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SCHOOL OF HEALTH SCIENCE AND EDUCATION

DEPARTMENT OF NUTRITION AND DIETETICS

POSTGRADUATE PROGRAMME: APPLIED NUTRITION AND DIETETICS

COURSE: CLINICAL NUTRITION

Correlates of adult obesity.

The "Feel4Diabetes" study

Master Thesis

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ΧΑΡΟΚΟΠΕΙΟ ΠΑΝΕΠΙΣΤΗΜΙΟ

ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ ΚΑΙ ΑΓΩΓΗΣ

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ΚΑΤΕΥΘΥΝΣΗ: ΚΛΙΝΙΚΗ ΔΙΑΤΡΟΦΗ

Διερεύνηση των επικρατέστερων κοινωνικο-δημογραφικών παραγόντων και του τρόπου ζωής που συσχετίζονται με την παχυσαρκία ενηλίκων.

Μελέτη "Feel4Diabetes"

Μεταπτυχιακή εργασία

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Table of Contents

Abstract in Greek

Τίτλος: Διερεύνηση των επικρατέστερων κοινωνικο-δημογραφικών παραγόντων και του τρόπου ζωής που συσχετίζονται με την παχυσαρκία ενηλίκων. Μελέτη "Feel4Diabetes"

Αντικείμενο και σκοπός: Η παχυσαρκία αποτελεί επιδημία με πολυπαραγοντική αιτιολογία και αυξανόμενο επιπολασμό παγκοσμίως. Στόχος της παρούσας μελέτης ήταν ο εντοπισμός των επικρατέστερων παραγόντων κινδύνου για υπερβαρότητα και παχυσαρκία ανάμεσα σε πληθώρα παραγόντων κοινωνικο-δημογραφικών, ιατρικών και τρόπου ζωής σε ενήλικες από οικογένειες υψηλού κινδύνου για σακχαρώδη διαβήτη τύπου ΙΙ.

Μεθοδολογία: Χρησιμοποιήθηκαν στοιχεία της μελέτης "Feel4Diabetes" από 19.761 ενήλικες χαμηλής κοινωνικο-οικονομικής τάξης από έξι χώρες σε Βόρεια, Ανατολική και Νότια Ευρώπη και μελετήθηκαν παράγοντες κοινωνικο-δημογραφικοί, ιατρικοί και τρόπου ζωής.

Αποτελέσματα: Οι κυριότεροι παράγοντες που αυξάνουν τον κίνδυνο υπερβαρότητας και παχυσαρκίας είναι: άρρεν φύλο (OR 4,55, 95% CI 4,26-4,87), λήψη αντιυπερτασικών φαρμάκων (OR 2,39, 95% CI 2,13-2,67), υψηλές τιμές γλυκόζης (OR 1,71, 95% CI 1,54-1,89), σακχαρώδης διαβήτης σε συγγενείς πρώτου (OR 1,46, 95% CI 1,35-1,58) και δευτέρου βαθμού (OR 1,18, 95% CI 1,09-1,28), δραστηριότητα <30 λεπτά/ημέρα (OR 1,46, 95% CI 1,35-1,57) και ηλικία >45 (OR 1,30, 95% CI 1,19-1,42). Οι κυριότεροι παράγοντες που μειώνουν τον κίνδυνο υπερβαρότητας και παχυσαρκίας είναι: εκπαίδευση >14 έτη (OR 0,70, 95% CI 0,66-0,75), οικονομική ασφάλεια (OR 0,79, 95% CI 0,74-0,84), εργασία (OR 0,84, 95% CI 0,76-0,92) και διαβίωση στις χώρες της Ανατολικής (OR 0,88, 95% CI 0,81-0,95) ή Νότιας Ευρώπης (OR 0,90, 95% CI 0,83-0,98) (p <0,05).

Συμπέρασμα: Σε ενήλικες οικογενειών υψηλού κινδύνου για σακχαρώδη διαβήτη, παράγοντες κινδύνου για υπερβαρότητα και παχυσαρκία είναι: άνδρες, ηλικία >45, μειωμένη σωματική άσκηση, λήψη αντιυπερτασικών, υψηλή γλυκόζη αίματος, σακχαρώδης διαβήτης σε συγγενείς πρώτου και δευτέρου βαθμού, χαμηλό επίπεδο εκπαίδευσης, κοινωνική ανασφάλεια, ανεργία και διαμονή στις χώρες της Βόρειας Ευρώπης. Συστήνεται μελλοντικά προγράμματα πρόληψης και αντιμετώπισης της παχυσαρκίας να δώσουν προτεραιότητα στις ευπαθείς ομάδες, με έμφαση σε άτομα με αυξημένο κίνδυνο για χρόνιες παθήσεις, όπως ο σακχαρώδης διαβήτης ΙΙ.

Λέξεις κλειδιά: Παχυσαρκία ενηλίκων, υπερβαρότητα, παράγοντες κινδύνου, τρόπος ζωής, κοινωνικο-οικονομικοί παράγοντες

Abstract in English

Title: Correlates of adult obesity. The "Feel4Diabetes" study

Object and aim: Obesity is an epidemic with multifactorial etiology and a constantly increasing prevalence worldwide. The aim of the present study was to identify the most significant risk factors for overweight and obesity from a wide range of sociodemographic, medical and lifestyle factors in adults from families at high risk of type II diabetes mellitus.

Methods: This project used data from the "Feel4Diabetes" study, from 19,761 adults from the lowest socioeconomic tertile of six countries of Northern, Eastern and Southern Europe. Analysis of multiple sociodemographic, lifestyle and medical factors was performed.

Results: The most important risk factors for overweight and obesity are male gender (OR 4.55, 95% CI 4.26-4.87), history of blood pressure medication (OR 2.39, 95% CI 2.13-2.67), high blood glucose (OR 1.71, 95% CI 1.54-1.89), history of diabetes mellitus in first- and second-degree relatives (OR 1.46, 95% CI 1.35-1.58 and OR 1.18, 95% CI 1.09-1.28 respectively), daily physical activity of less than 30 minutes (OR 1.46, 95% CI 1.35-1.57) and age above 45 (OR 1.30, 95% CI 1.19-1.42). The most important factors that reduce the risk of overweight and obesity are education of more than 14 years (OR 0.70, 95% CI 0.66-0.75) income security (OR 0.79, 95% CI 0.74-0.84), occupation (OR 0.84, 95% CI 0.76-0.92) and living in the countries of Eastern (OR 0.88, 95% CI 0.81-0.95) or Southern Europe (OR 0.90, 95% CI 0.83-0.98) ($p < 0.05$).

Conclusion: Among adults from families at high risk of diabetes mellitus, risk factors for overweight and obesity are men, age above 45, reduced physical activity, history of blood pressure medication, high blood glucose, history of diabetes mellitus in first- and second-degree relatives, unemployment, low education level, income insecurity and living in the countries of Northern Europe. Future programmes for prevention and management of obesity are recommended to prioritise vulnerable groups, mainly people with increased risk of chronic conditions such as type II diabetes mellitus.

Keywords: Adult obesity, overweight, risk factors, lifestyle, socioeconomic factors

List of Tables

Abbreviations

The following abbreviations have been used throughout this thesis:

BMI	Body mass index
CI	Confidence intervals
FINDRISC	Finnish Diabetes Risk Score
OR	Odds ratio
SPSS	Statistical Package for Social Sciences

1. Introduction

1.1. General background and risk factors for obesity

Obesity is a constantly increasing global health problem, as its worldwide prevalence has almost tripled in the past 40 years (World Health Organization Obesity and overweight fact sheet, 2021). In 2016, around 2 billion adults (39%) globally were overweight and 650 million (13%) were obese. Percentages of overweight were similar for men and women (39% and 40% respectively), whereas obesity was more prevalent in women (15%) compared with men (11%) (World Health Organization Obesity and overweight fact sheet, 2021). In Greece, obesity was found to be more prevalent in men (18.3% vs 16.4% in women) (Eurostat, 2016). In Europe the dynamics of obesity growth is higher for men (3.09% per year) than women (1.92% per year) and it is estimated that in 2030 obesity rates will reach 36.6% for men and 32.0% for women (Krzysztoszek et al., 2019).

Overweight and obesity are defined as an abnormal or excessive fat accumulation that presents a health risk and is caused by a positive energy balance. A body mass index (BMI) between 25-30 kg/m^2 is considered overweight and over 30 kg/m^2 is obese (World Health Organization Obesity and overweight fact sheet, 2021).

Developing campaigns and programmes for weight management and prevention of obesity is of great importance, as excess weight and obesity may affect the quality of life of people and are associated with a wide variety of conditions leading to high morbidity and mortality, including cardiovascular diseases (coronary heart disease and stroke), type II diabetes mellitus, hypertension, dyslipidemia, musculoskeletal diseases (osteoarthritis), respiratory conditions (sleep apnea), psychological disorders (anxiety, depression) and various forms of cancer (of gastrointestinal, endocrine and reproductive system) (Woolf et al., 2006; World Health Organization, 2009; National Cancer Institute, 2017; Centers for disease control and prevention, 2020a). Moreover, obesity may also be aggravated by conditions linked to it. For instance, obesity is implicated in the development of type II diabetes mellitus and hypertension; these conditions can also aggravate obesity (through insulin resistance resulting in increased deposition of fat in adipose tissue and other organs and through increased peripheral activity of the renin-angiotensin system leading to reduced resting metabolism respectively) leading to a vicious circle (Vaněčková et al., 2014; Sears and Perry, 2015; Littlejohn et al., 2016; Siddiqui, 2018; Fountain and Lappin, 2021). Nevertheless, obesity is difficult to be prevented or treated, as it is a multifactorial disease with various risk factors (genetic, environmental, social) that may interact

with each other (Lee et al., 2019; Diels et al., 2020; Hüls et al., 2021). Previous studies and meta-analyses examined the risk factors for overweight and obesity, which can be grouped into three large categories: biological, lifestyle and socioeconomic/demographic factors.

1.1.1. Biological factors

Genetic factors and hereditability have been found to influence the risk of excess weight and obesity (Venkatesan and Viswanathan, 2016). However, the 32 most common genetic variants account for less than 1.5% of the variation in BMI. Even people with more than 38 risk genes have just a 2.7 kg/m^2 higher BMI (+7 kg) compared with people with low genetic risk (Speliotes et al., 2010; Hruby and Hu, 2015). The literature estimates that genetic variation accounts for less than 20% of BMI variation and that genome-wide association studies can only explain 3-5% of obesity heritability. The "missing heritability" of obesity is hypothesised to be due to a large number of unknown rare variants, whereas epigenetic changes also play an important role (Chesi and Grant, 2015; Wallis and Raffan, 2020). Moreover, prenatal and perinatal factors also augment the risk of overweight and obesity and include increased parental BMI (mainly maternal obesity), gestational diabetes, maternal smoking during pregnancy, increased gestational weight gain, increased birth weight and rapid weight gain of infant (Birbilis et al., 2013; Morgen et al., 2018; Zou et al., 2019; Ardıç et al., 2020; Cissé et al., 2021).

