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The effects of olive oil consumption on blood lipids: a systematic review and dose–response meta-analysis of randomised controlled trials

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Abstract

We performed a systematic review and dose–response meta-analysis of randomised trials on the effects of olive oil consumption on blood lipids in adults. A systematic search was performed in PubMed, Scopus and Web of Science databases until May 2021. Randomised controlled trials (RCT) evaluating the effect of olive oil intake on serum total cholesterol (TC), TAG, LDL-cholesterol and HDL-cholesterol in adults were included. The mean difference (MD) and 95 % CI were calculated for each 10 g/d increment in olive oil intake using a random-effects model. A total of thirty-four RCT with 1730 participants were included. Each 10 g/d increase in olive oil consumption had minimal effects on blood lipids including TC (MD: 0·79 mg/dl; 95 % CI (−0·08, 1·66); $I^2 = 57$ %; *n* 31, GRADE = low certainty), LDL-cholesterol (MD: 0·04 mg/dl, 95 % CI (−1·01, 0·94); $I^2 = 80$ %; *n* 31, GRADE = very low certainty), HDL-cholesterol (MD: 0·22 mg/dl; 95 % CI (−0·01, 0·45); $I^2 = 38$ %; *n* 33, GRADE = low certainty) and TAG (MD: 0·39 mg/dl; 95 % CI (−0·33, 1·11); $I^2 = 7$ %; *n* 32, GRADE = low certainty). Levels of TC increased slightly with the increase in olive oil consumption up to 30 g/d ($MD_{30\ g/d}$: 2·76 mg/dl, 95 % CI (0·01, 5·51)) and then appeared to plateau with a slight downward curve. A trivial non-linear dose-dependent increment was seen for HDL-cholesterol, with the greatest increment at 20 g/d ($MD_{20\ g/d}$: 1·03 mg/dl, 95 % CI (−1·23, 3·29)). Based on existing evidence, olive oil consumption had trivial effects on levels of serum lipids in adults. More large-scale randomized trials are needed to present more reliable results.

Key words: **Dose–response: Lipid profile: Olive oil consumption: Randomised control trial studies**

Dyslipidemia is defined as high blood total cholesterol (TC), TAG or LDL-cholesterol concentrations, or low blood concentration of HDL-cholesterol[1]. Dyslipidemia has become a major public health challenge worldwide[2]. Among various types of dyslipidemia, hypercholesterolemia is the most common abnormality[1]. Dyslipidemia is responsible for about 2·6 million deaths and 29·7 million disability-adjusted life-years worldwide[3]. It has a primary role in the development of CVD[4]. Also, elevated plasma TAG levels are associated with weight gain and developing diabetes mellitus, non-alcoholic fatty liver disease, and acute pancreatitis[1].

An unhealthy diet is one of the main drivers of dyslipidemia. Western-style eating habits and higher fat and energetic intake can lead to raised plasma lipid levels[1,5]. In general, the Western dietary pattern has been characterised by high consumption of red meat, processed meat, high-fat dairy products, and sugar-sweetened and artificially sweetened beverages[6,7]. One of the most important pathways whereby the Western dietary pattern may influence overall cardiometabolic health is the high consumption of sugar-sweetened beverages that increases weight gain and central adiposity[6]. Sweets contain fructose. It is indicated that high fructose intake increases the expression of carbohydrate-response element-binding protein and acetyl-CoA carboxylase and thereby increases endogenous lipogenesis in the liver[8]. In addition, Western dietary pattern is rich in SFA. Evidence suggests that high intake of SFA is associated with higher serum cholesterol concentrations[9].

n-3 fatty acids can lower serum TAG and non-HDL-cholesterol concentrations[10]. In contrast, a higher intake of dietary sources of *trans*-fatty acids such as margarine was associated with increased LDL-cholesterol and decreased HDL-cholesterol concentrations[11]. It is indicated that substituting SFA with MUFA (e.g. replacing butter with olive oil) can favourably affect blood concentrations of TC, LDL-cholesterol and TAG[11]. Olive oil consists of oleic acid (55 % to 83 %), palmitic acid (7·5 % to 20 %), linoleic acid (3·5 % to 21 %) and phenolic compounds including hydroxytyrosol and tyrosol[12]. Olive oil is high in MUFA which may mediate the prevention and management of CVD and

Abbreviations: MD, mean difference; RCT, randomised controlled trials; TC, total cholesterol.

