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Sex differences in food choices, adherence to dietary recommendations and plasma lipid profile in type 2 diabetes – The TOSCA.IT study

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Abbreviations: CVD, cardiovascular disease; CV, cardiovascular; CHD, coronary heart disease; BMI, body mass index; HbA1c, glycated hemoglobin; DNSG, Diabetes and Nutrition Study Group; SID, Italian Diabetes Society; SAFA, saturated fatty acid.

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Abstract *Background and aims:* Diabetic women have a more adverse plasma lipid profile than men. Sex differences in dietary habits may play a role, but are little investigated. The study evaluates the quality of diet, adherence to the nutritional recommendations of the Diabetes and Nutrition Study Group and their relation with plasma lipid in men and women with diabetes.
Methods and results: We studied 2573 people, aged 50–75, enrolled in the TOSCA.IT study (clinicaltrials.gov; NCT00700856). Plasma lipids were measured centrally. Diet was assessed with a semi-quantitative food frequency questionnaire. Women had a more adverse plasma lipid profile than men. Women consumed significantly more legumes, vegetables, fruits, eggs, milk, vegetable oils, and added sugar, whereas men consumed more starchy foods, soft drinks and alcoholic beverages. This stands for a higher proportion (%) of energy intake from saturated fat and added sugar (12.0 ± 2.4 vs 11.5 ± 2.5 and 3.4 ± 3.2 vs 2.3 ± 3.2, $P < 0.04$), and a higher intake of fiber (11.2 ± 2.8 vs 10.4 ± 2.6 g/1000 Kcal/day) in women. Adherence to the recommendations for saturated fat and fiber consumption was associated with significantly lower LDL-cholesterol regardless of sex. Adherence to the recommendations for added sugars was associated with significantly lower triglycerides and higher HDL-cholesterol in men and women.
Conclusions: Men and women with diabetes show significant differences in adherence to nutritional recommendations, but sex differences in plasma lipid profile are unlikely to be explained by nutritional factors. Adherence to the nutritional recommendations is associated with a better plasma lipid profile regardless of sex, thus reinforcing the importance of substituting saturated for unsaturated fat sources, increasing fiber and reducing added sugar intake.
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Introduction

There is convincing evidence that diabetes increases the risk of cardiovascular disease (CVD) to a greater extent in women as compared with men [1]. Although the absolute cardiovascular risk remains lower in diabetic women as compared to diabetic men, relative risk for CVD morbidity and mortality in diabetic vs non-diabetic people is generally higher in women, ranging from 1 to 3 in men and from 2 to 5 in women.

The causes of this sex difference are not completely understood. Several hypotheses have been put forward. A greater burden and poorer control of CV risk factors in women with diabetes compared to men has been reported [2–4]; furthermore, a lower risk perception by the patients and/or by health care providers may lead to a less intensive treatment in women. Finally, response to treatments may differ in men and women [5,6]. Among others sex differences in dietary habits, due to biological, cultural, behavioral, psychological or socio-economic factors may play a role, but are little investigated.

The medical nutrition therapy is a cornerstone in the treatment of diabetes; the main goal is to improve glucose control and the cardiovascular risk factors profile. However, adherence to the nutritional guidelines is generally poor [7–9]. The most unattended recommendations are those on fat and fiber, whose consumption is respectively higher and lower than recommended, and reflects the wider problem of the overabundance of saturated fat and refined cereals in the western diet. In addition, the amount of added sugar that can be safely tolerated in people with diabetes is still debated. Recent prospective studies in non-diabetic people have shown a dose-dependent effect of the consumption of sweetened beverages on plasma lipids and CVD mortality [10,11].

No previous studies have evaluated sex differences in food choices and nutrients intake and their relation with the plasma lipid profile in people with type 2 diabetes. This is relevant to investigate in view of the more adverse lipid profile and the greater increase in CV risk conferred by diabetes in women.

Whether men and women with diabetes have different adherence to dietary recommendations for the management of diabetes, and to what extent this may contribute to the more adverse lipid profile reported in women, it is not known. A better knowledge of this issue would be in line with recent views of gender medicine and may potentially address therapeutic strategies.

The aim of the study is to investigate, in a large, nationally representative, cohort of men and women with type 2 diabetes, the quality of diet, the adherence to the nutritional recommendations with regard to fat, fiber and added sugars and their relation with the plasma lipid profile.

