diabetes [2]

1.1Type 1 Diabetes Mellitus in Brief

Type 1 diabetes mellitus (T1DM), often called autoimmune diabetes, is a chronic condition that causes elevated blood sugar levels due to a lack of insulin caused by pancreatic β-cell loss. Though it usually shows up in childhood or adolescence, T1DM can also evolve in the adulthood, with the name of latent autoimmune diabetes of adulthood (LADA)

The basic mechanism is the loss of the insulin-producing pancreatic β-cells due to an autoimmune response. To identify whether diabetes is present, blood sugar levels or glycated hemoglobin (HbA1C) levels are measured. It is customary to utilize autoantibodies and/or declining C-peptide levels or absence to distinguish type 1 diabetes from type 2 diabetes.(Knip, et al.2016).

1.2 Type 2 Diabetes

Type 2 diabetes mellitus (T2DM), accounting for 90-95% of diabetes cases, was previously known as non-insulin-dependent diabetes, or adult-onset diabetes. This condition involves individuals with insulin resistance and usually relative, rather than absolute, insulin deficiency. Initially, and often throughout their lives, these individuals do not need insulin treatment to survive. The causes of T2DM are varied and not entirely understood, but it does not involve autoimmune destruction of beta cells. Most patients with this form of diabetes are obese, leading to some degree of insulin resistance, although non-obese patients may have increased body fat, particularly in the abdominal area. Type 2 diabetes often goes undiagnosed for years due to the gradual development of hyperglycemia and the lack of severe symptoms in the early stages. Despite normal or elevated insulin levels, the higher blood glucose levels indicate defective insulin secretion insufficient to compensate for insulin resistance. Insulin resistance may improve with weight reduction or pharmacological treatment but seldom returns to normal. The risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity, and it is more common in women with prior gestational diabetes, individuals with hypertension or dyslipidemia, and varies across different racial and ethnic groups. It is strongly associated with a genetic predisposition, more so than type 1 diabetes, although the genetics are complex and not fully defined, since family history and lifestyle choices play a significant impact in the development of type 2 diabetes (Hossain, P.et al.2007, El Sayed et al, 2023)

Insulin resistance at the cellular level results in a relative insulin deficiency and a reduction in insulin production by beta cells, which produce type 2 diabetes. The decrease in beta cell mass could be due to apoptosis, or cell death, if there is no compensatory regeneration. Many factors, such as the deposition of islet cell amyloid, the infiltration of pro-inflammatory cytokines, and prolonged exposure to elevated glucose and fatty acid concentrations (lipotoxicity and glucotoxicity), have been implicated in the damage to the beta cells. (Butler, A. E.et al.2003). Figure 1.3 shows some pathological mechamisms involved in T2DM

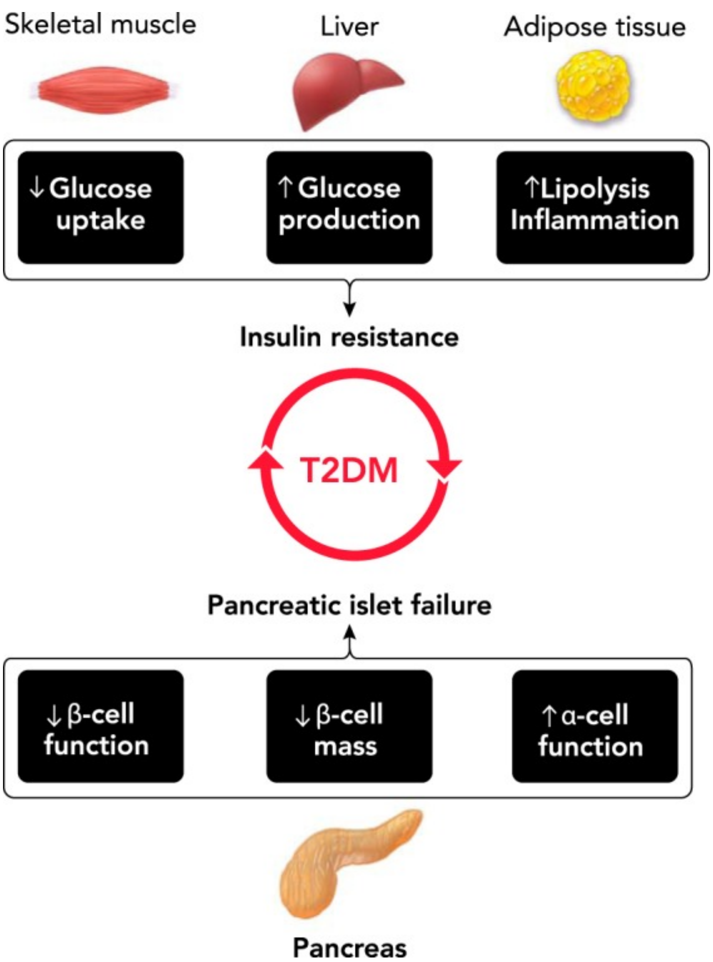

Figure 1.3 Main aspects involved in T2DM

The long-term effects of high blood sugar include heart disease, strokes, diabetic retinopathy, which can lead to blindness and renal failure, and insufficient blood supply in the limbs, which can lead to amputations. Due to an aging population, the illness is expected to afflict twice as many individuals in the next 10 years and is rapidly spreading to other regions of the world as a result of this trend. This will add to the already heavy workload for healthcare professionals, especially in developing countries. (Chatterjee, S.et al.2017)

Treatment options for the condition include lifestyle modifications, weight management, oral hypoglycemic medicines.

Treatment and prevention include dietary changes and exercise, like eating a balanced diet high in fruits, vegetables, and whole grains, staying physically active, and keeping a healthy weight, which can all help prevent or delay type 2 diabetes.

1.3 Gestational Diabetes

Gestational diabetes (GDM) is defined as any degree of abnormal glucose tolerance with first appearance or recognition during pregnancy. Pregnant women without a history of diabetes may develop gestational diabetes mellitus (GDM), characterized by elevated blood glucose levels. (Metzger, B. E.et al.2008)

Human placental lactogen and prolactin stimulate pancreatic B-cell hyperplasia during a normal pregnancy, raising insulin levels. Insulin resistance increases as a result of the placental release of diabetogenic hormones like progesterone, growth hormone, corticotropin-releasing hormone, and placental lactogen. (Omar, B. et al.2016).

Due to the rise in obesity and sedentary lifestyles, pregnancies complicated by glucose intolerance are becoming more common; these pregnancies are more common in ethnic communities and among those with lower incomes. Depending on the groups polled, current prevalence estimates range greatly, from 2% to 10% of all pregnancies. (Ferrara, A.etal.2012).

The usual hormonal balance is distorted during pregnancy, leading to decreased insulin production and insulin resistance. Insulin secretion rises throughout the first trimester, which promotes the buildup of fat. Later in pregnancy, lipolysis and insulin resistance appear. (Boney, C. M.et al.2005)

1.4 Insulin resistance and TDM

Insulin resistance IR is a metabolic condition marked by decreased sensitivity of target tissues to insulin, leading to several metabolic dysfunctions. These include the liver's inability to effectively inhibit gluconeogenesis, reduced glucose uptake in muscle and adipose tissues, and impaired regulation of lipolysis in adipose tissue by hormone-sensitive lipase (O'Neill et al., 2015).

Several factors contribute to insulin resistance, including obesity, physical inactivity, unhealthy diets, genetics, and aging. This condition prevents cells from efficiently absorbing glucose, resulting in elevated blood sugar levels (Samuel et al., 2016). In response, the pancreas increases insulin production, leading to hyperinsulinemia. Over time, this compensatory mechanism can increase the risk of cardiovascular disease, hypertension, and dyslipidemia (DeFronzo et al., 2010).

The causes of insulin resistance are still being widely studied, but the main hypotheses involve the presence of low-grade chronic inflammation and the production of free fatty acids exacerbated by the accumulation of fat in the liver and visceral tissue, which triggers the immune system (Choe et al., 2016; McLaughlin et al., 2014; Wensveen et al., 2015). The main mechanism explaining this association has been described by Jung et al. (2016), who suggested that the accumulation of visceral fat stores affects insulin metabolism by releasing free fatty acids. Elevated levels of free fatty acids can induce hepatic insulin resistance, particularly by enhancing gluconeogenesis. Diabetes and increased VLDL production are independent consequences of insulin resistance, leading to an overproduction of triglycerides and low levels of HDL (Ginsberg et al., 2005).

Inflammation and oxidative stress significantly contribute to the progression of insulin resistance. Elevated levels of reactive oxygen and nitrogen species (RONS) associated with obesity trigger inflammatory pathways that promote insulin resistance. Chronic low-grade systemic inflammation and oxidative stress in adipose tissue further exacerbate insulin resistance. Factors like hyperglycemia, persistent inflammation, and postprandial reactive oxygen species (ROS) production contribute to oxidative stress in obesity, leading to lipid peroxidation and declining antioxidant levels. Pancreatic β-cells, which have low antioxidant enzyme production, are particularly vulnerable to RONS damage (Hotamisligil et al., 2006; Shoelson et al., 2006).

Hyperglycemia develops when β-cells can no longer compensate for peripheral insulin resistance. Factors such as free fatty acids, hyperglycemia, and cytokines contribute to β-cell decompensation.

Additionally, improper coupling of insulin secretion and β-cell glucose metabolism exacerbates this decompensation (DeFronzo et al., 2009). In the early stages of insulin resistance, a compensatory response occurs, marked by an increase in pancreatic β-cells and enhanced insulin production to maintain normoglycemia. Over time, however, β-cells become insufficient, leading to a loss of mass and function, hyperglycemia, and the onset of type 2 diabetes mellitus (T2DM) (Dankner et al., 2009).

Insulin resistance is central to the development of metabolic syndrome, which includes obesity, hypertension, hypertriglyceridemia, and reduced HDL cholesterol. This syndrome significantly increases the risk of T2DM and cardiovascular diseases due to abdominal fat accumulation, elevated blood pressure, and dyslipidemia (DeFronzo et al., 2010). Obesity is closely linked to insulin resistance, particularly in peripheral tissues such as the liver, adipose tissue, and skeletal muscle. Peripheral insulin resistance increases insulin demand, leading to pancreatic β-cell adaptation and hyperinsulinemia, which exacerbates the metabolic dysregulations associated with obesity and T2DM (Eckel et al., 2005). The metabolic dysregulations associated with obesity and T2DM are further exacerbated by the peripheral insulin resistance-induced increase in insulin demand.

1.4Causes of Type 2 Diabetes Mellitus

The causes of diabetes mellitus are not fully known. It is now generally acknowledged that a combination of modificable and non modificable variables contribute to the development of diabetes mellitus. (Olokoba, A. B.et al.2012).

As previously said, two maininterrelated mechanisms are mostly responsible for type 2 diabetes: insulin resistance and insulin deficiency. Insulin-resistant cells develop in the liver, fat, and muscle tissues, contributing to an higher request of insulin. On the other hand too little insulin is produced by the pancreas to maintain blood sugar levels within a healthy range: when the balance between insulin demand and production is disrupted, blood sugar remains elevated in the bloodstream, leading to the glycation of haemoglobin. (Samuel et al. 2016; McCarthy, M. I. et al.2010).

T2DM is a result of a complex interaction of genetic, environmental, and metabolic risk factors, but whatever is responsible of an increase in insulin resistance or a decrease in insulin production might be associated with a higher T2DM risk.Like other chronic diseases, among the non modifiable factors, age and genetic predisposition are the two major causes, while among modifiable factors we have obesity,physical inactivity, diet, smoke, stress, drugsor other pollutants (Figure 1.4). The risk of developing type 2 diabetes mellitus is also higher in women with a history of gestational diabetes than in their offspring. In general, inappropriate lifestyle accounts for more than 50% of T2DM cases, and this is confirmed by the raise of T2DM prevalence in the latest years, mainly associated with obesity.Other pathological conditions may be related with T2DM, such as the polycystic ovary syndrome (PCOS), which is often characterized by hyperinsulinemia, a risk factor for developing T2DM (Kahn, S. E.et al. 2014).

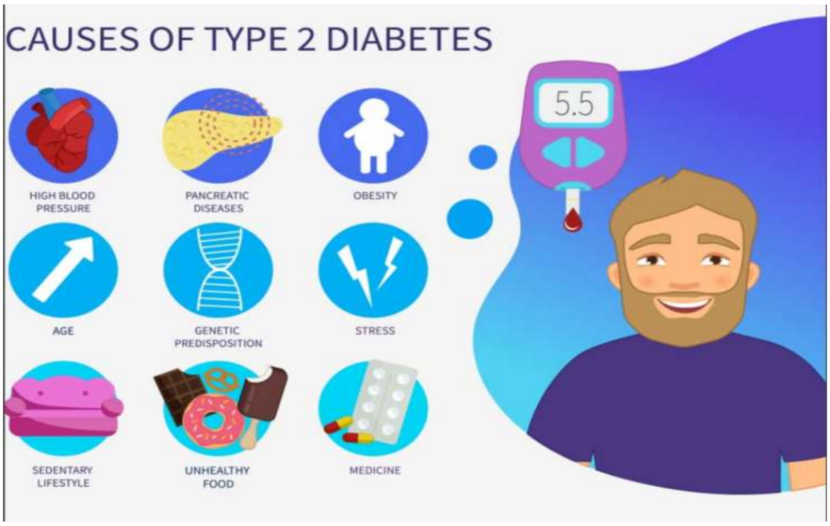

Figure 1.4: The causes of type 2 Diabetes Mellitus

Genetic Factor

The interaction between genetic and environmental factors in the development of type 2 diabetes mellitus (T2DM) is complex. Genome-wide association studies (GWAS) have identified over 100 loci associated with an increased risk of T2DM, including genetic polymorphisms in genes such as TCF7L2, WFS1, and INS. These genetic variations can influence the body's insulin production and glucose regulation mechanisms, contributing to the susceptibility to T2DM.

The impact of traditional risk factors like body mass index (BMI) and family history on the risk of T2DM is modified by an individual's genetic predisposition to the disease. This underscores the importance of genetic risk assessment in early diagnosis and preventive measures. Despite the identification of numerous loci, the genetic variants discovered so far only partially explain the heritability of T2DM. This indicates the necessity for further research to identify additional causative variants and understand their functional roles. This ongoing research is expected to lead to new discoveries that will enhance our understanding of the genetic basis of T2DM and improve strategies for its prevention and treatment.(Liu Y,et al.2022)

Ethnicity Factor

It seems that ethnicity may also influence an individual's chance of developing diabetes, suggesting that environmental factors are not the sole factors influencing the course of the disease. For instance, South African Indians have a significantly greater incidence of type II diabetes (8.9%) than Black South Africans (4.2%). Variations in the frequency of type II diabetes among individuals from various ethnic backgrounds across Asia have also been reported. Within the same population, Malays had a higher prevalence of type II diabetes (11.3%) than Aborigines (4.4%). Once more, research indicates that ethnicity may raise the risk of diabetes mellitus in addition to other factors. (Mbanya, J. C. N.et al.2010).

Gender Factor

Men and women tend to have similar rates of type II diabetes (T2D), yet there are significant geographical disparities and variations in risk factors.The International Diabetes Federation (IDF) reports that worldwide, males are a little more likely than women to have diabetes. Diabetes affected 9.8% of men and 9.2% of women worldwide in 2021.According to specific research, women may have a significantly greater frequency of T2D in particular areas or groups. For example, women are more common in several low- and middle-income nations because of things like increased obesity rates and various socioeconomic circumstances that impact healthcare availability.There are distinct risk factors for T2D development in men and women. MoreoverThere are distinct risk factors for T2D development in men and women. At a lower body mass index (BMI) than women, males are more likely to acquire type 2 diabetes (T2D). On the other hand, obesity is more common in women, which is a major risk factor for type 2 diabetes. (Kalyani RR,et al.2014)

Location (Urban vs Rural)

The impact of residency on the prevalence of diabetes mellitus has been demonstrated by numerous studies on the incidence of diabetes. The age-adjusted prevalence of diabetes mellitus was substantially higher in the urban population (12% for males and 14% for women) than in the rural population (7% for men and 7.7% for women), according to a recent study done in Saudi Arabia by Al-Nuaim. There has also been evidence of a difference in the prevalence of type II diabetes between rural and urban populations in Asia. A study looking at the incidence of diabetes mellitus among adult Malay residents of rural and urban areas discovered a very significant and noteworthy variation in the prevalence of type II diabetes between the two categories. Type II diabetes was more common in urban settings (8.2%) than in traditional hamlets (2.8%). (Mohammed, S. A.et al.2021).

Physical Activity

Regular exercise has been demonstrated to improve glucose tolerance and insulin sensitivity. Furthermore, new research has demonstrated that physical activity lowers the incidence of type II diabetes. A recent study conducted on an African American community in the United States found that diabetes prevalence rises with levels of obesity and inactivity. (Hawley, J. A.et al. 2008).

