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Systematic review and network meta-analysis about the effects of different oils and solid fats on blood lipid levels

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1

Introduction

This chapter states the motivation for carrying out this thesis. It follows a brief description of the research problem and a concluding outline of the methodological approach.

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In recent years, noncommunicable diseases (NCDs) have become the leading cause of death worldwide, with the majority occurring due to cardiovascular diseases (CVDs) (41.1 million - 17.8 million reported cases in 2017) [18, 166]. Therefore, the significant reduction in mortality rate caused by NCDs is one of the important subsets of the 'Sustainable Development Goals (SDGs)' [19].

1.1 Motivation

Due to the high mortality and morbidity, CVDs and their pathogenesis have become a highly investigated research field in the past decades. Several scientific publications show that both diet and lifestyle have an impact on the occurrence of CVDs [7, 40, 55, 91, 131]. Their development can be triggered by other diseases or by the presence of certain risk factors. One of these risk factors, atherogenetic dyslipidemia - a typical concomitant of obesity, type 2 diabetes mellitus and the metabolic syndrome - is characterised by increased low density lipoprotein cholesterol (LDL-C) and triglyceride (TG) levels as well as decreased high density lipoprotein cholesterol (HDL-C) concentrations [134]. Similar to blood lipid levels, saturated fatty acids (SFAs) and trans fatty acids (TFAs) are also linked to the development of various diseases, including CVDs [55, 131]. In contrast, benefits are attributed to unsaturated fatty acids (monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs)) [91, 132]. Since these fatty acids are primarily absorbed through edible oils and fats, the following research question arises: 'Which oils and fats are positively influencing blood lipid levels and might therefore have a preventive effect on CVDs?'
This work serves as an extension to the conducted research by Schwingshackl et al. [181], who investigated the effect of different oils and fats on the blood lipids LDL-C, total serum cholesterol (TC), HDL-C and TGs within the framework of a network meta-analysis (NMA) (including 13 oils / solid fats) by expanding the range of the investigated oils and solid fats.

1.2 Problem Statement

In the course of this work, a literature research is undertaken that aims to expand the existing analysis by integrating new study findings and taking additional oils and solid fats into consideration. Subsequently, a NMA is conducted in order to assess the effects of consuming one of the included oils and solid fats regarding their impact on the blood lipid concentrations of LDL-C, TC, HDL-C and TGs.

1.3 Methodological Approach

The first step is to identify all the studies that are eligible for the analysis based on a scientific literature search with predefined inclusion criteria. Next, a risk of bias assessment which allows a later sensitivity analysis is done. Finally, the actual NMA featuring an inconsistency as well as a sensitivity analysis is performed.

1.4 Structure of this Thesis

Chapter 2 provides additional background information about cardiovascular diseases and introduces the characteristics of different fatty acids and blood lipids.
Chapter 3 explains the literature search. Moreover, the concepts of the risk of bias assessment and the network meta-analysis are introduced.
Chapter 4 gives an overview of the included studies and their risk of bias and shows the results of the conducted network meta-analysis.
Chapter 5 discusses the findings and limitations of this work.
Chapter 6 gives a conclusion and outlines possible future work topics.
Chapter 7 contains a short summary of the thesis in English and German.

2

Background

This chapter provides additional background information about cardiovascular diseases and introduces the characteristics of different fatty acids and blood lipids.

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2.1 Burden of cardiovascular diseases

Cardiovascular diseases (CVDs) were among the leading causes of death worldwide in 2017 [166]. The associated clinical pictures are multifaceted and can affect different areas of the body (exemplary disease types are shown in Table 2.1). Heart

Table 2.1: Different clinical pictures of CVDs[1]

Type	Disease pattern
Coronary heart disease	Diseases of the blood vessels supplying the heart muscle
Cerebrovascular disease	Diseases of the blood vessels supplying the brain
Peripheral arterial disease	Diseases of blood vessels supplying blood to the arms and legs
Rheumatic arterial disease	Destruction of the heart muscle and valves by rheumatic fever caused by streptococcal bacteria
Congenital heart disease	Malformation of the heart structure from birth
Deep vein thrombosis and pulmonary embolism	Blood clots in the veins of the legs that can move to the heart and lungs

attacks and strokes are among the best-known consequences of CVDs - with a large proportion of them being due to a fatty deposit on the inside of blood vessels, which ultimately leads to the blood supply to the heart being inhibited or a small vein in the brain bursting[1]. Although the probability of developing one of these diseases has increased in recent years, the number of deaths attributable to CVDs appears to be decreasing slightly [166]. This is most likely due to the large amount of research interest and the resulting therapeutic approaches and recommendations for the prevention of CVDs. One example of such a preventive recommendation is the American Heart Association (AHA)'s concept of cardiovascular health, which is characterised by seven parameters (the so-called 'Life's Simple 7'®)[2]: Manage Blood Pressure, Control Cholesterol, Reduce Blood Sugar, Get Active, Eat Better, Lose Weight, Stop Smoking [18]. Non-compliance with the recommendations can lead to negative consequences, such as obesity, type 2 diabetes mellitus or metabolic syndrome and consequently promote the development

[1] World Health Organisation (WHO). Definition of cardiovascular disease - `https://www.euro.who.int/en/health-topics/noncommunicable-diseases/cardiovascular-diseases/cardiovascular-diseases2/definition-of-cardiovascular-diseases` Accessed January 17, 2021

[2] American Heart Association. My Life Check - Life's Simple 7 - `https://www.heart.org/en/healthy-living/healthy-lifestyle/my-life-check--lifes-simple-7`. Accessed November 9, 2020.

of a CVD. An important independent risk factor that may favour the occurrence of CVDs is the atherogenic dyslipidemia. This lipometabolic disorder is a common comorbidity of diabetes and the metabolic syndrome. It can be characterised by increased blood concentrations of low density lipoprotein (LDL) and triglyceride (TG) particles combined with a decreased high density lipoprotein (HDL) particle concentration [134, 166]. These blood lipid levels can be influenced by the individual dietary fat intake. Accordingly, various studies have shown that the composition of fatty acids (FAs) in the diet may influence the development of a CVD: While eating a diet high in saturated fatty acids (SFAs) can increase the risk, an intake of products high in monounsaturated fatty acids (MUFAs) and / or polyunsaturated fatty acids (PUFAs) might reduce it [119, 125, 134]. Based on the multitude of scientific evidence, a general recommendation is given to replace SFAs with MUFAs and PUFAs. This replacement should be beneficial in reducing cardiovascular morbidity and mortality [55, 91, 105, 119].

2.2 Blood lipids

As mentioned in Section 2.1, the concentrations of certain blood lipids can have different health consequences. In the following these blood lipids - TGs and lipoproteins (cholesterol) - are described in more detail.

2.2.1 Triglycerides

TGs can be absorbed into the body through the consumption of edible oils and fats as well as fatty food or are synthesised by the body itself, mainly in the liver [53, p. 103]. These blood lipids are among the major components of lipoproteins (see Section 2.2.2) [196, 204], consist of glycerol and three fatty acids [99] and cannot permeate the cell membrane until the lipases catabolise them into their individual components.
Moreover, high TG levels are associated with causal factors for the development of atherosclerotic cardiovascular diseases (ASCVDs), such as an elevated LDL particle concentration, insulin resistance and a low HDL-C level [18].

2.2.2 Cholesterol

Cholesterol is ingested via food (e.g. egg yolk, butter, cheese, beef) and can also be produced by the body itself. It is an essential component of biological membranes as well as a precursor of steroid hormones, Vitamin D and bile acids [53, p. 104]. Despite its important physiological role, elevated cholesterol and TG concentrations are associated with various diseases, such as diabetes and atherogenic dyslipidemia [134]. Furthermore, high cholesterol levels can cause plaque deposits in arteries, which may lead to myocardial infarction and the development of a metabolic syndrome (as described in Section 2.1) [3]. Cholesterol is transported in the blood by so-called lipoproteins - these are particles consisting of lipids and proteins [138]. Below, the different lipoproteins are briefly explained (in ascending order according to their density):

Chylomicrons These lipoproteins consists of only 1 - 2 % protein (apolipoprotein (Apo) B-48 and Apo E) and thus have the lowest density. They are formed in the intestinal mucosa from dietary fat and additionally comprise about 80 - 90 % TGs and a small amount of cholesterol. As they pass through the body, the chylomicrons can be broken down into remnants, which can be converted in the liver to very low density lipoprotein (VLDL) or HDL [53, p. 105].

VLDL-Cholesterol This triglyceride-rich lipoprotein is formed in the liver and consist predominantly of Apo B-100, Apo Cs and Apo E. Very low density lipoprotein cholesterol (VLDL-C) makes up 10 - 15 % of TC and is the precursor of intermediate-density lipoprotein cholesterol (IDL-C) and LDL-C [138].

IDL-Cholesterol IDL-C is a degradation product of VLDL. This lipoprotein contains less TGs, but more cholesterol than his precursor. IDL-C can be degraded in the liver and in the blood, where it can be converted to LDL-C subsequently [53, p. 105].

[3] National Heart, Lung, and Blood Institute (NIH). Blood Cholesterol - `https://www.nhlbi.nih.gov/health-topics/blood-cholesterol`; National Heart, Lung, and Blood Institute (NIH). High Blood Triglycerides - `https://www.nhlbi.nih.gov/health-topics/high-blood-triglycerides` Accessed January 11, 2021

LDL-Cholesterol This lipoprotein is also known as the 'bad' cholesterol and has a high content of cholesterol, phospholipids, Apo B-100 (25 %) and a small amount of TGs [53, p. 105]. LDL-C accounts for 60 - 70 % of TC and is the most important atherogenic lipoprotein, which is why low levels of LDL in the blood are associated with a lower risk of coronary heart disease (CHD) [138].

HDL-Cholesterol The lipoprotein with the highest density, also known as the 'good' cholesterol, contains 50 % protein (Apo A, Apo E) and 20 % cholesterol and is synthesised in the liver. The association between CHD risk and HDL-C appears to have an inverse effect compared to LDL-C and TC. Low levels of HDL-C and Apo A1 are associated with a higher risk of ASCVD in young and middle-aged adults [54, 89].

It is known that a long-term exposure to even modestly elevated cholesterol levels can lead to a CVD later in life [58, 134]. Nonetheless, the effect of cholesterol *being ingested with food* on blood lipid levels and the associated risk of developing a CVD is still a highly controversial issue, with some studies claiming that dietary cholesterol increases the risk [77, 100, 141] and others showing controversial non-significant findings [21, 69, 72].
Table 2.2 gives an overview of the recommended blood lipid values.

Table 2.2: Healthy blood lipid values

Abbreviation	Name	Normal values (mg/dl)	Normal values (mmol/l)
TC	Total cholesterol	< 200	< 5.16
LDL-C	Low density lipoprotein cholesterol	< 160	< 4.13
HDL-C	High density lipoprotein cholesterol	≥ 40	≥ 1.55
TG	Triglycerides	< 150	< 1.7

Source: Guidelines of the National Cholesterol Education Program 2001 [138]

2.3 Fatty acids

For a well-functioning human body different lipids and their derivatives are important. They can be ingested in the form of triglycerides via various (plant and

animal) foods and additionally bind various fatty acids (FAs), sterols (e.g. cholesterol), carotenoids and vitamins (e.g. vitamin A, D, E, K) [204].
The esterified FAs ingested via food are differentiated according the following characteristics [53, p. 100-102]:

- Chain length (straight or odd, short-chain, medium-chain or long-chain).
- Degree of saturation (saturated or unsaturated).
- Localisation of the first double bond.
- Isomerism of the double bond.

The most important dietary fatty acids are saturated, monounsaturated and polyunsaturated FAs. They are responsible for various physiological functions and provide - in appropriate amounts - good health [53, p. 103].

Saturated fatty acids are involved in metabolic processes such as energy production, energy storage and lipid transport. They are also required for the modification of numerous regulatory proteins as well as for the synthesis of phospho- and sphingolipids, which in turn are necessary for the membrane synthesis [189]. Notwithstanding, SFAs are considered to elevate plasma cholesterol, mainly that of LDL-C [45, 125].
Examples: Lauric acid, stearic acid, myristic acid and palmatic acid.
Oils / solid fats rich in SFAs are mainly animal fats, with butter being the best known example containing an average of 66 % of SFAs, 30 % of MUFAs and 4 % of PUFAs [34]. Other animal fats with high SFA levels are beef tallow, a primary source of dietary stearic acid in the United States [41] and ghee, a butter-like fat mainly used in Ayurveda [159].
Examples for vegetable oils / fats rich in SFAs are coconut oil and cocoa butter. In addition to its fatty acid pattern, coconut oil contains small amounts of tocopherols, tocotrienols as well as phytosterols and is known for its antibacterial effect and healing properties [95]. Cocoa butter, mainly known from chocolate production, contains palmitic, stearic, oleic and linoleic acids as well as antioxidants and flavonoids [108, 207].
Another vegetable oil with a high content of SFAs is palm oil, being extracted from the fruits of the oil palm. It is rich in antioxidants, β-carotenes and

vitamin E and is sold in various processed forms - palm oil, palm olein, palm stearin and red palm oil - that differ mainly in their melting points and fatty acid composition [51].

Monounsaturated fatty acids are involved in various regulatory and synthetic processes. In addition, these fatty acids play an essential role in ensuring optimal fluidity on the bilayer lipid membrane [189]. MUFA-rich fats and oils are also associated with a positive effect on blood lipids; a partial replacement of SFAs with MUFAs is supposed to eliminate the cholesterol-increasing effect of saturated fatty acids [85].

Example: Oleic acid.

Oils / solid fats rich in MUFAs are e.g. safflower, rapeseed and olive oil. Safflower oil is among those oils with the highest MUFA content and its consumption is associated with several positive biological parameters like healthier blood glucose and blood lipid levels [10].

Rapeseed oil similarly appears to have a positive effect on blood lipid profiles. Its consumption can improve TC, LDL-C as well as other lipid-related values like the TC/HDL and LDL/HDL ratios [5]. Rapeseed oil - in addition to its high MUFA content - is also rich in natural Ω-6-fatty acids. It is very stable to heat (up to 200°C) and is therefore also suitable for cooking at high temperatures [22].

Olive oil, on the other hand, is not very resistant to heat, but especially in the Mediterranean region it is a popular cooking oil. It mainly consists of TGs (98 - 99 %), which in turn are composed predominantly of MUFAs. In addition, the oil is rich in α- and γ-tocopherols, tocotrienols, β-carotenes, phytosterols, flavonoids and hydrophilic phenolic compounds [63].

Finally, also avocados feature high MUFA levels (73 % of total fat) [48]. The consumption of this fruit is associated with a positive effect on cardiovascular health [32, 113].

Polyunsaturated fatty acids must be supplied through the diet (in contrast to SFAs and MUFAs), which is why they are also called essential fatty acids [189]. They can be divided into Ω-6- (linoleic acid) and Ω-3- (α-linolenic acid) FAs, with the two most important fatty acids of Ω-3 being eicosapentaen-

oic acid (EPA) and decosahexaenoic acid (DHA) [17]. PUFAs are involved in the eicosanoid production, the signal transduction and the activation of the nuclear transcription factors. In addition, PUFAs are associated with the reduction of LDL-C [85, 125], whereby Ω-6-FAs potentially also decrease HDL-C [53, p. 102].
Examples for Ω-6-FAs: Linoleic acid, arachidonic acid.
Examples for Ω-3-FAs: a-linolenic acid, EPA, DHA.
Oils / solid fats rich in PUFAs are extracted from vegetable oil crops or are found in fatty fish. Oils with high levels of Ω-6-FA are especially represented in the Western diet, e.g. sunflower or corn oil. The latter consists of a high proportion of PUFAs, with the majority being attributed to linoleic acid [50]. Additionally, it contains vitamin E, which is supposed to have a positive effect on the reduction of oxidative stress in biological membranes and the prevention of atherosclerosis [101]. Sunflower oil is similarly rich in Ω-6-FAs with a low content of palmatic acid and a small amount of phospholipids, tocopherols, sterols and waxes [65].
High PUFA levels are also observed in camelina [142] and flaxseed oil [38] in combination with high total Ω-3-FA contents. The latter is also linked with a down-regulation of the growth factor of breast cancer [200] and a lowering effect on the blood pressure [135].
Hempseed oil naturally contains high levels of both Ω-6- and Ω-3-FAs. Due to its unique fatty acid composition and its bioactive secondary components - such as tocopherols, phenols and phytosterols, which are believed to have antioxidant effects - it is claimed to have health advantages [104]. These benefits include the reduction of cholesterol and blood pressure as well as the prevention of CVDs and cancer [176].
DHA and EPA are mainly found in (fatty) fish, such as salmon and tuna. As with the other PUFA-rich oils / solid fats, consumption of fatty fish is associated with health benefits in terms of blood pressure, cholesterol regulation and the prevention of CVDs [17, 25, 50, 185, 217].
Moreover also oils and solid fats rich in both, MUFAs and PUFAs exist.
Oils / solid fats rich in MUFAs & PUFAs are e.g. peanut, rice bran and argan oil. Peanut oil is derived from shelled, crushed peanuts and is nat-

urally TFA-free, cholesterol-free and low in SFAs. It has a very high smoking point 226.4°C) [211] and is linked to preventive effects on the development of CVDs as well as the protection against atherosclerosis [2]. Next, also argan oil has high amounts of unsaturated fatty acids. It is further composed of antioxidant components such as vitamin E. Due to its chemical composition, the oil is said to have positive and protective effects on hyperlipidaemic, hypertensive and antioxidant activities [34].

Another MUFA & PUFA-rich oil (but relatively unknown in Europe) is rice bran oil. It contains high levels of palmitic, oleic and linoleic acids and has a higher overall free fatty acid content than other vegetable oils [94]. Another compound of the oil is the antioxidant Γ-oryzanol [149] being associated with the reduction of plasma cholesterol [20] and hyperlipidaemia [136].

Finally, also sesame oil features high amounts of both MUFAs and PUFAs. It has one of the highest oil contents among oil plants [16] and the main FA components are linoleic, oleic, palmatic and stearic acids [210]. Sesame oil is very stable due to its antioxidants e.g. sesamin and sesamolin) [194] and can reduce cholesterol and high blood pressure in people [101, 175].

In addition to the negative effects of SFAs, TFAs are also associated with adverse health effects. These FAs are formed during the partial hydrogenation of vegetable oils while processing the product e.g. cooking, manufacturing processes). Further, they are also present in meat and dairy products, where they are built by bacteria in the stomach of the ruminant. Due to the negative effects associated with their intake via food, it should be kept to a minimum [131].

2.4 Dietary guidelines

Even though the intake of fat is essential for a functioning body, it is necessary to pay attention on how much and what kind of fat is being consumed. Despite the important functions that lipids maintain in the human body, care must be taken to exclude negative consequences such as obesity and CVDs [109]. Therefore, several recommendations and guidelines for the appropriate fat intake exist: The Institutions for Nutrition of Germany, Austria and Swiss recommend a fat intake of 30 - 35 % of total energy per day [43]. The European Food Safety Authority

(EFSA), on the other hand, has set the lower limit at 20 % of energy, at which level no adverse effects were observable [52]. Compared to these guidelines, the actual fat intake of the Austrian population is higher than the recommended intake (woman 37.6 % and man 36 % of total energy, as of 2017 [167]).
In addition to the dietary guidelines for total fat intake, also recommendations for the intake of individual fatty acids exist: The *D-A-CH Referenzwerte* - published by the German Institute for Nutrition - are shown in Table 2.3. According to this guideline, the proportion of PUFAs depends on the consumption of saturated FAs: If more than 10 % of saturated FAs are consumed, the proportion of PUFAs should be increased from 7 % to 10 % of total energy to prevent a rise in cholesterol levels. Further, the guideline highlights the relevance of an Ω-6- to Ω-3-FA intake ratio with a factor of 5:1. Moreover, a recommendation on fat intake is given, by favouring MUFAs and / or PUFAs as primary source when the total fat intake exceeds 30 %, with an ideal ratio of animal to vegetable oil sources being 1:2 [43].

Animal products / foods often contain plenty of cholesterol in addition to saturated FAs, which is why a reduced consumption of these products is often accompanied by reduced cholesterol intake. Although dietary cholesterol has little effect on plasma cholesterol levels on average, individual variations can be observed [59]. For this reason, the *D-A-CH Referenzwerte* recommend a daily intake of no more than 300 mg [43].

Table 2.3: Reference values for daily fat and cholesterol intake [43]

Fat type	References (Daily)
Total fat	30 - 35 E%
SFA	$<$ 10 E%
MUFA	$>$ 10 E%
PUFA	7 E%
Cholesterol	300 mg
TFA	$<$ 1 E%

3

Methods and Design

This chapter explains the literature search. Moreover, the concepts of the risk of bias assessment and the network meta-analysis are introduced.

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3.1 Literature search

The literature search was performed until January 2020 by using the electronic databases *PubMed®* [1] and *Cochrane* Central Register of Controlled Trials CENTRAL[2]. The databases were queried for randomised controlled trials (RCTs) including the following oils and fats: safflower oil*, sunflower oil*, rapeseed oil*, hempseed oil*, flaxseed oil*, corn oil*, olive oil*, soybean oil*, palm oil*, coconut oil*, butter*, lard*, beef fat*, cocoa butter, sesame oil, peanut oil, camelina oil, rice bran oil and argan oil, ghee and mustard oil[3].

3.1.1 Predefined search strategy

In the following the exact search strings for querying the databases are given (Variant 1 shows the search for the newly included oils / solid fats, Variant 2 is used to update the oils / solid fats already analysed by Schwingshackl et al. [181]):

PubMed

Variant 1 *("peanut oil"[tiab] OR "sesame oil"[tiab] OR "cocoa butter"[tiab] OR "cacao butter"[tiab] OR "camelina oil"[tiab] OR "rice bran"[tiab] OR"argan oil"[tiab] OR "mustard oil"[tiab] OR "ghee"[tiab] OR "hydrogenated oil"[tiab]) AND ("random*"[tiab] OR "Randomized Controlled Trial"[pt] OR "randomized"[tiab] OR "intervention"[tiab] OR "ward"[tiab] OR "feeding"[tiab] OR "trials"[tiab] OR "trial"[tiab] OR "supplements"[tiab] OR "supplement"[tiab] OR "supplementation"[tiab])*

Variant 2 *("coconut oil"[tiab] OR "butter"[tiab] OR "lard"[tiab] OR "seed oil"[tiab] OR "safflower oil"[tiab] OR "sunflower oil"[tiab] OR "hempseed oil"[tiab] OR "corn oil"[tiab] OR "sesame oil"[tiab] OR "soybean oil"[tiab] OR "soyabean oil"[tiab] OR "rapeseed oil"[tiab] OR "canola oil"[tiab] OR*

[1] National Library of Medicine. National Centre of Biotechnology Information - PubMed.gov - `https://pubmed.ncbi.nlm.nih.gov/` Accessed January 21, 2020

[2] Cochrane Library Central Register of Controlled Trials - CENTRAL - `https://www.cochranelibrary.com/central` Accessed January 21, 2020

[3]* Since the relevant literature collection for the oils and fats included in Schwingshackl et al. [181] could be consulted, it was only extended by new publications.

"olive oil"[tiab] OR "nut oil"[tiab] OR "linseed oil"[tiab] OR "flaxseed oil"[tiab] OR "grapeseed oil"[tiab] OR "peanut oil"[tiab] OR "avocado oil"[tiab] OR "cocoa butter"[tiab] OR "cacao butter" OR "palm oil"[tiab] OR "vegetable oil"[tiab] OR "margarine"[tiab] OR "camelina oil"[tiab] OR "rice bran"[tiab] OR "beef fat"[tiab] OR "argan oil"[tiab] OR "mustard oil"[tiab] OR "ghee"[tiab] OR "hydrogenated oil"[tiab]) AND ("random"[tiab] OR "Randomized Controlled Trial"[pt] "randomized"[tiab] OR"intervention"[tiab] OR "ward"[tiab] OR "feeding"[tiab] OR "trials"[tiab] OR "trial"[tiab] OR "supplements"[tiab] OR "supplement"[tiab] OR "supplementation"[tiab])*

Cochrane CENTRAL

Variant 1 *(peanut oil* or sesame oil* or cocoa butter* or cacao butter* or camelina oil* or rice bran* or argan oil* or mustard oil* or ghee* or hydrogenated oil*):ti,ab,kw AND (random*or randomized* or intervention* or ward* or feeding* or trials* or trial* or supplements* or supplement* or supplementation*):ti,ab,kw Randomized Controlled Trial"[pt]*

Variant 2 *coconut oil* or butter* or lard* or seed oil* or safflower oil* or sunflower oil* or hempseed oil* or corn oil* or sesame oil* or soybean oil* or soyabean oil* or rapeseed oil* or canola oil* or olive oil* or nut oil* or linseed oil or flaxseed oil or grapeseed oil or peanut oil* or avocado oil* or cocoa butter* or cacao butter* or palm oil* or vegetable oil* or margarine* or camelina oil* or rice bran* or beef fat* or argan oil* or mustard oil* or ghee* or hydrogenated oil*):ti,ab,kw AND (random*or "randomized* or intervention* or ward* or feeding* or trials* or trial* or supplements* or supplement* or supplementation*):ti,ab,kw Randomized Controlled Trial"[pt]*

3.1.2 Inclusion criteria

Studies are included for further analysis, if they fulfil the following predefined criteria:

Study design must be a RCT (parallel or crossover design) - comparing at least two of the following oils / solid fats: argan, safflower, sunflower, rapeseed, hempseed, flaxseed, rice bran, sesame, corn, olive, soybean, palm, mustard, camelina, peanut and coconut oil, and cocoa butter lard, beef-fat, ghee and butter.