Gene-environment interactions may also affect weight (Hruby and Hu, 2015). For instance, sugar-sweetened beverages, fried food, screen time and physical activity have been found to influence the genetic risk of overweight and obesity (Qi, Q. et al., 2012; Qi, Qibin et al., 2012; Qi et al., 2014; Hruby et al., 2016). Nevertheless, the increasing prevalence of obesity over the years points to the importance of environmental – modifiable variables, rather than genetic factors (Hruby and Hu, 2015).

1.1.2. Lifestyle factors

Diet plays a crucial role in weight maintenance, as the main cause of overweight and obesity is the positive energy balance (World Health Organization Obesity and overweight fact sheet, 2021). Various individual dietary factors have been found to affect body weight (Wadden et al., 2012), such as a Western type dietary pattern (increased consumption of red meat, potatoes and

sugar and reduced consumption of fruits, vegetables, whole grains, nuts and yogurt), which may augment the risk of overweight and obesity (Schulze et al., 2006; Mozaffarian et al., 2011; Hu, 2013; Fung et al., 2015). Nevertheless, more recent data show that factors such as macronutrient composition and glycemic load may not have such a significant impact on body weight and research focuses more on dietary habits such as restriction of caloric intake (for instance by reducing portion sizes or energy density of food), meal timing, size and composition of breakfast and dinner and intermittent fasting (Wadden et al., 2012; Xiao et al., 2019; Lopez-Minguez et al., 2019; Welton et al., 2020). Adopting healthy eating habits and consuming the majority of calories earlier in the day with a balanced breakfast, an early lunch and a light dinner may have a positive impact on circadian rhythm and metabolism (Allison and Goel, 2018; Lopez-Minguez et al., 2019). Intermittent fasting may also improve weight by affecting circadian rhythm and gene expression related to fat and glucose metabolism. Moreover, it may reduce inflammation and oxidative stress, interact with gut microbiome and improve insulin sensitivity (Stockman et al., 2018).

Another important lifestyle factor is physical activity, which may improve body weight through its beneficial effect on energy expenditure, glucose and fat metabolism and inflammatory processes (Soltani et al., 2020; Muscella et al., 2020). Overweight and obese people were reported to have significantly lower levels of physical activity compared to normal-weight individuals, which may also further increase their risk of obesity (Cassidy et al., 2017). In obese people, physical activity was found to be associated with age, gender and ethnicity (lower physical activity was reported for Hispanic ethnicity, male people and ages 18-34) (Tran et al., 2020). Research has shown that 150-250 minutes of moderate exercise per week is associated with weight loss or less weight gain (Wadden et al., 2012; Hruby and Hu, 2015) and the World Health Organisation recommends 150-300 minutes of moderate-intensity, or 75-150 minutes of vigorous-intensity aerobic physical activity for adults weekly (World Health Organization. Guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization, 2020.; Bull et al., 2020).

Limiting sedentary behaviour is also of great importance and it is distinct from physical inactivity, as it includes not only lack of physical exercise but also increased sedentary activities such as mental work/academic activities and screen-based tasks (television viewing and computer using) (Cassidy et al., 2017; Panahi and Tremblay, 2018; Martínez-Ramos et al., 2018). Sedentary activities may affect hormonal and neurophysiological pathways and influence dietary and stress factors thus increasing the risk of overweight and obesity, even with adequate physical activity

(Panahi and Tremblay, 2018). Although there is insufficient evidence to set specific recommendations on the duration and frequency of sedentary activities, it is advised to reduce sedentary time and increase physical activity (World Health Organization. Guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization, 2020.).

Another lifestyle factor associated with excess weight is sleep duration and quality (Ding et al., 2018). Sleeping less than seven hours per night or poor sleep quality may induce changes in eating habits (adoption of unhealthy eating patterns) and metabolism, imbalance of appetite-controlling hormones and reinforcement of hedonic brain pathways, leading to increased prevalence of obesity (St-Onge, 2017; Ding et al., 2018; Cooper et al., 2018; Krističević et al., 2018). Lastly, the risk of overweight and obesity augments in proportion to alcohol consumption, which affects appetite and fat oxidation (Shin, 2020; Kim et al., 2021; Traversy and Chaput, 2015) and it is also associated with smoking, which may induce dyslipidemia and endothelial dysfunction and increase insulin resistance and oxidative stress (Kim et al., 2016; Watanabe et al., 2016; Harris et al., 2016; Mons et al., 2016).

1.1.3. Socioeconomic and demographic factors

Body weight is affected by the economic and educational status of both the individual and the country. Until mid-20th century the prevalence of overweight and obesity was higher in wealthier classes. Nevertheless, over the past few decades, wealth has been negatively associated with obesity, which is positively associated with low socioeconomic status of both the individual and the neighbourhood surrounding, crime and racial isolation (Levine, 2011; Devaux and Sassi, 2013; Hruby and Hu, 2015; N. C. D. Risk Factor Collaboration, 2019; Mohammed et al., 2019; Sallis et al., 2020; Lam et al., 2021). Unemployment has also been reported to increase the risk of overweight and obesity (Monsivais et al., 2015). As regards the educational status, the risk of obesity decreases with increasing education level, a trend which seems to be more pronounced amongst women (Ogden et al., 2017; Hsieh et al., 2020). In addition, the increasing trend of obesity over the past few decades has been higher among people with lower educational status (Hoffmann et al., 2017).

Regarding the economic status, it was initially reported that low socioeconomic status, inequality (related with lack of knowledge and social support) and rural environment were associated with increased risk of overweight and obesity in developed countries, whereas in developing countries

obesity was more prevalent in higher-income classes and urban environment. Nevertheless, as the economy of developing countries improved, overweight and obesity became more prevalent in the low socioeconomic classes of these countries (Leal and Chaix, 2011; Monteiro et al., 2004; Glonti et al., 2016). In middle-income countries, for women with lower education, higher income was associated with higher prevalence of obesity, whereas in women with higher education, there was negative or no association between income and obesity (Aitsi-Selmi et al., 2014).

Geographical area is also important. In 2014 in Europe, the highest prevalence of overweight was observed in Czech Republic, Hungary and Lithuania and the highest prevalence of obesity in Slovenia, Estonia and the United Kingdom (Marques et al., 2017). In 2019, the highest obesity rates were observed in Ireland, Malta, Estonia and Latvia for women and in Ireland, Malta, Croatia and Hungary for men and the lowest obesity rates were noticed in Italy, Romania, Bulgaria and Cyprus for women and in Italy, Romania, France and the Netherlands for men (Eurostat, 2021).

As regards the effect of the built environment on obesity, higher rates of obesity have been observed in rural areas due to lack of education and scarcity of services and weight management programmes (Lundeen et al., 2018). Systematic reviews have reported a more consistent effect of physical activity installations rather than food environment on the prevalence of obesity. Increased fast-food exposure, urban sprawl and scarcity of mixed land use (which could enhance physical activity by providing grocery stores, retail shops and other services within a walking distance) are the most closely linked to excess body weight and obesity (Lam et al., 2021). Conversely, residential density, pedestrian infrastructure, park proximity and traffic safety, which indicate higher neighborhood walkability, reduce the risk of obesity (Sallis et al., 2020; Lam et al., 2021).

Lastly, non-modifiable demographic risk factors for obesity include increasing age, non-Hispanic black ethnicity and family history of obesity, cardiovascular and metabolic diseases (Mayega et al., 2012; Corica et al., 2018; Centers for disease control and prevention, 2020b).

1.2. The project

1.2.1. Project background and limitations of current studies

Obesity is a constantly increasing global health problem, which affects the quality of life of millions of people and it is associated with high morbidity and mortality. Nevertheless, as a multifactorial disease, it is difficult to be prevented or treated. Therefore, it is important to investigate its pathogenesis and the factors that lead to overweight and obesity or aggravate these conditions (World Health Organization Obesity and overweight fact sheet, 2021; Lee et al., 2019; Centers for disease control and prevention, 2020a; Diels et al., 2020; Hüls et al., 2021).

The literature includes a large number of studies on the risk factors for overweight and obesity. Nevertheless, limitations due to study design of many of them or due to study sample being small in size or consisting of a single gender, specific age groups or ethnicities do not allow pooling results from different studies and drawing robust conclusions (Hu et al., 2003; Schulze et al., 2006; Shahraki et al., 2012; Mayega et al., 2012; Fung et al., 2015). Even meta-analyses based on a large number of studies have limitations such as samples taken from high income countries only (Mohammed et al., 2019).

Also, many studies have investigated the association of solely one or two factors with overweight and obesity, which does not allow multiple comparisons in order to evaluate how these factors interact with one another or their effect size on these conditions (Lipek et al., 2015; Hruby and Hu, 2015; Mohammed et al., 2019). In addition, some studies that included several factors did not investigate their relative effect on obesity but only the unadjusted effect of each independent variable (Rabin et al., 2007), whereas a few studies only evaluated the relative effect of a couple of factors on obesity (Aitsi-Selmi et al., 2014; Wen et al., 2018).

The interaction between different variables and the heterogeneity of studies do not allow robust conclusions to be drawn (Mackenbach et al., 2014; Lakerveld and Mackenbach, 2017). The variation in study sample, variables and study design in previous research and the fact that the risk factors for overweight and obesity may affect and change the impact size of one another, increase the need for a more consistent future research on multiple variables simultaneously that may also take into account the interaction between various confounders (McCormack and Shiell, 2011; Hruby and Hu, 2015).

1.2.2. Aim and objectives of the project

In order to examine the relative effect of several factors on overweight and obesity simultaneously, this project used a large sample of both male and female adults from six European countries from different geographical areas. The sample was chosen randomly from low socioeconomic-status municipalities. The study collected data from medical history, socioeconomic, demographic and lifestyle factors of the participants in order to perform multiple comparisons and investigate the interaction between risk factors and their effect size on overweight and obesity. The ultimate aim was to identify the major risk factors for overweight and obesity amongst several lifestyle and sociodemographic data and determine the groups at high risk in order to facilitate the design of prevention programmes and reduce the prevalence of obesity.

2. Methods

2.1. Study design and sample

This project used data from the "Feel4Diabetes" study, a cluster randomised trial (National Clinical Trial number 02393872) conducted between 2015 and 2019, aiming in the identification of risk factors for overweight and obesity and the promotion of a healthy lifestyle in order to prevent obesity and type II diabetes mellitus (Manios et al., 2018). This multicenter study used the school setting, targeting the community and recruited adults and children from approximately 12,000 families from six European countries. The people were recruited randomly from low/middle-income countries (Bulgaria and Hungary) and from the lowest socioeconomic tertile of high-income countries (Belgium and Finland) and high-income countries under austerity measures (Greece and Spain) (Manios et al., 2018; Manios et al., 2020) (Table 2-1).

Table 2-1: The number of schools and families from each country that participated in the "Feel4Diabetes" study.