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associated risk factors through various mechanistic pathways including the favourable modulation of cholesterol levels[13] and improvement of insulin sensitivity[14]. Besides the high MUFA content, olive oil polyphenols have also been shown to be cardioprotective. Phenolic compounds scavenge free radicals through their antioxidant activity[12,15] and thus could protect LDL-cholesterol particles, circulating lipid markers and lipid peroxidation[12]. Olive oil may have cardioprotective properties alongside its anticancer activity and can lower the risk of type 2 diabetes by improving the metabolic and inflammatory biomarkers[16,17].

A previous meta-analysis of randomised controlled trials (RCT) has studied the effects of olive oil on blood lipid levels and has shown that increasing the consumption of olive oil can decrease serum TC, LDL-cholesterol, and TAG and increase HDL-cholesterol when compared with other plant oils[18]. However, another network meta-analysis of RCT indicated opposite findings[19]. In addition, the previous meta-analyses did not evaluate the potential dose-dependent effects of olive oil consumption on blood lipids. Pairwise comparisons used in standard meta-analyses cannot present valuable information about the dose-dependent effects of dietary interventions on continuous outcomes such as blood lipids. Therefore, we aimed to perform a systematic review and dose–response meta-analysis of RCT to evaluate the effects of different doses of olive oil consumption on levels of blood lipid in adults.

Methods

This meta-analysis has been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses: the PRISMA statement[20]. The protocol of the systematic review was registered on PROSPERO (CRD42022311168).

Systematic search

The systematic search was carried out by using related keywords in PubMed, Scopus and Web of Science until May 2021. The keywords related to intervention, outcome and study design were put together for finding eligible RCT. Our search has been restricted to English articles. The search strategy is illustrated in Supplementary Table 1. Titles and abstracts have been screened according to the pre-defined inclusion and exclusion criteria, and the full texts of eligible studies are checked by two review authors (BJ and AJ) independently. Disagreements were solved by consulting the third author (SS-B). We also searched the reference lists of related reviews and original research to find other potentially relevant studies.

Eligibility criteria

We applied PICOS (population, intervention, comparator, outcome and study design) framework to describe our inclusion and exclusion criteria. Inclusion criteria contain are as follows: (1) performed RCT, with either parallel or crossover design, in adults aged 18 years or more, regardless of health status; (2) evaluated the effect of olive oil, regardless of its form (refined, virgin or extra virgin olive oil) on blood lipids including TC, LDL-cholesterol, HDL-cholesterol and TAG; (3) compared the effects of various doses of olive oil (g/d) on blood lipids or compared the effects of a specific amount of olive oil (g/d) against a control (usual) diet (including trials that their only difference was olive oil intake); (4) considered change in blood lipids as the outcome; and (5) provided mean and standard deviation of change in serum TC, LDL-cholesterol, HDL-cholesterol, and TAG across study arms or reported sufficient information to estimate those values. We excluded trials that were conducted in adolescents (under 18 years of age) and pregnant and lactating women.

Data extraction

Two authors independently reviewed the full text of potentially eligible articles for eligibility. Then, data were extracted from these studies by two independent reviewers (BJ and AJ). The extracted data included author name, year of publication, population location, study design and duration, characteristics of the study population (% female, mean age ± SD, health status), total sample size, intervention characteristics (type and dose of olive oil consumption), comparison group, outcome measures, and main results for the outcomes included.

Risk of bias (quality) assessment

The quality assessment of the included studies was done by two reviewers (BJ and AJ) independently and in duplicate. We used the Cochrane risk of bias tool for this evaluation[21]. The Cochrane risk of bias tool covers six domains of bias including: (1) selection bias (random sequence generation and allocation concealment); (2) reporting bias (selective reporting of an outcome); (3) performance bias (participants and personnel blinding); (4) detection bias (outcome assessment blinding); (5) attrition bias (incomplete outcome data) and (6) other sources of bias. Each item scores high, low or unclear risk of bias. Then, the total quality would be scored as low risk (if all criteria were low), some concerns (if one criterion was high or two criteria were unclear) or high risk (if two or more criteria were high)[21]. The third author (SS-B) solved the disagreements about the risk of bias assessment.

