Update on lifestyle determinants of postprandial triacylglycerolemia with emphasis on the Mediterranean lifestyle.

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This review updates the effect of lifestyle on plasma triacylglycerols (TAG) in the postprandial state, commonly reported as postprandial lipemia (PPL), an independent risk factor for cardiovascular diseases (CVD). Numerous studies have shown that Mediterranean diet may reduce PPL. However, most of these studies were focused on the type of fat (i.e., monounsaturated fat from olive oil) and the other components of the Mediterranean lifestyle were neglected. Physical activity, an integral part of this lifestyle, is widely investigated on its own and shown to reduce PPL. In addition, preliminary results of studies examining other Mediterranean “ingredients”, such as legumes, fish and herbs, showed additional benefits; however, data on the long-term effects are limited. More studies are needed to confirm short-term results and investigate the effects of the whole Mediterranean lifestyle on PPL and whether these effects mediate its protective role on CVD. Moreover, investigation of the effects in non-healthy populations and the underlying mechanisms would be clinically helpful in individualizing the appropriate intervention.

Key words: triglycerides; olive; physical activity; diet; lipid metabolism.
INTRODUCTION

Free-living humans spent most of their time in a non-fasting, postprandial state; however, routine health screening is performed in the fasting state. Regarding lipids [mainly triacylglycerols (TAG) and their carriers, TAG-rich lipoproteins (TRL)], the most profound changes are taken place in the postprandial state, i.e., the hours after the consumption of dietary fat. TAG and TRL metabolism in the postprandial state are schematically shown in Figure 1.

Recent evidence suggests that elevated levels of plasma TAG in the postprandial state, commonly reported as postprandial lipemia (PPL) or non-fasting TAG, is associated with increased risk for atherosclerosis, independently of other known cardiovascular disease (CVD) risk factors (32, 61). In addition, TAG-TRL remnants [i.e., chylomicrons and VLDL with reduced amount or depleted of TAG after the action of lipoprotein lipase (LPL)] may penetrate the arterial wall and may be taken up by monocytes, forming foam cells. Several epidemiological studies have shown that CVD patients have increased levels of postprandial TRL (62), while VLDL remnants have also be found in atheromatique plaques. In addition, reduced TRL catabolism is associated with changes in the size of other lipoproteins (e.g., formation of HDL3 and LDL3; Figure 2) that are thought to be atherogenic (66, 74), as well as oxidative stress, endothelium dysfunction and inflammation (40, 87), thereby increasing CVD risk. Recent detailed reviews have highlighted the clinical importance of PPL (12, 37). Therefore, interventions that improve postprandial TAG and TRL metabolism may be valuable in reducing the risk of CVD.
Numerous epidemiological studies have shown that the Mediterranean lifestyle is associated with lower risk for several diseases, including CVD, and these results are also confirmed from interventional studies, such as the PREDIMED study (25) and others, as recently meta-analysed and reviewed (25, 36). The cardioprotective effect of this lifestyle may be mediated through favourably effects on several CVD risk factors, such as insulin sensitivity and fasting TAG levels (78). Whether improvements in postprandial TAG metabolism also mediate the protective role of the Mediterranean lifestyle on CVD is currently unknown.

The Mediterranean lifestyle is commonly depicted and summarized in the Mediterranean diet pyramid [Figure 3 (5)]. Although it has no particular definition, the main characteristics of the Mediterranean diet include high consumption of plant based foods, such as olive oil and olives (as the prevalent fat), vegetables, fruits, legumes, whole grain products and nuts, moderate wine consumption with meals, and low consumption of red meat and meat products. The result is an increased intake of carbohydrates (~50% of energy), mainly non-raffinates; fat (35-40%), mainly monounsaturated fatty acids (MUFA), and polyphenolics; moderate intake of alcohol; and low intake of saturated fatty acids (SFA). Other important, often neglected, characteristics of the Mediterranean lifestyle include regular physical activity, adequate rest (enough sleep duration and naps), use of herbs and spices, regular (weekly) consumption of fish and regular (daily) consumption of milk products (mainly cheese and yogurt).

Epidemiological studies investigating the association between Mediterranean lifestyle and PPL are scarce and focus only on the main characteristic of Mediterranean diet, i.e., the amount and type of fat, and not on the whole lifestyle pattern. In more detail, one study (89) found that Southern European males [consuming more percentage (%)
of energy as total fat and MUFA and less polyunsaturated fatty acids (PUFA)],
compared to Northern counterparts, presented differences in postprandial responses
after consumption of a high-MUFA or high-SFA meal. Southern Europeans
experienced an early postprandial TAG rise and a rapid return late postprandially,
accompanied by decreased apolipoprotein (apo)-B48 concentrations, reflecting
decreased chylomicron formation or increased clearance. On the other hand, another
study found no difference between Spanish (consuming more % of energy as MUFA)
and Dutch subjects in daylong self-measured TAGs (86). However, it should be noted
that the differences between Spanish and Dutch subjects in MUFA intake, while
statistically significant, were quite small (4-7gr/day or 3-3.5%).

