ATHENS,
2020

HAROKOPIO UNIVERSITY

Department of Nutrition and Dietetics

Postgraduate Program (P.P.) in Applied Nutrition and Dietetics Discipline of Clinical Nutrition

Assessment of dietary habits and their association with insulin resistance in the Feel4Diabetes study

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δηλώνω υπεύθυνα ότι:

1) Είμαι ο κάτοχος των πνευματικών δικαιωμάτων της πρωτότυπης αυτής εργασίας και από όσο γνωρίζω η εργασία μου δε συκοφαντεί πρόσωπα, ούτε προσβάλει τα πνευματικά δικαιώματα τρίτων.

2) Αποδέχομαι ότι η ΒΚΠ μπορεί, χωρίς να αλλάξει το περιεχόμενο της εργασίας μου, να τη διαθέσει σε ηλεκτρονική μορφή μέσα από τη ψηφιακή Βιβλιοθήκη της, να την αντιγράψει σε οποιοδήποτε μέσο ή/και σε οποιοδήποτε μορφότυπο καθώς και να κρατά περισσότερα από ένα αντίγραφα για λόγους συντήρησης και ασφάλειας.

THANKSGIVING

I would like to thank my supervisor, Professor Yannis Manios for giving me the opportunity to be part of his research team and participate in large research programs such as the present one.

I would also like to express my sincere thanks to Mrs Kalliopi Karatzi, for her solid help and guidance, as well as for her confidence, patience and kindness during the preparation of my thesis in order to be able to complete my work with the minimum number of misunderstandings and mistakes. I also owe her a big thanks for her valuable advice and suggestions which made me think more critically.

Last but not least, I would like to thank my family for their patience, support, love and constant encouragement.

Περιεχόμενα

ΠΕΡΙΛΗΨΗ

Σκοπός και εισαγωγή: Η ινσουλινοαντίσταση αποτελεί μια σημαντική μεταβολική κατάσταση η οποία μπορεί να οδηγήσει σε ποικίλες καρδιομεταβολικές διαταραχές, συμπεριλαμβανομένου του σακχαρώδη διαβήτη τύπου 2 (ΣΔτ2). Αρκετές μελέτες έχουν ερευνήσει τη συσχέτιση διαφόρων διαιτητικών συστατικών και προτύπων με την ινσουλινοαντίσταση τόσο σε υγιείς όσο και σε ασθενείς με ΣΔτ2. Σκοπός της παρούσας μελέτης είναι η διερεύνηση της πιθανής συσχέτισης διαφόρων διαιτητικών παραμέτρων με την ινσουλινοαντίσταση σε ενήλικες οι οποίοι βρίσκονται σε υψηλό κίνδυνο ανάπτυξης ΣΔτ2, σε ένα μεγάλο δείγμα από 6 Ευρωπαϊκές χώρες.

Μεθοδολογία: 2316 ενήλικες (41.13±5.5 χρονών) με υψηλό κίνδυνο ανάπτυξης ΣΔτ2 από 6 Ευρωπαϊκές χώρες (δεδομένα baseline από τη μελέτη Feel4Diabetes) συμμετείχαν στη συγκεκριμένη μελέτη. Οι ανθρωπομετρικές μετρήσεις, η αξιολόγηση των διατροφικών συμπεριφορών και οι εξετάσεις αίματος πραγματοποιήθηκαν μέσω τυποποιημένων διαδικασιών και επικυρωμένων ερωτηματολογίων. Η διατροφική αξιολόγηση έγινε είτε μέσω της χρήσης ομάδων τροφίμων είτε μέσω του δείκτη HealthyDietScore. Πολυπαραγοντικά μοντέλα λογιστικής παλινδρόμησης χρησιμοποιήθηκαν για τον έλεγχο της συσχέτισης των ομάδων τροφίμων ή του δείκτη HealthyDietScore με την ινσουλινοαντίσταση (μετρημένη μέσω του HOMA-IR) τόσο στο συνολικό δείγμα όσο και ανά περιοχή (Βόρεια, Νότια και Ανατολική Ευρώπη), ανά κοινωνικοοικονομικό επίπεδο (ΚΟΕ) (0-12 χρόνια και >12 χρόνια εκπαίδευσης) και ανά ηλικία (<45 και >45 χρονών) ύστερα από διόρθωση για τον ΔΜΣ, το κάπνισμα, το φύλο και τη φυσική δραστηριότητα.

Αποτελέσματα: Όσον αφορά τις ομάδες τροφίμων, η υψηλή κατανάλωση επεξεργασμένων δημητριακών και αναψυκτικών με ζάχαρη συσχετίστηκε θετικά με την ινσουλινοαντίσταση, ενώ η κατανάλωση χυμών χωρίς ζάχαρη, τσαγιού και καφέ συσχετίστηκε αρνητικά στο συνολικό δείγμα και τα περισσότερα από αυτά στο υψηλότερο ΚΟΕ και στους νεότερους συμμετέχοντες ύστερα από διόρθωση για τον ΔΜΣ, το κάπνισμα, το φύλο και τη φυσική δραστηριότητα. Σχετικά με την ποιότητα της δίαιτας, υψηλότερα σκορ του δείκτη HealthyDietScore συσχετίστηκαν αρνητικά με τον δείκτη HOMA-IR στο συνολικό δείγμα (0.66 (0.50-0.89) Exp(B) 95%C.Is), στην Βόρεια Ευρώπη (0.52 (0.29-0.94) Exp(B) 95%C.Is), στο υψηλότερο ΚΟΕ (0.61 (0.44-0.85) Exp(B) 95%C.Is) και στους νεότερους εθελοντές (0.66 (0.47-0.92) Exp(B) 95%C.Is) ανεξάρτητα από τον ΔΜΣ, το φύλο, το κάπνισμα και τη φυσική δραστηριότητα.

Συμπεράσματα: Η υψηλή συγκέντρωση επεξεργασμένων δημητριακών και αναψυκτικών με ζάχαρη συσχετίζεται θετικά με τον δείκτη HOMA-IR, ενώ η πρόσληψη χυμών χωρίς ζάχαρη, τσαγιού και καφέ εμφανίζει αρνητική συσχέτιση, σε άτομα με υψηλό κίνδυνο ανάπτυξης ΣΔτ2. Επιπλέον, η καλύτερη ποιότητα της δίαιτας συσχετίζεται αρνητικά με την ινσουλινοαντίσταση, κυρίως σε νεότερα άτομα υψηλού ΚΟΕ στη Βόρεια Ευρώπη. Επομένως, μελλοντικά προγράμματα παρέμβασης πρέπει να στοχεύσουν στον εντοπισμό και έγκαιρη αντιμετώπιση των ανθυγιεινών διατροφικών επιλογών στις πιο ευάλωτες πληθυσμιακές ομάδες, με στόχο την αποτελεσματικότερη μείωση του κινδύνου ανάπτυξης ΣΔτ2.

