Adherence to the Mediterranean diet is inversely associated with metabolic syndrome occurrence: a meta-analysis of observational studies

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ABSTRACT
Diet plays a role in the onset and progression of metabolic disorders, including metabolic syndrome (MetS). We aimed to systematically review and conduct a quantitative meta-analysis of results from observational cross-sectional and prospective cohort studies on adherence to the Mediterranean dietary pattern and risk of MetS. Literature databases including PubMed, SCOPUS and EMBASE were searched from the beginning to May 2016. Eight cross-sectional and four prospective studies were included in this meta-analysis, accounting for a total of 33,847 individuals and 6342 cases of MetS. High adherence to the Mediterranean diet was associated with a risk of MetS (RR: 0.81, 95% CI: 0.71, 0.92). Regarding individual components of the MetS, the inverse associations were significant for waist circumference, blood pressure and low HDL-C levels. In conclusion, adoption of a Mediterranean dietary pattern was associated with lower risk of the MetS and it can be proposed for the primary prevention of the MetS.

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Introduction
The metabolic syndrome (MetS) represents a clinical condition characterized by a number of metabolic risk factors that predispose to increased risk of developing diabetes mellitus and cardiovascular disease (CVD) (Grundy et al. 2004; Alberti et al. 2009). A chronic state of subclinical inflammation seems to be a key mechanism underlying the pathophysiology of MetS. Metabolic alterations characterizing the MetS involve blood glucose, blood lipids [triglycerides and high-density lipoprotein cholesterol (HDL-C)], blood pressure and abdominal obesity. Over the past decades, several criteria for the definition of MetS have been proposed. According to the National Cholesterol Education Program-Adult Treatment Panel-III (NCEP-ATP III), diagnosis of MetS requires three or more of the following: (i) waist circumference >102 cm in men and >88 cm in women; (ii) HDL-C <40 mg/dL (<1.04 mmol/L) in men and <50 mg/dL (<1.29 mmol/L) in women; (iii) triglycerides ≥150 mg/dL (≥1.7 mmol/L); (iv) blood pressure ≥130/85 mmHg and (v) fasting glucose ≥110 mg/dL (≥6.1 mmol/L) (Grundy et al. 2004). More recently, the Joint Interim Societies (including the International Diabetes Federation Task Force on Epidemiology and Prevention, the National Heart, Lung, and Blood Institute, the American Heart Association, the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity) proposed a harmonization of the criteria maintaining the same thresholds for blood pressure, triglycerides and HDL-C, but introduced population- and country-specific cutoff points for waist circumference and modified those for fasting glucose levels [≥100 mg/dL (≥5.6 mmol/L)] (Alberti et al. 2009). Despite MetS is characterized by a variety of metabolic alteration with no univocal pathogenetic mechanism, there are genetic and environmental factors that most likely are associated to this condition (Anagnostis 2012; Di Renzo et al. 2013; Di Renzo et al. 2014b). Besides the resulting hormonal abnormalities, engagement in unhealthy food patterns and
lifestyles, such as overnutrition and sedentary lifestyle, may worsen the clinical condition, with body fat accumulation and potential disregulation of the aforementioned parameters characterizing the MetS.

A dietary pattern following the principles of the traditional eating habits of individuals living in the Mediterranean areas during 1960s has been the focus of attention over the last decades for its potential ability to prevent and ameliorate metabolic disorders, including those associated with MetS (Grosso et al. 2014c). The Mediterranean diet is characterized by a number of key features: use of olive oil as the main or exclusive culinary fat, high intake of olive oil, fruits and nuts, vegetables, non-refined cereals and legumes as main sources of fiber and plant-derived antioxidants, such as vitamins and polyphenols (Zamora-Ros et al. 2012; Zamora-Ros et al. 2013; Grosso et al. 2014d); frequent consumption of fish as the main source of proteins and poly-unsaturated fatty acids (PUFA) (Marventano et al. 2015); a high intake of monounsaturated fatty acids (MUFA) derived from olive oil, and a high MUFA to saturated fat intake (Rondanelli et al. 2015); moderate consumption of wine (mainly red), which provides limited amount of alcohol and peculiar polyphenol compounds (such as stilbenes) (Giacosa et al. 2014); low consumption of meat and sweets, as sources of unhealthy fats, such as cholesterol and trans-fatty acids (Di Daniele et al. 2014) and low consumption of butter and cream. There are several peculiar foods characterizing diet of populations living in the Mediterranean region, such as oranges (Grosso et al. 2013b), prickly pears (Silveira et al. 2015), pomegranates (Gonzalez-Trujano et al. 2015) and artichoke (Rondanelli et al. 2013). The synergic effect of all the components of the diet, rather than any individual food or nutrient, has been considered the key for the success of this dietary pattern in improving human health and prolonging lifespan (Giacosa et al. 2013; Sofi et al. 2014). The peculiar profile of the MUFA:SFA ratio and the high intake of PUFA characterizing the Mediterranean diet, as well as the high content in fiber, antioxidants and polyphenols with anti-inflammatory properties, have been associated with lower risk of obesity and an overall better metabolic status (Abenavoli et al. 2014; Shin et al. 2015). Despite the evidence on the beneficial effect of the MedDiet on individual components of the MetS is convincing (Kastorini et al. 2011), no summary quantitative analyses have been conducted on population studies to explore whether this dietary pattern may exert preventive effects toward MetS itself. Thus, the aim of this study was to systematically review and perform meta-analysis of existing observational studies exploring the relation between adoption of a Mediterranean dietary pattern and the prevalence or the risk of MetS.

Methods

Search strategy and study selection

Literature databases including PubMed, SCOPUS and EMBASE were searched from the beginning through May 2016. Relevant keywords associated with Mediterranean diet ("mediterranean diet") were searched in combination with keywords associated with MetS ("metabolic syndrome” or “metabolic impairment” or “x syndrome” or “metabolic disease”) in combination with keywords relevant to the study methods ("incidence” or “cohort” or “follow-up” or “association”). Reference lists of retrieved articles were manually searched for missing citations. The literature search was limited to English. If more than one article was published using the same cohort, the most recent article with the longest follow-up period was considered. Studies included in this meta-analysis met the following inclusion criteria: (i) evaluated the risk or association between Mediterranean diet adherence and occurrence or risk of MetS with a prospective or case-control/cross-sectional design; (ii) used an a priori method to evaluate adherence to the diet; (iii) clearly defined the category of exposure (high versus low adherence) and provided risk measures. Articles were excluded if they did not report sufficient statistics. Two authors (JG and GZ) independently assessed the articles for compliance with the inclusion and exclusion criteria and solved disagreements through consensus.