Treatment should allow a comparison of an isocaloric exchange of the different oils / solid fats within a trial.

Outcome available for at least one of the following blood lipids: LDL-C, TC, HDL-C or TGs.

Study duration of at least 3 weeks.

Mean patient age must not be less than 18 years.

3.1.3 Exclusion criteria

Studies are excluded if they contain any of the following parameters:

- RCTs including pregnant woman, children / adolescents and patients with cancer, hemodialysis or type 1 diabetes.
- RCTs of acute (single meal) postprandial effects only or based on liquid / formula diets.
- RCTs using mixed oils or using butter plus mixed oils in the intervention arm.
- RCTs using encapsulated oil supplements; using fish oils or medium-chain triglyceride oils or ω-3-fatty enriched oils / solid fats.
- RCTs implementing enrichment of oils / solid fats with plant sterols or / and plant stanols.
- RCTs co-intervention (e.g. drug, diet, or exercise) not applied in all intervention arms.

In addition, all studies with examined oils / solid fats being labelled as high-oleic, refined or modified in any other form were excluded.

3.2 Risk of bias

The risk of bias (RoB) analysis is an important part of the Evidence-based Medicine (EbM). The EbM

> *'is the conscientious, explicit and rational use of the best external scientific evidence currently available to make decisions about the medical care of individual patients. The practice of EbM means the integration of individual clinical expertise with the best available external evidence from systematic research'* [168, p. 3].

The EbM considers the RCT to be the highest possible level of evidence among the study designs for assessing the efficacy and safety of an intervention, as these studies ensure better comparability of the study arms than non-randomised studies [120, 177]. In order to ensure a good study quality, (randomised) clinical trials should always follow a standardised concept such as the basic principles of the 'Good Clinical Practice'[4]. However, a good study quality itself does not guarantee the reliability of its results, since - despite a methodologically adequate implementation - distortions can occur due to possible weaknesses that are not directly related to the study quality [178]. These types of problems are defined as bias.
In the case of RCTs, according to Schmucker et al. [177] the most important bias are:

- **Selection bias**: Is a reflection of unequal study groups.
- **Performance bias**: Occurs when different settings or additional therapies are applied to the individual study groups.
- **Detection bias**: Occurs when study results are adjusted - consciously or unconsciously - in favour of personal / study investigators expectations.
- **Attrition bias**: Is attributable to systematic differences in the amount and causation of missing data.
- **Outcome reporting bias**: Arises from selective reporting / non-reporting of study results.

[4]European Medicines Agency. 2016. ICH E6 (R2) Good clinical practice - `https://www.ema.europa.eu/en/ich-e6-r2-good-clinical-practice` Accessed December 7, 2020

In order to prevent wrong decisions or adverse effects, RCTs and systematic reviews should be examined to identify the mentioned bias. A well-known approach therefor is the RoB assessment, for which various instruments are available [49, 177]: Scales e.g. Newcastle-Ottawa-Scale[5]), Checklists (e.g. Scottish Intercollegiate Guidelines Network checklist[6]) and Component ratings such as the Cochrane Risk of Bias 2 (RoB 2) tool [191]. Component rating - or domain-based assessment - instruments display potential bias separately and include supplementary qualitative evaluations such as randomisation and blinding.

Assessment Methodology

Upon completion of the literature search all eligible studies were examined in order to determine their RoB by using the Cochrane RoB 2 tool [191], which is a component rating system with criteria being derived from theoretical and empirical research results [78]. The RoB 2 tool includes the following five domains[7]:

- Domain 1: Bias arising from the randomisation process.
- Domain 2: Bias due to deviations from the intended interventions.
- Domain 3: Bias due to missing outcome data.
- Domain 4: Bias in measurement of the outcome.
- Domain 5: Bias in selection of the reported result.

For every trial, each individual domain has to be labelled with either a ‘low RoB’, ‘high RoB’ or ‘unclear RoB’ in order to assign an entire risk at the end. Each classification should be further substantiated either by a citation or a commentary [74].

[5] Wells GA et al. 2013. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non randomised studies in meta-analyses - http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp Accessed January 17, 2021

[6] Healthcare Improvement Scotland. Scottish Intercollegiate Guidelines Network (SIGN) - Checklists - https://www.sign.ac.uk/what-we-do/methodology/checklists/ Accessed January 17, 2021

[7] Higgins JPT, Savovi J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook. Accessed November 11, 2020

3.3 Network meta-analysis

Systematic reviews of RCTs are important evidence sources for the provision of efficacy and safety indications of a treatment [30, 103]. Most reviews - such as meta-analysis (MA) - perform paired, direct comparisons of treatments, often with a placebo / control group as a reference. These methods may be useful, but only permit a direct comparison of two studies. In the presence of many treatment options for a given clinical picture, a MA provides a large pool of useful information, but cannot determine which treatment is most appropriate [37, 169]. This problem can be solved by performing a network meta-analysis (NMA). As an extension of the pairwise meta-analysis, the NMA allows the comparison of several different treatment options in a single analysis and subsequently enables the identification of the optimal therapeutic intervention, based on the observed effects [122, 160, 169, 212]. It creates a coherent network while maintaining the internal randomisation of the individual trials and can be used to evaluate both direct and indirect evidence by comparing three or more treatments based on a pairwise or multi-armed comparative study [30]. Results obtained from a direct connection are denoted as direct evidence. If no direct comparisons exist, the interventions are compared via a common comparator. This technique contributes the so-called indirect evidence to the analysis [103]. Figure 3.1 shows an example of a network

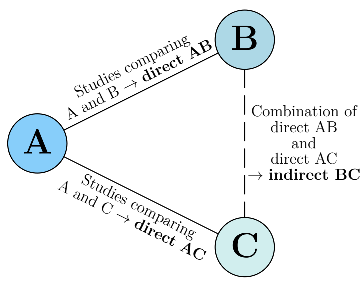

Figure 3.1: Example of direct and indirect effects in a hypothetical triangle comparing three interventions: A, B and C. Adapted from Schwingshackl et al. [181]

consisting of three interventions A, B and C, with solid lines denoting direct com-

parisons and a dashed line visualising an indirect comparison: A can be directly compared with B and C - thus A is the common comparator. For the indirect comparison between the two interventions B and C, the evidence of the direct comparison of A and B as well as the second direct comparison of A and C can be used. This allows the indirect estimation of the absolute effect measures (e.g. mean difference, risk difference) of intervention B relative to C [28, 103].
Finally, there is the concept called mixed evidence or closed-loop: it refers to a situation where both direct and indirect comparisons are available. A NMA, however, does not necessarily have to include all forms of evidence, since it can also be conducted with solely indirect comparisons of the different treatments [23, 171].
A NMA can be built on different (statistical) analytical approaches: the two methods - the frequentist and Bayesian approach - mainly differ in their interpretation for *probability* [115, 199] and are described below.

Frequentist analysis

Frequentism is a common theoretical approach for interpreting the probability of an event E to occur. With it, the likelihood from E occurring when the process (e.g. an intervention) is being repeated many times is defined. Frequentist ideas are the core of many statistical procedures used daily in quantitative research, e.g. significance tests, the calculation of confidence intervals (CIs) or the interpretation of p-values [115].
In the case of a frequentist NMA, a so-called P-score can be calculated, that allows to compare different treatments with one another and to rank them subsequently. It is based on the mean and variance of the observed relative effect estimates. First, P_{ij} denoting the probability of a treatment i producing a better outcome than treatment j is calculated [161]:

$$P_{ij} = \Phi\left(\frac{\widehat{\mu_i} - \widehat{\mu_j}}{s_{ij}}\right) \tag{3.1}$$

In this equation, Φ represents the cumulative density function of the standard normal distribution, while $\widehat{\mu_i} - \widehat{\mu_j}$ denotes the estimated difference between treatment i and j. Lastly, s_{ij} marks the standard error of said difference.

After retrieving these pairwise differences, the P-score for a given treatment is calculated via the following equation:

$$\overline{P}_i = \frac{1}{n-1} \sum_{j,j \neq i}^{n} P_{ij} \tag{3.2}$$

$\overline{P}_i$ finally yields the rank of the given treatment i in context to all investigated treatments on a normalised scale between 0 and 1 with higher values representing better treatment options.

Bayesian Inference

Besides the frequentist analysis technique, the Bayesian approach is another standard of inferential statistics [26]. In principle, Bayesian analysis pursues the same goal as the frequentist analysis technique: proper statistical inference [4]. With the Bayes' theorem serving as basis Bayesian theory allows to estimate the probability of an event A given the knowledge that another event B has occurred; this is known as conditional probability [83, 115]. Thus, to obtain the adjusted probability of A, the prior information available about the probability of A occurring is merged with the probability of B ('likelihood') given that A occurs [115].
The results of Bayesian inference are probabilistic and subjective in the sense that they represent an assumption about the actual parameter values. Bayesian inference therefore does not calculate confidence intervals around the estimators, but credibility intervals (CrIs) (CrIs can be regarded as the Bayesian equivalent of the frequentist CI) [4], which - taking into account the evidence of the observed data - enclose the true (unknown) estimator with correspondingly high probability within the given interval [73].
As an equivalent to the frequentist P-score [161], the Bayesian NMA approach makes use of the so-called Surface Under the Cumulative RAnking curve (SUCRA) [170] in order to rank the effectiveness of the analysed interventions. In a first step, $P(i,k)$ denoting the probability of treatment i being ranked at position k $(k = 1, ..., n)$ is calculated. Summing up these probabilities results in 1 $(\sum_{k=1}^{n} P(i,k) = 1)$, so that we can compute the probability of treatment i be-

ing ranked on place r or better by $F(i,r) = \sum_{k=1}^{r} P(i,k)$. The SUCRA value then represents the surface under the cumulative ranking distribution function for treatment i as [161, 170]:

$$\text{SUCRA}(i) = \frac{1}{n-1} \sum_{r=1}^{n-1} F(i,r). \tag{3.3}$$

Often, the property $E(\text{rank}(i)) = n - \sum_{r=1}^{n-1} F(i,r)$ is used in order to visualise the equation in an alternative fashion:

$$\text{SUCRA}(i) = \frac{n - \text{E}(\text{rank}(i))}{n-1}. \tag{3.4}$$

Analogous to the P-Score, also the SUCRA ranges between 0 and 1 with higher values denoting better treatment options [161].

Implementation of the network meta-analysis

A frequentist and Bayesian analysis was carried out with the tool 'MetaInsight' [144]. For this purpose, the following parameters were provided:

- Name of authors
- Year of publication
- Number of participants (per arm)
- Duration of the intervention (weeks)
- Treatment information
  - Investigated oil / solid fat
  - Blood lipid values (LDL-C, TC, HDL-C, TG) [mmol/L ± SD]

A random-effects model was used to determine the pooled relative effects of oils / solid fats against each other in terms of post interventional blood lipid levels of TC, LDL-C, HDL-C and TG (summarised in Table A.5).
Since assessing the consistency of effects across studies is an essential part of the NMA [74], inconsistency analyses were conducted. This kind of analysis is used

to determine biased estimates of treatments and / or effectiveness of interventions that can appear as a consequence of the direct and indirect evidence not being consistent with each other. Possible explanations for such inconsistency can be an uneven distribution of treatment effect modifiers or distortions of direct evidence due to different effects in the various comparisons [14, 79, 172, 173].
Furthermore, sensitivity analyses with studies either having a high RoB or *not* providing oils / solid fats to its participants being excluded were done.

4

Results

This chapter gives an overview of the included studies and their risk of bias and shows the results of the conducted network meta-analysis.

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4.1 Literature search

The queries yielded a total of 3,816 abstracts, which were subsequently screened in more detail by using the online tool 'rayyan'[1]. Out of 126 full-texts, 51 studies (52 reports) met the predefined inclusion criteria (see Section 3.1.2). A Prisma flow chart[2] representing the entire literature search workflow is shown in Figure 4.1.

Unfortunately, no suitable studies about ghee and mustard oil could be identified. In addition, 19 studies already investigated by Schwingshackl et al. [181] were excluded due to the usage of refined, hydrogenated or otherwise modified oils / solid fats.

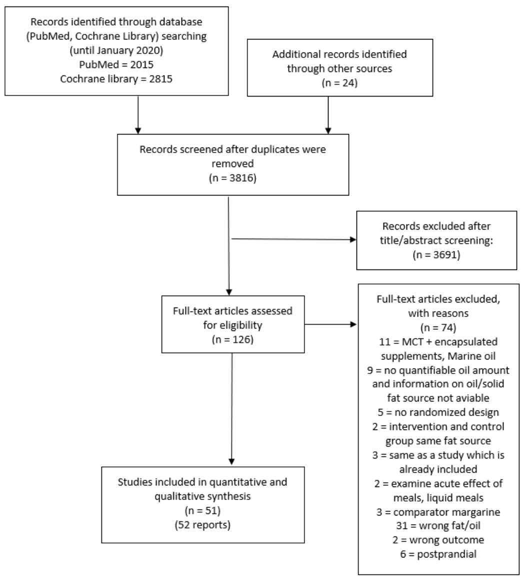

Figure 4.1: Prisma flow diagram of the search strategy

[1] Mourad Ouzzani, Hossam Hammady, Zbys Fedorowicz, and Ahmed Elmagarmid. Rayyan a web and mobile app for systematic reviews. Systematic Reviews (2016) 5:210, DOI: 10.1186/s13643-016-0384-4.- `https://rayyan.qcri.org/users/sign_in` Accessed June, 11 2020

[2] Prisma Flow Diagram. Transparent Reporting of Systematic Reviews and Meta-Analyses - `http://prisma-statement.org/prismastatement/flowdiagram.aspx` Accessed June 26, 2020

4.2 Data extraction

In order to gain an overview of the investigated oils / solid fats, they were extracted from the included studies and grouped according to their fatty acid composition (Table 4.1). In a next step the study characteristics were extracted: Information on the study authors and the different study arms is gathered in Table 4.2, additional information can be found in Table A.3 and Table A.4.
The 52 reports included a population of 2,178 study participants. The individual studies were published between 1984 and 2019 and span a study period of 3 to 27 weeks. The patients mean age ranged from 22 to 84 years and the mean BMI was between 20.2 and 31.1 kg/m^2. The trials were conducted in Europe (20), Asia (13), North America (12), Africa (3), South America (2) and Australia (1). Out of the 51 trials, 16 trials investigated healthy participants and 47 trials provided the oils / solid fats to their study participants.
Finally, the postintervention blood lipid levels with their corresponding SD were extracted (standardised to [mmol/L]). The exact values are collected in Table A.5.

Table 4.1: Included oils and solid fats - grouped by their most frequent fatty acid

SFA	SFA/MUFA	MUFA	MUFA/PUFA	PUFA
Coconut oil	Lard	Safflower oil	Argan oil	Sunflower oil
Beef fat		Rapeseed oil	Rice bran oil	Hempseed oil
Cocoa butter		Olive oil	Peanut oil	Flaxseed oil
Palm oil			Sesame oil	Corn oil
Butter				Soybean oil
				Camelina oil

Table 4.2: Study arms with associated amounts of fats and oils consumed

Study ID	Reference	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	Citation
1	Aguilera, 2004	Olive oil (8 g/d)	Sunflower oil (8g/d)	NR	NR	NR	[1]
2	Akrami, 2017	Flaxseed oil (25 ml/d)	Sunflower oil (25 ml/d)	NR	NR	NR	[3]
3	Assuncao, 2009	Coconut oil (30 ml/d)	Soybean oil (30 ml/d)	NR	NR	NR	[11]
4	Atefi,2018	Olive oil (30 g/d)	Rapeseed oil (30 g/d)	Sunflower oil (30 g/d)	NR	NR	[12]
5	Baudet, 1984	Palm oil (45 g/d)	Sunflower oil (45 g/d)	Peanut oil (45 g/d)	NR	NR	[15]
6	Binkoski, 2005	Olive oil (15 % of total energy)	Sunflowewr oil (15 % of total energy)	NR	NR	NR	[24]
7	Brassard, 2017	Butter (48.9 g/2500 kcal)	Corn oil (48.9 g/2500 kcal)	Olive oil (48.9 g/2500 kcal)	NR	NR	[27]
8	Candido, 2017	Olive oil (25 ml/d)	Soybean oil (25 ml/d)	NR	NR	NR	[62]
9	Cheng, 2018	Cacao butter (23 g/d)	Olive oil (23 g/d)	NR	NR	NR	[33]
10	Cicero, 2009	Corn oil (11 cans provided)	Olive oil (11 cans provided)	NR	NR	NR	[36]
11	Derouiche, 2005	Argan Oil (25 ml/day)	Olive oil (25 ml/d)	NR	NR	NR	[42]
12	Dittrich, 2015	Flaxseed oil (20 g/day)	Sunflower oil (20 g/d)	NR	NR	NR	[46]
13	Dobrzyñska, 2018	Camelina Oil (30 g/day)	Rapeseed oil (30 g/d)	NR	NR	NR	[47]
14	Farajabakhsh, 2019	Sesame oil (30 ml/d)	Sunflower oil (30 ml/d)	NR	NR	NR	[56]
15	Haimeur, 2013	Butter (20 g/d)	Argan oil (25 ml/d)	NR	NR	NR	[66]
16	Han, 2002	Butter (20 % of total energy)	Soybean oil (20 % of total energy)	NR	NR	NR	[67]
17	Harris, 2017	Coconut oil (30 ml/d)	Safflower oil (30 ml/d)	NR	NR	NR	[70]
18	Iggman, 2015	Palm oil (12 % of total energy)	Sunflower oil (12 % of total energy)	NR	NR	NR	[39]

Table 4.2: Study arms with associated amounts of fats and oils consumed (continued)

Study ID	Reference	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	Citation
19	Karvonen, 2002	(Camelina oil 30 g/day)	Olive oil (30 g/day)	Rapeseed oil (30 g/day)	NR	NR	[84]
20	Kawakami, 2015	Corn oil (10 g/d)	Flaxseed oil (10 g/d)	NR	NR	NR	[86]
21	Khaw, 2018	Butter (50 g/d)	Coconut oil (50 g/d)	Olive oil (50 g/d)	NR	NR	[88]
22	Kontogianni, 2013	Flaxseed oil (15 ml/d)	Olive oil (15 ml/d)	NR	NR	NR	[90]
23	Kris-Etherton, 1993	Butter (30 % of total energy)	Olive oil (30 % of total energy)	Soybean (30 % of total energy)	Cocoa butter (30 % of total energy)	NR	[92]
24	Kris-Etherton, 1993	Butter (30 % of total energy)	Cocoa butter (30 % of total energy)	NR	NR	NR	[92]
25	Kris-Etherton, 1999	Olive oil (17-21 % of total energy)	Peanut oil (17-21 % of total energy)	NR	NR	NR	[93]
26	Kruse, 2015	Olive oil (50 g/d)	Rapeseed oil (50 g/d)	NR	NR	NR	[96]
27	Lai, 2011	Soybean oil (18 g/d)	Rice bran oil (18 g/d)	NR	NR	NR	[98]
28	Lichtenstein, 1994 / Schwab, 1998	Beef fat (20 % of total energy)	Rapseed oil (20 % of total energy)	Corn oil (20 % of total energy)	Olive oil (20 % of total energy)	Rice bran oil (20 % of total energy)	[106, 180]
29	Lichtenstein, 1999	Butter (20 % of total energy)	Soybean oil (20 % of total energy)	NR	NR	NR	[107]
30	Lv, 2018	Soybean oil (20 - 22 g/d)	Cocoa butter (20 - 22 g/d)	NR	NR	NR	[114]
31	Maki, 2015	Corn oil (54 g/d)	Olive oil (54 g/d)	NR	NR	NR	[118]
32	Maki, 2018	Corn oil (54 g/d)	Coconut oil (54 g/d)	NR	NR	NR	[117]
33	Mohamedou, 2011	Argan oil (25 ml/d)	Butter (20 g/d)	NR	NR	NR	[128]
34	Mohamedou, 2011	Argan oil (25 ml/d)	Butter (25 g/d)	NR	NR	NR	[143]
35	Morillas-Ruiz, 2014	Butter (20 g/d)	Olive oil (20 g/d)	NR	NR	NR	[129]

Table 4.2: Study arms with associated amounts of fats and oils consumed (continued)

Study ID	Reference	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5	Citation
36	Nigam, 2014	Olive oil (20 g/d)	Rapeseed oil (20 g/d)	NR	NR	NR	[140]
37	Paschos, 2007	Flaxseed oil (15 ml/d)	Safflower oil (15 ml/d)	NR	NR	NR	[148]
38	Perona, 2004	Olive oil (60 g/d)	Sunflower oil (60 g/d)	NR	NR	NR	[151]
39	Rallidis, 2003	Flasxeed oil (15 ml/d)	Safflower oil (15 ml/d)	NR	NR	NR	[157]
40	Reiser, 1985	Beef fat (21 % of total energy)	Coconut oil (21 % of total energy)	Safflower oil (21 % of total energy)	NR	NR	[162]
41	Rezaei, 2018	Olive oil (20 g/d)	Sunflower oil (20 g/d)	NR	NR	NR	[164]
42	Salar, 2016	Rapeseed oil (30 g/d)	Sunflower oil (30 g/d)	Rice bran oil (30 g/d)	NR	NR	[174]
43	Schwab, 2006	Hempseed oil (30 ml/day)	Flaxseed oil (30 ml/day)	NR	NR	NR	[179]
44	Sirtori, 1986	Corn oil (45 g/d)	Olive oil (45 g/d)	NR	NR	NR	[188]
45	Sirtori, 1992	Corn oil (27-30 % fat of total energy)	Olive oil (27 - 30 % fat of total energy)	NR	NR	NR	[187]
46	Stonehouse, 2019	Cocoa butter (44 g/d)	Olive oil (44 g/d)	NR	NR	NR	[192]
47	Stricker, 2008	Rapeseed oil (2 tablespoons/d)	Sunflower oil (2 tablespoons/d)	NR	NR	NR	[193]
48	Tholstrup, 2011	Lard (17 % of total energy)	Olive oil (17 % of total energy)	NR	NR	NR	[197]
49	Utrawuthipong, 2009	Soybean oil (20 % of total energy)	Palm oil (20 % of total energy)	Rice bran oil (20 % of total energy)	NR	NR	[202]
50	Voon, 2011	Coconut oil (20 % of total energy)	Olive oil (20 % of total energy)	NR	NR	NR	[206]
51	Zhang, 1997	Soybean oil (30 % fat of total)	Lard (30 % fat of total)	Peanut oil (30 % fat of total)	NR	NR	[215]

4.3 Risk of bias

In order to assess the RoB for each study, the primary studies, the corresponding study protocols and statistical papers as well as older studies of the main authors were used. Based on the information contained therein, it was possible to record the RoB for every domain by filling in the blank templates available via the Cochrane RoB 2 tool[3] (see section 3.2) and to consequently define an overall RoB for each included study. The RoB classifications for the individual domains can be found in Figure 4.3 and a summarised overview is visualised in Figure 4.2.
The figures shown here have been created with aid of the online tool 'robvis' [123].
The analysis indicated, that only few studies have a low RoB (approx. 6 %) or

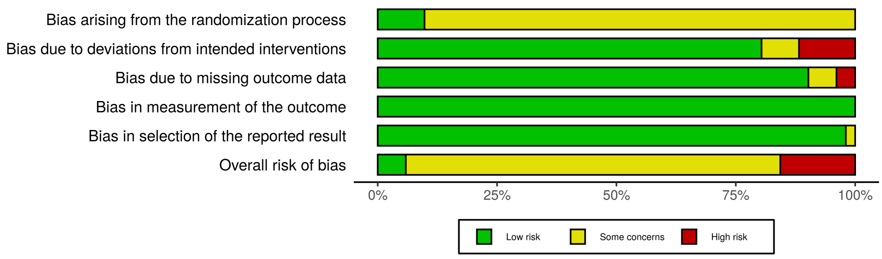

Figure 4.2: Risk of bias assessment - classification overview

a high RoB (approx. 16 %), while it is unclear for the vast majority. Most of the 'high risks' could be attributed to bias due to deviations from intended interventions - by lack of information on adherence and successful implementation of the intervention or the absence of a washout period between two interventions in crossover designs. Unsubstantiated absence of outcomes or a lack of evidence that they would be robust to the missing data led to bias due to missing outcome data. Finally, the lack of information on allocation concealing led to the bias arising from the randomisation process.