Λέξεις- κλειδιά: διατροφικές συνήθειες; διατροφή; αντίσταση στην ινσουλίνη; Σακχαρώδης Διαβήτης Τύπου 2;

ABSTRACT

Background and aim: Insulin resistance is a serious metabolic condition leading to many cardiometabolic health problems, including type 2 diabetes (T2DM). Several studies have examined the association between dietary components and dietary patterns with insulin resistance both in healthy and T2DM individuals, with inconsistent findings, while there is much less evidence regarding the above mentioned relation in people at risk for T2DM. Therefore, the aim of the present study is to investigate the possible associations between dietary indices and insulin resistance in adults at high risk for developing T2DM in a large sample from 6 European countries.

Methods: 2316 adults (41.13 ±5.5 years) at high risk for T2DM, from 6 European countries (baseline data collection of the Feel4Diabetes study) were used. Anthropometric measurements, dietary assessment and blood tests were performed through standard procedures and validated questionnaires. Diet was assessed either through use of food groups or as a whole using the HealthyDietScore. Logistic regression models were used to test the associations of food groups or the HealthyDietScore with insulin resistance (calculated by HOMA-IR) in the total sample and according to region (Northern, Southern and Eastern Europe), socioeconomic status (SES) (0-12 years and >12 years of education) and age (<45 and >45 years) after adjustment for BMI, smoking, sex and physical activity.

Results: Regarding food groups, high consumption of refined cereals and soft drinks with sugar has a positive association, while consumption of juice without sugar, tea and coffee has an inverse association with insulin resistance in the total sample and most of them in the higher SES groups and in younger participants, after adjustment for BMI, sex, smoking and physical activity. Regarding diet quality, higher scores of the HealthyDietScore were negatively associated with HOMA-IR in the total sample (0.66 (0.50-0.89) Exp(B) 95%C.Is), in Northern Europe (0.52 (0.29-0.94) Exp(B) 95%C.Is), in higher SES (0.61 (0.44-0.85) Exp(B) 95%C.Is) and in younger people <45 years (0.66 (0.47-0.92) Exp(B) 95%C.Is) independently of BMI, sex, smoking and physical activity.

Conclusion: High consumption of refined cereals and soft drinks with sugar is positively associated while consumption of juices without sugar, tea and coffee is inversely associated with HOMA-IR in people at risk of T2DM. Also, better diet quality is inversely associated with insulin resistance, especially in younger people of higher SES in Northern Europe. Therefore, future prevention programs should early identify and tackle unhealthy diet choices in the most vulnerable group of people in order to more efficiently reduce risk for T2DM.

Keywords: dietary habits; dietary pattern; insulin resistance; Type 2 Diabetes Mellitus; Feel4Diabetes;

LIST OF TABLES

LIST OF ABBREVIATIONS

T2DM	Type 2 Diabetes Mellitus
IR	Insulin Resistance
HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
BMI	Body Mass Index
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
RCT	Randomized Clinical Trial
FINDRISC	Finnish Diabetes Risk Score
SES	Socioeconomic Status
FFQ	Food Frequency Questionnaire
WC	Waist Circumference
TAG	Triacylglycerols
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
HbA1c	Hemoglobin A1c
SSBs	Sugar-sweetened beverages

1.1 DEFINITION

Insulin resistance is an abnormality which has been recognized since Himsworth's classic observations in the 1930s and provides a basis for the development of numerous metabolic, endocrine and cardiovascular diseases. It is defined as the inability of a specific quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual comparing with the respective procedure in a normal population [1]. Reaven in 1988 proposed that the cluster of insulin resistance (and by definition, hyperinsulinemia), impaired glucose tolerance, abnormalities of plasma lipids and hypertension was describing a syndrome which he called Syndrome X or insulin resistance syndrome or more commonly the metabolic syndrome [2]. There are several mechanisms which could lead to the development of the insulin resistance syndrome, as it enrolls a group of metabolic and cardiovascular risk factors, including the genetic background of the individual, fetal malnutrition, all enhanced by existence of visceral adiposity. All these risk factors may trigger the development of T2DM, accelerated atherosclerosis, hypertension or polycystic ovarian syndrome [1]. Insulin resistance can be measured by a hyperinsulinemic-euglycemic clamp, by HOMA (homeostasis model assessment) index or by dynamic oral glucose tolerance test. The first method is the gold standard method for estimating insulin resistance but it cannot be used for large population studies in contrast with HOMA-IR which is suitable for large epidemiological studies [3].

1.2 CONSEQUENCES

The consequences of insulin resistance syndrome are associated with the status of beta cell. If the function of beta cell is normal or well-preserved the major impact may be an increase in cardiovascular risk factors and the development of an atherogenic endothelial dysfunction or the polycystic ovary syndrome in susceptible women. Otherwise, if there is an insufficiency of beta cell, the major impact will be T2DM. Both status are strongly dependent on the interrelation of beta cell function and the genetic background of an individual [1].

An important meta-analysis which has been conducted in 2017 aimed to investigate the correlation between elevated fasting insulin/HOMA-IR and cardiovascular or all-

cause mortality risk in non-diabetic adults after collecting data of prospective observational studies. The results of this meta-analysis shown that there is an independent association of insulin resistance (which has been measured with HOMA-IR) and risk of cardiovascular and all-cause mortality. It was shown that participants on the highest HOMA-IR category had a 111% higher risk of cardiovascular and all-cause mortality compared to a 34% risk of the lowest HOMA-IR category. However this meta-analysis had several limitations as there was a small number of articles included (seven studies) highlighting the need of more well-designed prospective studies in order to confirm these findings [2].

Another important meta-analysis investigated the relationship between insulin resistance and the risk of hypertension in a general population. A total of 11 studies (prospective observational studies) were included in this meta-analysis. Hypertension was defined as SBP/DBP ≥ 140/90 mmHg. The results confirmed that an elevated fasting insulin or insulin resistance, which was calculated by HOMA-IR, was associated with a higher risk of hypertension in the general population. Women had a greater risk of hypertension than men which may be due to the different fasting insulin levels or the higher rates of obesity in women. A possible mechanism of hypertension caused by insulin resistance is the activation of the renin-angiotensin system which could lead to an increase in peripheral and renal vascular resistance. There are also several limitations in this meta-analysis including the small number of studies, the assessment of insulin resistance (HOMA-IR reflects only the hepatic insulin resistance) and other parameters such as medications, alcohol intake, smoking and physical activity [4].