Data extraction

The following information was extracted from each study: (i) name of the first author; (ii) year of publication; (iii) study cohort or name; (iv) country; (v) number of participants and cases; (vi) gender and age of the study population at baseline; (vii) follow-up period; (viii) endpoints and cases; (ix) diet adherence score; (x) MetS criteria; (xi) odds ratios (ORs) or hazard ratios (HRs) with 95% confidence intervals (CIs) of MetS and its components for the highest adherence versus the lowest category of exposure and (xii) covariates used in adjustments.

The quality of observational studies was assessed according to the Newcastle–Ottawa quality assessment scale (Wells et al. 1999), consisting of three parameters of quality: selection (four points), comparability
(two points) and outcome (three points), with a score of seven or more points reflecting high quality.

**Exposure and outcome measures**

Adherence to a Mediterranean was defined through scores that estimated the conformity of the dietary pattern of the studied population with the traditional Mediterranean dietary pattern (Davis et al. 2015). Overall, people more adherent to the Mediterranean diet were considered those included in the highest quantile of the score used in each study.

MetS was defined according the criteria set up by the study researchers in each included study. When the study provided also risk estimates for individual criteria included in the definition of MetS, we also performed separate meta-analyses for each of these outcomes to test whether the association with adherence to the Mediterranean diet was relying on a specific clinical feature rather than on the overall condition.

**Statistical analysis**

In this meta-analysis, ORs and HRs were deemed equivalent to relative risks (RRs) (Greenland 1987). ORs or HRs with 95% CIs for all categories of exposure were extracted for the analysis and random-effects models were used to calculate pooled RRs with 95% CIs for the highest compared with the lowest category of exposure. Heterogeneity was assessed by using the $Q$ test and $I^2$ statistic. The $I^2$ statistic represents the amount of total variation that could be attributed to heterogeneity. $I^2$ values <25%, <50% and <75% indicated little, moderate and significant heterogeneity, respectively. A sensitivity analysis was conducted by excluding one study at a time and by grouping studies by design, gender, sample size, Mediterranean diet assessment tool, MetS criteria and adjustment for diet-related (i.e. total energy intake) and health-related (i.e. history of CVD) variables. Publication bias was assessed by visual observation of funnel plot. All analyses were performed with Review Manager (RevMan) version 5.2 (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration).

**Results**

**Study characteristics**

The full process of identification and selection of studies is shown in Figure 1. The relevance of studies was assessed with a hierarchical approach on the basis of title, abstract and the full manuscript. Of the 21 studies considered relevant, 9 were excluded for the following reasons: 1 study had different design; 1 study evaluated different outcomes; 5 studies defined the Mediterranean dietary pattern through principal component analysis; 2 studies reported insufficient statistics. Overall, eight cross-sectional (Panagiotakos et al. 2004; Alvarez Leon et al. 2006; Babio et al. 2009; Gouveri et al. 2011; Grosso et al. 2014a; Grosso et al. 2015b; Veissi et al. 2016) and four prospective studies (Kesse-Guyot et al. 2013; Steffen et al. 2014; Mirmiran et al. 2015; Pimenta et al. 2015) were included in this meta-analysis, accounting for a total of 33,847 individuals and 6342 cases of MetS.