Statistical analysis

We considered the weighted mean difference (MD) and its 95 % CI of change in serum TC, LDL-cholesterol, HDL-cholesterol and TAG as the effect size to report the results of this systematic review.

We extracted mean values and standard deviations of changes in the outcomes in the control and intervention arm. If these changes were not reported in eligible articles, we calculated them by using measures before and after the intervention, according to the guidelines of the Cochrane Handbook[22]. If trials presented standard error as a dispersion parameter, we converted it to SD[23]. If studies reported median and interquartile ranges, we used the median instead of the mean and divided the interquartile range by 1·35 to compute the SD value[23]. At last, if there was not any dispersion parameter, we averaged the SD values of the other trials to calculate the missing one[24].

Then, we performed a random-effect meta-analysis. Two types of analyses were carried out in this meta-analysis. First,

we performed a random-effects dose–response meta-analysis to estimate the change in blood lipids for each 10 g/d increments in olive oil consumption in each primary trial according to the method introduced by Crippa and Orsini[25]. This method requires the dose of olive oil consumption (g/d) in each study arm, the number of participants in intervention and control groups, and the reported mean and SD of change in TC, LD-cholesterol, HDL-cholesterol and TAG. The Cochran Q and I^2 statistics were used to test for heterogeneity[23]. We performed a series of pre-defined subgroup analyses based on health status (with *v.* without hyperlipidemia), baseline weight (normal weight *v.* overweight/obese), baseline health status, control group (types of oil consumption) and types (virgin, extra virgin and refined) and forms (raw *v.* cooked) of olive oil. We used visual inspection of funnel plots for testing publication bias when more than ten trials were available for the analyses. Second, we performed a random-effects dose–response meta-analysis to clarify the shape of the dose–response effects of olive oil intake on blood lipids[25]. We used STATA version 16.0 for conducting our statistical analyses. A two-tailed *P*-value of less than 0·05 will be considered significant.

Grading the evidence

We used the GRADE approach to evaluate the certainty of evidence[26]. A detailed description of the GRADE domains is presented in Supplementary Text 1. Based on the GRADE approach, we rated the certainty of evidence as high, moderate, low or very low. Criteria to downgrade evidence included risk of bias, indirectness, inconsistency, imprecision and publication bias. We upgraded the certainty of evidence if there was a large effect size or dose–response gradient. We rated down for imprecision if the effect size did not surpass thresholds settled as the minimal clinically important difference (MCID), defined as 10 mg/dl for TC, 4 mg/dl for LDL-cholesterol and HDL-cholesterol, and 8 mg/dl for serum TAG[27].

Results

After a search in three databases, 8210 articles were found. Of these, we excluded 1256 duplicates and additional 6861 non-relevant articles based on screening of the title and abstract (online Supplementary Fig. 1). Finally, ninety-three full texts were screened and of these, thirty-four randomised trials with 1730 participants were eligible for inclusion in the dose–response meta-analysis[28–53,54–61]. Supplementary Table 2 presents the list of studies that were assessed in detail for eligibility with reasons for exclusions.

Characteristics of primary trials included in the systematic review

The characteristics of the thirty-four trials are shown in Supplementary Table 3. The publication year of the eligible studies was between 1988 and 2020. Of thirty-four trials, seventeen trials were performed on healthy participants[33–37,39,42–45,47,50,51,53,56,57,59], three trials on those with peripheral or coronary vascular disease[28,32,41], seven in patients with dyslipidemia[31,40,46,48,49,52,58], two in patients with type 2 diabetes[29,60], and one in patients with metabolic syndrome[30], rheumatoid arthritis[38], non-communicable disease[54], non-alcoholic fatty liver disease[55], and polycystic ovary syndrome[61]. Six trials were conducted in populations with overweight/obesity[37,45,55–57,61], nine in those with normal weight[34,36,39,43,44,52,53,58,59] and the rest in mixed populations[28–31,32,33,35,38,40–42,46–51,54,60]. The follow-up duration ranged between 3 weeks and 6 months. There is one trial in which the duration of intervention lasted 3 years[54].

