The long term effect of dietary habits and physical activity on type 2 diabetes incidence: 10-year follow up of the ATTICA study (2002-2012)

Diet, physical activity and diabetes

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Abstract

**Aim:** to record the 10-year diabetes incidence and investigate the effect of dietary habits and physical activity on its development.

**Material and methods:** from May 2001 to December 2002, 1514 men and 1528 women (>18 years) without any clinical evidence of CVD or any other chronic disease, at baseline, living in greater Athens area, were enrolled in ATTICA study. Socio-demographic, clinical, lifestyle and biochemical characteristics were evaluated. Dietary habits were assessed through a validated semi-quantitative, food frequency questionnaire and physical activity through a translated, validated, version of International Physical Activity Questionnaire (IPAQ). Diabetes diagnosis was defined as glucose>125mg/dL or use of antidiabetic medication. In 2011-2012, the 10-year follow-up was performed.

Citation


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Results: 191 incident cases of diabetes were documented, yielding an incidence of 12.9%. Medium and high adherence to the Mediterranean diet decreased 10-year diabetes risk by 49% (OR= 0.51; 95%CI: 0.30, 0.88) and 62% (OR=0.38; 95%CI: 0.16, 0.88) respectively. Moderate coffee consumption (≥250mL/day, adjusted for 28% caffeine containment) and low alcohol consumption (<1 glass/day) also decreased risk by 54% (OR=0.46; 95%CI: 0.24, 0.90) and 53% (OR=0.47; 95%CI: 0.26, 0.83), compared to abstention. Finally, moderate level of physical (331-1484 vs. <150 MET minutes/week) led to a risk reduction of 44% (OR=0.56, 95% CI: 0.34, 0.92).

Conclusions: The present work reported the importance of non-pharmacological interventions in the primary prevention of diabetes. Mediterranean diet, moderate coffee consumption, low alcohol consumption, and moderate level of physical activity exert a beneficial effect against diabetes onset.

Key words: diabetes incidence; Mediterranean diet; alcohol; coffee; physical activity

Introduction
Type 2 diabetes remains a global emergency, being responsible for approximately 16 million new cases annually, yielding a prevalence of 9%; while one in two people with diabetes still remain unaware of the disease. In 2015, diabetes cost the lives of 5 million people worldwide, imposing at the same time a significant economic cost on both the families of people with diabetes and countries with a high prevalence of the disease, accounting at the same time for 5-20% of the total cost of health care. These costs mainly result from the care or treatment of conditions related to diabetes; especially micro-and macrovascular complications (retinopathy, nephropathy, heart disease) and neuropathy [1].

While genetic predisposition is constantly gaining ground, with more than 60 polymorphisms being linked to diabetes development, as a whole they can explain only 10% of the disease’s inheritance [2], shifting the burden to environmental risk factors. Obesity, physical inactivity and poor nutrition are considered among the most important risk factors [1]; thus lifestyle changes constitute the cornerstone of the global response to the disease, with weight loss, medical nutrition therapy, regular exercise and smoking cessation being of the utmost importance for individuals with diabetes [3-7]. However, in terms of primary prevention, the long term effect of various dietary and biochemical parameters is not fully established. Specifically, the dietary pattern and exercise module that offer the greatest protection against diabetes onset, as well as the link of alcohol and coffee with the disease, particularly the quantity at which they could act beneficially, remain to be elucidated.

Thus, and under the context of the ATTICA study, the purpose of the present work was to investigate the long term effect of several dietary habits (adherence to the Mediterranean diet, coffee and alcohol consumption) and physical activity on 10-year diabetes incidence, in a Greek sample of cardiovascular free adults.

