AGRICULTURAL UNIVERSITY OF ATHENS
DEPARTMENT OF FOOD SCIENCE & HUMAN NUTRITION

POST GRADUATE PROGRAMME
FOOD, NUTRITION & HEALTH

Master Thesis

Consumption of vegetable protein sources and their association in individuals with impaired fasting glucose or type 2 diabetes mellitus

Eleni S. Mellou

Supervisor:
Magriplis Emmanuella, Assistant Professor AUA

Athens, 2024

AGRICULTURAL UNIVERSITY OF ATHENS
DEPARTMENT OF FOOD SCIENCE & HUMAN NUTRITION

Master Thesis

Consumption of vegetable protein sources and their association in individuals with impaired fasting glucose or type 2 diabetes mellitus

Κατανάλωση πηγών πρωτεΐνης φυτικής προέλευσης και η συσχέτισή τους σε άτομα με διαταραχές στη γλυκόζη ή σακχαρώδη διαβήτη τύπου 2

Eleni S. Mellou

Examination Committee:
Magriplis Emmanuella, Assistant Professor AUA (Supervisor)
Poulia Kalliopi Anna, Assistant Professor AUA
Zampelas Antonios, Professor AUA

Consumption of vegetable protein sources and their association in individuals with impaired fasting glucose or type 2 diabetes mellitus

MSc: Food, Nutrition & Health
Department of Food Science & Human Nutrition

Abstract

Aim: Vegetable protein sources are characterized by their rich content of fiber, antioxidants, and minerals, all of which have been scientifically demonstrated decrease the development of IFG and/or T2DM. The aim of this study was to assess the relationship between the consumption of vegetable protein sources, in Greek adults, using a representative sample and glucose status; Normal glucose levels, IFG and T2DM.

Methodology: For this study, from total HNNHS sample, a subgroup of 982 participants only from urban cities (Athens and Thessaloniki), were included, because all the necessary biochemical and anthropometric measurements were collected only in these cities. All the participants were adults and consisted of individuals that have reported/ diagnosed with T2DM, people on any diabetic medication/ treatment, irrespective of T2DM report and people that were unaware or undiagnosed, but post blood sampling results were classified as IFG or with T2DM. Clinical examinations such as blood results for fasting glucose and insulin levels, and other health indicators, were performed. Individuals were interviewed in order to collect data on their medical history and medication and supplement use, socioeconomical status, quality of life (QoL) and lifestyle status (alcohol intake, smoking, physical activity, sleeping). In order to measure the consumption of vegetable protein two 24-hour dietary recalls were collected. Vegetable protein consumption was analyzed in grams (gr) with the use of USDA food database and the mean average of the consumption was calculated for each participant. Logistic regression analyses was then performed to determine the relationship between vegetable protein consumption and glucose status. The analysis was stratified by total vegetable protein % of TEI, animal protein % of TEI, saturated fat % of TEI, total energy, MedDiet score, smoking status, sex, age, educational status and marital status.

Results: Individuals with impaired glucose status consumed more vegetable protein compared to those with normal glucose levels (4.8% to 5.4% of their total energy intake of their total caloric intake). Results showed that current smokers specifically with IFG/T2D were those with the highest consumption (5.5% of TEI compared to 4.9% of smokers with normal glucose. The likelihood of impaired glucose status increased for individuals at the highest tertile of intake for vegetable protein (OR: 1.44, 95%CI: 1.04-2.23). When analysis was stratified by smoking status, the relationship remained significant only for current smokers (OR: 2.5, 95%CI: 1.19-5.31).

Conclusions: From this study, a relation between smokers and the consumption of vegetable protein in individuals with IFG and/or T2DM. This effect is not yet understood as it isn't known whether a smoking-related mechanism is responsible or whether it comes from the type of vegetable sources that smokers consume. Therefore, it is important to perform additional research in Greek population that will categorize the

sources of vegetable protein to understand exactly the relation between vegetable protein, IFG and/or T2DM and smoking.

Scientific area: Human nutrition

Keywords: Diabetes mellitus type, Impaired fasting glucose, Glucose status, Vegetable protein, Animal protein, Saturated fat, Greek Population, Smoking, MedDiet score

Κατανάλωση πηγών πρωτεΐνης φυτικής προέλευσης και η συσχέτιση τους σε άτομα με διαταραχές στη γλυκόζη ή σακχαρώδη διαβήτη τύπου 2

MSc: Τρόφιμα, Διατροφή & Υγεία
Τμήμα Επιστήμης Τροφίμων & Διατροφής του Ανθρώπου

Περίληψη

Σκοπός: Οι φυτικές πηγές πρωτεΐνης χαρακτηρίζονται από την πλούσια περιεκτικότητά τους σε φυτικές ίνες, αντιοξειδωτικά και μέταλλα, τα οποία έχουν αποδειχθεί επιστημονικά ότι μειώνουν την ανάπτυξη διαταραχών της γλυκόζης νηστείας ή/και του Σακχαρώδη Διαβήτη τύπου 2 (ΣΔ2). Ο στόχος αυτής της μελέτης ήταν να αξιολογήσει τη σχέση μεταξύ της κατανάλωσης πηγών φυτικής πρωτεΐνης, σε Έλληνες ενήλικες, με τη χρήση αντιπροσωπευτικού δείγματος και της κατάστασης γλυκόζης. Φυσιολογικά επίπεδα γλυκόζης, IFG και ΣΔ2.

Μεθοδολογία: Για τη μελέτη αυτή, από το σύνολο του δείγματος HNNHS, συμπεριλήφθηκε μια υποομάδα 982 συμμετεχόντων μόνο από αστικές πόλεις (Αθήνα και Θεσσαλονίκη), επειδή όλες οι απαραίτητες βιοχημικές και ανθρωπομετρικές μετρήσεις συλλέχθηκαν μόνο σε αυτές τις πόλεις. Όλοι οι συμμετέχοντες ήταν ενήλικες και αποτελούνταν από άτομα που ανέφεραν/διαγνώστηκαν με ΣΔ2, άτομα σε οποιαδήποτε φαρμακευτική αγωγή/θεραπεία για διαβήτη, ανεξάρτητα από την αναφορά ΣΔ2 και άτομα που δεν γνώριζαν ή δεν είχαν διαγνωστεί, αλλά τα αποτελέσματα μετά την αιμοληψία ταξινομήθηκαν ως άτομα με διαταραχές στη γλυκόζη ή με ΣΔ2. Πραγματοποιήθηκαν κλινικές εξετάσεις όπως αποτελέσματα αίματος για επίπεδα γλυκόζης και ινσουλίνης νηστείας και άλλοι δείκτες υγείας. Τα άτομα ερωτήθηκαν για τη συλλογή δεδομένων σχετικά με το ιατρικό τους ιστορικό και τη χρήση φαρμάκων και συμπληρωμάτων, την κοινωνικοοικονομική κατάσταση, την ποιότητα ζωής (QoL) και την κατάσταση του τρόπου ζωής (κατανάλωση αλκοόλ, κάπνισμα, σωματική δραστηριότητα, ύπνος). Για τη μέτρηση της κατανάλωσης φυτικής πρωτεΐνης συλλέχθηκαν δύο 24ωρες διατροφικές ανακλήσεις. Η κατανάλωση φυτικής πρωτεΐνης αναλύθηκε σε γραμμάρια (gr) με τη χρήση της βάσης δεδομένων τροφίμων του USDA και υπολογίστηκε ο μέσος όρος της κατανάλωσης για κάθε συμμετέχοντα. Στη συνέχεια πραγματοποιήθηκαν αναλύσεις λογιστικής παλινδρόμησης για να προσδιοριστεί η σχέση μεταξύ της κατανάλωσης φυτικής πρωτεΐνης και της κατάστασης γλυκόζης. Η ανάλυση στρωματοποιήθηκε με βάση τη συνολική φυτική πρωτεΐνη % του TEI, τη ζωική πρωτεΐνη % του TEI, τα κορεσμένα λιπαρά % του TEI, τη συνολική ενέργεια, τη βαθμολογία MedDiet, την κατάσταση καπνίσματος, το φύλο, την ηλικία, την εκπαιδευτική κατάσταση και την οικογενειακή κατάσταση.

Αποτελέσματα: Τα άτομα με διαταραχές στη γλυκόζη κατανάλωναν περισσότερη φυτική πρωτεΐνη σε σύγκριση με εκείνα με φυσιολογικά επίπεδα γλυκόζης (4,8% έως 5,4% της συνολικής ενεργειακής πρόσληψης της συνολικής θερμιδικής τους πρόσληψης). Τα αποτελέσματα έδειξαν ότι οι σημερινοί καπνιστές ειδικά με IFG/T2D ήταν εκείνοι με την υψηλότερη κατανάλωση (5,5% του TEI σε σύγκριση με 4,9% των καπνιστών με φυσιολογική γλυκόζη. Η πιθανότητα μειωμένης κατάστασης γλυκόζης αυξήθηκε για τα άτομα με το υψηλότερο τριπλό πρόσληψης φυτικής πρωτεΐνης (OR:

1,44, 95%CI: 1,04-2,23) Όταν η ανάλυση στρωματοποιήθηκε με βάση την κατάσταση καπνίσματος, η σχέση παρέμεινε σημαντική μόνο για τους σημερινούς καπνιστές (OR: 2,5, 95%CI: 1,19-5,31).

Συμπεράσματα: Από αυτή τη μελέτη, μια σχέση μεταξύ των καπνιστών και της κατανάλωσης φυτικής πρωτεΐνης σε άτομα με IFG ή/και ΣΔ2. Αυτό το αποτέλεσμα δεν είναι ακόμη κατανοητό καθώς δεν είναι γνωστό εάν ένας μηχανισμός που σχετίζεται με το κάπνισμα ευθύνεται ή αν προέρχεται από τον τύπο φυτικών πηγών που καταναλώνουν οι καπνιστές. Ως εκ τούτου, είναι σημαντικό να πραγματοποιηθεί πρόσθετη έρευνα στον ελληνικό πληθυσμό που θα κατηγοριοποιήσει τις πηγές φυτικής πρωτεΐνης για να κατανοήσει ακριβώς τη σχέση μεταξύ φυτικής πρωτεΐνης, IFG ή/και ΣΔ2 και καπνίσματος.

Επιστημονικός περιοχή: Διατροφή ανθρώπου

Λέξεις κλειδιά: Σακχαρώδης διαβήτης τύπου 2, Διαταραγμένη γλυκόζη νηστείας, Κατάσταση γλυκόζης, Φυτική πρωτεΐνη, Ζωική πρωτεΐνη, Κορεσμένα λιπαρά, Ελληνικός πληθυσμός, Κάπνισμα, Βαθμολογία MedDiet

Acknowledgements

This thesis was conducted at the Agricultural University of Athens (AUA) as part of the postgraduate programme "Food, Nutrition & Health" in the field of "Nutrition, Public Health & Policies". Upon the conclusion of the study, I would want to express my sincere appreciation to all the people who provided me with their assistance during its process.

Initially, I would like to express my sincere gratitude to Assistant Professor Emmanuella Magripli, who was also my supervisor and member of the three-member examination committee. Her invaluable assistance was evident throughout all stages of the thesis, including organization and guidance and sharing all of her expertise in research and biostatistics.

I would like to express my gratitude to Assistant Professor, Anna Poulia and Professor, Antonios Zampelas for agreeing to serve as members of the assessment committee for my thesis.

Lastly, I would want to express my honest gratitude and thanks to my family and friends, and especially to Magda Kontogianni, for their constant encouragement and help.

With my permission, this paper has been checked by the Examining Board through plagiarism detection software available at the AUA and cross-checked for validity and originality

Table of contents

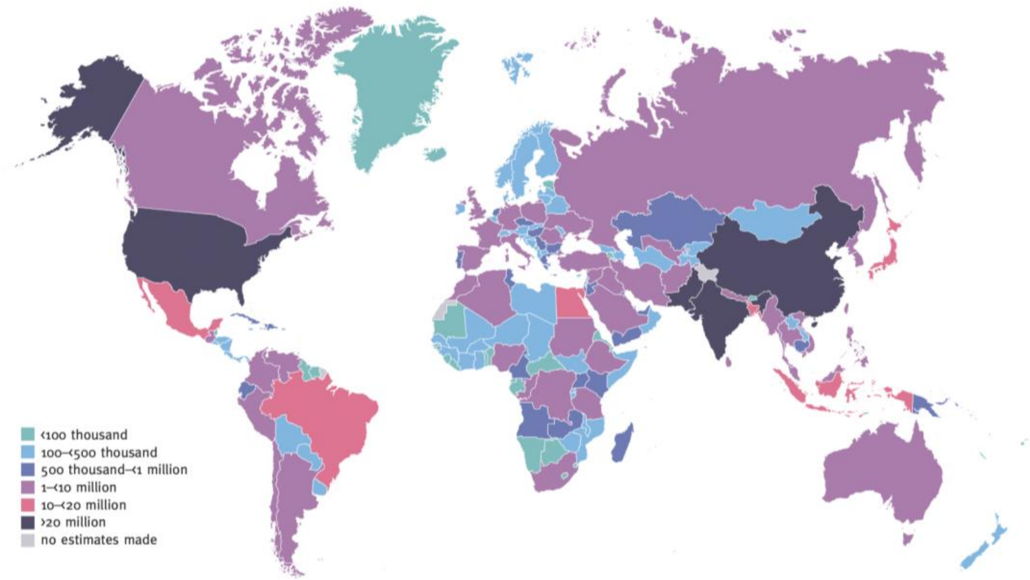
Graphs

Tables

1. Introduction

1.1 Type 2 Diabetes Mellitus

Type 2 Diabetes Mellitus (T2DM) is one of the most prevalent metabolic diseases worldwide, and its development is mostly due to a combination of two main factors: inadequate insulin secretion by pancreatic -cells and/or the failure of insulin-sensitive tissues to respond to insulin (1). Hence, the molecular mechanisms involved in the production and release of insulin, in addition to the insulin response in tissues, must be strictly regulated. Thus, errors in any of the relevant systems might result in a metabolic imbalance that contributes to the etiology of type 2 diabetes. Over 90% of all cases of diabetes, globally, are T2DM, making it the most prevalent. In T2DM, insulin resistance (IR), or the body's cells' failure to adequately respond to insulin, is the original cause of hyperglycemia. Insulin resistance causes the hormone to become less effective, which eventually causes an increase in insulin production. The inability of the pancreatic beta cells to meet demand over time can result in inadequate insulin production. Type 1 diabetes mellitus, often known as T1DM, and non-insulin-dependent diabetic mellitus, often known as T2DM, are the two main types of diabetes. Ninety to ninety-five percent of diabetic patients have T2DM, the most common type of the disease (1,2).