All trials investigated the effects of olive oil intake as a stand-alone intervention. The trials compared the effect of four types of olive oil against a usual diet or another kind of oil. Fourteen trials used extra virgin olive oil, fourteen trials used olive oil[29,31,35,38,44–46,49–52,55,58,61], four trials used refined olive oil[30,39–41] and two used virgin olive oil[28,33]. The dose of olive oil intake was between 11 and 77 g/d across trials, and the average intake was 37 g/d. Also, eleven trials reported the form of olive oil intake, of which three trials prescribed cooked olive oil[28,51,52], three trials prescribed olive oil intake a the raw form[41,45,61] and the other five trials prescribed both forms[33,42,55,56,60].

In the control groups, participants received usual diet[31,32,44,54,57] or different oils including canola oil[29,41,45,46,51,52,61], rapeseed oil[30,39,40,45,52,53], sunflower oil[28,29,31,33,39,53,55,61], maize oil[46,48,58], flaxseed oil[43,50], palm olein[34,35,59], maize oil[46,58], cocoa butter[34,59], extra virgin coconut oil[42], butter[42], soyabean oil[37], peanut oil[44], sesame oil[49], hybrid palm oil[47], evening promise oil[38] and virgin argan oil[36]. There were five trials with usual diet as control group. In two trials, the intervention and control groups received a diet with the same proportion of macronutrients, but the intervention group received an excess dose of olive oil[32,57]. In another trial, the percent of macronutrients were identical across study arms, and the differences between the two groups were the percent of energy from SFA and MUFA, wherein MUFA intake was higher in the intervention group[44]. In two other trials, participants in the control group followed a low-fat diet[54] and the average American diet[31].

Of the trials, only six trials reported the degree of adherence to the prescribed intervention, of which the degree of adherence was reported to be 94 % in one trial[50], 86 % in another trial[32], >75 % in one trial[42], high[45] and good[40] in two trials, and very high in another trial[36]. Of the trials, twenty-three were rated as high risk of bias[28–31,34–37,39,40,42,45–47,49–52,54,57–60], ten trials had some concerns[32,33,38,41,43,44,48,53,56,61] and one was rated to have a low risk of bias[55] (online Supplementary Table 4).

Total cholesterol

For the analysis of serum TC, thirty-one trials with 1574 participants were included in analysis[28–41,42,43,45–50,52–55,57–61]. For each 10 g/d increment in olive oil consumption, TC concentration slightly increased serum (MD: 0·79 mg/dl; 95 % CI (−0·08, 1·66); $I^2 = 57$ %, online Supplementary Fig. 2).

Supplementary Table 5 shows the results of the subgroup analyses. The results were the same across subgroups defined by type and form of olive oil, duration of intervention (≤12 *v.* >12 weeks), and weight and health status of the participants.

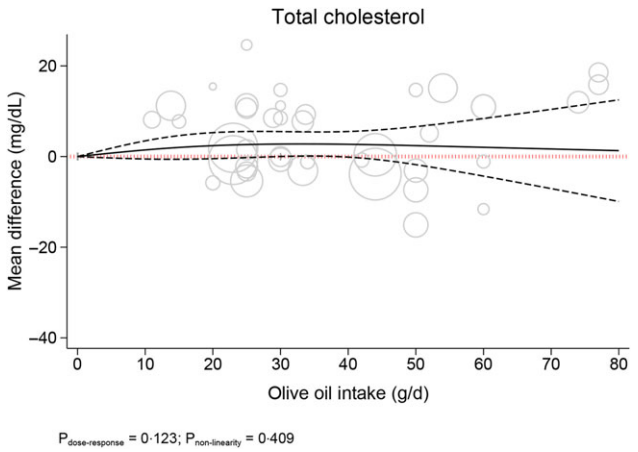

Fig. 1. Dose–response association between the olive oil consumption and the total cholesterol concentration. Solid line represents non-linear dose–response and dotted lines represent 95 % CI. Circles represent the effect size of each trial, with the size of the circles proportional to inverse of standard errors.

