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Postgraduate Program in Applied Nutrition and Dietetics

Discipline of **Clinical Nutrition**

«Diet and physical activity indices in relation to lipidemic profile in families at high risk for type 2 diabetes in Europe»

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Athens, 2019

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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 research programs such as the present one.

I would also like to thank *Dr. Kalliopi- Zafeirenia Karatzi* for her guidance and the time she has devoted during this process, for supporting me over the years, both undergraduate and postgraduate, for being so patient and always willing to help not only me but all of her students. I am pleased to have met her, to have been a student of her as well as worked with her during my time at the university.

I would like to thank my thesis committee members, Assistant Professor Tzortzis Nomikos and Professor Labros Sidosis for their guidance as well as their contribution during my studies.

I would especially like to thank my family for the love, support, and constant encouragement. In particular, I would like to thank my parents, *Maria* and *Theodoros* and my sister *Panagiota*. Without you being by my side all of my accomplishments would have been harder or impossible to achieve. Thank you for always being there.

Last but not least, I would like to thank my friends *Eftyhia, Anna, Jade* and *Irene* for being there over the years (no matter how far), for sharing the pressure, for always believing in me, for the times we've spent together as children, as adolescents and as adults and for the times that are about to come.

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Περίληψη

Εισαγωγή: Τα έως σήμερα διαθέσιμα δεδομένα είναι περιορισμένα όσον αφορά τις πιθανές συσχετίσεις της διατροφής και της φυσικής δραστηριότητας (ΦΔ) με το λιπιδαιμικό προφίλ σε ενήλικες υψηλού κινδύνου για ανάπτυξη Σακχαρώδους Διαβήτη Τύπου 2 (ΣΔΤ2).

Σκοπός: Σκοπός της παρούσας ερευνητικής εργασίας είναι να διερευνήσει συγχρονικά τις πιθανές συσχετίσεις ανάμεσα σε συμπεριφορές όπως η διατροφή και η ΦΔ με τα λιπίδια του αίματος [Ολική Χοληστερόλη, χοληστερόλη στις λιποπρωτεΐνες χαμηλής και υψηλής πυκνότητας (LDL-C και HDL-C), τριγλυκερίδια] σε οικογένειες υψηλού κινδύνου για ΣΔΤ2.

Μεθοδολογία: Η μελέτη Feel4Diabetes (F4D) είναι μία πολυκεντρική μελέτη παρέμβασης. Στην παρούσα ανάλυση, χρησιμοποιήθηκαν μόνο οι μετρήσεις κατά το baseline. Ο πληθυσμός της μελέτης κατά την έναρξη ήταν 2500 μη διαβητικοί ενήλικες. Οι συνήθειες διατροφής και ΦΔ ήταν αυτο-δηλούμενες σε ερωτηματολόγια και τα λιπίδια του αίματος μετρήθηκαν με τυποποιημένες μεθόδους. Για να εκτιμηθούν οι πιθανές ανεξάρτητες συσχετίσεις των παραγόντων διατροφής και ΦΔ με τα επίπεδα των λιπιδίων, πραγματοποιήθηκε πολυπαραγοντική ανάλυση γραμμικής παλινδρόμησης όλων των παραγόντων ταυτόχρονα με διόρθωση επίσης για το φύλο και το κάπνισμα τόσο σε άτομα χαμηλού, όσο και υψηλού κινδύνου σύμφωνα με το FINDRISK σκορ. Επίσης, διεξήχθη ανάλυση σε υποομάδες, κατά την οποία το δείγμα χωρίστηκε ανά περιοχή, ηλικία και κατηγορία κοινωνικοοικονομικού επιπέδου τόσο για τους χαμηλού όσο και για τους υψηλού κινδύνου για ΣΔΤ2 ενήλικες. Ο Δείκτης Μάζας Σώματος (ΔΜΣ) εισήχθη στο πολυπαραγοντικό μοντέλο προκειμένου να ανιχνευθούν εκείνοι οι παράγοντες που συσχετίζονται με τα λιπίδια του αίματος ανεξάρτητα από όλους τους παράγοντες που εξετάστηκαν καθώς και από τον ΔΜΣ.

Αποτελέσματα: Σύμφωνα με τα κύρια αποτελέσματα, στην ομάδα χαμηλού κινδύνου η υψηλή πρόσληψη φρούτων φάνηκε να έχει ευνοϊκή συσχέτιση ενώ τα οινοπνευματώδη και το κάπνισμα επιβαρυντική με το λιπιδαιμικό προφίλ. Όσον αφορά τους συμμετέχοντες υψηλού κινδύνου, η αυξημένη κατανάλωση γαλακτοκομικών προϊόντων με χαμηλή περιεκτικότητα σε λιπαρά βρέθηκε ότι έχει ευεργετική σχέση, ενώ η κατανάλωση γαλακτοκομικών με υψηλή περιεκτικότητα σε λιπαρά είχε επιβαρυντική σχέση με τα επίπεδα των λιπιδίων στο αίμα.

Συμπεράσματα: Η συγχρονική αυτή μελέτη σε άτομα υψηλού κινδύνου για ΣΔΤ2, έδειξε ότι η υψηλή κατανάλωση γαλακτοκομικών με χαμηλή περιεκτικότητα σε λιπαρά συσχετίζεται με ένα ευνοϊκότερο λιπιδαιμικό προφίλ σε σύγκριση με τα γαλακτοκομικά που είναι πλήρη σε λιπαρά τα οποία φάνηκε να έχουν επιβαρυντικό ρόλο. Στα άτομα χαμηλού κινδύνου, τα φρούτα φαίνεται να παίζουν ευεργετικό ρόλο στα λιπίδια του αίματος, ενώ τα οινοπνευματώδη ποτά δυσμενή. Τέλος, τα ευρήματά μας τονίζουν την ανάγκη για περαιτέρω διερεύνηση των πιθανών επιδράσεων των ομάδων τροφίμων και συνηθειών ΦΔ στο λιπιδαιμικό προφίλ και σε μελέτες παρέμβασης σε ενήλικες υψηλού κινδύνου για ΣΔΤ2, καθώς τα υπάρχοντα δεδομένα σε αυτήν την ομάδα ατόμων είναι ακόμη περιορισμένα.

Λέξεις- κλειδιά: λιπίδια; χοληστερόλη; δίαιτα; άσκηση; διαβήτης;

Abstract

Background: Current literature is limited regarding the possible associations of diet and PA on the lipid profile in adults at high risk of developing (Type 2 Diabetes Mellitus) T2DM.

Objectives: The purpose of the current report is to cross-sectionally investigate the possible associations of diet and PA with blood lipid levels [Total Cholesterol, Low Density Lipoprotein-Cholesterol (LDL-C), High Density Lipoprotein-Cholesterol, Triglycerides] in families at high-risk for developing T2DM in Europe.

Methods: The Feel4Diabetes (F4D) study is a multi-center, intervention study. For our analysis, only the baseline measurements were used. The study population at this initial point was 2500 non-diabetic individuals for T2DM from 6 European countries. Dietary and physical activity (PA) habits were self-reported in questionnaires and blood lipids were measured with standard procedures. To assess the possible independent associations of the dietary and PA factors with lipid levels, multivariate linear regression analysis was performed in the total sample divided in low- and high- risk categories according to the Finnish Diabetes Risk Score (FINDRISC) score, which was also adjusted for smoking and gender. A sub-group analysis was also carried out in which the sample was divided by region, by age and by SES categories for both low- and high-risk adults for T2DM. Body Mass Index (BMI) was entered in the linear multivariate model in order to detect those factors that were independently associated with blood lipids from all the factors examined and from BMI.

Results: According to the most dominant results, in the low-risk group high intake of fruits was favourably associated while spirits and smoking were negatively associated with the lipidemic profile. As for the high-risk participants, increased consumption of low-fat dairies was found to have a beneficial association [LDL-C: β = -0.18, CI=(-8.62--1.47)] while full-fat dairy a detrimental one with blood lipid levels.

Conclusion: In conclusion, this cross-sectional study in individuals at high-risk of developing T2DM demonstrates that high low-fat dairy consumption is associated with a more favourable lipidemic profile while full-fat dairy were found to have an adverse association. In low-risk individuals, fruits seem to play a promising role regarding blood lipids while spirits an unfavourable one. Our findings also highlight the need for additional investigation of the potential effects of specific food groups and PA patterns on the lipidemic profile in intervention trials, in adults at risk for T2DM, since such information in this group is still limited.

Keywords: lipids; cholesterol; diet; activity; diabetes;

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List of Abbreviations

TG	Triglycerides
ТС	Total Cholesterol
LDL-C	Low Density Lipoprotein-Cholesterol
HDL-C	High Density Lipoprotein-Cholesterol
FH	Familial Hypercholesterolemia
DM	Diabetes Mellitus
HIV	Human Immunodeficiency Virus
PCOS	Polycystic Ovary Syndrome
SFA	Saturated Fatty Acids
CVD	Cardiovascular Disease
T2DM	Type 2 Diabetes Mellitus
IR	Insulin Resistance
SES	Socioeconomic Status
DD	Diabetic Dyslipidemia
VLDL	Very Low Density Lipoprotein-Cholesterol
HL	Hepatic Lipase
RCT	Randomized Clinical Trial
MA	Meta- Analysis
F	Fruits
V	Vegetables
FU	Follow-Up
PA	Physical Activity
TV	Television
WC	Waist Circumference
MVPA	Moderate to Vigorous Physical Activity
ST	Sedentary Time
SR	Systematic Review
IGT	Impaired Glucose Tolerance
IFG	Impaired Fasting Glucose
SSP	Sugar Sweetened Products
F4D	Feel 4 Diabetes
FINDRISC	Finnish Diabetes Risk Score
BMI	Body Mass Index
WHO	World Health Organization
BP	Blood Pressure
VPA	Vigorous Physical Activity
FFQ	Food-Frequency Questionnaire

1. Introduction

1.1. Dyslipidemia

Cholesterol and triglycerides (TG) are the main lipids of the human body with numerous physiological functions. [1] TG mainly provide energy for the muscles and other organs, while the energy surplus is stored as TG within the adipocytes. Furthermore, TG insulate the skin and protect the surroundings of the organs. On the other hand, cholesterol is the precursor for important steroid molecules such as bile acids, steroid hormones and the active form of vitamin D. Last but not least, cholesterol plays a major role in the production of the cell membranes. [2]

Dyslipidemias are disorders in the lipid metabolism including increased levels of Total Cholesterol (TC) combined with increased Low Density Lipoprotein-Cholesterol (LDL-C) and/or TG and/or low High Density Lipoprotein-Cholesterol (HDL-C). [3, 4]

Dyslipidemias are divided in two categories (a) primary and (b) secondary dyslipidemias. The primary lipid disorders such as chylomicronemia, familial hypercholesterolemia (FH), mixed hyperlipidemia, familial hypertriglyceridemia and familial reduction in HDL-C levels have a genetic background. Whereas, the secondary lipid disorders are the result of other diseases or metabolic disorders such as uncontrolled diabetes mellitus (DM), hypothyroidism, renal disease, obesity, human immunodeficiency virus (HIV) infection, polycystic ovary syndrome (PCOS), or present due to drugs used (e.g. anabolic steroids, corticosteroids, beta blockers, retinoids, oestrogens). [1, 5] The dietary risk factors for developing secondary dyslipidemia include among others increased consumption of saturated (SFA) and trans fatty acids, excess calories and heavy alcohol consumption. Last but not least, sedentary lifestyle and smoking play a pivotal role in the development of dyslipidemia. [5, 6]

Screening for dyslipidemias, which is routinely done with a blood analysis test, should be considered in the following high-risk groups: men over 40 years of age and women who are either over 50 years old or postmenopausal, patients with chronic kidney disease, DM, organ damage, chronic inflammatory disease, severe hypertension, history of FH and/or Cardiovascular Disease (CVD) as well as obese and smokers. [7]

In Greece, the ATTICA study (2002-2012) showed that almost 40% of the study population had TC levels higher than 200 mg/dL. [8] In "the HYDRIA study" (2013-2014), the total prevalence of hypercholesterolemia in Greece, this time defined as TC>240 mg/dL, was 13,4% and it was almost the same for men (13,9%) and women (13%). [9] In 2015, a European study, showed

that about 67% of the Greeks had low HDL-C levels, which was more prevalent in women. The study also showed that 56% of the Greeks had high TG levels which was more commonly observed in men (61%) compared to women (50%). [10]

Dyslipidemia is a risk factor for CVD. More specifically, it increases the risk of coronary artery disease and coronary heart disease, atherosclerosis and atherosclerotic CVD as well as ischemic stroke. Individuals with dyslipidemia are therefore at increased risk of cardiovascular morbidity and mortality [3, 11, 12].

1.2. Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is a chronic disease characterized by hyperglycaemia, caused by the lack of insulin excretion or the body's inability to respond to insulin properly, which is a condition known as Insulin Resistance (IR). [13]

T2DM, has many clinical manifestations such as excessive thirst and dry mouth, frequent and abundant urination, lack of energy or extreme tiredness, tingling or numbness in hands and feet, repetitive fungal infections in the skin, slow wound healing and blurred vision, which are the result of uncontrolled hyperglycaemia. [13]

The progression of T2DM is frequently slow and as a result diabetic individuals can be asymptomatic for many years. If T2DM is left undiagnosed and uncontrolled, it can lead to serious clinical complications due to the chronic hyperglycaemia. These complications include macrovascular and microvascular complications, CVD, periodontitis, diabetic retinopathy, diabetic nephropathy, neuropathy and diabetic foot. [13]

According to the International Diabetes Federation Atlas, the prevalence of T2DM in Greece in 2017 and 2000 was 7,2% and 5,9% respectively. [13, 14] The European prevalence of T2DM in 2017 was 8,8% with 37,9% of them being undiagnosed. In 2045 it is estimated that the European prevalence of T2DM will increase up to 10,2%.[13] As for the worldwide prevalence of T2DM it raised from 3,6% to 8,8% in men and from 4,7% to 8,2% in women from 1980 to 2014. [15] It is noteworthy, that almost 80% of people with T2DM live in middle- and low-income countries. [16]

People with certain characteristics are more likely to develop T2DM and in these groups prevention is a key strategy to avoid early progression of the disease. More specifically, these characteristics include overweight and obesity, age 45 or older, family history of diabetes, high blood pressure, low HDL-C and high TG, history of gestational diabetes, physical inactivity,

depression, PCOS or IR. [17, 18] Other conditions that have been associated to increased risk of T2DM are smoking, short sleep duration and poor quality, low socioeconomic status (SES) and diet [19].

1.3. Pathophysiology of diabetic dyslipidemia

As aforementioned, T2DM is a risk factor for developing macrovascular complications; the major contributor to this relationship is diabetic dyslipidemia (DD) affecting 72-85% of the diabetics. [16, 20] It is worth to mention that dyslipidemia, may be present even before the onset of T2DM, under the IR state, expressed as either increased accumulation of TG rich lipoproteins [chylomicrons and Very Low Density Lipoproteins (VLDL)], or small dense LDL particles (which are more prone to oxidation) and/or reduced plasma HDL-C (which has atheroprotective, anti-inflammatory, anti-oxidative, anti-thrombotic and anti-apoptotic properties). [20]

Insulin, as an anabolic hormone, performs many physiological actions in lipid metabolism which are all disturbed during hyperinsulinemia, IR or β -cell failure all related to DD. [20]

More specifically, qualitative, quantitative and kinetic abnormalities have been observed in lipid metabolism in patients with T2DM. Raised TG as well as low HDL-C levels are the most common quantitative lipid aberrations. Regarding qualitative changes, there is an increase in VLDL1 (which is larger and less dense compared to the VLDL2 subfraction and preferentially taken up by the macrophages), in small dense, glycated and oxidised LDL-C, in the TG content of both LDL-C and HDL promoting the hepatic lipase (HL) activity and in the glycation of apolipoproteins. Regarding kinetic abnormalities, there is a rise in VLDL production (mainly VLDL1), reduced VLDL and chylomicron catabolism due to diminished lipoprotein lipase activity and increased HDL catabolism either due to low adiponectin levels or to increased HL activity. All of the above mentioned alterations contribute to the development of atherosclerosis in T2DM. [16, 20]

1.4. Diet and dyslipidemia

Diet plays an important role in the development of dyslipidemias. According to research, whole grains seem to positively affect blood lipids. For instance, in a Randomized Clinical Trial (RCT) in 46 healthy adults, the consumption of whole grain products resulted to a significant reduction in TC and LDL-C, which was mainly attributed to the fibre content, with no significant change in HDL-C or TG. [21] Similarly, oats is also a fiber rich food. A Meta- Analysis (MA) of 58 RCTs (N=3974), showed that β -glycans from oats lead to a dose dependent decrease in LDL-C. [22]

Evidence for the effects of increased fruits (F) and vegetables (V) intake on blood lipids is limited to date with most of the findings showing a neutral effect. In a RCT in 2002, 690 healthy adults were encouraged for 6 months to increase the consumption of F and V to at least 5 portions daily. The F and V consumption did increase, however, TC levels remained unchanged. [23] In another RCT conducted in 87 healthy adults, the intervention group increased F and V intake to 8 servings per day for 8 weeks. This led to no change in blood lipids compared to the control group. [24] Another MA of 19 trials (N=618) suggested that F juice consumption had no effect on TC, HDL-C, LDL-C concentrations. [25]

Interestingly here has been a controversy regarding dairy consumption and blood lipids due to their SFA content. In 2013, a MA of 20 RCTs in healthy adults (N=1677), with a median duration of 26 weeks and a mean increase in dairy food intake of 3,6 servings/day showed that there was no change in LDL-C and HDL-C with low versus whole fat dairy consumption. The results were similar for overweight and obese individuals. [26] A RCT in 15 healthy men, showed that independent of the fat content of the diet (high vs. low fat) a high calcium diet decreased TC by 4% and LDL-C by 10% but had no effect on HDL-C compared with the low calcium one, suggesting that milk minerals may mediate this effect. [27] A MA of 5 RCTs tested the effects of butter and hard cheese with equal polyunsaturated to SFA ratio on blood lipids. Cheese compared with butter was found to reduce LDL-C and HDL-C and to have no effect on TG levels. [28] As a result, dairy product consumption seems to not have a detrimental effect on the lipid profile of healthy adults.