Methods
Baseline sampling procedure (2001-2002)
The ATTICA study is a large-scale, health and nutrition, prospective survey, which was carried out during 2001-2002, in the province of Attica, where Athens is a major metropolis. People with history of CVD or other atherosclerotic disease, or having chronic viral infections or living in institutions were excluded from participation. Of the initially invited 4056 individuals and after excluding those with CVD (i.e., n=117) or those having chronic viral infections (n=107), 3042 finally agreed to participate.
(75% participation rate); 1514 of the participants were men (aged 46±13 years; range 18-87 years) and 1528 were women (aged 45±13 years; range: 18–89 years). Standardized procedures by trained personnel (i.e., cardiologists, general practitioners, dietitians and nurses) were followed for interviews of participants. More details about the aims, design and methods used in the ATTICA Study may be found elsewhere in the literature [8].

Baseline measurements
Baseline assessment included information about socio-demographic characteristics (age, sex, years of school), history of hypertension, hypercholesterolemia and diabetes, family history of CVD, dietary habits, smoking status and physical activity. Smokers were defined as those who smoked at least one cigarette per day or had quitted within the previous year; the rest were defined as non-smokers.

Weight (in Kg), height (in m), waist (in cm) and hip (in cm) circumferences, as well as clinical characteristics, were measured using standardized procedures. Arterial blood pressure was measured 3 times by using the right arm. All measurements were made at the end of the physical examination while subjects were in a sitting position for at least 30 min. Patients whose average blood pressure was ≥140/90 mmHg or those under antihypertensive medication were classified as hypertensive.

The evaluation of the nutritional habits was based on a validated semi-quantitative food-frequency questionnaire, the EPIC-Greek questionnaire that was kindly provided by the Unit of Nutrition of Athens Medical School; participants were asked to report the average intake of several food items and liquids consumed during the previous year [9]. Adherence to the Mediterranean diet was evaluated using MedDietScore (range 0-55, higher values indicating greater adherence) [10]. The tertiles of the score were calculated, yielding three categories, i.e., low, medium and high level of adherence.

Regarding coffee consumption, participants were asked about average coffee drinking habits during the preceding year. All reported types of coffee (that is, instant coffee, brewed coffee, Greek-type coffee, cappuccino or filtered coffee) were recorded in ml, and then recalculated in ml, after adjustment for 28% caffeine containment for analytical reasons. After this re-calculation, one ‘adjusted’ cup of coffee (that is, 150 ml) could be equivalent to 450 ml brewed coffee or 300 ml instant coffee. According to the observed distribution of coffee drinking pattern, four coffee categories were created: abstention, low (<250 ml/day), moderate (250–400 ml/day) and high (≥250 ml/day). However, because of the very small number of participants in the highest category (that is, n=64), the two higher groups were combined into one (≥250 ml/day). Coffee drinking of <250 ml/day was defined here as ‘casual’ and ≥250 ml/day as ‘habitual’. Information of decaffeinated coffee drinking was also recorded but not used in the analyses because of the very small number of participants reported drinking this type of coffee (n=47).

As for alcohol intake, alcoholic beverages usually consumed in Greece such as wine, beer, whisky, traditional alcoholic drinks (i.e., retsina, tsipouro, ouzo) and other spirits i.e., liqueur were recorded using a seven-day food record. For the present analyses, alcohol intake was categorized into five groups: abstention; low intake (>0 but <1 glass/day); moderate intake (1–2 glasses/day); high (>2 but <4 glasses/day); very high (> 4 glasses/day). One standard glass was the equivalent of 12g of alcohol. Due to the very small number of participants in the highest category (n = 28), again the two highest classes were combined into one (>2 glasses/day). Daily alcohol intake (in g) was calculated using food composition tables [11].

Physical activity was assessed through a translated version of the validated “International Physical Activity Questionnaire” (IPAQ), suitable for assessing population levels of self-reported physical activities [12]. The short version of IPAQ (7 items) that we used provided information on weekly time spent walking, in vigorous intensity, moderate intensity and sedentary activity. Participants were instructed to refer to all domains of physical activity and report only episodes of activities of at least 10 minutes, since this is the minimum required to
achieve health benefit. After, the sum of MET (Metabolic Equivalent of Task) minutes/week was calculated for each participant, and the quartiles of MET minutes/week were constructed, yielding four categories, i.e. very low, low, moderate and high physical activity level. This type of analysis was preferred in order to quantify total physical activity across all domains and thus provide an overall picture of physical activity's effect on diabetes development.