Methods

We studied 2573 people with type 2 diabetes, 1535 men and 1038 women, aged 50–75, enrolled in the TOSCA.IT study, a randomized clinical trial designed to compare the impact of glucose lowering drugs on cardiovascular events (clinicaltrials.gov NCT00700856). The study protocol has been published [12]. The study participants were recruited in 60 centers distributed all over Italy. The Ethics Review Committee of the Coordinating Center and of each participating center have approved the study protocol, and written informed consent was obtained from all participants.

In this study baseline data, collected prior to randomization to study treatments, were used. Patients with comorbidities requiring a special dietary treatment were excluded from the analysis. Among others body weight, height, waist and hip circumference were measured according to a standard protocol. Body Mass Index (BMI) was calculated as weight (kg)/height (m^2). Fasting blood samples were obtained, biochemical analyses were performed in a central laboratory. Total cholesterol, HDL-cholesterol and triglycerides were measured by standard methods. LDL-cholesterol was calculated according to the Friedewald equation only for triglycerides values < 400 mg/dl. Glycated hemoglobin (HbA1c) was measured with High Liquid Performance Chromatography. Use of medications was assessed. All patients were treated with metformin, as per study inclusions criteria. A high proportion (65%) was on lipid lowering medications.

The dietary habits were assessed with the Italian version of the European Prospective Investigation into Cancer and Nutrition (EPIC) questionnaire [13,14]. The questionnaire contains 248 items including the type of fat used as condiment, or added after cooking. The respondent indicates the absolute frequency of consumption of each item (per day, week, month or year). The quantity of the food consumed was assessed with the use of pictures of portions showing a small, medium and large portion, with additional quantifiers (e.g. "smaller than the small portion" or "between the small and medium portion" etc …). The nutrient's composition of the diet was calculated with the use of a software containing the Italian Food Tables [15,16]. Incomplete and/or implausible questionnaire (i.e. reporting energy intake less than 800 or greater than 5000 Kcal/day) were excluded from the analyses.

Statistical analysis

Data are given as mean and standard deviation ($M \pm$ SD), or number and proportion, as appropriate. Not normally distributed variables were logarithmically transformed for statistical analyses and back transformed to natural units for presentation in the text and tables. Means were compared by unpaired t-test. Differences between proportions were tested by χ^2 test. For analytical purposes, the adherence to the dietary recommendations was based on recommendations from the Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes endorsed by the Italian Diabetes Society (SID) [17,18]. The separate and combined effect of sex and adherence to dietary guidelines on plasma lipids was assessed with the two way analysis of variance with adjustment for BMI. All statistical analyses were performed with the SPSS software for Windows, version19.0.

Results

The general characteristics of the study participants are given in Table 1 for the total population and by sex. Age and diabetes duration were comparable in men and

Table 1 Clinical characteristics of the study participants.

	Total population	Men (n = 1535)	Women (n = 1038)
Age (years)	62.1 ± 6.5	62.0 ± 6.5	62.3 ± 6.4
Diabetes duration (years)	8.5 ± 5.7	8.4 ± 5.6	8.6 ± 5.8
BMI (kg/m^2)	30.3 ± 4.5	29.7 ± 4.0	31.2 ± 4.9*
HbA1c (%)	7.68 ± 0.51	7.71 ± 0.51	7.65 ± 0.50*
% on target (<7.5%)	41.0	38.6	44.6*
Systolic blood pressure (mm/Hg)	134.8 ± 15.4	135.0 ± 15.2	134.4 ± 15.8
Diastolic blood pressure (mm/Hg)	80.1 ± 9.1	80.7 ± 9.2	79.1 ± 8.7*
% on pressure lowering medications	92.5	91.0	94.5
HDL-cholesterol (mg/dl)	46.1 ± 12.0	43.5 ± 11.0	59.6 ± 10.1*
% on target (Men > 40; Women > 50 mg/dl)	53.5	59.4	44.7*
LDL-cholesterol (mg/dl)	102.8 ± 31.4	100.8 ± 31.2	103.5 ± 73.1*
% on target (<100 mg/dl)	49.1	51.0	46.4*
Triglycerides (mg/dl)	150.6 ± 75.0	151.5 ± 78.9	148.8 ± 31.5
% on target (<150 mg/dl)	60.4	60.2	60.6
% on lipid lowering medications	62.0	60.9	63.7
% on statins	51.7	51.2	52.8
% on other lipid lowering medications	10.3	9.7	10.9
% with metabolic syndrome	52.8	48.2	59.5*

$M \pm$ SD.
*$P < 0.05$ vs men.