[3]Sterne JAC, Savovi J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019; 366: l4898. `https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool` Accessed November 22, 2020

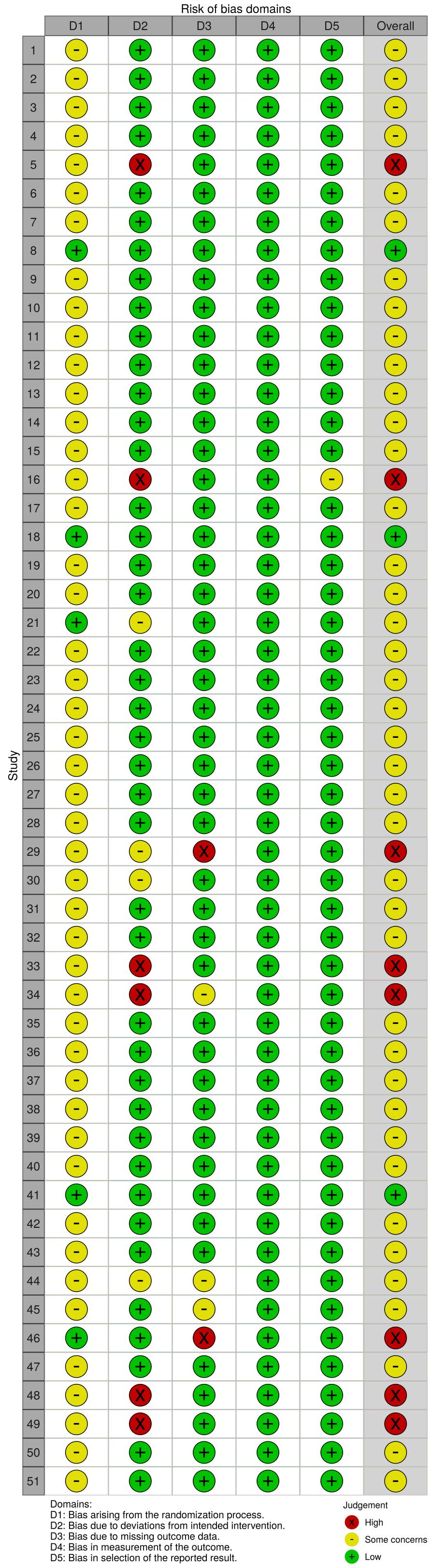

Figure 4.3: Risk of bias classification of each study individually

4.4 Network meta-analysis

This section shows the overall NMA results as well as the results of the sensitivity and inconsistency analysis. The input data of the respective analyses are illustrated with the network diagrams (one network per blood lipid) in Figure 4.4. The number of direct comparisons between two oils / solid fats is denoted via the line thickness between the respective nodes, whose size and fill opacity indicate the total number of participants for the given oil: The bigger and darker the node, the more individuals were assessed in the corresponding RCTs.

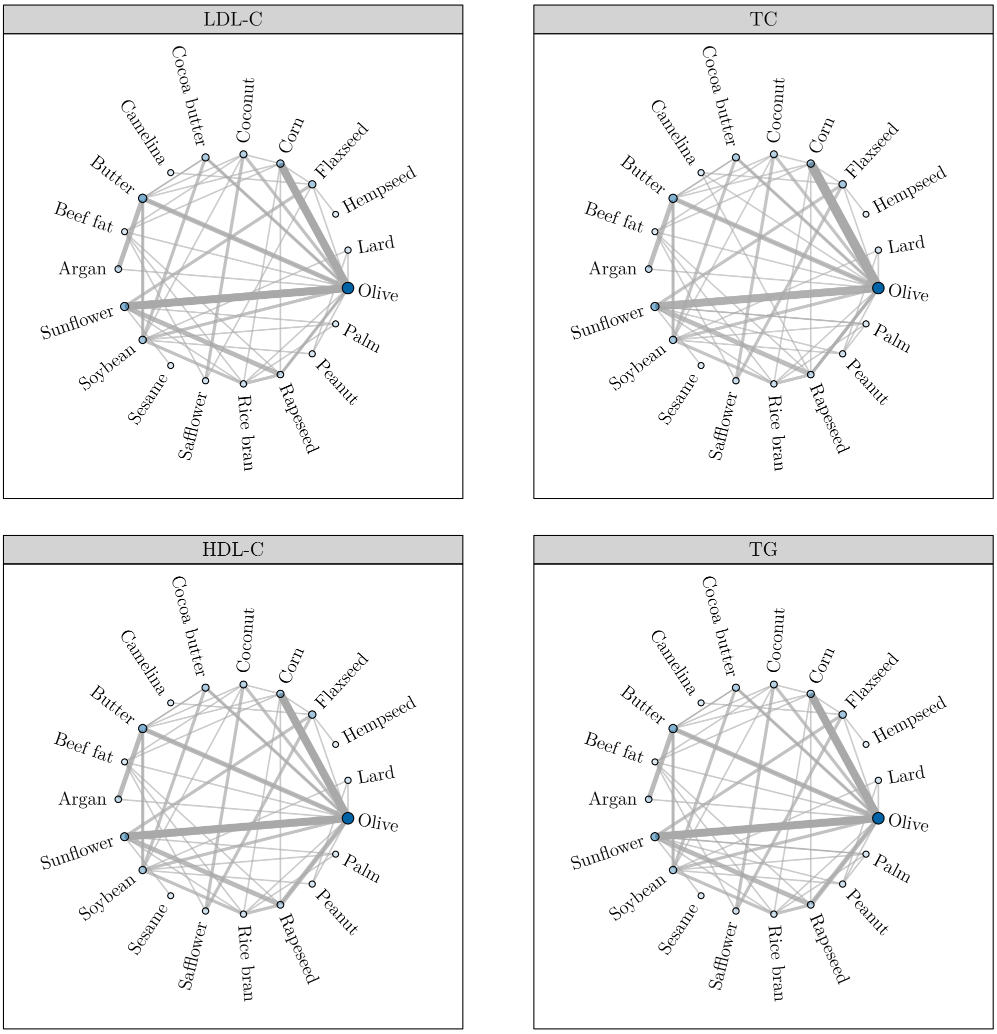

Figure 4.4: Network meta-analysis - underlying network structure

4.4.1 Frequentist analysis

In the following, the results of the frequentist analysis are presented. In a first step, the effects of the consumption of different oils and solid fats with regard to the individual blood lipid values are shown in terms of the corresponding mean differences (MDs). Subsequently, the overall ranking and the inconsistency analysis and lastly the sensitivity analysis are displayed.

Low density lipoprotein cholesterol In total, 46 studies were included in the LDL-C analysis. Out of the 171 ($\frac{n*n-1}{2}$) comparison pairs, 45 combinations were available as direct comparisons.

With the exception of palm and lard, all of the analysed oils and solid fats were effective in reducing LDL-C levels compared to butter (-0.74 to -0.35 [mmol/L]). Moreover, safflower, rapeseed, rice bran, camelina, sesame, flaxseed, soybean, hempseed, corn, sunflower, beef fat and olive oil were superior (-0.78 to -0.48 [mmol/L]) to palm oil. Safflower, rapeseed, rice bran, flaxseed, soybean, corn and sunflower oil had a more pronounced effect on LDL-C when compared with lard (-0.63 to -0.42 [mmol/L]). Safflower, rapeseed, rice bran, soybean and corn oil were also more effective than cocoa butter (-0.39 to -0.25 [mmol/L]). Except for corn oil, this also applied to the comparison with peanut oil (-0.39 to -0.25 [mmol/L]). Other significant lowering effects were seen by comparing safflower and rapeseed oil against coconut oil (-0.36 to -0.30 [mmol/L]), as well as rapeseed against olive oil (-0.23 [mmol/L]).

Total serum cholesterol 50 studies (49 direct comparisons) were subject of the TC analysis.

The comparison to butter revealed the same effect as in the case of the LDL-C analysis: apart from lard and palm oil, all oils and solid fats lowered the TC level (-1.00 to -0.35 [mmol/L]). Safflower, rice bran, rapeseed, camelina, sesame, soybean, flaxseed, corn, argan, sunflower and olive oil reduced the TC value significantly more than lard (-0.89 to -0.41 [mmol/L]). The mentioned oils (without olive oil) were also superior than palm oil (-0.83 to -0.43 [mmol/L]). A reduction was also observed for safflower, rice bran, rapeseed, camelina, soybean, flaxseed and corn oil in comparison to coconut oil (-0.32 to

-0.65 [mmol/L]) and cocoa butter (-0.61 to -0.28 [mmol/L]). A reducing effect was shown by safflower, rice bran, rapeseed, camelina and soybean against peanut oil (-0.60 to -0.34 [mmol/L]). Except of camelina oil this also applied for the comparison to olive oil (-0.48 to -0.22 [mmol/L]). Furthermore, rapeseed oil was more effective than sunflower oil (-0.25 [mmol/L]) and safflower oil was superior over beef fat, sunflower, corn and flaxseed oil (-0.32 to -0.46 [mmol/L]).

High density lipoprotein cholesterol A total of 48 studies (45 direct comparisons) were included in this analysis.

Argan oil showed a positive (increasing) effect on HDL levels compared to all other oils / solid fats (0.15 to 0.32 mmol/L) except for palm and hempseed oil. Further, coconut oil increased the levels compared to butter, soybean, peanut and safflower oil (0.09 to 0.17 mmol/L). Compared to safflower oil, lard, beef fat, sunflower and olive had an enhancing effect (0.11 to 0.15 [mmol/L]). An increasing effect was also observed for lard against peanut oil (0.11 [mmol/L]).

Triglyceride The TG analysis included 49 studies (47 direct comparisons). Here only soybean oil - compared to butter and sunflower oil - showed a significant reduction (-0.18 to -0.13 mmol/L) of the TG levels.

A graphical visualisation of the MDs and their corresponding CIs is given for LDL-C in Figure 4.5, TC in Figure 4.6, HDL-C in Figure 4.7 and TG in Figure 4.8 with the individual facets showing the effect of the oil / solid fat denoted in the respective header in relation to those being listed on the y-axis.

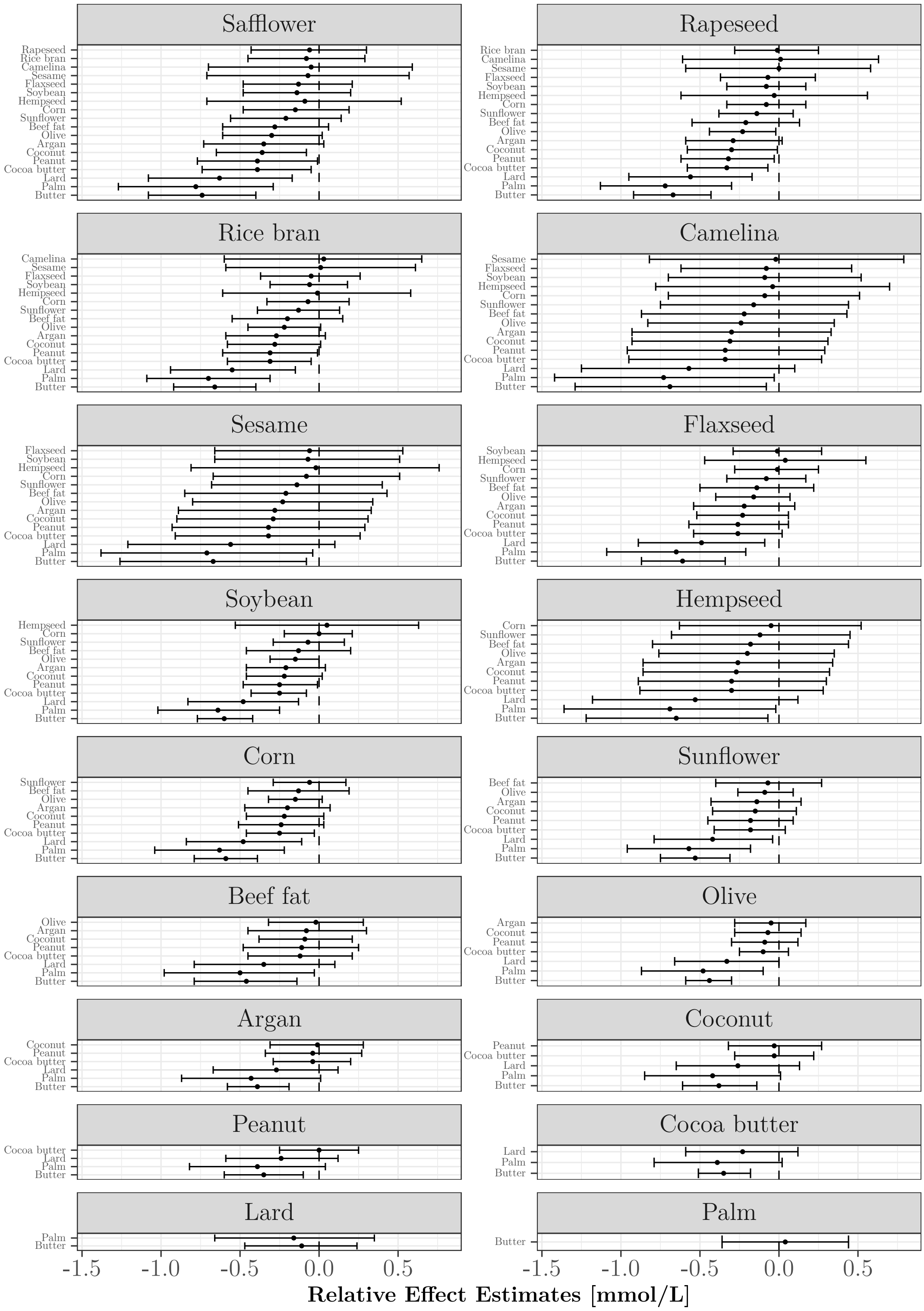

Figure 4.5: Effects of oils and solid fats on LDL-C (95 % CI) - for the individual effect magnitudes see Figure A.1

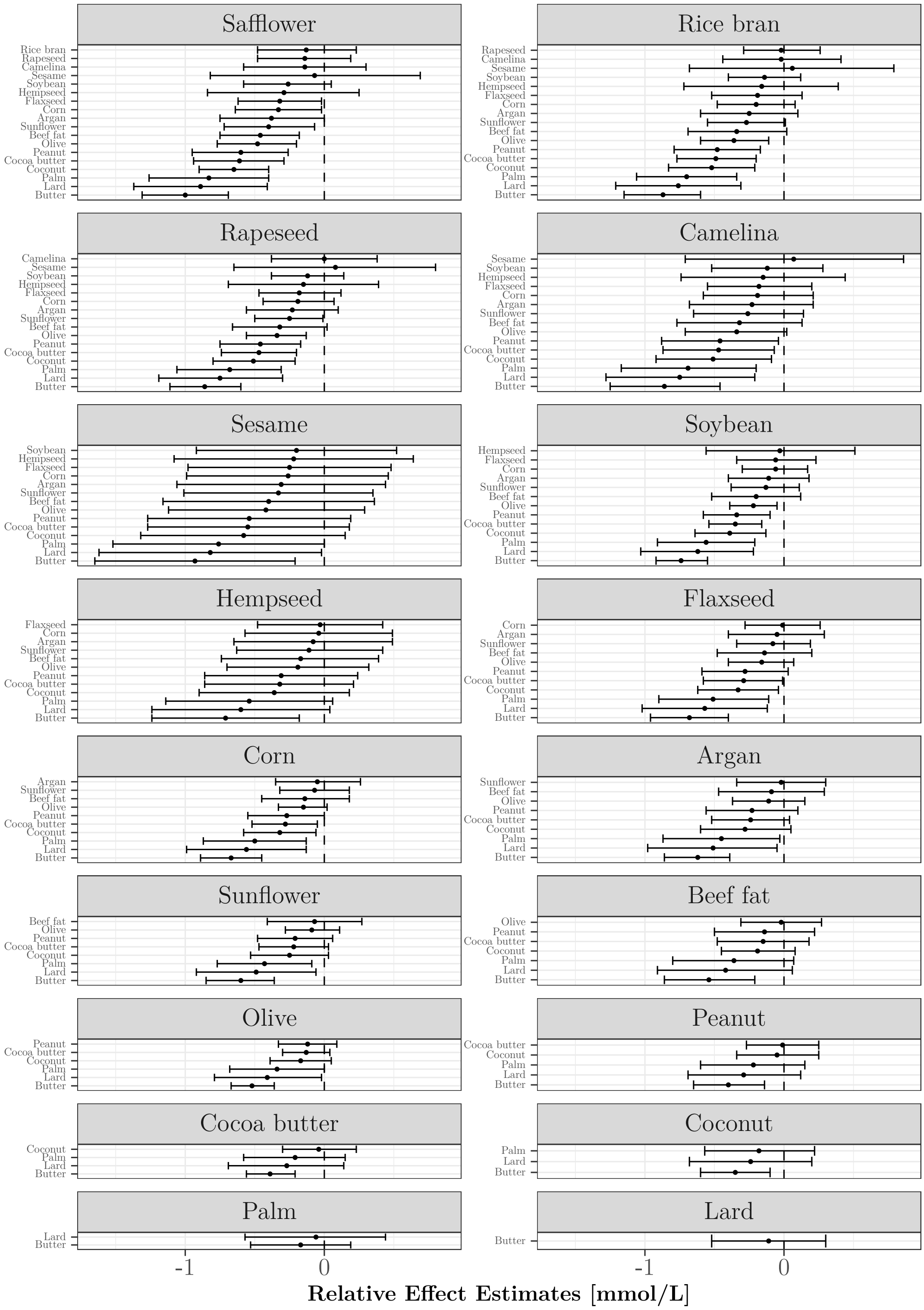

Figure 4.6: Effects of oils and solid fats on TC (95 % CI) - for the individual effect magnitudes see Figure A.2

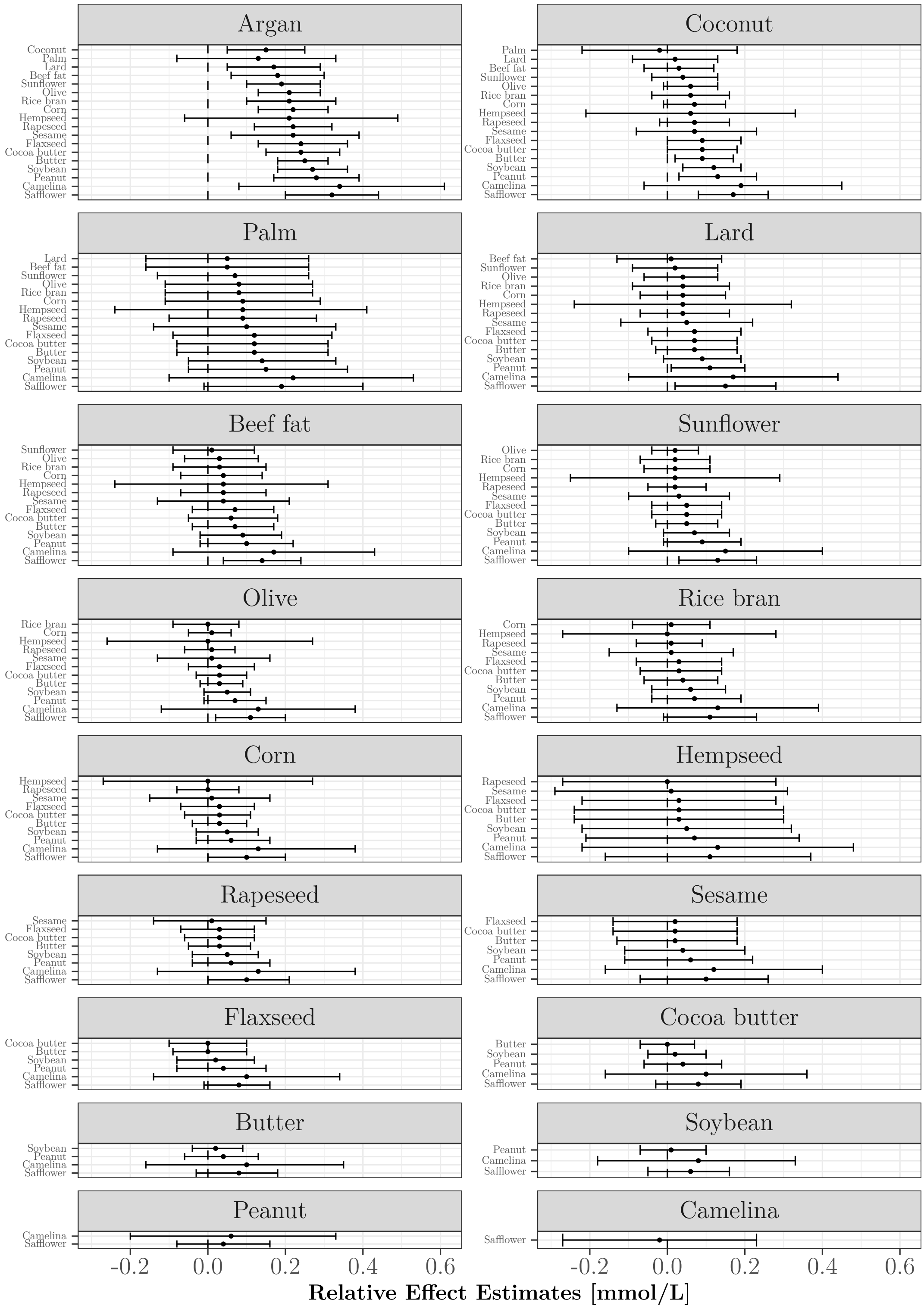

Figure 4.7: Effects of oils and solid fats on HDL-C (95 % CI) - for the individual effect magnitudes see Figure A.3

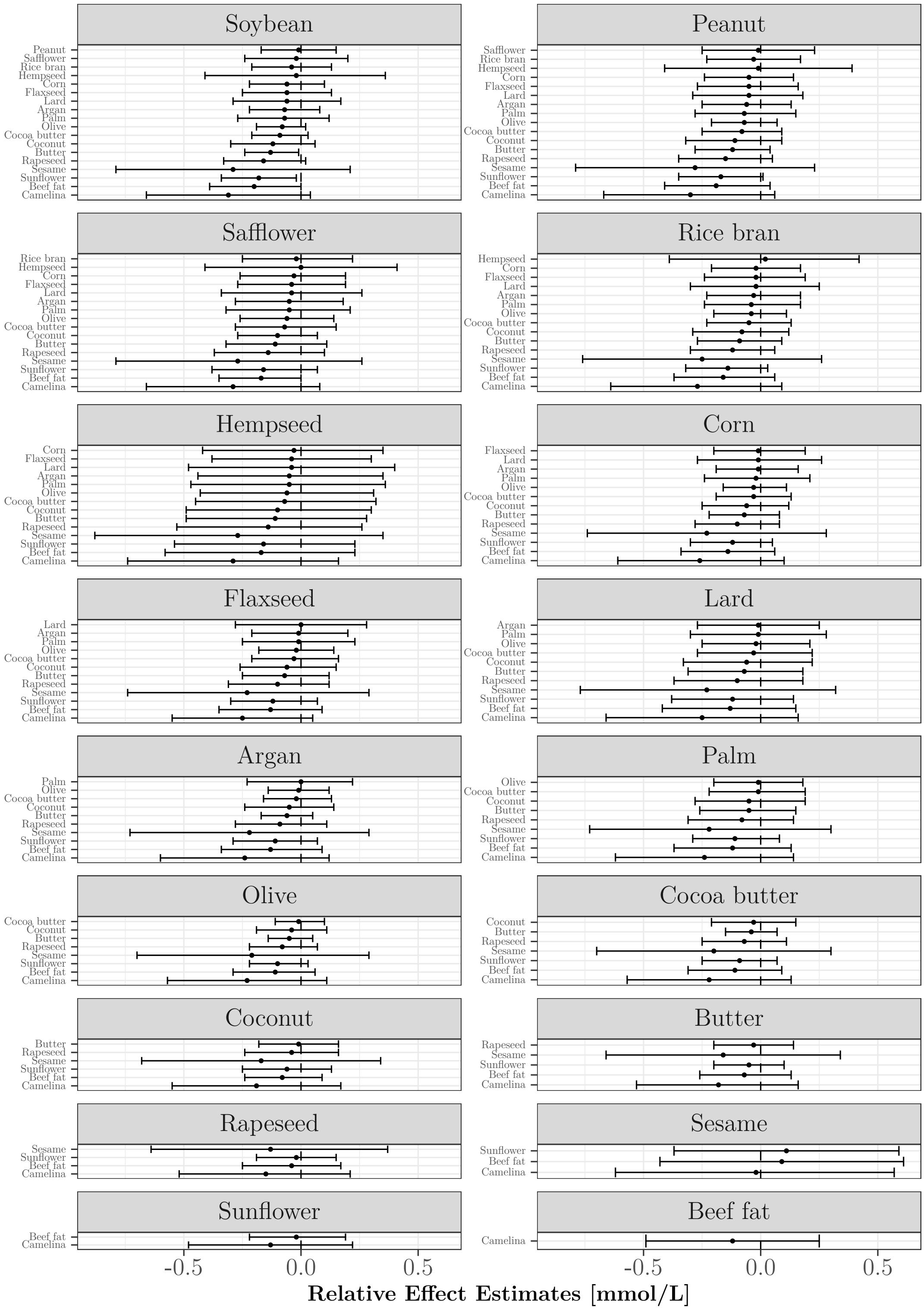

Figure 4.8: Effects of oils and solid fats on TC (95 % CI) - for the individual effect magnitudes see Figure A.4