Country	Belgium	Bulgaria	Finland	Greece	Hungary	Spain	**Total**
Number of participating schools	60	20	30	56	14	41	221
Number of participating families	1798	3032	1506	2286	1867	1704	12193

All participating families went through two screening stages (Manios et al., 2020). The first stage took place in the school setting using self-reported screening tools ("Finnish Diabetes Risk Score FINDRISC" and other questionnaires) (Lindström and Tuomilehto, 2003) (Appendix). The results showed that 4,513 parents had a FINDRISC score above 10 and underwent a second screening stage that included a detailed medical examination and an invitation to counselling courses. The "Feel4Diabetes" intervention part was divided into two arms: the "all-families" arm that took place in the school setting in collaboration with the local municipalities and included 12,193 families and the "high-risk families" arm, which included counselling sessions for families at high risk of type II diabetes mellitus, as identified by the "FINDRISC" questionnaire (Lindström and Tuomilehto, 2003) and included 2,230 families (Manios et al., 2018; Manios et al., 2020).

This project used data from 19,761 adults from the first screening stage of the "Feel4Diabetes" study (as described in chapter 2.3).

2.2. Ethical approval

The “Feel4Diabetes” study was conducted in accordance with the Declaration of Helsinki Ethical Principles (World Medical Association, 2013) and the Convention on Human Rights and Biomedicine developed by the Council of Europe (Dommel and Alexander, 1997). Ethical approval was granted from the local ethics committee of all participating countries and signed consent was obtained from all parents and caregivers (Manios et al., 2018; Manios et al., 2020).

2.3. Data collection

The “FINDRISC” questionnaire (Lindström and Tuomilehto, 2003) was used in order to obtain data regarding the age of participants, lifestyle factors (daily physical activity and consumption of fruits and vegetables) and medical history (current weight status, current or former regular use of high blood pressure medication, high blood glucose in a health examination and family history of type I or type II diabetes mellitus) (Appendix). Additional data regarding socioeconomic and demographic factors (gender, education, occupation, income security and region of residence) were also collected using standardised questionnaires (Manios et al., 2018; Manios et al., 2020; Anastasiou et al., 2020).

2.4. Statistical analysis

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) 21.0 statistics software (Chicago, USA). A probability value of $p < 0.05$ was considered statistically significant. The categorical variables were expressed as relative frequencies (%) and the continuous variables as mean ± standard deviation. The Kolmogorov-Smirnoff test was used to assess the distribution of the variables. The association between sociodemographic, lifestyle and medical factors with overweight and obesity was initially evaluated with univariate regression analysis. The factors that were found to be statistically significant were then included in the multivariate regression analysis (two-tailed statistical tests) in order to identify the ones that retained their statistical significance with overweight and obesity in the presence of the other variables that were used in the multivariate model.

3. Results

3.1. Descriptive statistics

The study sample consisted of 19,761 adults, with a slight female to male preponderance (1.2:1). Approximately 50% of them were either overweight or obese. The main characteristics of the participants are summarised in Table 3-1.

Table 3-1: Descriptive statistics of the study sample.

Variables[1]		Total sample N =19,761 n (%)
Sociodemographic factors		
Age	≤45 years	85.0
	>45 years	15.0
Gender	Female	54.7
	Male	45.3
Education	≤14 years	47.1
	>14 years	52.9
Occupation	Unemployed	14.8
	Employed	85.2
Income insecurity	Yes	47.0
	No	53.0
Region of residence	Northern Europe (Belgium & Finland)	27.6
	Southern Europe (Greece & Spain)	30.7
	Eastern Europe (Bulgaria & Hungary)	41.7
Lifestyle factors		
Fruits and vegetables	Every day	70.2
	Not every day	29.8
Physical activity (≥30 min/day)	Yes	79.1
	No	20.9
Medical history		
Blood pressure medication	No	89.7
	Yes	10.3
High blood glucose	No	89.5
	Yes	10.5
Family history of diabetes mellitus (type I or type II)	No	61.5
	1st degree relatives (parent, brother, sister, own child)	20.1
	2nd degree relatives (grandparent, aunt, uncle, first cousin)	18.4
Weight status	Underweight/normal weight (BMI <25 kg/m^2)	50.9
	Overweight (BMI =25-30 kg/m^2)	33.7
	Obesity (BMI >30 kg/m^2)	15.4

[1] Variables are presented as n (%) (N: sample size, BMI: body mass index)

3.2. Univariate analysis

The independent association of individual sociodemographic, lifestyle and medical history factors with overweight and obesity was initially evaluated with univariate regression analysis, in order to identify the factors that had a statistically significant association with obesity (Table 3-2).

According to the analysis (Table 3-2), the risk of overweight and obesity increased by 1.9 times for people above the age of 45 (odds ratio-OR 1.93, confidence intervals-CI 1.78-2.09) and by 4.4 times for male compared to female participants (OR 4.41, 95% CI 4.15-4.68).

High education level (above 14 years) and income security were associated with reduced risk of overweight and obesity (OR 0.59, 95% CI 0.56-0.63 and OR 0.74, 95% CI 0.70-0.79 respectively), whereas employment increased the risk of overweight and obesity by 1.2 times (OR 1.20, 95% CI 1.11-1.30). Participants from the Eastern and Southern European countries (Bulgaria, Hungary, Greece and Spain) had increased risk of overweight and obesity compared to participants from the Northern European countries (Belgium and Finland) (OR 1.08, 95% CI 1.00-1.15 and OR 1.11, 95% CI 1.03-1.20 respectively) (Table 3-2).

For individuals who did not engage in at least 30 minutes of daily physical activity or did not consume fruits and vegetables every day, the risk of overweight and obesity increased by 1.35 and 1.38 times respectively (OR 1.35, 95% CI 1.26-1.44 and OR 1.38, 95% CI 1.30-1.47 respectively). Lastly, as regards the medical history, current or former regular use of high blood pressure medication, high blood glucose in a health examination and family history of diabetes mellitus in first-degree relatives were also associated with increased risk of overweight and obesity (OR 3.25, 95% CI 2.93-3.60, OR 1.46, 95% CI 1.33-1.60 and OR 1.44, 95% CI 1.34-1.55 respectively) (Table 3-2).

Table 3-2: Univariate analysis of the correlates of overweight and obesity among adults in Europe.

Variables[2]		Overweight/Obesity Univariate analysis N =19,761 OR (95% CI)
Sociodemographic factors		
Age	≤45 years	1.00
	>45 years	**1.93 (1.78-2.09)***
Gender	Female	1.00
	Male	**4.41 (4.15-4.68)***
Education	≤14 years	1.00
	>14 years	**0.59 (0.56-0.63)***
Occupation	Unemployed	1.00
	Employed	**1.20 (1.11-1.30)***
Income insecurity	Yes	1.00
	No	**0.74 (0.70-0.79)***
Region of residence	Northern Europe (Belgium & Finland)	1.00
	Southern Europe (Greece & Spain)	**1.11 (1.03-1.20)***
	Eastern Europe (Bulgaria & Hungary)	**1.08 (1.00-1.15)***
Lifestyle factors		
Fruits and vegetables	Every day	1.00
	Not every day	**1.38 (1.30-1.47)***
Physical activity (≥30 min/day)	Yes	1.00
	No	**1.35 (1.26-1.44)***
Medical history		
Blood pressure medication	No	1.00
	Yes	**3.25 (2.93-3.60)***
High blood glucose	No	1.00
	Yes	**1.46 (1.33-1.60)***
Family history of diabetes mellitus (type I or type II)	No	1.00
	1st degree relatives (parent, brother, sister, own child)	**1.44 (1.34-1.55)***
	2nd degree relatives (grandparent, aunt, uncle, first cousin)	1.00 (0.93-1.08)

[2] Statistically significant odds ratios are highlighted, * p <0.05 (N: sample size; OR: odds ratio; CI: confidence intervals)

3.3. Multivariate analysis

The factors that were found to be statistically significantly associated with overweight and obesity in the univariate analysis were then included in the multivariate regression analysis, which analysed all variables simultaneously in order to identify the ones that retain their statistically significant association with overweight and obesity in the presence of the other variables (Table 3-3).

According to the results of Table 3-3, male gender had the highest association with overweight and obesity (OR 4.55, 95% CI 4.26-4.87), followed by current or former regular use of high blood pressure medication (OR 2.39, 95% CI 2.13-2.67) and high blood glucose in a health examination (OR 1.71, 95% CI 1.54-1.89).

Physical activity of less than 30 minutes per day increased the risk of overweight and obesity by 1.5 times (OR 1.46, 95% CI 1.35-1.57), similarly to first-degree relatives with diabetes mellitus (OR 1.46, 95% CI 1.35-1.58). Second-degree relatives with diabetes mellitus also increased the risk of overweight and obesity but to a lesser extent (OR 1.18, 95% CI 1.09-1.28). Also, people above the age of 45 had 1.3 times higher risk of being overweight or obese (OR 1.30, 95% CI 1.19-1.42) (Table 3-3).

As regards high education level (above 14 years), income security and employment, they were all associated with a reduced risk of overweight and obesity (OR 0.70, 95% CI 0.66-0.75, OR 0.79, 95% CI 0.74-0.84 and OR 0.84, 95% CI 0.76-0.92 respectively). Moreover, participants from the Eastern and Southern European countries (Bulgaria, Hungary, Greece and Spain) had lower risk of being overweight or obese (OR 0.88, 95% CI 0.81-0.95 and OR 0.90, 95% CI 0.83-0.98 respectively) compared to participants from the Northern European countries (Belgium and Finland). Lastly, in this multivariate model, daily consumption of fruits and vegetables was not associated with overweight and obesity ($p > 0.05$) (Table 3-3).

Table 3-3: Multivariate analysis of the correlates of overweight and obesity among adults in Europe.

Variables[3]		Overweight/Obesity Multivariate analysis N =19,761 OR (95% CI)
Sociodemographic factors		
Age	≤45 years	1.00
	>45 years	**1.30 (1.19-1.42)***
Gender	Female	1.00
	Male	**4.55 (4.26-4.87)***
Education	≤14 years	1.00
	>14 years	**0.70 (0.66-0.75)***
Occupation	Unemployed	1.00
	Employed	**0.84 (0.76-0.92)***
Income insecurity	Yes	1.00
	No	**0.79 (0.74-0.84)***
Region of residence	Northern Europe (Belgium & Finland)	1.00
	Southern Europe (Greece & Spain)	**0.90 (0.83-0.98)***
	Eastern Europe (Bulgaria & Hungary)	**0.88 (0.81-0.95)***
Lifestyle factors		
Fruits and vegetables	Every day	1.00
	Not every day	1.07 (1.00-1.15)
Physical activity (≥30 min/day)	Yes	1.00
	No	**1.46 (1.35-1.57)***
Medical history		
Blood pressure medication	No	1.00
	Yes	**2.39 (2.13-2.67)***
High blood glucose	No	1.00
	Yes	**1.71 (1.54-1.89)***
Family history of diabetes mellitus (type I or type II)	No	1.00
	1st degree relatives (parent, brother, sister, own child)	**1.46 (1.35-1.58)***
	2nd degree relatives (grandparent, aunt, uncle, first cousin)	**1.18 (1.09-1.28)***

[3] Statistically significant odds ratios are highlighted, * p <0.05 (N: sample size; OR: odds ratio; CI: confidence intervals)

4. Discussion

A diverse array of genetic, environmental and sociodemographic factors that may interact with one another has been implicated in the risk of overweight and obesity (Lee et al., 2019; Diels et al., 2020; Hüls et al., 2021). A deeper understanding of the effect of these factors on overweight and obesity and the identification of the major ones that increase their prevalence will contribute to the development of more targeted and effective prevention and treatment programmes to reduce the worldwide burden of obesity.