women, BMI was significantly higher in women and glucose control, evaluated as HbA1c, was marginally better in women. No significant differences were observed for systolic blood pressure; whereas diastolic blood pressure was slightly lower in women. Plasma LDL-cholesterol and the proportion of the cohort not meeting the treatment target of <100 mg/dl were significantly higher in women. HDL-cholesterol was significantly higher in women, however a significantly higher proportion of females as compared with males failed achieving the desirable value (i.e. >40 mg/dl for men; >50 mg/dl for women). No significant difference was observed for plasma triglycerides. Sex differences in plasma lipids hold true after correction for BMI. The proportion of people on lipid lowering medications was similarly high in men and in women, the most widely used class of drugs were statins. The findings were confirmed in a sensitivity analysis performed in the subsample of the cohort not on lipid lowering medications (Supplementary Table 1). Finally, the proportion of the cohort with metabolic syndrome was significantly higher in women.

The nutrients composition of the diet and the proportion of the cohort achieving the recommended intake is given in Table 2, along with the DNSG nutritional recommendations [17]. The least attended recommendations were those on saturated fat intake, cholesterol and fiber with 81.9%, 82.6% and 93.1% of the cohort not meeting the recommended intake. Adherence was fair for carbohydrates and good for added sugars, monounsaturated and polyunsaturated fat, and alcohol. However, there were sex differences. The proportion of energy from total fat and saturated fat was significantly higher in women, as well as the proportion of the cohort exceeding the recommended intake for saturated fat (Table 2). The intake of cholesterol and alcohol was significantly lower in women. The intake of fiber and the proportion of cohort achieving the recommend intake were generally low, and significantly higher in women; accordingly, the glycemic load of the diet was lower in women (Table 2).

The sex differences in the composition of the diet reflected different food choices: women consumed significantly more legumes, vegetables, fruits, eggs, milk, vegetable oils (mainly olive oil), and sugars added by the consumer, whereas men had a higher consumption of starchy foods (pasta and bread), soft drinks and alcoholic beverages (Table 3).

Table 4 gives plasma lipids and BMI according to sex and adherence to the recommendations for the intake of

Table 3 Food groups (g/1000 Kcal/day) in men and women with type 2 diabetes.

	Men	Women
Starch (Pasta, Rice, Bread)	102.9 ± 37.0	95.2 ± 38.1*
Legumes	43.1 ± 38.8	48.7 ± 36.7*
Vegetables	87.6 ± 44.9	102.6 ± 50.3*
Fresh fruit	160.9 ± 88.8	190.6 ± 99.6*
Meat and salami	56.8 ± 26.1	56.2 ± 26.4
Fish	21.7 ± 16.5	23.8 ± 16.0
Eggs	10.6 ± 7.6	12.4 ± 9.1*
Dairy products	18.9 ± 12.6	19.4 ± 12.9
Milk and yogurt (whole)	27.8 ± 38.2	36.8 ± 44.1*
Milk and yogurt (low fat)	56.1 ± 77.3	76.7 ± 84.3*
Vegetable oils (condiment)	12.8 ± 5.5	14.6 ± 6.2*
Olive oil	11.4 ± 4.6	13.5 ± 5.7*
Other vegetable oils	1.3 ± 1.7	1.2 ± 1.9
Animal fats (condiment)	1.4 ± 1.5	1.2 ± 1.3
Cake and pastries	18.7 ± 18.7	20.2 ± 20.1
Soft drinks	17.9 ± 43.6	15.6 ± 37.5*
Sugar added by consumer	2.6 ± 5.3	4.3 ± 7.1*
Wine and beer	89.1 ± 92.3	24.6 ± 48.2*

M ± SD.
*P < 0.05 vs men.

Table 2 Nutrient composition of the diet and adherence to the nutritional recommendations in men and women with type 2 diabetes.