Several interventional studies aimed to investigate the effect of the Mediterranean diet
on PPL. However, as for epidemiological studies, no intervention study to date has
investigated the effect of the Mediterranean lifestyle as a whole. Therefore, the
purpose of this manuscript is to review the effects of the Mediterranean lifestyle
“ingredients” and, where possible, of their combinations on PPL. Studies for this
review were retrieved via advanced PubMed search. Search terms used included the
followings: “Mediterranean”, or “olive”, or “monounsaturated”, or “nut”, or
“legume”, or “fibre”, or “fiber”, or “polyphenol”, or “fish”, or “n-3”, or “omega-3”, or
“exercise”, or “physical activity”, or “sleep”, or “nap” combined with “postprandial”
or “non-fasting”, and “lipemia”, or “lipaemia” or “triglyceride”, or “triacylglycerol”.
The search was restricted to articles published in English. The reference lists of
retrieved articles and other relevant published reviews were also reviewed. Where
available data exist, the underlying mechanisms are also discussed, in order for
physicians and researchers to focus on the most relevant interventions. Because of
space limitations, we cannot cite the vast number of papers that contributed to this
review and focus mainly on recent or the most important studies.

AMOUNT AND TYPE OF FAT

ACUTE EFFECTS

A typical Mediterranean meal contains enough fat (i.e., >30 g) to induce PPL. However, the degree of PPL depends on the type of fat ingested. Compared with butter (high in SFA), olive oil (high in MUFA) produced similar (6, 38, 60, 81), or greater (38, 56), or lower (42, 43, 82) PPL in healthy populations. Mixed results were also found when comparing olive oil with other fats and oils rich in SFA (palm oil or palm olein oil or cocoa butter), or PUFA (walnuts or corn oil or salmon oil or flaxseed oil or safflower oil or sunflower oil), or MUFA (rapeseed oil or high oleic sunflower oil).

It seems that subjects’ characteristics may influence the relationship between fat type and PPL. Higher weight subjects benefit more from the consumption of MUFA (olive oil) rather than PUFA (walnut), or SFA (butter) (45). Also, olive oil reduced PPL in men with fasting hypertriglyceridemia (42) and in overweight subjects with type 2 diabetes (83). Increases in postprandial insulin sensitivity after MUFA intake may increase LPL activity and therefore TAG clearance. Alternatively, or additionally, TRL particles after MUFA intake may have greater affinity to hepatic receptors that are responsible for TRL remnant clearance.

Lipid bioaccessibility may affect PPL. This fact is clinically important and should be taken into account when translating research evidence into practice. A recent study showed that whole almond seeds produced 70% lower PPL than almond oil with
defatted almond flour (given in order to provide the same nutrients) (9). Whether olives per se affect PPL differently than olive oil is currently unknown, and this issue is of great importance since the “original” Mediterranean diet includes mainly olives rather than their product. Interestingly, it has been recently revealed that pomace oil (i.e., the oil obtained by chemical processes from residues of the extraction of virgin olive oil, containing a number of unsaponifiable components from the olive skin) facilitates greater TAG clearance from TRL compared to olive oil, by increasing their particle size (16, 17). Nevertheless, whether olive oil is of low or high phenolic compounds does not seem to influence PPL responses, at least in those with hypercholesterolemia (72).

LONG-TERM EFFECTS

Several studies have compared the effects on PPL of a diet high in total fat and MUFA (HFMUFA) (olive oil) vs. low in fat and high in carbohydrates (LFHC) and / or vs. a diet high in fat and SFA (HFSFA) (butter). Many (21, 24, 33, 34, 39, 46, 68, 69, 76, 79, 90), but not all (4, 14, 20, 26, 65, 70, 71, 85), found that the HFMUFA diet was superior to the other two diets in several aspects of postprandial TAG metabolism in both healthy and non-healthy volunteers (Tables 1 & 2).