The main characteristics of the 12 studies included are presented in Table 1. Most studies comprised individuals of age ranging from 20–70 years old, while 1 study (Steffen et al. 2014) was conducted solely on younger participants (18–30 years old). Seven studies (Panagiotakos et al. 2004; Alvarez Leon et al. 2006; Babio et al. 2009; Gouveri et al. 2011; Kesse-Guyot et al. 2013; Grosso et al. 2014a; Pimenta et al. 2015) were conducted in Mediterranean countries, five involved individuals living in non-Mediterranean countries (Steffen et al. 2014; Grosso et al. 2015b; Mirmiran et al. 2015; Veissi et al. 2016). One study explored Mediterranean diet adherence in patients at high CVD risk (Babio et al. 2009), one was conducted on diabetic individuals (Veissi et al. 2016).
| Author, year | Cohort, country | No subjects/ No cases | Age, gender | Population characteristics | MED diet assessment | MetS criteria | Follow-up | Adjustments |
|-------------|-----------------|----------------------|-------------|---------------------------|-------------------|--------------|-----------|-------------|
| Cross-sectional<br>PanagiotaKos et al. 2004<br>Alvarez Leon et al. 2006<br>Babio et al. 2009<br>Gouveri et al. 2011<br>Yang et al. 2014<br>Grosso et al. 2014a<br>Grosso et al. 2015b<br>Veissi et al. 2016<br>Prospective<br>Kesse-Guyot et al. 2013<br>Pimenta et al. 2015<br>Steffen et al. 2014<br>Mirmiran et al. 2015 | ATTICA, Greece<br>ENCA, Spain<br>Reus-PREDIMED, Spain<br>Athens Study, Greece<br>USA<br>Italy<br>HAPIEE, Poland<br>Iran<br>SU.VI.MAX, France<br>SUN, Spain<br>CARDIA, USA<br>TLGS, Iran | 2282/453<br>578/141<br>808/505<br>2074/538<br>780/135<br>1889/226<br>8821/2461<br>158/131<br>3232/214<br>6851/346<br>4713/946<br>1661/246 | >18, M and F<br>18, M and F<br>Up to 80 y, M and F<br>46.0 (average), M and F<br>18, M<br>50.2 (average), M and F<br>45–69, M and F<br>54.3 (average)/M and F<br>49 (average), M and F<br>30–70, M and F<br>18–30, M and F<br>18–74, M and F<br> | General population with no evidence of CVD or diabetes<br>General population<br>High CVD risk patients<br>General population<br>Firefighters<br>General population<br>General population<br>General population<br> | Trichopoulou score (14-point)<br>Specific score (10-point)<br>Trichopoulou score (14-point)<br>Trichopoulou score (14-point)<br>Specific score (42-point)<br>Panagiotakos score (55-point)<br>Modified Panagiotakos score (60-point)<br>Panagiotakos score (55-point)<br>Trichopoulou score (14-point)<br>Modified Trichopoulou score (19-point)<br>Trichopoulou score (8-point)<br> | NCEP-ATP III<br>NCEP-ATP III<br>NCEP-ATP III<br>NCEP-ATP III<br>Joint Interim Societies<br>International Diabetes Federation<br>International Diabetes Federation<br>International Diabetes Federation<br>Joint Interim Societies<br>Joint Interim Societies<br>NCEP-ATP III<br>Joint Interim Societies<br> | NA<br>NA<br>NA<br>NA<br>NA<br>NA<br>NA<br> | Age, sex, smoking habits, educational status, several biochemical measurements,<br>Sex, age, educational level, physical activity level, BMI, tobacco consumption, diet in the past 12 months and energy intake<br>Sex, age, energy intake, smoking, physical activity, BMI<br>Age, sex, smoking, light physical activity, serum levels of LDL cholesterol and gamma-glutamyl transferase, CVD, type-2 diabetes, family history of hypertension and/or hyperlipidemia, age, physical activity.<br>Gender, age, BMI, educational level, socio-economic status, energy intake, smoking status, alcohol drinking, physical activity level, caffeine, source of caffeine.<br>Age, sex, education, occupation, physical activity, smoking status, alcohol drinking, total energy intake.<br>Age, sex, energy, macronutrient intake, physical activity.<br>Age, sex, supplementation group, energy intake, education level, tobacco smoking status, physical activity.<br>Age, sex, total energy intake, physical activity, smoking, special diets, eating between meals, and BMI at baseline<br>Age, sex, race, field center, education, energy intake, current smoking status, physical activity, vitamin/mineral supplement use, BMI, waist circumference at baseline.|
Adherence to the Mediterranean diet was assessed using scores mainly based on those developed by Trichopoulou (Panagiotakos et al. 2004; Babio et al. 2009; Steffen et al. 2014; Mirmiran et al. 2015; Pimenta, et al. 2015) and Panagiotakos (Gouveri et al. 2011; Grosso et al. 2014a; Grosso et al. 2015b; Veissi et al. 2016), while two studies (Alvarez Leon et al. 2006; Yang et al. 2014) developed their own ad hoc scores. The most used criteria for MetS were the NCEP-ATP III, while three studies (Grosso et al. 2014a; Grosso et al. 2015b; Veissi et al. 2016) used the International Diabetes Federation criteria and four studies (Steffen et al. 2014; Yang et al. 2014; Mirmiran et al. 2015; Pimenta, et al. 2015) the Joint Interim Societies ones. All studies included covariates that are considered to have significant influence on cardiovascular outcomes such as age, sex (when not analyzed separately), BMI, physical activity and smoking status. Furthermore, eight studies (Alvarez Leon et al. 2006; Kesse-Guyot et al. 2013; Grosso et al. 2014a; Steffen et al. 2014; Grosso et al. 2015b; Mirmiran et al. 2015; Pimenta, et al. 2015; Veissi et al. 2016) adjusted also for diet-related variables. Overall, all studies scored high quality.

**Association of Mediterranean diet and MetS**

Fourteen datasets from all 12 studies were pooled together to estimate the association between adherence to the Mediterranean diet and MetS. High adherence was inversely associated with decreased risk of MetS (RR: 0.81, 95%CI: 0.71, 0.92) compared to lowest adherence (Figure 2), with significant evidence of heterogeneity ($I^2=74\%$, $p < .001$) but no asymmetry of funnel plot (Supplementary Figure 1). Sensitivity analyses conducted by removing one study at a time showed that heterogeneity was driven mainly by one study (Babio et al. 2009), after exclusion of which results were substantially identical but without residual heterogeneity. Reason for such heterogeneity may depend on the fact that the study of Babio et al. (2009) was conducted on high CVD risk individuals, which may have a different sensibility to the potential effects of adherence to the Mediterranean diet. When considering studies by design, the association was found in both cross-sectional and prospective studies, despite with evidence of significant heterogeneity (Figure 2). Among the former, the contrasting results were due to the aforementioned study by Babio et al. (2009), while none of the prospective studies was primarily contributing to the heterogeneity. Stratification of analyses by variables of interest revealed that results were stable and significant when including studies with larger samples conducted on general population (rather than high CVD-risk patients) and using the Joint Interim Societies criteria for MetS (Table 2). Despite there was no difference in effect size either using the Trichopoulou or the Panagiotakos Mediterranean diet score, findings of studies adopting the latter definition resulted less heterogeneous (Table 2).

**Association of Mediterranean diet and MetS components**

A separate analysis was performed to evaluate the association between adherence to the Mediterranean diet and individual components of the MetS were

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**Figure 2.** Forest plot of summary RRs of MetS for the highest versus lowest (reference) category of adherence to the Mediterranean diet, by study design.
Table 2. Subgroup analyses of studies reporting occurrence or risk of MetS for the highest versus lowest (reference) category of adherence to the Mediterranean diet.