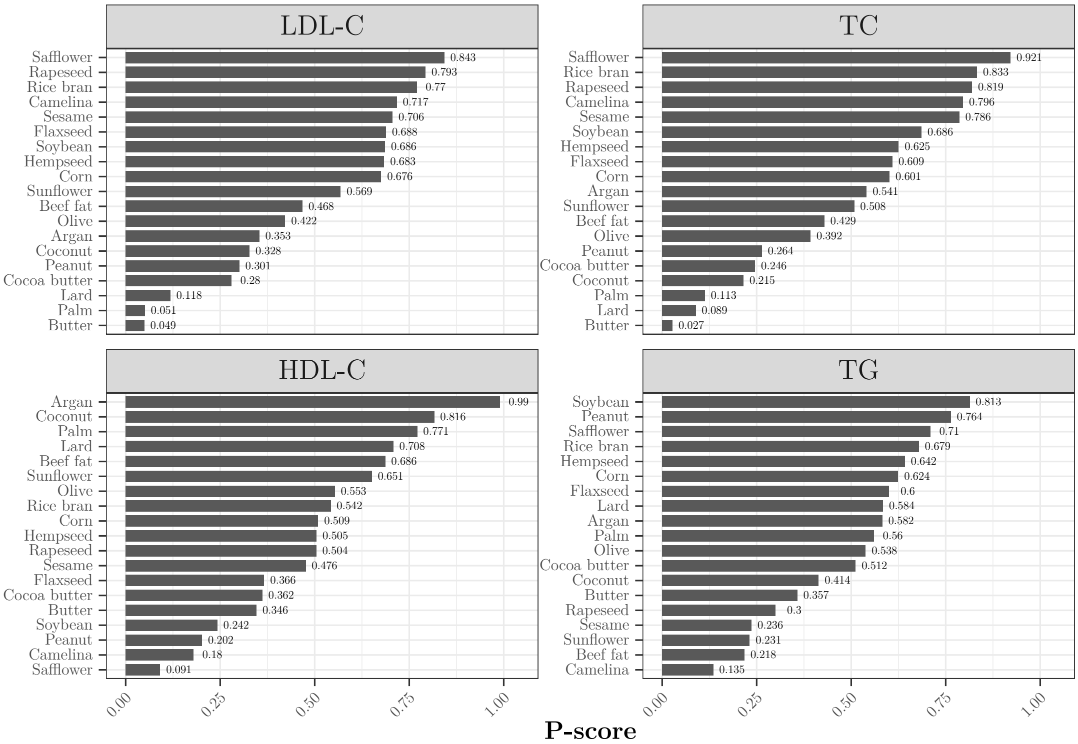

Figure 4.9: P-scores of the oils and solid fats

Ranking

The P-score ranking showed that safflower, rapeseed and rice bran oil were the most effective ones in terms of lowering LDL-C, while lard, palm oil and butter denote the worst treatment options. For lowering TC levels, safflower oil was the best option again - this time followed by rice bran and rapeseed oil. Butter, lard and palm oil showed the worst effect once more. If a HDL-C level increase is desired, argan oil was the optimal choice. Then, the best alternatives were coconut and palm oil; safflower, camelina and peanut oil represented the least suitable choices for this purpose. Lastly, the best options for lowering TG levels were soybean, peanut and safflower oil, while camelina, beef fat and sunflower oil showed the least effects.
Figure 4.9 shows the P-scores in relation to the individual blood lipids.

Inconsistency

The inconsistency analysis suggested significant inconsistency for LDL-C in the comparisons of coconut and soybean oil as well as rice bran and sunflower oil. For HDL-C the comparisons of argan oil with both butter and olive oil were inconsistent. For TC inconsistency was suggested for the comparisons of soybean oil with both cocoa butter and coconut as well as for the comparison of beef fat and corn oil. Furthermore, there was a significant inconsistency in the analysis for TG between cocoa butter and soybean oil.
Figure 4.10 shows the inconsistency of the mixed evidence with the compared oils / solid fats being aligned on the y-axis and the differences (direct versus indirect evidence) being plotted on the x-axis. In the figure, the p-value (p) and the amount of direct evidence per comparison (N) are given in addition to the MD and the 95 % CI.

Sensitivity analysis

According to the exclusion criteria specified in Section 3.3, the following studies were excluded for the sensitivity analysis: Akrami et al. [3], Baudet et al. [15], Cicero et al. [36], Kawakami et al. [86], Han et al. [67], Lichtenstein et al. [107], Mohamedou et al. [143], Mohamedou et al. [128], Stonehouse et al. [192], Tholstrup et al. [197] and Utarwuthipong et al. [202].
Despite some differences, the results largely supported the main analysis.

Low density lipoprotein cholesterol For LDL-C no more significant effects were visible between argan oil and butter as well as lard and sesame oil / beef fat. Moreover, the negative effect attributed to palm oil was vanished. Opposed to the main analysis, a significant LDL-C level reduction in relation to a treatment with argan oil was observable for safflower, rapeseed, rice bran, corn, soybean, sunflower and olive oil. Furthermore, a significant effect became apparent between corn and both olive and coconut oil.

Total serum cholesterol As with the LDL-C analysis, the TC analysis no longer showed any significant differences between the intake of palm oil and any other oil / solid fat. Further, sesame, sunflower and olive oil no longer showed

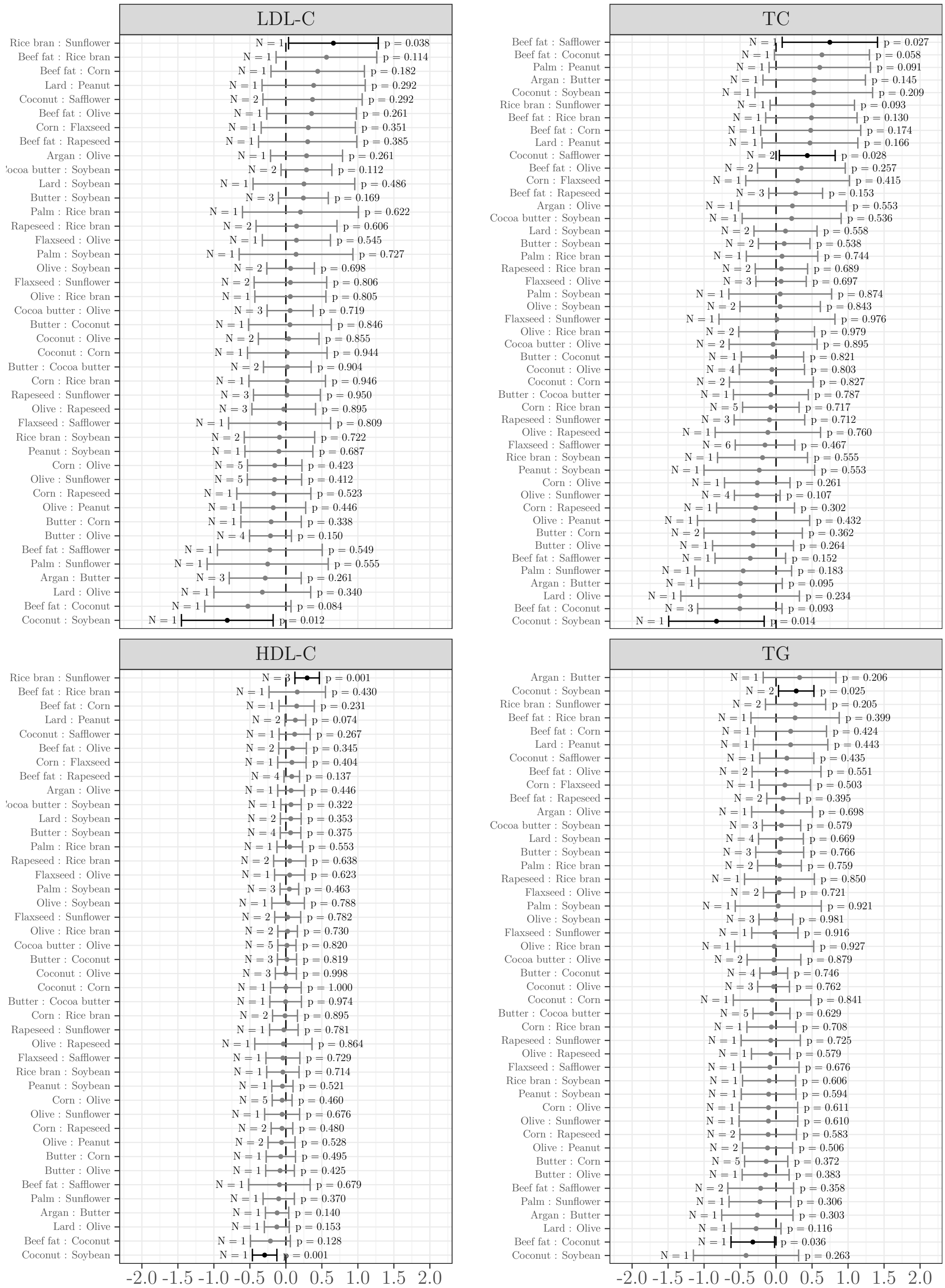

Figure 4.10: Frequentist inconsistency analysis - 95 % CI

a significant effect over lard. Also, the effects in reducing TC between safflower and corn, soybean and both peanut and olive, camelina and peanut oil as well as flaxseed oil against both cocoa butter and coconut had disappeared.

High density lipoprotein cholesterol The increasing effects of olive, sunflower and lard compared with safflower oil were no longer significant in this analysis. The same applied to the comparison of lard against peanut oil.

Triglycerides A reduction for soybean oil and safflower oil against beef fat was evident in this analysis.

4.4.2 Bayesian Analysis

This section reflects the results of the Bayesian approach: in a first step the resulting effects are outlined, before the SUCRA values, the inconsistency analysis and finally the sensitivity analysis are shown.
The following serves as a complement to the results of the frequentist analysis approach that have been shown in Section 4.4.1.

Low density lipoprotein cholesterol The significant effect of safflower oil over peanut oil was not discernible in this analysis; this also applied to rice bran oil versus soybean oil. Furthermore, rapeseed oil showed no more significance over peanut, olive and coconut oil. Also, beef fat lowered the LDL-C level only in comparison to butter.

Total serum cholesterol The effect of flaxseed oil versus cocoa butter found in the frequentist analysis could not be proven with this analysis. Furthermore, the comparisons of lard to both olive and sesame oil were no longer significant, nor was the comparison of rapeseed versus sunflower oil.

High density lipoprotein cholesterol The only difference obtained in the Bayesian analysis was lard having no significant effect versus both safflower and peanut oil.

Triglyceride While three effects were evident in the frequentist analysis, only one significant effect - namely soybean oil being favourable over sunflower oil - was found in this analysis.

A graphical visualisation of the MDs is given for LDL-C in Figure 4.11, TC in Figure 4.12, HDL-C in Figure 4.13 and TG in Figure 4.14 with the individual facets showing the effect of the oil / solid fat denoted in the respective header in relation to those being listed on the y-axis.

Rankings

The ranking according to the SUCRA value is displayed in Figure 4.15. As can be seen, the three best- and worst-placed oils did not differ between the SUCRA and the P-scores obtained via the frequentist analysis.

Inconsistency

The inconsistency analysis showed no deviations to the findings of the frequentist approach. The Appendix includes a complete overview for LDL-C (Table A.6), TC (Table A.7), HDL-C (Table A.8) and TG (Table A.9).

Sensitivity analysis

Low density lipoprotein cholesterol In comparison to the main analysis, the effects of argan oil versus butter, lard versus both olive and sesame oil as well as cocoa butter versus rice bran oil were no more significant. In addition, palm oil was no longer outperformed by any other oil or solid fat. Instead, safflower, rapeseed, rice bran, corn, soybean, sunflower and olive oil now showed a significantly greater effect than argan oil. Additionally, significant effects were observed for corn oil over peanut, safflower over soybean, peanut over rapeseed and olive over rapeseed oil.

Total serum cholesterol As already observed before (LDL-C), palm oil was no longer outperformed by any other oil or solid fat when it comes to the reduction of TC concentrations. Likewise, no effect resulted for soybean oil over peanut and olive oil. Also, argan and safflower oil were no longer superior than lard. Furthermore, the positive effect of flaxseed oil - when compared to coconut and safflower oil - was vanished. On the other hand, rapeseed oil was showing a significant reduction of TC levels compared to sunflower oil in this analysis.

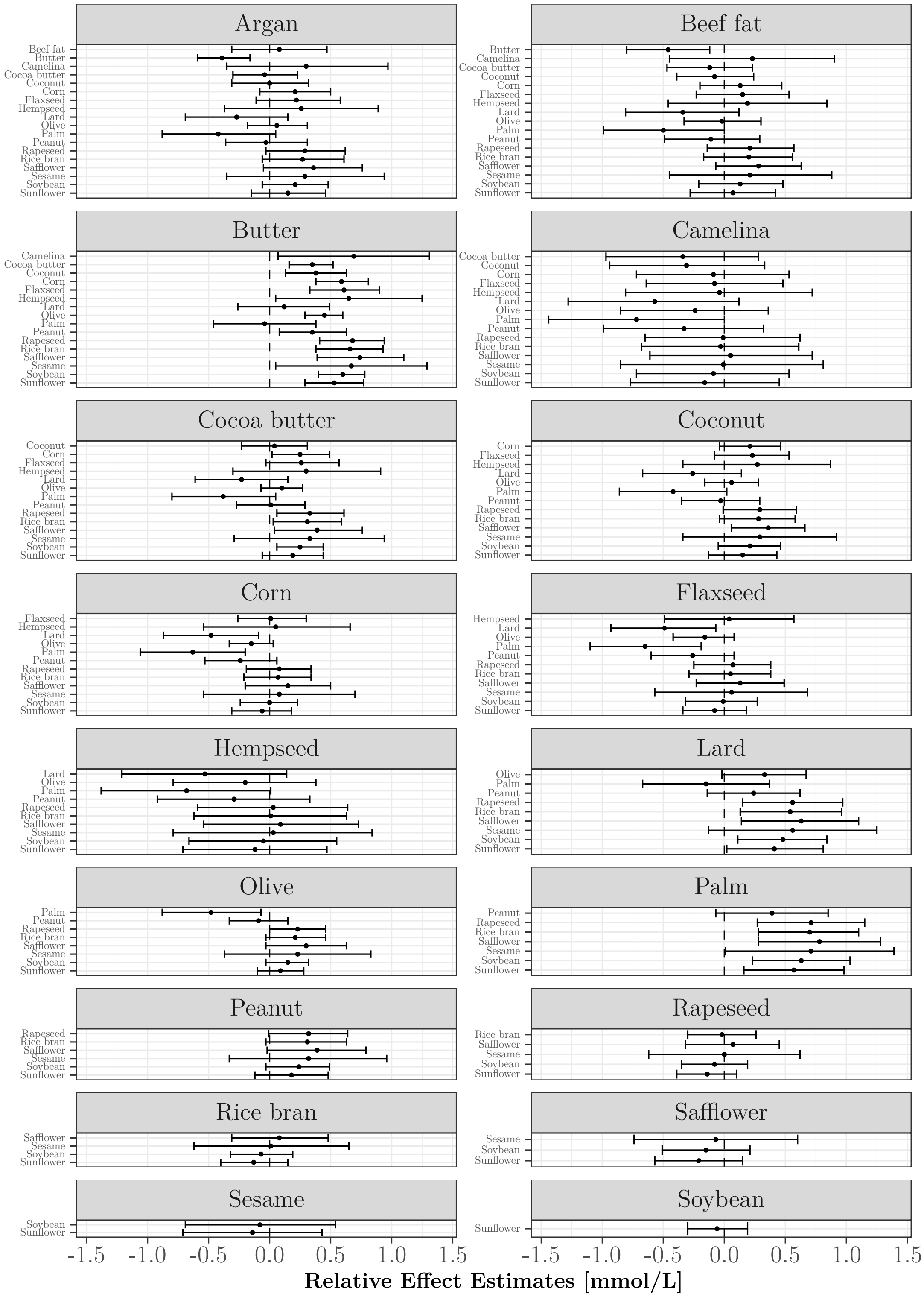

Figure 4.11: Effects of oils and solid fats on TC (95 % CI) - for the individual effect magnitudes see Figure A.9

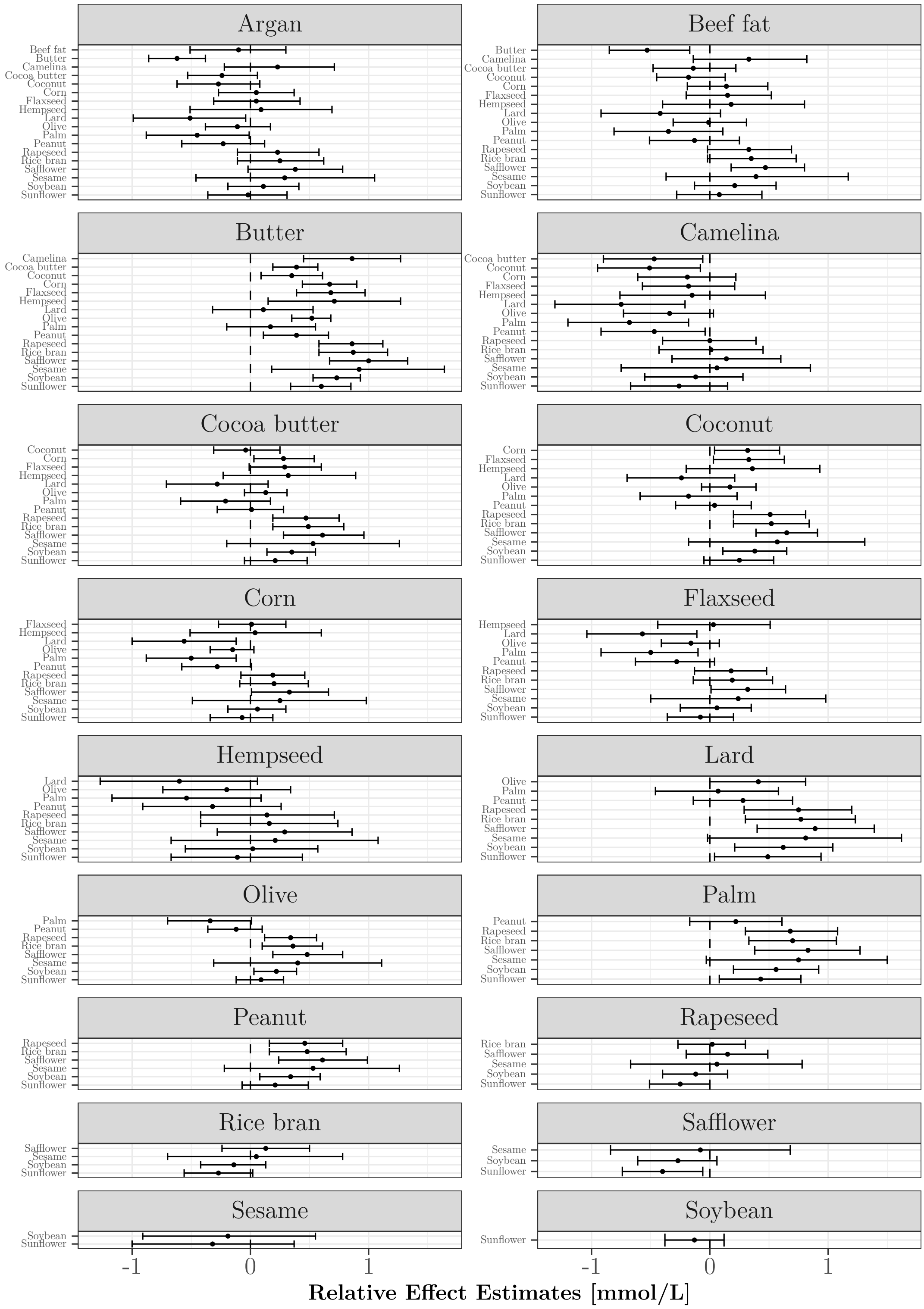

Figure 4.12: Effects of oils and solid fats on TC (95 % CI) - for the individual effect magnitudes see Figure A.10

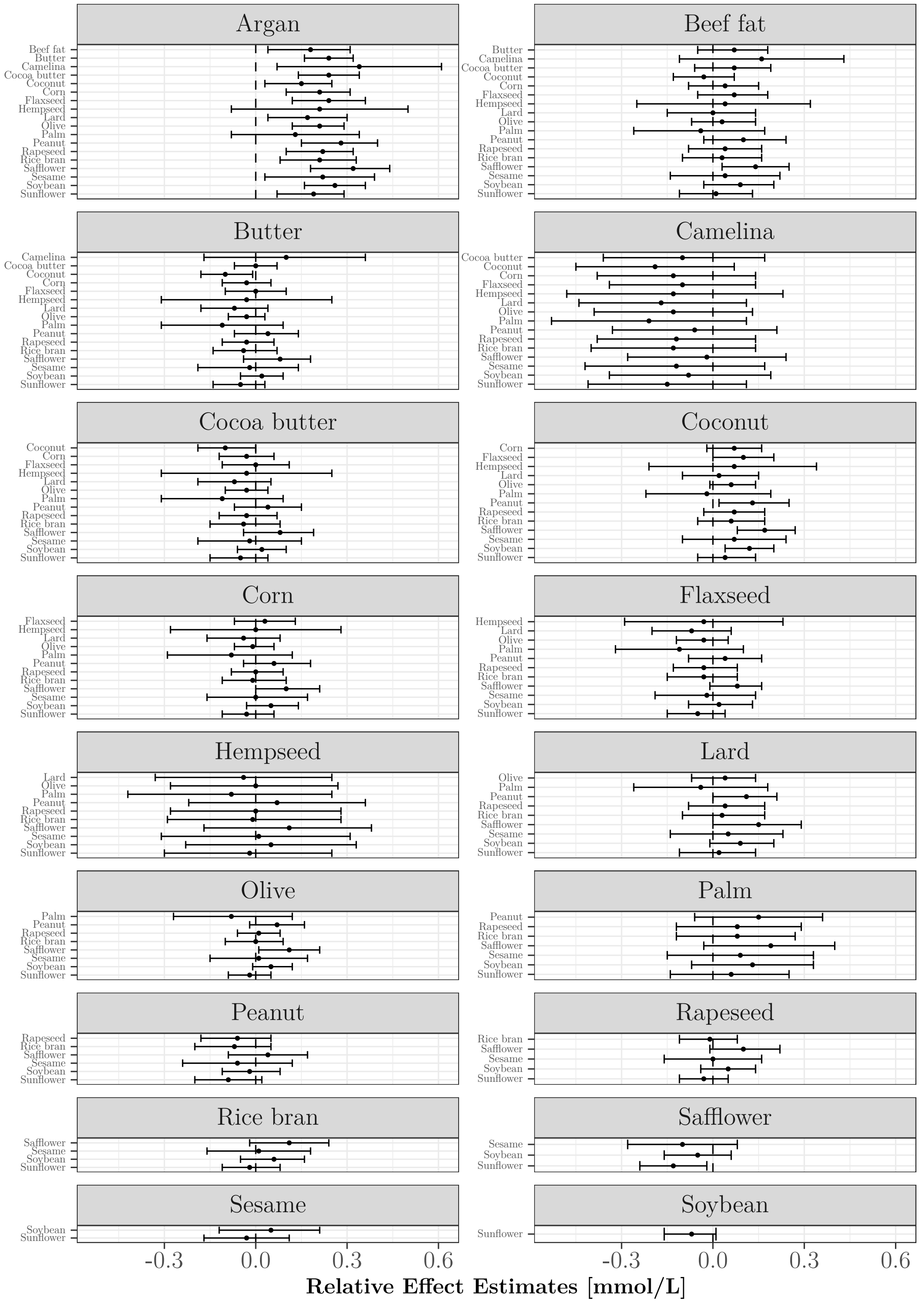

Figure 4.13: Effects of oils and solid fats on TC (95 % CI) - for the individual effect magnitudes see Figure A.11