Biochemical measurements were carried out in the same laboratory that followed the criteria of the World Health Organization Lipid Reference Laboratories. Blood samples were collected from the antecubital vein between 8 to 10 a.m., in a sitting position after 12 hours of fasting and avoiding of alcohol. Serum total cholesterol, HDL-cholesterol, triglycerides and glucose concentrations were measured using chromatographic enzymic method in a Technicon automatic analyser RA-1000. LDL cholesterol calculated using the Friedewald formulae. Hypercholesterolemia was defined as total serum cholesterol concentrations >200 mg/dL or the use of lipid-lowering agents. Diagnosis of diabetes mellitus (type 2) was based on the criteria of the American Diabetes Association [13], i.e., fasting blood glucose >125 mg/dL or the use of antidiabetic medication. Serum insulin concentrations were assayed by means of radioimmunoassay. Inflammatory markers were assayed using the following techniques: C-reactive protein (CRP) and Serum Amyloid-A (SAA) by particle-enhanced immunonephelometry, interleukin 6 (IL-6) by a high-sensitivity enzyme-linked immunoassay, human tumor necrosis factor -a (TNF-a) by the enzyme-linked immunosorbent assay method for the quantitative determination, homocysteine levels by an automatic analyzer based on the technology of fluorescence polarization immunoassay and fibrinogen by automatic nephelometry.

10-year follow-up (2011-2012)

During 2011-2012, the 10-year follow-up was performed. Of the n=3042 participants, n=2583 completed the follow-up (85% participation rate). Diagnosis of diabetes was based on ADA criteria, as performed in the baseline examination. Participants who did not provide biological samples-those who were reached only by telephone-were asked whether they had been diagnosed by a physician. Participants with diabetes at baseline (n=210) or with no information about diabetes status at the 10-year follow up (n=1347) were excluded for these analyses, yielding to a final sample of n=1485 subjects. Statistically, but not clinically significant, differences between our working sample (n=1485 individuals) and participants who were not included in these analyses (n=1347 participants), existed for age (43±13 vs. 45±13 years, p<0.001), hypertension status (30% vs. 26%, p=0.036), smoking status (58% vs. 54%, p=0.028), fasting glucose (88±12 vs. 80±13, p=0.005) and fasting insulin (12±3.0, 13±3.4μU/ml, p=0.014). No statistical significant differences existed for sex, years of education, hypercholesterolemia, family history of diabetes and BMI (ps>0.05). Further details about the baseline procedures and the 10-year follow-up of the study have been presented elsewhere [8, 14].

Statistical analysis

Incidence of diabetes was calculated as the ratio of new cases (n=191) to the total number (n=1485) of participants in the follow-up. Continuous variables are presented as mean values ± standard deviation and categorical variables as frequencies. Associations between categorical variables were tested using chi-squared test. Comparisons of mean values of normally distributed variables between those who developed diabetes and the rest of the participants were performed using Student’s t-test, after ensuring equality of variances using Levene’s test. For non-normally distributed variables, the Kruskall-Wallis test was applied, and next the Mann-Whitney test was performed between every two groups, so as to detect significant mean differences. Continuous variables were tested for normality through histograms. Multivariate logistic regression analysis was performed to evaluate independent associations. This type of analysis was preferred (instead of survival) because there were no accurate data about diabetes
Table 1. Demographic, lifestyle, clinical and biochemical factors among ATTICA participants, by T2DM status, at the 10-year follow up (n=1485).