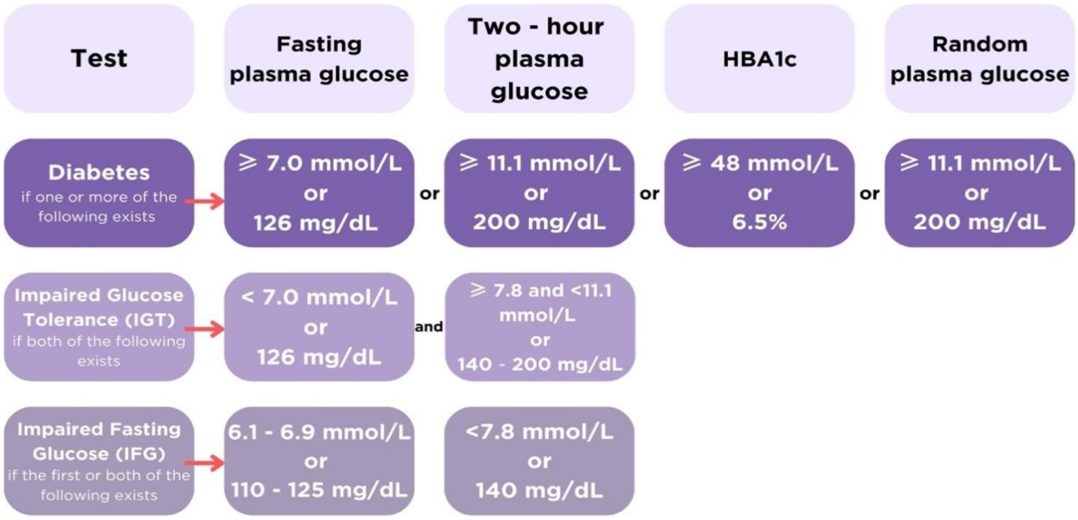


Graph 1. Diabetes Global Prevalence

DF Diabetes Atlas - Tenth Edition. IDF Diabetes Atlas. (n.d.). Retrieved January 26, 2023, from https://diabetesatlas.org/

1.2 Impaired glucose tolerance and impaired fasting glucose

Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) are conditions characterized by elevated blood glucose levels that are above the normal range but below the diabetes diagnostic cutoff. Alternative terminology includes "prediabetes," "non-diabetic hyperglycemia," and "intermediate hyperglycemia." IGT and IFG are significant for three reasons. First, they suggest a higher chance of developing T2DM in the future, second, they show an elevated risk of cardiovascular disease and third they can be used as an indicator for preventive therapies for T2DM (2).



Graph 2. Diagnostic criteria for T2DM, IGT and IFG

IDF Diabetes Atlas - Tenth Edition. IDF Diabetes Atlas. (n.d.). Retrieved January 26, 2023, from https://diabetesatlas.org/

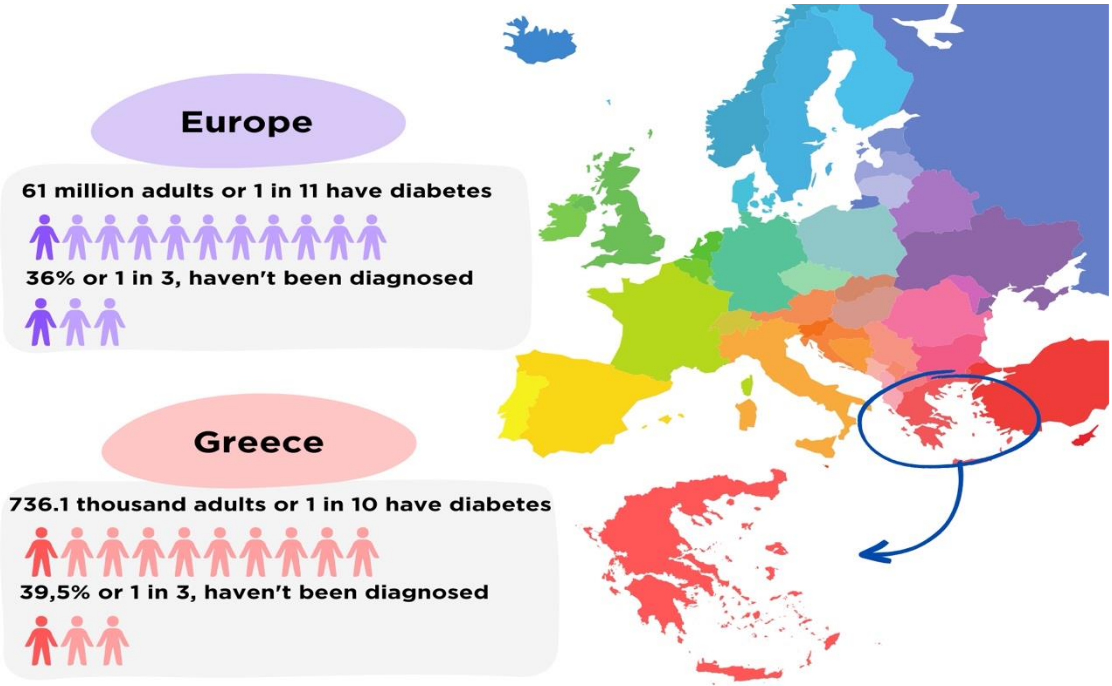
1.3 Type 2 Diabetes Mellitus and Public Health

Globally, T2DM is exceedingly prevalent and increasing. T2DM is expected to impact 462 million people worldwide, or 6.28% of the world's population. It is projected that 462 million individuals, or 6.28% worldwide, will have T2DM. This condition accounted for over one million deaths in 2017, ranking it as the ninth leading cause of death. In 1990, T2DM was listed as the eighteenth leading cause of mortality. This increase is concerning and is a result of urbanization, economic expansion, population ageing all of which encourage sedentary lifestyles and increased consumption of foods associated with obesity. (2)

Diabetes is the sixth most prevalent disease in terms of disability-adjusted life years (DALYs), which measure human suffering. In the world, 537 million individuals (20-79 years) have diabetes (1 in 10 people). (2) In 2019, there were 66.3 million DALYs attributable T2DM, and when they were stratified by age there was 801.5 DALYs per 100,000 population, which was 27.6% increased by 1990. (3) According to projections, there will be 643 million adults worldwide who have diabetes by 2030 and 784 million (1 in 8 adults) by 2045. The projected prevalence of diabetes in women between the ages of 20 and 79 is marginally lower than in men. Age is associated with a higher prevalence of diabetes, as indicated by diabetes prevalence data. (3,4) The lowest prevalence was found in ages from 20 to 24 (2.2% in 2021). Diabetes prevalence among adults aged 75–79 years is projected to reach 24.7% in 2045. The aging of the global population will result in an increase in the proportion of diabetics over the age of 60. (2) The global incidence of T2DM was marginally higher in men in 2019, and it exhibited an age-dependent increase until the 85-89 and 80-84 age groups for men and women, respectively, before declining. Similarly, the number of DALYs increased with age, peaking for males and females between the ages of 60 and 64 and 65 and 69, respectively, before declining with age. (4)

Nearly 90% of these individuals reside in low- and middle-income nations. The distribution pattern of T2DM prevalence corresponds to socioeconomic development. The prevalence rates in developed regions, such as Western Europe, are significantly higher and continue to rise despite public health measures. The rate of growth does not appear to be decelerating. (3,4) Globally, metabolic risk factors (i.e. high BMI > 25 kg/m^2) and lifestyle habits (i.e. poor nutrition, smoking and lack of physical activity) are strongly associated with the prevalence of diabetes. In 2017, elevated BMI, poor diet, and environmental pollution were the top three risk factors. Increased BMI accounted for 45.8% of DALYs and 30.8% of deaths. Dietary risk accounted for 24.7% of deaths and 34.9% of DALYs; environmental pollution caused 15.4% of DALYs and 13.4% of deaths. (3,4)

Around 240 million patients with diabetes are believed to go undiagnosed. In Europe specifically, 61 million persons (or one in eleven adults) have diabetes, and 36% (or one in three) haven't been diagnosed. (2,3,4) In Greece, 736.1 thousand adults (or 1 in 10) have diabetes, and 39,5% of persons lack a diagnosis. Approximately 453,000 individuals aged >18 years could have T2DM. (2,5).



Graph 3. Diabetes Europe and Greece Prevalence

Multiple organizations have established definitions for prediabetes based on diverse criteria. The World Health Organization (WHO) classifies prediabetes as intermediate hyperglycemia characterized by two specific parameters: impaired fasting glucose (IFG), which is defined as fasting plasma glucose (FPG) between 6.1-6.9 mmol/L (110-125 mg/dL), and impaired glucose tolerance (IGT), which is established after 75 g of oral glucose load ingestion results in plasma glucose levels between 7.8-11.0 mmol/L (140-200 mg/dL), after two hours. The American Diabetes Association (ADA) has added hemoglobin A1c (HbA1c) based criteria of a level of 5.7% to 6.4% for the definition of prediabetes, while maintaining the same cut-off value for IGT (140-200 mg/dL) and a lower cut-off value for IFG (100-125 mg/dL). The prevalence of those classified as having prediabetes increased due to the ADA's modification. This adjustment was made in an effort to balance the proportion of IFG and IGT people in the prediabetic population. There are divergent views regarding the justification for lowering the IFG cut-off values used to assess the likelihood of developing future T2DM. (6,7,8)

Multiple studies indicate that HbA1c and IFG and IGT do not correlate strongly. As a result of the inability of these blood glucoses cut points to identify diabetes-related pathologies and the probability of developing diabetes in the future, the diagnostic validity of prediabetes and diabetes using IFG and IGT has been called into question. The lack of repeatability of the assessments in both children and adults further undermines the validity of these cut-offs. (7,8)

The prevalence of IFG and IGT varies widely (9). Both are projected to rise in the near future. The prevalence of IGT among the adult population was evaluated by the IDF as 7.5% (373.9 million) in 2019. Projections indicate that this figure will increase to 8.6% by 2045, coinciding with the growth of the global population, and will thus impact 548.4 million individuals. (7). In addition, 541 million individuals, or one in ten, have impaired glucose tolerance, which increases their future risk of developing T2DM. Nonetheless, the increased survival rate and positive outcomes that result from earlier detection and more effective treatment are also factors in the increase in prevalence. Five years following IGT or IFG diagnosis, there is an estimated cumulative incidence of T2DM development of 26% and 50%, respectively. (2) In Greece, individuals with IFG were close to 30% in the two main metropolitan areas (Athens and Thessaloniki) where more than 60% of the country's population resides. (5).

Based on these findings, it appears that modifiable risk factors, including but not limited to physical inactivity, an energy dense and nutrient deficient diet, and overweight or obesity, can be targeted during prediabetes to prevent or postpone the development of type 2 diabetes mellitus. (10) Results from the Diabetes Prevention Program, showed that participants who tried to lose 7 percent of their body weight and maintain that weight loss by lowering their calorie and fat intake plus exercising 150 minutes per week continued to have a delay in the development of diabetes by 27 percent. (10). Both medication and lifestyle changes are successful at preventing the onset of T2DM in those with prediabetes, while lifestyle changes have longer-lasting results. In addition, patients with IGT benefit notably from lifestyle adjustment in contrast to those with IFG. Overall, risk stratification utilizing prediction models is advised, where the full range of glucose tolerance, including various pre-diabetic conditions, is considered. On this basis, risk group-specific interventions can be created. (6,7,8)

Graph 4. Modifiable T2DM risk factors

1.4 Risk factors and possible causes of type 2 Diabetes Mellitus

While the precise etiology of T2DM remains uncertain, a discernible association can be established between obesity and overweight, advancing age, ethnic origin, and genetics. It is postulated that environmental stimuli and polygenic factors, similar to those associated with T1DM, may elevate the susceptibility to T2DM. The cornerstone of T2DM care is the promotion of a lifestyle that consists of a balanced diet, regular exercise, ceasing smoking, and maintaining a healthy body weight. When lifestyle modifications fail to reduce blood glucose levels, oral medication is frequently initiated, with metformin being the initial treatment option. This contributes to enhanced T2DM management. (11).

Table 1. Risk factors for T2DM
Overweight or Obese
Family History
Genetic Factors
Diet
Sedentary Lifestyle
Metabolic Syndrome
Age
Smoking
Low socio-economic factors
Gestational Diabetes mellitus or delivery of neonates >4 kg in weight
Low quality of Sleep
Vitamin D deficiency
Psychosocial stress and depression

1.4.1 Lifestyle

The increase in T2DM is a consequence of lifestyle changes that have resulted in an increase weight (obesity or overweight), and low physical activity levels. Lifestyle changes on top of any underlying genetic susceptibility, exacerbate insulin resistance, which, in combination with progressive -cell failure, causes nondiabetic glycemia to rise. Insulin resistance and impaired insulin secretion come with a number of significant cardiovascular disease risk factors, such as hypertension and dyslipidemia, in addition to the risk for diabetes. As insulin secretion continues to decline over time, glycemia rises and diabetes develops, both of which are linked to the emergence of microvascular and cardiovascular problems. Diabetes can be prevented or delayed through lifestyle interventions. The main aspects of lifestyle include diet, physical activity, sleep and anxiety. T2DM is widely thought to be primarily caused by an energy-dense Western dietary pattern combined with a sedentary lifestyle (often referred to as inactivity). The present worldwide obesity pandemic, which is strongly linked with the growing prevalence of T2DM, is attributed to inactivity and energy dense (probably along with nutrient poor) diets (9,10).

1.4.2 Diet

Dietary patterns that lack of phytochemicals, fiber, or plant food in general increase the relative risk for T2DM by 44% to triple. (10) Regular intake of drinks with added sugar carries a 20–30% higher relative risk than abstinence. A diet abundant in high-quality lipids and carbohydrates (low in trans fatty acids, high in polyunsaturated fatty acids, and with a low glycemic index and glycemic load) is essential for the prevention of T2DM, as opposed to a diet deficient in these nutrients. A diet high in whole grains, fruits, vegetables, nuts, seeds, and legumes and low in refined grains, red or processed meat, and sugar-sweetened beverages is typically recommended for the prevention of T2DM. A substantial correlation exists between adhering to a high-quality diet, such as the Mediterranean diet, and a reduced prevalence of type 2 diabetes mellitus. (11,12)

Nowadays, there is a big interest towards the consumption of vegetable protein instead of animal protein and how it effects insulin resistance. Research has shown that vegetable diets lower insulin resistance and enhance glycemic control through a number of hypothesized mechanisms (13,14). Overall vegetable diets are also low in saturated fat, advanced glycation end products (AGEs), nitrosamines, factors associated to insulin resistance by several epidemiological and metabolic investigations (13,15).