This project identified sociodemographic, lifestyle and medical factors that have been reported to be associated with overweight and obesity (Lee et al., 2019; Diels et al., 2020; Hüls et al., 2021) and determined these variables in almost 20,000 adults from six European countries. It also attempted to detect the factors that were statistically significantly associated with overweight and obesity both independently and in a multivariate model.

The descriptive data of the study sample showed similar numbers of male and female participants, with a slight female preponderance (1.2:1) (Table 3-1). Moreover, approximately 34% of the participants were overweight and 15% were obese, similar to the worldwide percentages, according to the World Health Organisation (World Health Organization Obesity and overweight fact sheet, 2021) (Table 3-1).

Univariate analysis was initially performed in order to detect the factors that were statistically significantly associated with overweight and obesity. Then, a multivariate model analysed all the statistically significant variables simultaneously, by taking into account probable overlapping of the variables, in order to identify the factors that kept their statistically significant association with overweight and obesity in the presence of the other variables (Petrill and Kovas, 2016; Sherpa, 2021). The multivariate model showed that male gender was the most highly associated with overweight and obesity, increasing the risk by almost 4.6 times, followed by current or former regular use of high blood pressure medication, which increased the risk by 2.4 times (Table 3-3). In descending order, high blood glucose in a health examination, history of diabetes mellitus in first-degree relatives, daily physical activity of less than 30 minutes and age above 45 also increased the risk of overweight and obesity by 1.3-1.7 times. Second-degree relatives with diabetes mellitus increased the risk of overweight and obesity by 1.2 times. Conversely, in descending order, high education level (above 14 years), income security, employment and living in the Eastern and Southern European countries (Bulgaria, Hungary, Greece and Spain) reduced

the risk of overweight and obesity by 10-30%. Daily consumption of fruits and vegetables was not associated with overweight and obesity in the multivariate model (Table 3-3).

Age above 45 was shown to increase the risk of overweight and obesity (Table 3-3). Aging is followed by a decline in metabolic rate due to a decrease in skeletal muscle mass, redistribution of fat resulting in low-grade systemic inflammation and hormonal imbalance, including resistance to insulin and leptin (McKee and Morley, 2020; Rezuş et al., 2020). Moreover, physical activity is usually reduced with aging (Suryadinata et al., 2020) and if the energy intake is not adapted accordingly, a positive energy balance is created (Romieu et al., 2017). These mechanisms may explain the fact that the risk of obesity increases with increasing age.

As regards the association of gender with overweight and obesity, the results showed an increased risk for men compared to women (Table 3-3). Although worldwide percentages of overweight were reported to be similar for men and women (39% and 40% respectively) and obesity was more prevalent in women (15%) compared with men (11%), in some countries obesity is more prevalent in men (such as in the United States of America, the United Kingdom, France and Germany) and in Europe the dynamics of obesity growth is higher for men (3.09% per year) than women (1.92% per year) (Krzysztoszek et al., 2019; Kim and Shin, 2020; World Health Organization Obesity and overweight fact sheet, 2021). Therefore, there is a variation in the prevalence of overweight and obesity among men and women in different countries.

Regarding physical activity, the results of the multivariate analysis showed that less than 30 minutes of daily physical activity increased the risk of overweight and obesity by 1.5 times (Table 3-3). Physical activity has a positive impact on health and helps with weight loss or maintenance (Swift et al., 2018; Willis et al., 2020). Therefore, it is reasonable that people who do not engage to adequate physical activity are at higher risk of being overweight or obese (Niemiro et al., 2021). Although not the most significant factor associated with overweight and obesity, it is important for people to include some form of physical activity in their everyday life in order to maintain a healthier body weight (Swift et al., 2018; Willis et al., 2020). The World Health Organisation recommends 150-300 minutes of moderate intensity or 75-150 minutes of vigorous intensity of weekly aerobic exercise for adults (World Health Organization. Guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization, 2020.; Bull et al., 2020).

Fruits and vegetables are linked to a healthy diet (Wallace et al., 2020) and to weight loss or prevention of weight gain (Nour et al., 2018; Arnotti and Bamber, 2020). Although the univariate

analysis showed an increase in the risk of overweight and obesity by 1.4 times when fruits and vegetables were not consumed on a daily basis (Table 3-2), the multivariate analysis did not show a statistically significant association (Table 3-3). It is possible that lack of daily consumption of fruits and vegetables is not as significant for weight management as other factors. Recent data have reported that factors such as restriction of caloric intake, meal timing, size and composition of breakfast and dinner and intermittent fasting may play a more important role in weight management and prevention of overweight and obesity (Wadden et al., 2012; Xiao et al., 2019; Lopez-Minguez et al., 2019; Welton et al., 2020).

The multivariate analysis also showed that current or former regular intake of high blood pressure medication, which indicates hypertension, increased the risk of overweight and obesity by 2.4 times (Table 3-3). Although obesity is implicated in the development of hypertension, the latter may also aggravate obesity through increased peripheral activity of the renin-angiotensin system and reduced resting metabolism, leading to a vicious circle (Vaněčková et al., 2014; Littlejohn et al., 2016; Fountain and Lappin, 2021). Moreover, high blood glucose in a health examination was also found to be associated with a 1.7-times higher risk of overweight and obesity. Similar to hypertension, although obesity is implicated in the development of type II diabetes mellitus, the latter may also aggravate obesity through insulin resistance, resulting in increased deposition of fat in adipose tissue and other organs, leading to a vicious circle (Sears and Perry, 2015; Siddiqui, 2018). In addition, history of diabetes mellitus in first- and second-degree relatives augmented the risk of overweight and obesity by 1.5 and 1.2 times respectively (Table 3-3). Possibly, people who have relatives with diabetes mellitus are more prone to insulin resistance, which may also play a role in tissue fat deposition and obesity (Sears and Perry, 2015; Siddiqui, 2018). Therefore, it is important to detect populations with diabetes mellitus or hypertension, monitor their BMI and engage them in programmes for weight maintenance or weight loss.

As regards education and income, the results showed that high education level (above 14 years) and income security decreased the risk of overweight and obesity by approximately 20-30% (Table 3-3). Moreover, although in the univariate model employment increased the risk of overweight and obesity by 1.2 times (Table 3-2), the multivariate model, which analyses each factor in the presence of other variables, showed that employed people had 16% lower risk of being overweight or obese (Table 3-3). These results are in line with the latest research data, stating that over the past few decades high education level and socioeconomic status have been

inversely associated with obesity (Kim, 2016; Ogden et al., 2017; N. C. D. Risk Factor Collaboration, 2019; Mohammed et al., 2019; Hsieh et al., 2020). Possibly, education and employment may provide confidence and a higher income may ensure access to healthier food and physical activity facilities. During the recent economic development of countries, a significant increase in the prevalence of overweight and obesity in the lower economic classes has been observed. Unemployment and low income may increase the risk of obesity and conversely obese people tend to have a greater risk of unemployment and lower income (Monsivais et al., 2015; Kim and von dem Knesebeck, 2018; Templin et al., 2019; Norrbäck et al., 2019). This reverse causality highlights the need to address the most prevalent driving factors for overweight and obesity, in order to inhibit the vicious circle of low socioeconomic status – obesity.

The multivariate model, in which all statistically significant variables were added in the equation, showed that participants from Greece, Spain, Bulgaria and Hungary had about 10% lower risk of being overweight or obese compared to participants from Belgium and Finland (Table 3-3). There are several factors that could play a role in this variability of overweight and obesity amongst countries: environmental factors such as flat or inclined terrain that may affect the ways people commute and the weather or the presence of mountains, valleys and lakes that may influence agriculture, cultural factors such as customs, traditions, nutritional patterns and physical exercise habits, the educational and socioeconomic status and the mean age and genetic characteristics of the population (Blundell et al., 2017). Moreover, the rates of obesity do not follow the same trend in all countries, so it is important to focus on the populations that show the highest prevalence of obesity in order to decelerate their increasing rates (Janssen et al., 2020).

Overall, this project has identified the socioeconomic, medical and lifestyle risk factors for overweight and obesity that remain statistically significant in the presence of multiple variables. The modifiable factors more highly associated with overweight and obesity were current or former regular use of high blood pressure medication, high blood glucose in a health examination and inadequate daily physical activity (less than 30 minutes). Campaigns to inform people about obesity and its risk factors, as well as the importance of physical activity should be organised and populations at high risk of hypertension and diabetes mellitus should be monitored, in an effort to prevent these conditions and the subsequent increase in the risk of obesity. Education, employment and income security decrease the risk of overweight and obesity. This fact emphasises the need to address illiteracy and unemployment, offer psychological support and assure access of the population to healthy food options and physical activity installations.

Addressing the above-mentioned modifiable risk factors is important not only to reduce the prevalence of overweight and obesity but also because obesity can aggravate medical conditions (such as hypertension and diabetes mellitus) and can have an impact in various aspects of life (such as the opportunity for a high-income occupation), leading to a vicious circle. Male gender, the presence of diabetes mellitus in first- and second-degree relatives and increasing age are non-modifiable factors that may also increase the risk of overweight and obesity, which highlights the need to focus on these groups when organising campaigns to prevent obesity. As programmes for prevention and management of obesity are expensive and difficult to implement for the world population, this study suggests that priority should be given to the high-risk groups, in order to organise more targeted and effective health and weight management programmes and facilitate the worldwide effort to reduce the prevalence of obesity. Lastly, the variation of overweight and obesity rates amongst countries emphasises the complexity of driving factors of obesity and the need for prevention and management programmes that focus on the populations showing the highest obesity rates.

Limitations of the project include the fact that, as a cross-sectional study, it shows the association of obesity risk factors with overweight and obesity without being able to establish a causal relationship. Moreover, the existence of self-reported data, such as duration of daily physical activity, may be subject to the introspective ability and honesty of participants. Strengths of the study include the simultaneous analysis of multiple risk factors for overweight and obesity, the large sample from six countries of Northern, Eastern and Southern Europe and the use of standardised protocols and questionnaires from all data collection centres (Manios et al., 2018; Manios et al., 2020; Anastasiou et al., 2020).

In brief, this project found that male gender, age above 45, reduced physical activity, current or former regular use of high blood pressure medication, high blood glucose in a health examination, history of diabetes mellitus in first- and second-degree relatives, unemployment, low education level, income insecurity and living in the Northern European countries (Belgium and Finland) are associated with higher risk of overweight and obesity in adults from families at increased risk of type II diabetes mellitus. Future prevention and management programmes for obesity are recommended to focus on populations in greater need and prioritise the most vulnerable groups, such as people at increased risk of type II diabetes mellitus and other chronic diseases, in order to address obesity more effectively.

5. References

Aitsi-Selmi, A., Bell, R., Shipley, M.J. and Marmot, M.G. 2014. Education modifies the association of wealth with obesity in women in middle-income but not low-income countries: an interaction study using seven national datasets, 2005-2010. *PLoS One.* **9**(3), pe90403.