1.3 DIET COMPOSITION AND INSULIN RESISTANCE

Several studies have examined among many other risk factors the association of diet composition in the development of insulin resistance syndrome. It turned out that diet has a strong association with insulin resistance that may explain the striking effect of nutrition on the risk of T2DM and cardiovascular disease. Although many food groups and food items were found to be associated with insulin resistance those presenting with more robust results are red meat, vegetables, fruit juice, dairy intake as well as dietary fiber [5].

1.3.1 RED MEAT CONSUMPTION

Prospective studies have shown that elevated consumption of animal products and low intake of plant-based foods increase the risk of insulin resistance syndrome and T2DM [4]. A meta-analysis that was published in 2011, assessed the consumption of red meat (processed and unprocessed) with the risk of T2DM. The researchers concluded that a greater consumption (especially of processed red meat) is consistently associated with a higher risk of developing diabetes [6]. A more resent meta-analysis investigated again the relationship between red meat consumption (processed and unprocessed) and fasting glucose and insulin concentrations in Caucasians without diabetes mellitus. The meta-analysis included 14 epidemiologic studies and showed that the intake of processed meat was associated with higher fasting glucose and specifically every additional 50g of processed meat there was an increase of 0.021 mmol/L in fasting glucose. The same result was also found in the consumption of unprocessed red meat where a 0.037 mmol/L increase in fasting glucose was observed with every additional 100g consumption. The possible mechanism which could explain this result may concern nitrosamines, heme iron or advanced glycation end products that are present in red meat. Another possible explanation is the elevated consumption of saturated fat (such as processed meat and unprocessed red meat) which could promote obesity a disease that is strongly connected to glucose intolerance, insulin resistance and diabetes [7].

1.3.2 FRUIT JUICE CONSUMPTION

Accumulating evidence suggests that lifestyle changes can help prevent the appearance of insulin resistance and T2DM. Fruits are rich in fiber antioxidants and phytochemicals which may play a protective role against diabetes and insulin resistance [8]. In contrast, the dietary guidelines for Americans claim that fruit juices are less desirable than whole fruits as they have less dietary fiber than a whole fruit [9]. The same result emerged from another study which pointed out the small amount of fiber in fruit juices but emphasized in other important nutritional components such as antioxidants and phytochemicals [10]. A meta-analysis which has been conducted in 2014 included 12 randomized control trials (RCTs) that highlighted the association

between fruit juice consumption and glucose control and insulin sensitivity. The findings showed that there was no significant effect of the fruit juices in fasting glucose and insulin concentrations. This result may reveal the common knowledge that fruit juices have less fiber than whole fruits. Another possible explanation may be the increase in the consumption of sugars and energy in the participants. However, an important limitation of this meta-analysis is the small number of RCTs as well as the small sample sizes and the short periods of follow-up. Further well-designed studies are needed in order to clarify the association between fruit juice and glycemic control [8].

1.3.3 DAIRY CONSUMPTION

Several studies have shown that daily consumption of low-fat dairy products has a protective effect against diabetes [11, 12]. A recent meta-analysis of RCTs included 30 articles that correlated the effect of dairy intake in adults and insulin resistance and body mass index changes through weight loss. Findings suggest that a diet that includes low-fat dairy products leads to a decrease in HOMA-IR (-1.21 between dairy and placebo groups) and oxidative stress markers and therefore decreases the risk of insulin resistance and T2DM. A beneficial effect was also noticed in waist circumference and body weight. There are several possible mechanisms to explain this effect including vitamin D, casein and whey proteins which are all present in low-fat dairy products and play an important role in regulating body fat and insulin sensitivity. Calcium is also an important component which may promote fat cell apoptosis and inhibition of lipolysis via the expression of fatty acid synthase. Although these findings are of a great importance for healthcare providers, there is a need of conducting larger RCTs in order to have a more definitive answer concerning the effect of low-fat dairy intake and its impact on insulin resistance [13].

1.3.4 OATS, FRUIT AND VEGETABLE CONSUMPTION

The increase in the incidence rate of diabetes mellitus has led to the need of exploring many dietary components including oats, fruits and vegetables intake. Oats and oatmeal products are rich in β-glucans, minerals and other nutrients which could help in improving blood glucose concentrations. A meta-analysis of RCTs, which conducted

in 2014 and included 15 articles, indicated that oat intake leads to significantly lower fasting insulin concentrations with no significant effect on fasting glucose concentration, HbA1C and HOMA-IR. Further, long-term RCTs are required in order to investigate the effect of oat intake on fasting glucose concentrations [14]. Another more recent meta-analysis, included 4 RCTs in diabetic patients who followed an oat-enriched diet in the intervention group. Oat β-glycan intake for 3-8 weeks improved glycaemic control in diabetic patients (specifically fasting plasma glucose and HbA1c) but had no significant effect on fasting plasma insulin concentrations [15]. Concerning the intake of vegetables and fruits several studies have investigated their effect on insulin resistance and the risk of type 2 diabetes with controversial results. Some studies demonstrated a beneficial effect on insulin resistance and the risk of T2DM [16-19] and some others showed no significant effect [20, 21].

1.4 DIETARY PATTERNS AND INSULIN RESISTANCE

Nutritional epidemiology has focused on the effects of single nutrients or food groups creating the need of investigating the association of dietary patterns with insulin resistance, as nutrients and foods are consumed in combination. Several studies compared the adherence to a healthy-prudent dietary pattern (high in fruits, vegetables, whole grains, fish, poultry and legumes) with a western dietary pattern (high in refined grains, red meat, butter, processed meat, high-fat dairy products, sweets and desserts). The findings indicate that a dietary pattern characterized by high consumption of fruit, vegetables and whole grains is associated with a significantly reduced risk of insulin resistance and the metabolic syndrome, comparing to a western dietary pattern [22-24]. A recent meta-analysis included 28 articles which examined the association of metabolic syndrome with a prudent dietary pattern. The results confirmed that such a dietary pattern is associated with a lower prevalence of metabolic syndrome. An important mechanism concerns the antioxidant content of fruits, vegetables, whole grains and legumes which play a protective role against cardiovascular diseases [25]. Oxidative stress constitutes a confounding factor in the pathogenesis of diabetes mellitus and insulin resistance. A higher dietary antioxidant capacity is associated with a lower risk of T2DM, lower HOMA-IR not only in the total

population but also among people with prediabetes. Dietary antioxidants may improve insulin sensitivity by lowering oxidative stress, and suppress the apoptosis of pancreatic β-cells, sustaining in this way β-cell function [26].