<table>
<thead>
<tr>
<th></th>
<th>Did not develop T2DM (n = 1294)</th>
<th>Developed T2DM (n = 191)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>44±13</td>
<td>53±11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>629 (49)</td>
<td>97 (51)</td>
<td>0.57</td>
</tr>
<tr>
<td>Education, years</td>
<td>13±3.4</td>
<td>11±3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smokers now, n (%)</td>
<td>702 (54)</td>
<td>100 (52)</td>
<td>0.62</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>88±12</td>
<td>95±14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>13±3.4</td>
<td>14±3.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of T2DM, n (%)</td>
<td>230 (20)</td>
<td>61 (36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertensive, n (%)</td>
<td>333 (27)</td>
<td>82 (46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemic, n (%)</td>
<td>475 (37)</td>
<td>106 (56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Energy intake, kcal/day</td>
<td>2335±917</td>
<td>2616±1095</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Lifestyle behaviors

| MedDietScore (range 0-55)      | 26±6.8                          | 24±6.4                   | <0.001|
| Physically active, n (%)       | 552 (43)                        | 73 (38)                  | 0.25  |
| Coffee drinking (ml/day)       | 117±123                         | 103±123                  | 0.004 |
| Alcohol intake (g/day)         | 14±16                           | 21±16                    | <0.001|

Anthropometric indices

| BMI, kg/m²                     | 26±4.0                          | 29±5.0                   | <0.001|
| Waist circumference (cm)       | 88±14                           | 98±16                    | <0.001|
| Visceral obesity, as WC ≥102/88cm for men and women | 303 (27)                        | 92 (57)                  | <0.001|
| Visceral obesity, as WC ≥94/80cm for men and women | 598 (54)                        | 129 (80)                 | <0.001|

Inflammatory markers

| CRP, mg/L                      | 1.7±2.3                         | 2.7±2.8                  | <0.001|
| IL-6, pg/mL                    | 1.4±0.49                        | 1.6±0.42                 | <0.001|
| TNF-a, pg/mL                   | 6.1±4.4                         | 6.8±3.6                  | <0.001|
| Fibrinogen, mg/dL              | 302±66                          | 336±77                   | <0.001|
| SAA, mg/dL                     | 4.4±4.6                         | 4.6±3.8                  | 0.05  |
| Homocysteine, μmol/L           | 12±6.6                          | 12±5.5                   | 0.15  |

Data are presented as mean values and standard deviations for continuous variables; and absolute and relative frequencies for categorical variables. P-values derived from Student’s t-test for the normally distributed variables and Mann-Whitney test for the non-normally distributed variables (i.e., years of school, MedDietScore, fasting insulin, inflammatory markers), or chi-square test for the categorical variables.
onset, but only diagnosis. As previously demonstrated, the estimation of the odds ratio approximated the relative risk given an infrequent disease occurrence [15]. All known confounders were included in the models after testing for collinearity. Finally, interactions with the parameter of interest were checked in all steps, and when significant sub-group analyses were performed. The SPSS version 18 (Statistical Package for Social Sciences, IBM Hellas SA, Greece) software was used for all statistical calculations.

Results

10-year diabetes incidence

During the 10-year follow-up period, 191 diabetes cases were documented; yielding a crude incidence of 129 per 1000 participants (or 12.9%); of them, 97 (13.4%) were men and 94 (12.4%) were women (p=0.79 for gender difference).

The distribution of baseline demographic, lifestyle, clinical and biochemical parameters of ATTICA study participants, based on their diabetes status at the 10-year follow up is presented in Table 1. Unadjusted analysis revealed that people who developed diabetes were approximately 10 years older, less educated, had higher mean fasting glucose and insulin values; they were more likely to have family history of diabetes, hypertension and hypercholesterolemia. Also, they exhibited lower adherence to the Mediterranean diet and coffee consumption but higher alcohol consumption. No clinically or statistically significant differences existed for smoking status, energy intake or physical activity between the two groups. Individuals who developed diabetes had additionally higher mean BMI and waist circumference and they were more likely to have visceral obesity, defined as WC ≥94/80cm or ≥102/88cm. Finally, the group that developed diabetes had higher baseline mean CRP, IL-6, fibrinogen and TNF-a values, whereas SAA or homocysteine did not differ significantly.