There was no significant or credible subgroup difference, except for a subgroup analysis based on the type of the control group. According to the results, olive oil intake significantly increased TC concentration when was compared with canola oil (MD: 2·61 mg/dl, 95 % CI (1·31, 3·92); *n* 6), flaxseed oil (MD: 8 mg/dl, 95 % CI (2·61, 13·38); *n* 2), sunflower oil (MD: 1·86 mg/dl, 95 % CI (0·90, 2·83); *n* 8), and maize oil (MD: 2·22 mg/dl, 95 % CI (1·12, 3·32); *n* 3) and in contrast, decreased serum TC when was compared with butter (MD: −3·02 mg/dl; 95 % CI (−5·01, −1·03)). Dose-dependent effects of olive oil on levels of TC are shown in Fig. 1 and Table 1 ($P_{\text{non-linearity}} = 0{\cdot}41$, $P_{\text{dose–response}} = 0{\cdot}12$). Levels of TC increased slightly with the increase in olive oil consumption up to 30 g/d (MD $_{30\ \text{g/d}}$: 2·76 mg/dl; 95 % CI (0·01, 5·51)) and then reached plateau till 40 g/d (MD $_{40\ \text{g/d}}$: 2·70 mg/dl; 95 % CI (−0·12, 5·52)).

LDL-cholesterol

Thirty-one trials with 1547 participants assessed the effect of olive oil intake on LDL-cholesterol[28–37,39–41,42–50,52–60]. Each 10 g/d increment in olive oil consumption decreased LDL-cholesterol by 0·04 mg/dl (95 % CI (−1·01, 0·94); $I^2 = 80\,\%$, online Supplementary Fig. 3).

Supplementary Table 6 indicates the subgroup analyses. There was no significant subgroup difference across subgroups defined by type and form of olive oil, duration of intervention, and weight and health status of the participants. There was a significant and credible subgroup difference, where we compared the results across different types of the control groups. Olive oil intake significantly increased LDL-cholesterol concentration when was compared with canola oil (MD: 1·34 mg/dl, 95 % CI (0·44, 2·37); *n* 6) and flaxseed oil (MD: 4·77, 95 % CI (0·02, 9·51); *n* 2) and in contrast, reduced LDL-cholesterol when was compared with butter (MD: −3·02 mg/dl; 95 % CI (−4·70, −1·34)). Also, olive oil intake significantly but slightly increased serum LDL-cholesterol in those with hyperlipidemia (MD: 0·91 mg/dl, 95 % CI (0·23, 1·50); *n* 9) as compared with those with normal blood lipids. Dose-dependent effects of olive oil on

Table 1. The effects of different doses of olive oil on blood lipids form the non-linear dose–response meta-analysis (mean difference and 95 % confidence interval)

Olive oil intake (g/d)	0[67]	10		20		30		40		50		60		70		80	
		Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI
TC (mg/dl)	0	1·46	−0·54, 3·46	2·40	−0·47, 5·28	2·76	0·01, 5·51	2·70	−0·12, 5·52	2·41	−1·78, 6·60	2·04	−4·31, 8·40	1·67	−7·07, 10·41	1·30	−9·90, 12·51
LDL-cholesterol (mg/dl)	0	0·72	−1·12, 2·57	1·03	−1·23, 3·29	1·00	−1·00, 2·99	0·72	−2·06, 3·51	0·31	−4·65, 5·27	−0·15	−7·74, 7·44	−0·60	−10·93, 9·72	−1·06	−14·15, 12·03
HDL-cholesterol (mg/dl)	0	0·72	−1·12, 2·57	1·03	−1·23, 3·29	1·00	−1·00, 2·99	0·72	−2·06, 3·51	0·31	−4·65, 5·27	−0·15	−7·74, 7·44	−0·60	−10·93, 9·72	−1·06	−14·15, 12·03
TAG (mg/dl)	0	1·29	−0·68, 3·27	1·98	−0·85, 4·81	2·17	−0·70, 5·04	1·98	−0·68, 4·65	1·56	−1·47, 4·58	1·02	−3·18, 5·23	0·48	−5·30, 6·26	−0·07	−7·57, 7·44

TC, total cholesterol.