Nutritional Factors

Approximately 80% of people with type II diabetes are obese. Type II diabetes and obesity are strongly correlated. Foods high in calories, high in refined and simple sugars, high in saturated fats, and low in complex carbohydrates (fibers) may be a factor in the emergence of obesity and type II diabetes. (Malik, V. S.et al. 2015).

Stress Factor

The modern lifestyle's severe and protracted stress may also be linked to glucose intolerance, which could raise the risk of diabetes. Anxiety that is severe and protracted may activate adrenal hormones, especially glucocorticoids, which have been shown to induce glucose intolerance and contribute to the development of diabetes. (Aune, D.et al. 2013).

1.5 Treatment of Diabetes Mellitus

Diabetes mellitus (DM) is a progressive condition characterized by either insulin resistance or insulin insufficiency, leading to elevated blood glucose levels during fasting and after meals. This hyperglycemia can cause acute and chronic complications, including microvascular and macrovascular diseases, which can lead to blindness, kidney failure, heart disease, stroke, and amputations. Effective glycemic management is crucial for reducing the risk of these complications, and it often requires a dynamic approach to treatment as the disease progresses. Over the past five years, numerous novel pharmaceutical therapies have been developed to treat diabetes, complementing existing treatments focused on diet, exercise, and weight loss (American Diabetes Association, 2023).

1.5.1Insulin Therapy

Insulin therapy is essential for many individuals with type 2 diabetes, helping to maintain health and reduce the risk of complications. Daily insulin dosage varies among individuals and should be reviewed regularly. Adjustments should be based on blood glucose patterns and circadian rhythms, considering individual variations in dose distribution (Home et al., 2018).

1.5.2Non-Insulin Treatments

Metformin: is a cornerstone in the treatment of type 2 diabetes, primarily by lowering insulin resistance and improving vascular health. It is well-established for its benefits in glycemic management and reducing the risk of cardiovascular disease (CVD) (Foretz et al., 2014).

Sodium-Glucose Cotransporter 2 (SGLT2) Inhibitors:such as dapagliflozin, work by blocking glucose reabsorption in the kidney's proximal convoluted tubule, thereby increasing glucose excretion. They have beneficial effects on blood sugar levels, the kidneys, and the heart. However, they carry risks such as euglycemic diabetic ketoacidosis and can lead to genital and urinary infections (Marso et al., 2016).

GLP-1 Receptor Agonists: are incretin-based therapies that promote satiety, reduce postprandial glucagon, and improve insulin production. These treatments are advantageous for patients with T2DM, particularly those who are obese, as they effectively reduce cardiovascular events and enhance renal function (Mulvihill & Drucker, 2014).

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors :These medications enhance the effects of GLP-1 and glucose-dependent insulinotropic polypeptide (GIP), improving glycemic management and lowering A1C levels by 0.5-0.8%. They help manage glucose levels in T2DM patients without affecting cardiovascular risk (Scirica et al., 2013).

GLP-1: Functions and Implications

Production and Function GLP-1 is a 30-amino acid peptide hormone produced in L-type enteroendocrine cells of the intestine in response to food intake. It stimulates insulin secretion, inhibits glucagon release, and helps reduce postprandial glucose spikes by enhancing insulin release from pancreatic beta cells. GLP-1 is derived from the precursor molecule preproglucagon (Holst, 2007; Baggio & Drucker, 2007).

Metabolism and Inactivation :GLP-1 is rapidly metabolized and inactivated by the enzyme dipeptidyl peptidase IV (DPP-IV) before it can leave the intestine, limiting its bioavailability and functional duration (Drucker, 2006).

Role in Insulin Secretion and Glucose Homeostasis GLP-1 helps maintain glucose homeostasis and reduces insulin resistance by enhancing the absorption and utilization of glucose in peripheral tissues (Holst, 2007).

Impact on Obesity and Reactive Hypoglycemia Excessive GLP-1 production can cause postprandial reactive hypoglycemia due to overstimulation of insulin release. Reduced GLP-1 secretion may be linked to obesity, given its role in appetite and food intake regulation (Verdich et al., 2001).

Significance of GLP-1-Based Therapies GLP-1 receptor agonists not only enhance insulin production and reduce postprandial glucagon but also promote weight loss and lower cardiovascular risks in T2DM patients. They improve renal function and contribute to overall metabolic health (Mulvihill & Drucker, 2014).

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1.5.3The Medical Nutrion Theraphy (MNT) in T2D

Medical Nutrition Therapy (MNT) plays a crucial role in the management of type 2 diabetes (T2D) according to the Italian guidelines and its 2023 update, as well as the latest American Diabetes Association (ADA) guidelines. The Italian guidelines emphasize the efficacy of structured MNT, recommending a balanced Mediterranean diet and the use of low-glycemic index nutrientswhich has been linked to reductions in HbA1c levels and body weight, making it a beneficial choice for individuals with type 2 diabetes to improve glycemic control and body weight . Additionally, the ADA guidelines highlight the importance of MNT in T2D management, emphasizing the need for tailored dietary approaches to ethnic and family traditions, socioeconomic status, and educational background of the patient. Both sets of guidelines underscore the significance of MNT in achieving optimal outcomes for individuals with T2D, showcasing its role in enhancing overall health and well-being in patients with this metabolic condition.

Le raccomandazioni nutrizionali alla luce delle nuove linee guida italiane (e degli aggiornamenti) per il trattamento del diabete di tipo 2

The nutritional recommendations in light of Italy's new guidelines (and updates) for the treatment of type 2 diabetes

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ABSTRACT

***Background/aim**: this editorial is aimed at providing a reference for the medical nutritional therapy (MNT) in patients with type 2 diabetes, as recommended by the new Italian guidelines for the treatment of type 2 diabetes and its 2023-Update. **Methods and results**: the present paper revised the recently published Italian guidelines for the treatment of type 2 diabetes (outpatients) and its update, either in primary care or specialist referral. The guideline has been developed following the methods described in the Manual of the National Guideline System (http://www.snlg-iss.it) by a panel nominated by the Società Italiana di Diabetologia (SID) and Associazione Medici Diabetologi (AMD). Available literature on nutritional therapy showed a greater efficacy of: 1) MNT vs. unstructured nutritional advices, 2) Mediterranean diet vs. other dietary approaches, and the use of low- vs. high-glycemic index nutrients in reducing HbA1c and body weight.*

***Conclusions**: the present paper illustrates the recommendations of the Italian guidelines (and its 2023-update) for the treatment of type 2 diabetes on medical nutritional therapy. In synthesis, the panel suggests a structured medical therapy, balanced diet (Mediterranean), and the use of low-, rather than high-glycemic index nutrients due to the improvement of glycemic control and body weight.*

Figur 1.5.1The Medical Nutrion Theraphy (MNT) in T2D

Studies have shown that encouraging patients to adopt a Mediterranean diet and choose low-glycemic index foods can support long-term adherence to dietary changes and contribute to better health outcomes

However MNT is more effective than unstructured nutritional advice, and following a Mediterranean diet has shown better outcomes compared to other dietary approaches.
Thus the management of type 2 diabetes mellitus requires lifestyle changes and the development of self-management abilities. A change in eating habits is one of the biggest lifestyle adjustments and obstacles for diabetic people. For many years, diabetic patients were prescribed a standard carbohydrate portion-controlled diet; nevertheless, a variety of diets are currently being tested on this population. (Evert, A. B.et al.2014)

The Mediterranean Diet

Numerous diets have been suggested over time as being beneficial for people with diabetes, but no conclusive research has been done on them. The American Diabetes Association (ADA) recommends that nutritional therapy for adults with diabetes concentrate on encouraging healthy eating patterns based on essential nutrients that are varied, chosen, and integrated in the appropriate amount. The goal is to maintain a healthy weight and achieve optimal levels of blood pressure, cholesterol, and glycosylated hemoglobin (HbA1c), as well as blood pressure and lipid profile. The ADA stresses that in order to do this, cultural preferences,the places in which patients reside, their ability to obtain meals that are advised, and their openness to change should all be taken into account. Due to the pandemic of type 2 diabetes (T2D) in western nations, people with T2D are more vulnerable to other diseases like cancer and cardiovascular disease. Diet and lifestyle factors are linked to type 2 diabetes. Numerous cardiovascular risk factors, and diabetes specifically, are showing advantages to the standard Mediterranean diet. (Martínez-Gonzálezet al. 2017).

In this case, achieving appropriate diabetes management may depend on following a nutritious eating pattern like the traditional Mediterranean diet.

The phrase "Mediterranean diet" usually describes a nutritional pattern that is mostly plant-based. The Mediterranean diet, which emphasizes fruits, vegetables, nuts, grains, olive oil, grilled or steamed chicken and seafood, and a glass or two of red wine, is the diet that has historically been followed in Greece, Crete, southern France, and some regions of Italy. The conventional American diet is higher in butter and red meat than the Mediterranean diet. Because Mediterranean cuisine varies from country to country and region to region, there is no one Mediterranean diet. The Mediterranean diet, as it is commonly known, is characterized by a high intake of nutrient-dense foods such as fruits, vegetables, whole grains, legumes, nuts, and seeds; the essential source of monounsaturated fat is olive oil as shown in figure 1.5f below. The diet is low in red meat and animal products, high in omega-3 fatty acids foods like walnuts and fatty fish, and moderately (or rarely) high in wine. (Estruch, R.et al. 2018)

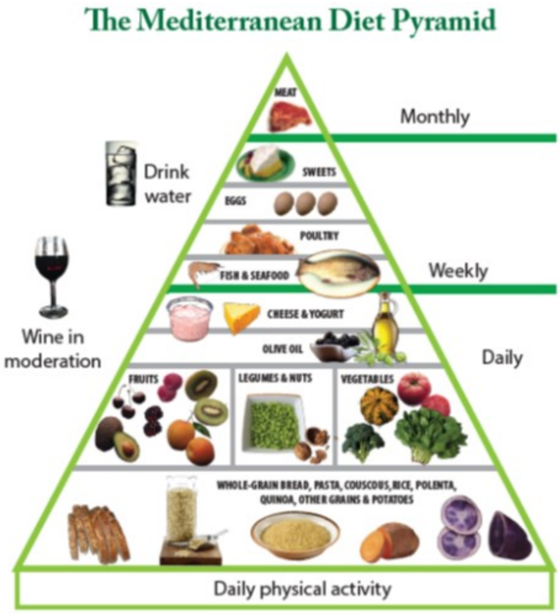


Figure 1.5.2 The Mediterranean Diet Pyramid.

Type 2 Diabetes and Mediterranean Diet

Researchers in medicine and science have been interested in the impact of the Mediterranean diet on general health for the past 80 years. Many studies carried out over the past 20 years have demonstrated the benefits of the Mediterranean lifestyle for those with type 2 diabetes mellitus or those at risk of getting the disease, corresponding with the ongoing global rise in type 2 diabetes incidence. Instead of being a set meal plan, the phrase "Mediterranean diet" refers to a way of life, with the dietary practices followed in traditional Mediterranean countries being linked to a lower risk of cardiovascular events and it demonstrated how the Mediterranean diet lowers the risk of metabolic syndrome and type 2 diabetes. (Salas-Salvadóet al. 2014).

Chronic hyperglycemia, which is brought on by decreased insulin secretion from pancreatic β-cells and/or insulin resistance (IR) in cells, is the main physio-pathological mechanism behind type 2 diabetes. This suggests either insufficient insulin production or an inability of insulin to get glucose into the cells, or both. In either case, the final effect is a disruption of the metabolism of proteins, fats, and carbohydrates, which ultimately causes macro- and microvascular issues. Apart from hereditary disorders, various other factors can impact the appropriate release of insulin by β-cells.

As was already mentioned, numerous researchers have discovered that the Mediterranean diet is beneficial for T2D. Reduced central obesity can lead to a decrease in chronic diseases like type 2 diabetes that are associated with obesity. In fact, for sustained weight loss, this diet is better than low-fatones.

Additionally, in comparison to other low-energy dietary strategies, it is linked to a significant improvement in insulin resistance in obese patients. Consequently, the benefits of T2D must be related to the makeup of the Mediterranean diet rather than the number of calories consumed. Furthermore, even while the individual effects of the various dietary components might not be significant enough to be noticed, their combined influence might be. (Kastorini, C. M.et al. 2011).

Low-carbohydrate and ketogenic diet

Lately, there has been a surge of curiosity regarding the effects of low-carb and ketogenic diets on weight reduction, diabetes management, and enhanced endurance and strength in sports. Because of the severe carbohydrate limitation, medical specialists continue to disagree with this diet. Dietary carbohydrate portion control consistently lowers elevated blood glucose since it is the main macronutrient that affects blood glucose levels. The food pyramid of this diet is shown below in the figure 1.5e. However severe carbohydrate restriction may raise the risk of hypoglycemia in diabetics, particularly in those receiving insulin and insulin secretagogues (sulfonylureas and incretin-based treatments). (Hallberg, S. J.et al. 2019). Few studies have demonstrated the benefits of very low-carb or ketogenic diets (less than 50 grams of carbohydrates per day); nevertheless, these diets are only appropriate for three to four months, depending on the individual. The ketogenic diet forces the body to use fat as its primary fuel source, simulating the metabolic effects of fasting. It is high in fat and low in carbohydrates. By simulating fasting, the ketogenic diet induces a condition of ketosis in the body's metabolism. Instead of a condition of glycolysis, where the majority of the body's energy comes from blood glucose, ketosis is a metabolic state where the majority of the body's energy comes from ketone bodies in the blood. Restricting carbohydrates causes the pancreas to release fatty acids from fat cells. These fatty acids are then absorbed by the liver, where they are transformed into ketones and released into the bloodstream. (Athinarayanan, S. J.et al.2019).

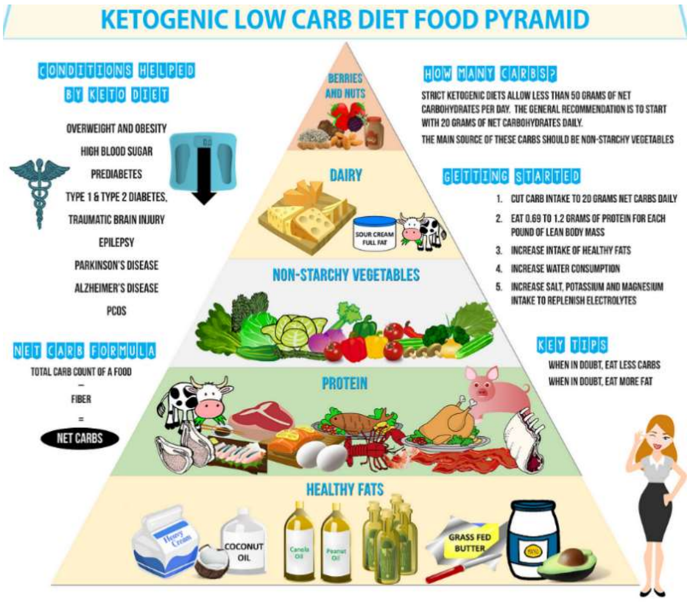


Figure 1.5.3 the low-carbohydrate ketogenic food pyramid.

Vegan Diet

People who follow plant-based and vegetarian diets have a comparatively low prevalence of diabetes, and clinical trials utilizing these diets have demonstrated advantages in cardiovascular health and glycemic management. A vegan diet excludes all animal products and meat, as well as any additional animal fats used in cooking as shown in below Figure 1.5e of the food pyramid of a vegan diet Numerous effects of a low-fat plant-based diet on nutrient intake and body composition may have an impact on insulin sensitivity. Firstly, because these diets are strong in fiber and low in fat, they usually result in reductions in calorie consumption and dietary energy density, which are not sufficiently offset by increased food intake. When meat is eliminated and replaced with foods high in carbohydrates, the intake of carbohydrates normally rises. (Kahleova, H.et al. 2017).

Figure 1.5.4 Food pyramid of the vegan diet.

1.5.4Eating Behavior

People develop consistent habits in their daily approach to food, adjusting the amount consumed based on the various functions it can have for them (Cavazza & Guidetti, 2020). Besides responding to physiological signals of hunger and satiety, eating can become a means to regulate emotions, control body weight, and respond to environmental stimuli. Three main eating styles are commonly considered: emotional eating, external eating, and restrictive eating.

Emotional eating refers to the tendency to consume food excessively in response to negative emotions, such as anxiety (Cavazza & Guidetti, 2020). This concept has roots in psychosomatic theory, which suggests that "emotional eaters" respond to stressful situations by increasing food intake, often oriented towards sweet and high-calorie foods, aiming to obtain comfort and a connection with positive memories. Studies have shown that individuals with emotional eating behaviors tend to consume fewer vegetables, which is associated with a higher risk of obesity and diabetes (Denney-Wilson et al., 2008).