In order to evaluate the association of lifestyle factors with 10-year diabetes risk, nested logistic regression models were constructed for each variable of interest. In Table 2, the results of fully adjusted models are presented for each variable:

- **Adherence to the Mediterranean diet:** individuals with medium adherence to the Mediterranean diet experienced 49% lower risk of developing diabetes, within the next 10 years (RR=0.51; 95%CI: 0.30, 0.88), whereas for individuals with high adherence, the risk was found decreased by 62% (RR=0.38; 95%CI: 0.16, 0.88), compared to participants with low level of adherence to the pattern. The interaction between MedDietScore and WC category was found significant (p=0.045) and was kept in the final model. Also, the analysis was repeated after stratification by WC, i.e., n=727 participants with increased WC (WC>94cm for men and >80cm for women) versus n=549 participants with normal WC. In the fully adjusted model, the protective effect remained only among participants with increased abdominal fat (RR=0.44, 95%CI: 0.25, 0.77 for medium adherence to the Mediterranean diet, and RR=0.26, 95%CI: 0.10, 0.70 for high adherence). For individuals with normal WC, results were not significant (RR=0.97, 95%CI: 0.29, 3.25 and RR=0.89, 95%CI: 0.16, 4.90 for medium and high adherence respectively).

- **Coffee consumption:** individuals who drank ≥250ml coffee daily experienced 54% lower risk of developing diabetes within 10 years, as compared to coffee abstainers (OR=0.46; 95%CI: 0.24, 0.90). When caffeinated drinks consumption (i.e., tea, cola) was taken into account, the protective association of coffee drinking was not altered; however significance was marginally reached (OR for ≥250ml coffee daily vs. abstainers =0.23; 95%CI: 0.04, 1.04). For casual coffee drinking results were not significant.

- **Alcohol consumption:** individuals who consumed <1 glass alcohol daily experienced 53% lower risk of developing T2DM within 10 years, as compared to alcohol abstainers (OR=0.47; 95%CI: 0.26, 0.83). However, moderate and high alcohol intake were not significantly associated with diabetes development (OR=1.05; 95%CI: 0.57, 1.93 and OR=1.25; 95%CI: 0.65, 2.37, respectively).

- **Physical activity:** participants with moderate physical activity level (MET minutes/week 331-
Table 2. Results from multiple logistic regression models (ORs and the corresponding CIs) that evaluated the association of various parameters with 10-year diabetes incidence, among ATTICA study participants (n=1485).

<table>
<thead>
<tr>
<th>Lifestyle behaviors</th>
<th>Tertile 1 (Low) (n=490)</th>
<th>Tertile 2 (Medium) (n=518)</th>
<th>Tertile 3 (High) (n=477)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases; incidence</strong></td>
<td>105; 21%</td>
<td>62; 12%</td>
<td>24; 5%</td>
</tr>
</tbody>
</table>
| **Fully adjusted model**
  a adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, education, physical activity and abnormal WC (i.e. WC>94 cm for men or>80 cm for women) | Reference | 0.51; 0.30, 0.88 | 0.38; 0.16, 0.88 |
| **Coffee consumption**                     | 0 ml/day (Abstention) (n=239) | <250 mL/day (Casual) (n=816) | ≥250 ml/day (Habitual) (n=385) |
| **Cases; incidence**                       | 23; 9.6%                | 57; 7%                    | 20; 5.2%                |
| **Fully adjusted model**
  b adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, education, physical activity, WC and adherence to the Mediterranean diet | Reference | 0.66; 0.39, 1.11 | 0.46; 0.24, 0.90 |
| **Alcohol consumption**                    | 0 glass/day (Abstention) (n=592) | 0 to < 1 glass/day (Low) (n=366) | 1–2 glasses/day (Moderate) (n=208) | >2 glasses/day (High) (n=137) |
| **Cases; incidence**                       | 100; 17%                | 21; 5.7%                  | 29; 14%                 | 23; 17%                 |
| **Fully adjusted model**
  c adjusted for confounders of models b,c plus fasting glucose and triglycerides | Reference | 0.47; 0.26, 0.83 | 1.05; 0.57, 1.93 | 1.25; 0.65, 2.37 |
| **Physical activity (MET-min/ wk)**        | Very low (<150) (n=509) | Low (150 – 330) (n=334) | Moderate (331 – 1484) (n=271) | High (>1484) (n=371) |
| **Cases; incidence**                       | 68; 13%                 | 48; 14%                   | 25; 9%                  | 50; 14%                 |
| **Fully adjusted model**
  d adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, physical activity and adherence to the Mediterranean diet | Reference | 0.77; 0.41, 1.49 | 0.47; 0.24, 0.93 | 1.04; 0.59, 1.82 |