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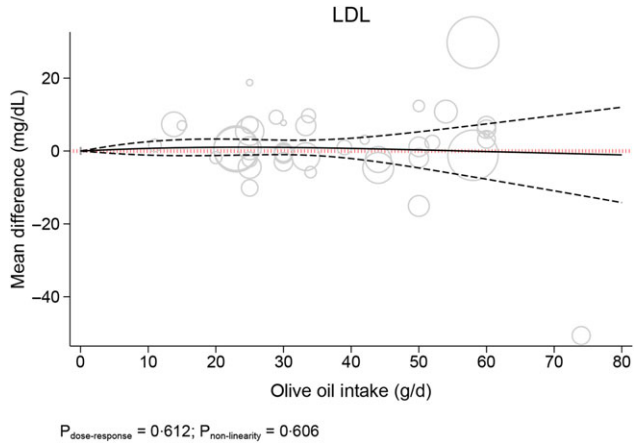

Fig. 2. Dose–response association between the olive oil consumption and the LDL-cholesterol concentration. Solid line represents non-linear dose–response and dotted lines represent 95 % CI. Circles represent the effect size of each trial, with the size of the circles proportional to inverse of standard errors.

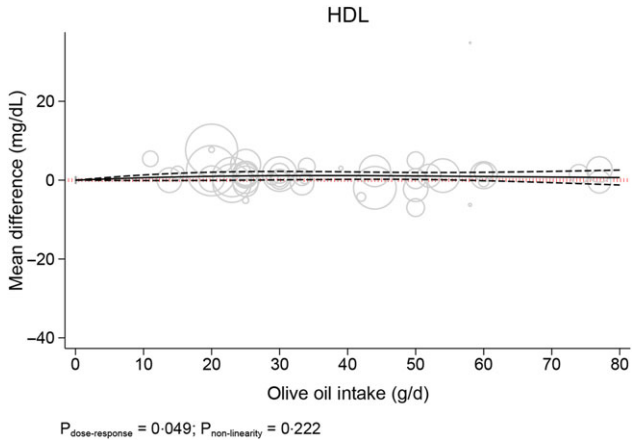

Fig. 3. Dose–response association between the olive oil consumption and the HDL-cholesterol concentration. Solid line represents non-linear dose–response and dotted lines represent 95 % CI. Circles represent the effect size of each trial, with the size of the circles proportional to inverse of standard errors.

levels of serum LDL-cholesterol are presented in Fig. 2 and Table 1 ($P_{\text{non-linearity}} = 0{\cdot}61$, $P_{\text{dose–response}} = 0{\cdot}61$), indicating that serum LDL-cholesterol concentrations did not change materially with the increase in olive oil intake.

HDL-cholesterol

All but one trial including 1685 participants were included in the analysis of HDL-cholesterol[28–39,41–61]. Supplementary Fig. 4 indicates that consumption of each 10 g/d olive oil resulted in a trivial increase in HDL-cholesterol concentrations (MD: 0·22 mg/dl; 95 % CI (−0·01, 0·45); $I^2 = 38\,\%$).

Supplementary Table 7 demonstrates the subgroup analyses. The results were similar across subgroups defined by type and form of olive oil, duration of intervention, and weight and health status of the participants. There was a significant and credible subgroup difference, where olive oil intake significantly increased HDL-cholesterol concentration when was compared with canola oil (MD: 0·53 mg/dl; 95 % CI (0·03, 1·04)) and, in contrast, reduced HDL-cholesterol when was compared with extra virgin coconut oil (MD: −1·39 mg/dl; 95 % CI (−2·30, −0·48)). Dose-dependent effects of olive oil on levels of HDL-cholesterol are indicated in Fig. 3 and Table 1, which indicated a small increase in HDL-cholesterol concentration ($P_{\text{non-linearity}} = 0{\cdot}22$, $P_{\text{dose–response}} = 0{\cdot}05$).