Regarding protein rich food groups, a MA of RCTs in adults, showed that consumption of ≥ 0.5 servings compared with <0.5 servings of total red meat per day does not influence blood lipid levels with 2 to 32 weeks duration. [29] This result is of great interest due to the high SFA content of red meat; however it could be explained by the different fat content of the various meat types. According to the current literature, fish consumption seems to positively affect the lipid profile. More specifically, according to a MA of 14 interventions in adults (N=1378) moderate (20-150 g/day) oily fish consumption was associated with significant reductions in TG and increases in HDL-C. No significant effect was observed in TC or LDL-C levels both after short term and long term consumption. [30] Noteworthy, another RCT with 38 young, healthy, normal-weight volunteers who consumed 750 g/week of lean or fatty fish or lean meat (control) for 4 weeks at dinner, showed that high intake of fatty but not lean fish, significantly reduced fasting TG and increased HDL-C when compared with control. [31]

Eggs, due to their high cholesterol content are also under debate regarding their effects on blood lipids. A MA of 27 RCTs, showed that frequent egg consumption (varying from 1 to 6 whole eggs/ day) for 15 to 365 days, increases TC, LDL-C and HDL-C with no effect on TG. [32] In a subsequent intervention study, in 37 healthy adults, the intake of 1 compared to 0 eggs/day resulted in a 10,9% reduction in plasma LDL-C and compared to 3 eggs/day it led to an increase in LDL-C levels. HDL-C increased by 4,4% with intake of 1 egg/day and remained elevated after consumption of 2 and 3 eggs/ day. TG and TC levels remained unchanged. [33]

Dietary non-oil seed pulses (beans, chickpeas, lentils and peas) is another food group which has been associated with lower cholesterol levels. For example, a recent MA of 26 RCTs (N=1037) which included both hyperlipidemic and normolipidemic subjects, showed that a median of 130 g pulses/day modestly reduces LDL-C by 5%. [34] In a subsequent intervention study 14 overweight and obese adults consumed 5 cups of canned navy beans per week for 4 weeks. According to the results, LDL-C and TC were decreased in men by 18% and 11,5% respectively while in women no change was observed. [35]

Nuts is lipid rich food group which is extensively studied regarding its beneficial effects on CVD risk and blood lipids. A MA of 61 interventions (N= 2582) with 3 to 26 weeks duration, showed that nut consumption (median 56 g/day) reduced TC, LDL-C and TG regardless of the nut type or the background diets. A stronger association between TC and LDL-C reduction was seen at \geq 60 g/day of nuts. [36]

In a cross-sectional study in healthy adults in which 5 major dietary patterns were identified, it was observed that the higher scores of the "junk food" pattern were significantly associated with raised TG levels [37] and this is in accordance with the results of a prospective study in India which showed that fast food consumption led to increased TG levels as well as to a higher TG/HDL-C ratio after 3 years of Follow-Up (FU). [38] Once again, junk food is associated with detrimental effects on the lipid profile even of healthy subjects.

In a network MA of 66 intervention trials the effects of specific food groups on the lipid profile where examined. Regarding LDL-C reduction, nuts were proven to be the most effective followed by legumes and whole grains. As for TG levels, fish had the strongest negative association followed by nuts and red meat. In addition, nuts were found to be the most promising food item for TC reduction and for HDL-C levels fish consumption had the strongest

positive association compared with the rest of the food groups. Red meat and eggs presented the weakest associations with LDL-C and TG respectively. [39]

Beverages have also been examined regarding their effects on the lipid profile. In a recent MA of 31 RCTs (N=1267) on healthy adults it was shown that moderate (up to 15 g alcohol/ day for women and 30 g alcohol/ day for men) alcohol consumption leads to lower LDL-C as well as to higher HDL-C and to no change in TC or TG. [40] Tea, according to studies, has a positive effect on some lipid profile parameters. Black tea consumption, ranging from 600 to 1800 ml/day for 4 weeks to 12 months, has been tested in a MA of 10 RCTs, and led to a significant reduction in LDL-C with no effect on TC or HDL-C in healthy individuals with a stronger effect on individuals with cardiovascular risk factors. [41] Another MA of 20 double-blind RCTs with a duration of at least 3 months on green tea extract (250-2304 mg/day) or catechins (398-1207 mg/day) consumption showed a reduction both in LDL-C (with higher effect in normolipidemics) and in TC (with higher effect in dyslipidemics). No effect was observed on TG or HDL-C. [42] Last but not least, a MA of 12 RCTs in adults showed that consumption of 2,4-8 cups of coffee per day, for 45 days on average, leads to increased TC, TG and LDL-C with a positive dose- response effect with the hyperlipidemics being more sensitive to the lipid -raising effect of coffee. [43] Nonetheless, available data is of low quality regarding the effect of coffee on blood lipids primarily due to the different coffee preparations and varieties.

Different types of oils can have different effects on the lipid profile due to the various types of fatty acids that they contain. Specifically, in a trial with 91 healthy adults with a mean age of 60 years, daily consumption of 50 g of extra virgin coconut oil, butter or extra virgin olive oil for 4 weeks resulted in increased levels of LDL-C after butter consumption compared with coconut and olive oil in which LDL-C was not significantly different. Coconut oil significantly increased HDL-C compared with butter and olive oil. [44]

1.5. Physical activity and dyslipidemia

Physical activity (PA) is defined as any body movement produced by skeletal muscles that results in energy expenditure. [45] PA helps to improve the lipid profile of individuals and plays a key role in the management of dyslipidemias. This was shown in a MA of 25 RCTs in apparently healthy individuals who exercised. Subjects who had medical issues in which treatments such as medication or special dietary interventions influence the effect of exercise where excluded. The effect of exercise itself was positive since HDL-C increased by 2,53 g/dL at 64,8% maximal aerobic capacity. [46] In another MA, aerobic exercise was shown to

significantly decrease TG levels in overweight and obese adults but no change was observed in HDL-C and LDL-C values. [47]

In Australia, 2.761 women and 2.103 men aged \geq 30 years self-reported their total sitting time and total television (TV) watching time. For both sexes, sitting time was harmfully associated with fasting TG and HDL-C. In addition, TV watching was positively associated with increased LDL-C, TC and TG in both men and women. In women sitting time was also associated with lower HDL-C levels. After adjustment for waist circumference (WC) the associations regarding TV watching and blood lipids lost their significance. [48] Another cross-sectional study, in 445 healthy adults with a mean age of 66 years, assessed the effects of sedentary activities substitution with light activity or Moderate to Vigorous Physical Activity (MVPA). The results showed that substitution of Sedentary Time (ST) with equal time spent on MVPA is associated with improved blood lipid levels. [49]

In a RCT, 24 sedentary overweight or obese volunteers with a mean age of 64 years wore an accelerometer to monitor their PA levels. The intervention was divided in two phases; the "Sit" period during which walking and standing were restricted to $\leq 1h/day$ and the "Sitless" one during which at least 7h/day where substituted with ≥ 4 hours of self-perceived light walking and ≥ 3 hours of standing. After the "Sitless" phase, TG decreased by 32% and HDL-C increased by 7%. [50] In a Systematic Review (SR), it was found that there is no significant association between the use of pedometer to monitor PA levels in relation to the lipid profile. [51] According to a SR, TC and LDL-C do not seem to be associated with total ST in cross- sectional studies and there are no available prospective studies. Findings on HDL-C and ST are inconclusive. Cross- sectional and prospective studies report either a null or a negative association. TG in general seem to be positively associated with ST in both cross-sectional and prospective studies. [52] In an intervention study, 36 community-dwelling physically active older people took part in a 59-week program aiming to increase the amount of walking measured by electronic pedometers. HDL-C significantly improved but no effect was found on the other blood lipids. [53]

1.6. Diet and dyslipidemia in individuals at risk for T2DM

As aforementioned, DD is a quite frequent comorbidity of T2DM. Therefore, the effect of diet on the lipid profile of this group of patients is of great interest. However, very few studies regarding the effect of specific food groups on the lipid profile in people at risk for T2DM are available. People considered to be at risk for T2DM are primarily those with Impaired Glucose

Tolerance (IGT), Impaired Fasting Glucose (IFG) or IR. Also, patient characteristics such as overweight and obesity, age 45 or older, family history of diabetes, hypertension, low HDL-C and high TG, history of gestational increase risk of developing T2DM. Many of these characteristics are components of the metabolic syndrome. [17, 18]

In a RCT in pre-diabetics, the intervention group consumed a diet consisting of 20% of the energy as almonds which led in significant declines only in LDL-C levels but not in TC, HDL-C or TG. [54] In a cross-over trial in adults with pre-diabetes a pistachio diet (57 g/day) compared to the placebo had no effect on blood lipids. [55] In an intervention study in 47 individuals, with IGT or IFG, a high low-fat dairy diet (4-6 servings/day) and a high red meat diet (200 g/day) were followed for 4 weeks (6 d/week) and led to no difference in TC, HDL-C, LDL-C and TG between both diets and control. [56] In a cross-over intervention trial in adults at risk of developing T2DM, participants consumed either dairy products or Sugar Sweetened Products (SSP). HDL-C declined by 4,2% with the SSP, compared with both the control and the dairy diet and remained unchanged during dairy consumption. LDL-C, TC and TG did not significantly change compared to baseline in none of the groups. [57] Furthermore, in a cross-over trial, in adults with family history of diabetes (N=26) it was shown that consumption of 4 servings of legumes per week for 6 weeks has no effect on blood lipids. [58] Last but not least, results from RCTs suggest that consumption of 6 to 12 eggs per week, in the context of a diet that promotes cardiovascular health, has no adverse effect on TC, LDL-C or TG in individuals at risk for developing diabetes or with T2DM while HDL-C levels seem to increase in the majority of the studies. [59]

1.7. Physical Activity and dyslipidemia in individuals at risk for T2DM

Research regarding PA and its effects on the lipid profile in individuals at risk for T2DM is still limited. According to the available data, in a SR of 14 studies, diet combined with PA in adults at risk for T2DM led to improved TC, LDL-C, HDL-C and TG levels. [60] PA alone was examined in a cross-sectional study, in 2326 adults with IGT or IFG, where MVPA, ST and total PA were objectively measured with a waist accelerometer. The results showed a negative association between MVPA and TG, while ST was positively associated with TG levels. Total PA was also positively associated with HDL-C and negatively associated with TG levels. Associations reported between total PA and blood lipids were comparable or even stronger than MVPA which may suggest that total PA is as important as MVPA in terms of blood lipid level regulation. [61]

1.8. Aim of the study

Current literature is limited regarding the possible associations of diet and PA on the lipid profile in adults at high risk of developing T2DM. Therefore the purpose of the current report is to cross-sectionally investigate the possible associations of diet and PA with blood lipid levels in families at high risk for developing T2DM in Europe.

2. Methodology

2.1. Ethical approvals and consent forms

The Feel4Diabetes (F4D) study complied with the Declaration of Helsinki as well as the conventions of the European Council on human rights and biomedicine. All countries, before the onset of the intervention obtained ethical clearance from the ethical committees and local authorities. In Greece the intervention was approved by the Bioethics Committee of Harokopio University as well as the Greek Ministry of Education. All parents provided signed consent forms before enrolment to the study.

2.2. Recruitment of the study participants

The study population consisted of "vulnerable groups" and was selected from low- or middleincome countries such as Bulgaria (Varna and Sofia) and Hungary (Debrecen), from low SES individuals in high- income countries such as Belgium (Oost-Vlaanderen and West-Vlaanderen) and Finland (Satakunta) or from countries such as Greece (Attica) and Spain (Zaragoza) which are subjected to austerity measures. The areas in Bulgaria and Hungary were considered as "vulnerable" in total, while in the other countries the areas were divided in tertiles according to SES indices retrieved from official resources and authorities. The "vulnerable" groups in the rest of the countries were randomly selected from the tertile with the lowest educational levels or the highest unemployment rate. In Finland, the areas were divided based on the SES index and the "vulnerable" ones were these at the lowest mean.

After taking all the official approvals from the local authorities, a list of all the primary schools within the "vulnerable" areas was provided and schools were randomly chosen from the list. Children in the first three grades of compulsory education were selected and recruited together with their families ("all-families"). Of these families the "high-risk families" were identified with the Finnish Diabetes Risk Score (FINDRISC). To be allocated in this group, at least one parent had to fulfil the country- specific cut- off point.

2.3. FINDRISC

The FINDRISC tool was completed by the children's parents (biological or foster) and contains 9 questions regarding the age, body weight, height, WC, the participation in at least 30 min/ day of PA, the daily consumption of F and V, history of anti-hypertensive medication or of increased glucose values and family history of T2DM. 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. [62]

2.4. F4D study protocol

The F4D intervention was implemented in 2016 until 1018 and is consisted of two parts. The "all families" part and the "high-risk for T2DM families" part. From the 236 primary schools, 30309 families were recruited in total. From these families, 20442 were screened and 12193 "all-families" and 2230 "high-risk-families" were measured at baseline. In May and June of 2016 the baseline measurements and procedures took place, during the academic years 2016-2017 and 2017-2018 the intervention was implemented and the 1st and 2nd FU were in May until June of 2017 and 2018 respectively.

• All- families

This component was delivered at schools by the teachers and at the local municipalities. The main goals were to increase water consumption (against sugary drinks); increase F and V consumption; consumption of a healthy and balanced breakfast and/or morning snack; increase PA; and decrease the prolonged sitting time. All teachers were trained in one session in the beginning of every school year, during which the material of the intervention and all the details on the implementation were presented. For the teachers who were not able to attend the training, extra training sessions were arranged. The control schools had no access to this information and material and they were asked to continue with their standard educational program. Trained teachers' objective was to create a more supportive social and physical environment, promoting a healthy and active lifestyle for children during the school hours by providing opportunities and by being the children's role models. At local municipality level, available infrastructure and human resources to support the lifestyle and behavioural changes of the families were identified and promoted.

• High-risk families

Trained health professionals were responsible for the implementation of this extra project, aiming to motivate "high-risk families" to participate in a more healthy and active lifestyle. The

adults of the high-risk families were invited to a local community centre within each municipality in order to be more extensively assessed. The intervention consisted of 7 counselling sessions regarding the participants' lifestyle and took place during the academic year 2016-2017. The first 6 sessions were completed until May 2017 while the 7th one was completed in September 2017 when the results of the 1st FU and the medical check-up were presented and the goals for the 2nd year of the intervention were set. These sessions included behavioural techniques to increase motivation, self-efficacy and self-regulation of this group as well as to set SMART goals (Specific, Measurable, Achievable, Relevant, Timely) in order to achieve the lifestyle recommendations. In each session, specific material and activities were provided either during the session or at home. The control group only received general advice on a healthy and active lifestyle during a 1-hour session. During the 2nd year of the implementation, volunteers received SMS-based feedback and guidance, sent during the academic year 2017-2018.

2.5. Measurements

The measurements were conducted in all of the individuals except of specific cases that are reported in detail below. In any case the reason why the measurement was not performed was reported. All measurements took place in a private area, so that the rest of the subjects could not see the value of height of the volunteer being measured.

2.5.1. Anthropometric measurements

The anthropometric characteristics that where collected from the participants were the following: height (in cm), body weight (in kg) as well as WC (in cm). The researcher ensured a private area to perform the measurements.

Height

The measurement was taken twice by the same researcher at baseline. A third measurement was conducted if the previous ones differed for more than 1 cm. The equipment was portable and included telescopic stadiometers of SECA 213, SECA 214, SECA 217 and SECA 225 types.

<u>Procedure</u>: The stadiometer was positioned on hard floor attached vertically to the wall. The volunteer was asked to remove his/ her shoes and any other outer garments or hair accessories. The participant was asked to stand in a natural straight standing position with his/her back attached to the vertical height rule, the legs slightly apart and the arms hanging loosely, palms facing at the sides of his/her body. The volunteer was asked to look straight and stay still while taking a deep breath. The measurement is taken at the end of the deep breath and was recorded to the nearest tenth of a centimeter (i.e. 0,1 cm). Volunteers who had

difficulties in standing straight, who were immobile or in a wheelchair, their hairstyle or accessories prevented the proper measurement, were taller than the maximum height of the stadiometer, pregnant or refused to perform the measurement were not measured.

Body weight

Weight was measured with an accredited electronic scale with EC type-examination certificate for medical use. Each measurement was done twice by the same researcher at each time point (baseline, 1st FU and 2nd FU) who ideally should be the same researcher in all time points. A third measurement was conducted if the first two differ for more than 100g. The equipment was portable and included electronic weight scales of SECA 813 and SECA 877 type. Each scale has a maximum capacity of 200 kg.

<u>Procedure:</u> The scale was placed on the floor or on a firm and flat surface. A carpenter's level should be used to verify that the scale is horizontal. Each scale was frequently calibrated. For the classification of the volunteers according to their body weight, the Body Mass Index (BMI) cut off points were used. A BMI of <18,5 kg/m² is classified as underweight, 18,5-24,9 kg/m² as normal weight, 25-29,9 kg/m² as overweight, 30-34,9 kg/m² as type 1 obesity, 35-39,9 kg/m² type 2 obesity and \geq 40 kg/m² as type 3 obesity. [63] The researcher asked the participants to remove his/her footwear and any other heavy clothes and/ or accessories or other objects (e.g. belt, coins, keys). The volunteer was asked to step onto scale with one foot on each side of the scale with their weight equally distributed to both of the legs, facing forward, standing still with the arms on the side and wait until he is asked to step off. The value was recorded to the nearest 0,1 kg by the investigator. Body weight was not measured if the volunteer was immobile or in a wheelchair, was heavier than the maximum weight of the scale, was pregnant or refused to perform the measurement.

Waist Circumference

Two measurements of the WC were conducted, in each session for each volunteer by the same researcher according to the steps below. A third measurement was taken in case the two first differed by >1 cm. For the classification of the volunteers based on their WC as high-risk or very-high-risk for metabolic disturbances, the World Health Organization (WHO) cut- off points were used. [63] The type of the measuring tape that was used was SECA 201.