	Men	Women	Recommendations (DNSG [17]/SID [18])	Non adherence % (men n = 1535)	Non adherence % (women n = 1038)
Energy (Kcal/day)	1934 ± 674	1680 ± 593*			
Proteins (% of total energy)	18.3 ± 2.5	18.2 ± 2.5	10–20%	22.3 (343)	21.8 (226)
Fat (% of total energy)	36.4 ± 5.9	37.0 ± 6.1*	<35%	59.9 (920)	63.7 (661)*
SFA (% of total energy)	11.5 ± 2.5	12.0 ± 2.4*	<10%	81.8 (1256)	82.4 (855)*
MUFA (% of total energy)	17.7 ± 3.6	18.1 ± 3.9	10–20%	24.3 (373)	28.4 (295)*
PUFA (% of total energy)	4.4 ± 1.0	4.5 ± 1.1	<10%	0.4 (6)	0.8 (8)
Cholesterol (mg/day)	344 ± 148	304 ± 135*	<200 mg	85.6 (1314)	79.6 (826)*
Carbohydrates (% of total energy)	45.3 ± 7.1	44.8 ± 7.3*	45–60%	51.2 (786)	53.8 (558)
Added sugars[a] (% of total energy)	2.3 ± 3.2	3.4 ± 3.2*	<10%	2.7 (41)	2.8 (29)
Fiber (g/1000 Kcal/day)	10.4 ± 2.6	11.2 ± 2.8*	>15 g/1000 Kcal	94.8 (1455)	90.6 (940)*
Glycemic index (%)	51.8 ± 3.4	51.6 ± 3.2			
Glycemic load	123.0 ± 53.3	103.4 ± 42.6*			
Alcohol (g/day)	15.9 ± 17.9	4.0 ± 8.2*	<20 g for men and <10 g for women	0.8 (12)	0.2 (3)

M ± SD.
*P < 0.05 vs men.
DNSG (Diabetes and Nutrition Study Group); SID (Italian Diabetes Society).
[a] Soft drinks + sugar added by consumer.

Table 4 Plasma lipid profile by sex and adherence to the recommendations for intake of saturated fat (panel a), fiber (panel b) and added sugars (panel c).

	Adherence		Non adherence		*P* for two-factors ANOVA		
	Men (*n* = 279)	Women (*n* = 183)	Men (*n* = 1252)	Women (*n* = 850)	Sex	Adherence	Sex × adherence
Panel a							
HDL-cholesterol (mg/dl)	43.0 ± 10.4	49.8 ± 12.1	43.6 ± 11.1	49.9 ± 12.3	0.001	0.142	0.912
LDL-cholesterol (mg/dl)	98.3 ± 32.1	102.7 ± 31.2	101.6 ± 30.8	106.0 ± 31.8	0.010	0.051	0.971
Triglycerides (mg/dl)	155.5 ± 77.4	150.6 ± 75.1	150.7 ± 79.2	149.0 ± 67.5	0.070	0.110	0.945
BMI (kg/m^2)	29.3 ± 4.0	30.0 ± 4.9	29.8 ± 4.0	31.4 ± 4.9	0.001	0.001	0.060
	Adherence		Non adherence		*P* for two-factors ANOVA		
	Men (*n* = 80)	Women (*n* = 98)	Men (*n* = 1455)	Women (*n* = 940)	Sex	Adherence	Sex × adherence
Panel b							
HDL-cholesterol (mg/dl)	43.5 ± 9.7	52.2 ± 11.9	43.5 ± 11.1	49.7 ± 12.3	0.001	0.343	0.260
LDL-cholesterol (mg/dl)	99.4 ± 32.0	103.8 ± 27.7	101.1 ± 31.0	105.6 ± 32.1	0.081	0.497	0.993
Triglycerides (mg/dl)	146.8 ± 60.8	143.1 ± 69.5	151.8 ± 79.7	149.9 ± 68.8	0.282	0.558	0.915
BMI (kg/m^2)	29.4 ± 4.0	30.0 ± 4.4	29.7 ± 4.0	31.3 ± 4.9	0.001	0.022	0.166
	Adherence		Non adherence		*P* for two-factors ANOVA		
	Men (*n* = 1488)	Women *n* = 1002)	Men (*n* = 41)	Women (*n* = 28)	Sex	Adherence	Sex × adherence
Panel c							
HDL-cholesterol (mg/dl)	43.6 ± 11.0	50.0 ± 12.4	39.6 ± 9.7	46.1 ± 9.4	0.001	0.009	0.901
LDL-cholesterol (mg/dl)	96.3 ± 34.7	105.3 ± 31.6	101.1 ± 31.0	110.2 ± 34.9	0.024	0.992	0.222
Triglycerides (mg/dl)	150.3 ± 78.1	148.7 ± 68.9	196.3 ± 94.0	170.3 ± 66.0	0.039	0.001	0.178
BMI (kg/m^2)	29.7 ± 4.0	31.2 ± 4.9	30.2 ± 3.5	31.7 ± 4.9	0.005	0.325	0.944

SAFA, fiber and added sugars. Adherence to the recommendations for SAFA intake was associated with significantly lower LDL-cholesterol and BMI in men and women. No significant association with HDL-cholesterol or triglycerides was observed. The findings were confirmed in a sensitivity analysis conducted after the exclusion of people on lipid lowering drugs (Table 5).