| Subgroup                        | Number of datasets | RR (95%CI) | I² | p heterogeneity |
|---------------------------------|--------------------|------------|----|----------------|
| Total                           | 14                 | 0.81 (0.71, 0.92) | 74% | <.001          |
| Study design                    |                    |            |    |                |
| Cross-sectional                 | 10                 | 0.84 (0.73, 0.97) | 71% | <.001          |
| Prospective                     | 4                  | 0.73 (0.54, 0.98) | 69% | .02            |
| Gender                          |                    |            |    |                |
| Men                             | 3                  | 0.69 (0.47, 1.03) | 66% | .05            |
| Women                           | 2                  | 0.93 (0.76, 1.14) | 78% | .03            |
| No. of participants             |                    |            |    |                |
| <1000                           | 5                  | 0.88 (0.62, 1.26) | 69% | .01            |
| >1000                           | 9                  | 0.79 (0.70, 0.88) | 42% | .09            |
| Geographical location           |                    |            |    |                |
| Mediterranean                   | 8                  | 0.79 (0.65, 0.96) | 80% | <.001          |
| Non-Mediterranean               | 6                  | 0.82 (0.72, 0.93) | 17% | .31            |
| Study population                |                    |            |    |                |
| General population              | 11                 | 0.79 (0.70, 0.89) | 45% | .06            |
| Patients with CVD risk factors  | 3                  | 0.86 (0.45, 1.64) | 71% | .03            |
| Mediterranean diet toola        |                    |            |    |                |
| Tricopoulou score               | 7                  | 0.77 (0.63, 0.95) | 82% | <.001          |
| Panagiotakos score              | 5                  | 0.83 (0.73, 0.96) | 21% | .28            |
| MetS criteria                   |                    |            |    |                |
| ATP III                         | 6                  | 0.83 (0.69, 1.01) | 78% | <.001          |
| International Diabetes Federation | 4           | 0.84 (0.69, 1.04) | 38% | .19            |
| Joint Interim Societies         | 4                  | 0.72 (0.53, 0.99) | 69% | .02            |
| Adjustment for:                 |                    |            |    |                |
| Smoking status                  | 13                 | 0.81 (0.71, 0.93) | 75% | <.001          |
| Diet-related variables          | 9                  | 0.79 (0.66, 0.95) | 59% | .02            |

*Including modified versions.

provided in four studies (Alvarez Leon et al. 2006; Babio et al. 2009; Grosso et al. 2015b; Mirmiran et al. 2015) (six datasets) (Figure 3). The resulting associations were significant for waist circumference (RR =0.82, 95%CI: 0.70, 0.96; I² =22%, p for heterogeneity =.27), blood pressure (RR =0.87, 95%CI: 0.77, 0.97; I² =0%, p for heterogeneity =.77) and HDL-C levels (RR =0.87, 95%CI: 0.77, 1.00; I² =0%, p for heterogeneity =.50) with no significant evidence of heterogeneity and asymmetry of funnel plot in any of the analysis (Supplemental Figure 1). The analysis on serum triglycerides showed an inverse non-significant association with high adherence to the Mediterranean diet (RR =0.84, 95%CI: 0.70, 1.01; I² =44%, p for heterogeneity =.11) with little evidence of heterogeneity due to the results of one study (Babio et al. 2009), after exclusion of which the association was not significant. Null results were found for the association between Mediterranean diet and blood glucose criterion for MetS (Figure 3).

Discussion

In the present meta-analysis, a significant and consistent inverse association between adherence to the Mediterranean diet and the risk of MetS was found all over the population and cohort studies investigated. Previous meta-analyses on Mediterranean diet and MetS have been conducted only on a limited number of studies or only on each specific criteria but not on the overall syndrome (Kastorini et al. 2011), while this is the first time that a quantitative meta-analysis using the overall MetS as the outcome has been performed involving a large number of individuals. Among the existing clinical trials evaluating MetS as an outcome (Esposito et al. 2013), only the PREDIMED study provided data on the potential efficacy of the Mediterranean diet in preventing this condition (Salas-Salvado et al. 2008). However, the researchers showed that the administration of a Mediterranean diet supplemented with extra-virgin olive oil or nuts led to null results on the risk of MetS (despite their finding of a significantly higher reversion with MedDiet of the condition in patients affected at baseline) (Babio et al. 2014). Current evidence is thus contrasting. Despite not conclusive, our findings are suggestive of an inverse association, though they are affected by small evidence of heterogeneity. Besides, evidence from a large randomized trial supported that the Mediterranean diet is able to ameliorate the MetS traits in subjects who have already developed it (i.e. a significantly higher reversion rate was apparent). However, further clinical trials conducted on high-risk individuals are needed to confirm that this dietary pattern could be considered as a first option for the primary prevention of MetS.
Among the components of the MetS, blood pressure, blood lipids and central obesity criteria resulted significantly inversely associated adherence to the Mediterranean diet. Overall, results on individual metabolic alterations are in line with previous summary analyses showing that Mediterranean diet is associated with decreased risk of hypertension (Nissensohn et al. 2016) as well as an improvements in blood lipid levels and body weight (Huo et al. 2015). However, we did not find any significant association between higher adherence to the Mediterranean diet and the blood glucose criterion. This finding is substantially in disagreement with existing meta-analyses of observational studies reporting that high adherence to this dietary pattern was associated with a reduced risk of developing type-2 diabetes (Koloverou et al. 2014). It is noteworthy that among the studies included in the aforementioned meta-analysis, those conducted in non-Mediterranean countries or involving multiethnic populations mainly reported null results. There is no clear reason for such a lack of association between a Mediterranean-type diet and diabetes risk in non-Mediterranean countries. Notably, we observed a similar lack of association also in the studies conducted in non-Mediterranean countries included in the present meta-analysis. The geographical localization of the population may condition whether or not the operational definition of the Mediterranean diet used in a study may truly capture or not the traditional Mediterranean dietary pattern.