<table>
<thead>
<tr>
<th>Inflammation status</th>
<th>Tertile 1 (0.01 – 0.58)</th>
<th>Tertile 2 (0.59 – 1.60)</th>
<th>Tertile 3 (1.61 – 15.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRP (mg/dL)</strong></td>
<td>35; 8.5%</td>
<td>44; 10.9%</td>
<td>80; 19.5%</td>
</tr>
</tbody>
</table>
| **Fully adjusted model**
  e adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, physical activity, WC and adherence to the Mediterranean diet | Reference | 0.87; 0.51, 1.50 | 1.46; 0.89, 2.40 |
| **IL-6 (pg/mL)**                           | Tertile 1 (0.3 – 1.25) | Tertile 2 (1.26 – 1.46) | Tertile 3 (1.47 – 7.1) |
| **Cases; incidence**                       | 21; 4.9%                | 39; 9.8%                 | 100; 23.4%              |
| **Fully adjusted model**
  f adjusted for age, sex, family history of diabetes, hypertension, hypercholesterolemia, smoking status, physical activity and adherence to the Mediterranean diet | Reference | 1.07; 0.55, 2.08 | 2.20; 1.13, 4.28 |

P<0.001
1484, e.g. half an hour of walking 4 days/week -
1 hour of walking everyday) had 44% lower 10-
year diabetes risk, compared to participants with
very low physical activity level (MET minutes/
week <150) (OR=0.56, 95% CI: 0.34, 0.92). For par-
ticipants in low and high physical activity groups
an inverse trend were observed, though not statisti-
cal significant.

• Inflammation status: the role of chronic sub-
clinical inflammation was also investigated. Elevat-
ed IL-6 levels increased by 2.2 times the 10-year
diabetes risk (OR3rd vs. 1st tertile=2.2, 95%CI: 1.13,
4.28), whereas for CRP results were not significant
in the fully-adjusted model. Interestingly, when
IL-6 model was further adjusted for BMI, statistical
significance was lost, indicating the potential medi-
ating effect of obesity in inflammation-diabetes link
(OR=1.30; 95%CI: 0.65, 2.60). For all other inflam-
matory markers results were not significant even in
age-sex adjusted models (results not shown).

Discussion
Diabetes is a chronic complex disease with a signif-
icant lifestyle basis. In the present work the 10-year
diabetes incidence was studied in relation to vari-
ous lifestyle factors. Medium and high adherence
to the Mediterranean diet, were found protective.
Firstly, even moderate adherence to the Mediterra-
ean diet was found to significantly decrease diabe-
tes risk by approximately 50%, which is very impor-
tant from a public health point of view, since even
small dietary changes are enough to achieve moder-
ate adherence to the pattern. In addition to this, the
benefit was maximized for individuals with viscer-
al obesity, a finding which was further confirmed by
the mediating effect of obesity in inflammation-diabetes relationship. With regards to the rest lifestyle
parameters, habitual coffee consumption (≥250ml/
day, i.e. 3 cups of brewed or 2 cups of instant cof-
f), low alcohol consumption (<1 glass/day, i.e.,
<120ml wine, 330ml beer or 45 ml of whisky, vod-
ka, gin etc) and moderate physical activity levels
(351-1484 MET-minutes; corresponding, for exam-
ples, to almost 30-60 minutes of walking 4-7 times/
week or 30-50 minutes of moderate intensity physi-
cal activity 3-7 times/week or 20-40 minutes of vig-
orous physical activity 2-5 times/week) were also
found to confer significant antidiabetic protection.
Despite the limitations of the present observational
study, the large, representative sample, the prospec-
tive design and follow-up of 10 years, as well as the
detailed assessment of lifestyle information, and,
therefore, the ability to adjust for several known
confounders, may guarantee that the reported find-
ings are of considerable public health importance,
as they shed light into the extent at which several
modifiable risk factors can decrease diabetes risk,
as well as the importance of obesity in the initia-
tion and/ or aggravation of inflammatory diathesis.