Saturated fat, predominantly present in animal-derived dietary sources, has a role in the occurrence of lipotoxicity. This phenomenon involves the accumulation of harmful fat metabolites, such as diacylglycerol and ceramide species, within cells of the liver and skeletal muscles. Consequently, this accumulation hinders insulin signaling and subsequently reduces the uptake of glucose. Numerous metabolic and epidemiological studies have established an association between saturated fat and oxidative stress, mitochondrial dysfunction, and insulin resistance. (13,15)

AGEs are oxidative molecules that are found in abundance in meat, particularly when subjected to cooking methods such as grilling, broiling, roasting, searing, or frying. Conversely, vegetable meals such as fruits, vegetables, legumes, and whole grains tend to have lower levels of AGEs. The involvement of AGEs in the development of type 2 diabetes has been suggested, and research has demonstrated that a diet low in these chemicals can enhance insulin resistance in individuals with type 2 diabetes. (13, 16)

The formation of nitrosamines occurs when nitrite and nitrate preservatives present in processed meat react with amino compounds inside the food. Research has demonstrated that these nitrosamines can expedite the process of DNA damage and the production of reactive oxygen species and pro-inflammatory cytokines. Consequently, this can result in oxidative stress and the development of insulin resistance. (13, 17)

Vegetable diets are also characterized by their rich content of fiber, antioxidants, and minerals, all of which have been scientifically demonstrated to exert positive effects on insulin sensitivity. Dietary fiber, only present in vegetable protein source, has a role in regulating the body's reaction to glucose after a meal. Additionally, it undergoes fermentation by gut bacteria, resulting in the production of short-chain fatty acids. These fatty acids further contribute to the improvement of glucose response, insulin signaling, and insulin sensitivity. In addition, dietary fiber has the capacity to lower the energy density of consumed foods, enhance feelings of fullness, and has been linked to the potential for weight reduction, thereby mitigating insulin resistance. In conclusion, adhering to a dietary pattern characterized by a higher consumption of vegetable protein and a lower intake of meat is expected to promote positive metabolic outcomes. This is primarily attributed to the facilitation of alterations in the composition of gut microbiota, leading to a reduction in the synthesis of trimethylamine N-oxide. It is worth noting that this chemical has been implicated in the development of insulin resistance (13).

1.4.3 Physical activity

Physical activity in adults has been found to have positive effects on various health outcomes. These include reducing the risk of all-cause mortality, cardiovascular disease mortality, incident hypertension, incident of type 2 diabetes, and various types of cancer. Additionally, engaging in physical activity has been associated with improved mental health, including reduced symptoms of anxiety and depression, as well as enhanced cognitive health and sleep. Furthermore, measures of adiposity, such as body fat percentage, may also show improvement with regular physical activity.

It is suggested that individuals of adult age engage in consistent physical activity. Specifically, adults should aim to complete a minimum of 150-300 minutes of moderate-intensity aerobic physical activity, or alternatively, 75-150 minutes of vigorous-intensity aerobic physical activity per week. 150 min of walking at an individually fast pace has shown to decrease progression to T2DM by 7% (10). The guidelines for physical activity for children and adolescents are 60min/day of moderate-to-vigorous intensity physical activity across the week (most of which should be aerobic). (18) Alternatively, a combination of moderate and vigorous-intensity activity can be pursued to achieve similar health benefits. Additionally, adults should incorporate muscle-strengthening activities into their routine, focusing on all major muscle groups, at a moderate or higher intensity for at least two days per week, as these activities offer supplementary health advantages. (18) Low levels of physical activity, either during leisure time or at work, have a relative risk that is 40% greater than levels of high overall physical activity. For the prevention of T2DM, increased physical activity as a key component. Research highlights that both weight training and aerobic exercise have positive benefits in preventing T2DM (18,19).

In parallel with enhanced mitochondrial function, short-term aerobic exercise training increases insulin sensitivity in adults with T2DM. Improved glycemia may be achieved through improved insulin-stimulated glucose clearance and reduction of hepatic glucose synthesis after only 7 days of vigorous aerobic exercise training. In individuals with obesity and T2DM, short-term aerobic exercise increases peripheral insulin sensitivity more than hepatic insulin sensitivity, thereby improving insulin action throughout the entire body. Multiple meta-analyses and systematic reviews have provided evidence supporting the notion that consistent aerobic exercise training yields positive effects on glycemia in individuals diagnosed with T2DM. These effects include a decrease in daily hyperglycemic excursions and a reduction of 0.5-0.7% in hemoglobin HbA1c levels. Regular training has been shown to enhance insulin sensitivity, lipids, blood pressure, other metabolic markers, and fitness levels, irrespective of any associated weight loss.

Resistance exercise training has been found to yield significant improvements in various health parameters among persons with T2DM. These gains include a 10-15% increase in strength, bone mineral density, blood pressure, lipid profiles, skeletal muscle mass, and insulin sensitivity. In conjunction with a slight reduction in body weight, the inclusion of resistance training in the exercise regimen of older persons with T2DM has been shown to result in a three-fold increase in lean skeletal muscle mass and a decrease in HA1c levels. This effect is notably superior to the outcomes observed in a group of individuals who only followed a calorie-restricted diet without engaging in any exercise, which led to a loss of skeletal muscle mass. According to a recent meta-analysis conducted on resistance exercise, it has been found that high-intensity training provides greater advantages compared to low-to-moderate-intensity training in terms of overall glucose control and reduction of insulin levels in people diagnosed with T2DM. The usage of anaerobic pathways during high-intensity training has been observed to potentially elevate blood glucose levels. This effect is attributed to the release of adrenaline and noradrenaline into the bloodstream, which then stimulates the liver to accelerate the release of glucose beyond typical rates.

Interventions involving the integration of aerobic and resistance exercise training have the potential to exhibit improved outcomes compared to either modality of exercise in isolation. According to a meta-analysis, it was found that all three exercise modalities have a positive effect on glycemia and insulin sensitivity. Additionally, it was seen that combined training may lead to higher reductions in HbA1c levels compared to any training mode used alone. (19)

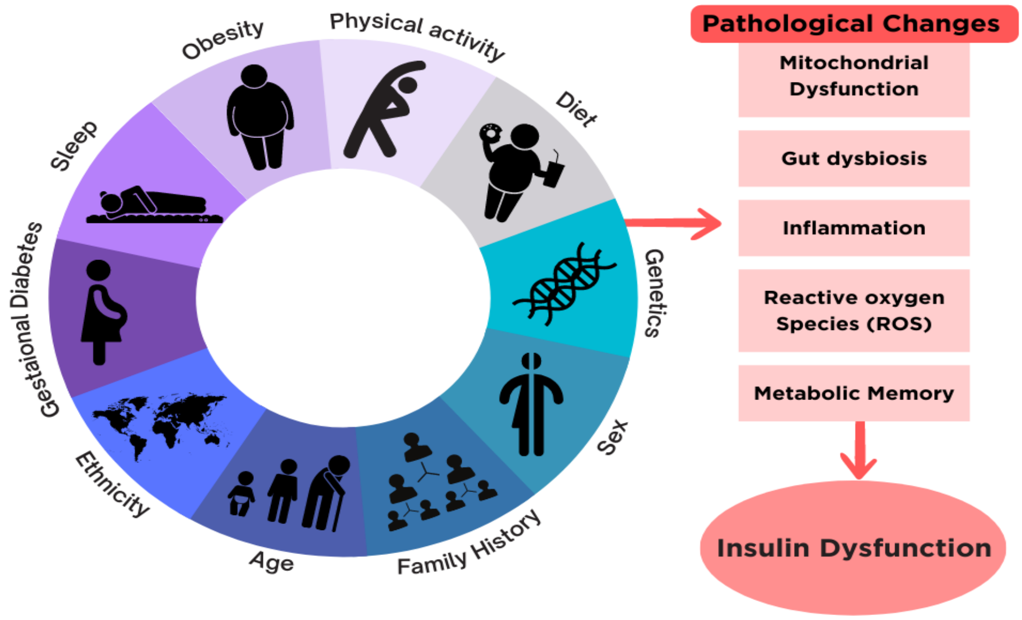
1.4.4 Sleep

Poor sleep quality and insufficient sleep are related with insulin resistance and T2DM. Respectively, each additional hour of insufficient sleep increases the relative risk by around 9% (9). A lack of sleep may cause aberrant glucose metabolism through a number of routes. Complete sleep deprivation dramatically reduces brain's use of glucose. Researchers have repeatedly shown that when sleep is restricted or fragmented, sympathetic nervous system activity rises. It is well established that the functioning of adipocytes, muscle insulin resistance, and insulin and glucagon production are all significantly influenced by sympathetic nervous system activity. Another potential contributing element is hypothalamic-pituitary-adrenal (HPA) axis activation. Several sleep restriction studies found that cortisol levels rise in the afternoon and evening, and these increases may be a factor in insulin resistance. Long-lasting nocturnal growth hormone (GH) release following sleep deprivation might also encourage morning insulin resistance. Additionally, inflammatory markers such as leukocytes, monocytes, IL-1, IL-6, IL-17, TNF-, and hsCRP are increased in response to sleep deprivation. Insulin resistance has been associated with several of these indicators. Inadequate sleep can deregulate hormones that control appetite, food intake, and energy and in this way can promote weight gain and indirectly affect glucose metabolism and diabetes risk (12,20).

1.4.5 Obesity

A significant rise in the risk of type 2 diabetes is one of the many medical, physical, and psychological problems of obesity, which is a chronic and frequently progressive condition. Overweight and obesity are defined as the abnormal or excessive deposition of adipose tissue, which creates a health risk. An individual is classified as overweight if their body mass index (BMI) exceeds 25, and as obese if it exceeds 30. According to the worldwide burden of illness estimates, the number of annual deaths caused by overweight or obesity exceeded 4 million in 2017. (21)

Obesity is the primary and most influential risk factor for T2DM and is associated with metabolic disorders that result in reduced responsiveness to insulin. The exact processes underlying the relationship between obesity, T2DM, and insulin resistance have not yet been fully understood. However, several factors have been linked to the progression of this disease, which includes both cell-specific and interorgan interactions. In contrast, lifestyle modifications such as increased physical activity and higher carbohydrate consumption are related with lower insulin resistance. (21, 22)



Graph 5. Obesity and other T2DM risk factors and pathological changes that finally lead to insulin dysfunction

Adipose tissue controls metabolism by the release of non-esterified fatty acids (NEFAs) and glycerol, hormones, such as leptin and adiponectin, and proinflammatory cytokines. In obese individuals, production of these is increased. Retinol-binding protein-4 (RBP4) develops insulin resistance. In comparison, adiponectin stimulates fatty acid oxidation in a way dependent on AMP-activated protein kinase (AMPK) and peroxisome proliferator- activated receptor- (PPAR-). (22) In addition to adipocyte-derived substances, the increased production of tumor necrosis factor- (TNF-), interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1) and other products of macrophages and other cells that fill adipose tissue may contribute to the development of insulin resistance. TNF- and IL-6 function via various pathways can lead to insulin resistance. (22) Mechanisms involving stimulation of suppression of cytokine signaling (SOCS) proteins and inducible nitric oxide synthase (iNOS) may promote cytokine-induced insulin resistance. (22)

When it comes to modulating insulin sensitivity, the release of NEFAs may be the single most important component. Obesity and T2DM are both associated with elevated NEFA levels, which are related to insulin resistance. Within hours of an acute increase in plasma NEFA levels in humans, insulin resistance occurs. In contrast, insulin-mediated glucose uptake and glucose tolerance improve with an initial drop in NEFA levels following acipimox therapy. The sequential suppression of pyruvate dehydrogenase, phosphofructokinase, and hexokinase II activity may occur from increased intracellular NEFAs due to competition with glucose for substrate oxidation. An increase in NEFA supply or a decrease in intracellular fatty acid metabolism may also raise the intracellular level of fatty acid metabolites such diacylglycerol (DAG), fatty acyl-coenzyme A (fatty acyl-CoA), and ceramides, which may then activate a serine/threonine kinase cascade that leads in serine/threonine phosphorylation of insulin receptor substrate-1 (IRS- Thus, processes subsequent to insulin-receptor signaling decline. Modest weight reduction in patients with type 2 diabetes who are overweight or obese improves glycemia and decreases the need for glucose-lowering medication, while significant weight loss has been found to support long-term diabetic remission for at least two years (11, 22).

1.4.6 Vitamin D

Vitamin D is a secosteroid produced in the skin as a result of UV specific rays. As such, it is very often regarded as a pre-hormone and not as a genuine vitamin. A series of fat steroids known collectively as vitamin D (calciferol) comes in two main forms: vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). To keep levels at normal levels, 10-15 minutes of daily sun exposure (focusing on the hands and face) is generally sufficient (6,7). Diet typically lacks vitamin D, with exceptions made by fatty fish and egg yolks. While vitamin D3 is mostly derived from animal sources, vitamin D2 is produced by plants and it exists in foods that have been fortified with vitamin D (such as milk) or dietary supplements. Vitamin D is easily absorbed by adipose tissue whether it is consumed or made chemically. The recommended dietary allowance (RDA) for vitamin D is 600 international units (IU) per day for those aged 9 to 70 and 800 IU for people over 70 (23).

There is sufficient proof that vitamin D insufficiency has a role in the development of metabolic regulation problems linked to insulin resistance and T2DM. With the development of T2DM comes dysfunction of the liver, muscles, and adipose tissue, which is also linked to vitamin D insufficiency. The connection between vitamin D insufficiency and insulin resistance with inflammatory markers, which are usually enhanced at vitamin D deficiency, is the one that is most commonly discussed among them.

Vitamin D deficiency has been associated with the epidemic of obesity although this remains controversial (24, 25). The prevalence of insufficient levels of vitamin D is frequently observed in individuals with obesity and insulin resistance. The association between low levels of vitamin D and obesity appears to have detrimental effects on insulin resistance and the regulation of glucose levels (25). Previous research has documented the inverse relationship between deficient levels of vitamin D and insulin resistance in several types of studies, including cross-sectional investigations (such as NHANES III) (26), prospective studies (27), and studies examining the effects of vitamin D supplementation (28). The precise mechanisms via which vitamin D reduces the likelihood of insulin resistance have not yet been fully elucidated. Multiple routes have been proposed to be implicated. An inverse relationship between fasting insulin levels or insulin resistance and 25(OH)D3 levels has been demonstrated; this relationship is independent of BMI. (25) The association between Vitamin D insufficiency and an elevation in parathyroid hormone (PTH) levels, which subsequently leads to a loss in insulin sensitivity, has been documented. (25) Moreover, vitamin D plays a crucial role in the regulation of calcium homeostasis and is involved in maintaining optimal intracellular levels of calcium for many intracellular processes in insulin-responsive tissues, including muscle cells. Moreover, it has been observed that pancreatic β-cells contain vitamin D receptors (VDR). Vitamin D plays a role in various biological processes related to insulin, such as regulating insulin production, promoting the development of insulin receptors, and enhancing insulin sensitivity for glucose transport.