### Table 1

| Study                      | Weight | RR, 95% CI | RR, 95% CI |
|----------------------------|--------|------------|------------|
| **Waist Circumference**    |        |            |            |
| Alvarez Leon, 2006         | 4.5%   | 0.77 [0.38, 1.56] |            |
| Babo, 2009 F               | 2.0%   | 1.23 [0.42, 3.60] |            |
| Babo, 2009 M               | 4.4%   | 0.49 [0.24, 1.00] |            |
| Grosso, 2015 F             | 40.2%  | 0.76 [0.64, 0.90] |            |
| Grosso, 2015 M             | 37.8%  | 0.96 [0.80, 1.15] |            |
| Mirmiran, 2015             | 11.0%  | 0.74 [0.48, 1.14] |            |
| **Total (95% CI)**         | 100.0% | 0.82 [0.70, 0.96] |            |
| Heterogeneity: Tau^2 = 0.01; Chi^2 = 6.38, df = 5 (P = 0.27); I^2 = 22% | | |
| Test for overall effect: Z = 1.51 (P = 0.03) | | |
| **Blood Pressure**         |        |            |            |
| Alvarez Leon, 2006         | 4.6%   | 0.58 [0.34, 0.99] |            |
| Babo, 2009 F               | 1.1%   | 1.04 [0.35, 3.08] |            |
| Babo, 2009 M               | 0.4%   | 0.60 [0.10, 3.60] |            |
| Grosso, 2015 F             | 43.5%  | 0.88 [0.74, 1.05] |            |
| Grosso, 2015 M             | 38.3%  | 0.89 [0.74, 1.07] |            |
| Mirmiran, 2015             | 12.0%  | 0.89 [0.64, 1.24] |            |
| **Total (95% CI)**         | 100.0% | 0.87 [0.77, 0.97] |            |
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 5.27, df = 5 (P = 0.77); I^2 = 0% | | |
| Test for overall effect: Z = 2.42 (P = 0.02) | | |
| **Triglycerides**          |        |            |            |
| Alvarez Leon, 2006         | 10.0%  | 1.05 [0.63, 1.75] |            |
| Babo, 2009 F               | 6.7%   | 0.48 [0.25, 0.92] |            |
| Babo, 2009 M               | 5.4%   | 0.46 [0.22, 0.96] |            |
| Grosso, 2015 F             | 31.4%  | 0.99 [0.83, 1.18] |            |
| Grosso, 2015 M             | 30.8%  | 0.84 [0.70, 1.01] |            |
| Mirmiran, 2015             | 15.8%  | 0.81 [0.56, 1.17] |            |
| **Total (95% CI)**         | 100.0% | 0.84 [0.70, 1.01] |            |
| Heterogeneity: Tau^2 = 0.02; Chi^2 = 8.91, df = 5 (P = 0.11); I^2 = 44% | | |
| Test for overall effect: Z = 1.89 (P = 0.06) | | |
| **HDL-C**                  |        |            |            |
| Alvarez Leon, 2006         | 7.6%   | 0.90 [0.56, 1.45] |            |
| Babo, 2009 F               | 3.1%   | 0.46 [0.22, 0.96] |            |
| Babo, 2009 M               | 2.3%   | 0.74 [0.31, 1.77] |            |
| Grosso, 2015 F             | 44.2%  | 0.84 [0.69, 1.02] |            |
| Grosso, 2015 M             | 36.8%  | 0.98 [0.79, 1.23] |            |
| Mirmiran, 2015             | 6.0%   | 0.82 [0.48, 1.40] |            |
| **Total (95% CI)**         | 100.0% | 0.87 [0.77, 1.00] |            |
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 4.36, df = 5 (P = 0.50); I^2 = 0% | | |
| Test for overall effect: Z = 2.03 (P = 0.04) | | |
| **Fasting Plasma Glucose** |        |            |            |
| Alvarez Leon, 2006         | 4.4%   | 2.46 [1.13, 5.36] |            |
| Babo, 2009 F               | 7.0%   | 1.00 [0.54, 1.83] |            |
| Babo, 2009 M               | 5.2%   | 0.86 [0.42, 1.76] |            |
| Grosso, 2015 F             | 25.9%  | 0.97 [0.71, 1.33] |            |
| Grosso, 2015 M             | 13.4%  | 1.01 [0.77, 1.32] |            |
| Mirmiran, 2015             | 24.0%  | 1.01 [0.73, 1.40] |            |
| **Total (95% CI)**         | 100.0% | 1.03 [0.87, 1.22] |            |
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 5.24, df = 5 (P = 0.39); I^2 = 5% | | |
| Test for overall effect: Z = 1.36 (P = 0.17) | | |

Figure 3. Forest plot of summary RRs of waist circumference, blood pressure, triglycerides, high-density lipoprotein cholesterol (HDL-C) and fasting plasma glucose criteria for MetS for the highest versus lowest (reference) category of adherence to the Mediterranean diet.
Despite a progressive shifting away from traditional dietary patterns have been documented in Mediterranean countries (De Lorenzo et al. 2001; Bonaccio et al. 2014; Grosso et al. 2014b), factors potentially related with quality of individual components of the Mediterranean diet (i.e. consumption of local organic products versus mass production) (De Lorenzo et al. 2010; Di Daniele et al. 2013; Grosso et al. 2013c), culinary practices, lifestyles linked to cultural and demographic backgrounds (Bonaccio et al. 2013; Grosso et al. 2013d; Buscemi et al. 2014), or genetic profiles (Di Daniele et al. 2014) may differ between Mediterranean and non-Mediterranean countries.

There are several Mechanisms relating the Mediterranean diet and its potential effects toward metabolic disorders. Known biological effects of the compounds characterizing this dietary pattern provide plausibility for its potential protective role against MetS. The synergic role of each of the Mediterranean diet components seems to provide protection against the chronic state of subclinical inflammation characterizing the early stage of MetS (Buscemi et al. 2013; Casas et al. 2014). Vitamins and flavonoids contained in fruit and vegetable have been extensively studied for their antioxidant and inflammatory properties (Grosso et al. 2013a; Gregorio et al. 2016). Vitamin C, vitamin E and carotenoids are free-radical scavengers, which mainly benefit toward MetS depends on their antioxidant activity (Dakshinamurti 2015). Flavonoids inhibit lipid peroxidation, promote vascular relaxation and ameliorate endothelial function via promoting antiatherogenic, antithrombotic and anti-inflammatory effects (Amiot et al. 2016). Intake of red wine naturally enriched with resveratrol has been demonstrated to lead to the expression of inflammation and oxidative stress-related genes and reduce post-prandial oxidation of blood lipids (Di Renzo et al. 2014a; Di Renzo et al. 2015). Whole grains have been demonstrated to protect against metabolic disorders due to their content of fiber, which are rich in several bioactive compounds (including minerals, trace elements, vitamins, carotenoids, polyphenols and alkylresorcinols) and act themselves in ameliorating carbohydrates metabolism (Mellen et al. 2008). Whole-grain wheat is also a source of methyl donors and lipotropes (methionine, betaine, choline, inositol and folates), which are involved in lipid metabolism and cardiovascular and hepatic protection (Borneo & Leon 2012). Finally, the high unsaturated:saturated fatty acid ratio has been suggested to exert beneficial effects toward insulin sensitivity, inflammation, vascular function and thrombosis (Siri-Tarino et al. 2015). Overall, all such compounds may counteract the release of pro-inflammatory cytokines occurring when the excess of adipose tissue trigger the inflammation and dis regulate immune function as well as insulin sensitivity, blood pressure homeostasis and lipid metabolism (Welty et al. 2016).