The aforementioned risk factors have been pre-
viously linked to a lower diabetes incidence. The
beneficial effect of the Mediterranean diet, also re-
ported in a meta-analysis of 10 prospective stud-
ies [16], may be ascribed among others to the pat-
tern’s increased content in dietary fiber, which
lower glucose absorption, mitigating insulin se-
cretion need [17], magnesium, an inadequacy of
which increases insulin resistance [18], as well as
antioxidants, which inhibit oxidative damage in
sensitive b-cells [19]. De Koning et al, have also
observed that Mediterranean diet yields its ben-
efit among individuals with high BMI [20], which
is in line with our findings. Indeed, under obesity
state fat tissue becomes the major producer of in-
flammatory molecules [21], which chronically get
implicated in the sustainment or aggravation of in-
sulin resistance [22]. Of the proposed inflammat-
ory markers in this work, IL-6 and CRP have been
well documented to independently increase dia-
betes risk, which was confirmed by a recent me-
ta-analysis [23]. In relation to the composite ef-
teffects CRP-IL-6 combined effect was expected, due
to the single aggravating effect of both markers,
however, this is the first study to document the
potential combined action of two acute phase pro-
teins, CRP and fibrinogen on diabetes incidence.
In relation to coffee consumption, consistency ex-
ists regarding its effect on diabetes development
[24, 25]. Coffee, a mixture of caffeine, chlorogenic
acid, micronutrients, helps maintain normal glu-
cose tolerance, improves insulin sensitivity, stimulates pancreatic insulin secretion and inhibits of glucose-6-phosphatase, which releases glucose to circulation [26]. Despite its observed beneficial effect, coffee should always be consumed in moderation, depending on individuals need, and not overconsumption is suggested. Alcohol’s protective effect at low doses has also been shown in previous studies [6, 27], which is mostly ethanol-related, since no significant differences have been proposed between types of drinks [28]. Alcohol increases anti-inflammatory adiponectin [29] and decreases plasma glucose and insulin [30] and fetuin-A, a glucoprotein implicated in disturbance of insulin signaling [31]. Last but not least, exercise normalizes liver and skeletal muscle insulin resistance, not only by itself but also through weight loss process [32]. Similarly to our findings, a very recent meta-analysis of 55 studies, concluded that the greatest antidiabetic benefit is attained in medium levels of physical activity [33].

Limitations
Regardless of the aforementioned findings, we cannot rule out the limitations of an observational study. Firstly, the baseline evaluation was performed once, and may be prone to measurement error. Also, for some individuals diabetes diagnosis was based upon self-report and/or physician-diagnosis, but this is common for prospective studies. Moreover, the accurate date of diabetes development was not accessible (only the date of diagnosis was identified); as a result hazard ratios were estimated through ORs that may have overestimated the true effect; however, it has been reported that, for low frequency diseases, OR is an accurate estimate (converges) of the relative risk. Another concern in prospective studies is that many lifestyle factors (i.e., physical activity, energy intake) may have changed during the 10-year time period without timely information updates.

Conclusions
In conclusion, the current study has provided additional evidence in the literature concerning the effect of lifestyle parameters on 10-year incidence of type 2 diabetes mellitus. The presented results carry a hopeful public health message suggesting that even medium adherence to different health behaviors can lead to a clinically significant reduction in diabetes risk. Targeting individuals who are very far from the Mediterranean diet or very sedentary might be particularly important from a public health perspective. It is consequently imperative to promote strategies to achieve small dietary changes and increase physical activity levels especially among obese and/or inactive individuals, while it is also important to recognize facilitators and barriers that patients with established prediabetes deal with, in terms of diet and physical activity compliance.

Conflict of Interest
All authors declare no conflict of interest.