1.5 AIM OF THE STUDY

This work has been carried out with data collected within the Feel4Diabetes program. The EU-funded Feel4Diabetes-study focused on the development, implementation and evaluation of a school and community-based intervention to prevent T2DM and obesity related metabolic risk factors in vulnerable families across Europe. The family environment, the community and the school environment play an important role in the determination of family lifestyle habits. These environments undoubtedly act as the main role models for kids leading to the need of a proper orientation and promotion of a healthy lifestyle. Glucose homeostasis and insulin sensitivity contribute to the prevention of type 2 diabetes in people at high risk or slow the progress of the disease development. Several cohort studies and randomized controlled trials in general population and in people with T2DM have investigated the relationship between different nutritional components and dietary patterns with insulin resistance. Despite much research the relevant evidence for several individual food items and dietary patterns is not clear yet. Nutritional components and dietary patterns need to be further examined for their efficacy in relation to glucose metabolism and insulin resistance specifically in people at high risk for developing T2DM, which is far less investigated and less evidenced. Therefore, the aim of this study is to investigate possible associations between dietary habits and insulin resistance in adults at high risk for developing T2DM in a large sample from 6 European countries.

2. METHODOLOGY

2.1 THE STUDY

Feel4Diabetes was a large school community-based study which was implemented within the academic years 2016-2017 and 2017-2018. The sample of the intervention was consisted of families (children, parents and grandparents) from vulnerable social groups in six European countries including low/middle income families (Bulgaria, Hungary), low socioeconomic areas in high income countries (Belgium, Finland) and countries with economic crisis (Greece, Spain). The aim of the study was the promotion of a healthy lifestyle including healthy eating and enhancing physical activities in order to alleviate the negative outcomes of obesity and obesity- related metabolic risk factors. The study complied with the declaration of Helsinki as well as the conventions of the European Council of human rights and biomedicine. All countries obtained ethical clearance from the ethical committees and local authorities. Concerning Greece, the intervention was approved by the Bioethics Committee of Harokopio University and the Greek Ministry of Education. In order to enroll in the study, parents provided signed consent forms.

2.2 RECRUITMENT

Children attending the first three grades of compulsory education and their families were recruited to the study ("all families" group). The final sample consisted of a total of 11.511 families ("all families") of whom 2.230 recruited the "high-risk families" group. In order to identify the "high-risk families" based on the risk possibility of developing T2DM the Finnish Risk Score (FIDRISC) was used. To be regarded as a "high-risk family", at least one parent in the family had to fulfill the country-specific cut-off point.

2.3 FINDRISC AND QUESTIONNAIRES

The FINDRISC tool was given to the parents and grandparents. This tool was completed by the parents (biological or adoptive) of the child at the first phase of recruitment and included six questions concerning a) age; b) weight; c) height; d) waist circumference; e) the existence of at least 30 minutes of physical activity daily f) daily

consumption of fruits and vegetables. If at least one parent of each family had a FINDRISC score above a country-specific cut-off point, the family was characterized as “high-risk”. For Greece this cut-off point was a score of at least 9. In addition to the FINDRISC tool there were questions about socioeconomic status (SES) and family status (the number and age of family members and the financial situation) as well as educational level, smoking sleeping hours, history of diabetes, hypertension and cholesterol. Moreover, parents filled out a short Food Frequency Questionnaire (FFQ), questions about the frequency and quality of breakfast, the quantity, quality and frequency of consumption of particular types of food (dairy products, bread, fats, fruits, vegetables, red meat, processed meat, white meat, fish, seafood, salty snacks, pastries, nuts, seeds, water, tea, coffee, alcoholic beverages, soft drinks with or without sugar) and their physical activity. Finally, the questionnaire included questions about the availability of food at home, eating habits, the parent's psychological condition and the existence of electronic devices in the child's room.

2.4 FEEL4DIABETES HEALTHY DIET SCORE

The Feel4Diabetes Healthy Diet Score was used in order to evaluate the diet of the population across this multinational project. Given that one of the aims was the identification of families at increased risk of T2DM and the provision of interventions in order to decrease that risk, this score was consisted of components that represent these goals, based on their importance as risk or protective factors for T2DM. These components were breakfast, vegetables, fruit and berries, sugary drinks, whole-grain cereals, nuts and seeds, low-fat dairy products, oils and fats, red meat, sweet snacks, salty snacks and family meals. Physical activity and sedentary behaviors were excluded from the score. Total score which is calculated as the sum of the component scores, ranges from 0 to 100. Higher scores indicate better quality of diet, regarding the risk of developing T2DM. It represents a reliable tool for measuring the level of and changes in the adherence to the goal of the intervention [27].

2.5 THE PROTOCOL

After the end of the initial recruitment and assessment of the study population the intervention of the study took place. Participants were divided in two groups. The “all-

families" group whose intervention was applied in the school environment and the "high-risk families" group whose intervention took place out of school. The initial measurements were carried out between April and June, whereas for Finland, Hungary and Bulgaria between August and September of 2016. The first level referred to "all families" regardless of the risk of developing T2DM and included improvements to the social and physical environment of the school and home and a session with general guidelines for a healthy and active lifestyle. The main goals were to increase the consumption of water, fruits and vegetables, breakfast and morning snacks. The adults of the "high-risk families" group were asked to attend the local community center of the municipality in order to undergo a more analytic assessment. This assessment included 7 counseling sessions about participants' lifestyle during the 1st year of the study, (academic year 2016 –2017). The first 6 sessions were completed by March 2017, whereas the 7th was held in September 2017. In the 7th session, the results from the 1st follow –up and the 1st check –up were presented to each family. In the last session the objectives of the second year of intervention were set. The counseling sessions included behavioral techniques in order to increase motivation and self –efficacy of participants in "high risk families" group, to improve self –regulation and establish measurable, feasible, realistic and time –specific goals. In every session, "high risk families" group was provided with relevant material and carried out specific activities, either during the session or at home. During the 2nd year of intervention, (academic year 2017 –2018), participants received incentive feedback and mobile message guidance. The present study used material only from the cross sectional part of the protocol.

2.6 MEASUREMENTS

One parent from each "high risk" family was invited in order to undergo anthropometric measurements (weight, height, and waist circumference), blood pressure measurement, and blood tests. They were also given pedometers or accelerometers to measure physical activity. In addition, the date of the assessments and any possible conditions during the measurements were recorded.