In contrast, there are some factors that may explain the correlation between obesity and low levels of Vitamin D that lead to insulin resistance. (24) Obese people have a higher body surface area that is available for the endogenous production of vitamin D in obese persons. In contrast to their leaner or normal-weight counterparts, obese individuals tend to have a sedentary lifestyle, engage in less outdoor activity, and cover up more when outside, hence reducing the endogenous generation of cholecalciferol in the skin. (24)

Vitamin D metabolites also affect the synthesis and secretion of adipokines by adipocytes. Vitamin D was found to have a negative association with leptin or resistin and a positive correlation with adiponectin, according to a number of studies. (25, 29) Adipose tissue inflammation is also significantly influenced by vitamin D3. Obesity is characterized by hypertrophic adipose tissue, which causes an imbalance in blood flow, hypoxia, and macrophage infiltration. Moreover, hypertrophied adipocytes exhibit an increase in the secretion of interleukins 6 and 8 (IL-6, IL-8), resistin, tumor necrosis factor-alpha (TNF-), and monocyte chemoattractant protein-1 (MCP1), and a decrease in the secretion of adiponectin.

Additionally, vitamin D can stop other epigenetic changes in cells and insulin-sensitive peripheral organs, as well as hypermethylation of DNA and the subsequent functional inactivation of numerous genes. Therefore, vitamin D insufficiency is one of the major reasons hastening the development of insulin resistance (25, 29).

1.5 Diabetes type 2 and Health Impact

T2DM develops symptoms that may resemble those of T1DM; however, these symptoms are typically less severe, and the condition can appear without any noticeable symptoms. Consequently, a considerable duration of time typically elapses prior to the formal diagnosis of type 2 diabetes, leading to a substantial proportion, ranging from one-third to one-half, of individuals within the population remaining undiagnosed. In the case of an extended delay in diagnosis, several consequences may arise, including visual impairment, poorly healing ulcers in the lower limbs, as well as the development of heart disease or stroke, which may ultimately prompt the diagnosis. (2, 11)

T2DM can lead to many health complications, particularly affecting the nervous system, vision, the kidneys function, circulatory system, and cardiovascular system. Adults with diabetes have a much higher risk of experiencing heart attacks and strokes, which is two to three times more compared to those without diabetes. When neuropathy occurs in the feet, it increases the likelihood of developing foot ulcers, infections, and ultimately the need for limb amputation, especially when there is reduced blood flow (6, 30). Diabetic retinopathy, a major cause of blindness, is due to progressive and chronic damage to the minuscule blood vessels in the retina. Diabetes leads to visual impairment in more than one million persons. (31). Last but not least, diabetes is one of the main reasons of kidney failure (32). Lastly, diabetes increases the risk of poor outcomes for a number of viral illnesses, including COVID-19 (33).

The fundamental aspect of managing T2DM revolves around the promotion of a lifestyle that encompasses a nutritious diet, consistent engagement in physical activity, cessation of smoking, and the maintenance of a healthy body weight. If lifestyle adjustments are insufficient in controlling blood glucose levels, oral medication, with metformin being the chosen initial option, has to begin. If monotherapy with an antidiabetic medicine is not sufficient, there are several combination treatment alternatives that can be examined. The available alternatives encompass sulphonylureas, thiazolidinediones, glucagon-like peptide 1 (GLP-1) agonists, alpha glucosidase inhibitors, dipeptidyl peptidase 4 (DPP-4) inhibitors, and sodium glucose co-transporter 2 inhibitors. If non-insulin therapies fail to achieve glycemic control, the use of insulin injections may be necessary to regulate hyperglycemia to the optimal levels. (2, 11) It is recommended that health care professionals utilize either an informal assessment of risk factors or an assessment tool to screen for prediabetes and assess the risk T2DM. (34) This aids in determining whether it is worthwhile to conduct a diagnostic test. Both prediabetes and T2DM fulfill the criteria for diseases which require early diagnosis through screening. (8, 34) Both conditions are prevalent and place substantial clinical and public health burdens. The diagnosis of T2DM is frequently preceded by a prolonged presymptomatic phase. (2, 34) The length of the period that an individual experiences glycemic burden is a robust indicator of negative consequences. Effective therapies are available to stop the development of diabetes from prediabetes. Risk models have investigated the benefit, with the overall conclusion that intervention has a higher benefit in individuals at highest risk of diabetes. (34)

According to the most recent National Institutes of Health (NIH) Diabetes Prevention Program Outcomes Study (DPPOS), preventing the transition from prediabetes to diabetes has led to lower rates of complications such as retinopathy and nephropathy. The U.K. Clinical Practice Research Datalink database shown comparable effects on diabetic complications through the implementation of screening, diagnosis, and comprehensive risk factor treatment. The analysis indicates that the transition from prediabetes to diabetes is associated with an increased likelihood of experiencing problems. (34)

Diabetes education, except from dietary modifications, physical activity, and pharmacological interventions, is the key component for a successful treatment. To be able to manage the condition, a patient with T2DM needs the necessary information, skills, and behaviors. (35). Health professionals can assist patients on how to reduce the negative effects of T2DM, prevent complications of the disease, and resume their social roles. The objectives of diabetes education involve the modification of patient behavior, enhancement of motivation to adhere to therapeutic guidelines, improvement of quality of life, establishment of a collaborative relationship within the treatment process, preparation for self-care, elevation of awareness regarding cardiovascular risk factors, and enhancement of psychological resilience. Education plays a crucial role as a highly effective element in the overall therapeutic process. (35) According to studies, it has been shown that only a small percentage, as low as 5%, of patients who get regular education exhibit an inability or unwillingness to adhere to their prescribed treatment. Patients who do not obtain adequate education are more likely to develop diabetes, and patients who did not receive any education are up to four times more likely to experience diabetic complications. (36) The most recent guidelines propose the establishment of a therapeutic team that actively engages in the provision of care for individuals with diabetes. The patients can be informed by medical and trained professionals, such as physicians and nurses, alongside specialized members like a dietitian, a psychologist or a social worker. (35, 37)

1.5.1 Diagnosis of diabetes

Diagnosis of diabetes may be based on plasma glucose criteria, either the fasting plasma glucose (FPG) value or the 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT), or A1C criterion (34).

1.5.2 Dietary Recommendations in Diabetes Mellitus

T2DM is a prevalent metabolic illness with significant systemic consequences that is mostly preventable by dietary changes and physical activity. The primary method for preventing T2DM is a balanced diet, and once encountered controlling diet and medical treatment are required. It is recommended that 3–7% weight loss can reduce the risk for diabetes in people at risk and it can improve glycemia in those with diabetes. Furthermore, it is suggested that overweight and obese patients should achieve and maintain >5% weight loss. This loss will result a better insulin response, better glucose levels and decrease in blood pressure and cholesterol levels. Additional weight loss may probably lead to more results in the management of diabetes and cardiovascular risk. (21, 38) Physical activity should be paired with regular mealtimes and a balanced diet (18, 23, 38).

There is no optimal specific percentage of calories from macronutrients. Recommendations for macronutrients range from 45 to 60% for carbs, 15 to 20% for proteins, and 20 to 35% for fats. To optimize glycemic management, LDL-cholesterol, and cardiovascular risk, high-fiber sources (30–50 g/day dietary fiber, 30% soluble fibers) and minimally processed, low-glycemic index carbohydrates should be favored. Overall, it has been proven that lowering carbohydrate intake improves blood glucose levels in patients with T2DM. (39)

The consumption of non-starchy vegetables, fruits, whole grains, and dairy products should be emphasized in dietary planning. By substituting nonnutritive sweeteners for added sugar (sucrose, high fructose corn syrup, fructose, glucose), daily calories and total carbs can be reduced. A low-calorie or unsweetened beverage can be an option for those who frequently use sweetened beverages, but both should be consumed with caution. (39, 40)

Additionally, guidelines for protein consumption are the same as for the general population (1.0-1.2 g/kg body weight or adjusted body weight for patients who are overweight or obese). However, protein intake for those with chronic diabetic nephropathy should be lowered to 0.8 g/kg body weight. (40)

It is advised to limit consumption of saturated fatty acids to 7-9% of total daily calories and to avoid trans-fatty acids as much as possible among dietary fats. Saturated fatty acids (SFAs) should be substituted by monounsaturated fatty acids (MUFAs) of vegetable origin found in whole grains, nuts, and seeds, as well as polyunsaturated fatty acids (PUFAs), which are mostly mixed sources of omega-3/omega-6 (rich in alpha-linolenic fatty acid) (23, 41, 42)

1.6 Protein Consumption in Type 2 Diabetes

When it comes to weight gain, scientists and nutritionists may still be debating whether "a calorie is a calorie," but it's apparent that different calorie sources have different impacts on glucose and insulin levels, fat and protein metabolism, and other metabolic parameters. Dietary fats, proteins, and carbohydrates all offer energy that can be measured in calories, but more significantly, the various macronutrients come in a wide variety of forms that can result in very different outcomes and functions in the body (43).

A healthy diet can reduce the risk of developing type 2 diabetes. Fewer studies have specifically examined the role of dietary protein in the onset of the disease, despite the fact that much is known about the impact of fats and carbs on risk of type 2 diabetes.

A great deal of attention has been placed on the impact of a high-quality protein diet on human health due to its potential advantages for weight control, metabolism, and healthy aging. Previous research, including meta-analyses of short-term clinical trials, has demonstrated that high-protein diets cause weight loss and fat mass reduction. This may be because of the negative energy balance brought on by prolonged satiety and increased energy expenditure. Moreover, cardiovascular measures, such as circulating lipid and lipoprotein profiles, blood pressure and glycemic regulation, have improved when protein replaces carbohydrates. Despite this supporting data and growing public awareness of the health benefits of dietary protein, no suggestions for the best food sources of protein have been offered. Given the different dimensions of nutritional profiles, including macronutrients, micronutrients, polyphenols, and amino acid combinations from various protein sources, a thorough analysis of the disparate long-term health outcomes resulting from dietary protein source selections (i.e., plant protein or animal protein) has yet to be completed (44).

1.6.1 Animal Protein: Protein-rich foods include red and processed meat, poultry (e.g chicken, turkey), fish and seafood, eggs and dairy products (e.g milk, cheese, yogurt, kefir). Several studies have shown the great benefits from replacing red and processed meat or even poultry or eggs with fish and seafood in health issues such as cardiovascular disease and diabetes mellitus (44, 45).

- **Red and processed meat:** The classification of meat can be delineated by two primary criteria: the first criterion refers to the origin of the product, while the second criterion refers to the processing of the meat, distinguishing between processed and unprocessed variants. There are numerous positive correlations between the consumption of red or processed meat and the development of chronic diseases. (46) The elevated presence of saturated fatty acids (SFAs) in red meat and due to higher concentrations of nitrates and nitrites in processed meat. (47) These components have been linked to a range of molecular pathways that have a role in the primary categories of chronic diseases, including cardiovascular diseases, T2DM, metabolic diseases, and some types of cancer. (46, 47)

- **Poultry:** This category includes meat such as chicken, turkey, duck etc. and are often known as "lean meat" because of their lower fat content in comparison with red meat. Many researches show a strong positive relationship between eating poultry and developing CVD. (48) That's because the consumption of poultry often includes fried chicken or processed meat products as well. Consuming fried food has a strong positive correlation with negative outcomes such as CVD and obesity, two major risk factors for T2DM. (43,48)

- **Fish and seafood:** A diet rich in seafood and fish is associated with a reduced risk of many chronic diseases such as cardiovascular disease and T2DM. (46). A serving size that consists two to three servings every week is associated with a lower risk of developing chronic diseases such as cardiovascular disease, coronary heart disease, myocardial infarction, stroke, and heart failure, compared to lower intakes of fish. (47) This result has been attributed to the omega-3 fatty acid content and substitution effect when fish and seafood replace other sources of animal protein (such as red and processed meat or full-fat dairy products). Fish and seafood preparation is important; fried varieties have low to no impact to health. Recent studies support weekly fish consumption of at least twice per week. Better results are realized when fish is substituted for diets high in saturated fat. (46, 47)

- **Eggs:** Eggs are an essential food source due to their high protein, lipid, and mineral content. A normal size egg (50gr) contains 6.29 gr of protein, 0.56 gr of carbohydrates, 1.6 gr of saturated fat, 2.0 gr of MUFA and 0.7 gr of PUFA. In addition, they contain numerous minerals (calcium, iron, magnesium, and phosphorus) and vitamins, with the exception of vitamin C. (49) After egg consumption, the intestines are accountable for cholesterol absorption. Absorption of cholesterol involves both dietary cholesterol and biliary cholesterol. Eggs and specifically egg yolks contain 200 mg of cholesterol, rendering it a notable source of dietary cholesterol. Eggs also possess supplementary elements that have the potential to lower the likelihood to develop cardiovascular disease. Furthermore, their lipid content is quite moderate, approximately 5 gr, predominantly including monounsaturated and polyunsaturated fatty acids. (47, 49)

- **Dairy products:** These products are considered as protein sources and provide a significant portion of the RDA's for calcium, iodine, riboflavin, and vitamin B-12 for adults (50). According to the International Dairy Federation, the consumption of dairy products is rising, globally. The global per capita consumption increased dramatically around 2006-2013. Recent research focus on categorizing various dairy products by type (fermented products, low- and high-fat dairy products, milk, yogurt, and cheese). (50, 51) Some epidemiologic studies have proposed that dairy product consumption may effect the prevention many chronic diseases, other studies have failed to discover this consequence. (51). Despite the fact that numerous previous meta-analyses have examined the association between T2DM, their conclusions are highly inconsistent. Latest evidence indicates the need for a more exhaustive systematic review. (51)

1.6.2 Vegetable protein: Protein-rich plant foods can be separated in three categories: nuts, pulses and grains (such as bulgur, rice, quinoa, amaranth, etc.). Most vegetable proteins consist of larger levels of non-protein substances than animal-based proteins, such as fiber and other minerals such as magnesium, potassium, and antioxidant phytonutrients, which are all linked to better health outcomes (44).

- **Nuts and seeds:** This category includes almonds, peanuts, hazelnuts, walnuts cashews, Brazil nuts, pumpkin seeds macadamias, sunflower seeds and pistachios. These types of foods typically contain protein, soluble and insoluble fibers, vitamins such as E and K, micronutrients such as folate and thiamine, minerals like magnesium, copper, potassium, and selenium, as well as compounds like zanthophyll carotenoids, antioxidants, and phytosterols. All these have a high impact human health. In addition, they consist of monounsaturated (MUFA) and polyunsaturated (PUFA) fatty acids. (43, 44)

Prior analyses, epidemiological studies, and/or clinical trials have proposed that regular nut consumption shows a positive impact on health, including chronic diseases such as obesity, diabetes and heart diseases, with a decrease in the mediators of chronic diseases, such as oxidative stress, inflammation, visceral adiposity, hyperglycemia, insulin resistance, endothelial dysfunction, and metabolic syndrome (52).