External eating is the propensity to eat in response to environmental or social cues related to food (Cavazza & Guidetti, 2020). This definition is influenced by Schachter's externality theory, which posits that obesity is related to individual differences in responsiveness to external stimuli, thereby contributing to overeating and weight gain.

Restrictive eating refers to the tendency to consume less food than desired to lose or maintain a particular body weight (Dakanalis et al., 2012; Dakanalis et al., 2013; Van Strien & Oosterveld, 2008). This concept derives from Herman and Polivy's (1980) theory of restrained eating, suggesting that those who consistently restrict their food intake may periodically succumb to episodes of overeating, generating vulnerability to dietary disinhibition (Cavazza & Guidetti, 2020). These eating styles, therefore, represent dysfunctional ways of relating to food, with consequent disadvantages for individual health and well-being, often interconnected.

1.5.5 Eating Disorders Associated with Obesity

Eating behavior results from the integration of biological signals with psychological factors, leading to disorders with prolonged effects on health and psychosocial balance, as established by the latest revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Some of these disorders are closely associated with weight gain and obesity; they have variable courses and outcomes, from brief episodes that resolve spontaneously to lifelong pathologies that shorten and reduce the overall quality of life (American Psychiatric Association, 2013).

Psychosocial stress, partly due to the stigmatization of people with obesity, contributes to the development of disordered eating behaviors, leading these individuals to social isolation, reduced access to healthcare, and decreased physical activity—all factors that worsen obesity and create further barriers to changing dysfunctional behaviors. Stress-induced eating, as well as emotional eating, predisposes individuals to eat in response to negative emotions, mainly energy-dense and nutrient-poor foods (Dakanalis et al., 2023).

The alteration of appetite during a period of stress is a common experience and seems to play a fundamental role in determining the final eating behavior for each individual (Sambal et al., 2021). In reality, it is not only stress that determines a variation in eating behavior, but also other emotions, moods, or external situations can generate deviations from habitual eating behavior and hinder the control of thought and reason over food intake, allowing the unconscious component to prevail.

Several terms have been coined in recent years to describe some types of disturbed eating behaviors that are not officially pathological. Among those related to obesity are hyperphagia (constant excess food intake not considered a binge), selective cravings (sweets, chocolate, etc.), grazing (nibbling), and food addiction. Alongside these unspecified eating disorders, recognized conditions by the DSM-5 include:

- Binge Eating Disorder (BED): Characterized by recurrent episodes of excessive food intake in a compulsive manner, often accompanied by feelings of anxiety, shame, disgust, and guilt towards oneself.
- Bulimia Nervosa: With or without purging behaviors.
- Night Eating Syndrome (NES): Characterized by recurrent episodes of uncontrolled eating and a constant focus on food, manifesting with food intake during nighttime, typically after waking up or due to difficulty falling asleep, or excessive food consumption after the evening meal.
- Anorexia Nervosa: Characterized by an intense fear of gaining weight, a distorted body image, and severe caloric restriction leading to dangerously low body weight.

1.5.6 The Effectsof Eating Behavior on Diet, Obesity, Diabetes, And Body Composition

Eating habits significantly influence diet, body composition, obesity, and diabetes. Studies reveal that a range of physiological, psychological, environmental, and social variables impact eating patterns from childhood, shaping future food choices and health consequences (Bellisle et al., 2003). High-calorie foods and sweets have a substantial impact on fat accumulation and the development of diabetes. Consuming high amounts of these foods can lead to an increase in body fat and contribute to the onset of diabetes due to their effects on insulin sensitivity and metabolic processes (Bhardwaj et al., 2023).

Disinhibition, a psychological trait characterized by a lack of control over eating, has been positively correlated with a higher body mass index (BMI) and body fat percentage, contributing to obesity (Denney-Wilson et al., 2008). Moreover, fast food consumption and eating until full have been associated with a higher risk of being overweight, emphasizing the significance of mindful eating practices in managing weight and preventing disease (Denney-Wilson et al., 2008).

Physiological elements such as hunger, satiety, and satiation greatly influence human eating behavior. These factors determine the types and quantities of food consumed, affecting the overall quality of the diet and body composition. Persistent dietary restriction and disinhibition are psychological traits that significantly impact eating habits, potentially leading to obesity and associated health problems by encouraging overeating or poor dietary choices (Bellisle et al., 2003).

Environmental factors, including portion sizes and food-related cues, can affect eating habits regardless of hunger. Continuous exposure to food and large portion sizes can cause excessive consumption, impacting body weight and health. Socioeconomic factors such as income and educational attainment also influence food choices and consumption patterns. A higher risk of obesity is linked to lower income and education levels, highlighting the influence of socioeconomic inequality on diet-related health issues (Bellisle et al., 2003).

The capacity to choose health-promoting foods depends on various biological and physiological factors, including current life stage, past developmental experiences, and the food environment. A significant factor contributing to higher calorie intake and increased food consumption rates is eating speed. Reducing food consumption rates and calorie intake through methods like product reformulation can be facilitated by understanding the neuroscience of eating behavior. Chronic illness complications may exacerbate obesity, underscoring the need to research eating habits in relation to nutrition and well-being (Stover et al., 2023).

1.5.7 Cognitive Behavioral Therapy in Eating Disorders:

Cognitive Behavioral Therapy (CBT) is widely regarded as one of the most effective treatments for eating disorders, including bulimia nervosa, binge eating disorder, and anorexia nervosa. CBT focuses on addressing the maladaptive behaviors and cognitive distortions that contribute to disordered eating. These distortions often involve rigid dieting, binge eating, purging, poor self-esteem, and body dissatisfaction (Wilson et al., 2007).

The CBT approach to treating eating disorders involves several stages. The initial phase aims to engage the patient in treatment, enhance motivation, and provide education about the disorder and the rationale for the therapeutic techniques. This stage often includes establishing regular eating patterns and addressing the immediate behaviors associated with the disorder, such as binge eating and purging (Mitchell et al., 2008).

As treatment progresses, CBT focuses on identifying and challenging the negative thoughts and beliefs about food, weight, and body image that sustain the disorder. Techniques such as cognitive restructuring help patients to recognize and alter these dysfunctional thoughts. Behavioral strategies are also employed to encourage the adoption of healthier eating habits and coping mechanisms, thereby reducing the reliance on maladaptive behaviors (Thompson-Brenner et al., 2013).

One of the critical components of CBT for eating disorders is relapse prevention. This involves preparing the patient for potential challenges and setbacks by developing skills to manage stress and other triggers without resorting to disordered eating behaviors. This stage also includes creating a long-term plan to maintain progress and prevent relapse, ensuring that the patient can sustain healthy eating patterns and a positive self-image after the conclusion of therapy (Lock et al., 2013).

Research has demonstrated the efficacy of CBT in significantly reducing the symptoms of eating disorders and improving overall psychological well-being. For example, a meta-analysis by (Linardon et al. 2017) found that CBT was effective in treating a broad range of eating disorders, showing significant improvements in patients' eating behaviors and cognitive distortions. Additionally, CBT has been adapted to be more inclusive of various eating disorders, with tailored protocols that address specific needs and comorbid conditions, making it a versatile and comprehensive approach to treatment (Grilo & Mitchell, 2011). Other studies have also highlighted the benefits of CBT in terms of long-term recovery and relapse prevention (Wonderlich et al., 2014).

CBT's structured and systematic approach, combined with its focus on both behavior and cognition, makes it particularly well-suited for addressing the complex and multifaceted nature of eating disorders. By targeting the underlying psychological issues and providing practical strategies for behavior change, CBT offers a robust framework for helping individuals achieve long-term recovery from eating disorders (Fairburn et al., 2003; Cooper & Fairburn, 2008).

2. AIM OF THE THESIS

Type 2 diabetes mellitus (T2DM) and insulin resistance currently pose critical public health challenges, with a significant increase in cases both in Western and developing countries. This trend is associated with an increase in disabilities, social stigmatization, higher healthcare costs, and a reduction in both overall quality of life and life expectancy.

While the importance of genetic and metabolic predisposition, along with the interaction with the obesogenic environment, is recognized in the development of overweight and obesity, exploring this phenomenon requires a multidisciplinary perspective that spans physiology, psychology, and human behavior.

The analysis and identification of eating behaviors play a fundamental role in the in-depth understanding of individual variations in the tendency to overeat and the complex causes of overweight and obesity. Despite established knowledge about the eating habits of the population, significant gaps remain in understanding the eating habits related to the development of diabetes.

In this context, this thesis aims to directly analyze newly diagnosed T2DM patients, focusing on observing adherence to the Mediterranean Diet, lifestyle, eating habits, and eating behavior prior to diagnosis. This approach aims to provide a detailed analysis for a deeper understanding of the dietary factors related to the onset of T2DM, with the goal of contributing to defining more effective preventive strategies and interventions.

3. MATERIALS AND METHODS

3.1_Study Population

The study included new patients diagnosed with type 2 diabetes within the past three months following the European Association for the study of Diabetes (EASD) guidelines (glycaemia ≥ 126 mg/dL or Hba1c ≥ 6,5% in two separate measurements). Patients were selected by the SCDU Endocrinology Department at their firsts endocrinological visits.Patients that were in doubt for other types of diabetes (such as LADA) were further excluded from the analyses if the different diagnosis was confirmed through blood tests (antibodies and c-peptide) in the subsequent days. Permission was obtained from all participants prior to the interviews.

3.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

- Newly diagnosed with type 2 diabetes (within the past three months).
- First endocrinological visit.
- Consent to participate in the study and complete questionnaires.
- Age between 18 and 85 years

Exclusion Criteria:

- Previous diagnosis of diabetes for more than three months
- Inability to provide consent

- Any medical condition that prevented the participation in the study

3.3 Blood Tests

Blood tests were conducted prior to the visit autonomously by the patient and indicated by the family doctor or other specialists to undergo a diabetologic visit.

The exams were always including :

-Glycamemic profile. Glucose and Glycated hemoglobin (Hba1c) are fundamental for a correct diagnosis. Hba1cis a kind of hemoglobin (Hb) that has a chemical bond with a sugar. When present in the circulation, the majority of monosaccharides, such as glucose, galactose, and fructose, naturally (i.e., non-enzymatically) bind with hemoglobin.

An excessive amount of sugar in the bloodstream is indicated by the creation of the sugar-hemoglobin linkage, which can be a sign of diabetes or other high-concentration hormone illnesses. As already said, EASD and other international guidelines reached a consensus on the cutoffs (Figure4):

-Less than 5.7% means no diabetes.

-5.7% to 6.4% signals prediabetes.

-6.5% or higher usually indicatesdiabetes (of any kind).

A1C and Estimated Average Glucose Levels

	A1C Percentage	Estimated Average Glucose (EAG)	
In-range	< 5.7%	< 117 mg/dL	6.5 mmol/L
Prediabetes	5.7-6.4%	117-137 mg/dL	6.5-7.6 mmol/L
Diabetes	> 6.4%	> 137 mg/dL	> 7.6 mmol/L
Increased risk of complications	6.5%	140 mg/dL	7.8 mmol/L
	7.0%	154 mg/dL	8.6 mmol/L
	7.5%	169 mg/dL	9.4 mmol/L
	8.0%	183 mg/dL	10.1 mmol/L
	8.5%	197 mg/dL	10.9 mmol/L
	9.0%	212 mg/dL	11.8 mmol/L
	9.5%	226 mg/dL	12.6 mmol/L
	10%	240 mg/dL	13.4 mmol/L

Cleveland Clinic

Figure3.1.example of the glucose levels and theGlycated hemoglobin numbers.

- Kidney function: creatinine and microalbuminuria;
- Lipid profile: Total cholesterol, HDL, LDL and tryglicerides;
- Liver profile: Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Gamma-Glutamyl Transferase (GGT);

3.4 Nurse Visit (Anthropometry and Blood Pressure)

Anthropometry:

- Measuring Weight:

Patients were measured using a calibrated scale (sensitivity of 0.1 kg) and a stadiometer(*Wunder Sa.Bi. srl).* Weight was recorded after ensuring the patient remained still on the scale, wearing minimal clothing, and without shoes.

After the scale stabilized, nurses recorded the weight shown on it to obtain the most accurate measurement. For diabetic patients to manage their disease and to keep track of any changes that can have an effect on their health, it is imperative that their weight be regularly monitored.

Figure 3.2 .Example.Mechanical Height and Weight Scale Medical Personal Scale.

- Measuring Height:

  At the same time, after the weight measurement process, after asking the patients to take off their shoes, hats, and any heavy clothing or accessories, their height was also measured. They were instructed to look straight ahead while maintaining their heads in the Frankfort horizontal plane (a horizontal line that should run parallel to the floor from the ear canal to the lower edge of the eye socket).

- Measuring the waist circumference:

  A standard measuring tape and a level platform for the patient to stand on were required in order to take a diabetic patient's waist circumference measurement. The measurement of the waist circumference is made by measuring the circumference of the abdomen, taking into account both the superior iliac spines and the anterior abdominal wall's umbilical point.

Figure 3.3. Body Mass Index Meter.

During the measurement, we were making sure the patient was standing upright, with their feet together and their arms at their sides. The measurements were obtained at the conclusion of a typical exhale, with the measuring tape tight but without squeezing the skin. To guarantee accuracy, we have repeated the measurement two or three times. The final waist circumference figure is determined by averaging the measurements.

Figure.3.4The correct way to measurethe waist circumference

- Blood Pressure:

Blood pressure was measured using a device called a sphygmomanometer. which consists of an inflated cuff and a pressure gauge. In order to momentarily block the blood flow in the artery, the cuff is inflated and placed around the upper arm at heart level. Using a stethoscope over the arm artery, the nurse listens for blood flow noises while the cuff deflates. During the procedure, the nurse records the following two measurements: the diastolic pressure, which measures the pressure in between heartbeats, and the systolic pressure, which measures the pressure while the heart beats. Two numbers are used to record blood pressure: the top number is the systolic pressure, and the bottom number is the diastolic pressure. An example of this would be 120/80 mm Hg.Prior to collecting the blood pressure reading, we were making sure that the patients were in a comfortable posture with their backs supported and their feet flat on the floor.

Figure 3.5. BLOOD PRESSURE MONITOR

3.5 Medical Visit

During the medical visit, the doctor:

- Reviewed the patient's medical history;
- Conducted a physical examination;
- Discussed the results of the blood tests and anthropometricmeasurements and eventually declared a diabetes diagnosis;
- Provided medical advice and treatment plans for managing diabetes.

3.6. Questionnaires

The patients completed three questionnaires with the help of a nutritionist and students after the nursing visit. The questionnaires covered a comprehensive range of commonly consumed foods in Italy and their respective quantities. Special attention was given to framing the questions to focus on the period prior to the onset and diagnosis of type 2 diabetes. Three different questionnaires were administered to the patients:

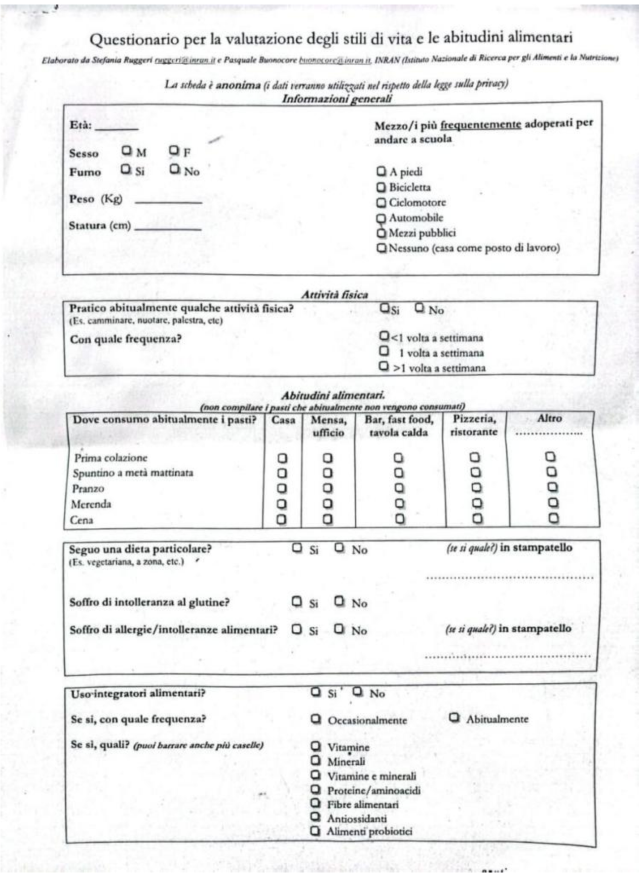
-INRAN questionnaire for eating habits and lifestyles.

-The PREDIMED.

-Dutch Eating Behavior Questionnaire.