2.6.1 ANTHROPOMETRIC MEASUREMENTS

Body weight

Body weight was measured twice in every session for each participant by the same examiner. Measurements were conducted by using weight scales SECA 813 and SECA 877. Participants were asked to remove their shoes, any heavy object (e.g. belt, keys) and clothes that could be removed. Then, participants were asked to stand in the center of the scale with their weight evenly distributed on both legs. They had to remain stable until the indication was stabilized in the scale. The indication was recorded at the nearest ten kilogram (0,1 Kg). A third measurement was performed only if the previous two varied by 100 g. Study participants were categorized for their body weight by using Body Mass Index (BMI), as defined by WHO [28]. Individuals unable to stand or in a wheel chair, pregnant women or participants who refused were excluded.

Height

The height measurement was taken twice by the same examiner. A third measurement was only conducted in the previous two differed for more than 1 cm. SECA 213, SECA 214, SECA 217 and SECA 225 were the stadiometers used. Researchers asked every participant to remove the shoes or any other garment or object that caused difficulties to the measurement (e.g. heavy clothing, hair accessories).Then, they had to stand in a natural position with the back turned to the stadiometer, focus on a point straight across and remain stable. The researcher had to confirm that the participant's position was correct and then the measurement was conducted at the end of a deep breath. Participants with difficulties in standing, unable to move or in a wheelchair, those being higher than the maximum height of the stadiometer, pregnant women or people that refused to get measured were excluded from the measurement.

Waist circumference

The waist circumference is an important indicator of visceral fat and is related to fat-free mass. This measurement was carried out twice in a private place and a third one took place only if the previous two varied more than 1 cm. The examiner asked the

participants to empty his/her bladder, if possible, and was remove heavy objects and clothes to reveal the waist. If the volunteer did not feel comfortable, the measurement could be done with light clothing and this information was recorded. The volunteer had to stand in a relaxed position with hands hanging loosely on the side of the body and the weight evenly distributed on both legs and breathe normally. The investigator asked the volunteer to breathe out normally and the measurement was recorded at the end of a normal exhalation. The limits used are: <80cm or <94cm, 80-88cm or 94-102cm,> 88cm or> 102cm for women and men respectively [28]. WC was not measured in individuals that had difficulties in standing straight, who were immobile or in a wheelchair, were pregnant, had colostomy, ileostomy, recent abdominal surgery or other problems/ devices that impeded proper measurement, their WC exceeded the maximum length of the tape used or denied to perform the measurement.

Blood tests

Blood samples were taken by qualified staff in the morning between 8:30 and 10:30. Participants had to follow fasting overnight (12 hours). Blood was collected in order to determine fasting glucose, HbA1, total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride (TAG) levels. A day before the blood tests, one investigator had to communicate with the parents to ensure the overnight fasting. The collection of blood samples (up to 16 mL of blood) was performed with venipuncture by professional staff. Some of the samples were left to coagulate for 30 to 120 minutes without the use of an anticoagulant to separate the serum. This blood was centrifuged at 3000 rpm for 10 minutes and the serum was divided into fractions and stored at -80 ° C. All serum samples were transferred to dry ice in the Dietetic and Clinical Dietetics Laboratory of Harokopio University of Athens where they were stored at -80^{o}C.

Glucose was determined by the GOD-PAP enzymatic reaction (hexokinase method). For the diagnosis of pre-diabetes, dysglycemia and diabetes, the criteria of the World Health Organization were used [29]. Blood lipids were determined by an automatic analyzer (Roche / Hitachi Modular) twice, using the Enzymatic Colorimetric Analysis (Roche Diagnostics SA, Vasilia, Switzerland). HOMA-IR for estimating insulin resistance

was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (mmol/L)/22.5 [30]. HOMA-IR values > 2.05 define insulin resistance in high risk adults for diabetes mellitus. This threshold is slightly lower than others in European healthy adult populations, with no metabolic risks taken into account [31, 32] and higher than values in non-European populations with metabolic risks [33]. It is also close to the value of ≥2.00 proposed by EGIR (the European Group for the Study of Insulin Resistance) from RISC study, yet proposed for healthy people with no signs or symptoms of disease [34]. After the completion of RISC study new data and research have emerged with new thresholds of HOMA-IR in various populations and by different methods. The threshold 2.05 of HOMA-IR was chosen based on a cross sectional study in a large and well characterized population based sample of non-diabetic Spanish adults with multiple metabolic risk factors, which best matched with the profile of the high risk group of this study [35, 36]. For those reasons the value 2.05 of HOMA-IR was estimated to be more suitable for the purpose of this study.

Blood Pressure

The automated Omron M6 AC and Omron M6 were used to measure systolic and diastolic blood pressure and pulses/minute. The measurement was conducted in a private, quiet place with the proper temperature. Participants were asked to sit down and relax for 5 minutes before the measurement. After, the researcher started the measurement and the indication of the device was recorded. Three measurements were conducted in total and the average of the three of them was calculated. The measurement was performed on the right hand, which was resting on a desk, so that the upper arm was at the level of the heart. Volunteers should abstain from food, beverages (except water), smoking and intense physical activity for at least 1 hour before the measurement.

2.6.2 PHYSICAL ACTIVITY

Physical activity was measured using electronic pedometers or accelerometers as steps per day in the “high-risk families”. The pedometers that were used were the following: OMRON model HJ-720IT-E2 Walking style Pro Pedometer and Omron HJ-322U-E Walking Style Pro 2.0 3D USB Accelerator Sensor Step Counter, while the

accelerometer types were the following: GT1M ActiGraph, GT3X ActiGraph, GT3X+ ActiGraph and Traxmeet.

Pacemakers and accelerometers were given to the participants with instructions to ensure proper use. A calendar of activities in order to keep a record was also provided. Every time the device had to be deactivated, they had to mention the reason why and the time that the device was not in use. Participants placed the device to the trouser/ skirt zone and specifically to the right hip side in alignment with the middle of the right knee. Participants with movement difficulties or restricted movement were excluded from this measurement. Questionnaires were also used in order to assess the physical activity. There were questions concerning the frequency, intensity, type of physical activity that the participant had the previous 7 days and contribution of other people to that decision. Finally, participants were asked to mention their opinion on the minimum recommended time for physical activity.

2.7 STATISTICAL ANALYSIS

For the statistical analysis of the study data, SPSS 21.0 (SPSS: Statistical package for social sciences, SPSS Inc., Chicago, IL, USA) was used and statistical significance level was set as $p \leq 0.05$. The categorical variables are presented as relative frequencies (%), while the continuous variables as mean ± standard deviation (SD). The normality of distribution of variables was determined by the Kolmogorov –Smirnov test. The independent associations of the dietary variables with the existence of insulin resistance (calculated by HOMA-IR) was tested by multiple logistic regression analysis. All the analysis were performed in the total sample as well as according to region, age and SES categories. The above mentioned statistical analyses was also adjusted for BMI, smoking, sex and physical activity in order to identify the most dominant behaviors independently associated with insulin resistance.