- **Legumes:** This category is described as the edible seeds extracted from eleven species of legume plants of the family Leguminosae that have been dried. This definition does not include crops that are harvested and produced for consumption as green vegetables, including hydrated green peas and beans; for sowing purposes, including clover seeds and alfalfa. It also does not include crops used for oil extraction, such as peanuts. The most popular varieties of pulses consumed globally, out of the many hundreds that are known, are beans, dry peas, chickpeas, and lentils. In general, pulses are low in calories and fat and highly rich sources of protein (18–30% dry weight) and carbohydrates (50–65% dry weight) (53,54).

- **Cereals:** The Gramineae (grasses) family, which also contains wheat, barley, oats, maize, rice, rye, millets, and sorghum, is where cereal grains are found. A typical serving of cereal has 70–72% carbs, 7–15% protein, and 1–12% fats. They can be ingested as whole grains or in their refined form and are a key source of energy in most diets (53).

1.6.3 Animal versus Vegetable Protein

The consumption of vegetable foods and dietary components, such as whole grain products, fiber, vegetable lipids, and vegetable protein, is connected with a reduced risk of T2DM. On the other hand, consuming more meat, particularly red and processed meat, as well as fat derived from animals has been associated with a greater risk of T2DM. Numerous prospective studies have consistently demonstrated a link between intake of animal proteins and an increased risk of developing T2DM in humans (44).

Most vegetable protein are richer in fiber, magnesium, potassium, and antioxidant phytonutrients, all of which are linked to better health outcomes, than animal-based protein. Because of this, plant sources of protein may have a number of positive impacts related to the treatment and prevention of T2DM, however these effects may be unrelated to the kind or quantity of protein present in the sources. In general, plant protein diets' preventive effects on the incidence of T2DM seem to be indirect. They probably come from their capacity to reduce associated risk factors such body weight, blood pressure, lipids, and inflammatory markers, which can reduce insulin resistance (44).

Prospective studies repeatedly demonstrate that dietary changes that boost the intake of vegetable protein at the expense of animal products lower the incidence of T2D, regardless of BMI. The mechanisms behind the negative effect of animal products and the preventive effect of vegetable meals on the risk of developing T2D are currently unknown. That’s why, there is a need for more research on the benefits of vegetable protein consumption in type 2 diabetes and insulin resistance (38).

Obesity, overweight and dietary habits are two main risk factors for developing T2DM or prediabetes. A diet that is energy dense and nutrient poor among with low levels of physical activity can lead to overweight or obesity. Obesity is related with metabolic abnormalities and finally may cause insulin resistance. The primary method for preventing T2DM is a balanced diet. Similarly, for the treatment of T2DM, controlled diet and usually among with medical treatment are required. Recommendations for the prevention and the treatment of T2DM and prediabetes focus on a diet with that is low in refined grains, red or processed meat, and sugar-sweetened beverages and high in whole grains, fruits, vegetables, nuts, and legumes. Protein consumption recommendations among healthy and diabetic patients (except those with diabetic nephropathy) are exactly the same. Animal protein and specifically some categories such as red and processed meat are high in saturated fat, advanced glycation end products (AGEs) and nitrosamines. In contrast, some other types of animal-based protein such as fish are low in saturated fat, high in polyunsaturated and monounsaturated fat, two types of fatty acids that are known for their positive health impacts. Vegetable diets are characterized by their rich content of fiber, antioxidants, and minerals, all of which have been scientifically demonstrated to exert positive effects on insulin sensitivity. For this reason, as the recommendations for protein consumption are staying the same neither for healthy or diabetic patients, there is the need to discover the effect from the consumption of vegetable protein instead of animal protein in people with T2DM and/or with IFG.

The aim of the study was to assess between consumption of vegetable protein sources, in Greek adults, using a representative sample and glucose status; Normal glucose levels, IFG and T2DM.

2. Methods

2.1 Study presentation

The Hellenic National Nutrition and Health Survey (PAMEDY) or Hellenic National Nutrition and Health Survey (HNNHS) is cross-sectional research with a nationally representative sample, irrespective of gender and age. It is the first survey in Greece to evaluate the nutritional and health status of Greek population. The respondents were selected through a random stratified design according to census information from 2011. The stratification process took into account the following factors:

(a) geographical density criteria by Greek area (7 regions)

(b) age group of the reference population (≤19; 20-65; ≥65 years), and

(c) sex distribution

More than one individual from the same age group could be chosen at random from each household, but only one per age age-group and two per household could enroll in the study at a time. At the end, total HNNHS sample population consisted of 4574 people (42.5 % men and 57.5 % women). Specifically, 47.2% of the participants were living in Athens Metropolitan Area thus only 18,5% in the Central Macedonia region.

2.2 Population Study Sample

Total HNNHS population consisted of 4574 people (42.5 % men and 57.5 % women). The sample distributed across Greece. Specifically, 47.2% of the participants were living in Athens Metropolitan Area thus only 18,5% in the Central Macedonia region. The remaining members were nearly equally dispersed across the entire nation. From the total population were excluded:

(a) people who don't speak Greek
(b) women who in gestation or in breastfeeding period
(c) people who were in the armed forces (including those who are currently serving their mandatory military service)
(d) residents of institutions (such as nursing homes, psychiatric institutions, prisons etc.)
(e) people who were unable to give informed consent due to any reason (mental or psychiatric condition, vision or hearing loss, drug abuse etc)

For this study, from total HNNHS sample, a group 982 participants only from urban cities (Athens and Thessaloniki), were included, because all the necessary biochemical and anthropometric measurements were collected only in these cities. All the participants were adults. Specifically, this study includes:

(a) individuals that have reported/ diagnosed with T2DM
(b) people on any diabetic medication/ treatment, irrespective of T2DM report
(c) people that were unaware or undiagnosed, but post blood sampling results were classified as IFG or with T2DM.

In addition, patients with CVD, were excluded. Patients with CVD probably have already changed their dietary habits because of their health condition. Latest diet recommendations for patients with CVD include (ref):

(a) High consumption of vegetables, fruits, legumes, nuts, whole grains, and fish
(b) Replacement of saturated fat with dietary monounsaturated and polyunsaturated fats

(c) Low consumption of red and processed meats. (55)

All the above dietary recommendations may influence the study's results.

2.3 Main Outcome

This study focus on whether there is an association between amount of vegetable protein intake and glucose status. For this purpose, clinical examinations such as blood results for fasting glucose and insulin levels, and other health indicators, were performed in a subgroup of the participants. HBA1c was only performed in individuals with diabetes and is not a sensitive marker for glucose status classification. It was therefore not used as a biomarker in this study. All samples were collected in the morning, from 8:00 and 10:00 am and the participant should have fasted at least 10 hours. To assure compliance all individuals were asked if they had fasted and when their last meal was. In order to reduce response biases and misclassification (minimize volunteer burden and increase the reliability of the data collected), an initial interview was conducted at the volunteer's home using a specially created computer program, (Computer Assisted Personal Interview – CAPI). In summary, the interviewing process included data on demographics, quality of life (QoL), medical history (ex. Chronic & autoimmune diseases, depression, anxiety), breastfeeding, medication and supplement use, memory impairment, eating habits, alcohol intake, smoking habits, physical activity, sleeping habits, overall patient health and effects of economic crisis. According to the study's protocol, the questions were chosen based on the volunteers' ages.

2.4 Main Exposure

To measure the consumption of vegetable protein in the study population a thorough 24-hour dietary recall was collected. According to the HNNHS study-protocol, the volunteers were also interviewed by telephone, for a second 24-hour dietary recall 8–20 days after the first interview on a separate day that wasn't consecutively chosen. From the two 24-hour dietary recalls, vegetable protein consumption was analyzed in grams (gr) with the use of USDA food database. The mean average of vegetable protein consumption was calculated for each participant.

2.5 Other variables

To have more accurate results it was important to take into account some more confounding variables that are associated with T2DM and IFG.

Socioeconomic variables

Low socioeconomic status is highly associated with T2DM. Socioeconomic factors may impact nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options and social determinants of health. Questionnaires were used to report residence area, educational level, employment and marital status.

Smoking & Alcohol:

There is a strong connection between smoking and an increased risk of T2DM, whereas clinical findings suggest an effect of smoking and nicotine on body composition, insulin sensitivity, and pancreatic β cell function. Also, alcohol consumption seems to be associated with the risk of developing type 2 diabetes. Questionnaires were used in order to report smokers or no – smokers and alcohol consumption.

Health status

Both hypertension and dyslipidemia are diabetes-related diseases. Prediabetes is associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides (>250 mg/dL) and/or low HDL cholesterol (<35 mg/dL), and hypertension (≥140/90 mmHg or on therapy for hypertension). The presence of prediabetes should prompt comprehensive screening for cardiovascular risk factors. The risk of developing type 2 diabetes increases in people with hypertension or dyslipidemia. Clinical examinations were performed on a subsample of 987 individuals.

Abdominal fat & Waist circumference:

Abdominal fat (visceral adipose tissue; VAT) is considered more crucial than subcutaneous fat. VAT release proteins that can lead to inflammation, atherosclerosis, dyslipidemia and hypertension. Moreover, VAT is associated with T2DM and IFG than other manifestations of obesity. In addition, other anthropometric methods such as waist circumference measurement can also give a lot of information about the distribution of body fat in each participant. For men, a waist circumference below 94 cm is ‘low risk’, 94–102cm is ‘high risk’ and more than 102cm is ‘very high’. For women, below 80cm is low risk, 80–88cm is high risk and more than 88cm is very high. These are the guidelines for people of white European, black African, Middle Eastern and mixed origin. For this purpose, additional components of the HNNHS included anthropometry examination which included weight, height, waist and hip circumference, and body composition. Then, BMI was calculated via kg/m^2 equation. In this study, waist circumstance was used in order to calculate the body composition of the participants.

Vitamin D:

There is evidence that suggests a correlation between low levels of vitamin D in the body and the development of T2DM. Consequently, several research have been conducted to examine the impact of vitamin D levels on the occurrence of diabetes, management of diabetes, and the occurrence of complications related to diabetes.

3. Statistical Analysis

Descriptive statistical analysis of the data was performed using STATA 14.0 software. The specific statistical program allows the grouping of data-variables, so that further analysis of the sample can be carried out, offering the possibility of graphical representation of the results.

First, normality was tested, since continuous variables following a normal distribution were expressed as mean ± standard deviation. While categorical variables were expressed as absolute numbers (n) or frequencies (%), to describe the demographic characteristics of the participants. The ANOVA test was used to determine the proportion of the population belonging to each control category, with a statistical significance level of 5%. For variables without normal distribution non-parametric test, Kruskal – Wallis, was used.

Logistic regression was performed to find the association of glucose status with adherence to socioeconomical and lifestyle factors, anthropometrical values and nutrient status and specifically vegetable protein. In order to observe these association study group, according to glucose status, was separated into two groups (participants with normal glucose status and participants with IFG or/and T2DM).

Finally, all estimates were based on two-way hypothesis tests with a significance level of 5% i.e. with a $p\text{-value}<0.05$.

4. Results

The study's sample characteristics are presented in the following three tables, all displayed in total and by glucose status. Table 2 contains the socioeconomic and lifestyle characteristics of the population sample, Table 3 includes anthropometric measurements, Vitamin D and health status data, and in Table 4 nutrient intake data are presented.

Table 2. ***Socioeconomical & lifestyle characteristics of population study sample by glucose status***

Characteristics	Total	Diabetes	IFG	Normal glucose levels	p-value
Age, (years)					<0.001
40.1661 ± 15.1					
≤19	555 (56.7%)	6 (13.0%)	103 (39.3%)	447 (66.4%)	
20-65	290 (29.6%)	15 (32.6%)	94 (35.9%)	181 (26.9%)	
≥65	135 (13.8%)	25 (54.3%)	65 (24.8%)	45 (6.7%)	
Sex					<0.001
Women	608 (61.9%)	20 (43.5%)	136 (51.9%)	452 (67.1%)	
Men	374 (38.1%)	26 (56.5%)	126 (48.1%)	222 (32.9%)	
Employment status					<0.000
Employed	540 (55.0%)	13 (28.3%)	131 (50.2%)	396 (58.7%)	
Unemployed	290 (29.6%)	12 (26.1%)	64 (24,5%)	214 (31.7%)	
Pension	151 (15.4%)	21 (45.6%)	66 (25.3%)	21 (45.6%)	
Marital status					<0.000
Single	490 (51.3%)	7 (15.5%)	93 (36.0%)	390 (59.8%)	
Married/ Cohabit	361 (37.8%)	28 (62.2%)	121 (46.9%)	212 (32.5%)	
Divorced/ Separated	60 (6.2%)	1 (2.2%)	21 (8.1%)	38 (5.8%)	
Widowed	44 (4.6%)	9 (20.0%)	23 (8.9%)	12 (1.8%)	

Characteristics	Total	Diabetes	IFG	Normal glucose levels	p-value
Educational Level					<0.000
Up to 6 years of school	50 (5.1%)	12 (26.1%)	19 (7.2%)	19 (2.8%)	
12 years of school	325 (33.1%)	15 (32.6%)	101 (38.5%)	209 (33.1%)	
Higher education inc. colleges	606 (61.8%)	19 (41.3%)	142 (54.2%)	445 (66.1%)	
Smoking status					<0.049
Smoker	336 (34.2%)	10 (21.7%)	80 (30.5%)	246 (36.6%)	
Ex-smoker	184 (18.7%)	13 (28.2%)	58 (22.1%)	113 (16.8%)	
Non-smoker	460 (46.9%)	23 (50.0%)	124 (47.3%)	313 (46.5%)	
Alcohol consumption					0.085
Yes	790 (82.5%)	33 (71.7%)	210 (81.1%)	547 (83.9%)	
No	167 (17.5%)	13 (28.3%)	49 (18.9%)	105 (16.1%)	
Physical Activity					0.127
Sedentary	41 (4.2%)	3 (6.6%)	17 (6.7%)	21 (3,1%)	
Low	151 (15.6%)	6 (13.3%)	31 (12.2%)	151 (15.6%)	
Moderate	417 (43.0%)	22 (48.9%)	109 (42.9%)	417 (43.1%)	
Very	359 (37.0%)	14 (31.1%)	97 (38.2%)	359 (37.1%)	
Sleep (hours)					0.407
6-8	465 (47.8%)	20 (45.5%)	136 (52.7%)	309 (46.1%)	
<6	162 (16.7%)	9 (20.5%)	41 (15.9%)	112 (16.6%)	
>8	345 (35.5%)	15 (34.1%)	81 (31.4%)	249 (37.1%)	

More specifically, 982 people were included, of which 608 (61.9 %) were women and 374 (38.1%) were men and the average age was 40 years (40.2 ± 15.1). A significant larger proportion of the population categorized with T2D being >65 years while those with IFG were of those ≤19 years of age (p<0.001). Significant differences in the distribution of individuals by glucose status, were also found for sex, employment status, marital status, educational level and smoking status. Specifically, a larger proportion of smokers were also with T2D and IFG (36.6% and 30.5%, 21.7%, and 21.7%, respectively) T2DM had a greater proportion of participants at pension (45.6%) compared to those who are currently employed (28.3%) or unemployed

(26.1%). Additionally, a greater proportion of employed individuals (50.2%) were classified with IFG, compared to the unemployed (24.5%) and retired (25.3%) (p<0.000). Higher prevalence of IFG and T2DM was found for those who were married (46.9% and 62.2%, respectively) compared to those who are single, divorced or widowed (p<0.000). Furthermore, in relation to level of education, IFG and T2DM was also more prevalent for participants with higher level of education (54.2% and 41.3%, respectively compared to up 6 year of school (7.2% and 26.1%, respectively) and 12 years of school (38.5 and 32.6, respectively). Regarding smoking status, it has been noted that non-smokers had a higher prevalence of IFG or/and T2DM (50.0 % and 47.3%) than current (21.7 and 30.5%) or former smokers (28.2 % and 22.1%).