Collectively, data from these studies suggest that a HFMUFA diet leads to significantly higher earlier (1-3h) (24, 34, 68, 69) but lower later (>4h) postprandial total TAG and TRL-TAG responses (21, 24, 33, 34, 68, 69). A reduced number of TRL (21, 46, 68, 76), increased production of TRL containing apoE (90) and increased size of TRL (68) (mainly chylomicrons) postprandially (note: larger chylomicrons have greater affinity to LPL and thereby cleared more efficiently) results in increased TRL catabolic rate (90) and, most importantly, increased
percentage of TRL that are cleared rather than being converted to the atherogenic particles, LDL (90).

Both normal and overweight subjects experienced similar reduction in PPL after a MUFA-rich Mediterranean-type diet (21). The same for subjects with normal or high fasting TAG levels, i.e., a MUFA-rich Mediterranean-type diet is an effective strategy to reduce an important CVD risk factor, independently of body mass index or fasting TAG levels. Advantages of a HFMUFA diet have also been found in subjects with metabolic syndrome (34) or type 2 diabetes (46, 69). Of two studies performed in type 1 diabetics, the first (26) found that 4 weeks on a HFMUFA diet increased PPL. However, a more recent study with a more prolonged intervention (6 months) showed that 24h TAG was lower after a HFMUFA compared to a LFHC diet (79).

Nevertheless, as mentioned above, some studies found higher or similar PPL after a HFMUFA vs. a LFHC diet. Small sample size, no washout period, only small differences (~3%) between diets in MUFA, higher fiber content in LFHC, or short postprandial time may account for the results of these studies. More importantly, in some of these studies, test meal composition was according to diet composition, and the LFHC meal had less (14, 20), or no (65) fat compared to the HFMUFA meal, and therefore this effect was expected since meal total fat amount is the main determinant of PPL (14, 20, 65). However, other studies found benefits of a HFMUFA vs. a LFHC diet, even if the test meal was according to diet composition and therefore of greater fat (24, 33, 68, 79).
LEGUMES, GRAINS AND OTHER HIGH FIBER FOODS

One of the main characteristics of the Mediterranean diet is the increased consumption of whole-grain products, i.e., products from grains that contain the germ, endosperm, and bran, in contrast to refined grains, which retain only the endosperm [Figure 3 (5)]. A 12-week whole-grain cereal-based diet, compared to one using refined cereals, reduced PPL and postprandial insulin levels in subjects with metabolic syndrome, without differences in postprandial apo-B48 or apo-B100 responses (27).

The Mediterranean diet includes frequent consumption of legumes, such as beans, lentils, fava, peas, etc.; however, little is known about their effects on PPL. Early study showed that fiber from beans added to a low-fat meal (23 g of fat) did not affect postprandial TAG, even though it increased postprandial apoB48 levels in healthy men (13). On the other hand, a recent study in overweight/obese type 2 diabetics showed that 275 g of almonga, but not Curruquilla, beans (Spanish types of beans) lowered postprandial TAG concentrations, compared to bread (64). The difference between these two types of beans on PPL may be mediated through differences in their antinutritional content, indicating the diversity in health effects of even the same legume. Moreover, the addition of pea fiber (~7 g more fiber in each of three main meals) for two days reduced postprandial TAG concentrations during breakfast and lunch the second day in healthy males (73). Carob is used in Mediterranean countries such as Cyprus, Malta, and Greece as a snack or cocoa substitute. Interestingly, carob pulp added to a low fat meal decreased PPL in a dose response manner (28).

However, more studies are needed in order to evaluate the long term effects of legumes on PPL and the underlying mechanisms.
OTHER CHARACTERISTICS OF THE MEDITERRANEAN DIET

DAIRY PRODUCTS

A recent study in healthy males found that increased calcium intake from dairy products (milk and yogurt) reduced PPL in a single high-fat meal, presumably due to reduced fat absorption, whereas supplementary calcium carbonate did not exert such an effect (44). Recent studies showed that a meal supplemented with whey protein lowers PPL, compared to cod- or glutein-meal, in both obese non-diabetics (30) and in type 2 diabetics (57), due to lower TAG in chylomicrons. Additionally, in obese non-diabetics, whey protein supplementation for 12 weeks decreased the postprandial apoB48 responses compared with casein, without affecting postprandial TAG concentrations, suggesting different short- and long-term effects of whey protein and/or each dairy product (11). Several types of cheeses consumed in the Mediterranean region include whey protein, such as ricotta in Italy, or anthotyros, manouri and mizithra in Greece. However, the effect of these dairy products on PPL is currently unknown.