3. RESULTS

3.1 Descriptive characteristics

The study sample consisted of 2316 adults with mean age 41.13 (±5.5) years, mean BMI 28.52 (±5.45) kg/m^2. Study participants' characteristics are shown in Table 1a.

Table 1α. Descriptive characteristics of the study sample

Variables	**Total** (N=2316)
Age	41.13 (±5.5)
Gender Female	 66.7%
Education 0-12 >12	 40.6% 59.4%
BMI (kg/m^2)	28.52 (±5.45)
Tchol (mg/dL)	194.53 (±37.91)
LDL (mg/dL)	120.62 (±33.11)
HDL (mg/dL)	53.17 (±13.98)
Dysglucaemia Normal (<110) Prediabetes (110-126) Diabetes (>126)	 93.0% 5.4% 1.7%
Glucose (mg/dL)	94.63 (± 14.28)
Insulin (pmol/L)	69.41(± 64.29)
HbA1c (%)	5.46 (±0.52)
SBP (mmHg)	117.83 (±16.68)
DBP (mmHg)	78.39 (±11.42)
MPA (min/day)	39.81 (±61.99)
Smoking status Never smoked Former smoker Current smoker	 45.5% 28.2% 26.3%
Low fat dairy (240mL/day)	0.83 (±1.21)
Full fat dairy (240mL/day)	0.43 (±0.77)
Vegetables (cups/day)	0.59 (±0.56)
Fruits and berries (cups/day)	0.52 (±0.51)
Refined cereals (30g)	0.15 (±0.59)
Whole grain cereals	0.47 (±0.89)
Legumes (cups/day)	0.29 (±0.26)
Red meat (g/day)	73.89 (±56.02)
White meat (g/day)	56.5 (±43.09)
Fish (g/day)	34.26 (±28.43)
Salty snacks (portions/day)	0.24 (±0.31)
Sweet snacks (40g/day)	0.56 (±0.7)

Nuts and seeds (30g/day)	0.31 (±0.49)
Tea (250mL/day)	0.35 (±0.72)
Coffee (250mL/day)	1.48 (±1.28)
Soft drinks with sugar (250mL/day)	0.20 (±0.48)
Soft drinks without sugar (250mL/day)	0.24 (±0.59)
Juice without sugar (250mL/day)	0.25 (±0.39)
Juice with sugar (250mL/day)	0.10 (±0.27)
Beer and cider (330mL/day)	0.27 (±0.60)
Wine (125mL/day)	0.18 (±0.35)
Spirits (40mL/day)	0.10 (±0.29)

BMI (Body Mass Index), Tchol (Total cholesterol), LDL (Low-density lipoprotein), HDL (high-density lipoprotein), HbA1c (Hemoglobin A1c), SBP (systolic blood pressure), DBP (diastolic blood pressure), MPA (moderate physical activity).

3.2 Association between dietary factors with insulin resistance in the total sample.

Higher consumption of refined cereals and soft drinks with sugar have a positive association with HOMA-IR, whereas higher consumption of tea, coffee and juices without sugar have a negative association with insulin resistance (table 1b).

Table 1b. Association between dietary factors with insulin resistance in the total sample of the study.

Variables (total)	**HOMA-IR** (n=752)
	OR (95% C.I.s)
Low fat dairies (cups/day, 240mL)	1.16 (0.91-1.47)
Full fat dairies (cups/day, 240mL)	0.95 (0.71-1.27)
Fruits and berries (cups/day)	1.03 (0.68-1.54)
Refined cereals (30g)	**1.44 (1.02-2.03)**
Whole grain cereals	0.91 (0.73-1.14)
Legumes (cups/day)	0.51 (0.25-1.08)
Red meat (g/day)	1.00 (0.99-1.01)
White meat (g/day)	1.00 (0.99-1.01)
Fish (g/day)	1.00 (1.00-1.01)
Salty snacks (*portions/day)	1.14 (0.68-1.91)
Sweet snacks (portions/day)**	1.01 (0.78-1.31)
Nuts and seeds (30g/day)	1.16 (0.83-1.61)
Tea (250mL/day)	**0.66 (0.47-0.93)**

Coffee (250mL/day)	**0.83 (0.70-0.99)**
Soft drinks with sugar (250mL/day)	**1.92 (1.15-3.20)**
Soft drinks without sugar (250mL/day)	0.93 (0.68-1.27)
Juice without sugar (250mL/day)	**0.52 (0.30-0.92)**
Juice with sugar (250mL/day)	0.91 (0.40-2.07)
Beer and cider (330mL/day)	1.06 (0.66-1.72)
Wine (125mL/day)	0.94 (0.49-1.80)
Spirits (40mL/day)	1.12 (0.47-2.67)

In bold letters, are the statistically significant findings after adjustment for sex, BMI, smoking and physical activity.* 1 portion of salty snacks = 1 small bag of crisps, 1 cheese pie or 1 piece of pizza, **1 portion of sweet snacks= 40 g of chocolate, ½ cup of sweets, biscuits or 1 scoop of ice cream.

3.3 Association between dietary indices with insulin resistance according to region, SES and age categories.

Higher consumption of soft drinks with sugar is positively associated with HOMA-IR in the lower SES and in the age group of <45 years, whereas higher consumption of coffee in these groups has a negative association. Additionally, juices without sugar is negatively associated with insulin resistance in the lower SES and the age group of <45 years (table 1c).

Table 1c. Association between dietary and physical factors, smoking, BMI and gender with insulin resistance are presented according to region, SES and age groups.

Variables	**HOMA-IR**						
	Northern Europe (n=165)	Southern Europe (n=447)	Eastern Europe (n=140)	0-12 (n=389)	>12 (n=363)	<45 (n=586)	>45 (n=162)
	OR (95% C.I.s)	OR (95% C.I.s)	OR (95% C.I.s)	OR (95% C.I.s)	OR (95% C.I.s)	OR (95% C.I.s)	OR (95% C.I.s)
Low fat dairies (cups/day, 240mL)	0.89 (0.55-1.43)	1.36 (0.94-1.98)	1.69 (0.81-3.50)	1.23 (0.86-1.76)	1.09 (0.77-1.54)	1.23 (0.96-1.59)	0.72 (0.28-1.85)
Full fat dairies (cups/day, 240mL)	0.91 (0.41-2.02)	1.04 (0.7-1.55)	0.78 (0.34-1.79)	0.89 (0.59-1.35)	1.04 (0.70-1.57)	0.83 (0.57-1.12)	1.26 (0.75-2.14)