TAG

Thirty-two trials with 1631 participants reported the effect of olive oil intake on serum TAG concentrations[28–33,34–39,41–47,49–61]. As indicated in Supplementary Fig. 5, there was no significant change in serum TAG concentration per each 10 g/d increase in olive oil intake (MD: 0·39 mg/dl; 95 % CI (−0·33, 1·11); $I^2 = 7\,\%$).

Supplementary Table 8 represents the subgroup analyses of the effect of olive oil intake on levels of serum TAG, where there was a significant increase in TAG levels when olive oil was compared with flaxseed oil (MD: 7·21 mg/dl, 95 % CI (1·01, 13·41); *n* 2). In addition, when we looked at the effect of olive oil intake

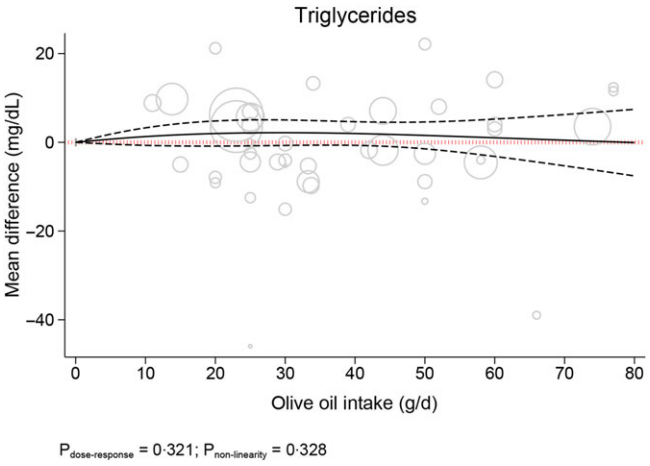

Fig. 4. Dose–response association between the olive oil consumption and the TAG concentration. Solid line represents non-linear dose–response and dotted lines represent 95 % CI. Circles represent the effect size of each trial, with the size of the circles proportional to inverse of standard errors.

in participants with type 2 diabetes, a significant decrease in TAG levels have been found (MD: −4·32 mg/dl, 95 % CI (−8·20, −0·45); *n* 4). However, *P* for subgroup difference was not significant and the credibility of subgroup differences was rated low. Dose-dependent effects of olive oil on levels of TAG are indicated in Fig. 4 and Table 1 ($P_{\text{non-linearity}} = 0{\cdot}33$, $P_{\text{dose–response}} = 0{\cdot}32$), indicating a small and non-significant increase in serum TAG concentrations with the increase in olive oil intake.

Publication bias

By looking at the funnel plots, we found that there was evidence of publication bias in the analyses of TC (Begg's test = 0·42, Egger's test = 0·17) and LDL-cholesterol (Begg's test = 0·03, Egger's test = 0·21) (online Supplementary Fig. 6 and 7). There was no evidence of publication bias in the analyses of HDL-cholesterol (Begg's test = 0·32, Egger's test = 0·36) and TAG

(Begg's test = 0·40, Egger's test = 0·54) (online Supplementary Fig. 8 and 9).

Grading the evidence

Supplementary Table 9 presents the details of the GRADE rating approach. The certainty of evidence was rated very low for LDL-cholesterol and low for other outcomes due to downgrades for serious risk of bias and inconsistency. The size of the effects for all outcomes did not surpass the MCID thresholds, suggesting trivial and unimportant effects.

Discussion

The present meta-analysis investigated the potential dose-dependent effects of olive oil intake on levels of blood lipids. The analyses indicated that each 10 g/d increment in olive oil intake did not have any significant beneficial effects on blood lipid concentrations. The subgroup analyses indicated that olive oil intake increased serum TC concentrations when was compared with canola, flaxseed, sunflower and maize oils, increased LDL-cholesterol concentrations when was compared with canola and flaxseed oils, and increased serum TAG when was compared with flaxseed oil. Although the effects of olive oil intake on blood lipids in comparison with other plant-based oil were trivial, it resulted in an important increase in serum LDL-cholesterol concentrations when was compared with flaxseed oil. The overall quality of evidence was rated very low to low for all outcomes, indicating that the true effect might be noticeably different from the estimated effect, and that future research might have a large impact on effect estimates[62].