<u>Procedure</u>: Volunteers were asked to stand upright with their feet about 25-30 cm apart, their weight equally balanced on both legs and hands hanging loosely beside the body. They were asked to reveal their waist and loosen their belt, lower their bottom wear and lift their blouse.

The measurement was taken preferably on bare skin at the end of a normal exhalation, at the midpoint of the lower rib and the top- front of the iliac crest (the spot was marked with a fine pen by the researcher). The tape had to be horizontal across the back and front of the participant. The researcher recorded to the nearest tenth of centimetre (i.e. 0,1 cm). 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.

2.5.2. Physical Activity

PA was measured with electronic pedometers or accelerometers as steps per day in the "highrisk 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.

<u>Procedure:</u> Before the PA-monitors were handed out, they were reset and checked for proper fit and function. Regarding accelerometers, the 15-second epoch length was selected. The device was fastened on the waistband of each participant's belt or bottom wear on the right hip in alignment with the midpoint of their right knee. The PA-monitor had to be attached immediately when the participant got up. An activity diary was handed over to the parents. In case the device needed to be taken off, the reason and time of removal were recorded in the activity diary. PA levels were not measured in volunteers who had any kinetic difficulty (e.g. arm or leg break).

As aforementioned, PA levels were measured only at high-risk families. However, both in the "high-risk" and "all families" groups, PA levels were assessed with a second questionnaire. The questions referred to the week before the completion of the questionnaire and had to do with the frequency, the intensity and the type of PA. It included also questions regarding sedentary activity patterns.

2.5.3. Blood Pressure (BP) measurement

BP was measured by the same investigator in all the participants. Each measurement was repeated three times at the same session, with one minute interval between two consecutive measurements. Both systolic and diastolic pressure were recorded in every BP estimation. Digital automatic BP monitors were used of the Omron M6 AC and Omron M6 type. The

European Society of Cardiology and the European Society of Hypertension (ESC/ESH, 2013) cutoff points were used for the classification of the volunteers based on their BP. [64]

<u>Procedure:</u> The volunteer should abstain from food, beverages (except water), smoking and intense PA for at least 1 hour before the measurement. On arrival, the participant was asked to sit still for 5 minutes, during which the procedure was explained, emphasizing that they should not move or talk during or between the measurements. The right cuff size was selected, after having measured the arm circumference of the participant. The cuff was placed on the right arm on bare skin. The participant was not told his/her BP at that point. Two more measurements were taken.

2.5.4. Blood Test

Blood samples were taken, by qualified staff, in the morning at 08:30 until 10:30. The subjects had fasted overnight (12 hour) as the protocol of the examination requires.

<u>Procedure</u>: The researcher collected up to 16 mL of blood from the participant. Some of the blood collected was left for 30-120 minutes without using an anticoagulant in order to separate the serum. After the blood clotted it was centrifuged at 3000 rpm for 10 minutes until the serum was divided into separate fractions and then stored at -80 °C. All participants' serum samples were stored at -80°C at the Nutrition and Clinical Dietetics Laboratory of Harokopio University of Athens.

TC, HDL-C, LDL-C and TG levels were measured with enzymatic colorimetric test (Roche Diagnostics SA, Vasilia, Switzerland) with an automatic analyser (Roche/Hitachi Modular). The National Cholesterol Education Program (NCEP) was used in order to detect any dyslipidemia cases. [5] Glucose levels were measured by an enzymatic endpoint method (Hexokinase/ enzymatic reaction GOD-PAP). Pre-diabetes, diabetes or dysglycemia cases were defined based on the WHO cut-off points. [65]

2.6. Demographic characteristics and dietary habits

Information regarding basic demographic characteristics and SES (birth record, race, marital status, smoking, sleep hours, awareness regarding existence of T2DM, medication prescribed by the doctor for T2DM, cholesterol and BP) was collected using questionnaires in all study participants. In addition, in the same questionnaire, dietary habits were recorded such as meal and snack frequency, breakfast patterns and food type consumed (F, V, breakfast cereal, bread, dairy, meat, sweet or salty snacks, eggs, water, soft drinks and juice, coffee and tea). In addition, participants were asked regarding the frequency of consumption of meals with family or friends, the quantity, quality and frequency of consumption of particular food groups (dairy,

bread, fats and oils, F, V, pulses, red and/ or processed meat, white meat, fish and seafood, salty snacks and/or snacks outside the house, pastries and pastries, nuts/seeds, water, tea and coffee, soft drinks with or without sugar, juice with or without sugar and alcoholic beverages). Last but not least, volunteers were asked for their opinion regarding their current body weight as well as the minimum amount of F and V that adults should consume during the day.

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 the statistical significance level was set at $p \le 0.05$. The categorical variables are presented as relative frequencies (%), while the continuous variables as mean \pm standard deviation (SD). The normality of distribution of variables was determined by the Kolmogorov – Smirnov test. To assess the possible independent associations of the dietary and PA variables, smoking and gender with TC, LDL-C, HDL-C or TG levels, multivariate linear regression analysis was performed. The analysis was performed in the total sample divided according to their risk for developing T2DM as follows: low risk (FINDRISC<12) and high risk (FINDRISC>12). In addition a sub-group analysis was carried out in which the sample was divided by region (Central North Europe and Southeast Europe), by age (<45 years and ≥45years) and by SES categories (0-14 or >15 years of education) for both low- and high- risk adults for T2DM. BMI was entered in the linear multivariate model in order to detect those factors that were independently associated with TC, LDL-C, HDL-C or TG from all the factors examined and from BMI.

3. Results

3.1. Participant Characteristics

Participants were 66% female with a mean age of 41.16±5.48 years. The total sample consisted of 2500 individuals free of T2DM. 890 were identified as being at high risk of developing T2DM (FINDRISC≥12) and 1550 as low risk (FINDRISC<12). High risk adults have higher mean BMI levels (27.11±4.90 kg/m² vs. 31.03±5.38 kg/m²). In addition they were found to have higher TC, LDL-C and TG as well as lower HDL-C levels. Participants' baseline characteristics are shown in *Table 1*.

3.2. Blood lipids

In the low risk group high F consumption was associated with desirable blood lipid levels. On the contrary, increased smoking and intake of spirits were found to have a positive association with TG and LDL-C and a negative one with HDL-C levels. Similarly, in the high risk group low consumption of low fat dairies and high consumption of full fat dairies were positively associated with unfavourable blood lipid levels. All of the above findings remained statistically significant after correction for BMI. In addition, BMI was found to be positively associated with HDL-C levels both in the low-risk and in high-risk group. The results are presented in *Table 3*.

In the sub-group analysis, various statistically significant results were observed, however the ones that were most repeatedly seen will be mainly discussed in this section. In general, regarding TC and LDL-C levels in the low and in the high risk group, increased F and low fat dairy consumption were associated with a more favourable lipidemic profile. On the contrary, spirits in the low risk group and full fat dairies together with smoking in the high risk group and especially in high SES participants were positively associated with TC and LDL-C levels. Most of these associations remained significant after adjustment for BMI in the high risk group while in the low risk group except from coffee and spirits the majority of the other associations lost significance. BMI was only significant in the low- and high-risk, >45 years subgroup as well as for low-SES in the low risk group only for LDL-C. Results are presented in *Table 4* and *5*.

Only in the low risk group both before and after adjustment for BMI, beer/cider consumption and smoking were positively and negatively associated with HDL-C levels respectively. It is worth to mention that BMI was statistically significant and negatively associated in almost all of the categories in the subgroup analysis. Results are presented in detail in *Table 6*. Regarding TG levels, in the low risk group, a positive relation was observed with higher intakes of juice with sugar, spirits as well as with increased smoking. On the contrary, in the high risk group, full fat dairy and beer/cider consumption were positively associated, while Vigorous Physical Activity (VPA) had a negative association with blood TG. All of these associations remained significant after adjustment for BMI. BMI was also statistically significant in the majority of the subgroups having a positive association with TG levels. Results are presented in *Table 7*.

Variables	Total	FINDRISC<12	FINDRISC≥12
	(n=2500)	(n=1550)	(n=890)
	Mean ±SD/ %	Mean ±SD/ %	Mean ±SD/ %
Gender			
Female	66.3%	66.7%	66.9%
Male	33.7%	33.3%	33.1%
Age	41.16	40.65	42.03
(years)	(±5.48)	(±5.24)	(±5.77)
Age			
<45 years	76.1%	81.7%	66.4%
>45 years	23.9%	18.3%	33.6%
Region			
Central North Europe	28.5%	28.1%	29.2%
Southeast Europe	71.5%	71.9%	70.8%
Education			
Low-risk	40.6%	38.7%	42.5%
High-risk	59.4%	61.3%	57.5%
BMI	28.53	27.11	31.03
(kg/m ²)	(±5.44)	(±4.90)	(±5.38)
Waist Circumference (cm)	94.68	91.20	100.88
	(±14.30)	(±13.49)	(±13.62)
Total Cholesterol	194.39	192.33	198.23
(mg/dL)	(±37.65)	(±36.79)	(±38.67)
LDL-C	120.58	118.21	124.54
(mg/dL)	(±32.88)	(±32.36)	(±33.25)
HDL-C	53.12	54.56	50.94
(mg/dL)	(±13.95)	(±14.46)	(±12.70)
Triglycerides	109.17	101.71	122.82
(mg/dL)	(±85.07)	(±72.12)	(±104.39)
Glucose	5.26	5.17	5.43
(mmol/L)	(±0.78)	(±0.66)	(±0.94)
Insulin	9.95	8.77	12.20
(mU/L or μIU/mL)	(±8.99)	±6.49)	(±11.24)
Cholesterol drugs			
No	96.5%	97.6%	94.7%
Yes	3.5%	2.4%	5.3%
Systolic Blood Pressure	117.77	116.06	120.93
(mmHg)	(±16.66)	(±16.36)	(±16.98)
Diastolic Blood Pressure	78.29	77.08	80.57
(mmHg)	(±11.42)	(±11.13)	(±11.64)
Smoking status			
Never smoked	45.9%	48.2%	41.8%
Former smoker	28.3%	26.5%	31.8%
Current smoker	25.9%	25.3%	26.4%
FINDRISC score	10.27	7.98	14.23
	(±4.06)	(±2.96)	(±2.25)

Continued...

Fruits	0.52	0.53	0.50
(cups*/day)	(±0.51)	(±0.50)	(±0.52)
Vegetables	0.58	0.60	0.56
(cups*/day)	(±0.55)	(±0.56)	(±0.54)
Whole grain cereals	0.47	0.48	0.45
(30g/day)	(±0.89)	(±0.89)	(±0.85)
Non- whole grain cereals	0.16	0.16	0.15
(30g/day)	(±0.59)	(±0.54)	±0.69)
Legumes	0.28	0.29	0.28
(cups*/day)	(±0.25)	(±0.26)	(±0.24)
Red meat	73.43	70.40	78.26
(grams/day)	(±55.70)	(±50.69)	(±62.71)
White meat	55.95	54.69	59.50
(grams/day)	(±42.87)	(±41.04)	(±45.65)
Fish	33.92	33.81	35.00
(grams/day)	(±28.10)	(±27.83)	(±28.67)
Salty snacks	0.24	0.23	0.25
(portions**/day)	(±0.31)	(±0.28)	(±0.33)
Sweet snacks	0.57	0.56	0.58
(portions**/day)	(±0.73)	(±0.69)	(±0.74)
Nuts and seeds	0.31	0.32	0.28
(30g/day)	(±0.49)	(±0.52)	(±0.42)
Теа	0.35	0.35	0.34
(250mL/day)	(±0.72)	(±0.73)	(±0.68)
Coffee	1.48	1.47	1.50
(250mL/day)	(±1.29)	(±1.22)	(±1.38)
Soft drinks with sugar	0.20	0.19	0.21
(250mL/day)	(±0.48)	(±0.47)	(±0.49)
Soft drinks without sugar	0.24	0.22	0.27
(250mL/day)	(±0.59)	(±0.58)	(±0.61)
Juice without sugar	0.24	0.25	0.24
(250mL/day)	(±0.38)	(±0.36)	(±0.43)
Juice with sugar	0.10	0.09	0.10
(250mL/day)	(±0.27)	(±0.27)	(±0.26)
Beer/cider	0.26	0.25	0.26
(330mL/day)	(±0.58)	(±0.46)	(±0.52)
Wine	0.18	0.18	0.17
(125mL/day)	(±0.35)	(±0.33)	(±0.39)
Spirits	0.10	0.09	0.10
(40mL/day)	(±0.29)	(±0.25)	(±0.33)
Low fat dairy	0.82	0.79	0.90
(cups*/day)	(±1.19)	(±1,17)	(±1.25)
Full fat dairy	0.43	0.45	0.42
(cups*/day)	(±0.76)	(±0.78)	(±0.4)
Sitting	5.35	5.26	5.52
(hours/day)	(±3.35)	(±3.34)	(±3.37)
Moderate Physical Activity	40.52	40.16	39.99
(min/day)	(±62.16)	(±61.61)	(±62.32)
Vigorous Physical Activity	44.46	44.27	43.75
(min/day)	(±87.52)	(±86.31)	(±85.89)
Walking	64.96	66.22	64.68
(min/day)	(±105.91)	(±105.55)	(±109.28)
*1 cup= 240 mL **1 portion of salty			

*1 cup= 240 mL, **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, LDL-C= Low Density Lipoprotein-Cholesterol, HDL-C= High Density Lipoprotein-Cholesterol

Table 2. Associations between dietary and PA factors with blood lipids (TC, LDL-C, HDL-C, TG) in high and low risk for T2DM participants.

Variables				т	DTAL			
		Low-risk grou	וע (FINDRISC <12)			High-risk grou	up (FINDRISC ≥12)	
	Total Cholesterol (n=595) Beta Coef. (95% Cl)	LDL- Cholesterol ⁺⁺ (n=593) Beta Coef. (95% Cl)	HDL- Cholesterol ⁺⁺ (n=595) Beta Coef. (95% CI)	Triglycerides ⁺⁺ (n=595) Beta Coef. (95% Cl)	Total Cholesterol (n=275) Beta Coef. (95% Cl)	LDL- Cholesterol (n=274) Beta Coef. (95% CI)	HDL- Cholesterol ⁺⁺ (n=275) Beta Coef. (95% Cl)	Triglycerides (n=275) Beta Coef. (95% Cl)
Low fat dairy (cups*/ day)	-0.01	-0.04 (-4.65-1.77)	0.05 (-0.49-2.30)	0.02	-0.18	-0.18 ⁺	-0.09 (-2.39-0.39)	0.00 (-7.62-8.19)
	(-4.21-3.24)	. ,	. ,	(-5.81-8.30)	(-10.361.78)	(-8.621.47)		
Full fat dairy (cups*/ day)	-0.06 (-7.28-1.25)	-0.05 (-6.02-1.34)	-0.01 (-1.87-1.34)	-0.02 (-10.04-6.14)	0.14 ⁺ (0.76-16.34)	0.10 (-1.28-11.82)	-0.02 (-2.91-2.14)	0.19 ⁺ (8.39-37.10
Vegetables	-0.01	-0.01	-0.05	0.02	-0.08	-0.07	-0.09 ^c	0.08
(cups*/ day)	(-5.85-4.95)	(-4.96-4.35)	(-3.18-0.88)	(-8.02-12.45)	(-14.41-3.31)	(-11.50-3.49)	(-4.96-0.78)	(-5.91-26.75
Fruits	-0.10+	-0.11	0.02	-0.04	0.05	0.06	0.02	-0.10
(cups*/ day)	(-15.300.83)	(-14.091.62)	(-1.99-3.45)	(-19.66-7.78)	(-6.86-14.35)	(-4.87-12.89)	(-2.81-4.06)	(-34.40-4.69
Ion whole grain cereals	-0.03	-0.01	-0.07	0.00	0.01	0.02	-0.01	0.00
(30 g/ day)	(-9.45-4.74)	(-7.13-5.10)	(-4.95-0.38)	(-12.97-13.93)	(-8.33-10.31)	(-6.30-9.18)	(-3.37-2.67)	(-16.78-17.5
Whole grain cereals	-0.01	-0.02	0.05	-0.02	0.02	0.05	-0.04	0.00
(30 g/ day)	(-3.84-3.36)	(-3.77-2.44)	(-0.59-2.11)	(-8.85-4.80)	(-4.15-5.68)	(-2.53-5.65)	(-2.18-1.01)	(-8.96-9.16
Legumes	-0.04	-0.03	-0.01	0.00	-0.09	-0.12	0.02	0.00
(cups*/ day)	(-12.14-7.22)	(-15.45-6.40)	(-5.45-4.08)	(-22.98-25.10)	(-33.48-5.65)	(-31.58-0.93)	(-5.31-7.37)	(-37.13-34.9
Red meat	0.02	0.00	-0.02	0.07	0.03	0.02	-0.02	-0.01
(grams/day)	(-0.05-0.09)	(-0.06-0.06)	(-0.03-0.02)	(-0.03-0.24)	(-0.07-0.11)	(-0.06-0.09)	(-0.03-0.03)	(-0.17-0.16)
White meat	0.00	0.03	-0.08	0.08	0.03	0.06	0.09	-0.10+
(grams/day)	(-0.10-0.10)	(-0.05-0.11)	(-0.07-0.00)	(-0.01-0.36)	(-0.11-0.16)	(-0.06-0.16)	(-0.02-0.07)	(-0.44-0.05
Fish	-0.08	-0.05	-0.04	-0.07	-0.04	-0.03	-0.09	-0.03
(grams/day)	(-0.31-0.02)	(-0.23-0.07)	(-0.09-0.03)	(-0.60-0.04)	(-0.31-0.16)	(-0.24-0.16)	(-0.13-0.02)	(-0.55-0.32)
Salty snacks	-0.01	-0.02	-0.03	0.04	-0.09	-0.08	-0.05	-0.09
(portions**/day)	(-9.39-8.33)	(-9.63-5.65)	(-4.55-2.11)	(-9.14-24.46)	(-22.23-5.79)	(-18.15-5.17)	(-6.01-3.07)	(-41.79-9.85
Sweet snacks	-0.06	-0.05	-0.03	0.00	0.13	0.14	0.10	0.07
(portions**/day)	(-7.84-7.22)	(-6.13-1.67)	(-2.23-1.17)	(-8.87-8.30)	(-0.80-15.87)	(-0.51-13.40)	(-0.88-4.52)	(-7.44-23.28
Nuts and seeds	0.01	-0.01	0.02	0.03	-0.10	-0.11	-0.04	0.04
(30 g/day)	(-4.97-5.93)	(-5.20-4.19)	(-1.61-2.48)	(-7.12-13.54)	(-14.92-1.88)	(-12.93-1.07)	(-3.60-1.84)	(-10.37-20.6
Теа	0.07	0.06	0.01	0.03	0.03	0.00	0.05	0.04
(250 mL/day)	(-1.00-8.65)	(-1.42-6.89)	(-1.62-2.00)	(-5.48-12.80)	(-5.05-8.37)	(-5.46-5.69)	(-1.19-3.15)	(-8.31-16.42
Coffee	-0.09 ⁺	-0.07	-0.07	-0.03	-0.02	-0.01	0.07	-0.12 ⁺
(250 mL/day)	(-5.310.17)	(-4.00-0.44)	(-1.85-0.09)	(-6.44-3.31)	(-4.01-3.10)	(-3.26-2.72)	(-0.51-1.79)	(-13.11- 0.00
Soft drinks with sugar	-0.04	3.57	-0.01	0.04	-0.05	-0.06	0.06	-0.02
(250 mL/day)	(-12.04-4.14)	(-9.71-4.31)	(-3.31-2.77)	(-8.14-22.54)	(-19.22-9.30)	(-17.15-6.71)	(-2.41-6.83)	(-29.84-22.7)
oft drinks without sugar	-0.06	-0.06	0.02	-0.03	0.01	-0.03	0.08	0.01
(250 mL/day)	(-9.68-1.64)	(-8.74-1.03)	(-1.57-2.69)	(-14.96-6.49)	(-6.85-7.70)	(-7.32-4.78)	(-0.84-3.88)	(-12.30-14.5
Juice without sugar	0.04	0.03	0.00	0.04	0.11	0.10	0.03	0.02
(250 mL/day)	(-4.28-14.88)	(-5.21-11.30)	(-3.55-3.65)	(-8.82-27.51)	(-1.53-29.67)	(-2.47-23.51)	(-3.68-6.43)	(-24.79-32.72
Juice with sugar	0.07	0.03	0.00	0.11	0.02	0.02	-0.05	0.09
(250 mL/day)	(-1.85-20.62)	(-6.04-13.36)	(-4.34-4.11)	(10.23-52.82)	(-16.20-22.24)	(-13.38-18.62)	(-8.81-3.64)	(-8.97-61.89