3.6.1INRAN Questionnaire for Eating Habits and Lifestyles

The INRAN Questionnaire for Lifestyles and Eating Habits, developed by the National Food and Nutrition Research Institute (INRAN), is a valuable tool for thoroughly evaluating lifestyles and dietary habits in scientific research.



Questionario per la valutazione degli stili di vita e le abitudini alimentari

Elaborato da Stefania Ruggeri ruggeri@inran.it e Pasquale Buonocore buonocore@inran.it, INRAN (Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione)

La scheda è **anonima** *(i dati verranno utilizzati nel rispetto della legge sulla privacy)*

Informazioni generali

Età: ______

Sesso ☐ M ☐ F

Fumo ☐ Si ☐ No

Peso (Kg) __________

Statura (cm) __________

Mezzo/i più frequentemente adoperati per andare a scuola

☐ A piedi
☐ Bicicletta
☐ Ciclomotore
☐ Automobile
☐ Mezzi pubblici
☐ Nessuno (casa come posto di lavoro)

Attività fisica

Pratico abitualmente qualche attività fisica? ☐ Si ☐ No
(Es. camminare, nuotare, palestra, etc)

Con quale frequenza?
☐ <1 volta a settimana
☐ 1 volta a settimana
☐ >1 volta a settimana

Abitudini alimentari.
(non compilare i pasti che abitualmente non vengono consumati)

Dove consumo abitualmente i pasti?	Casa	Mensa, ufficio	Bar, fast food, tavola calda	Pizzeria, ristorante	Altro ....
Prima colazione	☐	☐	☐	☐	☐
Spuntino a metà mattinata	☐	☐	☐	☐	☐
Pranzo	☐	☐	☐	☐	☐
Merenda	☐	☐	☐	☐	☐
Cena	☐	☐	☐	☐	☐

Seguo una dieta particolare? ☐ Si ☐ No *(se si quale?)* **in stampatello** ....
(Es. vegetariana, a zona, etc.)

Soffro di intolleranza al glutine? ☐ Si ☐ No

Soffro di allergie/intolleranze alimentari? ☐ Si ☐ No *(se si quale?)* **in stampatello** ....

Uso integratori alimentari? ☐ Si ☐ No

Se si, con quale frequenza? ☐ Occasionalmente ☐ Abitualmente

Se si, quali? *(puoi barrare anche più caselle)*
☐ Vitamine
☐ Minerali
☐ Vitamine e minerali
☐ Proteine/aminoacidi
☐ Fibre alimentari
☐ Antiossidanti
☐ Alimenti probiotici

Figure3.6.The INRAN Questionnaire for Lifestyles and Eating Habits

The questionnaire is structured into four sections:
General Information: This section collects basic details about the participant.
Physical Activity: This section includes questions about how often and what types of physical activities the participant engages in.
Eating Habits: This section explores various aspects of eating habits, such as where pastries are consumed, the type of diet followed, and the use of dietary supplements.
Food Consumption Frequency: This section gathers detailed information about how often the participant consumes different basic food categories and the typical portion sizes. These categories include fruits and vegetables, cereals, protein-rich foods (like meat, fish, eggs, dairy products, and legumes), nuts, sweets, alcoholic beverages, and sugary drinks.
To sum up, the INRAN Questionnaire is marketed as an easy-to-use yet comprehensive instrument that enables researchers to carefully analyze eating patterns and furnish essential data for evaluating nutritional consequences. Promoting a healthy lifestyle is the goal.(Leclercq, C.et al. 2009)

Frequenze di consumo per gruppi di alimenti

Per ogni riga riempire una sola casella, indicando quante volte vengono consumati gli alimenti corrispondenti.

		Numero di volte				
	Con quale frequenza consumo:	Anno	Giorno	Settimana	Mese	Mai (barrare)
1	Cereali e derivati? Es: pasta, riso, pane, pizza, farro, orzo, etc.	☐	☐	☐	☐	☐
2	Prodotti a base di cereali? Es: cornflakes, biscotti, fette biscottate, cracker etc.	☐	☐	☐	☐	☐
3	Carni fresche?	☐	☐	☐	☐	☐
4	Carni trasformate? Es: prosciutto, salame, wurstel, etc.	☐	☐	☐	☐	☐
5	Pesce, e altri prodotti della pesca? Es: spigola, polpo, gamberi.	☐	☐	☐	☐	☐
6	Latte e yogurt?	☐	☐	☐	☐	☐
7	Prodotti lattiero caseari? Es: formaggi freschi e stagionati.	☐	☐	☐	☐	☐
8	Frutta fresca?	☐	☐	☐	☐	☐
9	Frutta secca? Es: noci, nocciole, mandorle.	☐	☐	☐	☐	☐
10	Ortaggi o Verdura? Es: lattuga, radicchio, indivia, spinaci, bietole, etc.	☐	☐	☐	☐	☐
11	Legumi? Es: fagioli, lenticchie, piselli, ceci	☐	☐	☐	☐	☐
12	Uova?	☐	☐	☐	☐	☐
13	Dolci? Es: torte, gelati, cioccolato, etc.	☐	☐	☐	☐	☐
14	Bevande gassate? Es: Coca cola, gassosa, aranciata, etc.	☐	☐	☐	☐	☐
15	Bevande alcoliche? Es: vino, birra, superalcolici, etc.	☐	☐	☐	☐	☐

Figure3.7.Questions from The INRAN Questionnaire for Lifestyles and Eating Habits.

3.6.2 The PREDIMED

PREDIMED questionnaire was initiatedand developed by a team of scientistsas part of the PREDIMED study which began in the early 2000s to evaluate the adherence to the Mediterranean Diet on the primary prevention of cardiovascular diseases..(Ros E&Martínez-González MA, et al.2014). it Includes 14 questions. Some of them deal with eating habits (e.g., favoring white meat over red or using olive oil as the main cooking fat source), while others address the frequency of food consumption (e.g., the frequency of weekly consumption of nuts or carbonated/sweetened drinks). Each item received a score of 0 or 1, with one point given for behaviors that align with the Mediterranean Diet, such as regularly consuming fruits and vegetables, preferring white meat, or using olive oil.(Martínez-González MA et. al 2012)

The questions involve the usage of olive oil, the intake of fruits, vegetables, red meat, animal fat, sugary beverages, red wine, legumes, fish, sweets, nuts, andmeals with classic tomato sauce, garlic, onion, or leeks sautéed in olive oil. The overall adherence to the Mediterranean diet was assessed using the PREDIMED final score, which varied from 0 to 14. A total score equal or below five represents poor adherence; six to nine is moderate; and ten or above is good adhesion.

1. Utilizza olio extravergine di oliva come principale condimento in cucina? **si 1 no 0**
2. Quanto olio utilizza (compreso l'olio usato per friggere , insalate, etc) **$\geq$4 cucchiaini=1**
3. Quante porzioni di verdura consuma al giorno? (1 porzione : 200 g) **$\geq$2 porzioni=1**
4. Quanti frutti (compresi i succhi di frutta naturali) consuma al giorno? **$\geq$3 porzioni=1**
5. Quante porzioni di carne rossa, hamburger, o di prodotti a base di carne (prosciutto, salsicce, ecc), consuma al giorno? (1 porzione: 100-150 g) **$<$1 porzioni=1**
6. Quante porzioni di burro, margarina o grassi animali consuma al giorno? (1 porzione: 12 g), **$<$1 porzioni=1**
7. Quante bevande zuccherate o gassate bevi al giorno? **$<$1 porzioni=1**
8. Quanto vino bevi alla settimana? **$\geq$7 bicchieri=1**
9. Quante porzioni di legumi consuma a settimana? (1 porzione: 150 g) **$\geq$3 porzioni=1**
10. Quante porzioni di pesce o frutti di mare consuma a settimana? (1 porzione 100-150 g di pesce o 4-5 unità o 200 g di frutti di mare) **$\geq$3 porzioni=1**
11. Quante volte alla settimana consuma dolci o pasticcini commerciali (non fatti in casa), come torte, biscotti , biscotti, o crema pasticcera? **$<$3 porzioni=1**
12. Quante porzioni di frutta secca (noci, arachidi), consuma a settimana? (1 porzione 30 g) **$\geq$3 porzioni=1**
13. Preferenzialmente consuma carni bianchi quali pollo, tacchino o coniglio al posto delle carni rosse quali vitello, maiale , hamburger o salsicce? **si 1 no 0**
14. Quante volte alla settimana consuma verdure, pasta, riso o altri piatti conditi con soffritto (salsa fatta con pomodoro e cipolla, porro, o aglio e cotto con olio d'oliva)? **$\geq$2 porzioni=1**

Figure 3.8. Questions from the PREDIMED questionnaire.

3.6.3Dutch Eating Behavior Questionnaire (DEBQ)

The DEBQ was developed by Van Strien in 1986. It is a widely used tool to assess eating behavior, focusing on emotional eating, restrained eating, and external eating styles. It has been translated into various languages, including Dutch, Turkish, and Romanian, to assess eating behaviors in different populations, such as university students, preadolescents, and adults.(Cebolla A&Barrada JR van Strien TOliver & Baños R.et al. 2014)

It is a self-assessment scale composed of 33 questions for assessing three eating behavior domains:

-The restrained subscale (10 questions),

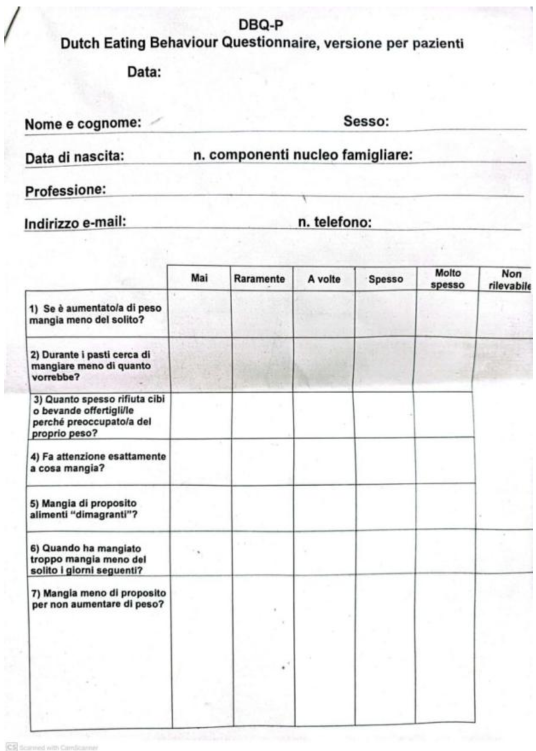
-The emotional eating subscale (13 questions),

-The external eating subscale (10 questions).

Restrained eating behavior is characterized by an ability to consciously limit food intake in order to control energy intake as well as the types of foods consumed, either to avoid weight gain or to encourage weight loss.

Emotional eating behavior: the tendency to overeat when experiencing negative mood states, such as loneliness, depression, or anxiety.

External eating behavior: the propensity to overeat in response to attractive meals.



DBQ-P

Dutch Eating Behaviour Questionnaire, versione per pazienti

Data:

Nome e cognome: Sesso:

Data di nascita: n. componenti nucleo famigliare:

Professione:

Indirizzo e-mail: n. telefono:

	Mai	Raramente	A volte	Spesso	Molto spesso	Non rilevabile
1) Se è aumentato/a di peso mangia meno del solito?						
2) Durante i pasti cerca di mangiare meno di quanto vorrebbe?						
3) Quanto spesso rifiuta cibi o bevande offertigli/le perché preoccupato/a del proprio peso?						
4) Fa attenzione esattamente a cosa mangia?						
5) Mangia di proposito alimenti "dimagranti"?						
6) Quando ha mangiato troppo mangia meno del solito i giorni seguenti?						
7) Mangia meno di proposito per non aumentare di peso?						

Figure 3.9 Questions from the Dutch Eating Behavior Questionnaire (DEBQ).

On a 5-point rating scale ranging from "never" to "very often," participants were asked to assess how frequently they felt the need to eat in reaction to certain emotions.
The thirty-three questions on the DEBQ fall into three different categories: containment (questions like "Do you purposefully eat less to not get heavier?"), external feeding (questions like "Do you eat more than usual when you see others eating?"), and emotional nutrition (questions like "Do you want to eat when you're irritated?"). With the exception of one question that has a reverse score ("Do you know how to eat delicious food?"), the response format is based on a Likert scale from 1 (never) to 5 (very often). The average scores of all the questions in a single category are used to get the overall score for each category.

The questionnaires provided comprehensive data on patients' eating behaviors, lifestyles, and adherence to dietary guidelines, which were essential for understanding the relationship between eating habits, eating behavior and the management of type 2 diabetes.(Cebolla A&Barrada JR van Strien TOliver & Baños R.et al. 2014)

4.**Statistical Analysis**

All analyses were performed using the Statistical Package for the Social Sciences, Version 26.0 (SPSS Inc., Chicago, IL, USA). Quantitative variables were presented as means and standard deviations (irrespectively on normal or non normal distribution) or absolute and percentage frequencies for categorical variables. For certain variables, differences between sexes were calculated using a Mann-Whitney U test. Dietary pattern analysis was evaluated through Principal component analysis (PCA). PCA replaces a set of possibly correlating food groups with a new set of comprehensive indexes (principal components) that are uncorrelated and retain as much of the foods' variance as possible. The sum of all factors for each individual always equals to 0. Linear correlations were calculated using Spearman's correlation. Statistical significance was set at $p<0.05$.

5. RESULTS

All questionnaires were answered by 45 patients enrolled at the Unit of Endocrinology between January and May 2024. After the medical confirmation,38 final patients were included in our analysis since 3 patients were found to be affected by LADA and 4 other patients were having diabetes due to other causes (pancreasectomy or steroid therapy). The 38 patients, consisting of 24 men and 14 women, had an age of 65.0 years (SD=10.6) (Table 1). Body weight was 83.9 ± 17.5 kg and BMI was 29.9 ± 5.3kg/m^2, indicating that most of the participants were overweight (42.1%) or had obesity (44.7%)(Table 1; Figure.4.1).

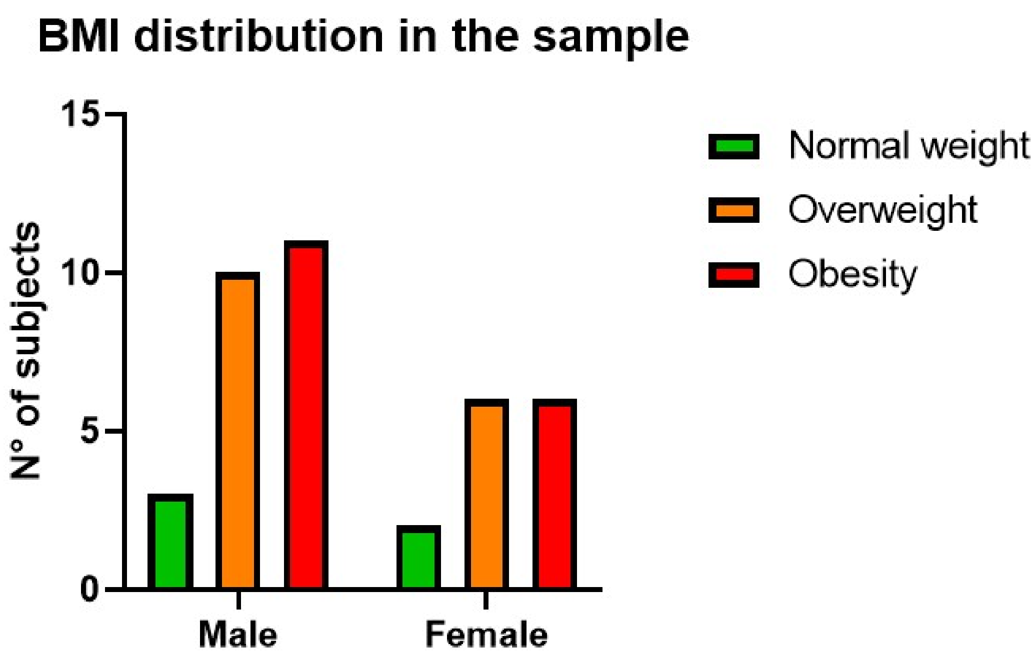


Figure 4.1. Distribution of BMI among the sample

TABLE 1. General characteristics, diseases and anthropometry

PARAMETERS	Mean	Standard deviation
Age (years)	65.03	10.60
Weight (kg)	83.95	17.54
Height (cm)	167.26	9.37
BMI (kg/m^2)	29.91	5.32
Waist circumference (cm)	107.16	14.55
N° of family members	2.74	1.54
	Frequency	
Gender	Female = 14(36.8%) Male = 24(63.2%)	
Smoke	NO = 31(81.6%) YES = 7(18.4%)	
Diabetes familiarity	NO =12(31.6%) YES =26(68.4%)	
Arterial hypertension	NO = 7 (18.4%) YES = 31 (81.6%)	
Total comorbidities (n°)	0 = 1 (2.6%) 1= 8 (21.0%) 2 = 5 (13.1%) 3 = 16 (42.1 %) 4 or more = 8 (21.0%)	

88% of patients had a waist circumference higher than the reference parameters.The waist circumference was 107.2 ± 14.5 cm.