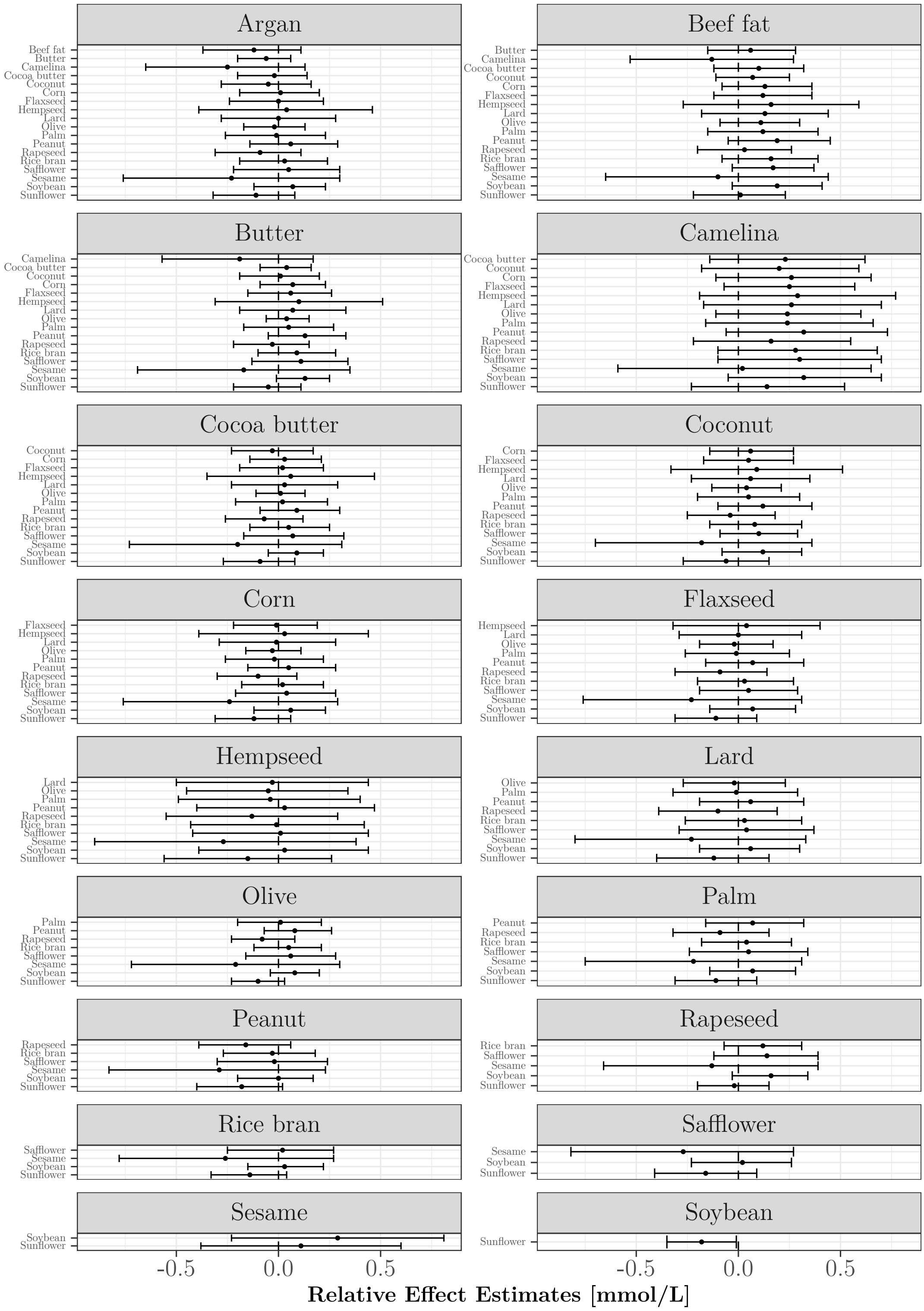

Figure 4.14: Effects of oils and solid fats on TC (95 % CI) - for the individual effect magnitudes see Figure A.12

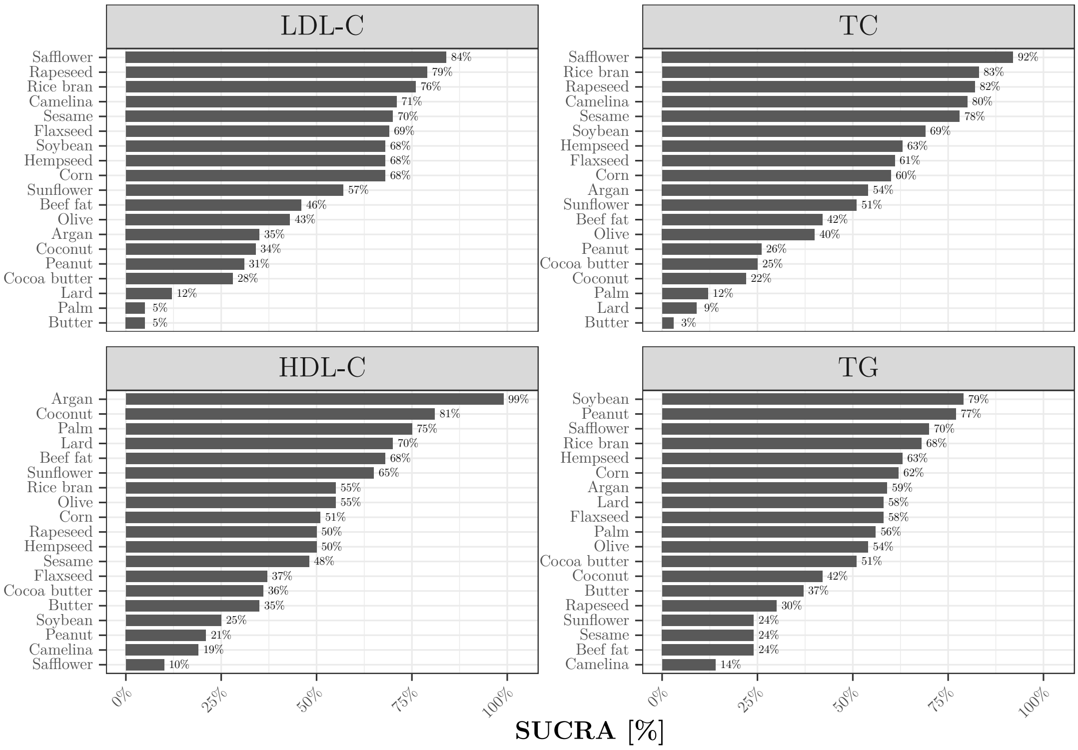

Figure 4.15: SUCRA value (%) of all oils and fats

High density lipoprotein cholesterol In terms of the HDL-C level investigation, no more significant effects could be attributed to olive, sunflower oil and lard with regard to safflower oil.

Total serum cholesterol No differences with respect to the main analysis were observable.

The Appendix contains a visualisation of the various effect magnitudes for both the frequentist and Bayesian sensitivity analysis regarding the individual blood lipids with Figures A.5 and A.13 showing LDL-C, Figures A.6 and A.14 showing TC, Figures A.7 and A.15 showing HDL-C and finally Figures A.7) and A.16 showing TG.

5

Discussion

This chapter discusses the findings and limitations of the present work.

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5.2 Relation to existing literature 55

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5.1 Results of the network meta-analysis

Comparison of the frequentist and Bayesian approach Whether to stick with either the frequentist or the Bayesian analysis method is a contentious issue with divergent views on when and why one of the two methods is most appropriate [23, 75].

In this work no major differences between the frequentist and Bayesian analysis can be seen, although the significance of some effects varies between the two approaches due to the slight differences in the underlying calculation methods. Such a behaviour can be observed in the LDL-C analysis where rapeseed oil shows a significant effect over olive oil upon using the frequentist approach: MD: -0.23 mmol/L (95 % CI: -0.44 to -0.02). Switching to the Bayesian analysis, the treatment effect of rapeseed oil over olive is denoted with MD: -0.23 mmol/L (95 % CI: -0.46 to 0). This minor change leads to the effect no longer being considered significant.

P-score and SUCRA Both analyses show the same results for the three best / worst ranked oils and solid fats. It can be observed, that PUFA- and MUFA-rich oils are ranked better than SFA- rich oils regrading the reduction of TC and LDL-C parameters in general. Furthermore, all vegetable oils - except palm oil - are more effective in reducing the aforementioned blood lipids than butter. The HDL-C value is mainly increased by SFA-rich oils and solid fats as the PUFA- and MUFA-rich argan oil. Interestingly, the latter shows the overall strongest potential. However, it must be taken into account that two inconsistencies are documented for argan oil, meaning that the effect should perhaps be viewed rather critically.

Inconsistency For each parameter (LDL-C, TC, HDL-C, TC), at least one inconsistency is found in the corresponding analyses. Since inconsistency is a property of evidence loops and not of specific treatment contrasts, it is difficult to determine the effect being responsible for it. Therefore, a further qualitative evaluation would be necessary in order to identify the exact cause [172].

Sensitivity analysis Both analyses show similar results. Compared to the main analyses, mostly only minor differences that can again be attributed to the circumstance discussed previously (weak significance of effects) are observable. A major difference, however, is the absence of significant comparisons with palm oil in terms of LDL-C and TC. Apart from these deviations, the sensitivity analysis supports the results of the main analysis and confirms that MUFA- and PUFA-rich oils have a better effect on LDL-C and TC compared to oils and solid fats high in SFAs.

5.2 Relation to existing literature

Comparison with Schwingshackl et al. [181]

The study outcomes support the findings of Schwingshackl et al. [181].
It can be confirmed, that safflower oil has the greatest effect in reducing TC and LDL-C and that vegetable oils have a bigger positive effect on TC (MDs from -1.00 to -0.17 [mmol/L]) and LDL-C (MDs from -0.74 to -0.35 [mmol/L]) than butter, while olive oil is less effective than other MUFA- and PUFA-rich oils (e.g. safflower and rice bran oil). Furthermore, the fact that soybean oil has the greatest impact on TG levels is again evident in this study.
A difference however emerges in the analysis of the effects on HDL-C levels: argan oil has the best effect in terms of increasing HDL-C.

Comparison with other studies

The lower effect of olive oil on TC and LDL-C compared to Ω-3- and Ω-6-rich oils is already observed in a meta-analysis by Ghobadi et al. [64]. In line with the meta-analysis results of Pan et al. [145], this analysis does not show any substantial effect of flaxseed oil (in relation to sunflower, rapeseed and olive oil) in reducing LDL-C and TC. Finally, the good performance of rice bran oil in lowering LDL-C and TC - as already reported via the meta-analysis by Jolfaie et al. [82] - can be approved.

Possible connections of oils / fats on the development of CVDs

Considering the different fatty acids and their effect on blood lipid levels, this work shows that PUFA- and MUFA-rich oils, such as safflower, rapeseed and rice bran oil, have a significant effect in reducing LDL-C and TC levels. Likewise, these oils show small changes in HDL-C levels, with the SFA-rich fats being the most effective. These results are also supported by Mensink et al. [125].
Looking at the above mentioned aspects in regard to the hard clinical endpoint, various studies show differing results. In a prospective observational study [57], the intake of Ω-6-FAs shows an inverse association with CHD risk in a dose-response manner. Further, a meta-analysis by Schwingshackl et al. [183] (including 42 observational studies) indicates a reduction in cardiovascular mortality, cardiovascular events and strokes when comparing the top versus bottom third of MUFA, olive oil, oleic acid and the MUFA:SFA ratio. In contrast, a dose-response meta-analysis of cohort studies shows no association between daily butter consumption and CVDs [152].
In addition to observational studies, several RCTs also deal with this topic. Two of the best known RCTs are the 'Lyon Heart Study' [91] and the 'PREvención con DIeta MEDiterránea (PREDIMED)' trial [119]. 'PREDIMED' is a multi-centre, randomised, nutritional intervention trial with the objective to evaluate possible prevention factors of CVDs. Over several years, more than 7,400 people - mainly with risk factors for a CVD - were screened. Participants were forced to follow a Mediterranean diet (MeDiet) with olive oil or nuts as the primary source of fat. It was concluded, that a MeDiet - either rich in olive oil or nuts - is suitable for the primary prevention of CVDs [119]. Just like the'PREDIMED' trial, also the 'Lyon Heart Study' investigated a MeDiet with rapeseed oil-based margarine being the main source of fat. According to it, a MeDiet can reduce the risk of CHD by 50 - 70 % [91].
While a meta-analysis by Mozaffarian et al. [132] (based on RCTs) shows that the replacement of SFAs by PUFAs leads to a reduction in cardiovascular events, Ramsden et al. [158] concludes that such a replacement is not related to CHD. Further this result is corroborated by a multivariate meta-regression by Schwingshackl et al. [182], which investigated MUFAs, PUFAs and SFAs in relation to

the CVD risk. However, despite various investigations with diverging conclusions, there is a basic agreement that replacing foods rich in saturated fatty acid with foods higher in unsaturated fats reduces the CHD risk [139].

Possible connections of blood lipids & CVDs

In addition to SFAs, elevated LDL-C levels are seen as a risk factor for developing CVDs. Baigent et al. [35] show with their meta-analysis (including 26 studies), that a reduction of LDL-C in the blood plasma by 1 mmol/L lowers the risk for developing a CVD by 20 %. The significantly higher reduction of LDL-C after consumption of vegetable oils and fats compared to butter (as shown in said study), is considered a valid factor regarding the prevention of cardiovascular events. The increased reduction of LDL-C by vegetable oils in contrast to butter can be confirmed in our work as well.
The extent to as which the HDL-C level has an effect on the development of CVDs has not been clarified yet. An inverse association between plasma HDL-C levels and CVD risk can be inferred from epidemiological studies [54, 156]. However, Mendelian randomisation studies have not shown any association of genetically reduced HDL-C in relation to an increased risk of myocardial infarction [76]. Due to the listed uncertainties, the main focus with regard to fat intake should not be put on HDL-C. Nevertheless, it is important to consider changes in HDL-C levels as a marker of cardiovascular health when discussing the effect of dietary oils / fats [181].

Potential biological mechanisms of oils and fats

A diet rich in oils with MUFAs and PUFAs is associated with beneficial effects for a number of physiological functions and the prevention of different diseases [80, 119, 124, 195]. Similarly, also antioxidants, polyphenols, carotenoids, etc. contained in edible oils and fats seem to have protective effects on the organism [8, 29, 163].

Lipid Metabolism The lipid metabolism can be affected in diverse ways depending on the intake of different FAs from oils and fats: Ω-3-FAs can influence the

TG synthesis by reducing fatty acid availability and enzyme activities which are responsible for the TG synthesis [71, 208]. In contrast, TFAs and SFAs are linked with negative effects on the lipid metabolism [121, 124]. TFAs can be incorporated into body lipids, oxidised and converted into longer SFAs. Moreover, they can modulate the metabolism of naturally occurring lipids and thereby alter the blood lipid profile [97]. Similarly to SFAs, TFAs also show an increasing effect on LDL, whereby the latter have a stronger reducing effect on HDL compared to saturated and unsaturated FAs [121, 124]. For further effects of SFAs, MUFAs and PUFAs on the blood lipids see section 5.2.

Phenols, which are found in vegetable oils have a positive effect on the lipid metabolism by inhibiting the pancreatic lipases in the small intestine and thus delaying the postprandial lipaemia [29]. Furthermore, polyphenols can increase the AMPK (AMP-activated protein kinase) mRNA - an enzyme able to reduce the activities of various enzymes of the lipid metabolism [155] -, which may indicate a dyslipidaemia-modulating effect [31]. In addition also different phytosterols seem to decrease the LDL-C values [154, 205].

Oxidative Stress Oxidative stress is characterised by the imbalance between pro- and antioxidative reactions in an organism. An overexpression of reactive oxygen species (ROS) leads to oxidative damage of biological molecules (DNA, proteins, lipids) [153] which in turn can be associated with chronic degenerative diseases such as cancer, metabolic diseases and CVDs [130, 190], while oxidised LDL-C plays a particular role in the formation of atherosclerosis and CVDs [184].

Fatty acids ingested via food apparently play an important role regarding the sensitivity of cells to oxidative stress, which is presumably due to alterations in the fatty acid composition of the cell membranes [137]. Evidence from observational [198] and interventional studies [81, 150] show that MUFAs - opposite to SFAs - have a positive effect on the protein and lipid oxidation. This can be attributed to the different chemical properties of these FAs, since the degree of unsaturated carbon chains can influence the biological membrane fluidity and the sensitivity to oxidation [203].

PUFAs are particularly susceptible to ROS due to their many double carbon-carbon bonds in their chains [203]. Studies investigating the effect of PUFAs on oxidative stress have yielded very different results: while no connection between PUFAs and oxidative stress is observed according to [213] and [60], other authors show a positive effect for Ω-3-FAs [147] and a disadvantageous effect for Ω-6-FAs [201].
Further, the presence of high TFA levels can lead to cell alterations due to ROS production and oxidative stress [110]. Thus, high concentrations of these FAs show an increased oxidative stress in rat livers due to a reduced efficiency of the antioxidant-enzymatic system [44].
Antioxidants - such as tocopherols, polyphenols and carotenoids - which are found in vegetable oils act preventive on oxidative processes [8, 116, 186, 216].

Inflammation Inflammation is an important aspect of the pathophysiology of chronic diseases such as CVDs, diabetes and various types of cancer [61]. When referring to fatty acids, SFAs and TFAs are often associated with a pro-inflammatory effect. SFAs are linked with the inflammatory markers HS-CRP [9] and TNF-α [102] and potential inflammations in the muscle tissue [87]. Also TFAs appear to increase the plasma concentrations of different inflammatory markers [67, 112, 133]. On the opposite, PUFA-rich oils seem to have a protective effect [102], which may be due to their fatty acid structure and its corresponding degradation metabolites. In healthy people, α-linolenic acid is converted into EPA and DHA. EPA and the γ-linoleic acid (GLA) - which is synthesised from Omega-6-FAs - can be transformed into hormone-like compounds called eicosanoids. These eicosanoids in turn have important functions in the body including vital organ functions, intracellular activities and anti-inflammatory properties [80].

Blood glucose Diets rich in fatty acids, mainly those with high levels of SFAs and TFAs, may cause an acute increase in insulin resistance independent of obesity [146]. Nonetheless, MUFAs seem to have a positive effect on insulin receptors [127]. Additionally, they can buffer the β-cell hyperactivity and insulin resistance in patients with hypertriglyceridemia, while this is not the case for SFAs [111].

Further, Ω-3-PUFAs seem to have a positive effect on the blood glucose level, whereas Ω-6-PUFAs may be associable with hyperinsulinaemia [209].
Moreover, also polyphenols can affect the glucose metabolism in a positive way: they have an inhibiting effect on carbohydrate digestion and absorption, reduce the glucose release from the liver and stimulate the uptake of glucose into the peripheral tissues [68] while being able to reduce the production of advanced glycation end products such as HBA1c using their antioxidant capabilities [214].

5.3 Limitations

Upon the interpretation of the results derived by the NMA the following limitations shall not be neglected: first, most of the evidences come from indirect comparisons, which leads to bigger uncertainty (wide confidence intervals and credibility intervals). Also, some of the observed effects are only significant in one or the other analysis approach (frequentist versus Bayesian). Furthermore, the mixed evidences show some inconsistencies that need to be considered when evaluating the effectiveness of the oils / solid fats.
Another limitation arises from not integrating the proportion of ingested oils and solid fats, as no standardisation has been performed. In addition, the study type (crossover or parallel trial) and the gender, age, origin as well as health status of the participants were not considered.
Moreover, only three of the included studies had a low risk of bias, no evaluation about the quality of evidence and investigation of small study effects has been done.
Finally, it must also be mentioned that only intermediate biomarkers for CVD risk have been evaluated.

6

Conclusion

This chapter gives a conclusion and outlines possible future work topics.

Conclusion

The results of the network meta-analysis show that oils higher in unsaturated fatty acids - such as safflower, rapeseed, rice bran, soybean and flaxseed oil - are more effective in reducing both LDL-C and TC than SFA-rich fats, such as butter and lard. In contrast, SFA-rich fats and oils appear to have a higher potential in increasing HDL-C.

Despite the prevailing limitations, the results are comparable to other studies dealing with the metabolic effects of fats [132, 181]. This work further strengthens the current recommendation [43, 105] of replacing SFA-rich fats with PUFA- and MUFA-rich oils due to their positive effect on cholesterol levels (compared to SFAs) [6, 45, 55, 165] in order to keep them constant and thus lessen the risk of developing a CVD.

Outlook on future research

In a future study, the quality of evidence should be investigated e.g. via the GRADE system of Salanti et al. [171]). In order to prevent a possible bias towards any of the examined treatment options, a standardisation of the fat intake should be done in order to create a common baseline that allows for a better comparability. Future work could also include an extension of the spectrum of investigated fats and oils by including omega-3 fatty acids of animal origin, which would allow a comparison of vegetable oils with the latter. Furthermore, an analysis of the gender-specific effects of oils and fats would be interesting.

7

Summary

The last chapter contains a short summary of the thesis in English and German.

Summary
Zusammenfassung

From a global perspective, cardiovascular diseases (CVDs) are the most common cause of death (as of 2017) [166]. Due to the multifaceted nature of the clinical picture, several risk factors can be associated with its development. For example, the intake of various fatty acids (mainly saturated fatty acids (SFAs)) - via the diet - can lead to an alteration in blood lipid concentrations [45, 125, 126] and therefore rise the risk of developing a CVD [58, 134]. Since the main sources of these fatty acids are edible oils and fats, the following question arises: "Which oils and fats are positively influencing blood lipid levels and might therefore have a preventive effect on CVDs?"
This systematic review addresses this issue and investigates - based on Schwingshackl et al. [181] - the effects of 19 different oils and fats on the blood lipid levels of low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), total serum cholesterol (TC) and triglyceride (TG) via a network meta-analysis (NMA).
It is shown that monounsaturated fatty acid (MUFA)- and polyunsaturated fatty acid (PUFA)-rich oils have the greatest effect in reducing TC and LDL-C. Furthermore, the findings suggest that vegetable oils should be favoured over butter. The results of the thesis are in line with the findings of similar studies [64, 82, 125, 145, 181] and thus support the current recommendations [18, 43, 52] of replacing fats rich in SFA with PUFA- and MUFA-rich oils / fats.

Bei globaler Betrachtung stellen Herz-Kreislauf-Erkrankungen die häufigste Todesursache dar (Stand 2017) [166]. Aufgrund der Komplexität dieses Krankheitsbildes können etliche Risikofaktoren, so beispielsweise auch erhöhte Blutfettwerte [58, 134], zur Entstehung von kardiovaskulären Ereignissen beitragen. Die Blutlipidkozentrationen können wiederum von verschiedenen Faktoren beinflusst werden, unter anderem von über die Nahrung aufgenommenen Fettsäuren (einfach ungesättigte (MUFA), mehrfach ungesättigte (PUFA) und gesättigte Fettsäuren (SFA)) [45, 125, 126]. Da die Hauptquellen dieser Fettsäuren Speiseöle und -fette bilden, stellt sich folgende Frage: "Welche Öle und Fette können die Blutfettwerte positiv

beeinflussen und indes präventiv auf eine Herz-Kreislauf-Erkrankung wirken?"
Die vorliegende systematische Übersichtsarbeit nimmt sich dieser Thematik an und untersucht basierend auf Schwingshackl et al. [181] - mittels einer Netzwerk Meta-Analyse - den Effekt von 19 verschiedenen Ölen und Fetten auf die Blutfettwerte (LDL-C, HDL-C, das Gesamtcholesterin (TC) und die Triglyceride (TG)).
Aus den Ergebnissen lässt sich schließen, dass MUFA- und PUFA-reiche Öle den größten Effekt hinsichtlich einer Reduktion von TC und LDL-C aufweisen. Des Weiteren sollten zur Senkung der eben genannten Blutfettwerte pflanzliche Öle gegenüber Butter favorisiert werden.
Die Resultate der vorliegenden Arbeit decken sich mit den Ergebnissen ähnlicher Studien [64, 82, 125, 145, 181] und bekräftigen somit die aktuellen Empfehlungen [18, 43, 52], wonach SFA-reiche Fette durch PUFA- und MUFA-reiche Öle / Fette ersetzt werden sollten.

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A

Appendix

Acronyms

Apo	Apolipoprotein
ASCVD	Atherosclerotic cardiovascular disease
CENTRAL	Central Register of Controlled Trials
CHD	Coronary heart disease
CI	Confidence interval
CrI	Credibility interval
CVD	Cardiovascular disease
DHA	Decosahexaenoic acid
EbM	Evidence-based Medicine
EFSA	European Food Safety Authority
EPA	Eicosapentaenoic acid
FA	Fatty acid
HDL	High density lipoprotein
HDL-C	High density lipoprotein cholesterol
IDL-C	Intermediate-density lipoprotein cholesterol
LDL	Low density lipoprotein
LDL-C	Low density lipoprotein cholesterol
MA	Meta-analysis
MD	Mean difference
MeDiet	Mediterranean diet
MUFA	Monounsaturated fatty acid
NCD	Noncommunicable disease
NMA	Network meta-analysis
PREDIMED	PREvención con DIeta MEDiterránea
PUFA	Polyunsaturated fatty acid
RCT	Randomised controlled trial
RoB	Risk of bias
SFA	Saturated fatty acid
SUCRA	Surface Under the Cumulative RAnking curve
TC	Total serum cholesterol
TFA	Trans fatty acid
TG	Triglyceride
VLDL	Very low density lipoprotein
VLDL-C	Very low density lipoprotein cholesterol

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Unless otherwise stated, each graph or table has been created using *R*[1] with the help of the packages *Tidyverse*[2] and *kableExtra*[3].