Beer cider serving	0.00	-0.04	0.13 ⁺	0.01	0.11	0.03	0.05	0.28 ⁺
(330mL/day)	(-6.72-7.27)	(-9.28-2.85)	(1.40-6.66)	(-11.11-15.40)	(-3.32-21.12)	(-8.83-13.32)	(-2.54-5.38)	(22.55-67.60)
Wine	-0.03	-0.02	0.04	-0.05	0.02	0.02	0.06	-0.06
(125 mL/day)	(-13.77-7.34)	(-11.14-7.27)	(-1.95-5.98)	(-32.10-7.92)	(-14.85-21.15)	(-13.43-17.05)	(-3.38-8.29)	(-47.54-18.82)
Spirits	0.15 ⁺	0.03	0.00	0.22 ⁺	0.01	0.02	-0.01	-0.02
(40mL/day)	(10.72-38.37)	(-9.49-19.11)	(-5.19-5.20)	(44.48-96.89)	(-13.13-14.85)	(-10.26-13.01)	(-4.84-4.23)	(-30.08-21.50)
Moderate Physical Activity	-0.03	-0.05	0.02	0.02	0.01	-0.05	0.06	0.09
(min/day)	(-0.08-0.03)	(-0.08-0.02)	(-0.02-0.03)	(-0.09-0.13)	(-0.08-0.09)	(-0.10-0.04)	(-0.01-0.04)	(-0.05-0.26)
Vigorous Physical Activity	0.02	0.02	0.09 ⁺	-0.03	-0.06	0.03	-0.02	-0.17 ⁺
(min/day)	(-0.03-0.05)	(-0.03-0.04)	(0.00-0.03)	(-0.10-0.05)	(-0.10-0.04)	(-0.05-0.07)	(-0.03-0.02)	(-0.290.04)
Walking	0.01	-0.02	0.05	0.03	0.07	0.05	0.07	0.01
(min/day)	(-0.03-0.03)	(-0.03-0.02)	(0.00-0.02)	(-0.04-0.08)	(-0.02-0.07)	(-0.02-0.06)	(-0.01-0.02)	(-0.08- 0.09)
Sitting	0.04	-0.01	0.11 ⁺	0.01	-0.03	-0.07	0.02	0.02
(hours/day)	(-0.52-1.45)	(-0.90-0.79)	(0.11-0.85)	(-1.62-2.11)	(-1.71-1.05)	(-1.75-0.55)	(-0.37-0.52)	(-2.10-2.99)
Smoking	0.07	0.09 ⁺	-0.11 ⁺	0.09 ⁺	0.10	0.13	-0.08	0.03
	(-0.54-6.87)	(0.27-6.65)	(-3.330.55)	(1.22-15.27)	(-1.14-10.42)	(0.26-9.86)	(-3.06-0.68)	(-7.66-13.64)

*1 cup= 240 mL, **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, ⁺The relationship was statistically significant after adjustment for BMI, ⁺⁺BMI was significant and positively associated after adjustment for BMI, ⁺⁺BMI was significant and negatively associated after adjustment for BMI, ⁺⁺BMI was significant and negatively associated after adjustment for BMI, Beta Coef.=

Table 3. Dietary and Physical Activity factors and TC levels in the sample examined by region, age and SES.

Variables	Total Cholesterol												
			Low-risk group	(FINDRISC <12)			High-risk group (FINDRISC ≥12)						
	Reg	Region Age		S	SES		Region		Age		ES		
	Central North Europe (n=187) Beta Coef. (95% CI)	Southeast Europe (n=408) Beta Coef. (95% CI)	<45 (n= 500) Beta Coef. (95% Cl)	>45 ⁺⁺ (n=95) Beta Coef. (95% CI)	0-14 (n=251) Beta Coef. (95% CI)	>15 (n= 344) Beta Coef. (95% Cl)	Central North Europe (n=101) Beta Coef. (95% CI)	Southeast Europe (n=174) Beta Coef. (95% CI)	<45 (n= 193) Beta Coef. (95% CI)	>45 (n=82) Beta Coef. (95% Cl)	0-14 (n=132) Beta Coef. (95% Cl)	>15 (n=143) Beta Coef. (95% CI)	
Low fat dairy (cups*/ day)	-0.04 (-6.78-3.84)	0.02 (-4.47-6.49)	-0.01 (-4.39-3.65)	-0.11 (-15.70-5.94)	-0.03 (-7.68-5.25)	0.01 (-4.32-5.49)	-0.12 (-9.11-2.66)	-0.19 (-20.81-0.11)	-0.22 ⁺ (-12.222.32)	0.00 (-11.16-10.99)	-0.17 (-12.98-1.56)	-0.26 ⁺ (-14.832.56)	
Full fat dairy (cups*/ day)	0.00 (-7.33-7.01)	-0.09 (-10.92-0.35)	-0.07 (-9.11-0.83)	-0.07 (-11.62-6.26)	-0.02 (-7.07-5.37)	-0.10 ⁺ (-11.63-0.66)	0.25 ⁺ (2.74-28.95)	0.10 (-4.57-16.81)	0.16 ⁺ (0.75-20.22)	-0.06 (-17.41-11.37)	-0.02 (-15.23-12.47)	0.28 ⁺ (5.80-27.60)	
Vegetables (cups*/ day)	0.00 (-9.70-9.51)	-0.02 (-8.38-5.38)	0.00 (-6.05-5.49)	0.05 (-13.19-19.93)	-0.07 (-12.92-4.57)	0.02 (-6.23-8.56)	-0.04 (-18.22-13.12)	-0.08 (-17.43-6.47)	-0.12 (-20.22-2.45)	-0.05 (-18.20-12.72)	-0.07 (-18.28-9.31)	-0.05 (-18.22-10.53)	
Fruits (cups*/ day)	-0.21 (-27.912.20)	-0.06 (-14.25-3.96)	-0.11 (-16.280.82)	0.02 (-23.85-26.65)	-0.05 (-15.10-7.49)	-0.12 (-20.190.26)	-0.13 (-32.58-9.52)	0.10 (-6.04-21.21)	0.00 (-12.77-12.88)	0.22 (-3.19-33.25)	-0.02 (-20.10-17.03)	0.08 (-8.08-21.68)	
Non whole grain cereals (30 g/ day)	-0.01 (-17.10-14.22)	-0.03 (-10.80-6.21)	-0.02 (-9.01-5.82)	-0.29 ⁺ (-93.5511.61)	0.03 (-8.26-13.29)	-0.07 (-16.44-3.74)	-0.05 (-30.93-18.73)	0.09 (-6.42-17.37)	-0.05 (-17.32-8.40)	0.12 (-10.78-22.92)	-0.07 (-23.59-12.26)	0.01 (-11.39-13.21)	
Whole grain cereals (30 g/ day)	0.06 (-3.50-7.97)	-0.01 (-5.64-4.29)	-0.01 (-4.65-3.86)	0.08 (-5.06-9.15)	0.06 (-3.03-7.80)	-0.04 (-6.93-3.25)	0.02 (-6.27-7.48)	0.09 (-4.62-12.73)	-0.04 (-7.47-4.12)	-0.03 (-10.56-8.57)	0.01 (-8.14-9.41)	-0.04 (-8.52-5.66)	
Legumes (cups*/ day)	0.17 (2.39-63.40)	-0.05 (-24.11-8.58)	-0.02 (-14.24-13.71)	-0.31 (-79.193.27)	-0.14 ⁺ (-40.401.10)	0.05 (-8.78-26.34)	0.03 (-90.37-120.78)	-0.13 (-41.80-6.10)	-0.07 (-38.57-14.48)	-0.22 (-56.21-6.80)	-0.09 (-40.77-16.21)	-0.22 ⁺ (-69.192.30)	
Red meat (grams/day)	0.11	0.02	0.04	-0.06	0.01	0.02	0.04	0.06	0.00	0.10	-0.12	0.21	

	(-0.04-0.21)	(-0.08-0.11)	(-0.05-0.11)	(-0.20-0.13)	(-0.11-0.12)	(-0.08-0.12)	(-0.26-0.34)	(-0.08-0.14)	(-0.11-0.12)	(-0.11-0.24)	(-0.20-0.07)	(0.02-0.31)
White meat	0.00	0.00	0.02	0.08	0.02	-0.01	0.01	0.06	0.04	0.31+	0.08	-0.03
(grams/day)	(-0.19-0.19)	(-0.13-0.12)	(-0.09-0.12)	(-0.18-0.34)	(-0.13-0.16)	(-0.15-0.13)	(-0.29-0.30)	(-0.12-0.22)	(-0.13-0.20)	(0.00-0.72)	(-0.150.31)	(-0.22-0.16)
Fish	0.01	-0.08	-0.12 ⁺	0.08	-0.02	-0.11	-0.01	-0.11	-0.02	-0.03	-0.10	0.10
(grams/day)	(-0.40-0.45)	(-0.35-0.05)	(-0.430.04)	(-0.26-0.51)	(-0.28-0.21)	(-0.49-0.01)	(-0.44-0.42)	(-0.51-0.15)	(-0.33-0.26)	(-0.47-0.38)	(-0.47-0.18)	(-0.19-0.64)
Salty snacks	-0.02	0.02	-0.04	-0.04	-0.01	-0.04	-0.09	-0.13	-0.19	-0.01	-0.11	-0.11
(portions**/ day)	(-16.01-12.83)	(-8.76-13.90)	(-18.50-6.14)	(-15.73-11.82)	(-12.25-11.34)	(-21.22-9.01)	(-60.61-32.20)	(-27.44-5.68)	(-31.780.45)	(-43.47-40.20)	(-52.49-19.33)	(-25.25-8.88)
Sweet snacks	0.04	-0.11	-0.07	-0.01	-0.04	-0.07	0.05	0.20	0.26	0.00	0.12	0.12
(portions**/ day)	(-4.48-7.11)	(-14.940.12)	(-9.15-1.16)	(-9.91-9.03)	(-9.96-5.53)	(-9.79-2.44)	(-14.91-23.00)	(-0.27-20.77)	(3.61-23.59)	(-18.02-17.66)	(-7.58-24.19)	(-4.89-17.02)
Nuts and	-0.10	0.05	0.03	-0.07	-0.06	0.04	-0.09	-0.08	-0.08	-0.29 ⁺	-0.08	-0.09
seeds (30 g/day)	(-11.73-3.22)	(-4.18-13.23)	(-4.33-7.60)	(-19.57-11.01)	(-10.51-4.88)	(-5.23-12.22)	(-29.10-12.39)	(-14.84-5.92)	(-16.85-5.09)	(-29.50-1.90)	(-15.77-7.64)	(-22.21-6.75)
Теа	0.01	0.06	0.05	0.07	0.07	0.03	0.11	-0.03	0.08	-0.10	0.06	0.01
(250 mL/day)	(-6.56-6.94)	(-3.17-11.87)	(-2.55-8.40)	(-7.63-13.75)	(-3.05-9.69)	(-5.57-10.33)	(-4.57-13.60)	(-15.68- 10.74)	(-3.49-11.99)	(-20.09-8.92)	(-7.00-13.44)	(-10.10-10.98)
Coffee	-0.22+	-0.07	-0.10 ⁺	0.14	-0.10	-0.09	-0.03	-0.04	-0.06	0.03	0.04	0.00
(250 mL/day)	(-7.500.96)	(-7.88-1.34)	(-5.870.17)	(-2.73-9.79)	(-7.00-1.32)	(-6.21-0.74)	(-5.23-4.14)	(-8.75-5.15)	(-5.62-2.40)	(-7.63-9.32)	(-4.61-6.66)	(-5.39-5.44)
Soft drinks	-0.08	-0.02	-0.06	0.02	-0.03	-0.04	-0.07	-0.07	-0.03	-0.01	0.11	-0.05
with sugar (250 mL/day)	(-17.20-5.65)	(-13.73-9.93)	(-14.69-2.72)	(-21.98-26.87)	(-16.40-11.20)	(-14.06-6.94)	(-27.77-14.34)	(-30.38- 15.24)	(-21.17-14.55)	(-30.31-29.22)	(-13.96-32.87)	(-30.17-16.51)
Soft drinks	-0.14	-0.03	-0.06	-0.18	-0.06	-0.04	0.04	-0.01	0.01	0.20	0.00	0.07
without	(-12.15-0.31)	(-18.46-10.16)	(-10.56-2.47)	(-20.43-2.41)	(-15.49-5.87)	(-9.44-4.57)	(-7.74-10.82)	(-17.78-	(-7.53-8.53)	(-5.07-35.75)	(-9.23-9.36)	(-8.55-20.73)
sugar (250 mL/day)								16.75)				
Juice	0.05	0.03	0.06	-0.22	0.03	0.06	0.21	0.06	0.14	-0.07	0.12	0.12
without	(-11.36-22.31)	(-8.85-15.60)	(-3.47-17.35)	(-51.20-0.51)	(-11.14-17.42)	(-6.41-21.05)	(-0.03-50.05)	(-14.60-	(-1.12-35.18)	(-38.18-22.37)	(-9.33-38.64)	(-6.55-38.63)
sugar (250 mL/day)								30.92)				
Juice with	0.03	0.05	0.10 ⁺	0.16	0.07	0.05	0.05	0.02	-0.01	0.02	-0.01	0.01
sugar	(1 1 0 6 22 7 1)								()			
(250 mL/day)	(-14.96-22.74)	(-7.18-22.10)	(1.32-28.25)	(-6.49-35.27)	(-11.88-32.89)	(-7.04-20.52)	(-25.09-37.20)	(-26.13- 30.78)	(-25.89-21.92)	(-31.61-37.63)	(-30.41-28.64)	(-29.11-32.51)
(250 mL/day) Beer cider	-0.06	(-7.18-22.10)		-0.13	(-11.88-32.89)	0.00	(-25.09-37.20)	30.78)	0.16	(-31.61-37.63)	(-30.41-28.64)	(-29.11-32.51)
Beer cider serving (serving of			(1.32-28.25)		· · ·			-				· · ·
Beer cider serving (serving of 330mL/day)	-0.06 (-16.24-8.02)	0.01 (-8.06-9.85)	(1.32-28.25) 0.01 (-7.28-8.23)	-0.13 (-24.28-35.67)	0.01 (-11.18-12.98)	0.00 (-8.97-8.86)	0.09 (-13.90-25.09)	30.78) 0.23 ⁺ (0.72-43.34)	0.16 (-2.10-28.78)	0.16 (-10.43-33.58)	0.01 (-23.44-24.85)	0.14 (-4.66-27.40)
Beer cider serving (serving of	-0.06	0.01	(1.32-28.25)	-0.13	0.01	0.00	0.09	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14-	0.16	0.16	0.01	0.14
Beer cider serving (serving of 330mL/day) Wine	-0.06 (-16.24-8.02) -0.11	0.01 (-8.06-9.85) -0.01 (-15.00-11.41)	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93)	-0.13 (-24.28-35.67) 0.08	0.01 (-11.18-12.98) 0.01	0.00 (-8.97-8.86) -0.04 (-19.05-8.13)	0.09 (-13.90-25.09) 0.14	30.78) 0.23 ⁺ (0.72-43.34) -0.01	0.16 (-2.10-28.78) -0.01	0.16 (-10.43-33.58) -0.04	0.01 (-23.44-24.85) 0.10	0.14 (-4.66-27.40) 0.04
Beer cider serving (serving of 330mL/day) Wine (125 mL/day)	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40)	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67)	0.01 (-11.18-12.98) 0.01 (-18.02-19.95)	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺	0.09 (-13.90-25.09) 0.14 (-13.10-60.13)	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57)	0.16 (-2.10-28.78) -0.01 (-23.29-21.76)	0.16 (-10.43-33.58) -0.04 (-36.70-26.47)	0.01 (-23.44-24.85) 0.10 (-17.47-41.27)	0.14 (-4.66-27.40) 0.04 (-22.63-35.40)
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06	0.01 (-8.06-9.85) -0.01 (-15.00-11.41)	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93)	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02	0.00 (-8.97-8.86) -0.04 (-19.05-8.13)	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical Activity	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06 (-21.08-47.52)	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺ (11.23-43.92)	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺ (13.71-43.97)	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12 (-56.04-18.48)	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02 (-32.34-24.49)	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺ (15.54-48.90)	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20 (-3.50-33.97)	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14 (-51.36-8.43)	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01 (-19.86-21.28)	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13 (-13.33-33.36)	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02 (-26.03-21.08)	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04 (-16.20-25.05)
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical Activity (min/day)	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06 (-21.08-47.52) 0.01	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺ (11.23-43.92) -0.04	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺ (13.71-43.97) -0.07	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12 (-56.04-18.48) 0.20	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02 (-32.34-24.49) -0.01	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺ (15.54-48.90) -0.08	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20 (-3.50-33.97) 0.07	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14 (-51.36-8.43) 0.00	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01 (-19.86-21.28) -0.09	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13 (-13.33-33.36) 0.14	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02 (-26.03-21.08) 0.04	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04 (-16.20-25.05) -0.08
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical Activity	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06 (-21.08-47.52) 0.01 (-0.09-0.09)	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺ (11.23-43.92) -0.04 (-0.10-0.05)	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺ (13.71-43.97) -0.07 (-0.11-0.02)	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12 (-56.04-18.48) 0.20 (-0.04-0.25)	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02 (-32.34-24.49) -0.01 (-0.08-0.07)	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺ (15.54-48.90) -0.08 (-0.15-0.03)	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20 (-3.50-33.97) 0.07 (-0.12-0.21)	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14 (-51.36-8.43) 0.00 (-0.11-0.11)	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01 (-19.86-21.28) -0.09 (-0.17-0.05)	$\begin{array}{c} 0.16\\(-10.43-33.58)\end{array}$ $\begin{array}{c} -0.04\\(-36.70-26.47)\end{array}$ $\begin{array}{c} 0.13\\(-13.33-33.36)\end{array}$ $\begin{array}{c} 0.14\\(-0.07-0.23)\end{array}$	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02 (-26.03-21.08) 0.04 (-0.10-0.15)	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04 (-16.20-25.05) -0.08 (-0.20-0.09)
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical Activity (min/day) Vigorous Physical Activity	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06 (-21.08-47.52) 0.01 (-0.09-0.09) -0.04	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺ (11.23-43.92) -0.04 (-0.10-0.05) 0.05	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺ (13.71-43.97) -0.07 (-0.11-0.02) -0.01	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12 (-56.04-18.48) 0.20 (-0.04-0.25) 0.18	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02 (-32.34-24.49) -0.01 (-0.08-0.07) 0.03	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺ (15.54-48.90) -0.08 (-0.15-0.03) 0.07	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20 (-3.50-33.97) 0.07 (-0.12-0.21) -0.17	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14 (-51.36-8.43) 0.00 (-0.11-0.11) -0.04	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01 (-19.86-21.28) -0.09 (-0.17-0.05) 0.09	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13 (-13.33-33.36) 0.14 (-0.07-0.23) -0.20	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02 (-26.03-21.08) 0.04 (-0.10-0.15) -0.15	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04 (-16.20-25.05) -0.08 (-0.20-0.09) 0.01
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical Activity (min/day) Vigorous Physical Activity (min/day)	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06 (-21.08-47.52) 0.01 (-0.09-0.09) -0.04 (-0.12-0.07)	$\begin{array}{c} 0.01 \\ (-8.06-9.85) \end{array}$ $\begin{array}{c} -0.01 \\ (-15.00-11.41) \end{array}$ $\begin{array}{c} 0.18^{+} \\ (11.23-43.92) \end{array}$ $\begin{array}{c} -0.04 \\ (-0.10-0.05) \end{array}$ $\begin{array}{c} 0.05 \\ (-0.02-0.07) \end{array}$	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺ (13.71-43.97) -0.07 (-0.11-0.02) -0.01 (-0.05-0.04)	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12 (-56.04-18.48) 0.20 (-0.04-0.25) 0.18 (-0.04-0.18)	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02 (-32.34-24.49) -0.01 (-0.08-0.07) 0.03 (-0.04-0.06)	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺ (15.54-48.90) -0.08 (-0.15-0.03) 0.07 (-0.03-0.13)	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20 (-3.50-33.97) 0.07 (-0.12-0.21) -0.17 (-0.30-0.05)	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14 (-51.36-8.43) 0.00 (-0.11-0.11) -0.04 (-0.11-0.07)	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01 (-19.86-21.28) -0.09 (-0.17-0.05) 0.09 (-0.04-0.13)	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13 (-13.33-33.36) 0.14 (-0.07-0.23) -0.20 (-0.25-0.07)	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02 (-26.03-21.08) 0.04 (-0.10-0.15) -0.15 (-0.15-0.03)	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04 (-16.20-25.05) -0.08 (-0.20-0.09) 0.01 (-0.13-0.14)
Beer cider serving (serving of 330mL/day) Wine (125 mL/day) Spirits (40mL/day) Moderate Physical Activity (min/day) Vigorous Physical Activity	-0.06 (-16.24-8.02) -0.11 (-33.38-7.40) 0.06 (-21.08-47.52) 0.01 (-0.09-0.09) -0.04	0.01 (-8.06-9.85) -0.01 (-15.00-11.41) 0.18 ⁺ (11.23-43.92) -0.04 (-0.10-0.05) 0.05	(1.32-28.25) 0.01 (-7.28-8.23) -0.05 (-18.43-4.93) 0.17 ⁺ (13.71-43.97) -0.07 (-0.11-0.02) -0.01	-0.13 (-24.28-35.67) 0.08 (-20.35-35.67) -0.12 (-56.04-18.48) 0.20 (-0.04-0.25) 0.18	0.01 (-11.18-12.98) 0.01 (-18.02-19.95) -0.02 (-32.34-24.49) -0.01 (-0.08-0.07) 0.03	0.00 (-8.97-8.86) -0.04 (-19.05-8.13) 0.22 ⁺⁺⁺ (15.54-48.90) -0.08 (-0.15-0.03) 0.07	0.09 (-13.90-25.09) 0.14 (-13.10-60.13) 0.20 (-3.50-33.97) 0.07 (-0.12-0.21) -0.17	30.78) 0.23 ⁺ (0.72-43.34) -0.01 (-26.14- 23.57) -0.14 (-51.36-8.43) 0.00 (-0.11-0.11) -0.04	0.16 (-2.10-28.78) -0.01 (-23.29-21.76) 0.01 (-19.86-21.28) -0.09 (-0.17-0.05) 0.09	0.16 (-10.43-33.58) -0.04 (-36.70-26.47) 0.13 (-13.33-33.36) 0.14 (-0.07-0.23) -0.20	0.01 (-23.44-24.85) 0.10 (-17.47-41.27) -0.02 (-26.03-21.08) 0.04 (-0.10-0.15) -0.15	0.14 (-4.66-27.40) 0.04 (-22.63-35.40) 0.04 (-16.20-25.05) -0.08 (-0.20-0.09) 0.01