Results of the present study should be considered in light of some limitations. First, most of the studies included in the meta-analysis had an observational design. Thus, long-term large-scale clinical trials are needed to confirm findings from this meta-analysis. Second, we found evidence of heterogeneity across the studies, which was not entirely explained. Third, the use of different dietary scores to evaluate the adherence to the Mediterranean diet may lead to some bias due to the non-uniformity of the indices, for instance, regarding food group classification (i.e. fish and nut consumption not considered separately) and quantification of food intake (such as frequency of consumption versus portion size). Forth, as mentioned above, investigations conducted in different geographical areas may lead to substantially different dietary intakes across individuals labeled as “highly adherent” to the Mediterranean diet, as those conducted in Mediterranean countries have reported higher intakes of fish and legumes than those in non-Mediterranean countries (Grosso et al. 2015a).

In conclusion, the adoption of a Mediterranean dietary pattern may be considered for the primary prevention of the MetS, but the available results are not entirely consistent. Most components of the MetS seem to be reduced by the Mediterranean dietary pattern, with the exception that conflicting results on the blood glucose criterion have been found. Background, cultural and geographical barriers may play a role with this regard, and further efforts should be made to better identify such factors and improve the efficacy of a Mediterranean-type dietary pattern also in non-Mediterranean countries.

**Disclosure statement**

The authors report no conflicts of interest.

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**References**

Abenavoli L, Milic N, Peta V, Alfieri F, De Lorenzo A, Bellentani S. 2014. Alimentary regimen in nonalcoholic
fatty liver disease: Mediterranean diet. World J Gastroenterol. 20:16831–16840.
Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr, et al. 2009. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 120:1640–1645.
Alvarez Leon E, Henriquez P, Serra-Majem L. 2006. Mediterranean diet and metabolic syndrome: a cross-sectional study in the Canary Islands. Public Health Nutr. 9:1089–1098.
Amiot MI, Riva C, Vinet A. 2016. Effects of dietary polyphenols on metabolic syndrome features in humans: a systematic review. Obes Rev. 17:573–586.
Anagnostis P. 2012. Metabolic syndrome in the Mediterranean region: current status. Indian J Endocrinol Metab. 16:72–80.
Babio N, Bulló M, Basora J, Martínez-González MA, Fernández-Ballart J, Márquez-Sandoval F, Molina C, Salas-Salvadó J; Nureta-PREDIMED Investigators. 2009. Adherence to the Mediterranean diet and risk of metabolic syndrome and its components. Nutr Metab Cardiovasc Dis. 19:563–570.
Babio N, Toledo E, Estruch R, Ros E, Martinez-Gonzalez MA, Castaner O, Bullo M, Corella D, Arós F, Gómez-Gracia E, et al. 2014. Mediterranean diets and metabolic syndrome status in the PREIDIM randomized trial. CMAJ. 186:E649–E657.
Bonaccio M, Di Castelnuovo A, Bonanni A, Costanzo S, De Luca F, Persichillo M, Zito F, Donati MB, de Gaetano G, Iacoviello L. 2014. Decline of the Mediterranean diet at a time of economic crisis. Results from the Moli-sani study. Nutr Metab Cardiovasc Dis. 24:853–860.
Bonaccio M, Di Castelnuovo A, Costanzo S, De Luca F, Olivieri M, Donati MB, de Gaetano G, Iacoviello L, Bonanni A; Moli-sani Project Investigators. 2013. Nutrition knowledge is associated with higher adherence to Mediterranean diet and lower prevalence of obesity. Results from the Moli-sani study. Appetite. 68:139–146.
Borneo R, Leon AE. 2012. Whole grain cereals: functional components and health benefits. Food Funct. 3:110–119.
Buscemi S, Nicolucci A, Mattina A, Rosafio G, Massenti FM, Lucisano G, Galvan F, Amadio E, Pellegrini F, Barile AM, et al. 2013. Association of dietary patterns with insulin resistance and clinically silent carotid atherosclerosis in apparently healthy people. Eur J Clin Nutr. 67:1284–1290.
Buscemi S, Sprini D, Grosso G, Galvano F, Nicolucci A, Lucisano G, Massenti FM, Amadio E, Rini GB. 2014. Impact of lifestyle on metabolic syndrome in apparently healthy people. Eat Weight Disord. 19:225–232.
Casas R, Sacanella E, Estruch R. 2014. The immune protective effect of the Mediterranean diet against chronic low-grade inflammatory diseases. Endocr Metab Immune Disord Drug Targets. 14:245–254.
Dakshinamurti K. 2015. Vitamins and their derivatives in the prevention and treatment of metabolic syndrome diseases (diabetes). Can J Physiol Pharmacol. 93:355–362.
Davis C, Bryan J, Hodgson J, Murphy K. 2015. Definition of the Mediterranean diet; a literature review. Nutrients. 7:9139–9153.
De Lorenzo A, Alberti A, Andreoli A, Iacopino L, Serrano P, Perriello G. 2001. Food habits in a southern Italian town (Nicotera) in 1960 and 1996: still a reference Italian Mediterranean diet? Diabetes Nutr Metab. 14:121–125.
De Lorenzo A, Noce A, Bigioni M, Calabrese V, Della Rocca DG, Di Daniele N, Tozzo C, Di Renzo L. 2010. The effects of Italian Mediterranean organic diet (IMOD) on health status. Curr Pharm Des. 16:814–824.
Di Daniele N, Di Renzo L, Noce A, Iacopino L, Ferraro PM, Rizzo M, Sarlo F, Domino E, De Lorenzo A. 2014. Effects of Italian Mediterranean organic diet vs. low-protein diet in nephropathic patients according to MTHFR genotypes. J Nephrol. 27:529–536.
Di Daniele N, Petrimala L, Di Renzo L, Sarlo F, Della Rocca DG, Rizzo M, Fondacaro V, Iacopino L, Pepine CJ, De Lorenzo A. 2013. Body composition changes and cardiometabolic benefits of a balanced Italian Mediterranean diet in obese patients with metabolic syndrome. Acta Diabetol. 50:409–416.
Di Renzo L, Carraro A, Valente R, Iacopino L, Colica C, De Lorenzo A. 2014a. Intake of red wine in different meals modulates oxidized LDL level, oxidative and inflammatory gene expression in healthy people: a randomized crossover trial. Oxid Med Cell Longev. 2014:681318.
Di Renzo L, Marsella LT, Carraro A, Valente R, Gualtieri P, Gratteri S, Tomasi D, Giaiotti F, De Lorenzo A. 2015. Changes in LDL oxidative status and oxidative and inflammatory gene expression after red wine intake in healthy people: a randomized trial. Mediators Inflamm. 2015:317348.
Di Renzo L, Marsella LT, Sarlo F, Soldati L, Gratteri S, Abenavoli L, De Lorenzo A. 2014b. C677T gene polymorphism of MTHFR and metabolic syndrome: response to dietary intervention. J Transl Med. 12:329.
Di Renzo L, Rizzo M, Iacopino L, Sarlo F, Domino E, Jacongeli F, Colica C, Sergi D, De Lorenzo A. 2013. Body composition phenotype: Italian Mediterranean diet and C677T MTHFR gene polymorphism interaction. Eur Rev Med Pharmacol Sci. 17:2555–2565.
Esposito K, Kastorini CM, Panagiotakos DB, Giugliano D. 2013. Mediterranean diet and metabolic syndrome: an updated systematic review. Rev Endocr Metab Disord. 14:255–263.
Giacosa A, Barale R, Bavaresco L, Faliva MA, Gerbi V, La Vecchia C, Negri E, Opizzi A, Perna S, Pezzotti M, Rondanelli M. 2014. Mediterranean way of drinking and longevity. Crit Rev Food Sci Nutr. 56:635–640.
Giacosa A, Barale R, Bavaresco L, Gatenby P, Gerbi V, Janssens J, Johnston B, Kas K, La Vecchia C, Mainguet P, et al. 2013. Cancer prevention in Europe: the Mediterranean diet as a protective choice. Eur J Cancer Prev. 22:90–95.
Gonzalez-Trujano ME, Pellicer F, Mená P, Moreno DA, Garcia-Viguera C. 2015. Antinoceptive and anti-inflammatory activities of a pomegranate (Punica granatum L.) extract rich in ellagitannins. Int J Food Sci Nutr. 66:395–399.
Gouvier ET, Tzavara C, Drakopanagiotakis F, Tsoussoglou M, Marakichelakis GE, Tountas Y, Diamantopoulos
EJ. 2011. Mediterranean diet and metabolic syndrome in an urban population: the Athens Study. Nutr Clin Pract. 26:598–606.