FISH

Several studies have investigated the effects of fish oil supplementation; however, little is known regarding the effect of fish intake per se on PPL. In the short-term, baked herring produced higher TAG clearance than baked minced beef in overweight men (80). In the long-term, a diet naturally rich in long chain n-3 fatty acids (salmon, dentex or anchovies) for eight weeks significantly reduced VLDL-apoB48, and tended to decrease postprandial TRL, total TAG concentrations and chylomicron remnants in overweight subjects (3). It should be noted that the amount and frequency of fish
consumption in this study (330g, 3 times per week) is ordinary in the Mediterranean diet. A previous study of longer duration also found decreases in healthy males in postprandial total and chylomicron-TAG responses after 15 weeks on a fish-rich diet (~4 fish-containing meals per week) (1).

**ALCOHOL & WINE**

Although an early study showed that acute consumption of ~1-2 glasses of wine along with a high-fat meal did not significantly affect PPL in healthy volunteers (22), a more recent study in dyslipidemic postmenopausal women showed that 400ml of red wine acutely increased postprandial TAG concentrations and the incremental area under the TAG concentration-versus time curve:apoB48 ratio, compared with water, suggesting an increase in larger, TAG-enriched chylomicron particles (59); however, this effect was abolished when red wine was dealcoholized (59). Other studies found similar results, as reviewed (67). However, it is currently unknown whether this unfavorable effect of wine is transient or not. A recent study, investigating another alcohol drink (vodka), showed that the effect on PPL is transient and abolished ~12h after alcohol intake (58). Indeed, epidemiological studies indicate that low or moderate consumption of alcohol is associated with lower postprandial TAG concentrations in a white population (75, 84) and this may be one, albeit not the sole, mechanism by which low to moderate alcohol consumption is associated with reduced CVD risk (23, 31, 54).
OTHER FOODS HIGH IN PHENOLIC COMPOUNDS

Herbs, spices, tea, etc.

One of the main characteristics of several popular diets (Indian diet, Mediterranean diet, etc.), often neglected, is the frequent use of herbs and spices in meal preparation. A recent study in healthy slightly overweight men (77) showed that adding 14 g of a mixed herb/spice blend (black pepper, cinnamon, cloves, garlic powder, ginger, Mediterranean oregano, paprika, rosemary, turmeric) to a moderate fat meal (~50 g of fat) significantly reduced PPL by 31%, presumably due to the high concentration of phenolic antioxidants in spices, which may have delayed gastric emptying and directly inhibited pancreatic lipases. On the other hand, in a previous study in overweight/obese men with type 2 diabetes (41), adding ~12 g of a similar mix to 250 g of ground beef did not influence PPL; however, the low fat content (~25 g) and/or medication used by the participants may have influenced the results. Nevertheless, 3 g of cinnamon does not affect PPL in healthy subjects (52) although investigated only for 3h.

Acute coffee consumption after a meal does not influence PPL (10); neither does black tea (29). The effect of other herbal teas used in the Mediterranean diet, such as linden, flamouri, diktamo, louiza, etc., is currently unknown.

Phenolics from fruits

The addition of 1 L of red orange juice (high in anthocyanin) to a high-fat meal results in a reduced increase in postprandial TAG concentrations compared to water and blond orange juice in healthy subjects (19). On the other hand, the addition of a
pomegranate extract (high in other polyphenols, but with very small amounts of anthocyanins) did not influence PPL for 4h in healthy males (53).

**Long-term effects**

Two recent studies investigated the long term effects of a diet rich in polyphenols on PPL. Six weeks’ dietary supplementation with an active strawberry beverage, equivalent to 110 g/d of fresh strawberries, reduced postprandial TAG responses to a high-fat meal (15). A diet rich in polyphenols of different sources (decaffeinated green tea and coffee, dark chocolate, blueberry jam, artichokes, onions, spinach, rocket, and extra-virgin olive oil) for eight weeks significantly reduced PPL, mainly by reducing postprandial large VLDL-TAG concentrations in overweight subjects (3). It should be noted that the amounts of foods high in polyphenols used in this study are ordinary in the Mediterranean diet.

**EFFECTS OF OTHER “INGREDIENTS” OF THE MEDITERRANEAN LIFESTYLE**

**PHYSICAL ACTIVITY**

It is well established that a single bout of exercise reduces PPL (50, 51), mainly by increasing TRL-TAG clearance, and to a lesser extent by reducing VLDL-TAG production (7, 8). The main moderator of this effect is exercise energy expenditure (48, 49); an energy expenditure of ~30 kJ/kg of body mass (or ~2-2.5 MJ) is required; for resistance or high intensity interval exercise, for those following a moderate rather than a high fat diet, and for those with obesity or fasting hypertriacylglycerolemia, a smaller energy expenditure is probably sufficient (51). Furthermore, if a prudent diet
Mediterranean lifestyle and lipemia

(with moderate fat intake, high in MUFA, like the Mediterranean diet) is followed, exercise may be of less load. However, since training studies have shown that the effect of exercise is transient, exercise should be included as a part of daily living, as in the Mediterranean lifestyle, and not performed only occasionally, although the effort need not be a single continuous bout but instead could be spread out throughout the day, since the benefits of intermittent compared to continuous exercise on PPL are equal or possibly even greater (2).