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Sitting	0.00	0.04	0.07	-0.19	0.01	0.05	-0.11	-0.02	0.04	-0.31	-0.02	-0.09
(hours/day)	(-1.77-1.71)	(-0.78-1.73)	(-0.21-1.95)	(-4.33-0.57)	(-1.38-1.63)	(-0.74-2.13)	(-3.42-1.25)	(-2.13-1.67)	(-1.28-2.03)	(-6.17-0.18)	(-2.64-2.14)	(-3.10-1.22)
Smoking	0.19 ⁺	0.05	0.05	0.24 ⁺	0.09	0.05	0.29 ⁺	0.03	0.06	0.12	0.01	0.20 ⁺
	(1.63-17.07)	(-2.54-6.71)	(-1.91-6.35)	(0.53-17.80)	(-1.80-9.70)	(-2.80-2.13)	(3.08-28.97)	(-5.75-8.58)	(-4.17-9.27)	(-8.37-18.14)	(-8.03-9.05)	(0.55-18.58)

*1 cup= 240 mL, **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, ⁺The relationship was statistically significant after adjustment for BMI, ⁺⁺⁺The association was reversed from negative to positive or vice versa after adjustment for BMI, Beta Coef.= Standardized Coefficients/ Beta, Cl= Confidence Interval, Central North Europe= Belgium, Finland and Southeast Europe= Spain, Greece, Hungary, Bulgaria

Table 4. Dietary and Physical Activity factors and LDL-C levels in the sample examined by region, age and SES.

Variables				npie examined by re		LDL-Chol	esterol						
			Low-risk group	(FINDRISC <12)			High-risk group (FINDRISC ≥12)						
	Reg	ion	A	Age		ES	Regi	ion	A	ge	SI	ES	
	Central North Europe (n=187) Beta Coef. (95% CI)	Southeast Europe ⁺⁺ (n=406) Beta Coef. (95% CI)	<45 (n=498) Beta Coef. (95% CI)	>45 ⁺⁺ (n=95) Beta Coef. (95% CI)	0-14 ⁺⁺ (n=251) Beta Coef. (95% CI)	>15 (n=342) Beta Coef. (95% CI)	Central North Europe (n=100) Beta Coef. (95% Cl)	Southeast Europe (n=174) Beta Coef. (95% CI)	<45 (n=193) Beta Coef. (95% CI)	>45 (n=81) Beta Coef. (95% CI)	0-14 (n=132) Beta Coef. (95% CI)	>15 (n=142) Beta Coef. (95% CI)	
Low fat dairy	-0.04	-0.02	-0.03	-0.18	-0.06	0.00 ⁺	-0.09	-0.17	-0.25 ⁺	0.15	-0.11	-0.29 ⁺	
(cups*/ day)	(-5.85- 3.65)	(-5.36-3.96)	(-4.49-2.45)	(-16.53-2.35)	(-8.08-3.46)	(-4.19-3.98)	(-6.86-3.04)	(-16.88-0.84)	(-11.162.84)	(-5.00-14.43)	(-9.81-2.92)	(-12.582.77)	
Full fat dairy	-0.01	-0.09	-0.08	0.02	-0.01	-0.10	0.20	0.07	0.09	0.05	0.00	0.23 ⁺	
(cups*/ day)	(-6.79-6.03)	(-8.85-0.71)	(-8.08-0.49)	(-7.26-8.35)	(-6.07-5.02)	(-9.83-0.41)	(-0.89-21.60)	(-5.31-12.80)	(-3.38-13.00)	(-10.12-14.83)	(-12.31-11.95)	(2.40-20.26)	
Vegetables	0.02	-0.02	0.00	0.07	-0.05	0.01	-0.02	-0.08	-0.11	-0.01	-0.08	-0.03	
(cups*/ day)	(-7.52-9.65)	(-6.92-4.81)	(-4.98-5.00)	(-10.00-18.90)	(-10.44-5.17)	(-5.83-6.55)	(-15.03-12.58)	(-14.43-5.82)	(-15.96-3.09)	(-13.51-13.01)	(-16.52-7.64)	(-13.94-9.85)	
Fruits	-0.20	-0.10	-0.12 ⁺	-0.04	-0.07	-0.12	-0.09	0.11	0.01	0.21	-0.03	0.12	
(cups*/ day)	(-24.781.79)	(-14.48-1.01)	(-14.911.57)	(-24.77-19.29)	(-14.25-5.91)	(-17.080.48)	(-24.60-11.60)	(-4.43-18.65)	(-10.22-11.34)	(-3.72-28.40)	(-18.40-14.12)	(-4.11-19.84)	
Non whole grain cereals (30 g/ day)	-0.04 (-18.21-9.78)	-0.01 (-7.59-6.86)	-0.01 (-6.79- 6.01)	-0.29 ⁺ (-83.9112.41)	0.07 (-4.44-14.79)	-0.08 (-13.99-2.80)	-0.02 (-22.34-19.14)	0.08 (-5.82-14.34)	-0.04 (-13.95-7.67)	0.03 (-12.83-15.54)	-0.03 (-17.85-13.55)	0.02 (-8.66-10.96)	
Whole grain cereals (30 g/ day)	0.00 (-5.09-5.16)	0.01 (-4.01-4.44)	-0.02 (-4.37- 2.98)	0.03 (-5.45-6.95)	0.06 (-2.77-6.89)	-0.08 (-7.15-1.33)	0.06 (-4.27-7.25)	0.09 (-3.82-10.87)	0.00 (-4.81-4.93)	-0.02 (-8.75-7.38)	0.01 (-7.39-7.98)	0.03 (-4.93-6.37)	
Legumes	0.14	-0.06	0.00	-0.32 ⁺	-0.15 ⁺	0.07	-0.01	-0.16 ⁺	-0.10	-0.23	-0.09	-0.26 ⁺	
(cups*/ day)	(-1.96-52.58)	(-21.96-5.81)	(-11.95- 12.17)	(-71.585.34)	(-37.332.25)	(-5.22-24.00)	(-91.74-84.81)	(-39.75-0.83)	(-37.13-7.46)	(-48.25-4.47)	(-35.28-14.61)	(-60.276.97)	
Red meat	0.06	0.01	0.02	-0.05	0.01	0.00	0.05	0.03	-0.01	0.12	-0.12	0.23 ⁺	
(grams/day)	(-0.07-0.16)	(-0.07-0.09)	(-0.06- 0.09)	(-0.17-0.12)	(-0.10- 0.10)	(-0.09-0.08)	(-0.20-0.30)	(-0.08-0.11)	(-0.10-0.09)	(-0.08-0.21)	(-0.18-0.06)	(0.03-0.26)	
White meat	0.01	0.04	0.06	0.04	0.05	0.02	0.02	0.09	0.04	0.31 ⁺	0.12	-0.03	
(grams/day)	(-0.16-0.19)	(-0.07-0.14)	(-0.04-0.14)	(-0.19-0.26)	(-0.09-0.17)	(-0.10-0.14)	(-0.23-0.28)	(-0.08-0.21)	(-0.10-0.17)	(0.01-0.61)	(-0.10-0.31)	(-0.18-0.13)	
Fish	0.01	-0.05	-0.11	0.14	0.03	-0.11	-0.04	-0.05	-0.01	0.03	-0.07	0.10	
(grams/day)	(-0.36-0.39)	(-0.25-0.09)	(-0.350.01)	(-0.14-0.54)	(-0.18-0.27)	(-0.40-0.02)	(-0.43-0.30)	(-0.36-0.20)	(-0.26-0.24)	(-0.32-0.39)	(-0.38-0.20)	(-0.16-0.51)	
Salty snacks (portions**/ day)	0.03 (-10.57-15.20)	-0.02 (-11.64-7.64)	-0.04 (-15.63-5.66)	-0.06 (-14.82-9.22)	-0.03 (-12.55-8.50)	-0.05 (-18.12-7.08)	-0.09 (-50.55-27.65)	-0.12 (-22.67-5.39)	-0.19 (-26.880.55)	0.06 (-27.54-43.47)	-0.12 (-48.12-14.78)	-0.08 (-18.68-8.61)	
Sweet snacks (portions**/ day)	0.06 (-3.12-7.24)	-0.11 (-12.680.09)	-0.05 (-6.88- 2.02)	-0.03 (-9.29-7.24)	0.00 (-7.06-6.77)	-0.06 (-7.89-2.29)	0.02 (-14.66-17.37)	0.21 (-0.16-17.99)	0.27 ⁺ (3.44-20.24)	0.03 (-13.78-16.97)	0.12 (-6.56-21.26)	0.13 (-3.62-13.93)	