More than 40% of patients were showing the presence of at least 3 comorbidities, with dyslipidemia, arterial hypertension and heart disease as the most common. The prevalence of arterial hypertension was 81.6%.

4.1 Biochemical parameters

The mean HbA1c value of 8.4% and mean fasting blood glucose level of 177.22 mg/dL were far from perfect glycaemic control, as expected. GGT (57.8 U/L ± 54.7) was above the upper normal range. Lipid profile mean values were generally within the ranges, with a moderate prevalence of low HDL (21%) and hypertrigliceridemia (37%). Uric acid was at normal range, and also kidney functionality was generally retained (eGFR = 85.4 ± 18.2). Microalbuminuria was relevant in 17 % of patients.

Table 2 represents biochemical parameters at the first visit.

TABLE 2. Biochemical parameters

Parameters	Mean	Standard deviation
Hba1c (%)	8.39	1.87
Glucose levels (mg/dL)	177.22	78.63
AST (U/L)	25.23	10.13
ALT (U/L)	31.35	20.83
GGT (U/L)	57.76	54.72
Total Cholesterol (mg/dL)	167.91	50.07
HDL Cholesterol (mg/dL)	51.87	17.35

LDL Cholesterol (mg/dL)	85.96	43.25
Triglycerides (mg/dL)	140.71	68.67
Uric Acid (mg/dL)	5.21	1.20
eGFR	85.37	18.18
Pathological microalbuminuria	Yes = 17.4 % No = 82.6 %	

Hba1c: glycated hemoglobin; AST: aspartate aminotransferase; ALT alanine aminotransferase; GGT gamma-glutamyl transferase; HDL: high density lipoprotein; LDL: low density lipoprotein; eGFR = estimated glumerular filtration rate

4.2 Eating habits

TABLE 3. Food habits from PREDIMED questionnaire

Predimed	**Mean**	**Standard deviation**
Total Predimed score	7.42	2.33
Adherence class	Low adherence = 7 (18.4%) Medium adherence = 23 (60.5%) Good adherence = 8 (21.1%)	
Single answers	**Frequency**	
USE OF EVOO as preferential fat source	**Yes (1)**	33 (86.8%)
	No (0)	5 (13.2%)

How much EVOO is used	**Less than 4 spoon (0)**	13 (34.2%)
	At least 4 spoon (1)	23 (65.8%)
How many vegetables are consumed daily	**Less than 2 servings (0)**	26 (68.4%)
	At least 2 servings (1)	12 (31.6%)
How many fruits are consumed daily	**Less than 3 servings (0)**	22 (57.9%)
	At least 3 servings (1)	16 (42.1%)
Consumption of Red meat and processed meat at least 1 serving perday	**Yes (0)**	12 (31.6%)
	No (1)	26 (68.4%)
Butter/ margarine/ creams consumed at least once daily	**Yes (0)**	4 (10.5%)
	No (1)	34 (89.5%)
Sweets /sweet beverages consumed at least once daily	**Yes (0)**	11 (28.9%)
	No (1)	27 (71.1%)
1 glass of winedaily	**Yes (1)**	11 (28.9%)
	No (0)	27 (71.1%)
3 legumesservings per week	**Yes (1)**	15 (39.5%)
	No (0)	23 (60.5%)
At least 3 servings of seafood per week	**Yes (1)**	13 (34.2%)
	No (0)	25 (65.8%)

Ultra-processed sweets per week	**Less than 3 (1)**	12 (31.6%)
	More than 3 (0)	26 (68.4%)
At least 3 servings per week of nuts, seeds	**Yes (1)**	15 (39.5%)
	No (0)	23 (60.5%)
White meat > red meat	**Yes (1)**	21 (55.3%)
	No (0)	17 (44.7%)
At least 2 servings per week of rice, pasta, or cereals with "soffritto" seasoning	**Yes (1)**	22 (57.9%)
	No (0)	16 (42.1%)

The PREDIMED questionnaire has been used to assess Mediterranean diet adherence (Table 3). Results indicated an average score of 7.4 ± 2.3 points. 7 patients (18,4%) displayed allow adherence to the Mediterranean diet, 23(60.5%) had a medium adherence and 8 (21.1%) of patients adhered well to the Mediterranean diet well.
Mediterranean diet principles were supported by a high use ofextra virgin olive oil (86.8% of subjects using it as main added fat) and low consumption of butter, margarine, and creams(10.5% consuming them daily).

68.4% of patients consumed less than 2 servings of vegetables daily and 57.9% of patients consume less than 3 servings of fruits daily.
Moreover, 31.6% consume at least one serving daily of red meat and processed meat and 55.3% were prioritizing white meat over red meat.

The consumption of at least three times a week of seafood (34.2%), legumes (39.5%) and nuts (39.5%) was low. 57.9% consumedrice, pasta, or cereals with "soffritto" seasoning at least twice a week, reflecting a common dietary practice in the Mediterranean Diet.

On the other hand, dietary habits have been investigated more deeply through the use of the INRAN questionnaire (Table 4)

TABLE 4. Food habits (INRAN FFQ) servings per day

Food frequency INRAN	**Mean**	**Standard deviation**
Cereals	2.00	0.86
Cereal based	0.96	0.71
Meat	0.56	0.36
Processed meat	0.42	0.27
Fish and seafood	0.24	0.13
Milk and yogurt	0.73	0.66
Dairies	0.71	0.46
Fruit	1.73	0.85
Nuts	0.28	0.31
Vegetables	0.95	0.61
Legumes	0.31	0.28
Egg	0.26	0.26

Sweets	0.95	0.87
Sugar sweetened beverages	0.43	0.90
Alcoholic beverages	0.59	0.86

The low intake of seafood (0.24 servings/day), legumes (0.31 servings/day) and nuts (0.28 servings/day), together with a low consumption of eggs (0.26 servings/day) was confirmed by food frequency data.

Particularly concerning was the high consumption of sweets (0.95 servings/day), sugar sweetened beverages (0.43 servings/day), processed meat (0.42 servings/day) and the low consumption of vegetables (0.95 servings/day) and low fat dairies (0.73 servings/day).

The qualitative FFQ data were compared to suggested healthy frequencies from the Italian"Consiglio per la ricerca in agricoltura e analisi dell'economia agraria" (CREA), which advocates for specific frequencies of consumption based on the Mediterranean diet principles. Comparison between frequencies in our sample and CREA are showed in (Figure 4.2)

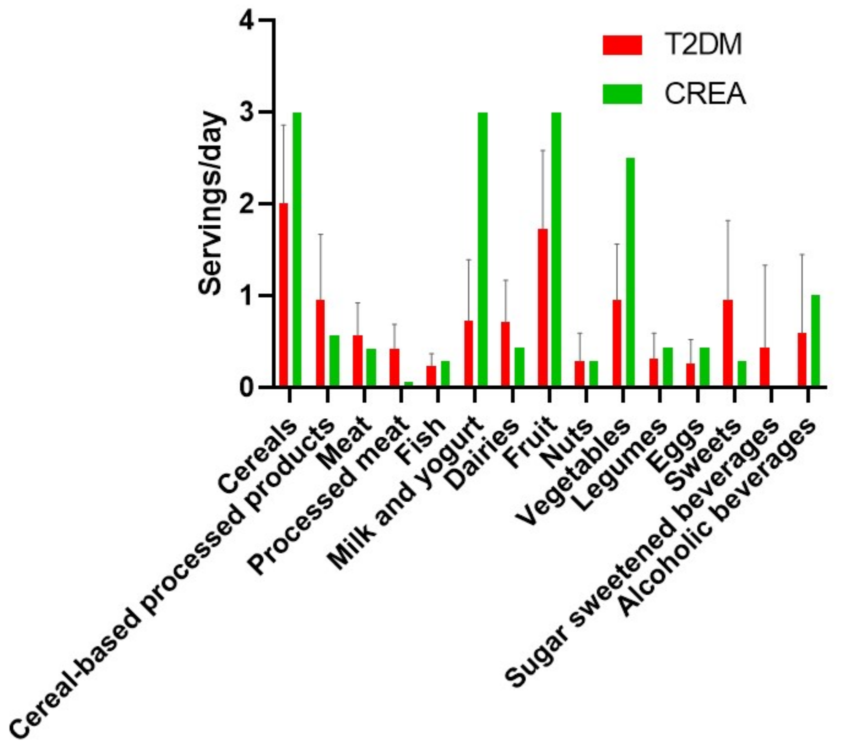


Figure 4.2. Comparison between T2DM onset food frequency and CREA guidelines.

In our sample, patients had a relatively lower consumption of cereals compared to guidelines (2 servings/day vs 3 servings/day) and a higher consumption of cereal based processed products. Meat and processed meat was higher, as well as for sweets, sugar sweetened beverages and high fat dairies. Consumption of fish, nuts, eggs, low fat dairies, vegetables, fruits, legumes and wine was registered lower than recommended.

4.3 Eating behavior

TABLE 5. Eating behavior synthesis scores from DEBQ

DEBQ PARAMETERS	AVERAGE	Standard. Deviation
Restrictive eating	1.99	0.78

Emotional eating	1.66	0.91
External eating	2.43	0.69

DEBQ data are resumed in Table 5.

External eating score was recorded to be the highest (2.43) among the three eating behavior patterns, followed by restrictive eating (1.99) and emotional eating (1.66). A high variance was registered among the sample in terms of answers to the DEBQ questionnaire.

4.4 Food patterns

The analysis of food patterns was built to assess whether there was a trend in consumption of a certain food in association with other food and which patterns were the most iconic among our sample. Principal component analysis (PCA) (Table 6) resulted in five main dietary patterns there were classified based on most representative scores:

1 = Western pattern (high in grains, meat, milk, eggs and sweets)

2= Mediterranean pattern (high in fish, nuts and vegetables)

3 = Sweets pattern (high in cereal-based processed products, dairies, sweets and sugar sweetened beverages)

4 = High proteins and alcohol pattern (high in meat, processed meat, legumes and alcoholic beverages)

5 = Prudent, high fruit pattern (moderate consumption of dairies and high in fruits).

Table 6. Principal component analysis (PCA) scores for food groups for each main dietary pattern

Rotated components matrix					
	Components				
	1	2	3	4	5
Grains	0.714	0.148	0.248	-0.157	-0.202
Grain processed products	0.009	0.148	0.819	-0.044	-0.159
Meat	0.569	-0.319	0.212	0.472	0.250
Processed meat	-0.129	-0.159	0.194	0.696	-0.275
Fish	0.029	0.580	-0.148	-0.139	0.377
Milk and yogurt	0.632	0.234	-0.192	-0.022	-0.181
Dairies	-0.285	0.144	0.526	0.231	0.437
Fruit	-0.013	-0.049	0.053	-0.147	0.820
Nuts	0.158	0.797	0.254	-0.050	-0.134
Vegetables	0.052	0.733	0.109	0.073	0.019
Legumes	0.173	0.228	-0.103	0.549	0.320
Eggs	0.735	-0.032	0.068	0.192	0.370
Sweets	0.440	0.094	0.689	0.023	0.102
Sugar-sweetened beverages	0.022	-0.536	0.592	-0.003	0.297
Alcoholic beverages	0.025	-0.011	-0.069	0.813	-0.096

4.5 Gender differences

A separate analysis based on gender differences was conducted (Table 7) to assess differences in eating patterns and behavior among genders. Women displayed an higher emotional eating score ($p<0.05$) compared to men, but a lower tendency to follow a “high proteins and alcohol” dietary pattern.

Table 7. Gender differences in dietary patterns and eating behavior

	Men (Mean ± SD)	**Women (Mean ± SD)**	**P-value**
Restrictive	2.03 ± 0.83	1.92 ± 0.68	0.846
Emotional	1.40 ± 0.58	2.11 ± 1.19	**<0.05**
External	2.40 ± 0.62	2.50 ± 0.83	0.731
Western pattern factor	-0.12 ± 1.02	0.18 ± 0.97	0.249
Mediterranean pattern factor	-0.09 ± 0.97	0.14 ± 1.07	0.474
Sweets pattern factor	-0.17 ± 0.96	0.25 ± 1.04	0.186
High proteins and alcohol pattern factor	0.29 ± 1.15	-0.43 ± 0.50	**<0.05**
Prudent high fruit pattern factor	0.05 ± 1.05	-0.08 ± 0.95	0.907

4.6 Correlations between measures

Western dietary pattern was found to be correlated with emotional eating ($\rho = 0.406$; $p<0.05$) and external eating behavior ($\rho = 0.336$; $p<0.05$). It was also associated with higher levels of AST ($\rho = 0.376$; $p<0.05$) and ALT ($\rho = 0.447$; $p<0.05$). On the contrary, Mediterranean dietary pattern seemed to be correlated with a higher restrictive eating behavior ($\rho = 0.321$; $p = 0.06$).
The restrictive eating behavior was correlated with a lower intake of sweets and sugar sweetened beverages ($\rho = 0.610$; $p<0.001$) and a higher total PREDIMED score ($\rho = 0.429$; $p <0.01$)
Emotional eating behavior was positively correlated with external eating ($\rho = 0.406$; $p <0.05$), female gender ($\rho = 0.336$; $p<0.05$), grains ($\rho = 0.379$; $p<0.05$) and sweets consumption ($\rho = 0.441$; $p<0.01$). It was also negatively correlated with wine consumption ($\rho = -0.522$; $p<0.001$) and total alcoholic beverages consumption ($\rho = -0.423$; $p<0.01$).

External eating behavior was also positively correlated with smoke habit ($\rho = 0.347$; $p<0.05$), milk and yogurt ($\rho = 0.322$; $p<0.05$) and sweets consumption ($\rho = 0.442$; $p<0.01$).

6. DISCUSSION

This study focused on the analysis of patients recently diagnosed with T2DM, with particular attention to adherence to the Mediterranean Diet, lifestyle, dietary habits, and eating behavior prior to diagnosis through the use of three simple questionnaires. The evaluation of disease-specific dietary patterns and rating the level of dysfunctional eating allowed to categorize T2DM patients based on a wider perspective.

Patients that answered our questionnaires were definitely not lacking of problematic health conditions, with over 80% of the sample having hypertension and almost 70% diagnosed with metabolic syndrome. The dysregulation of neuro-humoral and neuro-immune systems, resulting in chronic low-grade inflammation, is involved in the pathophysiology of both insulin resistance and hypertension, and insulin resistance plays also a key role in the pathogenesis and progression of hypertension-induced target organ damage (Mancusi et al. 2020). In addition, the presence of prediabetes and hypertension are most likely to predict the high prevalence of metabolic syndrome in our sample.

Dietary habits were most likely the main responsible of T2DM onset, with only 21% of patients that showed an high adherence to the Mediterranean Diet and the majority reporting moderate or poor adherence.As regards PREDIMED answers, the most detrimental data was the low prevalence of patients consuming at least two portions per day of vegetables (31.6%) and three portions (80g) of fruits (42.1%). A recent meta-analysis has confirmed that fruit and vegetable intake is associated with a reduced risk of developing T2DM and this is mainly due to the high presence of antioxidants and dietary fibers (Wang et al. 2016). As confirmed by the INRAN FFQ, important foods such as legumes, fish and nuts intakes were far below the recommended intakes and weekly frequencies. On the other hand, we observed an high intake of processed and ultra processed products (cereal based, meat, sweets and beverages) which have been recognized to be enormously impactful in the genesis of prediabetes and T2DM. In particular a recent review claimed that the consumption of sweet drinks and salty processed foods could increase the risk of prediabetes by 248% and 48%, respectively, and the risk of T2DM by 219% and 600%, respectively, compared to individuals who did not consume these products or had a rare consumption ratio (Almarshad et al. 2022)

We also found a notable reduction in the consumption of milk and yogurt compared to the recommended standards (32% of participants reported never consuming them).