Allison, K.C. and Goel, N. 2018. Timing of eating in adults across the weight spectrum: Metabolic factors and potential circadian mechanisms. *Physiology & behavior.* **192**, pp.158-166.

Anastasiou, C.A., Fappa, E., Zachari, K., Mavrogianni, C., Van Stappen, V., Kivelä, J., Virtanen, E., González-Gil, E.M., Flores-Barrantes, P., Nánási, A., Semánová, C., Dimova, R., Usheva, N., Iotova, V., Cardon, G., Manios, Y., Makrilakis, K. and Feel4Diabetes-study, g. 2020. Development and reliability of questionnaires for the assessment of diet and physical activity behaviors in a multi-country sample in Europe the Feel4Diabetes Study. *BMC endocrine disorders.* **20**(Suppl 1), pp.135-135.

Ardıç, C., Çolak, S., Uzun, K., Salı, G., Aydemir, T. and Telatar, G. 2020. Maternal Gestational Diabetes and Early Childhood Obesity: A Retrospective Cohort Study. *Child Obes.* **16**(8), pp.579-585.

Arnotti, K. and Bamber, M. 2020. Fruit and Vegetable Consumption in Overweight or Obese Individuals: A Meta-Analysis. *West J Nurs Res.* **42**(4), pp.306-314.

Birbilis, M., Moschonis, G., Mougios, V., Manios, Y. and on behalf of the 'Healthy Growth Study', g. 2013. Obesity in adolescence is associated with perinatal risk factors, parental BMI and sociodemographic characteristics. *European Journal of Clinical Nutrition.* **67**(1), pp.115-121.

Blundell, J.E., Baker, J.L., Boyland, E., Blaak, E., Charzewska, J., de Henauw, S., Frühbeck, G., Gonzalez-Gross, M., Hebebrand, J., Holm, L., Kriaucioniene, V., Lissner, L., Oppert, J.-M., Schindler, K., Silva, A.L. and Woodward, E. 2017. Variations in the Prevalence of Obesity Among European Countries, and a Consideration of Possible Causes. *Obesity facts.* **10**(1), pp.25-37.

Bull, F.C., Al-Ansari, S.S., Biddle, S., Borodulin, K., Buman, M.P., Cardon, G., Carty, C., Chaput, J.P., Chastin, S., Chou, R., Dempsey, P.C., DiPietro, L., Ekelund, U., Firth, J., Friedenreich, C.M., Garcia, L., Gichu, M., Jago, R., Katzmarzyk, P.T., Lambert, E., Leitzmann, M., Milton, K., Ortega, F.B., Ranasinghe, C., Stamatakis, E., Tiedemann, A., Troiano, R.P., van der Ploeg, H.P., Wari, V. and Willumsen, J.F. 2020. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med.* **54**(24), pp.1451-1462.

Cassidy, S., Chau, J.Y., Catt, M., Bauman, A. and Trenell, M.I. 2017. Low physical activity, high television viewing and poor sleep duration cluster in overweight and obese adults; a cross-sectional study of 398,984 participants from the UK Biobank. *International Journal of Behavioral Nutrition and Physical Activity.* **14**(1), p57.

Centers for disease control and prevention. 2020a. The Health Effects of Overweight and Obesity.

Centers for disease control and prevention. 2020b. Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017–2018.

Chesi, A. and Grant, S.F.A. 2015. The Genetics of Pediatric Obesity. *Trends in endocrinology and metabolism: TEM.* **26**(12), pp.711-721.

Cissé, A.H., Lioret, S., de Lauzon-Guillain, B., Forhan, A., Ong, K.K., Charles, M.A. and Heude, B. 2021. Association between perinatal factors, genetic susceptibility to obesity and age at adiposity rebound in children of the EDEN mother–child cohort. *International Journal of Obesity.* **45**(8), pp.1802-1810.

Cooper, C.B., Neufeld, E.V., Dolezal, B.A. and Martin, J.L. 2018. Sleep deprivation and obesity in adults: a brief narrative review. *BMJ Open Sport & Exercise Medicine.* **4**(1), pe000392.

Corica, D., Aversa, T., Valenzise, M., Messina, M.F., Alibrandi, A., De Luca, F. and Wasniewska, M. 2018. Does Family History of Obesity, Cardiovascular, and Metabolic Diseases Influence Onset and Severity of Childhood Obesity? *Frontiers in endocrinology.* **9**, pp.187-187.

Devaux, M. and Sassi, F. 2013. Social inequalities in obesity and overweight in 11 OECD countries. *Eur J Public Health.* **23**(3), pp.464-469.

Diels, S., Vanden Berghe, W. and Van Hul, W. 2020. Insights into the multifactorial causation of obesity by integrated genetic and epigenetic analysis. *Obes Rev.* **21**(7), pe13019.

Ding, C., Lim, L.L., Xu, L. and Kong, A.P.S. 2018. Sleep and Obesity. *Journal of obesity & metabolic syndrome.* **27**(1), pp.4-24.

Dommel, F.W. and Alexander, D. 1997. The Convention on Human Rights and Biomedicine of the Council of Europe. *Kennedy Inst Ethics J.* **7**(3), pp.259-276.

Eurostat. 2016. European Health Interview Survey. Almost 1 adult in 6 in the EU is considered obese.

Eurostat. 2021. Overweight and obesity - BMI statistics.

Fountain, J.H. and Lappin, S.L. 2021. Physiology, Renin Angiotensin System. *StatPearls.* Treasure Island (FL): StatPearls Publishing. Copyright © 2021, StatPearls Publishing LLC.

Fung, T.T., Pan, A., Hou, T., Chiuve, S.E., Tobias, D.K., Mozaffarian, D., Willett, W.C. and Hu, F.B. 2015. Long-Term Change in Diet Quality Is Associated with Body Weight Change in Men and Women. *The Journal of nutrition.* **145**(8), pp.1850-1856.

Glonti, K., Mackenbach, J.D., Ng, J., Lakerveld, J., Oppert, J.M., Bárdos, H., McKee, M. and Rutter, H. 2016. Psychosocial environment: definitions, measures and associations with weight status--a systematic review. *Obes Rev.* **17 Suppl 1**, pp.81-95.

Hüls, A., Wright, M.N., Bogl, L.H., Kaprio, J., Lissner, L., Molnár, D., Moreno, L.A., De Henauw, S., Siani, A., Veidebaum, T., Ahrens, W., Pigeot, I. and Foraita, R. 2021. Polygenic risk for obesity and its interaction with lifestyle and sociodemographic factors in European children and adolescents. *International Journal of Obesity.* **45**(6), pp.1321-1330.

Harris, K.K., Zopey, M. and Friedman, T.C. 2016. Metabolic effects of smoking cessation. *Nature reviews. Endocrinology.* **12**(5), pp.299-308.

Hoffmann, K., De Gelder, R., Hu, Y., Bopp, M., Vitrai, J., Lahelma, E., Menvielle, G., Santana, P., Regidor, E., Ekholm, O., Mackenbach, J.P. and van Lenthe, F.J. 2017. Trends in educational inequalities in obesity in 15 European countries between 1990 and 2010. *The international journal of behavioral nutrition and physical activity.* **14**(1), pp.63-63.

Hruby, A. and Hu, F.B. 2015. The Epidemiology of Obesity: A Big Picture. *PharmacoEconomics.* **33**(7), pp.673-689.

Hruby, A., Manson, J.E., Qi, L., Malik, V.S., Rimm, E.B., Sun, Q., Willett, W.C. and Hu, F.B. 2016. Determinants and Consequences of Obesity. *American journal of public health.* **106**(9), pp.1656-1662.

Hsieh, T.-H., Lee, J.J., Yu, E.W.-R., Hu, H.-Y., Lin, S.-Y. and Ho, C.-Y. 2020. Association between obesity and education level among the elderly in Taipei, Taiwan between 2013 and 2015: a cross-sectional study. *Scientific Reports.* **10**(1), p20285.

Hu, F.B. 2013. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obes Rev.* **14**(8), pp.606-619.

Hu, F.B., Li, T.Y., Colditz, G.A., Willett, W.C. and Manson, J.E. 2003. Television watching and other sedentary behaviors in relation to risk of obesity and type 2 diabetes mellitus in women. *Jama.* **289**(14), pp.1785-1791.

Janssen, F., Bardoutsos, A. and Vidra, N. 2020. Obesity Prevalence in the Long-Term Future in 18 European Countries and in the USA. *Obesity Facts.* **13**(5), pp.514-527.

Kim, B.-Y., Nam, H., Yoo, J.-J., Cho, Y.-Y., Choi, D.-H., Jung, C.-H., Mok, J.-O. and Kim, C.-H. 2021. Association between alcohol consumption status and obesity-related comorbidities in men: data from the 2016 Korean community health survey. *BMC Public Health.* **21**(1), p733.

Kim, K.-B. and Shin, Y.-A. 2020. Males with Obesity and Overweight. *Journal of obesity & metabolic syndrome.* **29**(1), pp.18-25.

Kim, T.J. and von dem Knesebeck, O. 2018. Income and obesity: what is the direction of the relationship? A systematic review and meta-analysis. *BMJ Open.* **8**(1), pe019862.

Kim, Y.-J. 2016. The long-run effect of education on obesity in the US. *Economics & Human Biology.* **21**, pp.100-109.

Kim, Y., Jeong, S.M., Yoo, B., Oh, B. and Kang, H.-C. 2016. Associations of smoking with overall obesity, and central obesity: a cross-sectional study from the Korea National Health and Nutrition Examination Survey (2010-2013). *Epidemiology and health.* **38**, pp.e2016020-e2016020.

Krističević, T., Štefan, L. and Sporiš, G. 2018. The Associations between Sleep Duration and Sleep Quality with Body-Mass Index in a Large Sample of Young Adults. *International journal of environmental research and public health.* **15**(4), p758.

Krzysztoszek, J., Laudańska-Krzemińska, I. and Bronikowski, M. 2019. Assessment of epidemiological obesity among adults in EU countries. *Ann Agric Environ Med.* **26**(2), pp.341-349.

Lakerveld, J. and Mackenbach, J. 2017. The Upstream Determinants of Adult Obesity. *Obesity facts.* **10**(3), pp.216-222.

Lam, T.M., Vaartjes, I., Grobbee, D.E., Karssenberg, D. and Lakerveld, J. 2021. Associations between the built environment and obesity: an umbrella review. *International Journal of Health Geographics.* **20**(1), p7.

Leal, C. and Chaix, B. 2011. The influence of geographic life environments on cardiometabolic risk factors: a systematic review, a methodological assessment and a research agenda. *Obes Rev.* **12**(3), pp.217-230.

Lee, A., Cardel, M. and Donahoo, W. 2019. Social and Environmental Factors Influencing Obesity. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. *South Dartmouth (MA): MDText.com, Inc.*

Levine, J.A. 2011. Poverty and obesity in the U.S. *Diabetes.* **60**(11), pp.2667-2668.

Lindström, J. and Tuomilehto, J. 2003. The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care.* **26**(3), pp.725-731.