Nuts and seeds	-0.08	0.01	0.00	-0.05	-0.12	0.07	-0.04	-0.11	-0.08	-0.34 ⁺	-0.10	-0.07
(30 g/day)	(-9.51-3.85)	(-6.38-8.40)	(-4.93- 5.36)	(-16.42-10.25)	(-12.32-1.41)	(-2.64-11.88)	(-20.11-14.69)	(-14.19-3.39)	(-14.16-4.28)	(-26.913.79)	(-14.90-5.60)	(-15.97-7.14)
Tea (250 mL/day)	-0.04 (-7.46-4.61)	0.08 (-1.75-11.03)	0.03 (-3.19-6.26)	0.16 (-3.11-15.54)	0.07 (-2.67-8.69)	0.00 (-6.78-6.44)	0.10 (-4.50-10.67)	-0.05 (-14.55-7.83)	0.03 (-5.10-7.91)	-0.09 (-16.48-7.86)	0.02 (-7.96-9.94)	-0.01 (-8.64-8.17)
Coffee (250 mL/day)	-0.23 ⁺ (-7.101.26)	-0.03 (-4.88-2.97)	-0.08 (-4.47-0.45)	0.09 (-3.33-7.60)	-0.07 (-5.73-1.70)	-0.08 (-4.79-1.01)	0.02 (-3.66-4.34)	-0.02 (-6.73-5.05)	-0.04 (-4.22-2.53)	-0.03 (-8.06-6.56)	0.04 (-4.07-5.79)	-0.03 (-5.16-3.53)
Soft drinks with sugar (250 mL/day)	-0.09 (-15.93-4.50)	0.00 (-10.13-10.07)	-0.04 (-10.79-4.33)	-0.07 (-27.78-14.85)	-0.05 (-17.00-7.63)	-0.02 (-10.16-7.38)	-0.09 (-24.26-11.75)	-0.06 (-25.33- 13.32)	-0.03 (-17.45-12.58)	-0.15 (-39.32-15.24)	0.04 (-17.44-23.57)	-0.05 (-24.40-13.04)
Soft drinks without sugar (250 mL/day)	-0.13 (-10.53-0.61)	-0.07 (-19.89-4.53)	-0.08 (-10.31-0.96)	-0.11 (-15.20-4.74)	-0.12 (-18.57- 0.49)	-0.02 (-6.69-4.98)	0.01 (-7.5-8.03)	-0.04 (-17.90- 11.35)	-0.03 (-7.96-5.55)	0.06 (-13.24-21.35)	-0.04 (-9.91-6.36)	0.04 (-9.41-14.04)
Juice without sugar (250 mL/day)	0.02 (-12.49-17.61)	0.01 (-9.12-11.66)	0.03 (-5.67-12.30)	-0.15 (-38.24-6.89)	0.00 (-12.47-13.02)	0.05 (-5.80-17.07)	0.22 (-0.87-41.58)	0.05 (-13.55- 25.01)	0.13 (-1.11-29.39)	-0.12 (-38.71-15.01)	0.11 (-9.02-32.99)	0.10 (-7.23-28.93)
Juice with sugar (250 mL/day)	0.01 (-15.99-17.71)	0.02 (-9.65-15.33)	0.04 (-6.60-16.66)	0.13 (-7.88-28.56)	0.00 (-20.60-19.35)	0.03 (-8.02-14.94)	0.05 (-20.96-31.20)	0.04 (-18.61- 29.60)	0.01 (-19.08-21.10)	-0.01 (-29.72-28.23)	0.01 (-24.52-27.20)	-0.02 (-26.69-22.90)
Beer cider serving (330mL/day)	-0.10 (-17.09-4.60)	-0.04 (-10.77-4.60)	-0.05 (-10.41-3.08)	-0.15 (-22.55-5.52)	-0.02 (-12.23-9.33)	-0.07 (-11.82-3.19)	0.08 (-14.73-23.87)	0.12 (-7.89-28.21)	0.07 (-7.93-18.03)	0.09 (-19.38-33.07)	-0.04 (-23.75-18.54)	0.08 (-8.91-20.44)
Wine (125 mL/day)	-0.14 (-33.13-3.33)	0.01 (-10.81-12.00)	-0.05 (-15.58-4.84)	0.06 (-18.65-30.23)	0.00 (-17.24-16.65)	-0.03 (-14.84-8.13)	0.13 (-13.87-47.27)	0.00 (-21.50- 20.61)	-0.02 (-20.86-17.01)	-0.08 (-36.71-19.03)	0.08 (-17.51-33.93)	0.02 (-21.40-25.45)
Spirits (40mL/day)	0.07 (-17.49-43.84)	0.02 (-13.90-20.60)	0.04 (-9.00-23.28)	-0.06 (-41.03-23.99)	-0.07 (-37.75-12.96)	0.09 (-3.95-31.94)	0.22 ⁺ (-2.27-29.39)	-0.11 (-39.20- 11.44)	0.02 (-14.90-19.68)	0.07 (-14.69-24.37)	0.01 (-19.45-21.81)	0.04 (-12.81-20.06)
Moderate Physical Activity (min/day)	-0.04 (-0.10-0.06)	-0.06 (-0.10-0.03)	-0.09 (-0.11-0.00)	0.22 (-0.02-0.23)	-0.04 (-0.09-0.05)	-0.09 (-0.13-0.02)	-0.02 (-0.15-0.13)	-0.03 (-0.11-0.08)	-0.15 (-0.17-0.01)	0.08 (-0.09-0.17)	-0.02 (-0.12-0.10)	-0.14 (-0.19-0.04)
Vigorous Physical Activity (min/day)	0.00 (-0.08-0.09)	0.04 (-0.02-0.05)	-0.01 (-0.04-0.03)	0.14 (-0.05-0.14)	-0.01 (-0.05-0.04)	0.10 (-0.01-0.12)	-0.06 (-0.18-0.11)	0.03 (-0.06-0.08)	0.16 (0.00-0.14)	-0.06 (-0.16-0.11)	-0.03 (-0.09-0.07)	0.09 (-0.06-0.15)
Walking	-0.02	-0.03	-0.02	-0.06	-0.02	0.01	0.04	0.05	0.14	-0.24	0.05	0.13
(min/day)	(-0.06-0.04)	(-0.04-0.02)	(-0.04-0.02)	(-0.07-0.04)	(-0.04-0.03)	(-0.05-0.06)	(-0.05-0.07)	(-0.05-0.10)	(0.00-0.09)	(-0.19-0.04)	(-0.04-0.07)	(-0.03-0.14)
Sitting (hours/day)	-0.04 (-1.92-1.20)	0.00 (-1.07-1.07)	0.03 (-0.64-1.23)	-0.20 (-3.95-0.33)	-0.02 (-1.49-1.19)	0.00 (-1.17-1.22)	-0.11 (-2.79-1.10)	-0.05 (-2.07-1.15)	-0.03 (-1.71-1.08)	-0.23 (-4.54-0.78)	-0.06 (-2.65-1.53)	-0.10 (-2.57-0.87)
Smoking	0.21 ⁺	0.05	0.08	0.21	0.11	0.06	0.24	0.09	0.09	0.19	0.05	0.22 ⁺
	0.21 (2.35-16.15)	(-2.07-5.79)	(-0.59-6.53)	0.21 (-0.27-14.80)	(-1.07-9.19)	(-2.08-6.91)	(-0.30-21.31)	(-2.58-9.57)	(-2.10-9.20)	0.19 (-4.37-17.83)	(-5.61-9.34)	0.22 (1.16-15.56)

*1 cup= 240 mL, **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, ⁺The relationship was statistically significant after adjustment for BMI, ⁺⁺⁺The association was reversed from negative to positive or vice versa after adjustment for BMI, Beta Coef.= Standardized Coefficients/ Beta, CI= Confidence Interval, Central North Europe= Belgium, Finland and Southeast Europe= Spain, Greece, Hungary, Bulgaria

Table 5. Dietary and Physical Activity factors and HDL-C levels in the sample examined by region, age and SES.

Variables	HDL-Cholesterol												
			Low-risk gro	up (FINDRISC <12)		High-risk group (FINDRISC ≥12)							
	Region			Age	s	ES	Regi	ion	Age		S	ES	
	Central North	Southeast	<45++	>45++	0-14++	>15++	Central North	Southeast	<45++	>45	0-14++	>15	
	Europe (n=187) Beta Coef. (95% CI)	Europe (n=408) Beta Coef. (95% CI)	(n=500) Beta Coef. (95% CI)	(n=95) Beta Coef. (95% CI)	(n=251) Beta Coef. (95% CI)	(n=344) Beta Coef. (95% CI)	Europe (n=101) Beta Coef. (95% CI)	Europe (n=174) Beta Coef. (95% CI)	(n=193) Beta Coef. (95% CI)	(n=82) Beta Coef. (95% CI)	(n=132) Beta Coef. (95% CI)	(n=143) Beta Coef. (95% Cl)	
Low fat dairy (cups*/ day)	-0.06 (-3.01-1.21)	0.10 (-0.17-3.80)	0.02 (-1.13-1.85)	0.20 ⁺⁺⁺ (-0.56-8.85)	0.07 (-1.14-3.84)	0.03 (-1.38-2.23)	-0.22 (-3.280.06)	0.01 (-3.17-3.76)	-0.09 (-2.65-0.74)	0.00 (-3.29-3.33)	-0.09 (-3.53-1.19)	-0.08 (-2.85- 1.10)	
Full fat dairy (cups*/ day)	0.07 (-1.44-4.27)	-0.06 (-3.28-0.80)	0.01 (-1.56-2.12)	-0.22 (-7.67-0.11)	0.05 (-1.34-3.45)	-0.06 (-3.60-0.92)	-0.02 (-3.92-3.26)	-0.01 (-3.66-3.42)	0.08 (-1.54-5.11)	-0.29 ⁺ (-9.731.13)	-0.04 (-5.32-3.67)	0.05 (-2.58-4.43)	
Vegetables (cups*/ day)	-0.10 (-3.34-1.31)	-0.02 (-3.02-1.96)	-0.05 (-3.38-0.90)	-0.01 (-7.40-7.01)	-0.11 (-6.10-0.63)	0.00 (-2.70-2.73)	-0.08 (-5.85-2.73)	-0.07 (-5.74-2.18)	-0.08 ⁺ (-5.86-1.88)	-0.19 (-8.57-0.66)	-0.10 (-6.68-2.26)	-0.05 (-5.81-3.44)	
Fruits (cups*/ day)	0.07 (-2.94-7.29)	0.04 (-2.13-4.46)	0.03 (-1.90-3.83)	0.14 (-5.72-16.25)	0.04 (-3.30-5.40)	0.02 (-2.95-4.38)	-0.16 (-9.86-1.68)	0.05 (-3.09-5.94)	0.08 (-2.34-6.42)	-0.08 (-7.51-3.37)	0.09 (-6.59-8.45)	-0.02 (-5.22-4.35)	
Non whole grain cereals (30 g/ day)	0.07 (-3.31-9.16)	-0.11 ⁺ (-6.480.32)	-0.07 (-4.99-0.50)	0.00 (-17.95-17.70)	-0.06 (-6.18-2.22)	-0.05 (-5.31-2.11)	-0.10 (-9.96-3.64)	-0.01 (-4.12-3.77)	-0.07 (-6.51-2.28)	0.14 (-2.27-7.79)	-0.09 (8.81-2.81)	-0.01 (-4.18-3.74)	
Whole grain cereals (30 g/ day)	0.14 (-0.26-4.31)	-0.02 (-2.20-1.40)	0.01 (-1.36-1.79)	0.07 (-2.16-4.02)	-0.03 (-2.54-1.63)	0.12 ⁺ (0.12-3.86)	0.03 (-1.62-2.15)	-0.03 (-3.37-2.38)	-0.03 (-2.39-1.57)	-0.10 (-4.29-1.43)	0.01 (-2.69-3.01)	-0.12 (-3.64-0.93)	
Legumes (cups*/ day)	0.02 (-10.81- 13.48)	-0.01 (-6.77-5.06)	-0.01 (-5.63-4.72)	0.03 (-14.46-18.57)	-0.05 (-10.72-4.41)	0.01 (-5.77-7.14)	0.15 (-8.10-49.75)	0.00 (-7.80-8.06)	0.01 (-8.34-9.78)	0.01 (-8.85-9.96)	-0.02 (-10.15-8.33)	-0.02 (-11.86-9.67)	
Red meat (grams/day)	0.04 (-0.04-0.06)	-0.05 (-0.05-0.02)	-0.03 (-0.04-0.02)	-0.04 (-0.08-0.06)	0.01 (-0.04-0.05)	-0.05 (-0.05-0.02)	0.15 (-0.03-0.13)	0.00 (-0.04-0.04)	0.04 (-0.03-0.05)	-0.04 (-0.06-0.04)	-0.09 (-0.06-0.02)	0.07 (-0.03-0.06)	
White meat (grams/day) Fish	-0.07 (-0.11-0.04)	-0.10 (-0.09-0.00)	-0.09 (-0.08-0.00)	0.02 (-0.11-0.12)	-0.06 (-0.08-0.03)	-0.10 (-0.10-0.00)	0.03 (-0.07-0.09)	0.11 (-0.02-0.09)	0.11 (-0.02-0.09)	-0.03 (-0.12-0.10)	0.03 (-0.06-0.09)	0.11 (-0.03-0.10)	
(grams/day)	0.02 (-0.15-0.19) -0.07	-0.03 (-0.09-0.05) -0.02	-0.04 (-0.10-0.04) 0.02	0.05 (-0.13-0.20) - 0.25	0.01 (-0.09-0.10) -0.05	-0.06 (-0.14-0.05) -0.02	0.05 (-0.09-0.15) -0.05	-0.12 (-0.18-0.04) -0.05	-0.14 (-0.18-0.02) -0.06	0.04 (-0.10-0.15) 0.14	-0.06 (-0.14-0.07) 0.06	-0.07 (-0.18-0.09)	
(portions** /day)	(-8.62-2.86)	(-4.90-3.30)	(-3.75-5.37)	(-12.040.06)	(-6.08-3.00)	(-6.34-4.77)	(-15.03-10.40)	(-6.80-4.17)	(-6.99-3.72)	(-4.79-20.20)	(-8.00-15.29)	-0.14 (-8.91-2.08)	
Sweet snacks (portions** /day)	-0.10 (-3.85-0.76)	0.03 (-2.02-3.35)	-0.02 (-2.30-1.52)	-0.11 (-6.37-1.87)	-0.07 (-4.58-1.38)	-0.01 (-2.37-2.12)	0.21 (-0.59-9.79)	0.05 (-2.50-4.47)	0.09 (-1.90-4.93)	0.04 (-4.33-6.32)	0.03 (-4.45-5.85)	0.14 (-1.18-5.87)	
Nuts and seeds (30 g/day)	-0.13 (-5.14-0.81)	0.11 ⁺ (0.39-6.69)	0.02 (-1.72-2.69)	0.03 (-5.89-7.42)	0.10 (-1.03-4.89)	-0.02 (-3.88-2.54)	-0.17 (-10.36-1.01)	0.01 (-3.32-3.56)	0.01 (-3.55-3.95)	-0.03 (-4.68-3.56)	-0.03 (-4.41-3.18)	-0.08 (-6.74-2.58)	
Tea (250 mL/day)	0.06 (-1.61-3.76)	-0.05 (-4.07-1.37)	0.02 (-1.48-2.58)	-0.22 ⁺ (-9.12-0.18)	-0.04 (-3.26-1.65)	0.04 (-1.70-4.14)	-0.01 (-2.62-2.36)	0.10 (-1.75-7.00)	0.08 (-1.14-4.15)	0.04 (-3.55-5.11)	0.08 (-1.82-4.81)	0.00 (-3.39-3.39)	
Coffee (250 mL/day)	0.05 (-0.89-1.71)	-0.15 ⁺ (-4.140.80)	-0.08 (-2.00-0.10)	0.07 (-1.86-3.59)	-0.01 (-1.76-1.45)	-0.11 ⁺ (-2.53-0.02)	-0.03 (-1.45-1.11)	0.02 (-2.08-2.53)	0.04 (-1.06-1.68)	-0.10 (-3.68-1.39)	0.08 (-1.10-2.55)	0.11 (-0.64-2.84)	

Soft drinks with sugar (250 mL/day)	-0.09 (-7.09-2.01)	0.04 (-2.74-5.83)	-0.05 (-4.83-1.61)	0.18 (-1.94-19.31)	0.02 (-4.56-6.06)	-0.02 (-4.51-3.21)	-0.10 ⁺⁺⁺ (-8.37-3.17)	0.11 (-2.97-12.14)	0.10 (-2.70-9.51)	-0.12 (-13.23-4.55)	0.22 ⁺ (-0.73-14.46)	0.00 (-7.57-7.45)
Soft drinks without sugar (250 mL/day)	0.04 (-1.76-3.20)	0.04 (-3.20-7.16)	0.04 (-1.21-3.62)	-0.09 (-7.12-2.82)	0.07 (-1.80-6.42)	-0.01 (-2.91-2.24)	0.16 (-0.69-4.40)	-0.03 (-6.90-4.53)	0.10 (-0.89-4.59)	0.01 (-5.88-6.31)	0.12 ⁺ (-0.93-5.09)	0.03 (-3.95-5.47)
Juice without sugar (250 mL/day)	-0.02 (-7.71-5.70)	0.02 (-3.57-5.28)	0.04 (-2.27-5.44)	-0.21 ⁺ (-22.760.26)	-0.09 (-9.42-1.58)	0.07 (-1.65-8.45)	-0.09 (-9.98-3.74)	0.03 (-5.99-9.08)	0.05 (-4.05-8.35)	-0.01 (-9.56-8.52)	0.15 (-1.21-14.35)	-0.08 (-10.68-3.86)
Juice with sugar (250 mL/day)	-0.05 (-10.19-4.82)	-0.01 (-5.78-4.82)	0.04 (-2.92-7.06)	0.01 (-8.74-9.43)	-0.12 (-16.36-0.87)	0.02 (-3.94-6.19)	-0.10 (-12.40-4.67)	-0.08 (-13.98-4.86)	-0.08 (-12.23-4.10)	0.09 (-5.84-14.83)	-0.13 (-15.63-3.53)	-0.01 (-10.16-9.66)
Beer cider serving (330mL/day)	0.12 (-1.65-8.01)	0.13 ⁺ (1.08-7.56)	0.17 ⁺ (2.34-8.09)	-0.12 (-10.80-3.20)	0.01 (-4.31-4.99)	0.17 ⁺ (1.65-8.20)	0.03 (-4.70-5.98)	0.03 (-6.14-7.97)	0.13 (-1.67-8.88)	0.10 (-3.85-9.29)	-0.16 (-12.53-3.13)	0.19 ⁺ (-0.17-10.14)
Wine (125 mL/day)	0.07 (-4.56-11.68)	0.03 (-3.14-6.41)	0.02 (-3.34-5.31)	0.25 (-0.28-24.10)	0.07 (-3.66-10.96)	0.02 (-3.99-6.01)	0.00 (-9.97-10.09)	0.08 (-4.62-11.84)	0.01 (-7.35-8.04)	0.10 (-4.54-14.32)	0.18 ⁺ (-2.10-16.95)	0.08 (-5.32-13.36)
Spirits (40mL/day)	-0.05 (-18.28-9.03)	0.00 (-5.93-5.90)	0.00 (-5.62-5.59)	-0.13 (-25.37-7.05)	0.02 (-9.20-12.68)	-0.02 (-7.35-4.92)	0.08 (-3.25-7.02)	-0.10 (-15.18-4.62)	-0.10 (-11.03-3.03)	0.17 (-1.93-12.01)	-0.10 (-11.29-3.99)	0.11 (-2.83-10.44)
Moderate Physical Activity (min/day)	0.06 (-0.02-0.05)	0.02 (-0.02-0.03)	0.01 (-0.02-0.03)	-0.01 (-0.07-0.06)	0.05 (-0.02-0.04)	0.00 (-0.03-0.03)	0.25 ⁺ (0.00-0.09)	0.00 (-0.04-0.04)	0.09 (-0.02-0.06)	-0.11 (-0.07-0.02)	0.05 (-0.03-0.05)	0.02 (-0.04-0.05)
Vigorous Physical Activity (min/day)	-0.04 (-0.05-0.03)	0.12 ⁺ (0.00-0.04)	0.08 ⁺ (0.00-0.03)	0.07 (-0.03-0.06)	0.11 (0.00-0.03)	0.05 (-0.02-0.04)	-0.27 ⁺ (-0.110.01)	0.04 (-0.03-0.04)	-0.06 (-0.04-0.02)	0.19 (-0.01-0.08)	-0.10 (-0.04-0.02)	0.03 (-0.04-0.05)
Walking (min/day)	-0.04 (-0.03-0.02)	0.08 (0.00-0.02)	0.08 (0.00-0.03)	-0.12 (-0.04-0.01)	0.09 (0.00-0.02)	0.01 (-0.02-0.03)	-0.02 (-0.02-0.02)	0.03 (-0.02-0.03)	0.07 (-0.01-0.03)	-0.05 (-0.05-0.03)	0.03 (-0.02-0.02)	0.13 (-0.01-0.06)
Sitting (hours/day)	0.04 (-0.51-0.88)	0.12 (-0.09-1.00)	0.13 ⁺ (0.19-0.99)	-0.13 (-1.65-0.48)	0.06 (-0.29-0.86)	0.12 ⁺ (0.06-1.11)	-0.08 (-0.86-0.42)	0.00 (0.62-0.64)	0.10 (-0.22-0.91)	-0.15 (-1.50-0.40)	0.01 (-0.74-0.81)	-0.05 (-0.88-0.51)
Smoking	-0.11 (-5.34-0.81)	-0.09 (-3.14-0.21)	-0.11 ⁺ (-3.40-0.34)	-0.10 (-5.46-2.05)	-0.16 ⁺ (-4.94-0.51)	-0.05 (-2.93-1.04)	0.12 (-1.56-5.53)	-0.13 (-4.44-0.31)	-0.06 (-3.19-1.40)	0.00 (-4.03-3.89)	-0.13 (-4.74-0.80)	-0.09 (-4.35-1.45)

*1 cup= 240 mL, **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, ⁺The relationship was statistically significant and positively associated after adjustment for BMI, ⁺⁺BMI was statistically significant and negatively associated after adjustment for BMI, ⁺⁺BMI was statistically significant and positively associated after adjustment for BMI, ⁺⁺BMI was statistically significant and negatively associated after adjustment for BMI, ⁺⁺The association was reversed from negative to positive or vice versa after adjustment for BMI, Beta Coef.= Standardized Coefficients/ Beta, CI= Confidence Interval, Central North Europe= Belgium, Finland and Southeast Europe= Spain, Greece, Hungary, Bulgaria

Table 6. Dietary and Physical Activity factors and TG levels in the sample examined by region, age and SES.