Adherence to the recommendations for fiber intake (Table 4) was associated with lower BMI in men and women. No differences were observed for plasma lipids; however, in the subsample of cohort not on lipid lowering medications, the adherence to the recommendations for fiber intake was associated with significantly lower LDL-cholesterol and triglycerides in both men and women (Table 5).

The adherence to the recommendations for added sugars was generally good with only a small proportion of the cohort (2.7% in men and 2.8% in women) not meeting the recommended intake. Notwithstanding the small numbers and the limited statistical power, adherence to the

Table 5 Plasma lipid profile by sex and adherence to the recommendations for intake of saturated fat (panel a), fiber (panel b) and added sugars (panel c) in population not on lipid lowering medications.

	Adherence		Non adherence		*P* for two-factors ANOVA		
	Men (*n* = 90)	Women (*n* = 62)	Men (*n* = 448)	Women (*n* = 289)	Sex	Adherence	Sex × adherence
Panel a							
HDL-cholesterol (mg/dl)	43.8 ± 10.8	48.0 ± 12.5	43.6 ± 10.5	49.6 ± 12.0	0.001	0.252	0.457
LDL-cholesterol (mg/dl)	109.4 ± 28.6	116.7 ± 32.0	115.9 ± 28.3	121.0 ± 29.3	0.021	0.049	0.656
Triglycerides (mg/dl)	157.1 ± 80.8	159.4 ± 80.8	153.3 ± 76.9	145.5 ± 66.4	0.464	0.124	0.544
BMI (kg/m^2)	29.7 ± 4.2	30.9 ± 5.4	29.9 ± 4.0	32.0 ± 5.2	0.001	0.141	0.309
	Adherence		Non adherence		*P* for two-factors ANOVA		
	Men (*n* = 31)	Women (*n* = 62)	Men (*n* = 509)	Women (*n* = 319)	Sex	Adherence	Sex × adherence
Panel b							
HDL-cholesterol (mg/dl)	46.5 ± 11.3	53.7 ± 12.1	43.4 ± 10.5	48.9 ± 12.0	0.001	0.142	0.254
LDL-cholesterol (mg/dl)	107.5 ± 20.3	118.4 ± 24.8	115.2 ± 28.8	120.5 ± 30.3	0.154	0.032	0.523
Triglycerides (mg/dl)	124.6 ± 55.4	134.1 ± 53.9	155.5 ± 78.2	149.3 ± 70.5	0.987	0.036	0.588
BMI (kg/m^2)	28.5 ± 3.9	30.1 ± 4.4	29.9 ± 4.0	32.0 ± 5.3	0.003	0.008	0.755
	Adherence		Non adherence		*P* for two-factors ANOVA		
	Men (*n* = 525)	Women (*n* = 341)	Men (*n* = 9)	Women (*n* = 8)	Sex	Adherence	Sex × adherence
Panel c							
HDL-cholesterol (mg/dl)	43.6 ± 10.6	49.4 ± 12.2	42.4 ± 12.2	45.3 ± 6.5	0.154	0.294	0.597
LDL-cholesterol (mg/dl)	114.7 ± 28.4	120.3 ± 29.9	118.6 ± 34.4	119.5 ± 25.6	0.547	0.252	0.780
Triglycerides (mg/dl)	152.3 ± 76.1	146.7 ± 68.7	252.2 ± 96.6	198.5 ± 80.1	0.056	0.001	0.216
BMI (kg/m^2)	29.9 ± 4.0	31.8 ± 5.2	29.8 ± 2.8	33.4 ± 6.3	0.013	0.481	0.440

recommendations for added sugars intake was associated with significantly lower triglycerides and higher HDL-cholesterol, both in men and women independent of BMI (Table 4). The finding on triglycerides was confirmed in the subsample not taking lipid lowering medications (Table 5).