SLEEP HABITS

Sleep habits (duration and quality) in western-type societies have changed due to lifestyle and workload, affecting insulin sensitivity and several other CVD risk factors (18, 55). U-shaped associations between sleep duration and high fasting TAG levels were observed among women only (35), with those sleeping 6-7 h presenting the lowest levels. However, to the best of our knowledge, associations between sleep duration and/or quality and PPL have not been investigated. The only relevant data come from two interventional studies, one on the effect of short-term partial sleep deprivation on 24h TAG levels and the other on the effect of total sleep deprivation followed by normal sleep in night shift workers. In more detail, four days of partial sleep deprivation (4h sleep/night) did not affect 24h TAG levels on the 4th day, compared to normal sleep (9h sleep/night) (63). Even though subjects in this study were under controlled isocaloric feeding, observed weight loss may have influenced the results. In the other study, although total sleep deprivation did not affect PPL immediately (during the following breakfast), PPL was increased after recovery sleep (during the breakfast the next day after recovery sleep), mainly due to increases in fasting TAG levels (88). In addition, no study to date has investigated the effect on
PPL of daytime nap, a habit in the Mediterranean lifestyle. Therefore, more studies are needed in order to clarify the role of sleep habits on PPL.

CONCLUSIONS

It seems that most components of the Mediterranean lifestyle may reduce PPL, an important CVD risk factor, with the exception of wine. Although olive oil is a main component of this pattern, preliminary results of studies of several other components — such as fish, legumes, herbs and physical activity — are very promising. More studies are needed to confirm these results, investigate long-term effects and, most importantly, investigate the lifestyle as a whole. In addition, investigation of the underlying mechanisms would increase our knowledge and may be also helpful in the clinical setting. Finally, studies are needed in order to investigate whether the effect of the Mediterranean lifestyle and its components on PPL mediate the overall well-established protective role of this lifestyle on CVD.
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of HDL and LDL in individuals with the metabolic syndrome and patients with type 2


Figure Legends

Figure 1. Triacylglycerol (TAG) and TAG-rich lipoprotein (TRL) metabolism in the postprandial state. Adapted from (47). Apo, apolipoprotein; CM, chylomicron; CMr, chylomicron remnants; DNL, de novo lipogenesis; HL, hepatic lipase; HSL, hormone sensitive lipase; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; LDLR, LDL receptor; LPL, lipoprotein lipase; LRP, lipoprotein related protein; MAG, monoacylglycerol; NEFA, non-esterified fatty acid; TAG, triacylglycerol; VLDLr, VLDL remnant.

Figure 2. Atherogenic changes induced by the accumulation of triacylglycerol-rich lipoproteins (TRL). Elevated levels of TRL, i.e., chylomicron (CM), VLDL and their remnants (CMr and VLDLr; i.e., chylomicrons and VLDL with reduced amount or depleted of TAG after the action of lipoprotein lipase), lead to the formation of cholesterol-ester (CE) enriched small dense LDL (LDL3) and HDL (HDL3). LDL3 are the more atherogenic forms of LDL due to increased binding affinity to the artery wall, while HDL3 are more easily catabolised, thereby decreasing HDL cholesterol. HL, hepatic lipase; CETP, cholesterol-ester transfer protein.

Figure 3. The Mediterranean diet pyramid. Reproduced from (5), who recommends use of this image without restriction.
Table 1: Interventional studies on the long term effect of MUFA-rich vs. other diets on PPL in a healthy population a, b