Table 3. ***Anthropometric measurements, Vitamin D and health status of population study sample by glucose status***

Characteristics	Total	Diabetes	IFG	Normal glucose levels	p-value
BMI (kg/m^2)					<0.001
25,1739 ± 4,64					
≤18,5	23 (2.3%)	0 (0.0%)	1 (0.4%)	22 (3.3%)	
18,5- 24,9	529 (54.1%)	8 (17.4%)	106 (40.9%)	415 (61.7%)	
25-29,9	285 (29.1%)	170 (25.3%)	94 (26.3%)	21 (45.6%)	
≥30	141 (14.4%)	17 (37.0%)	58 (22.4%)	66 (9.8%)	
Waist circumstance (cm)					<0.001
	86.7 ± 14.0	98.6 ± 12.6	92.1 ± 14.5	83.8 ± 13	
Vitamin D status (µg/dl)					0.991
≤19	344 (35.1%)	16 (34.8%)	88 (33.8%)	240 (35.7%)	
20-29	311 (31.7%)	15 (32.6%)	84 (32.3%)	212 (31.5%)	
≥30	324 (33.1%)	15 (32.6%)	88 (33.8%)	221 (32.8%)	
Hypertension					<0.001
Yes	108 (11.2%)	18 (40.0%)	53 (20.8%)	37 (5.56%)	
No	858 (88.8%)	27 (60.0%)	202 (79.2%)	629 (94.4%)	
Dyslipidemia					<0.001
Yes	491 (54.9%)	38 (88,3%)	159 (67.6%)	294 (47.8%)	
No	402 (45.0%)	5 (11,6%)	76 (32.3%)	321 (52.2%)	

Table 4. ***Nutrient intake of population study sample by glucose status***

Characteristics	Total	Diabetes	IFG	Normal glucose levels	p-value
Total protein % of TEI	16.3 (± 5.7)	16.4 (± 4.7)	16.4 (± 5.2)	16.2 (± 6.0)	0.9377
Total protein intake (gr/kg)	1.0 (0.6, 1.5)	5.0 (3.4, 11.5)	1.0 (0.6, 1.4)	1.0 (0.6, 1.5)	0.1591
Vegetable protein % of TEI	5.0 (3.5, 6.8)	5.7 (3.4, 8.3)	5.2 (3.7, 7.1)	4.9 (3.4, 6.7)	0.1900
Vegetable protein intake (gr/kg)	0.3 (0.2, 0.5)	0.3 (0.1, 0.4)	0.3 (0.2, 0.5)	0.3 (0.2, 0.5)	0.3771
Vegetable protein intake (gr)	23.0 (14.9, 36.5)	23.3 (11.3, 39.8)	24.7 (15.2, 39.7)	22.5 (14.9, 34.8)	0.3086
Animal protein % of TEI	15.6 (12.5, 18.9)	16.1 (13.1, 18.7)	15.5 (12.5, 19.2)	15.5 (12.3, 18.8)	0.5666
Animal protein intake (gr/kg)	0.4 (0.2, 0.7)	0.4 (0.2, 0.6)	0.4 (0.2, 0.7)	0.4 (0.2, 0.7)	0.3336
Animal protein intake (gr)	31.7 (17.1, 50.7)	28.5 (17.0, 49.7)	32.3 (16.8, 56.7)	31.7 (17.3, 49.7)	0.8063
Total carbohydrates % of TEI	0.46 (37.7, 57.3)	49.9 (38.6, 58.6)	44.8 (37,5, 57,6)	46.2 (38.0, 57.0)	0.5789
Total fiber intake (gr)	20.6 (13.6, 37.4)	26.0 (17.5, 45.2)	22.9 (14.3, 42.5)	19.9 (13.2, 36.1)	0.0685
Total fat % of TEI	37.6 (± 12.0)	36.7 (± 11.4)	38.6 (± 12.0)	36.7 (± 12.0)	0.2779
Saturated fat % of TEI	12.3 (± 5.1)	12.1 (± 4.7)	12.3 (± 5.0)	12.3 (± 5.3)	0.9602
Monosaturated fat % od TEI	16.6 (± 7.0)	16.3 (± 6.9)	17.3 (± 7.2)	16.7 (± 6.5)	0.1862
Polysaturated fat % of TEI	5.1 (4.0, 6.5)	4.9 (3.8, 6.1)	5.2 (4.1, 6.7)	5.0 (4.0, 6.5)	0.1255
Meddiet_score	29 (25, 34)	30 (28, 35)	29 (24, 34)	29 (25,33)	0.1281
% population by tertile					
1st tertile	322 (34,7%)	10 (24.3%)	96 (38.5%)	216 (33.9%)	0.031
2nd tertile	328 (35.4%)	15 (36.5%)	70 (28.1%)	243 (38.2%)	0.031
3rd tertile	276 (29.8%)	16 (39.0%)	83 (33.3%)	177 (27.8%)	0.031

**TEI: total energy intake*

According to anthropometric measurements in Table 3, the average BMI of the sample was 25,1 kg/m^2 (25.1 ± 4.6). Significant differences were also found for waist circumstance, hypertension and dyslipidemia. T2DM a greater proportion of participants at pension (45.6%) compared to those who are currently employed (28.3%) or unemployed (26.1%). Additionally, a greater proportion of the majority of individuals with IFG (40.9%) had a normal BMI while a significant proportion of those with T2DM are obese (37.0%) (p<0.001). Moreover, as the average waist size of the research participants grows, it is noticeable a corresponding impairment in their glucose condition. Participants with normal glucose levels had a reduced waist circumference (83.8 ± 13) compared to those with IFG (92.1 ± 14.5). Similarly, participants with IFG also demonstrate a significantly lowered waist circumference compared to those with T2DM (98.6 ± 12.6) (p<0.001) In relation to the participants' health status, it was observable that participants with T2DM had a higher prevalence of hypertension (40.0%) than those with IFG (20.8%) and normal glucose levels (5.5%) (p<000.1). The same applies in regard to dyslipidemia. T2DM occurs in a higher proportion of participants with dyslipidemia (88.3%) than in those with IFG (32.3%) or normal fasting glucose levels (52.2%) (p<000.1).

In relation to dietary intake in Table 4, there was no statistically significant differences observed between the consumption of particular macronutrients and IFG and/or T2DM. According to Table 4, the amount of total protein % of TEI (16.3 ± 5.7) and vegetable protein % of TEI (5.0), among the different groups of the participants, didn't have a significant difference. Table 4, a trend was only found for fiber with those with IFG and/or T2DM (grey zone) having higher intake of total fiber.

Table 5. Multiple logistic regression that evaluates the odds ratio of IFG or/and T2DM depending on the amount of vegetable protein consumption in relation to consumption of animal protein, saturated fat, total energy, smoking status, sex, educational level, marital status and the level of adherence to the Mediterranean diet (MedDietScore).

Glucose status	**Odds Ratio**	**Std. Err.**	**[95% Conf. Interval]**	
Total vegetable protein % of TEI				
2nd tertile	1.14	0.23	0.77	1.70
3rd tertile	1.44	0.32	1.04	2.32
Animal protein % of TEI	1.00	0.14	0.97	1.03
Saturated fat % of TEI	1.176	0.20	0.83	1.65
Total Energy	1.00	0.00	0.99	1.00
MedDietScore				
2nd tertile	0.62	0.11	0.42	0.90
3rd tertile	0.80	0.16	0.54	1.20
Smoking status				
Ex smoker	1.30	0.30	0.33	2.04
Non smoker	1.53	0.28	1.07	2.20
Sex	0.40	0.67	0.28	0.55
Age				
20-65	3.33	0.66	2.26	4.91
≥65	10.03	2.61	6.0	16.72
Educational Status				
Higher education inc. colleges	0.80	0.13	0.57	1.11
Up to 6 years of school	1.29	0.50	0.61	2.73
Marital Status	1.14	0.14	0.90	1.50

Table 6. Multiple logistic regression that evaluates the odds ratio of IFG or T2DM depending on the amount of vegetable protein consumption and smoking status in relation to the consumption of animal protein, saturated fat, total energy, sex, educational level, marital status and the level of adherence to the Mediterranean diet (MedDietScore).

	Smoker				Ex Smoker				Non smoker			
	Odds Ratio	**Std. Err.**	**[95% Conf. Interval]**		**Odds Ratio**	**Std. Err.**	**[95% Conf. Interval]**		**Odds Ratio**	**Std. Err.**	**[95% Conf. Interval]**	
Total vegetable protein % of TEI												
2nd tertile	1.38	0.54	0.64	2.99	0.66	0.30	0.27	1.60	1.33	0.38	0.75	2.35
3rd tertile	2.5	0.95	1.19	5.31	0.73	0.34	0.30	1.84	1.70	0.51	0.94	3.07
Animal protein % of TEI	1.00	0.30	0.95	1.06	1.04	0.33	0.98	1.11	0.98	0.02	0.94	1.02
Saturated fat % of TEI	2.54	0.87	1.29	5.00	0.63	0.25	0.29	1.37	0.98	0.25	0.60	1.62
Total Energy	1.00	0.00	0.99	1.00	1.00	0.00	0.99	1.00	1.00	0.00	0.99	1.00
MedDietScore												
2nd tertile	0.56	0.20	0.29	1.12	0.57	0.27	0.23	1.43	0.66	0.19	0.39	1.16
3rd tertile	1.08	0.42	0.50	2.32	0.66	0.32	0.26	1.70	0.84	0.25	0.47	1.49
Sex	0.36	0.12	0.20	0.70	4.29	2.39	1.44	12.80	0.32	0.08	0.19	0.53
Age												
20-65	3.68	1.37	1.29	5.00	2.58	1.13	1.10	6.07	3.94	1.19	2.18	7.10
≥65	34.0	18.63	11.63	99.52	4.29	2.40	1.44	12.80	9.2	3.71	4.19	20.29
Educational Status												
Higher education inc. colleges	0.88	0.28	0.47	1.64	0.93	0.38	0.42	2.06	0.65	0.16	0.40	1.05
Up to 6 years of school	0.30	0.25	0.05	1.59	2.54	2.12	0.49	13.05	1.62	0.92	0.53	4.94
Marital Status	1.19	0.29	0.74	1.90	0.99	0.27	0.59	1.69	1.16	0.21	0.81	1.67

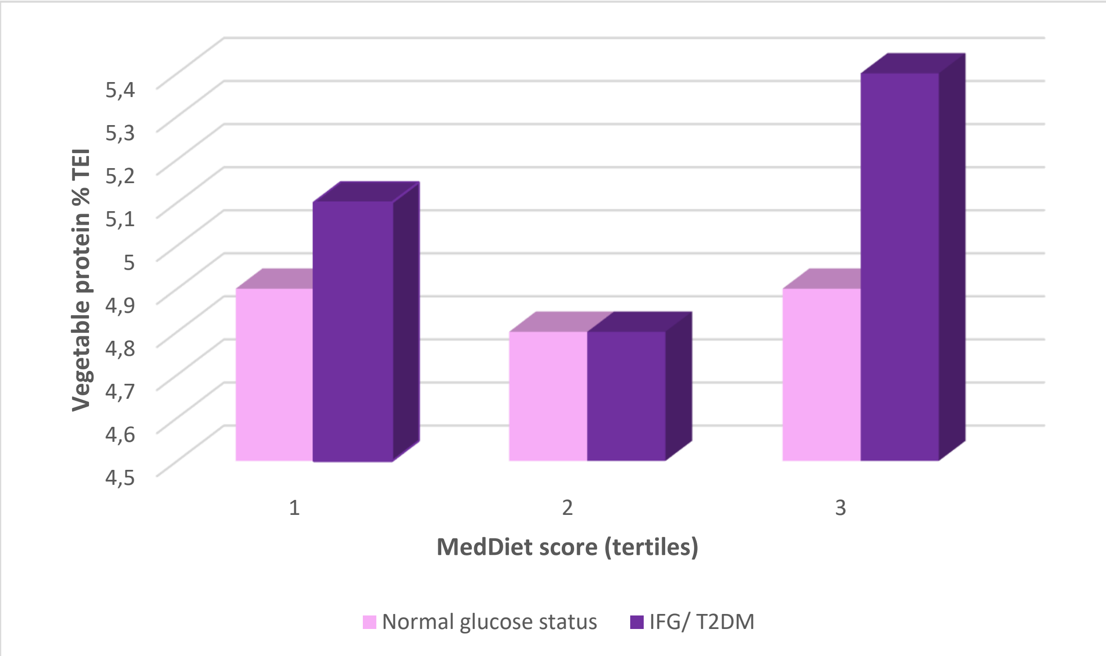
TEI: Total Energy Intake

Marital status has been categorized as single, married, divorced and widowed

Sex has been categorized as male and female

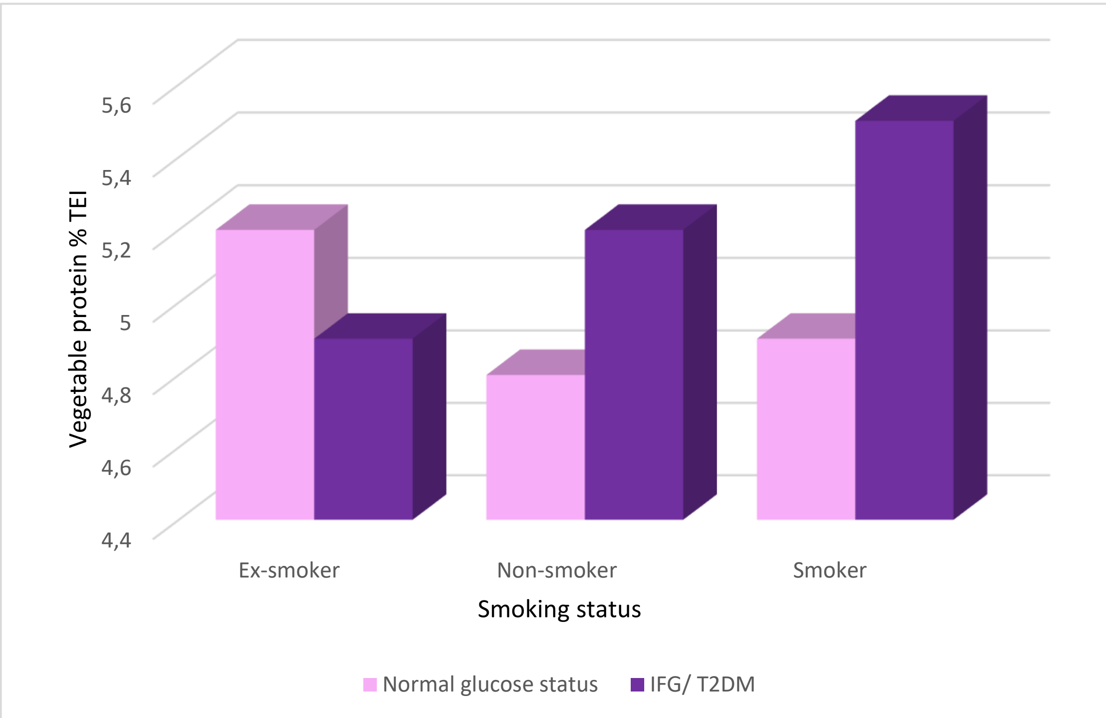
A multiple logistic regression that examined the odds of developing T2DM and/or IFG in the study population in relation to vegetable protein intake (% of TEI in tertiles) is depicted in Table 5. The model was adjusted for animal protein, saturated