Greenland S. 1987. Quantitative methods in the review of epidemiologic literature. Epidemiol Rev. 9:1–30.

Gregorio BM, De Souza DB, de Morais Nascimento FA, Pereira LM, Fernandes-Santos C. 2016. The potential role of antioxidants in metabolic syndrome. Curr Pharm Des. 22:859–869.

Grosso G, Bei R, Mistretta A, Marventano S, Calabrese G, Masuelli L, Giganti MG, Modesti A, Galvano F, Gazzolo D. 2013a. Effects of vitamin C on health: a review of evidence. Front Biosci (Landmark Ed). 18:1017–1029.

Grosso G, Galvano F, Mistretta A, Marventano S, Nolfo F, Calabrese G, Buscemi S, Drago F, Veronesi U, Scuderi A. 2013b. Red orange: experimental models and epidemiological evidence of its benefits on human health. Oxid Med Cell Longev. 2013:157240.

Grosso G, Marventano S, Buscemi S, Scuderi A, Matalone M, Platania A, Giorgianni G, Rametta S, Nolfo F, Galvano F, Mistretta A. 2013c. Factors associated with adherence to the Mediterranean diet among adolescents living in Sicily, Southern Italy. Nutrients. 5:4908–4923.

Grosso G, Marventano S, Galvano F, Pajak A, Mistretta A. 2014a. Factors associated with metabolic syndrome in a Mediterranean population: role of caffeinated beverages. J Epidemiol. 24:327–333.

Grosso G, Marventano S, Giorgianni G, Raciti T, Galvano F, Mistretta A. 2014b. Mediterranean diet adherence rates in Sicily, southern Italy. Public Health Nutr. 17:2001–2009.

Grosso G, Marventano S, Yang J, Micek A, Pajak A, Scalfi L, Galvano F, Kales SN. 2015a. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: are individual components equal? Crit Rev Food Sci Nutr. [Epub ahead of print]. doi: 10.1080/10408398.2015.1107021.

Grosso G, Mistretta A, Marventano S, Purrello A, Vitaglione P, Calabrese G, Drago F, Galvano F. 2014c. Beneficial effects of the Mediterranean diet on metabolic syndrome. Curr Pharm Des. 20:5039–5044.

Grosso G, Mistretta A, Turconi G, Cena H, Roggi C, Galvano F. 2013d. Nutrition knowledge and other determinants of food intake and lifestyle habits in children and young adolescents living in a rural area of Sicily, South Italy. Public Health Nutr. 16:1827–1836.

Grosso G, Stepaniak U, Micek A, Topor-Madry R, Steller D, Szafrańczyk K, Bobak M, Pajak A. 2015b. A Mediterranean-type diet is associated with better metabolic profile in urban Polish adults: results from the HAPIEE study. Metabolism. 64:738–746.

Grosso G, Stepaniak U, Topor-Madry R, Szafrańczyk K, Pajak A. 2014d. Estimated dietary intake and major food sources of polyphenols in the Polish arm of the HAPIEE study. Nutrition. 30:1398–1403.

Grundy SM, Hansen B, Smith SC, Jr., Cleeman JI, Kahn RA. American Heart Association, National Heart Lung and Blood Institute. 2004. Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/ American Diabetes Association conference on scientific issues related to management. Circulation. 109:551–556.