Lipek, T., Igel, U., Gausche, R., Kiess, W. and Grande, G. 2015. Obesogenic environments: environmental approaches to obesity prevention. *J Pediatr Endocrinol Metab.* **28**(5-6), pp.485-495.

Littlejohn, N.K., Keen, H.L., Weidemann, B.J., Claflin, K.E., Tobin, K.V., Markan, K.R., Park, S., Naber, M.C., Gourronc, F.A., Pearson, N.A., Liu, X., Morgan, D.A., Klingelhutz, A.J., Potthoff, M.J., Rahmouni, K., Sigmund, C.D. and Grobe, J.L. 2016. Suppression of Resting Metabolism by the Angiotensin AT2 Receptor. *Cell Rep.* **16**(6), pp.1548-1560.

Lopez-Minguez, J., Gómez-Abellán, P. and Garaulet, M. 2019. Timing of Breakfast, Lunch, and Dinner. Effects on Obesity and Metabolic Risk. *Nutrients.* **11**(11), p2624.

Lundeen, E., Park, S., Pan, L., O'Toole, T., Matthews, K. and Blanck, H. 2018. Obesity Prevalence Among Adults Living in Metropolitan and Nonmetropolitan Counties — United States, 2016. *MMWR Morb Mortal Wkly Rep.* (67), pp.653-658.

Mackenbach, J.D., Rutter, H., Compernolle, S., Glonti, K., Oppert, J.M., Charreire, H., De Bourdeaudhuij, I., Brug, J., Nijpels, G. and Lakerveld, J. 2014. Obesogenic environments: a systematic review of the association between the physical environment and adult weight status, the SPOTLIGHT project. *BMC Public Health.* **14**, p233.

Manios, Y., Androutsos, O., Lambrinou, C.P., Cardon, G., Lindstrom, J., Annemans, L., Mateo-Gallego, R., de Sabata, M.S., Iotova, V., Kivela, J., Martinez, R., Moreno, L.A., Rurik, I., Schwarz, P., Tankova, T., Liatis, S. and Makrilakis, K. 2018. A school- and community-based intervention to promote healthy lifestyle and prevent type 2 diabetes in vulnerable families across Europe: design and implementation of the Feel4Diabetes-study. *Public Health Nutr.* **21**(17), pp.3281-3290.

Manios, Y., Mavrogianni, C., Lambrinou, C.-P., Cardon, G., Lindström, J., Iotova, V., Tankova, T., Civeira, F., Kivelä, J., Jancsó, Z., Shadid, S., Tsochev, K., Mateo-Gallego, R., Radó, S., Dafoulas, G., Makrilakis, K., Androutsos, O., Manios, Y., Cardon, G., Lindström, J., Schwarz, P., Makrilakis, K., Annemans, L., Garamendi, I., Kontogianni, M., Androutsos, O., Mavrogianni, C., Tsoutsoulopoulou, K., Katsarou, C., Karaglani, E., Qira, I., Skoufas, E., Maragkopoulou, K., Tsiafitsa, A., Sotiropoulou, I., Tsolakos, M., Argyri, E., Nikolaou, M., Vampouli, E.-A., Filippou, C., Gatsiou, K., Dimitriadis, E., Laatikainen, T., Wikström, K., Kivelä, J., Valve, P., Levälahti, E., Virtanen, E., Van Stappen, V., Huys, N., Willems, R., Shadid, S., Panchyrz, I., Holland, M., Timpel, P., Liatis, S., Dafoulas, G., Lambrinou, C.-P., Giannopoulou, A., Tsirigoti, L., Fappa, E., Anastasiou, C., Zachari, K., Rabemananjara, L., de Sabata, M.S., Ko, W., Moreno, L., Civeira, F., Bueno, G., De Miguel-Etayo, P., Gonzalez-Gil, E.M., Mesana, M.I., Vicente-Rodriguez, G., Rodriguez, G., Baila-Rueda, L., Cenarro, A., Jarauta, E., Mateo-Gallego, R., Iotova, V., Tankova, T., Usheva, N., Tsochev, K., Chakarova, N., Galcheva, S., Dimova, R., Bocheva, Y., Radkova, Z., Marinova, V., Bazdarska, Y., Stefanova, T., Rurik, I., Ungvari, T., Jancsó, Z., Nánási, A., Kolozsvári, L., Semánova, C., Martinez, R., Tong, M., Joutsenniemi, K., Wendel-Mitoraj, K. and on behalf of the Feel4Diabetes-study, g. 2020. Two-stage, school and community-based population screening successfully identifies individuals and families at high-risk for type 2 diabetes: the Feel4Diabetes-study. *BMC Endocrine Disorders.* **20**(1), p12.

Marques, A., Peralta, M., Naia, A., Loureiro, N. and de Matos, M.G. 2017. Prevalence of adult overweight and obesity in 20 European countries, 2014. *European Journal of Public Health.* **28**(2), pp.295-300.

Martínez-Ramos, E., Beltran, A.-M., Martín-Borràs, C., Lasaosa-Medina, L., Real, J., Trujillo, J.-M., Solà-Gonfaus, M., Puigdomenech, E., Castillo-Ramos, E., Puig-Ribera, A., Giné-Garriga, M., Serra-Paya, N., Rodriguez-Roca, B., Gascón-Catalán, A., Martín-Cantera, C. and for the, S.g. 2018. Patterns of sedentary behavior in overweight and moderately obese users of the Catalan primary-health care system. *PLOS ONE.* **13**(1), pe0190750.

Mayega, R.W., Makumbi, F., Rutebemberwa, E., Peterson, S., Östenson, C.-G., Tomson, G. and Guwatudde, D. 2012. Modifiable Socio-Behavioural Factors Associated with Overweight and Hypertension among Persons Aged 35 to 60 Years in Eastern Uganda. *PLOS ONE.* **7**(10), pe47632.

McCormack, G.R. and Shiell, A. 2011. In search of causality: a systematic review of the relationship between the built environment and physical activity among adults. *Int J Behav Nutr Phys Act.* **8**, p125.

McKee, A. and Morley, J. 2020. Obesity in the Elderly. *In: Feingold KR, Anawalt B, Boyce A, et al., editors. [Updated 2018 Oct 12]. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.*

Mohammed, S.H., Habtewold, T.D., Birhanu, M.M., Sissay, T.A., Tegegne, B.S., Abuzerr, S. and Esmaillzadeh, A. 2019. Neighbourhood socioeconomic status and overweight/obesity: a systematic review and meta-analysis of epidemiological studies. *BMJ open.* **9**(11), pp.e028238-e028238.

Mons, U., Muscat, J.E., Modesto, J., Richie, J.P., Jr. and Brenner, H. 2016. Effect of smoking reduction and cessation on the plasma levels of the oxidative stress biomarker glutathione--Post-hoc analysis of data from a smoking cessation trial. *Free radical biology & medicine.* **91**, pp.172-177.

Monsivais, P., Martin, A., Suhrcke, M., Forouhi, N.G. and Wareham, N.J. 2015. Job-loss and weight gain in British adults: Evidence from two longitudinal studies. *Social science & medicine (1982).* **143**, pp.223-231.

Monteiro, C.A., Moura, E.C., Conde, W.L. and Popkin, B.M. 2004. Socioeconomic status and obesity in adult populations of developing countries: a review. *Bull World Health Organ.* **82**(12), pp.940-946.

Morgen, C.S., Ängquist, L., Baker, J.L., Andersen, A.M.N., Michaelsen, K.F. and Sørensen, T.I.A. 2018. Prenatal risk factors influencing childhood BMI and overweight independent of birth weight and infancy BMI: a path analysis within the Danish National Birth Cohort. *International Journal of Obesity.* **42**(4), pp.594-602.

Mozaffarian, D., Hao, T., Rimm, E.B., Willett, W.C. and Hu, F.B. 2011. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med.* **364**(25), pp.2392-2404.

Muscella, A., Stefàno, E., Lunetti, P., Capobianco, L. and Marsigliante, S. 2020. The Regulation of Fat Metabolism During Aerobic Exercise. *Biomolecules.* **10**(12), p1699.

N. C. D. Risk Factor Collaboration. 2019. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature.* **569**(7755), pp.260-264.

National Cancer Institute. 2017. Obesity and Cancer.

Niemiro, G., Rewane, A. and Algotar, A. 2021. Exercise and Fitness Effect On Obesity. *In: StatPearls [Internet]. [Updated 2021 Jun 8]. Treasure Island (FL): StatPearls Publishing.*

Norrbäck, M., Tynelius, P., Ahlström, G. and Rasmussen, F. 2019. The association of mobility disability and obesity with risk of unemployment in two cohorts from Sweden. *BMC Public Health.* **19**(1), p347.

Nour, M., Lutze, S.A., Grech, A. and Allman-Farinelli, M. 2018. The Relationship between Vegetable Intake and Weight Outcomes: A Systematic Review of Cohort Studies. *Nutrients.* **10**(11), p1626.

Ogden, C.L., Fakhouri, T.H., Carroll, M.D., Hales, C.M., Fryar, C.D., Li, X. and Freedman, D.S. 2017. Prevalence of Obesity Among Adults, by Household Income and Education - United States, 2011-2014. *MMWR. Morbidity and mortality weekly report.* **66**(50), pp.1369-1373.

Panahi, S. and Tremblay, A. 2018. Sedentariness and Health: Is Sedentary Behavior More Than Just Physical Inactivity? *Frontiers in public health.* **6**, pp.258-258.

Petrill, S.A. and Kovas, Y. 2016. Chapter 11 - Individual Differences in Mathematics Ability: A Behavioral Genetic Approach. In: Berch, D.B., et al. eds. *Development of Mathematical Cognition.* San Diego: Academic Press, pp.299-323.

Qi, Q., Chu, A.Y., Kang, J.H., Huang, J., Rose, L.M., Jensen, M.K., Liang, L., Curhan, G.C., Pasquale, L.R., Wiggs, J.L., De Vivo, I., Chan, A.T., Choi, H.K., Tamimi, R.M., Ridker, P.M., Hunter, D.J., Willett, W.C., Rimm, E.B., Chasman, D.I., Hu, F.B. and Qi, L. 2014. Fried food consumption, genetic risk, and body mass index: gene-diet interaction analysis in three US cohort studies. *Bmj.* **348**, pg1610.

Qi, Q., Chu, A.Y., Kang, J.H., Jensen, M.K., Curhan, G.C., Pasquale, L.R., Ridker, P.M., Hunter, D.J., Willett, W.C., Rimm, E.B., Chasman, D.I., Hu, F.B. and Qi, L. 2012. Sugar-sweetened beverages and genetic risk of obesity. *The New England journal of medicine.* **367**(15), pp.1387-1396.

Qi, Q., Li, Y., Chomistek, A.K., Kang, J.H., Curhan, G.C., Pasquale, L.R., Willett, W.C., Rimm, E.B., Hu, F.B. and Qi, L. 2012. Television watching, leisure time physical activity, and the genetic predisposition in relation to body mass index in women and men. *Circulation.* **126**(15), pp.1821-1827.