<table>
<thead>
<tr>
<th>Sex (n)</th>
<th>Subjects’ important characteristics</th>
<th>Experimental diet</th>
<th>Duration</th>
<th>Crossover</th>
<th>Test meal</th>
<th>Pre &amp; post</th>
<th>Test</th>
<th>PPL responses</th>
<th>Important Notes</th>
<th>Reference</th>
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<tbody>
<tr>
<td>M(20)</td>
<td>Young</td>
<td>HFMUFA (olive oil) vs. HFSFA (butter) vs. LFHC/ALA (walnuts)</td>
<td>4 wks</td>
<td>Y</td>
<td>Different bw diets (corresponding to diet composition)</td>
<td>N</td>
<td>8</td>
<td>ppTAG at 2h: HFMUFA &gt; HFSFA = LFHC/ALA</td>
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<td>ppTAG at 6h: HFMUFA &gt; HFSFA = LFHC/ALA</td>
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<td>M(20)</td>
<td>Young</td>
<td>HFMUFA (olive oil) vs. HFSFA (butter) vs. LFHC/ALA (walnuts)</td>
<td>4 wks</td>
<td>Y</td>
<td>Different bw diets (corresponding to diet composition)</td>
<td>N</td>
<td>11</td>
<td>ppTAG &amp; ppTRL-TAG early (1-3h): HFMUFA &gt; HFSFA = LFHC/ALA</td>
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<td>(68)</td>
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<td>ppTAG, ppTRL-TAG late (4-8.5h): HFMUFA &lt; HFSFA = LFHC/ALA</td>
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<td>ppTRL particles: HFMUFA &lt; HFSFA = LFHC/ALA</td>
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<td>ppTRL particle size: HFMUFA &gt; HFSFA = LFHC/ALA</td>
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<td>HFMUFA (olive oil) vs. HFSFA (butter) vs. LFHC/ALA (walnuts)</td>
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<td>Y</td>
<td>Different bw diets (corresponding to diet composition)</td>
<td>N</td>
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<td>ppTAG at 6h: HFSFA &gt; HFMUFA = LFHC/ALA &lt;</td>
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<td>ppTAG at 9h: HFMUFA &lt; LFHC/ALA</td>
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<td>B(25)</td>
<td>Young</td>
<td>HSFA vs. MMUFA</td>
<td>8 wks</td>
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<td>Same after all diets</td>
<td>N</td>
<td>8</td>
<td>TAG AUC &amp; iAUC: ns</td>
<td>Differences in MUFA content between diets only 3 or 4.5%</td>
<td>(76)</td>
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<td>B(26)</td>
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<td>HSFA vs. HMUFA</td>
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<td>apoB48 AUC &amp; peak: HMFUFA &gt; MMUFA &lt; HSFA</td>
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<td>MMUFA vs. HMUFA</td>
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<td>Differences in MUFA content between diets only 3 or 4.5%</td>
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<td>M(23)</td>
<td>Young</td>
<td>HMUFA (manufactured fat) vs. HSFA</td>
<td>8 wks</td>
<td>Y</td>
<td>Same after both diets</td>
<td>N</td>
<td>9</td>
<td>TAG AUC &amp; iAUC: ns</td>
<td>Differences in diet MUFA content between diets only 4.5%</td>
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<td>ppTAG &amp; ppTRL-apoB48 at 3.4.5h: MUFA &gt; SFA</td>
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<td>M(23)</td>
<td>NW/OW</td>
<td>HFMUFA (olive oil) vs. LFHC</td>
<td>6-7 wks</td>
<td>N</td>
<td>HFMUFA before &amp; after both diets</td>
<td>Y</td>
<td>8</td>
<td>Pre vs. post in each diet: TAG AUC: ns</td>
<td>Differences in diet fiber content LFHC &gt; HFMUFA</td>
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<td>Bw diets: TAG AUC: ns</td>
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<td>M(19)</td>
<td>NW/OW</td>
<td>HFMUFA (olive oil) vs. LFHC</td>
<td>7 wks</td>
<td>N</td>
<td>Same standard meal before &amp;</td>
<td>Y</td>
<td>8</td>
<td>TAG AUC: Pre vs. post: ↓ only in HFMUFA</td>
<td>Small weight loss: HFMUFA &lt;</td>
<td>(39)</td>
</tr>
</tbody>
</table>

a. Studies involving healthy populations

b. Studies involving young subjects

Notes:
- HFMUFA: High Monounsaturated Fat
- HFSFA: High Saturated Fat
- LFHC/ALA: Low Fat, High Carbohydrate, ALA
- MUFA: Monounsaturated Fat
- SFA: Saturated Fat
- MUFA (manufactured fat): Artificially manufactured diet high in MUFA
- Same after all diets
- Differences in MUFA content between diets only 3 or 4.5%
| B(20) | NW/OW | HFMUFA (olive oil) vs. LFHC | 3 wks | Y | Small frequent meals corresponding to diet composition | N | 14 | TRL-apoE, TRL fractional catabolic rate, %TRL cleared rather than converted to LDL; HFMUFA>LFHC | Differences in diet fiber content: LFHC> HFMUFA (90) |

a For clarity, **bold** studies reported significant reduction in postprandial lipemia after MUFA-rich diet or/and compared to other diets, while non-bold studies did not.