As widely supported by the literature, key elements of the Mediterranean Diet, such as omega-3, whole grains, nuts, and moderate alcohol consumption (wine), if integrated into the diet in a balanced manner, can have a positive impact on systemic inflammation and cardiovascular risk factors associated with type 2 diabetes (Martínez-González M. 2008). Furthermore, various studies indicate an inverse association between daily dairy intake and T2DM, suggesting a beneficial effect of dairy consumption in the prevention of T2DM (Aune D. et al., 2013). Schwingshackl L. and colleagues (2017) confirmed that increased consumption of vegetables, fruits, and dairy, and reduced consumption of red and processed meats and eggs, can lead to a significant reduction in the risk of T2DM.ok up to here

Furthermore, studies have shown that emotional stress, including depression, is associated with increased emotional eating, and that eating caused by depression, anxiety/anger, and boredom is related to worse psychological well-being, more severe eating disorder symptoms, and more emotion regulation complications. However, eating caused by positive emotions was not related to negative outcomes. Emotional eating is a multidimensional feature, and it is important to consider it as a multidimensional issue. In addition to the general emotional stress, anxiety, sleeping problems, anger, and hostility, is associated with an increased risk for developing type 2 diabetes mellitus, showing that when individuals experiencing a chronic emotional stress are more likely to develop type 2 diabetes. .(Pouwer, F, et al.2010). In our sample, women showed higher scores in emotional style than men. This suggests a potential difference in emotional management of food between the two genders. Infact, on the opposite side, we not only found that men were more likely to follow a dietary pattern rich in alcohol and high protein meals, but also that alcohol consumption was negatively correlated with sweets intake and emotional eating. Some articles conducted on university students confirm this trend, hypothesizing that both emotional eating and alcohol consumption should be considered as addictions, but they are associated with different psychosocial contexts. In particular, emotional eating appear more associated with anxiety and depression, while alcohol has a strong external factor, especially in young people, since it forms a part of the recreational culture (ILópez-Moreno et al. 2021; Marchena-Giráldez et al., 2014). Indeed, our population was mainly composed of older people and for this reason we believe that the alcohol consumption mainly stands as an addiction in our sample.

On the other hand, no significant gender differences emerged for the external and restrictive styles, but emotional eating resulted to be linked to external eating, highlighting that the lack of self control and a high impulsiveness could be key factors that determine these kinds of eating behaviors (ILópez-Moreno et al. 2021).

The results of this study are consistent with the conclusions of the article by Dakanalis and colleagues (2013), who observed that in Italy external eating is prevalent, followed by restrictive and emotional eating, reflecting what was found in the analyzed data. Furthermore, the same study shows that older people, compared to younger ones, exhibit lower levels of emotional eating, a result consistent with the average age of our patients,

Study limitations

However, the discrepancy between these dietary principles and the eating habits of diabetic patients indicates the need for further studies. In fact, the analysis of consumption frequency does not provide details on the actual quantities consumed by each individual in each food category, as portion sizes were estimated, but it offers a general overview. Evaluating the quality of individual dietary habits, on the other hand, would require further investigation to obtain a more complete understanding of eating behaviors and their relationship with the risk of type 2 diabetes. Focusing on food groups can still help understand the role that dietary factors play in the risk of developing type 2 diabetes in a way more accessible to the public and could form the basis for dietary recommendations aimed at preventing chronic diseases.Also,it is more difficult to compare the results with a baseline or non-diabetic population when there is no control group. A control group would improve the results' validity and give a more accurate picture of how dietary practices affect the risk of diabetes. Moreover, the study most likely uses self-reported data, which is prone to errors and memory biases. There is a chance that participants would record or forget their food consumption incorrectly, which could cause mistakes in the results.

7. CONCLUSION

Despite the widespread recognition of the Mediterranean Diet as an effective model for the prevention, control, and management of Type 2 Diabetes Mellitus (T2DM) complications, research on dietary habits at the onset of diabetes remains limited. Additionally, the link between eating disorders or dysfunctional eating behaviors and T2DM is a largely unexplored research area. Understanding the dietary and behavioral patterns associated with T2DM development could reveal crucial dietary interventions and behavioral modifications necessary for early prevention and improved disease management. This knowledge could potentially reduce the incidence and severity of T2DM-related complications. Such insights could inform public health strategies and clinical practices, addressing T2DM not only as a metabolic disease but also in relation to psychological factors.

8. BIBLIOGRAPHY

1. Abbasi J. Interest in the Ketogenic Diet Grows for Weight Loss and Type 2 Diabetes. JAMA. 2018 Jan 16;319(3):215-217. doi: 10.1001/jama.2017.20639. PMID: 29340675
2. ADEGHATE, E., SCHATTNER, P. and DUNN, E. (2006), An Update on the Etiology and Epidemiology of Diabetes Mellitus. Annals of the New York Academy of Sciences, 1084: 1-29.
3. akalamba, C. B. (2013). The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *J Physiol Pathophysiol* , *4* (4), 46-57.
4. Almarshad, M. I., Algonaiman, R., Alharbi, H. F., Almujaydil, M. S., & Barakat, H. (2022). Relationship between ultra-processed food consumption and risk of diabetes mellitus: a mini-review. *Nutrients*, *14*(12), 2366.
5. Al-Nuaim, A.R. 1997. Prevalence of glucose intolerance in urban and rural communities in Saudi Arabia. Diabet. Med. 14: 595–602.
6. American Diabetes Association (ADA). (2023). Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2023. *Diabetes Care*, 46(Supplement 1), S19-S40. doi:10.2337/dc23-S002.
7. American Diabetes Association; Bantle JP, Wylie-Rosett J, Albright AL, Apovian CM, Clark NG, Franz MJ, Hoogwerf BJ, Lichtenstein AH, Mayer-Davis E, Mooradian AD, Wheeler ML. Nutrition recommendations and interventions for diabetes: a position statement of the American Diabetes Association. Diabetes Care. 2008 Jan;31 Suppl 1:S61-78. doi: 10.2337/dc08-S061. Erratum in: Diabetes Care. 2010 Aug;33(8):1911. PMID: 18165339.

8. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington DC: Author.
9. Andersen SSH, Heller JMF, Hansen TT, Raben A. Comparison of Low Glycaemic Index and High Glycaemic Index Potatoes in Relation to Satiety: A Single-Blinded, Randomised Crossover Study in Humans. Nutrients. 2018 Nov 10;10(11):1726. doi: 10.3390/nu10111726. PMID: 30423848; PMCID: PMC6266898.
10. Anderson, Pat Baird, Richard H Davis, Stefanie Ferreri, Mary Knudtson, Ashraf Koraym, Valerie Waters, Christine L Williams. Health benefits of dietary fiber. Nutrition Reviews, Volume 67, Issue 4, 1 April 2009, Pages 188–205, https://doi.org/10.1111/j.1753-4887.2009.00189.x
11. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med. 2017 Jun 15;376(24):2367-2375. doi: 10.1056/NEJMra1615439. PMID: 28614678.
12. Athinarayanan SJ, Adams RN, Hallberg SJ, McKenzie AL, Bhanpuri NH, Campbell WW, Volek JS, Phinney SD, McCarter JP. Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial. Front Endocrinol (Lausanne). 2019 Jun 5;10:348. doi: 10.3389/fendo.2019.00348. PMID: 31231311; PMCID: PMC6561315.
13. Atkinson FS, Brand-Miller JC, Foster-Powell K, Buyken AE, Goletzke J. International tables of glycemic index and glycemic load values 2021: a systematic review. Am J Clin Nutr. 2021 Nov 8;114(5):1625-1632. doi: 10.1093/ajcn/nqab233. PMID: 34258626.
14. Augustin LSA, Kendall CWC, Jenkins DJA, Willett WC, Astrup A, Barclay AW, Björck I, Brand-Miller JC, Brighenti F, Buyken AE,

Ceriello A, La Vecchia C, Livesey G, Liu S, Riccardi G, Rizkalla SW, Sievenpiper JL, Trichopoulou A, Wolever TMS, Baer-Sinnott S, Poli A. Glycemic index, glycemic load and glycemic response: An International Scientific Consensus Summit from the International Carbohydrate Quality Consortium (ICQC). Nutr Metab Cardiovasc Dis. 2015 Sep;25(9):795-815. doi: 10.1016/j.numecd.2015.05.005. Epub 2015 May 16. PMID: 26160327.

15. Aune D, Ursin G, Veierød MB. Meat consumption and the risk of type 2 diabetes: a systematic review and meta-analysis of cohort studies. Diabetologia. 2009 Nov;52(11):2277-87. doi: 10.1007/s00125-009-1481-x. Epub 2009 Aug 7. PMID: 19662376.
16. Bailey Clifford J., Peter R. Flatt, J. Michael Conlon. An update on peptide-based therapies for type 2 diabetes and obesity. Peptides, Volume 161, 2023.
17. Bailey, Clifford J., and Robert C. Turner. "Metformin."*New England Journal of Medicine* 334.9 (1996): 574-579.
18. Barclay, A.W., Petocz, P., McMillan-Price, J., Flood, V.M., Prvan, T., Mitchell, P., Brand-Miller, J.C. Glycemic index, glycemic load, and chronic disease risk, a meta-analysis of observational studies, The American Journal of Clinical Nutrition. 87, 627–637 (2008).
19. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA. 2002 May 15;287(19):2570-81. doi: 10.1001/jama.287.19.2570. PMID: 12020339.
20. Belgardt BF, Okamura T, Brüning JC. Hormone and glucose signalling in POMC and AgRP neurons. J Physiol. 2009 Nov 15;587(Pt 22):5305-14. doi: 10.1113/jphysiol.2009.179192. Epub 2009 Sep 21. PMID: 19770186; PMCID: PMC2793863.

21. Bellisle F. Why should we study human food intake behaviour? Nutr Metab Cardiovasc Dis. 2003 Aug;13(4):189-93. doi: 10.1016/s0939-4753(03)80010-8. PMID: 14650350.
22. Bellisle F., Dalix A. M., & Slama G. (2003). Nonfood-related environmental stimuli induce increased meal intake in healthy women: comparison of television viewing versus listening to a recorded story in laboratory settings. Appetite, 41(1), 7-13.
23. Bhardwaj M., Denney-Wilson E., Baur L. A., & Wen L. M. (2023). Eating Behaviour, Diet Quality, and Obesity Risk in Children and Adolescents: A Narrative Review. Nutrients, 15(3), 688.
24. Boucher JL. Mediterranean Eating Pattern. Diabetes Spectr. 2017 May;30(2):72-76. doi: 10.2337/ds16-0074. PMID: 28588371; PMCID: PMC5439355.
25. Browning K. N., Mendelowitz D., & Travagli R. A. (2021). Neurocircuitry underlying control of the stomach. Nature Reviews Gastroenterology & Hepatology, 18(8), 478-492.
26. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature. 2001 Dec 13;414(6865):813-20. doi: 10.1038/414813a. PMID: 11742414.
27. Cavazza N., & Guidetti M. (2020). Eating behaviors in response to external and internal cues: Development and validation of the Emotional and External Eating Scale. Appetite, 144, 104473.
28. Cebolla A, Barrada JR, van Strien T, Oliver E, Baños R. Validation of the Dutch Eating Behavior Questionnaire (DEBQ) in a sample of Spanish women. Appetite. 2014 Feb;73:58-64. doi: 10.1016/j.appet.2013.10.014. Epub 2013 Oct 28. PMID: 24177441.

29. Cebolla A, Barrada JR, van Strien T, Oliver E, Baños R. Validation of the Dutch Eating Behavior Questionnaire (DEBQ) in a sample of Spanish women. Appetite. 2014 Feb;73:58-64. doi: 10.1016/j.appet.2013.10.014. Epub 2013 Oct 28. PMID: 24177441.
30. Cebolla A, Barrada JR, van Strien T, Oliver E, Baños R. Validation of the Dutch Eating Behavior Questionnaire (DEBQ) in a sample of Spanish women. Appetite. 2014 Feb;73:58-64. doi: 10.1016/j.appet.2013.10.014. Epub 2013 Oct 28. PMID: 24177441.
31. Chaturvedi N, Stevens L, Fuller JH. Which features of smoking determine mortality risk in former cigarette smokers with diabetes? The World Health Organization Multinational Study Group. Diabetes Care. 1997 Aug;20(8):1266-72. doi: 10.2337/diacare.20.8.1266. PMID: 9250452.DOI: 10.2337/diacare.24.7.1261
32. Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: Distinct or continuum? Indian J Endocrinol Metab. 2016 Jul-Aug;20(4):546-51. doi: 10.4103/2230-8210.183480. PMID: 27366724; PMCID: PMC4911847.
33. Chester, B., Babu, J. R., Greene, M. W., & Geetha, T. (2019). The effects of popular diets on type 2 diabetes management. *Diabetes/metabolism research and reviews*, *35*(8), e3188.
34. Choe, S.S.; Huh, J.Y.; Hwang, I.J.; Kim, J.I.; Kim, J.B. Adipose tissue remodeling: Its role in energy metabolism and metabolic disorders. *Front. Endocrinol. (Lausanne)*. 2016, *7*.
35. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, Horton ES, Castorino K, Tate DF. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association.

Diabetes Care. 2016 Nov;39(11):2065-2079. doi: 10.2337/dc16-1728. PMID: 27926890; PMCID: PMC6908414.

36. Cooper, Z., & Fairburn, C. G. (2008). The evolution of "enhanced" cognitive behavior therapy for eating disorders: Learning from treatment nonresponse. Cognitive and Behavioral Practice, 15(4), 386-401.
37. Cosmi F, D'Orazio S, Mariottoni B, Tarquini B, Cosmi D. Processo all'insulina nella terapia del diabete mellito di tipo 2 [Process to insulin for type 2 diabetes mellitus therapy]. G Ital Cardiol (Rome). 2022 Jan;23(1):52-62. Italian. doi: 10.1714/3715.37063. PMID: 34985463.
38. Cryer PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Seaquist ER, Service FJ; Endocrine Society. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009 Mar;94(3):709-28. doi: 10.1210/jc.2008-1410. Epub 2008 Dec 16. PMID: 19088155.
39. Cryer PE. The barrier of hypoglycemia in diabetes. Diabetes. 2008 Dec;57(12):3169-76. doi: 10.2337/db08-1084. PMID: 19033403; PMCID: PMC2584119.
40. Cui H., López M., & Rahmouni K. (2017). The cellular and molecular bases of leptin and ghrelin resistance in obesity. Nature Reviews Endocrinology, 13(6), 338-351.
41. Dakanalis A, Mentzelou M, Papadopoulou SK, Papandreou D, Spanoudaki M, Vasios GK, Pavlidou E, Mantzorou M, Giaginis C. The Association of Emotional Eating with Overweight/Obesity, Depression, Anxiety/Stress, and Dietary Patterns: A Review of the Current Clinical Evidence. Nutrients. 2023 Feb 26;15(5):1173. doi: 10.3390/nu15051173. PMID: 36904172; PMCID: PMC10005347.

42. Dakanalis A., Carrà G., Calogero R. M., Zanetti M. A., Riva G., & Clerici M. (2013). Predictors of initiation and persistence of recurrent binge eating and inappropriate weight compensatory behaviors in college men. International Journal of Eating Disorders, 46(8), 785-792.
43. Dakanalis A., Colmegna F., Riva G., & Clerici M. (2012). Disordered eating behaviors among Italian men: Objectifying media and sexual orientation differences. Eating Disorders, 20(5), 356-367.
44. De la Cruz-Concepción B., Navarro E., González-Puga C., & Guerrero J. M. (2023). Molecular mechanisms underlying the role of oxidative stress in insulin resistance: The impact of the antioxidant melatonin. International Journal of Molecular Sciences, 24(6), 3242.
45. DeFronzo RA, Abdul-Ghani M. Type 2 diabetes can be prevented with early pharmacological intervention. Diabetes Care. 2011 May;34 Suppl 2(Suppl 2):S202-9. doi: 10.2337/dc11-s221. PMID: 21525456; PMCID: PMC3632162.
46. Defronzo RA. Bromocriptine: a sympatholytic, d2-dopamine agonist for the treatment of type 2 diabetes. Diabetes Care. 2011 Apr;34(4):789-94. doi: 10.2337/dc11-0064. Erratum in: Diabetes Care. 2011 Jun;34(6):1442. Dosage error in article text. PMID: 21447659; PMCID: PMC3064029.
47. Denney-Wilson E., Campbell K. J., Hesketh K. D., & Ridgers N. D. (2008). Eating behaviours of two-year-old children and associations with BMI and TV viewing. Obesity research & clinical practice, 2(2), 131-138.
48. Diabetes UK - Treatments: https://www.diabetes.org.uk/diabetes-the-basics/diabetes-treatments

49. Diabetes UK - Type 1 Diabetes Causes: https://www.diabetes.org.uk/diabetes-the-basics/types-of-diabetes/type-1/causes
50. Dostou J, Gerich J. Pathogenesis of type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes. 2001;109 Suppl 2:S149-56. doi: 10.1055/s-2001-18577. PMID: 11460566.
51. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005 Apr 16-22;365(9468):1415-28. doi: 10.1016/S0140-6736(05)66378-7. PMID: 15836891.
52. Elizabeth Denney-Wilson J. R., & Dunbar J. A. (2008). Association of disinhibition and dietary restraint with BMI in Australian adults. Public Health Nutrition, 11(2), 174-180.
53. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, Collins BS, Hilliard ME, Isaacs D, Johnson EL, Kahan S, Khunti K, Leon J, Lyons SK, Perry ML, Prahalad P, Pratley RE, Seley JJ, Stanton RC, Gabbay RA, on behalf of the American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes-2023. Diabetes Care. 2023 Jan 1;46(Suppl 1):S19-S40. doi: 10.2337/dc23-S002. Erratum in: Diabetes Care. 2023 May 1;46(5):1106. doi: 10.2337/dc23-er05. Erratum in: Diabetes Care. 2023 Sep 1;46(9):1715. doi: 10.2337/dc23-ad08. PMID: 36507649; PMCID: PMC9810477.
54. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Basora J, Muñoz MA, Sorlí JV, Martínez JA, Fitó M, Gea A, Hernán MA, Martínez-González MA; PREDIMED Study Investigators. Primary Prevention of Cardiovascular

Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. N Engl J Med. 2018 Jun 21;378(25):e34. doi: 10.1056/NEJMoa1800389. Epub 2018 Jun 13. PMID: 29897866.

55. Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, Neumiller JJ, Nwankwo R, Verdi CL, Urbanski P, Yancy WS Jr. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care. 2014 Jan;37 Suppl 1:S120-43. doi: 10.2337/dc14-S120. PMID: 24357208.
56. Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, Mitri J, Pereira RF, Rawlings K, Robinson S, Saslow L, Uelmen S, Urbanski PB, Yancy WS Jr. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. Diabetes Care. 2019 May;42(5):731-754. doi: 10.2337/dci19-0014. Epub 2019 Apr 18. PMID: 31000505; PMCID: PMC7011201.
57. EZMed Learning - Type 1 Diabetes: https://www.ezmedlearning.com/blog/type-1-diabetes-mellitus-symptoms-treatment
58. Fairburn C. G., & Beglin S. J. (1994). Assessment of eating disorders: Interview or self-report questionnaire?. International Journal of Eating Disorders, 16(4), 363-370.
59. Fairburn C. G., Cooper Z., & Shafran R. (2003). Cognitive behaviour therapy for eating disorders: A "transdiagnostic" theory and treatment. Behaviour research and therapy, 41(5), 509-528.
60. Fairburn CG, Beglin SJ. Assessment of eating disorders: interview or self-report questionnaire? Int J Eat Disord. 1994 Dec;16(4):363-70. PMID: 7866415.

61. Fairburn, C. G. (2008). Cognitive behavior therapy and eating disorders. Guilford Press.
62. -Farmaki P, Damaskos C, Garmpis N, Garmpi A, Savvanis S, Diamantis E. Complications of the Type 2 Diabetes Mellitus. Curr Cardiol Rev. 2020;16(4):249-251. doi: 10.2174/1573403X1604201229115531. PMID: 33407062; PMCID: PMC7903505.
63. Feldman, E.L., Callaghan, B.C., Pop-Busui, R. *et al.* Diabetic neuropathy. *Nat Rev Dis Primers*5, 41 (2019).
64. Fletcher, Barbara RN, MN, FAAN; Gulanick, Meg PhD, RN; Lamendola, Cindy RN, MSN, ANP. Risk Factors for Type 2 Diabetes Mellitus. The Journal of Cardiovascular Nursing 16(2):p 17-23, January 2002.
65. Fong, D. S., Aiello, L. P., Ferris III, F. L., & Klein, R. (2004). Diabetic retinopathy. *Diabetes care*, *27*(10), 2540-2553.
66. Forbes JM, Cooper ME. Mechanisms of diabetic complications. Physiol Rev. 2013 Jan;93(1):137-88. doi: 10.1152/physrev.00045.2011. PMID: 23303908.
67. Fowler, M. J. (2008). Microvascular and Macrovascular Complications of Diabetes. *Clinical Diabetes*, 26(2), 77-82. doi:10.2337/diaclin.26.2.77.
68. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med. 2008 Feb 7;358(6):580-91. doi: 10.1056/NEJMoa0706245. PMID: 18256393.
69. Gibson E. L., & Green M. W. (2006). Nutritional influences on cognitive function: mechanisms of susceptibility. Nutrition Research Reviews, 19(1), 35-48.

70. Gibson EL. Emotional influences on food choice: sensory, physiological and psychological pathways. Physiol Behav. 2006 Aug 30;89(1):53-61. doi: 10.1016/j.physbeh.2006.01.024. Epub 2006 Mar 20. PMID: 16545403.
71. Giglio RV, Papanas N, Rizvi AA, Ciaccio M, Patti AM, Ilias I, Pantea Stoian A, Sahebkar A, Janez A, Rizzo M. An Update on the Current and Emerging Use of Thiazolidinediones for Type 2 Diabetes. *Medicina*. 2022; 58(10):1475.
72. Ginsberg, H.N.; Zhang, Y.L.; Hernandez-Ono, A. Regulation of plasma triglycerides in insulin resistance and diabetes. *Arch. Med. Res.* 2005, *36*, 232–240.
73. Green, Andrew J., Kathleen M. Fox, and Susan Grandy. "Impact of regular exercise and attempted weight loss on quality of life among adults with and without type 2 diabetes mellitus." Journal of Obesity 2011 (2011).
74. Grilo, C. M., & Mitchell, J. E. (2011). The treatment of eating disorders: A clinical handbook. Guilford Press.
75. Guillermo E. Umpierrez, Mary Beth Murphy, Abbas E. Kitabchi; Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar Syndrome. *Diabetes Spectr* 1 January 2002; 15 (1): 28–36.
76. Hallberg SJ, McKenzie AL, Williams PT, Bhanpuri NH, Peters AL, Campbell WW, Hazbun TL, Volk BM, McCarter JP, Phinney SD, Volek JS. Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study. Diabetes Ther. 2018 Apr;9(2):583-612. doi: 10.1007/s13300-018-0373-9. Epub 2018 Feb 7. Erratum in: Diabetes

Ther. 2018 Apr;9(2):613-621. doi: 10.1007/s13300-018-0386-4. PMID: 29417495; PMCID: PMC6104272.

77. Hansen JB, Kristiansen K. Regulatory circuits controlling white versus brown adipocyte differentiation. Biochem J. 2006 Sep 1;398(2):153-68. doi: 10.1042/BJ20060402. PMID: 16898874; PMCID: PMC1550312.
78. Hawley JA, Lessard SJ. Exercise training-induced improvements in insulin action. Acta Physiol (Oxf). 2008 Jan;192(1):127-35. doi: 10.1111/j.1748-1716.2007.01783.x. PMID: 18171435.
79. Helmrich, S.P., D.R. Ragland, R.W. Leung & R.S. Paffenbarger Jr. 1991. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. N. Engl. J. Med. 325: 147–152.
80. Hirsch IB, Brownlee M. Should minimal blood glucose variability become the gold standard of glycemic control? J Diabetes Complications. 2005 May-Jun;19(3):178-81. doi: 10.1016/j.jdiacomp.2004.10.001. PMID: 15866065.
81. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006 Dec 14;444(7121):860-7. doi: 10.1038/nature05485. PMID: 17167474.
82. https://diabetesjournals.org/care/article/46/Supplement_1/S19/148056/2-Classification-and-Diagnosis-of-Diabetes
83. Hudson J. I., Hiripi E., Pope H. G., & Kessler R. C. (2007). The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. Biological Psychiatry, 61(3), 348-358.
84. Hudson JI, Hiripi E, Pope HG Jr, Kessler RC. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. Biol Psychiatry. 2007 Feb 1;61(3):348-58. doi: 10.1016/j.biopsych.2006.03.040. Epub 2006 Jul 3. Erratum in: Biol

Psychiatry. 2012 Jul 15;72(2):164. PMID: 16815322; PMCID: PMC1892232.

85. Javeed N, Matveyenko AV. Circadian Etiology of Type 2 Diabetes Mellitus. Physiology (Bethesda). 2018 Mar 1;33(2):138-150. doi: 10.1152/physiol.00003.2018. PMID: 29412061; PMCID: PMC5899235.
86. Jorge L. Gross, Mirela J. de Azevedo, Sandra P. Silveiro, Luís Henrique Canani, Maria Luiza Caramori, Themis Zelmanovitz; Diabetic Nephropathy: Diagnosis, Prevention, and Treatment. Diabetes Care 1 January 2005; 28 (1): 164–176.
87. Jung, S.H.; Ha, K.H.; Kim, D.J. Visceral fat mass has stronger associations with diabetes and prediabetes than other anthropometric obesity indicators among Korean adults. *Yonsei Med. J.*2016, *57*, 674–680.
88. Kahleova H, Tura A, Hill M, Holubkov R, Barnard ND. A Plant-Based Dietary Intervention Improves Beta-Cell Function and Insulin Resistance in Overweight Adults: A 16-Week Randomized Clinical Trial. Nutrients. 2018 Feb 9;10(2):189. doi: 10.3390/nu10020189. PMID: 29425120; PMCID: PMC5852765.
89. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. Lancet. 2014 Mar 22;383(9922):1068-83. doi: 10.1016/S0140-6736(13)62154-6. Epub 2013 Dec 3. PMID: 24315620; PMCID: PMC4226760
90. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. Lancet. 2014 Mar 22;383(9922):1068-83. doi: 10.1016/S0140-6736(13)62154-6. Epub 2013 Dec 3. PMID: 24315620; PMCID: PMC4226760.

91. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. Lancet. 2014 Mar 22;383(9922):1068-83. doi: 10.1016/S0140-6736(13)62154-6. Epub 2013 Dec 3. PMID: 24315620; PMCID: PMC4226760.
92. Kanaley JA, Colberg SR, Corcoran MH, Malin SK, Rodriguez NR, Crespo CJ, Kirwan JP, Zierath JR. Exercise/Physical Activity in Individuals with Type 2 Diabetes: A Consensus Statement from the American College of Sports Medicine. Med Sci Sports Exerc. 2022 Feb 1;54(2):353-368. doi: 10.1249/MSS.0000000000002800. PMID: 35029593; PMCID: PMC8802999.
93. Kane, Kelly, 1969- author, editor. | Prelack, Kathy, author, editor. Title: Advanced medical nutrition therapy / Kelly Kane and Kathy Prelack. Description: Burlington, Massachusetts : Jones & Bartlett Learning,
94. Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. J Am Coll Cardiol. 2011 Mar 15;57(11):1299-313. doi: 10.1016/j.jacc.2010.09.073. PMID: 21392646.
95. Katsarou, A., Gudbjörnsdottir, S., Rawshani, A. *et al.*Type 1 diabetes mellitus. *Nat Rev Dis Primers*3, 17016 (2017).
96. Keel P. K., & Klump K. L. (2003). Are eating disorders culture-bound syndromes? Implications for conceptualizing their etiology. Psychological Bulletin, 129(5), 747-769.
97. Keel, P. K., & Klump, K. L. (2003). Are eating disorders culture-bound syndromes? Implications for conceptualizing their etiology. Psychological Bulletin, 129(5), 747–769. https://doi.org/10.1037/0033-2909.129.5.747

98. Kellar D., & Craft S. (2020). Brain insulin resistance in Alzheimer's disease and related disorders: mechanisms and therapeutic approaches. The Lancet Neurology, 19(9), 758-766.
99. Kissebah, A.H., N. Vydelingum, R. Murray, et al . 1982. Relation of body fat distribution to metabolic complications of obesity. J. Clin. Endocrinol. Metab. 54: 254–260.
100. Kruger R, De Bray JG, Beck KL, Conlon CA, Stonehouse W. Exploring the Relationship between Body Composition and Eating Behavior Using the Three Factor Eating Questionnaire (TFEQ) in Young New Zealand Women. Nutrients. 2016 Jun 23;8(7):386. doi: 10.3390/nu8070386. PMID: 27347997; PMCID: PMC4963862.
101. Leclercq C, Arcella D, Piccinelli R, Sette S, Le Donne C, Turrini A; INRAN-SCAI 2005-06 Study Group. The Italian National Food Consumption Survey INRAN-SCAI 2005-06: main results in terms of food consumption. Public Health Nutr. 2009 Dec;12(12):2504-32. doi: 10.1017/S1368980009005035. Epub 2009 Mar 12. PMID: 19278564.
102. Lenzen S. The mechanisms of alloxan- and streptozotocin-induced diabetes. Diabetologia. 2008 Feb;51(2):216-26. doi: 10.1007/s00125-007-0886-7. Epub 2007 Dec 18. PMID: 18087688.
103. Lerman, I.G., Villa, A.R., Martinez, C.L., Turrubiatez, L.C., Salinas, C.A.A., Wong, B., Pérez, F.J.G. and Robledo, L.M.G. (1998), The Prevalence of Diabetes and Associated Coronary Risk Factors in Urban and Rural Older Mexican Populations. Journal of the American Geriatrics Society, 46: 1387-1395.
104. Linardon, J., Wade, T. D., de la Piedad Garcia, X., & Brennan, L. (2017). The efficacy of cognitive-behavioral therapy for eating

disorders: A systematic review and meta-analysis. Journal of Consulting and Clinical Psychology, 85(11), 1080-1094.

105. Liu Y, Wang Y, Qin S, Jin X, Jin L, Gu W, Mu Y. Insights Into Genome-Wide Association Study for Diabetes: A Bibliometric and Visual Analysis From 2001 to 2021. Front Endocrinol (Lausanne). 2022 Mar 11;13:817620. doi: 10.3389/fendo.2022.817620. PMID: 35360064; PMCID: PMC8963272.

106. Lock, J., Agras, W. S., Bryson, S. W., & Kraemer, H. C. (2013). A comparison of short- and long-term family therapy for adolescent anorexia nervosa. Journal of the American Academy of Child & Adolescent Psychiatry, 52(9), 911-919.

107. López-Moreno M, Garcés-Rimón M, Miguel M, Iglesias López MT. Adherence to Mediterranean Diet, Alcohol Consumption and Emotional Eating in Spanish University Students. *Nutrients*. 2021; 13(9):3174. https://doi.org/10.3390/nu13093174

108. Low Wang, Cecilia C., et al. "Clinical update: cardiovascular disease in diabetes mellitus: atherosclerotic cardiovascular disease and heart failure in type 2 diabetes mellitus–mechanisms, management, and clinical considerations."*Circulation* 133.24 (2016): 2459-2502.

109. LSU AgCenter - Diabetes: https://www.lsuagcenter.com/profiles/rmiller/articles/page1656610049514

110. M.P. Khanolkar, S.C. Bain, J.W. Stephens, The diabetic foot, QJM: An International Journal of Medicine, Volume 101, Issue 9, September 2008, Pages 685–695

111. Mack LR, Tomich PG. Gestational Diabetes: Diagnosis, Classification, and Clinical Care. Obstet Gynecol Clin North Am. 2017 Jun;44(2):207-217. doi: 10.1016/j.ogc.2017.02.002. PMID: 28499531.

112. Macroangiopathy in diabetes mellitus Manuela Birrer Vasa 2001 30:3, 168-174

113. Malik VS, Hu FB. Fructose and Cardiometabolic Health: What the Evidence From Sugar-Sweetened Beverages Tells Us. J Am Coll Cardiol. 2015 Oct 6;66(14):1615-1624. doi: 10.1016/j.jacc.2015.08.025. PMID: 26429086; PMCID: PMC4592517.

114. Mancusi, C., Izzo, R., di Gioia, G., Losi, M. A., Barbato, E., & Morisco, C. (2020). Insulin resistance the hinge between hypertension and type 2 diabetes. *High blood pressure & cardiovascular prevention*, *27*, 515-526.

115. Marchena-Giráldez, C., Carbonell-Colomer, M., & Bernabéu-Brotons, E. (2024). Emotional eating, internet overuse, and alcohol intake among college students: a pilot study with virtual reality. *Frontiers in Nutrition*, *11*, 1400815.

116. Martínez-González MA, García-Arellano A, Toledo E, Salas-Salvadó J, Buil-Cosiales P, Corella D, Covas MI, Schröder H, Arós F, Gómez-Gracia E, Fiol M, Ruiz-Gutiérrez V, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pintó X, Muñoz MA, Wärnberg J, Ros E, Estruch R; PREDIMED Study Investigators. A 14-item Mediterranean diet assessment tool and obesity indexes among high-risk subjects: the PREDIMED trial. PLoS One. 2012;7(8):e43134. doi: 10.1371/journal.pone.0043134. Epub 2012 Aug 14. PMID: 22905215; PMCID: PMC3419206.