Variables	Triglycerides												
			Low-risk grou	up (FINDRISC <12)		High-risk group (FINDRISC ≥12)							
	Region			Age	S	ES	Reg	ion	Age		SES		
	Central North Europe ⁺⁺ (n=187) Beta Coef. (95% Cl)	Southeast Europe (n=408) Beta Coef. (95% Cl)	<45 ⁺⁺ (n=251) Beta Coef. (95% Cl)	>45 ⁺⁺ (n=344) Beta Coef. (95% CI)	0-14 ⁺⁺ (n=500) Beta Coef. (95% CI)	>15 (n=95) Beta Coef. (95% Cl)	Central North Europe (n=101) Beta Coef. (95% CI)	Southeast Europe ⁺⁺ (n=174) Beta Coef. (95% Cl)	<45 ⁺⁺ (n=132) Beta Coef. (95% Cl)	>45 (n=143) Beta Coef. (95% CI)	0-14 ⁺⁺ (n=193) Beta Coef. (95% Cl)	>15 (n=82) Beta Coef. (95% Cl)	
Low fat dairy (cups*/ day)	0.05 (-5.52-10.90)	0.01 (-9.63-12.36)	0.03 (-5.18-10.24)	-0.12 (-28.71-9.25)	0.02 (-12.04-15.03)	0.02 (-7.07-9.61)	0.09 (-6.29-15.65)	-0.11 (-31.17-6.87)	0.01 (-7.41-8.87)	-0.06 (-30.27-19.69)	-0.12 (-17.48-4.24)	0.01 (-11.72-13.60)	
Full fat dairy (cups*/ day)	-0.08 (-17.11-5.06)	0.00 (-11.12-11.47)	-0.03 (-12.62-6.43)	0.04 (-13.00-18.37)	-0.06 (-19.28-6.75)	0.03 (-7.74-13.13)	0.32 ⁺ (17.70-66.57)	0.07 (-11.90- 26.97)	0.18 ⁺ (3.32-35.35)	0.13 (-14.94-49.96)	-0.02 (-22.86- 18.51)	0.26 ⁺ (11.18-56.12)	
Vegetables (cups*/ day)	0.07 (-7.92-21.78)	-0.01 (-15.09-12.49)	0.01 (-9.70-12.45)	-0.04 (-33.59-24.52)	0.02 (-15.40-21.22)	0.03 (-9.20-15.91)	0.16 (-6.43-51.99)	0.05 (-15.75- 27.70)	-0.03 (-22.30-14.98)	0.15 (-12.49-57.23)	0.10 (-10.62- 30.58)	0.13 (-9.19-50.08)	
Fruits (cups*/ day)	-0.17 (-39.95 0.20)	0.00 (-17.72-18.78)	-0.05 (-22.18-7.48)	-0.04 (-50.10-38.50)	-0.03 (-29.03-18.27)	-0.07 (-27.60-6.24)	-0.15 (-65.56-12.92)	-0.07 (-34.62- 14.92)	-0.14 (-38.24-3.95)	-0.04 (-48.73-33.43)	-0.15 (-46.03-9.42)	-0.09 (-47.24-14.12)	
Non whole grain cereals (30 g/ day)	-0.01 (-25.23- 23.18)	0.02 (-14.38-19.72)	0.00 (-13.84- 14.60)	-0.06 (-93.00-50.77)	-0.05 (-31.51-13.60)	0.01 (-15.75-18.52)	-0.01 (-48.76-43.81)	0.06 (-14.04- 29.22)	0.03 (-16.31-25.99)	0.00 (-37.99-38.00)	-0.01 (-28.56- 24.99)	-0.01 (-27.31-23.40)	
Whole grain cereals (30 g/ day)	0.02 (-7.87-9.86)	-0.03 (-12.83-7.09)	0.00 (-8.34-7.99)	0.04 (-10.61-14.32)	0.03 (-8.86-13.79)	-0.05 (-13.00-4.28)	-0.05 (-16.22-9.41)	0.06 (-10.24- 21.28)	-0.10 (-16.05-3.01)	0.07 (-15.04-28.10)	-0.01 (-13.66- 12.55)	-0.02 (-16.35-12.89)	
Legumes (cups*/ day)	0.10 (-15.91- 78.41)	0.02 (-27.85-37.71)	0.01 (-23.78- 29.84)	-0.10 (-90.78-42.41)	0.05 (-25.16-57.11)	-0.02 (-36.88-22.76)	-0.04 (-234.66- 158.97)	-0.01 (-46.99- 40.09)	0.03 (-34.98-52.29)	-0.04 (-82.75-59.33)	-0.03 (-49.36- 35.72)	-0.01 (-73.44-64.49)	
Red meat (grams/day)	0.10 (-0.06-0.32)	0.06 (-0.09-0.28)	0.07 (-0.03-0.28)	0.02 (-0.26-0.32)	0.05 (-0.16-0.31)	0.08 (-0.05-0.29)	-0.10 (-0.81-0.30)	0.01 (-0.20-0.21)	-0.05 (-0.24-0.13)	0.02 (-0.35-0.43)	-0.02 (-0.22-0.18)	0.00 (-0.30-0.31)	
White meat (grams/day)	0.06 (-0.18-0.41)	0.07 (-0.09-0.40)	0.07 (-0.04-0.36)	0.10 (-0.27-0.64)	0.08 (-0.13-0.48)	0.07 (-0.07-0.40)	0.03 (-0.47-0.63)	-0.11 ⁺ (-0.49-0.13)	-0.06 (-0.35-0.18)	0.06 (-0.63-1.00)	-0.01 (-0.36-0.33)	-0.11 (-0.63-0.16)	
Fish (grams/day)	-0.01 (-0.68-0.63)	-0.08 (-0.72-0.09)	-0.06 (-0.63-0.12)	-0.18 (-1.21-0.15)	-0.16 ⁺ (-1.110.07)	-0.03 (-0.53-0.32)	0.00 (-0.80-0.81)	-0.10 (-0.93-0.26)	0.08 (-0.28-0.70)	-0.19 (-1.79-0.13)	-0.10 (-0.72-0.26)	0.03 (-0.73-0.98)	
Salty snacks (portions** /day)	-0.03 (-27.29- 17.29)	0.08 (-5.21-40.23)	-0.06 (-39.23-8.03)	0.35 ⁺ (10.28-58.60)	0.05 (-15.75-33.63)	0.00 (-25.59-25.77)	-0.08 (-115.38-57.63)	-0.11 (-46.83- 13.38)	-0.12 (-42.03-9.50)	-0.19 (-170.42-18.24)	-0.19 (-101.90- 5.36)	-0.03 (-39.98-30.40)	
Sweet snacks (portions** /day)	0.06 (-5.05-12.86)	-0.04 (-20.89-8.82)	-0.03 (-12.89-6.89)	0.17 (-2.41-30.81)	0.01 (-15.48-16.94)	-0.02 (-12.06-8.71)	0.02 (-32.89-37.78)	0.10 (-9.14-29.11)	0.13 (-5.44-27.43)	0.03 (-34.71-45.74)	0.19 (-2.39-45.05)	-0.03 (-25.60-19.58)	
Nuts and seeds (30 g/day)	0.05 (-7.95-15.16)	-0.01 (-18.61-16.28)	0.04 (-6.51-16.36)	-0.08 (-36.56-17.08)	0.04 (-11.18-21.01)	-0.02 (-17.33-12.31)	0.02 (-34.63-42.71)	0.05 (-13.28- 24.45)	-0.04 (-22.32-13.76)	0.01 (-29.52-32.71)	0.11 (-7.56-27.40)	0.00 (-30.37-29.35)	
Tea (250 mL/day)	0.04 (-7.71-13.16)	0.03 (-11.09-19.08)	0.03 (-6.91-14.10)	0.08 (-12.17-25.34)	0.05 (-8.46-18.20)	0.04 (-8.17-18.82)	0.10 (-8.81-25.05)	-0.03 (-28.41- 19.61)	0.10 (-4.57-20.89)	-0.11 (-48.78-16.61)	0.06 (-10.51- 20.02)	0.05 (-15.71-27.75)	

Coffee (250 mL/day)	-0.07 (-7.30-2.80)	-0.02 (-10.99-7.52)	-0.03 (-7.26-3.67)	0.06 (-8.34-13.64)	-0.09 (-14.43-2.99)	0.03 (-4.48-7.32)	-0.20 (-16.57-0.88)	-0.06 (-17.28-8.00)	-0.13 (-11.99-1.21)	0.06 (-14.35-23.88)	-0.05 (-10.45-6.37)	-0.07 (-15.80-6.52)
Soft drinks with sugar (250 mL/day)	0.11 (-5.22-30.11)	0.02 (-17.99-29.45)	0.04 (-9.98-23.41)	0.01 (-41.73-43.98)	0.08 (-11.82-45.95)	0.01 (-15.39-20.26)	-0.05 (-47.73-30.77)	0.01 (-39.33- 43.62)	0.02 (-26.89-31.88)	0.05 (-54.60-79.64)	0.17 (-10.08- 59.85)	-0.08 (-71.80-24.44)
Soft drinks without sugar (250 mL/day)	-0.13 (-18.10-1.15)	0.05 (-15.52-41.87)	-0.03 (-16.66-8.33)	-0.09 (-28.31-11.77)	0.05 (-12.70-32.00)	-0.06 (-19.47-4.33)	-0.06 (-22.01-12.59)	0.13 (-6.23-56.54)	0.02 (-11.64-14.79)	0.19 (-7.52-84.52)	0.02 (-12.63- 15.12)	0.04 (-22.20-38.16)
Juice without sugar (250 mL/day)	0.11 (-6.27-45.78)	0.01 (-21.16-27.87)	0.03 (-11.78- 28.16)	0.04 (-36.03-54.70)	0.15 ⁺ (6.37-66.15)	-0.06 (-37.16-9.48)	0.09 (-24.99-68.38)	-0.02 (-45.20- 37.54)	0.00 (-29.70-30.01)	-0.09 (-95.46-41.06)	-0.13 (-61.67-9.97)	0.12 (-13.09-80.08)
Juice with sugar (250 mL/day)	0.14 ⁺ (-0.10-58.18)	0.09 (-0.94-57.76)	0.13 ⁺ (13.33-64.99)	0.11 (-18.05-55.21)	0.29 ⁺ (58.79-152.48)	0.03 (-15.64-31.16)	0.12 (-24.37-91.75)	0.12 (-17.92- 85.53)	0.11 (-13.09-65.55)	0.00 (-77.01-79.11)	0.18 (-5.42-82.77)	0.01 (-59.99-67.07)
Beer cider serving (330mL/day)	-0.05 (-23.76- 13.75)	0.03 (-12.35-23.56)	-0.01 (-15.93- 13.83)	0.17 ⁺ (-7.13-49.31)	0.06 (-14.02-36.55)	0.02 (-12.62-17.66)	0.39 ⁺ (16.25-88.92)	0.27 ⁺ (11.05-88.52)	0.13 ⁺ (-8.11-42.69)	0.57 ⁺ (61.27-160.50)	0.17 (-12.91- 59.22)	0.25 ⁺ (11.43-77.52)
Wine (serving of 125 mL/day)	-0.05 (-40.21- 22.83)	-0.05 (-38.81-14.14)	-0.03 (-30.55- 14.26)	-0.27 ⁺ (-99.971.69)	-0.07 (-58.58-20.91)	-0.04 (-31.21-14.96)	0.09 (-39.52-96.99)	-0.06 (-59.21- 31.15)	0.08 (-19.57-54.54)	-0.19 (-134.61-7.82)	0.06 (-32.25- 55.47)	-0.08 (-85.70-33.96)
Spirits (40mL/day)	0.07 (-29.66- 76.39)	0.26 ⁺ (50.21-115.75)	0.25 ⁺ (55.46- 113.49)	-0.02 (-70.83-59.90)	0.10 (-14.65-104.30)	0.29 ⁺ (50.61-107.26)	0.07 (-24.26-45.59)	-0.04 (-66.00- 42.68)	0.00 (-34.56-33.11)	0.04 (-43.58-61.70)	-0.10 (-51.15- 19.20)	-0.03 (-50.65-34.40)
Moderate Physical Activity (min/day)	0.05 (-0.09-0.19)	0.00 (-0.15-0.15)	0.01 (-0.11-0.14)	0.01 (-0.25-0.26)	0.02 (-0.14-0.19)	-0.02 (-0.17-0.13)	-0.08 (-0.41-0.20)	0.15 (-0.03-0.38)	0.00 (-0.18-0.17)	0.21 (-0.03-0.66)	0.13 (-0.06-0.31)	0.05 (-0.22-0.37)
Vigorous Physical Activity (min/day)	-0.07 (-0.22-0.07)	-0.01 (-0.10-0.08)	-0.03 (-0.11-0.05)	0.03 -0.17-0.21	0.05 (-0.06-0.14)	-0.08 (-0.24-0.04)	-0.02 (-0.34-0.30)	-0.27 ⁺⁺⁺ (-0.390.08)	-0.04 (-0.18-0.10)	-0.30 (-0.710.01)	-0.23 ⁺ (-0.300.02)	-0.14 (-0.47-0.08)
Walking (min/day)	0.09 (-0.03-0.14)	0.02 (-0.06-0.09)	0.03 (-0.04-0.09)	0.11 (-0.06-0.15)	-0.02 (-0.08-0.06)	0.06 (-0.04-0.18)	0.04 (-0.10-0.15)	0.06 (-0.11-0.21)	0.15 (-0.01-0.18)	-0.16 (-0.45-0.15)	0.08 (-0.05-0.13)	0.04 (-0.16-0.27)
Sitting	0.04	0.00	0.00	0.14	0.01	0.00	0.01	0.01	0.06	-0.16	0.04	0.01
(hours/day)	(-1.96-3.42)	(-2.50-2.54)	(-2.06-2.10)	(-1.71-6.90)	(-2.98-3.31)	-2.38-2.49	(-4.20-4.51)	(-3.15-3.75)	(-1.67-3.78)	(-11.30-3.02)	(-2.91-4.22)	(-4.26-4.65)
Smoking	0.15 (0.04-23.90)	0.09 ⁺ (-1.09-17.46)	0.06 (-2.04-13.78)	0.25 ⁺ (2.89-33.19)	0.17 ⁺ (3.74-27.80)	0.05 (-4.86-13.49)	0.17 (-5.09-43.16)	-0.01 (-14.00- 12.06)	-0.02 (-12.58-9.52)	-0.04 (-33.86-25.92)	-0.01 (-13.65- 11.85)	0.12 (-6.22-30.97)

*1 cup= 240 mL, **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, ⁺The relationship was statistically significant after adjustment for BMI, ⁺⁺The association was reversed from negative to positive or vice versa after adjustment for BMI, Beta Coef.= Standardized Coefficients/ Beta, CI= Confidence Interval, Central North Europe= Belgium, Finland and Southeast Europe= Spain, Greece, Hungary, Bulgaria

4. Discussion

In the present work, the possible associations of diet and PA with blood lipid levels in high- and low-risk adults for developing T2DM were investigated. A sub-group analysis according to region, SES and age was also performed. According to the most dominant results, high intake of F in the low-risk and low-fat dairies in the high-risk participants were found to have a favourable association with blood lipid levels. Higher intakes of full-fat dairy in the high-risk as well as spirits and smoking in the low-risk group were negatively associated with the lipidemic profile.