b **apo**, apolipoprotein; **AUC**, area under the concentration-versus time curve in the postprandial state; **B**, both sexes; **bw**, between; **HFMUFA**, high in total fat and MUFA; **HFSFA**, high in total fat and SFA; **HMUFA**, high in MUFA; **HSFA**, high in SFA; **iAUC**, incremental area under the concentration-versus time curve in the postprandial state; **LFHC**, low in fat and high in carbohydrates; **LFHC/ALA, LFHC** enriched in α-linolenic acid; **M**, men; **MUFA**, monounsaturated fatty acids; **MMUFA**, moderate in MUFA; **ns**, not significant (p>0.05); **NW**, normal weight; **OW**, overweight; **pp**, postprandial; **PPL**, postprandial lipemia; **SFA**, saturated fatty acids; **TAG**, triacylglycerols;

c whether study was of crossover design; **Y**, Yes; **N**, no

d information regarding the test meal given to investigate PPL

e whether the test meal was given before and after each experimental diet; **Y** Yes, both; **N**, No, only after each experimental diet

f duration of postprandial investigation in hours.
### Table 2: Interventional studies on the long term effect of MUFA-rich vs. other diets on PPL in a non-healthy population a, b

<table>
<thead>
<tr>
<th>Sex (n)</th>
<th>Subjects' important characteristics</th>
<th>Experimental diet</th>
<th>Duration</th>
<th>Cross over</th>
<th>Test meal</th>
<th>Pre &amp; post</th>
<th>PPL responses</th>
<th>Important Notes</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>B(72) B(63)</td>
<td>At least one CVD risk factor</td>
<td>LFHMUFA (olive oil, Mediterranean type) vs. LF-AHA</td>
<td>3 mo</td>
<td>N</td>
<td>Same continental breakfast before and after both diets</td>
<td>Y</td>
<td>5</td>
<td>Pre vs. post in each diet: TAG AUC &amp; iAUC: ns Both diets ↓ ppTAG at5h Both diets ↓ apoB48 AUC &amp; iAUC (LFHMUFA more pronounced effects) Bw diets: ns</td>
<td>Very small difference in MUFA intake (1-2%), not HMUFA (15%), not HF</td>
</tr>
<tr>
<td>M(6) M(7) M(8) M(8)</td>
<td>MS</td>
<td>HFMUFA (manufactured fat) vs. HSFA vs. LFHC vs. LFHCn3</td>
<td>12 wks</td>
<td>N</td>
<td>Same before &amp; after all diets</td>
<td>Y</td>
<td>4</td>
<td>Pre vs. post in each diet: TAGAUC: ns Bw diets: TAGAUC: LFHC&gt;HFHCn3&lt;HF-SFA</td>
<td>Too small sample size</td>
</tr>
<tr>
<td>B(26) B(32) B(31) B(28)</td>
<td>MS</td>
<td>HFMUFA vs. HSFA vs. LFHC vs. LFHCn3</td>
<td>12 wks</td>
<td>N</td>
<td>Fat composition according to diet</td>
<td>Y</td>
<td>8h</td>
<td>Pre vs. post in each diet: TAGAUC &amp; large TRL-TAG iAUC: ↑ in LFHC large TRL-apo: ↑ in LFHC &amp; LFHCn3 Bw diets post-intervention: TAGAUC: LFHC&gt;the others ppTAG: LFHC n3&lt;the others HFMUFA earlier increase and faster clearance of pTAG and large TRL-TAG compared to HSFA and LFHC</td>
<td></td>
</tr>
<tr>
<td>B(17)</td>
<td>IR, COB, offsprings of OB, DB2</td>
<td>HFMUFA (olive oil) vs. HSFA (butter) vs. LFHC</td>
<td>4 wks</td>
<td>Y</td>
<td>Different bw diets (corresponding to diet composition) No fast after LFHC</td>
<td>N</td>
<td>3</td>
<td>TAGAUC: LFHC&lt; the others</td>
<td>Due to main differences in fat content of test meal Only 3h</td>
</tr>
<tr>
<td>M(11)</td>
<td>DB2</td>
<td>MUFA (30ml olive oil) vs. PUFA (30ml sunflower oil)</td>
<td>2 wks</td>
<td>Y</td>
<td>Different bw diets (corresponding to diet composition)</td>
<td>N</td>
<td>8</td>
<td>TAGAUC: ns ppChylomicron- &amp; ppvldl-ppapoB48 &amp; ppapoB100: MUFA&lt;PUFA</td>
<td>No washout period Only 2 wks</td>
</tr>
<tr>
<td>B(12)</td>
<td>DB2, BMI&lt;30</td>
<td>HFMUFA (olive oil) vs. LFHC</td>
<td>6 wks</td>
<td>Y</td>
<td>Same after both diets</td>
<td>N</td>
<td>6</td>
<td>TAGAUC &amp; VLDL-TAG iAUC:ns</td>
<td>No washout period Differences in diet fiber content: LFHC&gt; HFMUFA</td>
</tr>
<tr>
<td>M(11)</td>
<td>OW/OB, DB2</td>
<td>HMUFA (olive oil) vs. HSFA (butter)</td>
<td>3 wks</td>
<td>Y</td>
<td>Same after both diets</td>
<td>N</td>
<td>6</td>
<td>Small VLDL-TAG IAUC: MUFA&gt;SFA ppchylomicron-TAG at 2h, LPL activity in</td>
<td></td>
</tr>
</tbody>
</table>
## Mediterranean lifestyle and lipemia