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Table A.2: Oils and solid fat content

	SFA (g/100g)	MUFA (g/100g)	PUFA (g/100g)
Safflower oil	7	79	14
Sunflower oil	10	20	66
Rapseed oil	7	63	28
Hempseed oil	7	13	73
Flaxseed oil	9	18	68
Corn oil	13	28	55
Olive oil	14	73	11
Soybean oil	16	23	58
Palm oil	49	37	9
Coconut oil	82	6	2
Butter	51	22	3
Lard	39	45	11
Beef Fat	50	41	4
Cacao Butter	60	33	3
Sesame oil	14	40	42
Peanut oil	17	46	32
Camelina oil*	8	35	57
Rice Bran	20	39	35
Argan oil	18	43	38

Note:
Sources accessed May 1, 2020: USDA. FoodData Central.
https://fdc.nal.usda.gov/ndb/
** - Government of Canada. Food and Nutrition.*
https://www.canada.ca/en/health-canada/services/food-nutrition

Table A.3: More detailed information about the study site and the study participants

Study ID	Reference	Country	Study Design	Comparison Oils/Solid fat	Sample Size	Disease Status	Mean Age	Mean Baseline BMI	Type 2 Diabetes (%)	Female (%)	Duration (Weeks)
1	Aguilera, 2004	Spain	RCT, parallel	Olive oil vs. Sunflower oil	20	Peripheral vascular disease	65	26.7	0	0	16
2	Akrami, 2017	Iran	RCT, parallel	Flaxseed oil vs. Sunflower oil	52	Metabolic syndrome	48.5	NR	0	37	7
3	Assuncao, 2009	Brazil	RCT, parallel	Coconut oil vs. Soybean oil	40	Abdominal obesity	28.5	31.1	0	100	12
4	Atefi, 2018	Iran	RCT, parallel	Olive oil vs. Rapeseed oil vs. Sunflower oil	77	Type 2 diabetes and overweight	58.01	28.6	100	100	8
5	Baudet, 1984	France	RCT, crossover	Sunflower oil vs. Palm oil vs. Peanut oil	24	50 % hypercholesterolemia	45.9	NR	0	100	20
6	Binkoski, 2005	USA	RCT, crossover	Olive oil vs. Sunflower oil	31	Moderate hypercholesterolemia	46.2	26.1	0	61	4
7	Brassard, 2017	Canada	RCT, crossover	Butter vs. Corn oil vs. Olive oil	92	Abdominal obesity and relatively low HDL-C	38	30.5	0	53	4
8	Candido, 2017	Brazil	RCT, parallel	Olive oil vs. Soybean oil	41	Exess body fat	27	30.1	0	100	9
9	Cheng, 2018	China	RCT, crossover	Cocoa butter vs. Olive oil	67	Healthy	23.16	20.9	0	51	18
10	Cicero, 2009	Italy	RCT, parallel	Corn oil vs. Olive oil	22	Moderate hypercholesterolemia	50	25.7	0	50	6.5
11	Derouiche, 2005	France	RCT, parallel	Argan oil vs. Olive oil	60	Healthy	23.4	22.3	0	0	3
12	Dittrich, 2015	Germany	RCT, crossover	Flaxseed oil vs. Sunflower oil	46	Moderate hypertriacylglyceridemia	61	NR	NR	NR	10
13	Dobrzyńska 2018	Poland	RCT, parallel	Camelina oil vs. Rapeseed oil	60	Postmenopusal with dyslipidaemia	45-65	26.8	0	100	6

Table A.3: More detailed information about the study site and the study participants *(continued)*

Study ID	Reference	Country	Study Design	Comparison Oils/Solid fat	Sample Size	Disease Status	Mean Age	Mean Baseline BMI	Type 2 Diabetes (%)	Female (%)	Duration (Weeks)
14	Farajabakhsh, 2019	Iran	RCT, parallel	Sesame oil vs. Sunflower oil	47	Metabolic syndrome	49.08	29.8	NR	64	8
15	Haimeur, 2013	Morocco	RCT, parallel	Butter vs. Virgin Argan oil	39	Dyslipidemia	53	29.7	NR	79	3
16	Han, 2002	USA	RCT, crossover	Butter vs. Soybean oil	19	Moderately elevated LDL-C levels	64.7	28.8	0	58	4.5
17	Harris, 2017	USA	RCT, crossover	Coconut oil vs. Safflower oil	12	Healthy	58.8	26.4	0	100	4
18	Iggman, 2015	Sweden	RCT, parallel	Palm oil vs. Sunflower oil	39	Healthy	26.9	20.2	0	31	7
19	Karvonen, 2002	Finnland	RCT, parallel	Olive oil vs. Rapeseed oil vs. Camelina Oil	68	Mild hypercholesterolemia	51.3	25.6	0	60	6
20	Kawakami, 2015	Japan	RCT, crossover	Corn oil vs. Flaxseed oil	15	Healty	59.9	25.1	0	0	12
21	Khaw, 2018	United Kingdom	RCT, parallel	Butter vs. Coconut oil vs. Olive oil	91	Healthy	59.9	25.1	0	69	4
22	Kontogianni, 2013	Greece	RCT, crossover	Flaxseed oil vs. Olive oil	37	Healthy	25.6	21.9	0	78	6
23	Kris-Etherton, 1993	USA	RCT, crossover	Butter vs. Olive oil vs. Soybean oil vs. Cocoa butter	18	Healthy	26	23	0	0	4
24	Kris-Etherton, 1993	USA	RCT, crossover	Butter vs. Cocoa butter	15	Healthy	27	24	0	0	4
25	Kris-Etherton, 1999	USA	RCT, crossover	Olive oil vs. Peanut oil	22	Healthy	34	20 - 27	0	59	3.5

Table A.3: More detailed information about the study site and the study participants *(continued)*

Study ID	Reference	Country	Study Design	Comparison Oils/Solid fat	Sample Size	Disease Status	Mean Age	Mean Baseline BMI	Type 2 Diabetes (%)	Female (%)	Duration (Weeks)
26	Kruse, 2015	Germany	RCT, parallel	Olive oil vs. Rapeseed oil	18	Obese	55	29.5	0	0	4
27	Lai, 2011	Taiwan	RCT, parallel	Soybean oil vs. Rice bran oil	35	Type 2 diabetes	56.8	NR	100	NR	5
28	Lichtenstein, 1994 / Schwab, 1998	USA	RCT, crossover	Beef tallow vs. Rapeseed oil vs. Corn oil vs. Olive oil vs. Rice bran oil	15	Elevated LDL-C levels	61	27.4	0	53	4
29	Lichtenstein, 1999	USA	RCT, crossover	Butter vs. Soybean oil	36	Elevated LDL-C levels	63	27.4	0	50	5
30	Lv, 2018	China	RCT, parallel	Soybean oil vs. Cocoa butter	60	Healthy	21.59	21.03	0	NR	16
31	Maki, 2015	USA	RCT, crossover	Corn oil vs. Olive oil	54	Hypercholesterolemia	53.8	28.2	0	65	3
32	Maki, 2018	USA	RCT, crossover	Corn oil vs. Coconut oil	24	Healthy	45.2	27.7	0	57	4
33	Mohamedou, 2011	Morocco	RCT, parallel	Argan oil vs. Butter	24	Dyslipidemia	48	23.6	0	71	3
34	Mohamedou, 2011	Morocco	RCT, parallel	Argan oil vs. Butter	86	Typ 2 diabetes and dyslipidemia	52	29.7	100	48	3
35	Morillas-Ruiz, 2014	Spain	RCT, crossover	Butter vs. Olive oil	53	Hypercholesterolemia	63.5	27.8	13	100	4
36	Nigam, 2014	India	RCT, parallel	Olive oil vs. Rapeseed oil	93	Non-alcoholic fatty liver disease	37.1	27.3	0	0	27
37	Paschos, 2007	Greece	RCT, parallel	Flaxseed oil vs. Safflower oil	35	Hypercholesterolemia	51.4	28	0	0	12

Table A.3: More detailed information about the study site and the study participants *(continued)*

Study ID	Reference	Country	Study Design	Comparison Oils/Solid fat	Sample Size	Disease Status	Mean Age	Mean Baseline BMI	Type 2 Diabetes (%)	Female (%)	Duration (Weeks)
38	Perona, 2004	Spain	RCT, crossover	Olive oil vs. Sunflower oil	62	Hypertensive	84	28.8	0	0	4
39	Rallidis, 2003	Greece	RCT, parallel	Flaxseed vs. Safflower oil	76	Hypercholester-olemia	51	28.3	0	0	12
40	Reiser, 1985	USA	RCT, crossover	Beef fat vs. Cocout oil vs. Safflower oil	19	Healthy	25.6	NR	0	0	5
41	Rezaei, 2018	Iran	RCT, parallel	Olive oil vs. Sunflower oil	66	Non-alcoholic fatty liver disease	43.47	30.1	0	56	12
42	Salar, 2016	Iran	RCT, parallel	Rapeseed oil vs. Sunflower oil vs. Rice bran oil	72	Type 2 diabetes	51.4	29.9	100	100	8
43	Schwab, 2006	Finland	RCT, crossover	Hempseed oil vs. Flaxseed oil	14	Healthy	45	24.5	0	43	4
44	Sirtori, 1986	Italy	RCT, crossover	Corn oil vs. Olive oil	23	High artherosclerotic risk	47.4	NR	50	NR	8
45	Sirtori, 1992	Italy	RCT, crossover	Corn oil vs. Olive oil	12	Hypercholester-olemia	NR	NR	NR	NR	6
46	Stone-house, 2019	Australia	RCT, crossover	Cocoa butter vs. Olive oil	38	Healthy	20 - 40	18 - 25	0	NR	4
47	Stricker, 2008	Switzer-land	RCT, parallel	Rapeseed oil vs. Sunflower oil	40	Peripheral artery disease	65.2	NR	33	13	8
48	Tholstrup, 2011	Denmark	RCT, crossover	Lard vs. Olive oil	43	Healthy	29.6	22.9	0	0	3
49	Ut-rawuthi-pong, 2009	Thailand	RCT, crossover	Soybean oil vs. Palm oil vs. Rice bran oil	16	Hyperlipidemia	44 -67	< 25	0	100	10
50	Voon, 2011	Malaysia	RCT, crossover	Coconut oil vs. Olive oil	45	Healthy	30.1	23.1	80	0	5
51	Zhang, 1997	China	RCT, parallel	Soybean oil vs. Lard vs. Peanut oil	120	Healthy	18 - 25	18.5 - 25	0	0	6

Note: NR = Not Reported

Table A.4: Information on study outcomes and any potential conflicts of interest

Study ID	Reference	Diet Advice	Oils/solid fat provided by investigators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
1	Aguilera, 2004	Healthy diet advice	Yes	None	LDL-oxidation suspectibility	TC, HDL-C, LDL-C, TG	Ministerio de Education y Cienica, Instituto Danone
2	Akrami, 2017	Healthy diet advice	Oils advised	Yes, in both arms	Blood Pressure (systolic and diastolic), Fasting Blood Glucose, TG, HDL-C, LDL-C, waistcircumference, MDA	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
3	Assuncao, 2009	Healthy diet advice	Yes	Yes, in both arms	NR	TC, HDL-C, LDL-C, TG	NR
4	Atefi, 2018	Healhty diet by investigators	Yes	None	Lipid profile	TC, HDL-C, LDL-C, TG	Extractetd from Msc thesis written by Masoumeh Atefi which was funded by Shiraz University of Medical Sciences (SUMS)
5	Baudet, 1984	Healthy diet advice	Oils advised	None	NR	TC, TG	International Olive Council
6	Binkoski, 2005	Helthy diet by investigators	Yes	None	Lipid and lipoprotein levels, measures of oxidative stress	TC, HDL-C, LDL-C, TG	Grant from the National Sunflower Association
7	Brassard, 2017	Healthy diet by investigators	Yes	None	HDL-C	TC, HDL-C, LDL-C, TG	Dairy Research Cluster Initiative (Agriculture and Agri-Food Canada, Dairy Farmers of Canada, the Canadian Dairy Network, and the Canadian Dairy Commission

Table A.4: Information on study outcomes and any potential conflicts of interest *(continued)*

Study ID	Reference	Diet Advice	Oils/solid fat provided by investig-ators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
8	Candido, 2017	Habitual diet advice	Yes	Yes, in both arms	NR	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
9	Cheng, 2018	Healthy diet by investig-ators	Yes	None	NR	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
10	Cicero, 2009	Healthy diet advice	Oils advised	None	NR	TC	Unrestricted grant form Bonomelli Srl
11	Derouiche, 2005	Healthy diet advice	Yes	None	NR	TC, HDL-C, LDL-C, TG	Finicial support from the Institute AICHA Santé et Nutrition (Meknès)
12	Dittrich, 2015	Healthy diet by investig-ators	Yes	None (weight gain in sunflower oil arm)	TG	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
13	Dobrzyska, 2018	Habitual diet advice	Yes	None	NR	TC, LDL-C, HDL-C, TG	No conflict of interest was reported by the authors
14	Fara-jabakhsh, 2019	Partially provided by investigat-ors	Yes	None	Lipid profile, fasting blood glucose, malondialdehyde, high-sensitivity C-reactive protein, homeostatic model assessment, blood pressure	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
15	Haimeur, 2013	Healthy diet advice	Yes	NR	NR	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors

Table A.4: Information on study outcomes and any potential conflicts of interest *(continued)*

Study ID	Reference	Diet Advice	Oils/solid fat provided by investigators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
16	Han, 2002	Healthy diet by investigators	Yes	NR	NR	TC, HDL-C, LDL-C, TG	NR
17	Harris, 2017	NR	Yes	None	NR	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
18	Iggman, 2015	Habitual diet by investigators	Yes	None	Liver fat content, body composition	TC, HDL-C, LDL-C	No conflict of interest was reported by the authors
19	Karvonen, 2002	Habitual diet advice	Yes	None	Serum lipids, fatty acid composition of total lipids	TC	Camelina Ltd
20	Kawakami, 2015	Habitual diet advice	Oils advised	None	NR	TC, HDL-C, LDL-C, TG	Supported by Sadamitsu food industry
21	Khaw, 2018	Habitual diet advice	Yes	None	Change in LDL-C	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
22	Kontogianni, 2013	Habitual diet advice	Yes	None	Adiponectin, HDL-C and TG levels	TC, HDL-C, LDL-C, TG	Minerva S.A. for the supply of the extra virgin olive oil
23	Kris-Etherton, 1993	High fat diet by investigators	Yes	None	NR	TC, HDL C, LDL-C, TG	American Cocoa Research Institute
24	Kris-Etherton, 1993	High fat diet by investigators	Yes	None	Plasma levels of lipids, lipoproteins and apolipoproteins	TC, HDL-C, LDL-C, TG	American Cocoa Research Institute
25	Kris-Etherton, 1999	Healthy diet by investigators	Yes	None	NR	TC, HDL-C, LDL-C, TG	NR

Table A.4: Information on study outcomes and any potential conflicts of interest *(continued)*

Study ID	Reference	Diet Advice	Oils/solid fat provided by investigators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
26	Kruse, 2015	Habitual diet advice	Yes	None	Body composition, serum lipids, serum liver enzymes, inflammatory gene espression in subcutaneous adipose tissue	TC, HDL-C, LDL-C, TG	Union zur Förderung von Öl- und Proteinpflanzen
27	Lai, 2011	Partially provided by investigators; Habitual diet advice	Yes	None	Plasma lipids, insulin resistance	TC, HDL-C, LDL-C, TG	NR
28	Lichtenstein, 1994 / Schwab, 1998	Healthy diet by investigators	Yes	None	NR	TC, HDL-C, LDL-C, TG	Grant from Uncle Bens
29	Lichtenstein, 1999	Healthy diet by investigators	Yes	None	NR	TC, HDL-C, LDL-C, TG	NR
30	Lv, 2018	Healthy diet by investigators	Yes	None	Composition and serum Lipids	TC, HDL-C, LDL-C, TG	Supported by Mutual fund of the Chinese Nutrition Society and Malaysian palm bureau, no conflict of interest was declared by the authors
31	Maki, 2015	Habitual diet by investigators	Yes	None	Change in LDL-C	TC, HDL-C, LDL-C, TG	Funded by ACH Food Companies
32	Maki, 2018	Habitual diet advice	Yes	None	NR	TC, LDL-C, HDL-C, TG	NR

Table A.4: Information on study outcomes and any potential conflicts of interest *(continued)*

Study ID	Reference	Diet Advice	Oils/solid fat provided by investigators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
33	Mohamedou, 2011	Lifestyle and diet recomended for dyslipidemic patients	Yes	NR	NR	TC, LDL-C, HDL-C, TG	Argan oil Company, Agrotech Association SMD; no conflict of interest was reported by the authors
34	Mohamedou, 2011	Habitaul diet advice	Yes	NR	Serum lipids, apolipoproteins (AI and B), CRP, and LDL susceptibility to oxidation	TC, LDL-C, HDL-C, TG	No conflict of interest was reported by the authors
35	Morillas-Ruiz, 2014	Habitual diet advice	Yes	None (measured as BMI)	NR	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors
36	Nigam, 2014	Healthy diet advice	Yes	Yes, only in Olive oil arm	NR	HDL-C, TG	No conflict of interest was reported by the authors
37	Paschos, 2007	Habitual diet advice	Yes	None	NR	TC, HDL-C, TG	NR
38	Perona, 2004	Habitual diet by investigators	Yes	NR	NR	TC, HDL-C, LDL-C, TG	NR
39	Rallidis, 2003	Habitual diet advice	Yes	None (measured as BMI)	NR	TC, HDL-C, LDL-C, TG	NR
40	Reiser, 1985	Healthy diet by investigators	Yes	None	NR	TC, HDL-C, LDL-C, TG	National Live Stock and Meat Board, the Texas Cattle Feeders Association, and the Standard Meat Co of Fort Worht, Texas

Table A.4: Information on study outcomes and any potential conflicts of interest *(continued)*

Study ID	Reference	Diet Advice	Oils/solid fat provided by investigators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
41	Rezaei, 2018	Hypocaloric diet (-500 kcal/d) recommanded by investigators	Yes	Yes, in both arms	Severity of fatty liver and cardiometabolic markers	TC, LDL-C, HDL-C, TG	Oil Version Factory, Goorgan
42	Salar, 2016	Healthy diet by investigators	Yes	None	Blood lipids	TC, LDL-C, HDL-C, TG	No conflict of intererst was reported by the authors
43	Schwab, 2006	Healthy diet advice	Yes	None	serum lipids and fasting concentrations of serum total and lipoprotein lipids, plasma glucose, insulin and haemostatic factors	TC, HDL-C, LDL-C, TG	Financially supported by the National Technology Agency, Finland
44	Sirtori, 1986	Habitual diet advice	Yes	None	NR	TC, HDL-C, LDL-C, TG	Grant from the European Economic Community
45	Sirtori, 1992	Habitual diet advice	Yes	None	NR	TC, HDL-C, LDL-C, TG	Grant from the European Economic Community
46	Stonehouse, 2019	Healthy diet by investigators	Yes	None	Evaluate the assumption of the sn-2 position of dietary TAGs	TC, LDL-C, HDL-C, TG	No conflict of interest was reported by the authors
47	Stricker, 2008	Habitual diet advice	Yes	NR	NR	TC, HDL-C, LDL-C, TG	Partly funded by the Fondo Balli
48	Tholstrup, 2011	Habitual diet advice	Yes	None	NR	TC, HDL-C, LDL-C, TG	Supported by Malaysian Palm Oil Board
49	Utrawuthipong, 2009	Healthy diet by investigators	Yes	None	NR	TC, HDL-C, LDL-C, TG	No conflict of interest was reported by the authors

Table A.4: Information on study outcomes and any potential conflicts of interest *(continued)*

Study ID	Reference	Diet Advice	Oils/solid fat provided by investigators	Weight loss	Primary outcome of the study	Outcomes	Conflict of interest
50	Voon, 2011	Habitaul dietby investigators	Yes	None	Change in total homocysteine	TC, HDL-C, LDL-C, TG	Malaysion Palm Oil Board
51	Zhang, 1997	Habitual diet by investigators	Yes	NR	NR	TC, HDL-C, LDL-C, TG	Malaysian Palm Oil Promotion Council

Note: NR = Not Reported

Table A.5: Blood lipids postinterventional

Reference	Comparison	TC ± SD [mmol/L]	LDL-C ± SD [mmol/L]	HDL-C ± SD [mmol/L]	TG ± SD [mmol/L]
Aguilera, 2004	Olive oil	6.30 ± 1.23	4.42 ± 1.37	1.21 ± 0.37	1.45 ± 0.30
Aguilara, 2004	Sunflower oil	6.05 ± 0.93	3.83 ± 0.97	1.19 ± 0.54	2.24 ± 0.46
Akrami, 2017	Flaxseed oil	5.10 ± 0.96	3.13 ± 0.70	1.09 ± 0.27	1.77 ± 0.74
Akrami, 2017	Sunflower oil	4.93 ± 0.86	3.05 ± 0.72	1.13 ± 0.22	1.61 ± 0.85
Assuncao, 2009	Coconut oil	5.13 ± 1.01	3.02 ± 0.95	1.26 ± 0.06	2.03 ± 1.06
Assuncao, 2009	Soybean oil	5.42 ± 0.74	3.47 ± 0.75	1.17 ± 0.15	1.67 ± 0.73
Atefi, 2018	Olive oil	4.44 ± 1.03	2.35 ± 0.74	1.06 ± 0.21	1.46 ± 0.66
Atefi, 2018	Rapeseed oil	4.03 ± 0.75	2.07 ± 0.53	1.00 ± 0.20	1.49 ± 0.69
Atefi, 2018	Sunflower oil	4.42 ± 1.06	2.34 ± 0.72	1.06 ± 0.16	1.51 ± 0.61
Baudet, 1984	Sunflower oil	4.54 ± 0.59	NR	NR	1.23 ± 1.12
Baudet, 1984	Palm oil	5.12 ± 0.88	NR	NR	0.89 ± 0.58
Baudet, 1984	Peanut oil	5.25 ± 0.74**	NR	NR	0.67 ± 0.48**
Binkoski, 2005	Olive oil	5.67 ± 0.78	3.72 ± 0.61	1.34 ± 0.33	1.28 ± 0.61
Binkoski, 2005	Sunflower oil	5.47 ± 0.78	3.54 ± 0.61	1.32 ± 0.33	1.34 ± 0.61
Brassard, 2017	Butter	5.10 ± 0.95	3.30 ± 0.84	1.11 ± 0.21	1.36 ± 0.73
Brassard, 2017	Corn oil	4.60 ± 0.81	2.84 ± 0.69	1.10 ± 0.20	1.30 ± 0.62
Brassard, 2017	Olive oil	4.82 ± 0.89	3.03 ± 0.78	1.10 ± 0.19	1.38 ± 0.67
Candido, 2017	Olive oil	4.25 ± 0.92	2.48 ± 0.69	1.28 ± 0.32	0.89 ± 0.54
Candido, 2017	Soybean oil	4.12 ± 0.85	2.36 ± 0.67	1.12 ± 0.27	0.90 ± 0.54
Cheng, 2018	Cocoa butter	4.13 ± 0.59	2.28 ± 0.47	1.48 ± 0.27	0.84 ± 0.31
Cheng, 2018	Olive oil	4.11 ± 0.63	2.29 ± 0.50	1.47 ± 0.27	0.88 ± 0.31
Cicero, 2009	Corn oil	6.35 ± 0.76	NR	NR	NR
Cicero, 2009	Olive oil	6.00 ± 0.55	NR	NR	NR
Derouiche, 2005	Argan oil	3.97 ± 0.93	2.36 ± 0.82	1.28 ± 0.18	0.71 ± 0.24
Derouiche, 2005	Olive oil	3.71 ± 0.81	2.10 ± 0.56	1.27 ± 0.27	0.77 ± 0.33
Dittrich, 2015	Flaxseed oil	5.38 ± 1.21	3.45 ± 1.09	1.20 ± 0.28	1.87 ± 0.89
Dittrich, 2015	Sunflower oil	5.83 ± 1.37	3.77 ± 1.15	1.29 ± 0.48	1.91 ± 1.06
Dobrzyńska, 2018	Camelina oil	5.77 ± 0.98	3.42 ± 0.91	1.76 ± 0.37	1.31 ± 0.61
Dobrzyñska, 2018	Flaxseed oil	5.83 ± 0.94	3.50 ± 1.03	1.86 ± 0.50	1.06 ± 0.36
Farajabakhsh, 2019	Sesame oil	4.59 ± 1.17	2.54 ± 0.87	0.94 ± 0.16	1.78 ± 0.79
Farajabakhsh, 2019	Sunflower oil	4.92 ± 1.05	2.68 ± 0.85	0.97 ± 0.20	1.67 ± 0.79
Haimeur, 2013	Butter	5.83 ± 0.2**	2.75 ± 0.28**	1.25 ± 0.05**	1.66 ± 0.06**
Haimeur, 2013	Argan oil	4.92 ± 0.68**	2.67 ± 0.51**	1.64 ± 0.14**	1.75 ± 0.17**
Han, 2002	Butter	6.66 ± 1.13	4.58 ± 1.00	1.24 ± 0.22	1.73 ± 0.74
Han, 2002	Soybean oil	5.88 ± 0.92	3.89 ± 0.78	1.17 ± 0.22	1.79 ± 0.78
Harris, 2017	Coconut oil	6.16 ± 0.62	3.56 ± 0.70	1.83 ± 0.49	1.21 ± 0.91
Harris, 2017	Safflower oil	5.68 ± 0.59	3.28 ± 0.67	1.68 ± 0.38	1.34 ± 1.27
Iggman, 2015	Palm oil	4.20 ± 1.03	2.40 ± 0.80	1.40 ± 0.57	0.56 ± 0.27
Iggman, 2015	Sunflower oil	4.20 ± 0.87	2.00 ± 1.22	1.40 ± 0.56	0.65 ± 0.37
Karvonen, 2002	Camelina oil	5.60 ± 0.80	NR	NR	NR
Karvonen. 2002	Rapeseed oil	5.70 ± 0.70	NR	NR	NR
Karvonen, 2002	Olive oil	6.00 ± 0.80	NR	NR	NR
Kawakami, 2015	Corn oil	5.62 ± 0.77	3.57 ± 0.77	1.42 ± 0.31	1.44 ± 0.74