Rabin, B.A., Boehmer, T.K. and Brownson, R.C. 2007. Cross-national comparison of environmental and policy correlates of obesity in Europe. *Eur J Public Health.* **17**(1), pp.53-61.

Rezuş, E., Burlui, A., Cardoneanu, A., Rezuş, C., Codreanu, C., Pârvu, M., Rusu Zota, G. and Tamba, B.I. 2020. Inactivity and Skeletal Muscle Metabolism: A Vicious Cycle in Old Age. *International journal of molecular sciences.* **21**(2), p592.

Romieu, I., Dossus, L., Barquera, S., Blottière, H.M., Franks, P.W., Gunter, M., Hwalla, N., Hursting, S.D., Leitzmann, M., Margetts, B., Nishida, C., Potischman, N., Seidell, J., Stepien, M., Wang, Y., Westerterp, K., Winichagoon, P., Wiseman, M., Willett, W.C., Balance, I.w.g.o.E. and Obesity. 2017. Energy balance and obesity: what are the main drivers? *Cancer causes & control : CCC.* **28**(3), pp.247-258.

Sallis, J.F., Cerin, E., Kerr, J., Adams, M.A., Sugiyama, T., Christiansen, L.B., Schipperijn, J., Davey, R., Salvo, D., Frank, L.D., Bourdeaudhuij, I.D. and Owen, N. 2020. Built Environment, Physical Activity, and Obesity: Findings from the International Physical Activity and Environment Network (IPEN) Adult Study. *Annual Review of Public Health.* **41**(1), pp.119-139.

Schulze, M.B., Fung, T.T., Manson, J.E., Willett, W.C. and Hu, F.B. 2006. Dietary patterns and changes in body weight in women. *Obesity (Silver Spring).* **14**(8), pp.1444-1453.

Sears, B. and Perry, M. 2015. The role of fatty acids in insulin resistance. *Lipids in health and disease.* **14**, pp.121-121.

Shahraki, M., Shahraki, T., Shidfar, F. and Ansari, H. 2012. Which modifiable, non-modifiable, and socioeconomic factors have more effect on cardiovascular risk factors in overweight and obese women? *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences.* **17**(7), pp.676-680.

Sherpa, D. 2021. *Introduction to Univariate, Bivariate and Multivariate Analysis, Analytics Vidhya community of Analytics and Data Science professionals.* [Online]. Available from: https://medium.com/analytics-vidhya/univariate-bivariate-and-multivariate-analysis-8b4fc3d8202c

Shin, H. 2020. *Even light alcohol consumption linked to higher risk of obesity and metabolic syndrome in study of 27 million adults. European Association for the Study of Obesity.* [Online]. Available from: https://www.eurekalert.org/news-releases/605322

Siddiqui, S. 2018. Obesity and diabetes: interrelationship. *Adv Obes Weight Manag Control.* **8**(2), pp.155-158.

Soltani, N., Marandi, S.M., Kazemi, M. and Esmaeil, N. 2020. The Exercise Training Modulatory Effects on the Obesity-Induced Immunometabolic Dysfunctions. *Diabetes, metabolic syndrome and obesity : targets and therapy.* **13**, pp.785-810.

Speliotes, E.K., Willer, C.J., Berndt, S.I., Monda, K.L., Thorleifsson, G., Jackson, A.U., Lango Allen, H., Lindgren, C.M., Luan, J., Mägi, R., Randall, J.C., Vedantam, S., Winkler, T.W., Qi, L., Workalemahu, T., Heid, I.M., Steinthorsdottir, V., Stringham, H.M., Weedon, M.N., Wheeler, E., Wood, A.R., Ferreira, T., Weyant, R.J., Segrè, A.V., Estrada, K., Liang, L., Nemesh, J., Park, J.H., Gustafsson, S., Kilpeläinen, T.O., Yang, J., Bouatia-Naji, N., Esko, T., Feitosa, M.F., Kutalik, Z., Mangino, M., Raychaudhuri, S., Scherag, A., Smith, A.V.,

Welch, R., Zhao, J.H., Aben, K.K., Absher, D.M., Amin, N., Dixon, A.L., Fisher, E., Glazer, N.L., Goddard, M.E., Heard-Costa, N.L., Hoesel, V., Hottenga, J.J., Johansson, A., Johnson, T., Ketkar, S., Lamina, C., Li, S., Moffatt, M.F., Myers, R.H., Narisu, N., Perry, J.R., Peters, M.J., Preuss, M., Ripatti, S., Rivadeneira, F., Sandholt, C., Scott, L.J., Timpson, N.J., Tyrer, J.P., van Wingerden, S., Watanabe, R.M., White, C.C., Wiklund, F., Barlassina, C., Chasman, D.I., Cooper, M.N., Jansson, J.O., Lawrence, R.W., Pellikka, N., Prokopenko, I., Shi, J., Thiering, E., Alavere, H., Alibrandi, M.T., Almgren, P., Arnold, A.M., Aspelund, T., Atwood, L.D., Balkau, B., Balmforth, A.J., Bennett, A.J., Ben-Shlomo, Y., Bergman, R.N., Bergmann, S., Biebermann, H., Blakemore, A.I., Boes, T., Bonnycastle, L.L., Bornstein, S.R., Brown, M.J., Buchanan, T.A., Busonero, F., Campbell, H., Cappuccio, F.P., Cavalcanti-Proença, C., Chen, Y.D., Chen, C.M., Chines, P.S., Clarke, R., Coin, L., Connell, J., Day, I.N., den Heijer, M., Duan, J., Ebrahim, S., Elliott, P., Elosua, R., Eiriksdottir, G., Erdos, M.R., Eriksson, J.G., Facheris, M.F., Felix, S.B., Fischer-Posovszky, P., Folsom, A.R., Friedrich, N., Freimer, N.B., Fu, M., Gaget, S., Gejman, P.V., Geus, E.J., Gieger, C., Gjesing, A.P., Goel, A., Goyette, P., Grallert, H., Grässler, J., Greenawalt, D.M., Groves, C.J., Gudnason, V., Guiducci, C., Hartikainen, A.L., Hassanali, N., Hall, A.S., Havulinna, A.S., Hayward, C., Heath, A.C., Hengstenberg, C., Hicks, A.A., Hinney, A., Hofman, A., Homuth, G., Hui, J., Igl, W., Iribarren, C., Isomaa, B., Jacobs, K.B., Jarick, I., Jewell, E., John, U., Jørgensen, T., Jousilahti, P., Jula, A., Kaakinen, M., Kajantie, E., Kaplan, L.M., Kathiresan, S., Kettunen, J., Kinnunen, L., Knowles, J.W., Kolcic, I., König, I.R., Koskinen, S., Kovacs, P., Kuusisto, J., Kraft, P., Kvaløy, K., Laitinen, J., Lantieri, O., Lanzani, C., Launer, L.J., Lecoeur, C., Lehtimäki, T., Lettre, G., Liu, J., Lokki, M.L., Lorentzon, M., Luben, R.N., Ludwig, B., Manunta, P., Marek, D., Marre, M., Martin, N.G., McArdle, W.L., McCarthy, A., McKnight, B., Meitinger, T., Melander, O., Meyre, D., Midthjell, K., Montgomery, G.W., Morken, M.A., Morris, A.P., Mulic, R., Ngwa, J.S., Nelis, M., Neville, M.J., Nyholt, D.R., O'Donnell, C.J., O'Rahilly, S., Ong, K.K., Oostra, B., Paré, G., Parker, A.N., Perola, M., Pichler, I., Pietiläinen, K.H., Platou, C.G., Polasek, O., Pouta, A., Rafelt, S., Raitakari, O., Rayner, N.W., Ridderstråle, M., Rief, W., Ruokonen, A., Robertson, N.R., Rzehak, P., Salomaa, V., Sanders, A.R., Sandhu, M.S., Sanna, S., Saramies, J., Savolainen, M.J., Scherag, S., Schipf, S., Schreiber, S., Schunkert, H., Silander, K., Sinisalo, J., Siscovick, D.S., Smit, J.H., Soranzo, N., Sovio, U., Stephens, J., Surakka, I., Swift, A.J., Tammesoo, M.L., Tardif, J.C., Teder-Laving, M., Teslovich, T.M., Thompson, J.R., Thomson, B., Tönjes, A., Tuomi, T., van Meurs, J.B., van Ommen, G.J., Vatin, V., Viikari, J., Visvikis-Siest, S., Vitart, V., Vogel, C.I., Voight, B.F., Waite, L.L., Wallaschofski, H., Walters, G.B., Widen, E., Wiegand, S., Wild, S.H., Willemsen, G., Witte, D.R., Witteman, J.C., Xu, J., Zhang, Q., Zgaga, L., Ziegler, A., Zitting, P., Beilby, J.P., Farooqi, I.S., Hebebrand, J., Huikuri, H.V., James, A.L., Kähönen, M., Levinson, D.F., Macciardi, F., Nieminen, M.S., Ohlsson, C., Palmer, L.J., Ridker, P.M., Stumvoll, M., Beckmann, J.S., Boeing, H., Boerwinkle, E., Boomsma, D.I., Caulfield, M.J., Chanock, S.J., Collins, F.S., Cupples, L.A., Smith, G.D., Erdmann, J., Froguel, P., Grönberg, H., Gyllensten, U., Hall, P., Hansen, T., Harris, T.B., Hattersley, A.T., Hayes, R.B., Heinrich, J., Hu, F.B., Hveem, K., Illig, T., Jarvelin, M.R., Kaprio, J., Karpe, F., Khaw, K.T., Kiemeney, L.A., Krude, H., Laakso, M., Lawlor, D.A., Metspalu, A., Munroe, P.B., Ouwehand, W.H., Pedersen, O., Penninx, B.W., Peters, A., Pramstaller, P.P., Quertermous, T., Reinehr, T., Rissanen, A., Rudan, I., Samani, N.J., Schwarz, P.E., Shuldiner, A.R., Spector, T.D., Tuomilehto, J., Uda, M., Uitterlinden, A., Valle, T.T., Wabitsch, M., Waeber, G., Wareham, N.J., Watkins, H., Wilson, J.F., Wright, A.F., Zillikens, M.C., Chatterjee, N., McCarroll, S.A., Purcell, S., Schadt, E.E., Visscher, P.M., Assimes, T.L., Borecki, I.B., Deloukas, P., Fox, C.S., Groop, L.C., Haritunians, T., Hunter, D.J., Kaplan, R.C., Mohlke, K.L., O'Connell, J.R., Peltonen, L., Schlessinger, D., Strachan, D.P., van Duijn, C.M., Wichmann, H.E., Frayling, T.M., Thorsteinsdottir, U., Abecasis, G.R., Barroso, I., Boehnke, M., Stefansson, K., North, K.E., McCarthy, M.I., Hirschhorn, J.N., Ingelsson, E. and Loos, R.J. 2010. Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index. *Nat Genet.* **42**(11), pp.937-948.

St-Onge, M.-P. 2017. Sleep–obesity relation: underlying mechanisms and consequences for treatment. *Obesity Reviews.* **18**(S1), pp.34-39.