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Περίληψη

Η μακροχρόνια επίδραση της διατροφής και άσκησης στην ανάπτυξη σακχαρώδη διαβήτη τύπου 2: 10ετής επανέλεγχος της μελέτης ΑΤΤΙΚΗ (2002-2012)

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Α Πανεπιστημιακή Καρδιολογική κλινική Ιπποκρατείου ΓΝΑ, Ιατρική Σχολή Αθηνών, ΕΚΠΑ

Σκοπός: να καταγραφεί η 10-ετής επίπτωση σακχαρώδη διαβήτη τύπου 2 και να διερευνηθεί η επίδραση των διατροφικών συνηθειών και της σωματικής δραστηριότητας στην ανάπτυξη του.

Υλικό και Μέθοδος: από τον Μάιο 2001 έως το Δεκέμβριο 2002, εντάχθηκαν στη μελέτη ΑΤΤΙΚΗ 1514 άνδρες και 1528 γυναίκες (> 18 ετών) χωρίς κλινική ένδειξη καρδιαγγειακής νόσου ή άλλης χρόνιας νόσου, που ζούσαν στην ευρύτερη περιοχή της Αθήνας. Αξιολογήθηκαν κοινωνικο-δημογραφικά, κλινικά, βιοχημικά χαρακτηριστικά και στοιχεία του τρόπου ζωής. Οι διατροφικές συνήθειες αξιολογήθηκαν μέσω έγκυρου ημι-ποσοτικού ερωτηματολογίου συχνότητας κατανάλωσης τροφίμων και η φυσική δραστηριότητα με το έγκυρο Διεθνές Ερωτηματολόγιο Σωματικής Δραστηριότητας (IPAQ). Η διάγνωση του σακχαρώδη διαβήτη ορίστηκε ως γλυκόζη> 125mg/dL ή/και χρήση αντιδιαβητικής αγωγής. Μεταξύ 2011-2012 πραγματοποιήθηκε ο 10ετής επανέλεγχος.

Αποτελέσματα: 191 περιπτώσεις σακχαρώδη διαβήτη καταγράφηκαν, διαμορφώνοντας την επίπτωση στο 12.9%. Η μέση και υψηλή προσκόλληση στη Μεσογειακή Δίαιτα μείωσε τον 10ετή κίνδυνο ανάπτξης σακχαρώδη διαβήτη κατά 49% (ΣΛ=0,51, 95%ΔΕ: 0,30, 0,88) και 62% (ΣΛ= 0,38, 95% ΔΕ: 0,16, 0,88) αντίστοιχα. Η μέτρια κατανάλωση καφέ (≥250mL/ημέρα, προσαρμοσμένο για 28% περιεκτικότητα σε καφεΐνη) και η χαμηλή κατανάλωση αλκοόλ (<1 ποτήρι/ημέρα) μείωσαν επίσης τον κίνδυνο κατά 54% (ΣΛ=0.46, 95%ΔΕ: 0.24, 0.47) και 3% (ΣΛ=0.47, 95% CI: 0.26, 0.83), σε σύγκριση με την αποχή. Τέλος, το μέτριο επίπεδο φυσικής δραστηριότητας (331-1484 έναντι <150 ΜΕΤ / εβδομάδα) οδήγησε σε μείωση κινδύνου 44% (ΣΛ=0.56, 95%ΔΕ: 0.34, 0.92).

Συμπεράσματα: η παρούσα εργασία τόνισε τη σημασία μη φαρμακολογικών παρεμβάσεων στην πρωτειογενή πρόληψη του σακχαρώδη διαβήτη. Η μεσογειακή δίαιτα, η μετριά κατανάλωση αλκοόλ και το μέτριο επίπεδο φυσικής δραστηριότητας ασκούν ευεργετική δράση ενάντια στην ανάπτξη της νόσου.

Λέξεις ευρετηρίου: συχνότητα εμφάνισης σακχαρώδη διαβήτη, μεσογειακή δίαιτα, αλκοόλ, καφές, σωματική δραστηριότητα

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