In contrast to our findings, a previous pairwise meta-analysis indicated a significant effect of olive oil intake on blood lipids. A meta-analysis of twenty-seven randomised trials[18] indicated that olive oil consumption, compared with other plant oils, significantly increased HDL-cholesterol levels by 1·37 mg/dl. The study also showed that olive oil consumption reduced TC, LDL-cholesterol and TAG concentrations by 6·27, 4·2 and 4·31 mg/l, respectively. Although the previous meta-analysis indicated some suggestions of favourable effects of olive oil intake on blood lipids, it did report small and unimportant effects on levels of blood lipids. We included ten new eligible trials which were not included in the previous pairwise meta-analysis. In addition, our findings are in line with those of a network meta-analysis of randomised trials that compared the effects of different oils on blood lipids[19]. In a network meta-analysis of fifty-four randomised trials, Schwingshackl *et al.* indicated that olive oil intake had no significant effects on blood lipids in comparison with other plant-based oils[19].

Although the results indicated that olive oil intake had no significant and important effects on blood lipids, the subgroup analyses suggested that it can improve blood lipids when was compared with butter. However, only a very small number of trials were included in the subgroups. In addition, evidence is lacking to compare the effects of olive oil in comparison with other dietary sources of SFA. Thus, more research is needed to assess the effects of olive oil intake on blood lipids in comparison with other dietary sources of SFA.

There was another obvious significant difference between olive oil intake and flaxseed oil. In the present work, flaxseed oil intake resulted in significant and important improvements in blood lipids when was compared with olive oil. Flaxseed oil is a source of *n*-3 fatty acids[43] which could explain these results. By decreasing the activity of lipogenic enzymes such as fatty acid synthesis, acyl-CoA carboxylase and malic enzyme, *n*-3 PUFA can regulate gene expression and could affect lipid metabolism through induction of b-oxidation and inhibition of lipogenesis[18].

A previous meta-analysis of prospective cohort studies indicated a significant inverse association between higher intake of olive oil and risk of all-cause mortality, cardiovascular events, and stroke[63]. In addition, olive oil is a major component of the Mediterranean dietary pattern[64]. Considering the null findings on blood lipids in the present meta-analysis, it seems that the favourable effects of olive oil intake on human health may be mediated by other mechanisms.

Besides the notable amounts of MUFA in olive oil, it also has other biologically active components. Oleuropein is a polyphenol and is a potent scavenger of superoxide radicals and inhibits LDL-cholesterol oxidation[65]. Olive oil has anti-inflammatory properties[66] and thus may protect against the pathogenesis of CVD. In addition, Pedersen *et al.* showed that olive oil contains high amounts of squalene compared with some plant oils. It is a kind of hydrocarbon that might have hypercholesterolemic effects[53].

Our meta-analysis had some limitations which should be noted. We had limited data about the macronutrient composition of the diets across study arms in each trial. In addition, limited trials were available to compare the effects of olive oil with dietary sources of SFA. Of thirty-four trials included in the present review, twenty-eight trials lasted shorter than 12 weeks and thus, we had insufficient evidence on long-term effects of olive oil intake on blood lipids. In addition, only a small number of trials reported the degree of adherence to the prescribed intervention, as well as information about the form of olive oil intake (cooked *v.* raw). There might be a potential interaction between olive oil intake and consumption/cooking methods that should be considered in future research.

Strengths of the study include the comprehensive systematic search, performing dose–response meta-analysis, evaluating the effects across various subgroups especially subgroups defined by type of olive oil, control group, and health status, and rating the certainty of evidence using the GRADE approach.

Conclusion

The present dose–response meta-analysis of thirty-four small randomised trials indicated that olive oil intake did not significantly improve blood lipids when was compared with other plant-based oils. The subgroup analyses suggested some favourable effects in comparison with butter, but the number of trials was very small. In addition, the overall quality of evidence was rated very low to low, indicating that the true effect might be noticeably different from the estimated effect, and that future research might have a large impact on effect estimates.

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There are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114522003683

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