Fruits and berries (cups/day)	0.58 (0.16-2.16)	0.82 (0.45-1.48)	2.02 (0.82-4.97)	0.86 (0.47-1.58)	1.26 (0.70-2.29)	1.07 (0.69-1.67)	0.71 (0.22-2.28)
Refined cereals (30g)	1.80 (0.68-4.79)	1.36 (0.86-2.15)	2.35 (0.54-10.28)	1.62 (0.94-2.78)	1.40 (0.87-2.26)	1.38 (0.96-1.98)	2.59 (0.50-13.39)
Whole grain cereals	0.96 (0.56-1.64)	0.80 (0.58-1.11)	0.92 (0.48-1.75)	0.89 (0.62-1.28)	0.87 (0.65-1.16)	0.97 (0.76-1.23)	0.78 (0.37-1.65)
Legumes (cups/day)	0.54 (0.03-11.82)	0.63 (0.22-1.78)	1.19 (0.16-8.80)	0.70 (0.24-2.07)	0.40 (0.12-1.27)	0.69 (0.29-1.62)	0.19 (0.02-1.55)
Red meat (g/day)	1.00 (0.99-1.01)	1.01 (1.00-1.01)	0.99 (0.99-1.01)	1.01 (0.99-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (0.99-1.01)
White meat (g/day)	1.00 (0.99-1.01)	0.99 (0.99-1.00)	1.00 (0.99-1.02)	**0.99 (0.98-0.99)**	1.01 (1.00-1.02)	1.00 (1.00-1.01)	0.99 (0.97-1.00)
Fish (g/day)	0.99 (0.97-1.02)	0.99 (0.98-1.01)	0.99 (0.97-1.02)	0.99 (0.98-1.01)	1.00 (0.98-1.02)	1.00 (0.99-1.01)	0.99 (0.97-1.01)
Salty snacks (portions/day)	1.44 (0.22-9.63)	1.54 (0.77-3.08)	0.40 (0.07-2.36)	1.16 (0.58-2.30)	1.23 (0.50-3.03)	0.86 (0.44-1.67)	2.65 (0.95-7.44)
Sweet snacks (40g/day)	1.25 (0.78-2.01)	0.81 (0.53-1.26)	0.46 (0.13-1.60)	1.66 (0.96-2.86)	0.97 (0.69-1.37)	1.12 (0.82-1.55)	0.72 (0.41-1.28)
Nuts and seeds (30g/day)	1.55 (0.63-3.82)	0.89 (0.55-1.47)	1.07 (0.49-2.34)	0.88 (0.55-1.41)	1.55 (0.96-2.51)	1.22 (0.86-1.73)	0.79 (0.31-1.99)
Tea (250mL/day)	0.44 (0.19-1.05)	0.89 (0.55-1.46)	**0.29 (0.09-0.91)**	0.97 (0.65-1.43)	**0.31 (0.15-0.61)**	0.67 (0.42-1.06)	0.87 (0.43-1.77)
Coffee (250mL/day)	0.76 (0.56-1.03)	0.89 (0.68-1.16)	0.78 (0.37-1.64)	1.02 (0.77-1.35)	**0.76 (0.59-0.96)**	**0.79 (0.65-0.96)**	0.95 (0.59-1.51)
Soft drinks with sugar (250mL/day)	**3.82 (1.62-8.99)**	1.62 (0.53-5.01)	0.69 (0.17-2.78)	1.37 (0.66-2.83)	**2.68 (1.23-5.84)**	**1.87 (1.06-3.30)**	1.48 (0.35-6.30)
Soft drinks without sugar (250mL/day)	0.74 (0.47-1.19)	1.49 (0.69-3.21)	1.61 (0.24-10.75)	0.80 (0.52-1.24)	1.06 (0.67-1.67)	0.97 (0.69-1.36)	0.72 (0.30-1.75)
Juice without sugar (250mL/day)	0.39 (0.66-2.35)	0.52 (0.26-1.03)	0.37 (0.08-1.84)	**0.45 (0.22-0.93)**	0.74 (0.27-2.06)	**0.44 (0.23-0.85)**	1.89 (0.33-10.86)
Juice with sugar (250mL/day)	0.68 (0.12-3.86)	0.75 (0.11-5.01)	1.39 (0.37-5.30)	1.27 (0.27-6.07)	0.82 (0.25-2.68)	0.79 (0.28-2.18)	1.10 (0.18-6.80)
Beer and cider (330mL/day)	2.45 (0.73-8.26)	0.98 (0.34-2.85)	0.99 (0.44-2.25)	1.15 (0.51-2.58)	1.32 (0.66-2.66)	1.04 (0.60-1.79)	0.92 (0.23-3.65)
Wine (125mL/day)	0.46 (0.09-2.47)	0.69 (0.25-1.94)	1.28 (0.32-5.19)	0.70 (0.23-2.14)	1.20 (0.49-2.96)	1.18 (0.56-2.47)	0.33 (0.07-1.52)
Spirits (40mL/day)	1.11 (0.07-17.32)	1.23 (0.28-5.45)	1.30 (0.18-9.20)	1.79 (0.45-7.01)	0.86 (0.23-3.26)	1.06 (0.40-2.83)	2.99 (0.27-33.29)

In bold letters, are the statistically significant findings after adjustment for sex, BMI, smoking and physical activity.

3.4 Association between the HealthyDietScore with insulin resistance in the total sample and according to region, SES and age categories.

Higher scores in the HealthyDietScore had a negative association with insulin resistance in the total sample, in Northern Europe, in higher SES and in the age group <45 years. Moderate scores (second tertile) had also a statistically significant negative association with HOMA-IR in higher SES category (table 1d).

Table 1d. Association between the HealthyDietScore with insulin resistance in the total sample and according to region, SES and age categories

	1st tertile (<40)	2nd tertile (40-60) OR (95% CI)	3d tertile (>60) OR (95% CI)
TOTAL (N = 1645)			
Diet Score	1	0.78 (0.60-1.03)	**0.66 (0.50-0.89)**
REGION			
NORTHERN EUROPE (N= 418)			
Diet Score	1	0.61 (0.34 – 1.09)	**0.52 (0.29-0.94)**
SOUTHERN EUROPE (N= 851)			
Diet Score	1	0.75 (0.50-1.13)	0.69 (0.45-1.08)
EASTERN EUROPE (N=376)			
	1	1.16 (0.68-1.97)	1.05 (0.56-1.98)
EDUCATION			
<12years (N=332)			
Diet Score	1	1.02 (0.56-1.89)	0.89 (0.44-1.78)

>12years (N=1313)			
Diet Score	1	**0.70 (0.52-0.96)**	**0.61 (0.44-0.85)**
		AGE	
<45 (N=1240)			
Diet Score	1	0.75 (0.55-1.03)	**0.66 (0.47-0.92)**
>45 (N=413)			
	1	0.94 (0.53-1.66)	0.71 (0.38-1.31)

In bold letters, are the statistically significant findings, after adjustment for sex, BMI, smoking and physical activity.