Huo R, Du T, Xu Y, Xu W, Chen X, Sun K, Yu X. 2015. Effects of Mediterranean-style diet on glycemic control, weight loss and cardiovascular risk factors among type 2 diabetes individuals: a meta-analysis. Eur J Clin Nutr. 69:1200–1208.

Kastorini CM, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. 2011. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. J Am Coll Cardiol. 57:1299–1313.

Kesse-Guyot E, Ahluwalia N, Lassale C, Hercberg S, Fezeu L, Lairon D. 2013. Adherence to Mediterranean diet reduces the risk of metabolic syndrome: a 6-year prospective study. Nutr Metab Cardiovasc Dis. 23:677–683.

Koloverou E, Esposito K, Giugliano D, Panagiotakos D. 2014. The effect of Mediterranean diet on the development of type 2 diabetes mellitus: a meta-analysis of 10 prospective studies and 136,846 participants. Metab Clin Exp. 63:903–911.

Marventano S, Kolacz P, Castellano S, Galvano F, Buscemi S, Mistretta A, Grosso G. 2015. A review of recent evidence in human studies of n-3 and n-6 PUFA intake on cardiovascular disease, cancer, and depressive disorders: does the ratio really matter? Int J Food Sci Nutr. 66:611–622.

Mellen PB, Walsh TF, Herrington DM. 2008. Whole grain intake and cardiovascular disease: a meta-analysis. Nutr Metab Cardiovasc Dis. 18:283–290.

Mirmiran P, Moslehi N, Mahmoudof H, Sadeghi M, Azizi F. 2015. A longitudinal study of adherence to the Mediterranean dietary pattern and metabolic syndrome in a non-Mediterranean population. Int J Endocrinol Metab. 13:e26128.

Nissensohn M, Roman-Vinas B, Sanchez-Villegas A, Pisco S, Serra-Majem L. 2016. The effect of the Mediterranean diet on hypertension: a systematic review and meta-analysis. J Nutr Educ Behav. 48:42–53.

Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas J, Tousoulis D, Toutouza M, Toutouzas P, Stefanadis C. 2004. Impact of lifestyle habits on the prevalence of the metabolic syndrome among Greek adults from the ATTICA study. Am Heart J. 147:106–112.

Pimenta AM, Toledo E, Rodriguez-Diez MC, Gea A, Lopez-Iracheta R, Shivappa N, Hebert JR, Martinez-Gonzalez MA. 2015. Dietary indexes, food patterns and incidence of metabolic syndrome in a Mediterranean cohort: the SUN project. Clin Nutr. 34:508–514.

Rondanelli M, Faliva MA, Peroni G, Moncaglieri F, Infantino V, Naso M, Perna S. 2015. Focus on pivotal role of dietary intake (diet and supplement) and blood levels of tocopherols and tocotrienols in obtaining successful aging. Int J Mol Sci. 16:23227–23249.

Rondanelli M, Monteferrario F, Perna S, Faliva MA, Opizzi A. 2013. Health-promoting properties of artichoke in preventing cardiovascular disease by its lipidic and glycemic-reducing action. Monaldi Arch Chest Dis. 80:17–26.

Salas-Salvadó J, Fernández-Ballart J, Ros E, Martinez-González MA, Fitó M, Estruch R, Corella D, Fiol M, Gómez-Gracia E, Arós F, et al. 2008. Effect of a Mediterranean diet supplemented with nuts on metabolic syndrome status: one-year results of the PREDIMED randomized trial. Arch Intern Med. 168:2449–2458.
Shin JY, Kim JY, Kang HT, Han KH, Shim JY. 2015. Effect of fruits and vegetables on metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. Int J Food Sci Nutr. 66:416–425.

Silveira JQ, Dourado GK, Cesar TB. 2015. Red-fleshed sweet orange juice improves the risk factors for metabolic syndrome. Int J Food Sci Nutr. 66:830–836.

Siri-Tarino PW, Chiu S, Bergeron N, Krauss RM. 2015. Saturated fats versus polyunsaturated fats versus carbohydrates for cardiovascular disease prevention and treatment. Annu Rev Nutr. 35:517–543.

Sofi F, Macchi C, Abbate R, Gensini GF, Casini A. 2014. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. Public Health Nutr. 17:2769–2782.

Steffen LM, Van Horn L, Daviglus ML, Zhou X, Reis JP, Loria CM, Jacobs DR, Duffey KJ. 2014. A modified Mediterranean diet score is associated with a lower risk of incident metabolic syndrome over 25 years among young adults: the CARDIA (Coronary Artery Risk Development in Young Adults) study. Br J Nutr. 112:1654–1661.

Veissi M, Anari R, Amani R, Shahbazian H, Latifi SM. 2016. Mediterranean diet and metabolic syndrome prevalence in type 2 diabetes patients in Ahvaz, southwest of Iran. Diabetes Metab Syndr. [Epub ahead of print]. doi:10.1016/j.dsx.2016.01.015.

Wells GA, Shea B, O’connell D, Peterson J, Welch V, Losos M, Tugwell P. [Internet]. 1999. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. [Journal]. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.

Welty FK, Alfaddagh A, Elajami TK. 2016. Targeting inflammation in metabolic syndrome. Transl Res. 167:257–280.

Yang J, Farioli A, Korre M, Kales SN. 2014. Modified Mediterranean diet score and cardiovascular risk in a North American working population. PLoS One. 9:e87539.

Zamora-Ros R, Knaze V, Lujan-Barroso L, Kuhnle GG, Mulligan AA, Touillaud M, Slimani N, Romieu I, Powell N, Tumino R, et al. 2012. Dietary intakes and food sources of phytoestrogens in the European Prospective Investigation into Cancer and Nutrition (EPIC) 24-hour dietary recall cohort. Eur J Clin Nutr. 66:932–941.

Zamora-Ros R, Knaze V, Lujan-Barroso L, Romieu I, Scalbert A, Slimani N, Hjartaker A, Engeset D, Skeie G, Overvad K, et al. 2013. Differences in dietary intakes, food sources and determinants of total flavonoids between Mediterranean and non-Mediterranean countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Br J Nutr. 109:1498–1507.