Table A.5: Blood lipids after the intervention *(continued)*

Reference	Comparison	TC ± SD [mmol/L]	LDL-C ± SD [mmol/L]	HDL-C ± SD [mmol/L]	TG ± SD [mmol/L]
Kawakami, 2015	Flaxseed oil	5.24 ± 0.74	3.31 ± 0.72	1.27 ± 0.27	1.28 ± 0.39
Khaw, 2018	Butter	6.32 ± 1.00	3.83 ± 0.90	1.99 ± 0.50	0.92 ± 0.96
Khaw, 2018	Coconut oil	6.12 ± 1.00	3.41 ± 0.90	2.28 ± 0.50	0.96 ± 0.96
Khaw, 2018	Olive oil	6.03 ± 0.90	3.64 ± 1.00	1.90 ± 0.50	0.91 ± 0.96
Kontogianni, 2013	Flaxseed oil	4.40 ± 0.70	2.51 ± 0.60	1.57 ± 0.30	0.68 ± 0.20
Kontogianni, 2013	Olive oil	4.51 ± 0.70	2.59 ± 0.60	1.55 ± 0.30	0.76 ± 0.40
Kris-Etherton, 1993	Olive oil	3.94 ± 0.34	2.38 ± 0.34	1.24 ± 0.22	0.95 ± 0.13
Kris-Etherton, 1993	Cocoa butter	4.27 ± 0.34	2.67 ± 0.34	1.14 ± 0.22	0.98 ± 0.13
Kris-Etherton, 1993	Soybean oil	3.60 ± 0.34	2.15 ± 0.34	1.17 ± 0.22	0.82 ± 0.13
Kris-Etherton, 1993	Butter	4.56 ± 0.34	2.93 ± 0.34	1.17 ± 0.22	0.99 ± 0.13
Kris-Etherton, 1993 (2)	Butter	4.90 ± 0.20	3.24 ± 0.20	1.35 ± 0.11	0.90 ± 0.17
Kris-Etherton, 1993 (2)	Cocoa butter	4.40 ± 0.20	2.82 ± 0.20	1.35 ± 0.11	0.75 ± 0.17
Kris-Etherton, 1999	Olive oil	4.79 ± 0.23	2.98 ± 0.20	1.28 ± 0.11	1.15 ± 0.13
Kris-Etherton, 1999	Peanut oil	4.93 ± 0.23	3.13 ± 0.20	1.26 ± 0.11	1.18 ± 0.13
Kruse, 2015	Olive oil	4.98 ± 0.78	3.18 ± 0.68	1.19 ± 0.31	1.35 ± 0.72
Kruse, 2015	Rapeseed oil	4.69 ± 0.78	2.94 ± 0.53	1.09 ± 0.20	1.46 ± 0.69
Lai, 2011	Soybean oil	4.98 ± 0.99	2.94 ± 0.95	1.11 ± 0.23	1.68 ± 1.12
Lai, 2011	Rice bran oil	4.60 ± 0.59	2.80 ± 0.33	1.12 ± 0.73	1.47 ± 0.56
Lichtenstein, 1993 / Schwab, 1998	Beef fat	5.63 ± 0.79	3.62 ± 0.70	1.15 ± 0.24	1.31 ± 0.38
Lichtenstein, 1993 / Schwab, 1998	Rapeseed oil	5.02 ± 0.53	3.26 ± 0.44	1.14 ± 0.26	1.23 ± 0.35
Lichtenstein, 1993 / Schwab, 1998	Corn oil	5.02 ± 0.49	3.24 ± 0.49	1.14 ± 0.23	1.22 ± 0.35
Lichtenstein. 1993/Schwab, 1998	Olive oil	5.31 ± 0.49	3.42 ± 0.49	1.19 ± 0.23	1.26 ± 0.33
Lichtenstein, 1993 / Schwab, 1998	Rice bran oil	5.00 ± 0.49	3.16 ± 0.44	1.15 ± 0.24	1.26 ± 0.33
Lichtenstein, 1999	Butter	6.50 ± 0.93	4.58 ± 0.83	1.17 ± 0.26	1.64 ± 0.64
Lichtenstein, 1999	Soybean oil	5.83 ± 0.83	3.99 ± 0.73	1.11 ± 0.23	1.61 ± 0.72

Table A.5: Blood lipids after the intervention *(continued)*

Reference	Comparison	TC ± SD [mmol/L]	LDL-C ± SD [mmol/L]	HDL-C ± SD [mmol/L]	TG ± SD [mmol/L]
Lv, 2018	Cocoa butter	4.29 ± 0.67	2.21 ± 0.56	1.46 ± 0.22	0.96 ± 0.50
Lv, 2018	Soybean oil	3.96 ± 0.59	2.00 ± 0.43	1.45 ± 0.32	0.73 ± 0.22
Maki, 2015	Corn oil	5.36 ± 0.76	3.52 ± 0.63	1.18 ± 0.29	1.56 ± 0.79
Maki, 2015	Olive oil	5.72 ± 0.76	3.81 ± 0.65	1.20 ± 0.30	1.43 ± 0.72
Maki, 2018	Coconut oil	5.21 ± 1.08*	3.33 ± 0.74*	1.27 ± 0.29*	1.11 ± 0.96*
Maki, 2018	Corn oil	4.84 ± 1.08*	3.10 ± 0.74*	1.26 ± 0.29*	1.02 ± 0.96*
Mohamedou, 2011	Butter	4.70 ± 0.80	2.90 ± 0.44	1.04 ± 0.29	1.68 ± 0.31
Mohamedou, 2011	Argan oil	4.07 ± 0.57	2.15 ± 0.54	1.24 ± 0.31	1.48 ± 0.29
Mohamedou, 2011 (2)	Butter	4.97 ± 0.91	3.29 ± 0.88	0.91 ± 0.13	1.67 ± 0.61
Mohamedou, 2011 (2)	Argan oil	4.64 ± 0.93	2.90 ± 0.85	1.11 ± 0.26	1.51 ± 0.49
Morillas-Ruiz. 2014	Butter	5.39 ± 0.88	3.13 ± 0.76	1.77 ± 0.35	1.07 ± 0.47
Morillas-Ruiz, 2014	Olive oil	5.07 ± 0.98	2.87 ± 0.90	1.75 ± 0.35	1.00 ± 0.50
Nigam, 2014	Olive oil	NR	NR	1.05 ± 0.15	1.75 ± 0.55
Nigam, 2014	Rapeseed oil	NR	NR	1.07 ± 0.12	1.92 ± 0.66
Paschos, 2007	Flaxseed oil	6.16 ± 0.85	NR	1.00 ± 0.19	1.89 ± 0.96
Paschos, 2007	Safflower oil	5.23 ± 1.06	NR	0.90 ± 0.16	1.65 ± 0.96
Perona, 2004	Olive oil	4.48 ± 1.07	2.66 ± 0.80	1.29 ± 0.42	1.09 ± 0.48
Perona, 2004	Sunflower oil	4.80 ± 1.01	2.92 ± 0.82	1.45 ± 0.47	0.97 ± 0.37
Rallidis, 2003	Flaxseed oil	5.85 ± 0.93	3.94 ± 0.93	1.06 ± 0.26	1.84 ± 0.98
Rallidis, 2003	Safflower oil	5.65 ± 1.19	3.86 ± 1.14	0.99 ± 0.21	1.76 ± 0.97
Reiser, 1985	Beef fat	4.01 ± 0.32	2.54 ± 0.48	1.19 ± 0.12	0.99 ± 0.16
Reiser, 1985	Coconut oil	4.35 ± 0.32	2.85 ± 0.44	1.19 ± 0.12	0.88 ± 0.17
Reiser, 1985	Safflower oil	3.65 ± 0.32	2.33 ± 0.49	1.04 ± 0.12	0.81 ± 0.17
Rezaei, 2018	Olive oil	4.83 ± 1.25	2.76 ± 0.84	1.09 ± 0.26	1.59 ± 1.26
Rezaei, 2018	Sunflower oil	4.67 ± 0.74	2.72 ± 0.88	1.09 ± 0.21	1.61 ± 1.00
Salar, 2016	Rapeseed oil	4.07 ± 0.70	2.50 ± 1.06	1.08 ± 0.18	2.10 ± 0.46
Salar, 2016	Rice bran oil	4.11 ± 0.96	2.61 ± 0.82	1.05 ± 0.14	1.87 ± 0.52
Salar, 2016	Sunflower oil	4.21 ± 1.02	2.23 ± 0.93	1.04 ± 0.20	2.09 ± 0.59
Schwab, 2006	Hempseed oil	5.57 ± 0.60	3.58 ± 0.68	1.53 ± 0.30	1.03 ± 0.44
Schwab, 2006	Flaxseed oil	5.60 ± 0.42	3.62 ± 0.53	1.50 ± 0.35	1.07 ± 0.37
Sirtori, 1986	Corn oil	6.12 ± 1.52	4.47 ± 1.32	1.05 ± 0.21	1.67 ± 0.73
Sirtori, 1986	Olive oil	6.37 ± 1.40	4.63 ± 1.17	1.08 ± 0.23	1.74 ± 0.64
Sirtori, 1992	Corn oil	6.94 ± 0.76	5.17 ± 0.69	1.31 ± 0.24	1.29 ± 0.42
Sirtori, 1992	Olive oil	7.09 ± 0.80	5.19 ± 0.76	1.34 ± 0.28	1.51 ± 0.55
Stonehouse, 2019	Cocoa butter	4.43 ± 1.08*	2.78 ± 0.74*	1.42 ± 0.29*	0.84 ± 0.96*
Stonehouse, 2019	Olive oil	4.36 ± 1.08*	2.68 ± 0.74*	1.44 ± 0.29*	0.86 ± 0.96*
Stricker, 2008	Rapeseed oil	4.42 ± 0.89	2.42 ± 0.65	1.46 ± 0.40	1.29 ± 0.96
Stricker, 2008	Sunflower oil	4.87 ± 1.46	2.71 ± 1.31	1.63 ± 0.60	1.24 ± 0.96
Tholstrup, 2011	Lard	4.17 ± 1.08	2.31 ± 0.74	1.22 ± 0.29	0.83 ± 0.96
Tholstrup, 2011	Olive oil	3.93 ± 1.08	2.11 ± 0.74	1.20 ± 0.29	0.87 ± 0.96

Table A.5: Blood lipids after the intervention *(continued)*

Reference	Comparison	TC ± SD [mmol/L]	LDL-C ± SD [mmol/L]	HDL-C ± SD [mmol/L]	TG ± SD [mmol/L]
Utrawuthipong, 2009	Soybean oil	5.95 ± 0.72	4.09 ± 0.61	1.34 ± 0.32	1.16 ± 0.42
Utrawuthipong, 2009	Palm oil	6.86 ± 0.65	4.78 ± 0.63	1.54 ± 0.35	1.17 ± 0.38
Utrawuthipong, 2009	Rice bran oil	6.01 ± 0.64	4.00 ± 0.66	1.47 ± 0.30	1.17 ± 0.32
Voon, 2011	Coconut oil	4.95 ± 0.69	3.30 ± 0.75	1.37 ± 0.26	0.90 ± 0.39
Voon, 2011	Olive oil	4.65 ± 0.71	3.06 ± 0.64	1.28 ± 0.23	0.84 ± 0.37
Zhang, 1997	Soybean oil	3.36 ± 0.67	2.22 ± 0.62	0.90 ± 0.22	1.23 ± 0.45
Zhang, 1997	Lard	3.99 ± 1.24	2.85 ± 1.23	0.96 ±0.16	1.21 ± 0.47
Zhang, 1997	Peanut oil	3.48 ± 0.50	2.41 ± 0.45	0.82 ± 0.15	1.05 ± 0.50

Note: * = self-calculated. ** = calculated with [13, p. 328]

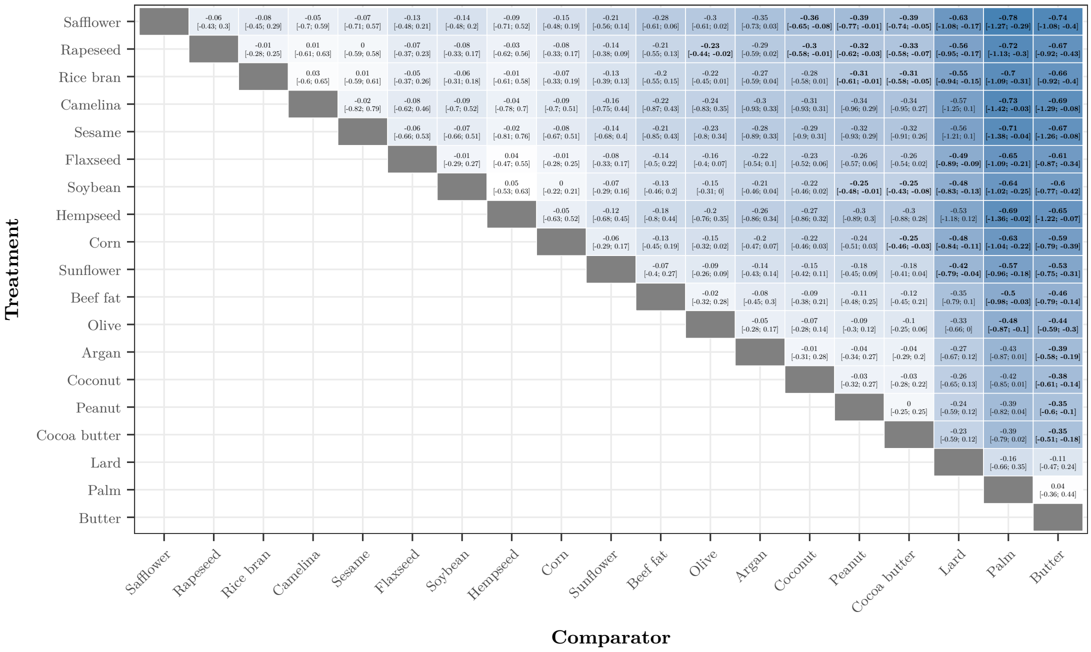

Figure A.1: Relative effect estimates - LDL-C (frequentist analysis)

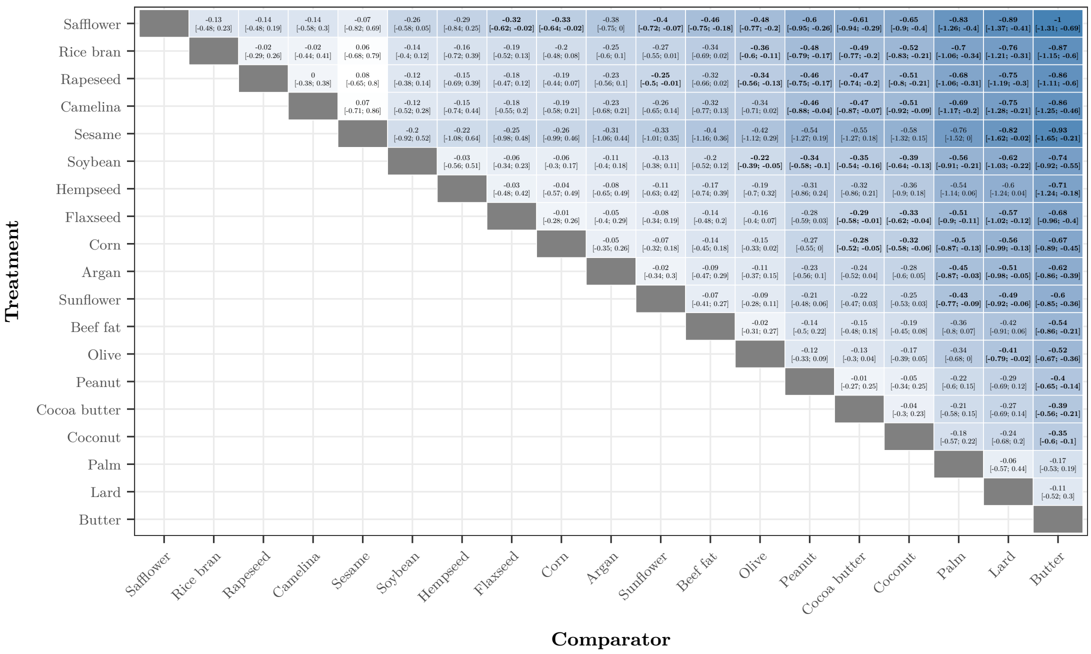

Figure A.2: Relative effect estimates - TC (frequentist analysis)

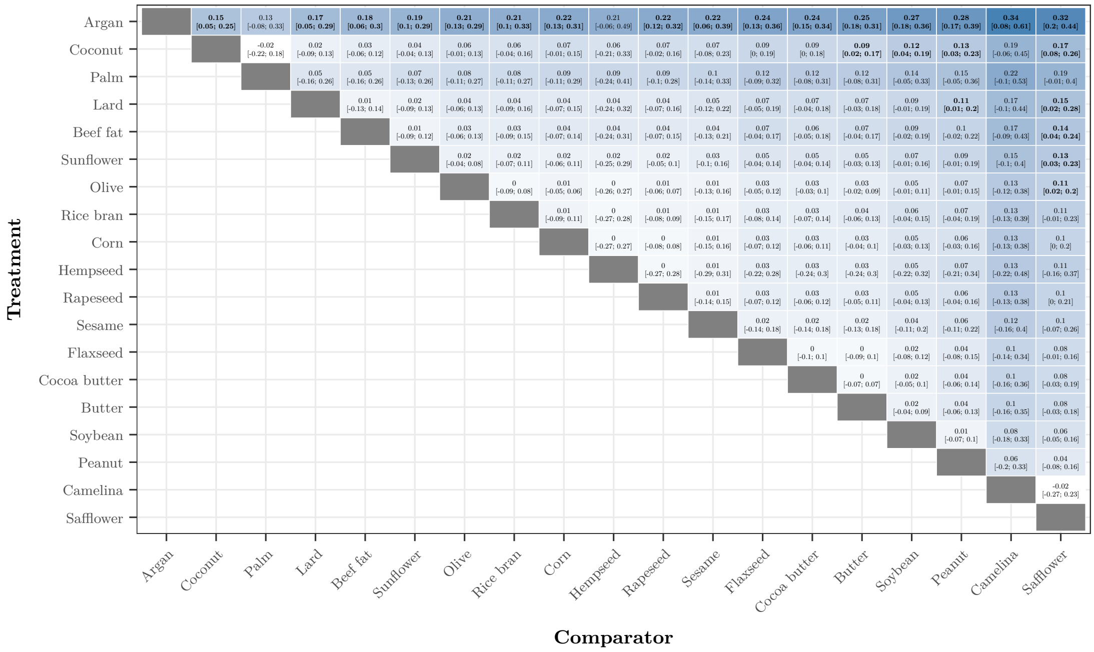

Figure A.3: Relative effect estimates - HDL-C (frequentist analysis)

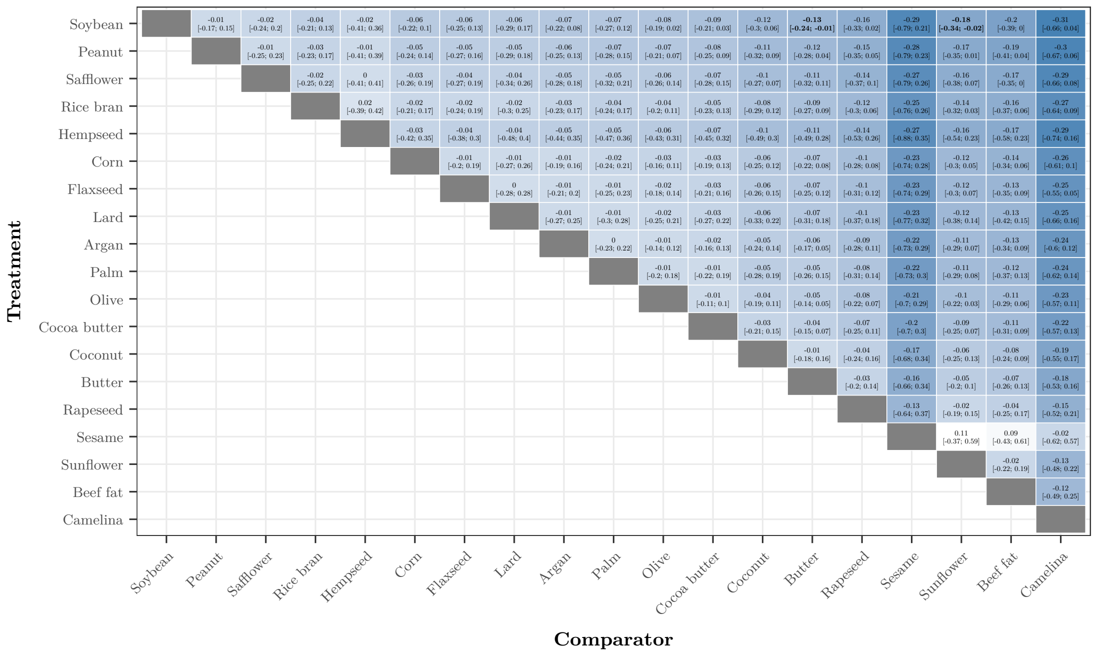

Figure A.4: Relative effect estimates - TG (frequentist analysis)

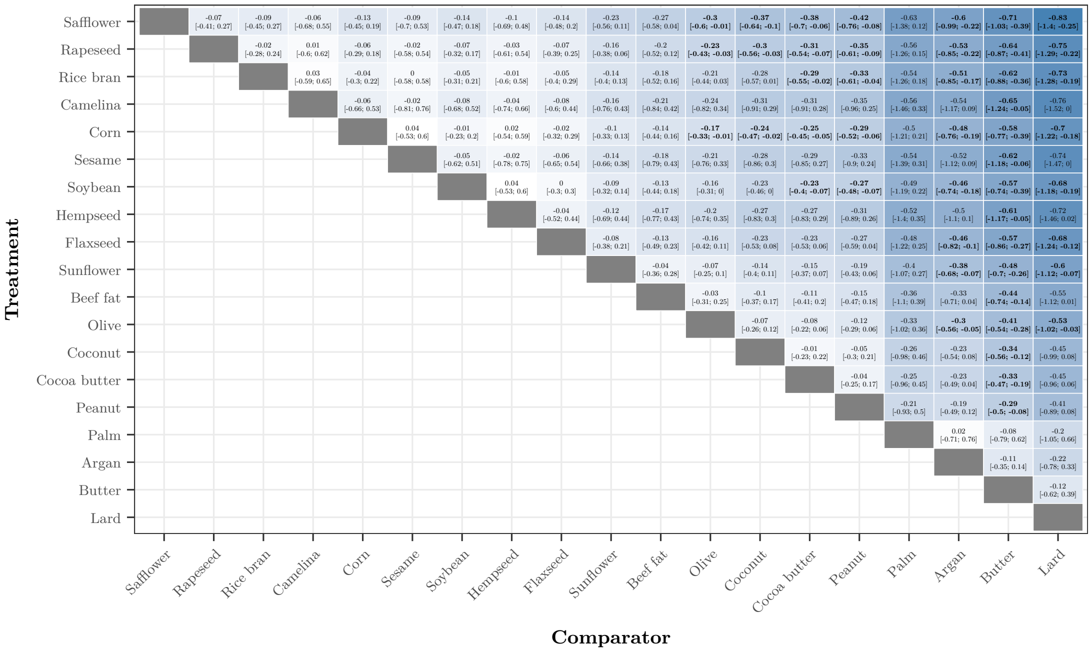

Figure A.5: Relative effect estimates - LDL-C (frequentist sensitivity analysis)