4. DISCUSSION

In the present work possible associations between dietary indices with insulin resistance were investigated in adults at high risk for developing T2DM. Diet was assessed either through use of food groups or as a whole using the HealthyDietScore. A sub-group analysis according to region, SES and age categories was also performed after adjustment for BMI, smoking, sex and physical activity in order to identify the most dominant behaviors independently associated with insulin resistance.

Results showed that high consumption of refined cereals and soft drinks with sugar is positively associated with insulin resistance, whereas high consumption of tea, coffee and juices without sugar is negatively associated with HOMA-IR in the total sample.

According to region, high consumption of tea is inversely associated with insulin resistance in Eastern Europe and high consumption of soft drinks with sugar is positively associated with HOMA-IR in Northern Europe. Regarding different SES categories, high consumption of white meat and juices without sugar is negatively associated with insulin resistance in the lower SES. In the higher SES, high consumption of coffee and tea is negatively associated with insulin resistance, whereas consumption of soft drinks with sugar has a positive association. Concerning the age groups, in participants <45 years, high consumption of soft drinks with sugar

has a positive association with HOMA-IR, while consumption of coffee and juices without sugar has an inverse association.

In the present study HealthyDietScore was used in order to evaluate the quality of diet and the association with insulin resistance. Higher scores indicate better quality of diet. Findings indicate that higher scores are negatively associated with insulin resistance in the total sample, in Northern Europe, in higher SES and in younger participants (<45 years).

Current literature focus on associations of dietary components and several dietary patterns with insulin resistance in healthy and/or T2DM individuals, with very few studies conducted in adults with high risk for type 2 diabetes. In line with the present findings, a prospective cohort study in middle-aged adults, investigated the association between sugar-sweetened beverages (SSB) and the incidence of prediabetes and insulin resistance. Consumption of SSB was estimated by using food-frequency questionnaires. Findings showed that higher consumption of SSBs was positively associated with a higher incidence of prediabetes and a greater increase in insulin resistance (as assessed by HOMA-IR), after adjustment for multiple confounders, including BMI [37]. With regard to SSBs, a meta-analysis of prospective cohort studies came to the conclusion that despite the weight gain, higher consumption of SSBs is associated with development of metabolic syndrome and T2DM [38]. Regarding refined cereal consumption, the longitudinal Framingham Offspring Study with 2.834 non diabetic subjects, showed a positive association between glycemic index and glycemic load with HOMA-IR [39]. In the same extent, the cross-sectional Baltimore Longitudinal Study of Aging showed in a subgroup analyses that refined grains were positively associated with fasting insulin, only among healthy women [40]. Also, the association between insulin resistance and coffee and tea consumption has been investigated with several controversial results. A cross-sectional study in non-diabetic subjects concluded that coffee and tea consumption were related to improved insulin sensitivity [41]. To similar conclusions came Pham et al. who showed that coffee consumption was inversely associated with HOMA-IR in a Japanese working population, especially among healthy overweight individuals [42].

An inverse association between coffee consumption and HOMA-IR in the present study has been observed in several observational studies [43-47] whereas clinical trials failed to confirm this association [48-49]. A systemic review of eight clinical trials (six of them evaluated healthy individuals, one evaluated individuals with T2DM and one enrolled overweight individuals diagnosed with impaired glucose tolerance) found no significant changes in insulin sensitivity, which must be interpreted with caution due to the limited number of studies enrolled in the review [50].

Insulin resistance is a serious metabolic condition that develops as a result of interaction between genetic and environmental factors. The composition and quality of diet is recognized as one of the most important modifiable factors in the development of insulin resistance and T2DM. Therefore, it is important to assess the achieved changes in the quality of diet and investigate their associations with insulin resistance using validated methods. In the present study HealthyDietScore was used for that purpose. The HealthyDietScore is comprised of components that represent the goals of the Feel4Diabetes high-risk intervention, weighted based on their appraised importance as risk or protective factors for T2DM. This is the first study which used this score in order to investigate the association with a clinical outcome (HOMA-IR), with no other available studies in bibliography to compare the findings. Several studies have used different diet scores. For example, the PREDIMED study where Mediterranean Diet Score was calculated as the sum of dichotomized goals [51] and the DPS (Diabetes Prevention Study) where the score varied from 0 to 5 according to the number of intervention goals (total fat intake <30% of total energy consumed, saturated fat <10% of total energy, and dietary fibre 15g/1000 kcal or more) [52]. Although in both studies an inverse association was confirmed between T2DM and better quality of diet, none of them investigated the association with insulin resistance. Also, Lavigne-Robichaud et al. in order to assess diet quality and correlate it with the metabolic syndrome, used two scores aHEI-2010 (based on a combination of eleven nutrients or food previously associated with chronic diseases and mortality and ranged from 0 to 110) and the FQS (based solely on the consumption frequency of fourteen foods [53]. In addition to the previous studies mentioned, neither the later studied the correlation with insulin resistance.

This study has several strengths. First of all, there are not sufficient number of studies investigating the relationship between dietary indices and insulin resistance among adults at high risk for developing T2DM as the majority enrolls healthy or T2DM individuals. Also, the large study sample, the standardized protocols and procedures followed across all centers, and the objectively collected data (i.e. blood and anthropometric indices) safeguard the more objective and reliable assessment and increase the generalizability of findings. Furthermore, regarding the evaluation of the quality of the diet, HealthyDietScore was used, which is a sensitive tool for all beneficial changes in diet (e.g. increase in consumption of fruit from once per day to twice per day, even if the actual goal (five portions per day) is not achieved) and of which clinical validity has been tested [27].

Potential limitations should be considered. First, the cross-sectional design does not enable us to draw conclusions regarding cause and effect. Also, part of the collected data is self-reported thus prone to recall bias and social desirability. Concerning the results of the study, in the subgroup analysis the number of participants in each group was significantly lowered compared with the analysis in the total sample which may affect the accuracy of these results.

5. CONCLUSION

In conclusion, the present study in individuals at increased risk of developing T2DM demonstrates that high consumption of refined cereals and soft drinks with sugar is positively associated while consumption of juices without sugar, tea and coffee is inversely associated with HOMA-IR. Also, better diet quality is inversely associated with insulin resistance, especially in younger people of higher SES in Northern Europe. Therefore, future research is needed in order to further investigate unhealthy diet choices in people at high risk for developing T2DM and consequently to use their outcomes in order to early prevent T2DM targeting primarily to the most vulnerable groups.

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