From the literature review, only a few studies were found to examine the effects of specific food groups on the lipid profile in high-risk individuals for T2DM. Interestingly, our findings regarding dairy consumption are not in line with previous studies. A recent MA of RCTs in healthy adults showed that consumption of 3,6 servings/day, for a mean duration of 24 weeks, led to no change in LDL-C and HDL-C levels independently of the fat content of the dairy product. [26] In high risk adults, a RCT showed that the intake of 4-6 servings of low fat dairy per day had a neutral effect on blood lipids. On the contrary, our results highlighted a beneficial role of low-fat dairy intake as well as a detrimental one with increased high-fat dairy consumption on blood lipids which may be mediated by its higher SFA content which are known to raise blood LDL-C levels. [66] The association of F consumption with blood lipids has not been previously investigated in high-risk for T2DM individuals. In our study, F were repeatedly observed to have a beneficial association with the lipidemic profile mainly of lowbut not of high-risk participants. Existing intervention studies in healthy individuals have shown a neutral effect of F intake on the lipid profile, which may be due to the different design of the studies. [23, 24] However, the relationship between F and blood lipids remains to be elucidated in future studies. All of the associations, in our study, were found to be independent of the participant's BMI. Yet, BMI was also an independent determinant, positively associated with TG and negatively with HDL-C levels both in the low-risk and in high-risk group. Despite the dietary associations that were found, unsurprisingly, smoking was also demonstrated to play a detrimental role on blood lipids. It was associated with higher LDL-C and TG as well as with lower HDL-C levels independently of BMI but only in the low-risk group. Smoking is known for its detrimental effects on blood lipids. [67]

It is worth to mention, that several food groups or PA habits were expected to have significant associations with blood lipids, however, such associations were not observed in our results. For

instance, increased red meat intake due to its high SFA content would be anticipated to have an adverse association with the lipidemic profile. However, no significant associations were observed in our analysis which is in accordance with a recent MA in healthy adults [29] and a RCT in pre-diabetics where 200 g/day of red meat were consumed for 4 weeks and led to no difference in TC, LDL-C, HDL-C or TG. [55] In addition, nuts intake which has been extensively studied in previous studies, both in healthy and in high-risk individuals, was not observed to have any significant associations in our study. Previous data suggest that, in healthy adults, a mean intake of 56 g/day of nuts leads to decreased TC, LDL-C and TG levels. [36] Similar effects were observed in a RCT in high-risk individuals where increased almond intake was found to lower LDL-C levels. [55] Last but not least, regarding PA, in a cross-sectional study objectively measured PA was shown to be favourably associated with TG and HDL-C levels while sitting time was found to play a detrimental role on TG levels. [61] In our analysis, a positive association between VPA and HDL-C was observed in low-risk adults. In the high-risk group, VPA was also negatively associated with TG levels. Other associations with PA were not observed and this could be attributed to the fact that PA levels were self-reported.

In the sub-group analysis, from all the factors that were investigated similar associations with low- and full- fat dairy were repeatedly observed. Interestingly, full-fat dairy seem to have a positive association with TC and TG levels in the following subgroups of the high-risk category: Central North Europe, <45 years of age and high-SES. In the same subgroups, high F intake was found to play a beneficial role in TC as well as LDL-C levels this time in the low-risk group. Lowfat dairy, were negatively associated with TC and LDL-C levels in high-risk adults aged <45 years as well as in those of the high-SES group. Alcoholic beverages are known for their effects on blood lipids. A MA of RCTs showed that moderate alcohol consumption has LDL-C lowering effects, which was not observed in our study as well as HDL-C increasing effects similarly to our findings in the subgroup analysis. No change was observed in TC or TG levels. [40] According to the present results, spirits and beer/cider were positively associated with TC levels and HDL-C levels respectively which was also observed in the total sample where a positive association for spirits with TC and TG and beer/cider with HDL-C levels was shown. Regarding TG, beer/cider and spirits intake were positively associated both in low- and in high-risk individuals independently of the BMI. Beer/cider higher intakes were associated with higher TG levels in both of the regions examined while spirits were significant only in Southeast Europe. In addition, beer/cider and spirits were both observed to be associated with higher-SES independently of the BMI.

Our study has several strengths. To begin with, it is the first large-scale study to crosssectionally investigate the association between various food groups and PA indices on the lipid profile of individuals who are at risk of T2DM. Secondly, the majority of the food groups and PA indices under study was examined as part of a multi-variate model and therefore the strongest association could be distinguished. In addition, other benefits include the large study sample as well as the standardized protocols and procedures.

Potential limitations should be considered. First of all, the cross-sectional design does not allow us to find any potential cause-effect relationships since the exposure and the outcome are simultaneously assessed. In addition, part of the data that was collected was self-reported and therefore prone to recall bias, social desirability as well as under- and over- reporting. Also, information regarding the dietary habits was not collected as part of a structured Food Frequency Questionnaire (FFQ) and this may lead to less accurate information reporting as well as to less information regarding people's dietary habits. Last but not least, 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 the results among the different subgroups.

In conclusion, this cross-sectional study in individuals at increased risk of developing T2DM demonstrates that increased low fat dairy consumption is associated with a more favourable lipidemic profile while full fat dairy were found to have an adverse association in high-risk adults. In low-risk individuals, F seem to play a promising role regarding blood lipids while spirits an unfavourable one. Our findings also highlight the need for additional investigation of the potential effects of specific food groups and PA patterns on the lipidemic profile in intervention studies as well, in adults at risk for T2DM, since such information in this group of patients is still limited.

References

- 1. Elisaf, M., et al., Updated guidelines of the Hellenic Society of Atherosclerosis for the diagnosis and treatment of dyslipidemia-2014. Hellenic Journal of Atherosclerosis, 2014. **5**(3).
- 2. Langsted, A. and B.G. Nordestgaard, *Nonfasting versus fasting lipid profile for cardiovascular risk prediction.* Pathology, 2019. **51**(2): p. 131-141.
- 3. Kopin, L. and C. Lowenstein, *Dyslipidemia*. Ann Intern Med, 2017. **167**(11): p. ITC81-ITC96.
- 4. Nelson, R.H., *Hyperlipidemia as a risk factor for cardiovascular disease*. Prim Care, 2013. **40**(1): p. 195-211.
- 5. Grundy, S.M., et al., *Detection, evaluation, and treatment of high blood cholesterol in adults* (*Adult Treatment Panel III*). Circulation, 2002. **106**(25): p. 3143-3421.
- 6. Karr, S., *Epidemiology and management of hyperlipidemia*. Am J Manag Care, 2017. **23**(9 Suppl): p. S139-S148.
- 7. Galema-Boers, J.M. and J.E. van Lennep, *Dyslipidemia testing: Why, for whom and when.* Maturitas, 2015. **81**(4): p. 442-5.
- 8. Panagiotakos, D.B., et al., *Ten-year (2002-2012) cardiovascular disease incidence and all-cause mortality, in urban Greek population: the ATTICA Study.* Int J Cardiol, 2015. **180**: p. 178-84.
- 9. Martimianaki, G., et al., *Methods and introductory results of the Greek national health and nutrition survey-HYDRIA*. Epidemiology, Biostatistics and Public Health, 2018. **15**(2).
- 10. Scuteri, A., et al., *Metabolic syndrome across Europe: different clusters of risk factors.* European journal of preventive cardiology, 2015. **22**(4): p. 486-491.
- 11. Ference, B.A., et al., Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. European heart journal, 2017. **38**(32): p. 2459-2472.
- Grace, M., et al., Role of dyslipidemia in stroke and comparison of lipid profile in ischemic and hemorrhagic stroke-a case control study. International Journal of Advances in Medicine, 2016.
 3(3): p. 694-698.
- 13. IDF Diabetes Atlas, t.e., *International Diabetes Federation*. Brussels, Belgium: International Diabetes Federation 2017(<u>http://www.diabetesatlas.org</u>).
- 14. Federation, I.D., *Diabetes Atlas 2000*. Brussels, Belgium: International Diabetes Federation 2000(<u>http://www.diabetesatlas.org</u>).
- 15. Collaboration, N.R.F., Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4 · 4 million participants. The Lancet, 2016. **387**(10027): p. 1513-1530.
- 16. Athyros, V.G., et al., *Diabetes and lipid metabolism*. Hormones, 2018: p. 1-7.
- 17. Yu, M., et al., *Depression and risk for diabetes: a meta-analysis.* Canadian journal of diabetes, 2015. **39**(4): p. 266-272.
- 18. Diseases, N.I.o.D.a.D.a.K., *Risk Factors for Type 2 Diabetes*. <u>www.niddk.nih.gov</u>, November 2016. **last visited: 16-12-2018**.
- 19. Kolb, H. and S. Martin, *Environmental/lifestyle factors in the pathogenesis and prevention of type 2 diabetes.* BMC medicine, 2017. **15**(1): p. 131.
- 20. Verges, B., *Pathophysiology of diabetic dyslipidaemia: where are we?* Diabetologia, 2015. **58**(5): p. 886-99.
- 21. Cooper, D.N., et al., *The Effects of Moderate Whole Grain Consumption on Fasting Glucose and Lipids, Gastrointestinal Symptoms, and Microbiota.* Nutrients, 2017. **9**(2).
- 22. Ho, H.V., et al., *The effect of oat beta-glucan on LDL-cholesterol, non-HDL-cholesterol and apoB* for CVD risk reduction: a systematic review and meta-analysis of randomised-controlled trials. Br J Nutr, 2016. **116**(8): p. 1369-1382.
- 23. John, J.H., et al., *Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: a randomised controlled trial.* Lancet, 2002. **359**(9322): p. 1969-74.

- 24. Zino, S., et al., *Randomised controlled trial of effect of fruit and vegetable consumption on plasma concentrations of lipids and antioxidants.* BMJ, 1997. **314**(7097): p. 1787-91.
- 25. Liu, K., et al., *Effect of fruit juice on cholesterol and blood pressure in adults: a meta-analysis of 19 randomized controlled trials.* PLoS One, 2013. **8**(4): p. e61420.
- 26. Benatar, J.R., K. Sidhu, and R.A. Stewart, *Effects of high and low fat dairy food on cardiometabolic risk factors: a meta-analysis of randomized studies.* PLoS One, 2013. **8**(10): p. e76480.
- 27. Lorenzen, J.K. and A. Astrup, *Dairy calcium intake modifies responsiveness of fat metabolism and blood lipids to a high-fat diet*. Br J Nutr, 2011. **105**(12): p. 1823-31.
- 28. de Goede, J., et al., *Effect of cheese consumption on blood lipids: a systematic review and metaanalysis of randomized controlled trials.* Nutr Rev, 2015. **73**(5): p. 259-75.
- 29. O'Connor, L.E., J.E. Kim, and W.W. Campbell, *Total red meat intake of >/=0.5 servings/d does not negatively influence cardiovascular disease risk factors: a systemically searched meta-analysis of randomized controlled trials.* Am J Clin Nutr, 2017. **105**(1): p. 57-69.
- 30. Alhassan, A., et al., *Consumption of fish and vascular risk factors: A systematic review and metaanalysis of intervention studies.* Atherosclerosis, 2017. **266**: p. 87-94.
- Hagen, I.V., et al., High intake of fatty fish, but not of lean fish, affects serum concentrations of TAG and HDL-cholesterol in healthy, normal-weight adults: a randomised trial. Br J Nutr, 2016.
 116(4): p. 648-57.
- 32. Rouhani, M.H., et al., *Effects of Egg Consumption on Blood Lipids: A Systematic Review and Meta-Analysis of Randomized Clinical Trials.* J Am Coll Nutr, 2018. **37**(2): p. 99-110.
- 33. DiMarco, D.M., et al., Intake of up to 3 Eggs/Day Increases HDL Cholesterol and Plasma Choline While Plasma Trimethylamine-N-oxide is Unchanged in a Healthy Population. Lipids, 2017. 52(3): p. 255-263.
- 34. Ha, V., et al., *Effect of dietary pulse intake on established therapeutic lipid targets for cardiovascular risk reduction: a systematic review and meta-analysis of randomized controlled trials.* CMAJ, 2014. **186**(8): p. E252-62.
- 35. Luhovyy, B.L., et al., *Canned Navy Bean Consumption Reduces Metabolic Risk Factors Associated with Obesity.* Can J Diet Pract Res, 2015. **76**(1): p. 33-7.
- 36. Del Gobbo, L.C., et al., *Effects of tree nuts on blood lipids, apolipoproteins, and blood pressure: systematic review, meta-analysis, and dose-response of 61 controlled intervention trials.* Am J Clin Nutr, 2015. **102**(6): p. 1347-56.
- 37. Bogl, L.H., et al., *Association between habitual dietary intake and lipoprotein subclass profile in healthy young adults.* Nutr Metab Cardiovasc Dis, 2013. **23**(11): p. 1071-8.
- 38. Bahadoran, Z., et al., *Fast food consumption and the risk of metabolic syndrome after 3-years of follow-up: Tehran Lipid and Glucose Study.* Eur J Clin Nutr, 2013. **67**(12): p. 1303-9.
- 39. Schwingshackl, L., et al., *Food groups and intermediate disease markers: a systematic review and network meta-analysis of randomized trials.* Am J Clin Nutr, 2018. **108**(3): p. 576-586.
- 40. Huang, Y., et al., *Moderate alcohol consumption and atherosclerosis : Meta-analysis of effects on lipids and inflammation.* Wien Klin Wochenschr, 2017. **129**(21-22): p. 835-843.
- 41. Zhao, Y., et al., *Black tea consumption and serum cholesterol concentration: Systematic review and meta-analysis of randomized controlled trials.* Clin Nutr, 2015. **34**(4): p. 612-9.
- 42. Onakpoya, I., et al., *The effect of green tea on blood pressure and lipid profile: a systematic review and meta-analysis of randomized clinical trials.* Nutrition, Metabolism and Cardiovascular Diseases, 2014. **24**(8): p. 823-836.
- 43. Cai, L., et al., *The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials.* European journal of clinical nutrition, 2012. **66**(8): p. 872.
- 44. Khaw, K.-T., et al., *Randomised trial of coconut oil, olive oil or butter on blood lipids and other cardiovascular risk factors in healthy men and women.* BMJ open, 2018. **8**(3): p. e020167.
- 45. Caspersen, C.J., K.E. Powell, and G.M. Christenson, *Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research*. Public health reports, 1985. **100**(2): p. 126.
- 46. Kodama, S., et al., *Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis.* Archives of internal medicine, 2007. **167**(10): p. 999-1008.

- 47. Kelley, G., K. Kelley, and Z.V. Tran, *Aerobic exercise, lipids and lipoproteins in overweight and obese adults: a meta-analysis of randomized controlled trials.* International journal of obesity, 2005. **29**(8): p. 881.
- 48. Thorp, A.A., et al., *Deleterious associations of sitting time and television viewing time with cardiometabolic risk biomarkers: Australian Diabetes, Obesity and Lifestyle (AusDiab) study 2004–2005.* Diabetes care, 2010. **33**(2): p. 327-334.
- 49. Hamer, M., E. Stamatakis, and A. Steptoe, *Effects of substituting sedentary time with physical activity on metabolic risk.* Medicine and science in sports and exercise, 2014. **46**(10): p. 1946.
- 50. Duvivier, B.M., et al., *Benefits of substituting sitting with standing and walking in free-living conditions for cardiometabolic risk markers, cognition and mood in overweight adults.* Frontiers in physiology, 2017. **8**: p. 353.
- 51. Bravata, D.M., et al., Using pedometers to increase physical activity and improve health: a systematic review. Jama, 2007. **298**(19): p. 2296-2304.
- 52. Brocklebank, L.A., et al., *Accelerometer-measured sedentary time and cardiometabolic biomarkers: A systematic review.* Preventive medicine, 2015. **76**: p. 92-102.
- 53. Miyazaki, R., et al., *Effects of a year-long pedometer-based walking program on cardiovascular disease risk factors in active older people.* Asia Pacific Journal of Public Health, 2015. **27**(2): p. 155-163.
- 54. Wien, M., et al., *Almond consumption and cardiovascular risk factors in adults with prediabetes.* Journal of the American College of Nutrition, 2010. **29**(3): p. 189-197.
- 55. Hernández-Alonso, P., et al., *Effect of pistachio consumption on plasma lipoprotein subclasses in pre-diabetic subjects.* Nutrition, Metabolism and Cardiovascular Diseases, 2015. **25**(4): p. 396-402.
- 56. Turner, K.M., et al., *Changes in lipids and inflammatory markers after consuming diets high in red meat or dairy for four weeks.* Nutrients, 2017. **9**(8): p. 886.
- 57. Maki, K.C., et al., Sugar-Sweetened Product Consumption Alters Glucose Homeostasis Compared with Dairy Product Consumption in Men and Women at Risk of Type 2 Diabetes Mellitus1–3. The Journal of nutrition, 2015. **145**(3): p. 459-466.
- 58. Saraf-Bank, S., et al., *Effects of legume-enriched diet on cardiometabolic risk factors among individuals at risk for diabetes: a crossover study.* Journal of the American College of Nutrition, 2016. **35**(1): p. 31-40.
- 59. Richard, C., et al., Impact of egg consumption on cardiovascular risk factors in individuals with type 2 diabetes and at risk for developing diabetes: a systematic review of randomized nutritional intervention studies. Canadian journal of diabetes, 2017. **41**(4): p. 453-463.
- 60. Balk, E.M., et al., *Combined diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk: a systematic review for the Community Preventive Services Task Force.* Annals of internal medicine, 2015. **163**(6): p. 437-451.
- 61. Swindell, N., et al., *Objectively measured physical activity and sedentary time are associated with cardiometabolic risk factors in adults with prediabetes: the PREVIEW study.* Diabetes care, 2018. **41**(3): p. 562-569.
- 62. Lindstrom, J. and J. Tuomilehto, *The diabetes risk score: a practical tool to predict type 2 diabetes risk*. Diabetes Care, 2003. **26**(3): p. 725-31.
- 63. *Obesity: preventing and managing the global epidemic. Report of a WHO consultation.* World Health Organ Tech Rep Ser, 2000. **894**: p. i-xii, 1-253.
- 64. Mancia, G., et al., 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens, 2013. **31**(7): p. 1281-357.
- 65. WHO, *Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia.* WHO/IDF consultation, 2006.
- 66. Siri-Tarino, P.W., et al., *Saturated fatty acids and risk of coronary heart disease: modulation by replacement nutrients.* Curr Atheroscler Rep, 2010. **12**(6): p. 384-90.
- 67. Jain, R.B. and A. Ducatman, Associations between smoking and lipid/lipoprotein concentrations among US adults aged≥ 20 years. Journal of circulating biomarkers, 2018. **7**: p. 1849454418779310.