Discussion

The study evaluated sex differences in food choices, nutrient intake, adherence to the nutritional recommendations and their relation with the plasma lipid profile in men and women with type 2 diabetes in real life clinical practice. Data on the quality of diet in people with type 2 diabetes are scant [8,9]. To the best of our knowledge no prior data on sex differences were reported. In this study, women consumed more legumes, vegetables, fruits, eggs, milk, vegetable oils, and sugars added by the consumer, but less starchy foods (pasta and bread), soft drinks and alcoholic beverages. This translated into slightly, but significantly lower adherence to the recommendations for SAFA intake and higher adherence to the recommendations for fiber intake in women as compared to men. Sugar intake was higher in women and was counterbalanced by a lower consumption of soft drinks. The consumption of whole grain cereals was negligible in both men and women and their effect could not be evaluated. The DNSG recommendations for people with diabetes are close to the Mediterranean style diet, which has been shown effective in the prevention of diabetes and its complications [23,24]. In theory in Italy, due to their gastronomic background, people with diabetes should be facilitated in following the nutritional recommendations, yet this was not the case as far as SAFA and fiber intake is concerned. A low adherence to SAFA and fiber intake in people with type 2 diabetes was also reported in a prior Italian study and was also described in other cohorts [7–9]. A recent study conducted in Ireland in people with type 2 diabetes [8] reports average fat intake of 38.8% that is close to what we found in our cohort, and is a reflection of the more general problem of saturated fat and refined carbohydrates overabundance in the western diet.

Notwithstanding some debate as to which diet is best for people with type 2 diabetes, there is a general consensus on the need to reduce the intake of saturated fat while increasing the intake of dietary fiber, particularly from whole grain cereals [19]. One general criticism is that the nutritional recommendations are insufficiently evidence based. Our study provided strong observational data in support of the DNSG recommendations. As a matter of fact, adherence to SAFA and fiber intake was associated with better plasma lipid profile in both men and women, independent of BMI and, to some extent, independent of lipid lowering treatment. The amount of added sugars that can be safely tolerated is debated [20,21]. In the present study adherence to the DNSG nutritional guidelines (i.e., added sugars below 10% of energy intake) was associated with significantly higher HDL-cholesterol and lower triglycerides in both men and women, so reinforcing the importance of this recommendation. The indication of maintaining the added sugars intake well below 10% of total energy is further sustained by recent studies showing a dose-related response of plasma lipid and CVD mortality with progressively increasing consumption of sweetened beverages [10,11].

Our observations were in line with recent studies showing that a Mediterranean style diet has beneficial effects on diabetes control and cardiovascular risk factors modification (reviewed in Ref. [23]). The more adverse plasma lipid profile observed in women in the present study was coherent with findings of other studies [2,3,22] and it was unlikely to be explained by differences in adherence to the nutritional guidelines, as it persisted when limiting the analyses to people with good adherence to the dietary recommendations.

The major study strengths relayed on the large sample size, the selection of a cohort representative of real life clinical practice, the standardized collection of nutritional data and the centralized measurement of plasma lipids. Among the study limitations we acknowledge the cross-sectional design that did not allow to explore "cause–consequence" relationships. In addition, the dietary data were collected only once and could be prone to recall bias and seasonal variation. Finally, the extensive use of hypolipidemic drugs could have partly offset the quantitative effect of nutritional factors. In this regard the appreciation of the impact of diet adherence in the face of pharmacological treatment was even more relevant.

In conclusion, this study showed that men and women with diabetes make different food choices, but sex differences in plasma lipids are unlikely to be explained by nutritional factors. Adherence to the nutritional recommendations for SAFA, fiber and added sugars intake was associated with a better plasma lipid profile within men and women over and above the effect of medications. These findings reinforced the importance of substituting saturated for unsaturated fat sources, increasing fiber intake and reducing the consumption of added sugars, and provided strong observational data in support of the DNSG nutritional recommendations. Although small in magnitude, the observed differences in plasma lipids were coherent with the results of lifestyle interventions studies [25] and, at the population level, may significantly impact on the population's absolute cardiovascular risk.

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Conflict of interest

No conflicts of interest to report.

Authors' contributions to manuscript

O. V., G. R., M. M., E. B., F. C., and S. S. designed research; S. C., R. A., A. C. B., M. B., R. B., R. C., C. C., E. C., M. C., G. C., G. C., A. C., L. C., A. D. G., P. D. B., G. D. C., L. F., M. G., C. B. G., C. G., C. I., S. L., G. M., C. M., V. M., M. M., G. P., M. E. R., M. C. R., L. S., G. S., C. S., L. T., C. Z., and A. Z. conducted research; V. K. and S. G. provided essential materials; M. V., S. G., F. C., and S. S. analyzed data and performed statistical analysis; O. V., G. R., and M. V. wrote paper; O. V., M. V., and G. R. had primary responsibility for final content.

All authors have read and approved the final manuscript.

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Appendix A. Supplementary material

Supplementary material associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.numecd.2016.04.006.

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