Stockman, M.-C., Thomas, D., Burke, J. and Apovian, C.M. 2018. Intermittent Fasting: Is the Wait Worth the Weight? *Current obesity reports.* **7**(2), pp.172-185.

Suryadinata, R.V., Wirjatmadi, B., Adriani, M. and Lorensia, A. 2020. Effect of age and weight on physical activity. *Journal of public health research.* **9**(2), pp.1840-1840.

Swift, D.L., McGee, J.E., Earnest, C.P., Carlisle, E., Nygard, M. and Johannsen, N.M. 2018. The Effects of Exercise and Physical Activity on Weight Loss and Maintenance. *Prog Cardiovasc Dis.* **61**(2), pp.206-213.

Templin, T., Cravo Oliveira Hashiguchi, T., Thomson, B., Dieleman, J. and Bendavid, E. 2019. The overweight and obesity transition from the wealthy to the poor in low- and middle-income countries: A survey of household data from 103 countries. *PLOS Medicine.* **16**(11), pe1002968.

Tran, L., Tran, P. and Tran, L. 2020. A cross-sectional examination of sociodemographic factors associated with meeting physical activity recommendations in overweight and obese US adults. *Obes Res Clin Pract.* **14**(1), pp.91-98.

Traversy, G. and Chaput, J.-P. 2015. Alcohol Consumption and Obesity: An Update. *Current obesity reports.* **4**(1), pp.122-130.

Type 2 diabetes risk assessment form. c2021. [Online]. Available from: https://www.diabetes.fi/files/502/eRiskitestilomake.pdf

Vaněčková, I., Maletínská, L., Behuliak, M., Nagelová, V., Zicha, J. and Kuneš, J. 2014. Obesity-related hypertension: possible pathophysiological mechanisms. *Journal of Endocrinology.* **223**(3), pp.R63-R78.

Venkatesan, R. and Viswanathan, M. 2016. Obesity – Are we continuing to play the genetic "blame game"? *Advances in Genomics and Genetics.* **6**, pp.11-23.

Wadden, T.A., Webb, V.L., Moran, C.H. and Bailer, B.A. 2012. Lifestyle modification for obesity: new developments in diet, physical activity, and behavior therapy. *Circulation.* **125**(9), pp.1157-1170.

Wallace, T.C., Bailey, R.L., Blumberg, J.B., Burton-Freeman, B., Chen, C.O., Crowe-White, K.M., Drewnowski, A., Hooshmand, S., Johnson, E., Lewis, R., Murray, R., Shapses, S.A. and Wang, D.D. 2020. Fruits, vegetables, and health: A comprehensive narrative, umbrella review of the science and recommendations for enhanced public policy to improve intake. *Crit Rev Food Sci Nutr.* **60**(13), pp.2174-2211.

Wallis, N. and Raffan, E. 2020. The Genetic Basis of Obesity and Related Metabolic Diseases in Humans and Companion Animals. *Genes (Basel).* **11**(11).

Watanabe, T., Tsujino, I., Konno, S., Ito, Y.M., Takashina, C., Sato, T., Isada, A., Ohira, H., Ohtsuka, Y., Fukutomi, Y., Nakamura, H., Kawagishi, Y., Okada, C., Hizawa, N., Taniguchi, M., Akasawa, A. and Nishimura, M. 2016. Association between Smoking Status and Obesity in a Nationwide Survey of Japanese Adults. *PloS one.* **11**(3), pp.e0148926-e0148926.

Welton, S., Minty, R., O'Driscoll, T., Willms, H., Poirier, D., Madden, S. and Kelly, L. 2020. Intermittent fasting and weight loss: Systematic review. *Canadian family physician Medecin de famille canadien.* **66**(2), pp.117-125.

Wen, M., Fan, J.X., Kowaleski-Jones, L. and Wan, N. 2018. Rural-Urban Disparities in Obesity Prevalence Among Working Age Adults in the United States: Exploring the Mechanisms. *Am J Health Promot.* **32**(2), pp.400-408.

Willis, E.A., Creasy, S.A., Honas, J.J., Melanson, E.L. and Donnelly, J.E. 2020. The effects of exercise session timing on weight loss and components of energy balance: midwest exercise trial 2. *International journal of obesity (2005).* **44**(1), pp.114-124.

Woolf, A.D., Breedveld, F. and Kvien, T.K. 2006. Controlling the obesity epidemic is important for maintaining musculoskeletal health. *Annals of the rheumatic diseases.* **65**(11), pp.1401-1402.

World Health Organization. 2009. Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks. Geneva: WHO.

World Health Organization Obesity and overweight fact sheet, 2021.

World Health Organization. Guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization, 2020.

World Medical Association. 2013. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *Jama.* **310**(20), pp.2191-2194.

Xiao, Q., Garaulet, M. and Scheer, F.A.J.L. 2019. Meal timing and obesity: interactions with macronutrient intake and chronotype. *International journal of obesity (2005).* **43**(9), pp.1701-1711.

Zou, Z., Yang, Z., Yang, Z., Wang, X., Gao, D., Dong, Y., Ma, J. and Ma, Y. 2019. Association of high birth weight with overweight and obesity in Chinese students aged 6–18 years: a national, cross-sectional study in China. *BMJ Open.* **9**(5), pe024532.

6. Appendix

The Finnish Diabetes Risk Score (FINDRISC)

Finnish Diabetes Association

TYPE 2 DIABETES RISK ASSESSMENT FORM

Circle the right alternative and add up your points.

1. Age

0 p. Under 45 years
2 p. 45–54 years
3 p. 55–64 years
4 p. Over 64 years

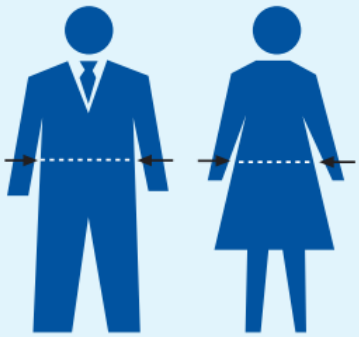
2. Body-mass index

(See reverse of form)

0 p. Lower than 25 kg/m^2
1 p. 25–30 kg/m^2
3 p. Higher than 30 kg/m^2

3. Waist circumference measured below the ribs (usually at the level of the navel)

	MEN	WOMEN
0 p.	Less than 94 cm	Less than 80 cm
3 p.	94–102 cm	80–88 cm
4 p.	More than 102 cm	More than 88 cm



4. Do you usually have daily at least 30 minutes of physical activity at work and/or during leisure time (including normal daily activity)?

0 p. Yes
2 p. No

5. How often do you eat vegetables, fruit or berries?

0 p. Every day
1 p. Not every day

6. Have you ever taken medication for high blood pressure on regular basis?

0 p. No
2 p. Yes

7. Have you ever been found to have high blood glucose (eg in a health examination, during an illness, during pregnancy)?

0 p. No
5 p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?

0 p. No
3 p. Yes: grandparent, aunt, uncle or first cousin (but no own parent, brother, sister or child)
5 p. Yes: parent, brother, sister or own child

Total Risk Score

☐ **The risk of developing type 2 diabetes within 10 years is**

Lower than 7	**Low:** estimated 1 in 100 will develop disease
7–11	**Slightly elevated:** estimated 1 in 25 will develop disease
12–14	**Moderate:** estimated 1 in 6 will develop disease
15–20	**High:** estimated 1 in 3 will develop disease
Higher than 20	**Very high:** estimated 1 in 2 will develop disease

Please turn over

Test designed by Professor Jaakko Tuomilehto, Department of Public Health, University of Helsinki, and Jaana Lindström, MFS, National Public Health Institute.

Finnish Diabetes Association

WHAT CAN YOU DO TO LOWER YOUR RISK OF DEVELOPING TYPE 2 DIABETES?

You can't do anything about your age or your genetic predisposition. On the other hand, the rest of the factors predisposing to diabetes, such as overweightness, abdominal obesity, sedentary lifestyle, eating habits and smoking, are up to you. Your lifestyle choices can completely prevent type 2 diabetes or at least delay its onset until a much greater age.

If there is diabetes in your family, you should be careful not to put on weight over the years. Growth of the waistline, in particular, increases the risk of diabetes, whereas regular moderate physical activity will lower the risk. You should also pay attention to your diet: take care to eat plenty of fibre-rich cereal products and vegetables every day. Omit excess hard fats from your diet and favour soft vegetable fats.

Early stages of type 2 diabetes seldom cause any symptoms. If you scored 12–14 points in the Risk Test, you would be well advised to seriously consider your physical activity and eating habits and pay attention to your weight, to prevent yourself from developing diabetes. Please contact a public-health nurse or your own doctor for further guidance and tests.

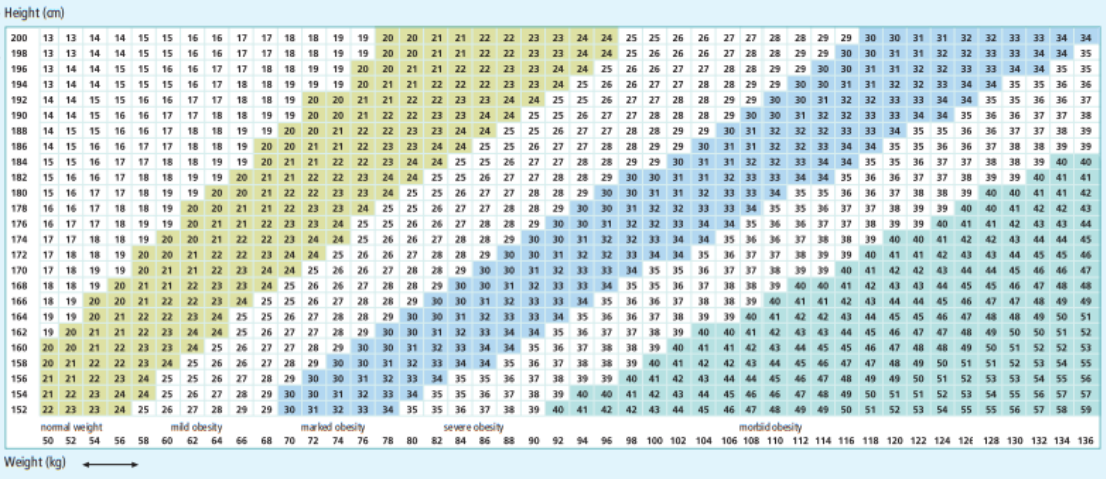
If you scored 15 points or more in the Risk Test, you should have your blood glucose measured (both fasting value and value after a dose of glucose or a meal) to determine if you have diabetes without symptoms.

BODY-MASS INDEX

The body-mass index is used to assess whether a person is normal weight or not. The index is calculated by dividing body weight (kg) by the square of body height (m). For example, if your height is 165 cm and your weight 70 kg, your body-mass index will be 70/(1.65 x 1.65), or 25.7.

If your body-mass index is 25–30, you will benefit from losing weight; at least you should take care that your weight doesn't increase beyond this. If your body-mass index is higher than 30, the adverse health effects of obesity will start to show, and it will be essential to lose weight.

BODY-MASS INDEX CHART



(Lindström and Tuomilehto, 2003; *Type 2 diabetes risk assessment form*, c2021)