117. Martínez-González MÁ, Hershey MS, Zazpe I, Trichopoulou A. Transferability of the Mediterranean Diet to Non-Mediterranean Countries. What Is and What Is Not the Mediterranean Diet. Nutrients. 2017 Nov 8;9(11):1226. doi: 10.3390/nu9111226. Erratum in: Nutrients. 2018 Jun 26;10(7):E823. doi: 10.3390/nu10070823. PMID: 29117146; PMCID: PMC5707698.
118. Martín-Peláez S, Fito M, Castaner O. Mediterranean Diet Effects on Type 2 Diabetes Prevention, Disease Progression, and Related Mechanisms. A Review. Nutrients. 2020 Jul 27;12(8):2236. doi: 10.3390/nu12082236. PMID: 32726990; PMCID: PMC7468821.
119. Mbanya JC, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. Lancet. 2010 Jun 26;375(9733):2254-66. doi: 10.1016/S0140-6736(10)60550-8. PMID: 20609971.
120. McCarthy MI. Genomics, type 2 diabetes, and obesity. N Engl J Med. 2010 Dec 9;363(24):2339-50. doi: 10.1056/NEJMra0906948. PMID: 21142536.
121. Micha R, Peñalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association Between Dietary Factors and Mortality From Heart Disease, Stroke, and Type 2 Diabetes in the United States. JAMA. 2017 Mar 7;317(9):912-924. doi: 10.1001/jama.2017.0947. PMID: 28267855; PMCID: PMC5852674.
122. Milenkovic T, Bozhinovska N, Macut D, Bjekic-Macut J, Rahelic D, Velija Asimi Z, Burekovic A. Mediterranean Diet and Type 2 Diabetes Mellitus: A Perpetual Inspiration for the Scientific World. A Review. Nutrients. 2021 Apr 15;13(4):1307. doi: 10.3390/nu13041307. PMID: 33920947; PMCID: PMC8071242.

123. Mitchell, J. E., Agras, S., & Wonderlich, S. (2008). Treatment of bulimia nervosa: Where are we and where are we going?. International Journal of Eating Disorders, 41(5), 493-496.

124. Modi, Pankaj. "Diabetes beyond insulin: review of new drugs for treatment of diabetes mellitus." Current drug discovery technologies 4.1 (2007): 39-47.

125. Mohsen S. Eledrisi, Mohammed S. Alshanti, M. Faiq Shah, Basem Brolosy, Nermeen Jaha, Overview of the Diagnosis and Management of Diabetic Ketoacidosis, The American Journal of the Medical Sciences, Volume 331, Issue 5, 2006, Pages 243-251, ISSN 0002-9629

126. Müller TD, Finan B, Bloom SR, D'Alessio D, Drucker DJ, Flatt PR, Fritsche A, Gribble F, Grill HJ, Habener JF, Holst JJ, Langhans W, Meier JJ, Nauck MA, Perez-Tilve D, Pocai A, Reimann F, Sandoval DA, Schwartz TW, Seeley RJ, Stemmer K, Tang-Christensen M, Woods SC, DiMarchi RD, Tschöp MH. Glucagon-like peptide 1 (GLP-1). Mol Metab. 2019 Dec;30:72-130. doi: 10.1016/j.molmet.2019.09.010. Epub 2019 Sep 30. PMID: 31767182; PMCID: PMC6812410.

127. Murphy R, Straebler S, Cooper Z, Fairburn CG. Cognitive behavioral therapy for eating disorders. Psychiatr Clin North Am. 2010 Sep;33(3):611-27. doi: 10.1016/j.psc.2010.04.004. PMID: 20599136; PMCID: PMC2928448.

128. Murphy, R., Straebler, S., Cooper Z., & Fairburn C. G. (2010). Cognitive behavioral therapy for eating disorders. The Psychiatric Clinics of North America, 33(3), 611-627.

129. Nichols G.A., Reinier K., Chugh S.S., et al. Independent contribution of diabetes to increased prevalence and incidence of atrial fibrillation. Diabetes Care. 2009;32:1851–1856.

130. Nolte Kennedy, M. S., & Rodgers, V. M. (2006). Type 1 diabetes: current perspective. *Diabetes Spectrum*, 19(2), 86-92. doi:10.2337/diaspect.19.2.86

131. Norhammar A, Tenerz A, Nilsson G, Hamsten A, Efendíc S, Rydén L, Malmberg K. Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study. Lancet. 2002 Jun 22;359(9324):2140-4. doi: 10.1016/S0140-6736(02)09089-X. PMID: 12090978.

132. Oh R, Gilani B, Uppaluri KR. Low-Carbohydrate Diet. [Updated 2023 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537084/

133. Okur, Mehmet Evren, Ioannis D. Karantas, and Panoraia I. Siafaka. "Diabetes mellitus: A review on pathophysiology, current status of oral medications and future perspectives." (2017).

134. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman Med J. 2012 Jul;27(4):269-73. doi: 10.5001/omj.2012.68. PMID: 23071876; PMCID: PMC3464757.

135. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman Med J. 2012 Jul;27(4):269-73. doi: 10.5001/omj.2012.68. PMID: 23071876; PMCID: PMC3464757.

136. Ozougwu, J. C., Obimba, K. C., Belonwu, C. D., & Un

137. Pasquel F.J., Umpierrez G.E. Hyperosmolar hyperglycemic state: A historic review of the clinical presentation, diagnosis, and treatment. Diabetes Care. 2014;37(11):3124–3131. doi: 10.2337/dc14-0984.

138. Petersen MC, Shulman GI. Mechanisms of Insulin Action and Insulin Resistance. Physiol Rev. 2018 Oct 1;98(4):2133-2223. doi: 10.1152/physrev.00063.2017. PMID: 30067154; PMCID: PMC6170977.

139. Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in Type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabet Med. 2008 Jul;25(7):765-74. doi: 10.1111/j.1464-5491.2008.02486.x. PMID: 18644063.

140. Pouwer, F., Kupper, N., & Adriaanse, M. C. (2010). Does emotional stress cause type 2 diabetes mellitus? A review from the European Depression in Diabetes (EDID) Research Consortium. *Discovery medicine*, *9*(45), 112-118.

141. Rachdaoui N. Insulin: The Friend and the Foe in the Development of Type 2 Diabetes Mellitus. Int J Mol Sci. 2020 Mar 5;21(5):1770. doi: 10.3390/ijms21051770. PMID: 32150819; PMCID: PMC7084909.

142. Ralph A. DeFronzo MD,, Ele Ferrannini MD,, Paul Zimmet AO, MD, PhD, FRACP, FRCP, FTSE,, K. George M. M. Alberti, 6 March 2015

143. Riddle MC, Bolli GB, Ziemen M, Muehlen-Bartmer I, Bizet F, Home PD; EDITION 1 Study Investigators. New insulin glargine 300 units/mL versus glargine 100 units/mL in people with type 2 diabetes using basal and mealtime insulin: glucose control and hypoglycemia in a 6-month randomized controlled trial (EDITION 1). Diabetes Care. 2014 Oct;37(10):2755-62. doi: 10.2337/dc14-0991. Epub 2014 Jul 30. PMID: 25078900.

144. Roglic, Gojka. WHO Global report on diabetes: A summary. International Journal of Noncommunicable Diseases 1(1):p 3-8, Apr–Jun 2016. | DOI: 10.4103/2468-8827.184853

145. Rorsman P, Ashcroft FM. Pancreatic β-Cell Electrical Activity and Insulin Secretion: Of Mice and Men. Physiol Rev. 2018 Jan 1;98(1):117-214. doi: 10.1152/physrev.00008.2017. PMID: 29212789; PMCID: PMC5866358.

146. Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, McManus K, Champagne CM, Bishop LM, Laranjo N, Leboff MS, Rood JC, de Jonge L, Greenway FL, Loria CM, Obarzanek E, Williamson DA. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med. 2009 Feb 26;360(9):859-73. doi: 10.1056/NEJMoa0804748. PMID: 19246357; PMCID: PMC2763382.

147. Salas-Salvadó J, Bulló M, Babio N, Martínez-González MÁ, Ibarrola-Jurado N, Basora J, Estruch R, Covas MI, Corella D, Arós F, Ruiz-Gutiérrez V, Ros E; PREDIMED Study Investigators. Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care. 2011 Jan;34(1):14-9. doi: 10.2337/dc10-1288. Epub 2010 Oct 7. Erratum in: Diabetes Care. 2018 Oct;41(10):2259-2260. doi: 10.2337/dc18-er10. PMID: 20929998; PMCID: PMC3005482.

148. Sambal H., De Backer C., & Van Houtte M. (2021). The mediating role of stress in the relation between food insecurity and emotional eating in European young adults. Appetite, 157, 104986.

149. Samuel VT, Shulman GI. The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. J Clin Invest. 2016 Jan;126(1):12-22. doi: 10.1172/JCI77812. Epub 2016 Jan 4. PMID: 26727229; PMCID: PMC4701542.

150. Samuel VT, Shulman GI. The pathogenesis of insulin resistance: integrating signaling pathways and substrate flux. J Clin Invest. 2016 Jan;126(1):12-22. doi: 10.1172/JCI77812. Epub 2016 Jan 4. PMID: 26727229; PMCID: PMC4701542.
151. Scheiner, Gary, et al. "Insulin pump therapy guidelines for successful outcomes." The diabetes educator 35.2_suppl (2009): 29S-41S.
152. Schramm TK, Gislason GH, Køber L, Rasmussen S, Rasmussen JN, Abildstrøm SZ, Hansen ML, Folke F, Buch P, Madsen M, Vaag A, Torp-Pedersen C. Diabetes patients requiring glucose-lowering therapy and nondiabetics with a prior myocardial infarction carry the same cardiovascular risk: a population study of 3.3 million people. Circulation. 2008 Apr 15;117(15):1945-54. doi: 10.1161/CIRCULATIONAHA.107.720847. Epub 2008 Mar 31. PMID: 18378618.
153. Secrest AM, Becker DJ, Kelsey SF, Laporte RE, Orchard TJ. Cause-specific mortality trends in a large population-based cohort with long-standing childhood-onset type 1 diabetes. Diabetes. 2010 Dec;59(12):3216-22. doi: 10.2337/db10-0862. Epub 2010 Aug 25. PMID: 20739685; PMCID: PMC2992785.
154. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest. 2006 Jul;116(7):1793-801. doi: 10.1172/JCI29069. Erratum in: J Clin Invest. 2006 Aug;116(8):2308. PMID: 16823477; PMCID: PMC1483173.
155. Shomali M. Optimizing the Care of Patients with Type 2 Diabetes Using Incretin-Based Therapy: Focus on GLP-1 Receptor Agonists. Clin Diabetes. 2014 Jan;32(1):32-43. doi: 10.2337/diaclin.32.1.32. PMID: 26246677; PMCID: PMC4521427.

156. Shuai HeYue Yu, Peng-quan Chen, Hui-min Sun, Xin-ran Gao, Huai-zhi Sun, Jin-fang Ge, 03 July 2024.
157. Slavin J, Carlson J. Carbohydrates. Adv Nutr. 2014 Nov 14;5(6):760-1. doi: 10.3945/an.114.006163. PMID: 25398736; PMCID: PMC4224210.
158. Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: a meta-analysis. Diabetes Care. 2006 Nov;29(11):2518-27. doi: 10.2337/dc06-1317. PMID: 17065697.
159. Stover P. J., Caudill M. A., Field M. S., & Julian M. V. (2023). Genomics and epigenomics in nutrition and health. Nutrition Reviews, 81(5), 405-425.
160. Stover PJ, Field MS, Andermann ML, Bailey RL, Batterham RL, Cauffman E, Frühbeck G, Iversen PO, Starke-Reed P, Sternson SM, Vinoy S, Witte AV, Zuker CS, Angelin B. Neurobiology of eating behavior, nutrition, and health. J Intern Med. 2023 Nov;294(5):582-604. doi: 10.1111/joim.13699. Epub 2023 Aug 3. PMID: 37424220.
161. Sunday S. R., Halmi K. A., & Einhorn A. (1997). The Yale-Brown-Cornell Eating Disorder Scale: a new scale to assess eating disorder symptomatology. International Journal of Eating Disorders, 21(3), 315-319.
162. Sunday SR, Halmi KA. Eating behavior and eating disorders: the interface between clinical research and clinical practice. Psychopharmacol Bull. 1997;33(3):373-9. PMID: 9550881.
163. Sung J, Lee K, Song YM, Lee MK, Lee DH. Heritability of eating behavior assessed using the DEBQ (Dutch Eating Behavior Questionnaire) and weight-related traits: the Healthy Twin Study.

Obesity (Silver Spring). 2010 May;18(5):1000-5. doi: 10.1038/oby.2009.389. Epub 2009 Oct 29. PMID: 19876000.

164. Sung J., & Lee K. (2010). The effects of stress on eating behavior among women with high and low disinhibition. Eating Behaviors, 11(4), 218-222.

165. T.; Liu, L.F.; Lamendola, C.; Shen, L.; Morton, J.; Rivas, H.; Winer, D.; Tolentino, L.; Choi, O.; Zhang, H.; et al. T-cell profile in adipose tissue is associated with insulin resistance and systemic inflammation in humans. *Arterioscler. Thromb. Vasc. Biol.*2014.

166. Tabák, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimäki, M. (2012). Prediabetes: a high-risk state for diabetes development. *The Lancet*, 379(9833), 2279-2290. doi:10.1016/S0140-6736(12)60283-9.

167. Thompson-Brenner, H., Shingleton, R. M., & Thompson, D. R. (2013). Reducing dropout in the treatment of eating disorders: Outcomes at 1-year follow-up. Behaviour Research and Therapy, 51(12), 732-739.

168. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001 May 3;344(18):1343-50. doi: 10.1056/NEJM200105033441801. PMID: 11333990.

169. Ueno N., Inui A., Iwasaki T., & Otani K. (2016). Neural circuits of feeding regulation in the hypothalamus. Obesity Research & Clinical Practice, 10(5), 574-585.

170. Umpierre D, Ribeiro PA, Schaan BD, Ribeiro JP. Volume of supervised exercise training impacts glycaemic control in patients with

type 2 diabetes: a systematic review with meta-regression analysis. Diabetologia. 2013 Feb;56(2):242-51. doi: 10.1007/s00125-012-2774-z. Epub 2012 Nov 16. PMID: 23160642.

171. Umpierrez GE, P Kovatchev B. Glycemic Variability: How to Measure and Its Clinical Implication for Type 2 Diabetes. Am J Med Sci. 2018 Dec;356(6):518-527. doi: 10.1016/j.amjms.2018.09.010. Epub 2018 Oct 2. PMID: 30447705; PMCID: PMC6709582.

172. Valensi P. Biphasic insulin aspart 30/70 (BIAsp 30) in the treatment of type 1 and type 2 diabetes. Diabetes Metab Syndr Obes. 2009 Jun 3;2:61-71. doi: 10.2147/dmsott.s3408. PMID: 21437119; PMCID: PMC3048020.

173. Van Strien T., &Oosterveld P. (2008). The concurrent validity of the DEBQ Emotional Eating Scale with emotional eating behavior and Body Mass Index in a community sample. Psychological Reports, 102(2), 289-297.

174. Walsh BT. The importance of eating behavior in eating disorders. Physiol Behav. 2011 Sep 26;104(4):525-9. doi: 10.1016/j.physbeh.2011.05.007. Epub 2011 May 8. PMID: 21570418; PMCID: PMC3139829.

175. Wang, P. Y., Fang, J. C., Gao, Z. H., Zhang, C., & Xie, S. Y. (2016). Higher intake of fruits, vegetables or their fiber reduces the risk of type 2 diabetes: A meta-analysis. *Journal of diabetes investigation*, *7*(1), 56-69.

176. Wellen KE, Hotamisligil GS. Inflammation, stress, and diabetes. J Clin Invest. 2005 May;115(5):1111-9. doi: 10.1172/JCI25102. PMID: 15864338; PMCID: PMC1087185.

177. Wensveen, F.M.; Valentić, S.; Šestan, M.; Turk Wensveen, T.; Polić, B. The “Big Bang” in obese fat: Events initiating obesity-induced adipose tissue inflammation. *Eur. J. Immunol.* 2015, *45*, 2446–2456.

178. WHO - Diabetes Fact Sheet: https://www.who.int/news-room/fact-sheets/detail/diabetes#

179. William B. Kannel, Lipids, diabetes, and coronary heart disease: Insights from the Framingham Study, American Heart Journal, Volume 110, Issue 5, 1985, Pages 1100-1107, ISSN 0002-8703

180. Wilson, G. T., Grilo, C. M., &Vitousek, K. M. (2007). Psychological treatment of eating disorders. American Psychologist, 62(3), 199-216.

181. Wingard, Deborah L., and Elizabeth Barrett-Connor. "Heart disease and diabetes."*Diabetes in America* 2.1 (1995): 429-448.

182. Wonderlich, S. A., Peterson, C. B., Crosby, R. D., Smith, T. L., Klein, M. H., Mitchell, J. E., ... & Crow, S. J. (2014). A randomized controlled comparison of integrative cognitive-affective therapy (ICAT) and enhanced cognitive-behavioral therapy (CBT-E) for bulimia nervosa. Psychological Medicine, 44(3), 543-553.

183. Zigman J. M., Bouret S. G., & Andrews Z. B. (2016). Obesity impairs the action of the neuroendocrine ghrelin system. Trends in Endocrinology & Metabolism, 27(1), 54-63.