<table>
<thead>
<tr>
<th>Study (Ref)</th>
<th>Type</th>
<th>Intervention</th>
<th>Duration</th>
<th>Design</th>
<th>Outcome Measures</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>B(12) OB, DB2</td>
<td>HFMUFA vs. LFHC</td>
<td>Different bw diets</td>
<td>4 wks</td>
<td>Y</td>
<td>TAG iAUC, Chylomeron TAG iAUC, large VLDL-TAG iAUC, LDL-TAG iAUC, self-measured TAG 3h after lunch: HFMUFA&gt;HCHOHfiber</td>
<td>Main differences in fat content of test meal</td>
</tr>
<tr>
<td>B(17) OB, DB2</td>
<td>HFMUFA vs. LFHC</td>
<td>Different bw diets</td>
<td>8 wks</td>
<td>N</td>
<td>Pre vs. post in each diet: HFMUFA: ↑% ppTAG increase at 4&amp; 6h HCHOHfiber: ↓ppTAG at 6h Bw diets: TAG iAUC: HFMUFA &gt;HCHOHfiber</td>
<td>Main differences in fat content of test meal</td>
</tr>
<tr>
<td>B(17) DB1</td>
<td>HFMUFA vs. LFHC</td>
<td>Both types</td>
<td>4 wks</td>
<td>Y</td>
<td>Same breakfast &amp; lunch; dinner according to diet</td>
<td>N</td>
</tr>
<tr>
<td>B(15) DB1 (olive oil) vs. LFHC</td>
<td></td>
<td></td>
<td>6 mo</td>
<td>N</td>
<td>Same breakfast &amp; lunch; dinner according to diet</td>
<td>N</td>
</tr>
</tbody>
</table>

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**a** For clarity, **bold** studies reported significant reduction in postprandial lipemia after MUFA-rich diet or/and compared to other diets, while non-bold studies did not.

**b** **apo**, apolipoprotein; **AUC**, area under the concentration-versus time curve in the postprandial state; **B**, both sexes; **bw**, between; **COB**, centrally obese; **CVD**, cardiovascular disease; **DB1**, type 1 diabetes; **DB2**, type 2 diabetes; **HFMUFA**, high in total fat and MUFA; **HFSFA**, high in total fat and SFA; **HMUFA**, high in MUFA; **HSFA**, high in SFA; **iAUC**, incremental area under the concentration-versus time curve in the postprandial state; **IR**=insulin resistant; **LF-AHA**=low fat, American Heart Association type; **LFHC**, low in fat and high in carbohydrates; **LFHCn3**, LFHC supplemented with n-3; **LFHCHfiber**, LFHC and high in fiber; **LFHMUFA**, low in fat and high in MUFA; **M**, men; **mo**, months; **MS**, metabolic syndrome; **MUFA**, monounsaturated fatty acids; **ns**, not significant (p>0.05); **OB**, obese; **OW**, overweight; **pp**, postprandial; **PPL**, postprandial lipemia; **PUFA**, polyunsaturated fatty acids; **SFA**, saturated fatty acids; **TAG**, triacylglycerols; **TRL**, TAG-rich lipoproteins; **wks**, weeks

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**c** whether study was of crossover design; **Y**, Yes; **N**, no

**d** information regarding the test meal given to investigate PPL

**e** whether the test meal was given before and after each experimental diet; **Y**, Yes, both; **N**, No, only after each experimental diet

**f** duration of postprandial investigation in hours
Figure 2

TAG-rich lipoproteins (TRL):
CM, VLDL & their remnants