fat, total energy (in calories), adherence to the Mediterranean Diet (MedDiet score), smoking, sex, age, education, and marital status. Results showed that individuals in the highest tertile of vegetable protein were 1,4 times more likely to develop T2DM and/or IFG compared to those with the lowest intakes found in the 1st tertile (OR: 1.44; 95%CI: 1.04 – 2.32; p-value <0.029). Furthermore, men had 39% more risk of having TD2M and/or IFG compared to women (p-value <0.000). Simultaneously, participants aged between 20 and 65, as well as those aged 65 or older, had 3.33 and 10 times greater chances, respectively, of having TD2M and/or IFG compared to participants aged 19 or younger (p-value <0.000 in both cases). Non-smokers had a 53% higher likelihood of acquiring TD2M and/or IFG compared to smokers (p-value <0.018). In relation to adherence to the Mediterranean diet, participants in the second tertile had 38% less likelihood of experiencing the specified outcome (p-value < 0.013). A lower likelihood was also for those in 3rd tertile which means highest adherence to the Mediterranean diet but this was not significant (0.54,1.20).



Graph 6. *Average vegetable protein consumption according to MedDiet score and glucose status*

The model in Table 6 depicts results of the same multiple logistic regression stratified by smoking status. The effect of vegetable protein on the likelihood of IFG & T2D remained significant only in smokers (OR: 2.5; 95%CI: 1.19-5.31). Within the group of smokers, we observed that sex, age, and the proportion of energy obtained from vegetable protein and saturated fat had a significant effect on the occurrence of T2DM and/or IFG (p-value <0.05). More specifically, participants who consume a percentage of their daily intake of vegetable protein and were in the 3rd tertile are 2.5 times more likely to develop T2DM and/or IFG compared to people who consume in the 1st tertile (p-value <0.015). Similarly, to Table 5, male smokers again had 64% less likelihood of developing T2DM/IFG (p-value <0.002). Individuals from 20-65 years old had 3.6 times greater chances to develop T2DM/IFG (p-value <0.000).



Graph 7. Average vegetable protein consumption according to smoking and glucose status

5. Discussion

The present study assessed the association between the amount of vegetable protein intake and glucose status in a representative sample of the Greek population. This study found a 16% total protein intake and 12% SFA intake. This is in accordance with other studies in Greek population which have reported a protein and SFA intake of Greek population accounted for 15% and 13% of the total energy, respectively (62). The power of the analysis is low because there is no significant range among study groups (normal glucose levels, T2DM, IFG) and total protein intake % TEI and vegetable protein intake % TEI.

According to many studies, animal protein consumption was linked to an increased risk of T2DM, whereas plant protein consumption was associated with a decreased risk. (43,57,60). It has been hypothesized that a number of nutrients found in processed and red meat, such as saturated fats are risk factors of T2DM and/or IFG. (13,15) On the contrary, protein derived from plants, including nuts, legumes, and whole cereals, has been linked to a reduced likelihood of developing type 2 diabetes. (13,15) Other researches of dietary habits of Greek population present that younger Greeks have higher consumption of meat, mainly red meat, alcohol, cereals, saturated fats, and sugar products (particularly women). (62)

The substitution of 5% plant protein energy (especially from nuts and whole grains) for animal protein was associated with a 21% reduction in the risk of T2DM. (43,57,60). In addition, according to Melbourne Collaborative Cohort Study (MCCS), higher total and animal protein consumption was associated with an increased risk of T2DM, and plant protein consumption was inversely associated with incident T2DM, but only in women. (58) Still, the exact plant protein sources that were consumed and were responsible for these results, weren't justified. (58) Furthermore, another study that assessed the findings of three additional prospective studies showed that a vegetable diet with low animal consumption was linked to an approximate 20% decrease in the likelihood of developing T2DM. However, the introduction of a vegetable diet with an emphasis on consuming nutritious plant foods resulted in a more substantial reduction (34%), in terms of diabetes risk. In particular, adherence to a vegetable diet that was abundant in plant foods that are comparatively less nutritious was linked to a 16% increase in the likelihood of developing T2DM. According to the study, healthy vegetable foods are whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and tea/coffee. Conversely, fruit juices, sweetened beverages, refined cereals, potatoes, and sweets/desserts were categorized as less healthy plant foods. (58)

The findings of this study are inconsistent with those of other research indicating that an increased intake of vegetable protein reduces the risk of developing T2DM and/or IFG. In this study people with IFG and/ or T2DM consume higher percentage of vegetable protein in contrast to those that have normal glucose levels. Particularly, participants on the 3rd tertile of total vegetable protein % TEI had higher likelihood to develop T2DM or/and IFG. On the contrary, the percentage of the participants on the highest tertile was small which means that the sample was also small which led to a low power of the analysis. In this study, the sources of vegetables protein aren't justified. This can probably explain the different outcomes between our study and others studies. According to other cohort studies, a reduced risk of T2DM was observed when 5% of energy intake was replaced with vegetable protein in place of animal protein and carbohydrates derived from refined grains, potatoes, and added sugar. These results indicate that substituting vegetable protein for animal protein and low-quality carbohydrates may reduce the risk of T2DM. The primary vegetable protein sources consumed in these studies were whole grains, nuts, peanut butter, and legumes. (60) In contrary, EPIC-IntercAct study had as primary vegetable protein sources foods like bread, pasta, rice, and potatoes, which could potentially contribute to an elevated dietary glycemic load. It has been demonstrated that glycemic load-rich diets increase the risk of T2DM. (61)

In this study, non-smokers had higher likelihood of acquiring TD2M and/or IFG compared to smokers. To understand the reason why non-smokers had higher likelihood we performed a logistic regression analysis by smoking status. When this was performed an interesting finding arose. The higher likelihood of T2DM and/or IFG with increasing tertile of total vegetable protein % TEI, remained only for smokers.

From this study, there is a relation between smokers and the consumption of vegetable protein in people with IFG and/or T2DM. This effect is not yet understood as it isn't known whether a smoking-related mechanism is responsible or whether it comes from the type of plant protein sources that smokers consume. In this particular research, limitations that existed concern the categorization of plant protein sources. In addition, people with T2DM and are aware with their condition, change their dietary habits (eg increase fiber consumption, decrease sugar or processed foods). Different types of vegetable proteins may have led to completely different results as reported in other studies. Whole grain products, legumes, nuts and vegetables are sources of vegetable protein that contribute to a better glycemic response. In contrast, ultra-processed foods, processed grains, etc. are plant-protein sources that may lead to disturbed fasting glucose.

Also, in this particular study, for a better understanding of the results, a multiple logistic regression was performed only for people with IFG. Between the group of people with T2DM there wasn't any significant relation with the increase of vegetable protein consumption. This could be attributed to the limited number of the sample size.

6. Conclusion

This is the first study to examine the relationship of vegetable protein with glucose status using representative population data. Overall, mean intake was low, although individuals that reported being current smokers had the highest intake as a percent of their total daily caloric intake. Results were found to contradict the preventive effect of vegetable protein although this remained the case only for current smokers. It is important to carry out further research in the Greek population that will categorize the sources of vegetable protein in order to understand exactly the relation between vegetable protein, IFG and/or T2DM and smoking. Understanding the exact relationship between these factors may lead to more accurate guidelines for the prevention of IFG and T2DM.

7. Bibliography

1. Wu, Y., Ding, Y., Tanaka, Y., & Zhang, W. (2014). Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. International Journal of Medical Sciences, 11(11), 1185–1200. https://doi.org/10.7150/ijms.10001
2. *IDF Diabetes Atlas – Tenth Edition*. IDF Diabetes Atlas. (n.d.). Retrieved January 26, 2023, from https://diabetesatlas.org/
3. Lin, Xiling, et al. "Global, Regional, and National Burden and Trend of Diabetes in 195 Countries and Territories: An Analysis from 1990 to 2025." *Scientific Reports*, vol. 10, no. 1, 2020, https://doi.org/10.1038/s41598-020-71908-9.
4. Safiri, Saeid, et al. "Prevalence, Deaths and Disability-Adjusted-Life-Years (Dalys) Due to Type 2 Diabetes and Its Attributable Risk Factors in 204 Countries and Territories, 1990-2019: Results from the Global Burden of Disease Study 2019." *Frontiers in Endocrinology*, vol. 13, 2022, https://doi.org/10.3389/fendo.2022.838027.
5. Magriplis, E., et al. "Prevalence of Type 2 Diabetes Mellitus in a Representative Sample of Greek Adults and Its Association with Modifiable Risk Factors: Results from the Hellenic National Nutrition and Health Survey." *Public Health*, vol. 197, 2021, pp. 75–82., https://doi.org/10.1016/j.puhe.2020.10.002.
6. Marx, Nikolaus. "Cardiovascular Risk Assessment in Diabetes and Pre-Diabetes." *ESC CardioMed*, 2018, pp. 923–924., https://doi.org/10.1093/med/9780198784906.003.0216.
7. Schlesinger, Sabrina, et al. "Prediabetes and Risk of Mortality, Diabetes-Related Complications and Comorbidities: Umbrella Review of Meta-Analyses of Prospective Studies." *Diabetologia*, vol. 65, no. 2, 2021, pp. 275–285., https://doi.org/10.1007/s00125-021-05592-3.
8. Bansal, Nidhi. "Prediabetes Diagnosis and Treatment: A Review." *World Journal of Diabetes*, vol. 6, no. 2, 2015, p. 296., https://doi.org/10.4239/wjd.v6.i2.296.
9. Leahy, J.L. "Impaired Fasting Glucose and Impaired Glucose Tolerance: Implications for Care." *Yearbook of Medicine*, vol. 2008, 2008, pp. 498–501, https://doi.org/10.1016/s0084-3873(08)79281-2.
10. "Diabetes Prevention Program (DPP) – NIDDK." *National Institute of Diabetes and Digestive and Kidney Diseases*, www.niddk.nih.gov/about-niddk/research-areas/diabetes/diabetes-prevention-program-dpp. Accessed 12 Aug. 2023.
11. Zheng, Yan, et al. "Global Aetiology and Epidemiology of Type 2 Diabetes Mellitus and Its Complications." *Nature Reviews Endocrinology*, vol. 14, no. 2, 2017, pp. 88–98., https://doi.org/10.1038/nrendo.2017.151.
12. Kolb, Hubert, and Stephan Martin. "Environmental/Lifestyle Factors in the Pathogenesis and Prevention of Type 2 Diabetes." *BMC Medicine*, vol. 15, no. 1, 2017, https://doi.org/10.1186/s12916-017-0901-x.
13. Rose, Stewart. "The Prevention and Treatment of Type 2 Diabetes Mellitus with a Vegetable Diet." *Endocrinology& Metabolism International Journal*, vol. 5, no. 5, 2017, https://doi.org/10.15406/emij.2017.05.00138.

14. von Frankenberg AD, Marina A, Song X, *et al.* A high-fat, 59 high-saturated fat diet decreases insulin sensitivity without changing intra-abdominal fat in weight-stable overweight and 60 obese adults. *Eur J Nutr* 2017; 56:431–443
15. Imamura F, Micha R, Wu JH, *et al.* Effects of saturated fat, polyunsaturated fat, monounsaturated fat, and carbohydrate on glucose-insulin homeostasis: a systematic review and meta-analysis of 53 randomized controlled feeding trials. *PloS Med* 2016; 13: e1002087.
16. Uribarri J, Cai W, Ramdas M, et al. Restriction of advanced glycation end products improves insulin resistance in human type 2 diabetes: potential role of AGER1 and SIRT1. Diabetes Care. 2011;34:1610–1616.
17. Kim Y, Keogh J, Clifton P. A review of potential metabolic etiologies of the observed association between red meat consumption and development of type 2 diabetes mellitus. Metabolism. 2015;64:768–779.
18. Cataletto, Mary. "World Health Organization Issues New Guidelines on Physical Activity and Sedentary Behavior." *Pediatric Allergy, Immunology, and Pulmonology*, vol. 33, no. 4, 2020, pp. 167–167, https://doi.org/10.1089/ped.2020.29005.mca.
19. KANALEY, JILL A., et al. "Exercise/Physical Activity in Individuals with Type 2 Diabetes: A Consensus Statement from the American College of Sports Medicine." *Medicine & Science in Sports & Exercise*, vol. 54, no. 2, 2022, pp. 353–368, https://doi.org/10.1249/mss.0000000000002800.
20. Reutrakul, Sirimon, and Eve Van Cauter. "Sleep Influences on Obesity, Insulin Resistance, and Risk of Type 2 Diabetes." *Metabolism*, vol. 84, 2018, pp. 56–66., https://doi.org/10.1016/j.metabol.2018.02.010.
21. Obesity and weight management for the prevention and treatment of type 2 diabetes:*standards of medical care in diabetes—2022*. (2021). *Diabetes Care*, *45*(Supplement_1). https://doi.org/10.2337/dc22-s008
22. Kahn, Steven E., et al. "Mechanisms Linking Obesity to Insulin Resistance and Type 2 Diabetes." *Nature*, vol. 444, no. 7121, 2006, pp. 840–846, https://doi.org/10.1038/nature05482.
23. Petroni, M. L., Brodosi, L., Marchignoli, F., Sasdelli, A. S., Caraceni, P., Marchesini, G., & Ravaioli, F. (2021). Nutrition in patients with type 2 diabetes: Present knowledge and remaining challenges. Nutrients, 13(8), 2748.
24. Vondra, Karel, and Richard Hampl. "Vitamin D and New Insights into Pathophysiology of Type 2 Diabetes." *Hormone Molecular Biology and Clinical Investigation*, vol. 42, no. 2, 2021, pp. 203–208., https://doi.org/10.1515/hmbci-2020-0055.
25. Savastano, Silvia, et al. "Low Vitamin D Status and Obesity: Role of Nutritionist." *Reviews in Endocrine and Metabolic Disorders*, vol. 18, no. 2, 2017, pp. 215–225, https://doi.org/10.1007/s11154-017-9410-7.
26. Zhao G, Ford ES, Li C. Associations of serum concentrations of 25-hydroxyvitamin D and parathyroid hormone with surrogate markers of insulin resistance among U.S. adults without physician-diagnosed diabetes: NHANES, 2003-2006. Diabetes Care. 2010;33(2):344–7.

27. Forouhi, Nita G., et al. "Baseline Serum 25-Hydroxy Vitamin D Is Predictive of Future Glycemic Status and Insulin Resistance." *Diabetes*, vol. 57, no. 10, 2008, pp. 2619–2625, https://doi.org/10.2337/db08-0593.
28. Davidson MB. Response to comment on: Davidson et al. High- dose vitamin D supplementation in people with prediabetes and hypovitaminosis D. Diabetes Care 2013;36:260–266. Diabetes Care. 2013;36(5):e72.
29. Cavalier, E. "Vitamin D and Type 2 Diabetes Mellitus." *Bioactive Food as Dietary Interventions for Diabetes*, 2013, pp. 195–205., https://doi.org/10.1016/b978-0-12-397153-1.00019-6.
30. Diabetes Mellitus, Fasting Blood Glucose Concentration, and Risk of Vascular Disease: A Collaborative Meta-Analysis of 102 Prospective Studies. *Journal of Vascular Surgery*, vol. 53, no. 2, 2011, pp. 548–549., https://doi.org/10.1016/j.jvs.2010.12.016.
31. Pawar, Shrikant. "Causes of Blindness and Vision Impairment in 2020 and Trends over 30 Years, and Prevalence of Avoidable Blindness in Relation to Vision 2020: The Right to Sight: An Analysis for the Global Burden of Disease Study." *SSRN Electronic Journal*, 2021, https://doi.org/10.2139/ssrn.3939242.
32. US Renal Data System 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States." *American Journal of Kidney Diseases*, vol. 75, no. 1, 2020, https://doi.org/10.1053/j.ajkd.2019.09.002.
33. Khunti, Kamlesh, et al. "Covid-19, Hyperglycemia, and New-Onset Diabetes." *Diabetes Care*, vol. 44, no. 12, 2021, pp. 2645–2655., https://doi.org/10.2337/dc21-1318.
34. Classification and diagnosis of diabetes: *standards of medical care in diabetes—2022*. (2021). *Diabetes Care*, *45*(Supplement_1). https://doi.org/10.2337/dc22-s002
35. Świątoniowska, Natalia, et al. "The Role of Education in Type 2 Diabetes Treatment." *Diabetes Research and Clinical Practice*, vol. 151, 2019, pp. 237–246, https://doi.org/10.1016/j.diabres.2019.04.004.
36. Siminerio L, Zgibor J, Solano Jr FX. Implementing the chronic care model for improvements in diabetes practice and outcomes in primary care: the University of Pittsburgh Medical Center experience. Clin Diabetes 2004;22(2):54–8.
37. Chatterjee, Sudesna, et al. "Diabetes Structured Self-Management Education Programmes: A Narrative Review and Current Innovations." *The Lancet Diabetes & Endocrinology*, vol. 6, no. 2, 2018, pp. 130–142, https://doi.org/10.1016/s2213-8587(17)30239-5.
38. Adeva-Andany, M. M., Rañal-Muíño, E., Vila-Altesor, M., Fernández-Fernández, C., Funcasta-Calderón, R., & Castro-Quintela, E. (2019). Dietary habits contribute to define the risk of type 2 diabetes in humans. *Clinical Nutrition ESPEN*, *34*, 8–17. https://doi.org/10.1016/j.clnesp.2019.08.002
39. Papamichou, D., et al. "Dietary Patterns and Management of Type 2 Diabetes: A Systematic Review of Randomised Clinical Trials." *Nutrition, Metabolism and Cardiovascular Diseases*, vol. 29, no. 6, 2019, pp. 531–543, https://doi.org/10.1016/j.numecd.2019.02.004.
40. Mocanu, Carmen-Antonia, et al. "Vegetable versus Animal-Based Low Protein Diets in the Management of Chronic Kidney Disease." *Nutrients*, vol. 13, no. 11, 2021, p. 3721, https://doi.org/10.3390/nu13113721.

41. Sievenpiper, J.L.; Chan, C.B.; Dworatzek, P.D.; Freeze, C.; Williams, S.L. Diabetes Canada Clinical Practice Guidelines Expert Committee. Nutrition therapy. *Can. J. Diabetes* 2018, *42* (Suppl. S1), S64–S79.
42. Ojo, O.; Ojo, O.O.; Adebowale, F.; Wang, X.H. The effect of dietary glycaemic index on glycaemia in patients with type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *Nutrients* 2018, *10*, 373.
43. Li, J., Glenn, A. J., Yang, Q., Ding, D., Zheng, L., Bao, W., Beasley, J., LeBlanc, E., Lo, K., Manson, J. A. E., Philips, L., Tinker, L., & Liu, S. (2022). Dietary protein sources, mediating biomarkers, and incidence of type 2 diabetes: Findings from the Women's Health Initiative and the UK Biobank. https://doi.org/10.2337/figshare.19860148
44. Comerford, Kevin, and Gonca Pasin. "Emerging Evidence for the Importance of Dietary Protein Source on Glucoregulatory Markers and Type 2 Diabetes: Different Effects of Dairy, Meat, Fish, Egg, and Plant Protein Foods." *Nutrients*, vol. 8, no. 8, 2016, p. 446., https://doi.org/10.3390/nu8080446.
45. Huang, J., Liao, L. M., Weinstein, S. J., Sinha, R., Graubard, B. I., & Albanes, D. (2020). Association between plant and animal protein intake and overall and cause-specific mortality. *JAMA Internal Medicine*, *180*(9), 1173. https://doi.org/10.1001/jamainternmed.2020.2790
46. Ferrari, Luca, et al. "Animal- and Vegetable Protein Sources: A Scoping Review of Human Health Outcomes and Environmental Impact." *Nutrients*, vol. 14, no. 23, 2022, p. 5115, https://doi.org/10.3390/nu14235115.
47. Wong, Nathan. "Faculty Opinions Recommendation of 2021 Dietary Guidance to Improve Cardiovascular Health: A Scientific Statement from the American Heart Association." *Faculty Opinions – Post-Publication Peer Review of the Biomedical Literature*, 2021, https://doi.org/10.3410/f.741097836.793589958.
48. Petersen, Kristina S, et al. "Healthy Dietary Patterns for Preventing Cardiometabolic Disease: The Role of Vegetable Foods and Animal Products." *Current Developments in Nutrition*, vol. 1, no. 12, 2017, https://doi.org/10.3945/cdn.117.001289.
49. Li, Man-Yun, et al. "Association between Egg Consumption and Cholesterol Concentration: A Systematic Review and Meta-Analysis of Randomized Controlled Trials." *Nutrients*, vol. 12, no. 7, 2020, p. 1995, https://doi.org/10.3390/nu12071995.
50. Mozaffarian D, Wu JHY. Flavonoids, dairy foods, and cardiovascular and metabolic health: a review of emerging biologic pathways. Circ Res 2018;122(2):369–84.
51. Feng, Yifei, et al. "Consumption of Dairy Products and the Risk of Overweight or Obesity, Hypertension, and Type 2 Diabetes Mellitus: A Dose–Response Meta-Analysis and Systematic Review of Cohort Studies." *Advances in Nutrition*, vol. 13, no. 6, 2022, pp. 2165–2179, https://doi.org/10.1093/advances/nmac096.
52. Schincaglia, Raquel, et al. "Nuts and Human Health Outcomes: A Systematic Review." *Nutrients*, vol. 9, no. 12, 2017, p. 1311., https://doi.org/10.3390/nu9121311.

53. Bouchard, J., Malalgoda, M., Storsley, J., Malunga, L., Netticadan, T., & Thandapilly, S. (2022). Health benefits of cereal grain- and pulse-derived proteins. *Molecules*, *27*(12), 3746. https://doi.org/10.3390/molecules27123746
54. “The Future of Food.” *Pulse Canada*, 18 Nov. 2022, https://pulsecanada.com/.
55. Mach, François, et al. “2019 ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk.” *European Heart Journal*, no. 1, Oxford University Press (OUP), Aug. 2019, pp. 111–88. *Crossref*, doi:10.1093/eurheartj/ehz455.
56. Magriplis, Emmanouella & Panagiotakos, Demosthenes & Karageorgou, Dimitra & Mitsopoulou, A. & Dimakopoulos, I. & Bakogianni, Ioanna & Zampelas, Antonis. (2018). Dietary intake of macronutrients and micronutrients, among the Greek population: HEL-NHANES ∗ Hellenic National Health and Nutrition Examination Survey 2013–2015. Clinical Nutrition ESPEN. 24. 185. 10.1016/j.clnesp.2018.01.050.
57. Alysha S. Thompson, Catharina J. Candussi, Anna Tresserra-Rimbau, Amy Jennings, Nicola P. Bondonno, Claire Hill, Solomon A. Sowah, Aedín Cassidy, Tilman Kühn, A healthful vegetable diet is associated with lower type 2 diabetes risk via improved metabolic state and organ function: A prospective cohort study, Volume 851, Issue 1, 10/2023, Pages 7-119, ISSN 1262-3636, http://dx.doi.org/10.1016/j.diabet.2023.101499
58. Shang, X., Scott, D., Hodge, A. M., English, D. R., Giles, G. G., Ebeling, P. R., & Sanders, K. M. (2016). Dietary protein intake and risk of type 2 diabetes: results from the Melbourne Collaborative Cohort Study and a meta-analysis of prospective studies. The American Journal of Clinical Nutrition, 104(5), 1352–1365. doi:10.3945/ajcn.116.140954
59. Satija A., Bhupathiraju S.N., Rimm E.B., Spiegelman D., Chiuve S.E., Borgi L., Willett W.C., Manson J.E., Sun Q., Hu F.B. Vegetable Dietary Patterns and Incidence of Type 2 Diabetes in US Men and Women: Results from Three Prospective Cohort Studies. PLoS Med. 2016;13:e1002039. doi: 10.1371/journal.pmed.1002039.
60. Vasanti S. Malik, Yanping Li, Deirdre K. Tobias, An Pan, Frank B. Hu, Dietary Protein Intake and Risk of Type 2 Diabetes in US Men and Women, American Journal of Epidemiology, Volume 183, Issue 8, 15 April 2016, Pages 715–728, https://doi.org/10.1093/aje/kwv268
61. van Nielen M., Feskens E.J.M., Mensink M., Sluijs I., Molina E., Amiano P., Ardanaz E., Balkau B., Beulens J.W.J., Boeing H., et al. Dietary Protein Intake and Incidence of Type 2 Diabetes in Europe: The EPIC-InterAct Case-Cohort Study. Diabetes Care. 2014;37:1854–1862. doi: 10.2337/dc13-2627.
62. Martimianaki G, Peppa E, Valanou E, Papatesta EM, Klinaki E, Trichopoulou A. Today's Mediterranean Diet in Greece: Findings from the National Health and

Nutrition Survey-HYDRIA (2013-2014). Nutrients. 2022 Mar 11;14(6):1193. doi: 10.3390/nu14061193. PMID: 35334847; PMCID: PMC8949101.

8. Appendix

Table 7. Multiple logistic regression that evaluates the odds ratio of IFG compared to Normal glucose status depending on the amount of vegetable protein consumption and smoking status in relation to the consumption of animal protein, saturated fat, total energy, sex, educational level, marital status and the level of adherence to the Mediterranean diet (MedDietScore), excluding T2DM for sensitivity analyses.

	Smoker				Ex Smoker				Non smoker			
	Odds Ratio	**Std. Err.**	**[95% Conf.**	**Interval]**	**Odds Ratio**	**Std. Err.**	**[95% Conf.**	**Interval]**	**Odds Ratio**	**Std. Err.**	**[95% Conf.**	**Interval]**
Total vegetable protein % of TEI												
2nd tertile	1.53	0.61	0.69	3.37	0.56	0.27	0.22	1.45	1.31	0.39	0.73	2.37
3rd tertile	2.66	1.04	1.23	5.74	0.78	0.37	0.30	2.01	1.77	0.55	0.96	3.26
Animal protein % of TEI	1.00	0.03	0.95	1.06	1.05	0.34	0.98	1.12	0.97	0.02	0.93	1.02
Saturated fat % of TEI	2.49	0.88	1.25	4.98	0.56	0.23	0.25	1.24	0.94	0.24	0.57	1.58
Total Energy	1.00	0.00	0.99	1.00	1.00	1.00	0.99	1.00	1.00	0.00	0.99	1.00
MedDietScore												
2nd tertile	0.57	0.20	0.29	1.17	0.54	0.26	0.20	1.41	0.61	0.18	0.34	1.09
3rd tertile	1.08	0.43	0.49	2.37	0.59	0.30	0.21	1.62	0.83	0.25	0.46	1.51
Sex	0.41	0.13	0.21	0.78	0.47	0.18	0.21	1.02	0.35	0.98	0.20	0.61
Age												
20-65	3.41	1.29	1.62	7.18	2.17	0.99	0.88	5.34	3.67	1.14	1.99	6.76
≥65	27.06	15.49	8.81	83.09	4.31	2.53	1.36	13.66	7.21	3.03	3.16	16.42
Educational Status												
Higher education inc. colleges	0.85	0.27	0.45	1.60	1.16	0.51	0.49	2.78	0.66	0.16	0.40	1.07
Up to 6 years of school	0.34	0.29	0.06	1.87	2.85	2.57	0.48	16.76	1.39	0.83	0.43	4.51
Marital Status	1.20	0.29	0.72	1.91	1.02	0.28	0.59	5.70	1.13	0.22	0.77	1.64