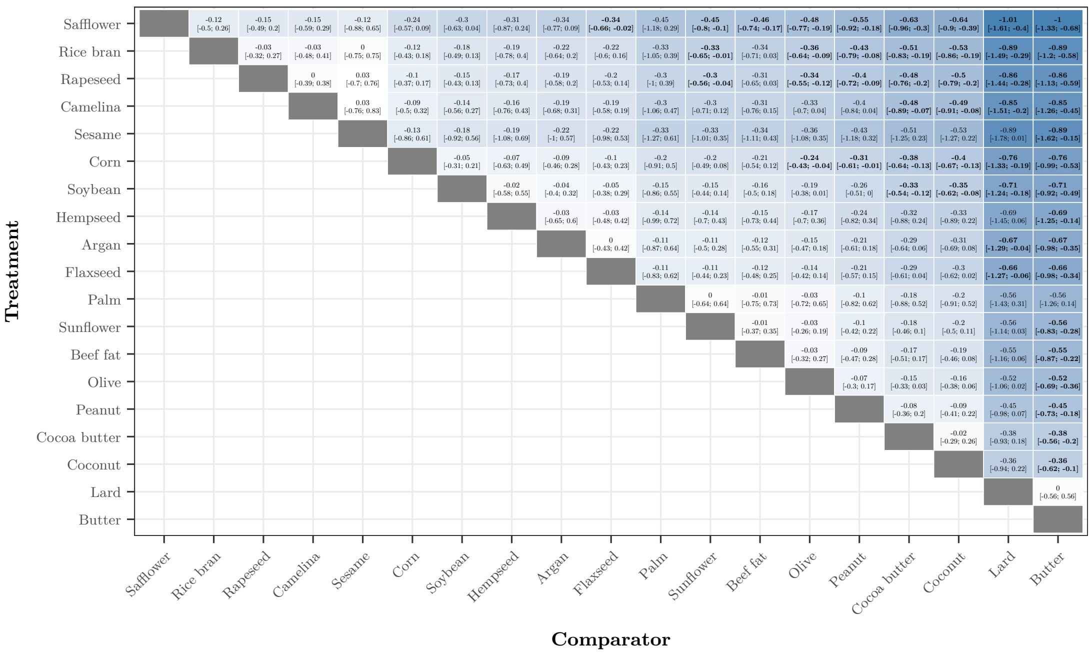

Figure A.6: Relative effect estimates - TC (frequentist sensitivity analysis)

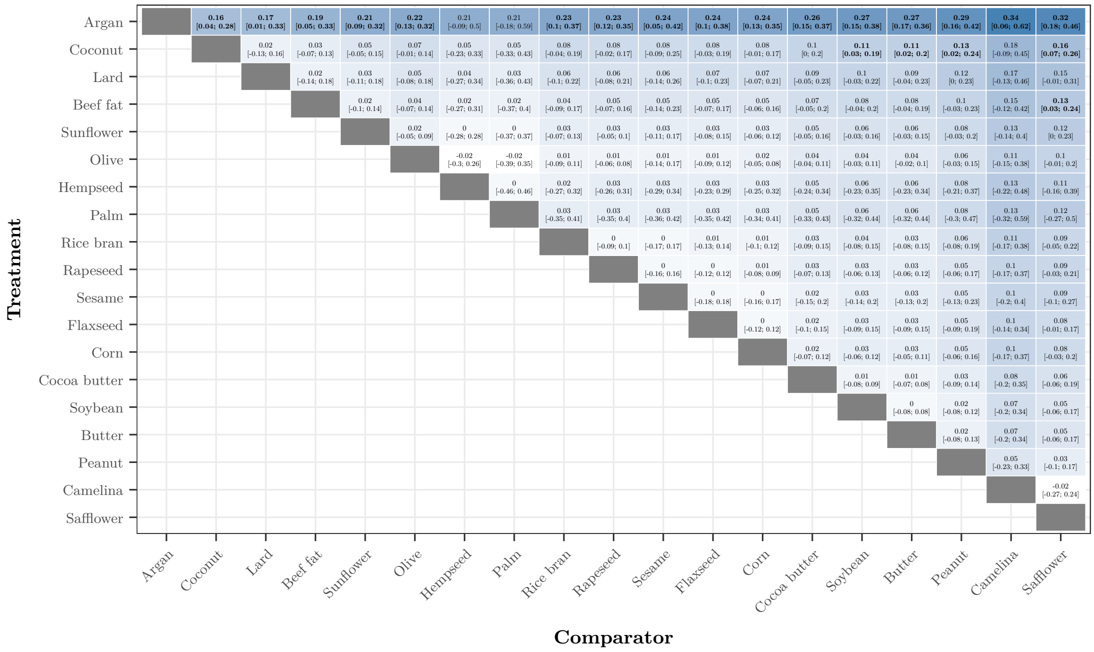

Figure A.7: Relative effect estimates - HDL-C (frequentist sensitivity analysis)

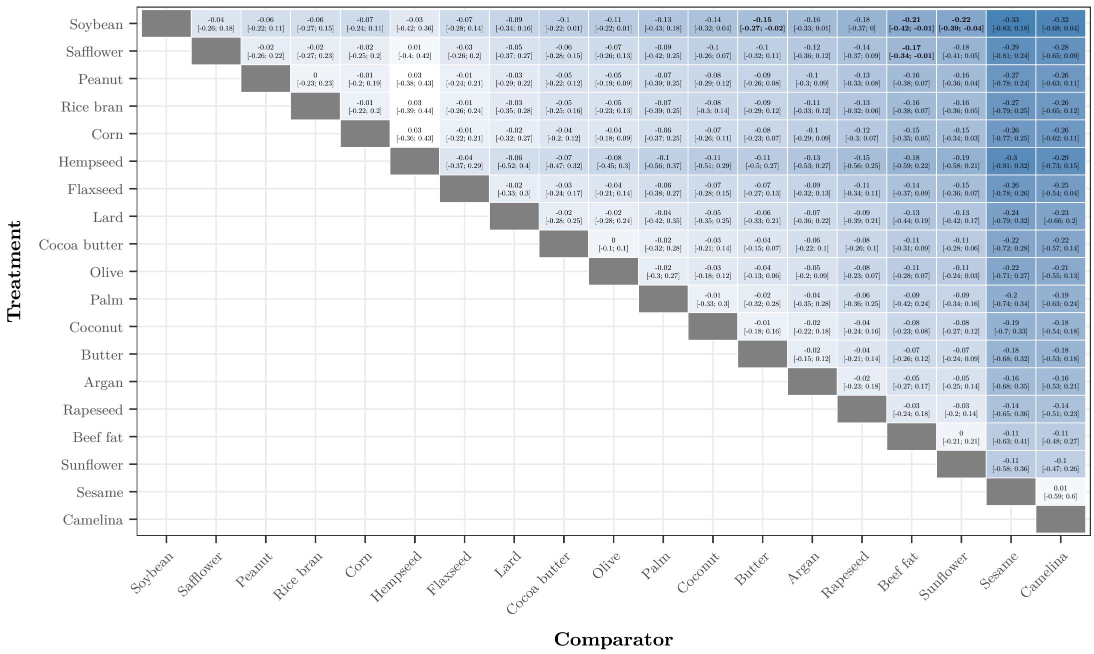

Figure A.8: Relative effect estimates - TG (frequentist sensitivity analysis)

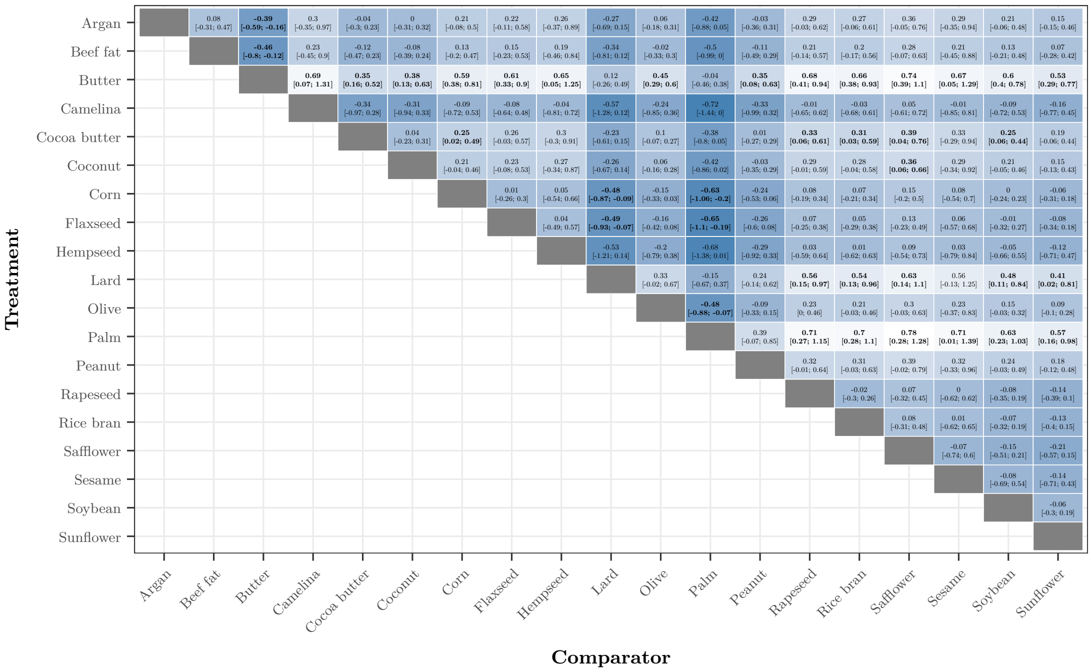

Figure A.9: Relative effect estimates - LDL-C (Bayesian analysis)

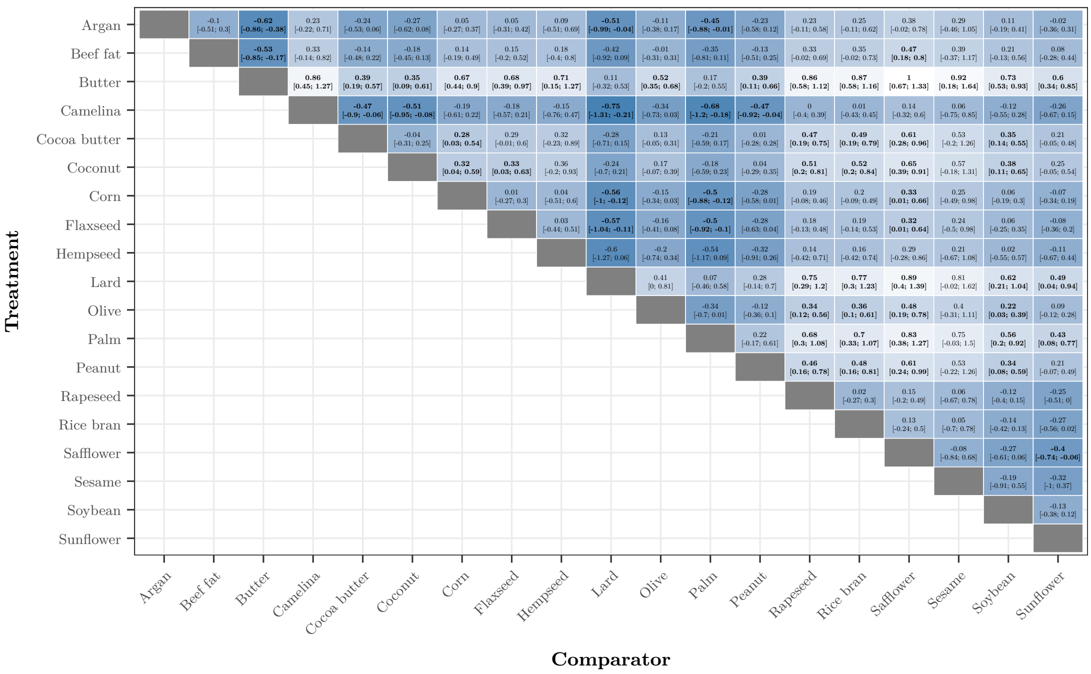

Figure A.10: Relative effect estimates - TC (Bayesian analysis)

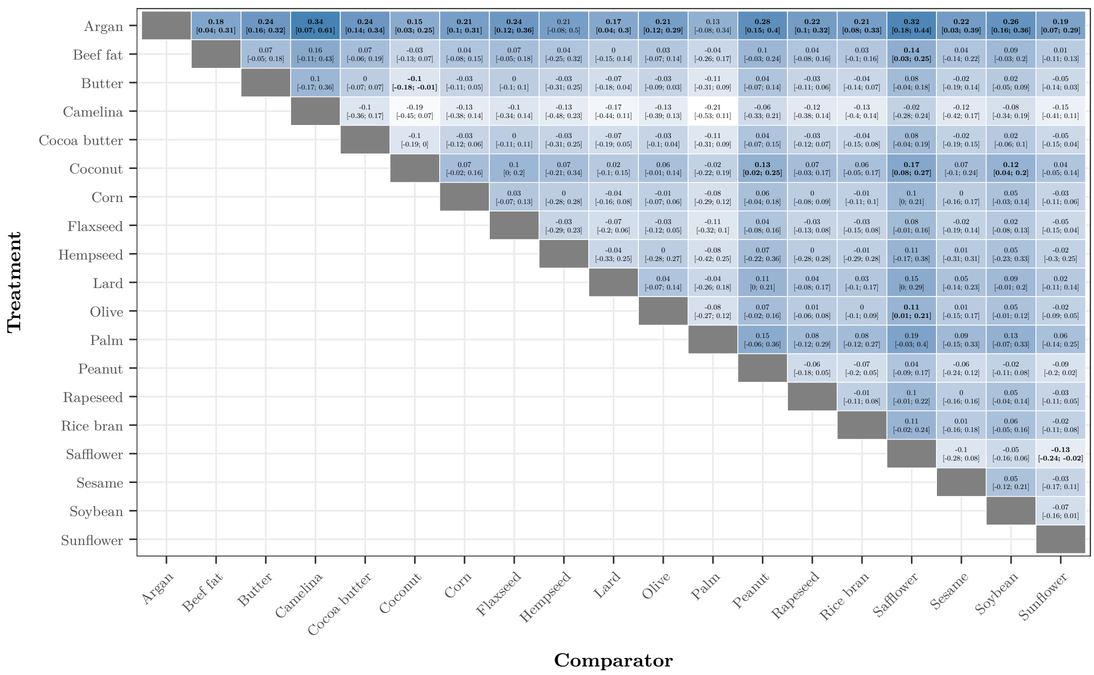

Figure A.11: Relative effect estimates - HDL-C (Bayesian analysis)

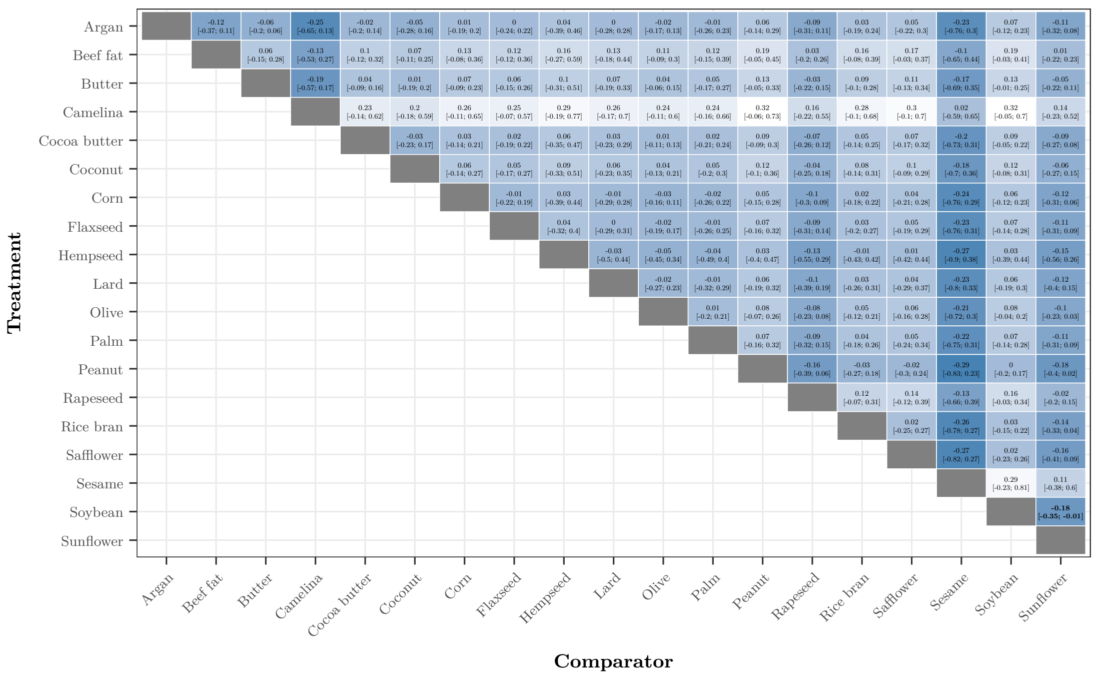

Figure A.12: Relative effect estimates - TG (Bayesian analysis)

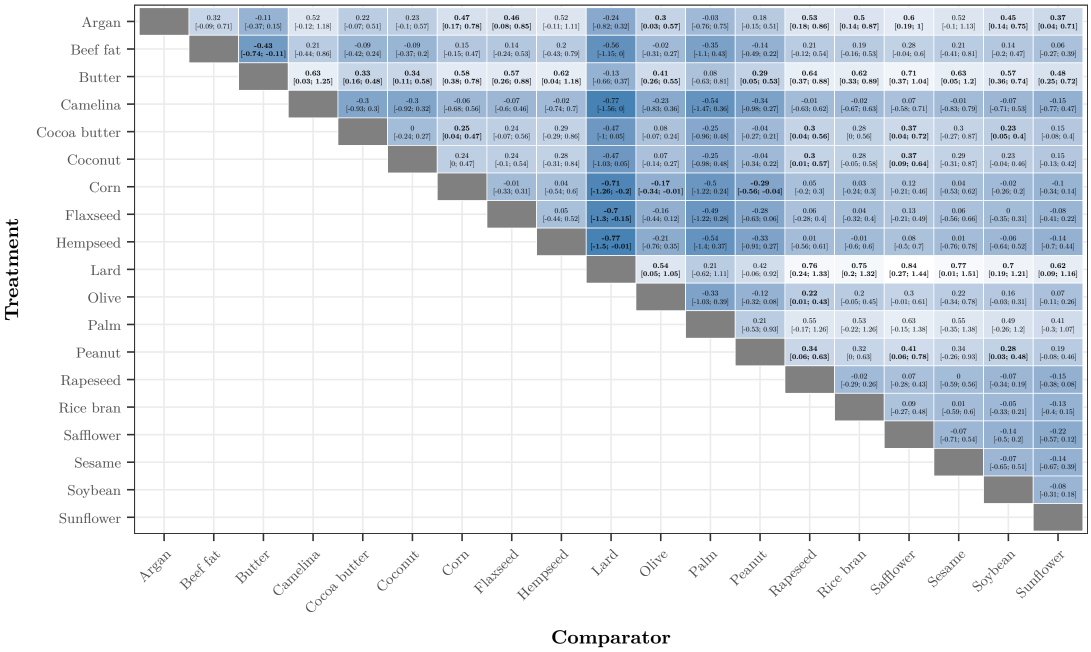

Figure A.13: Relative effect estimates - LDL-C (Bayesian sensitivity analysis)

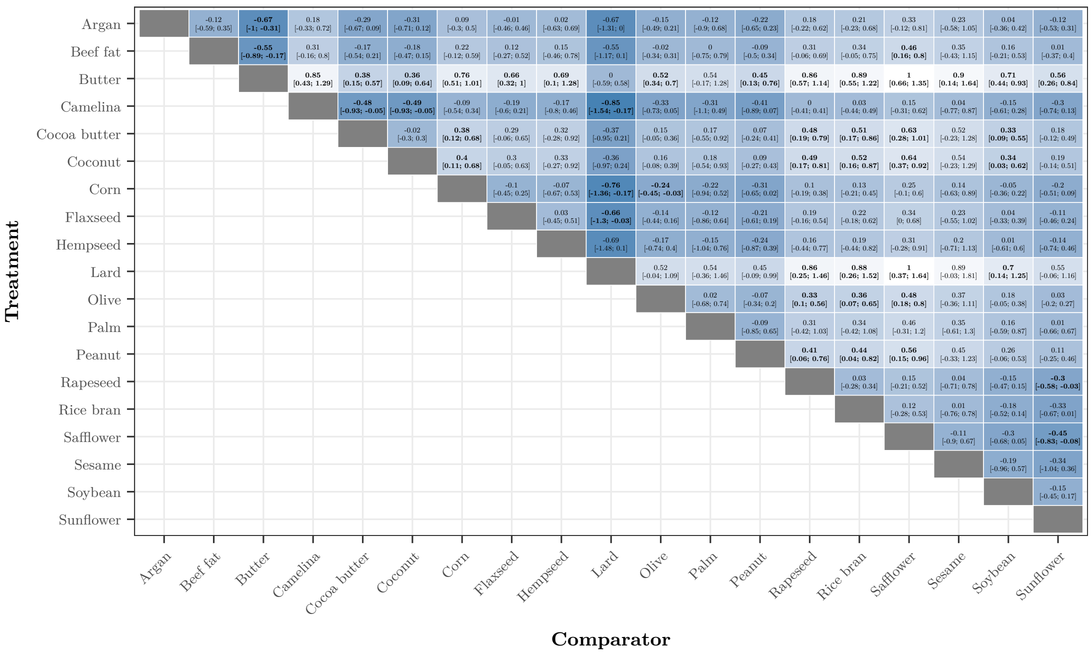

Figure A.14: Relative effect estimates - TC (Bayesian sensitivity analysis)

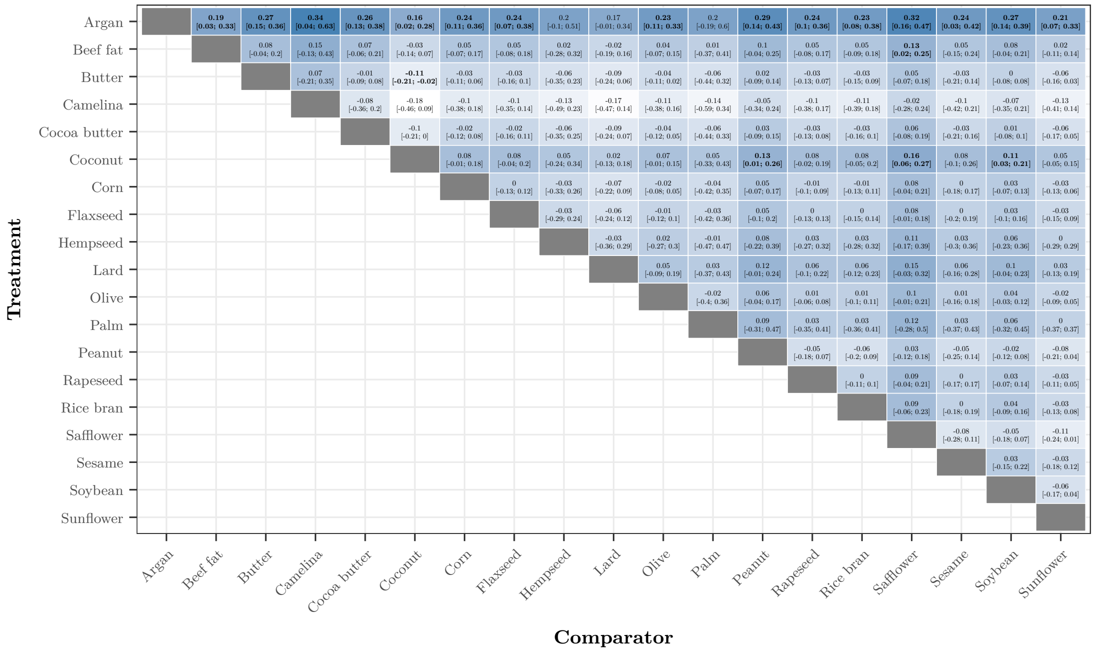

Figure A.15: Relative effect estimates - HDL-C (Bayesian sensitivity analysis)

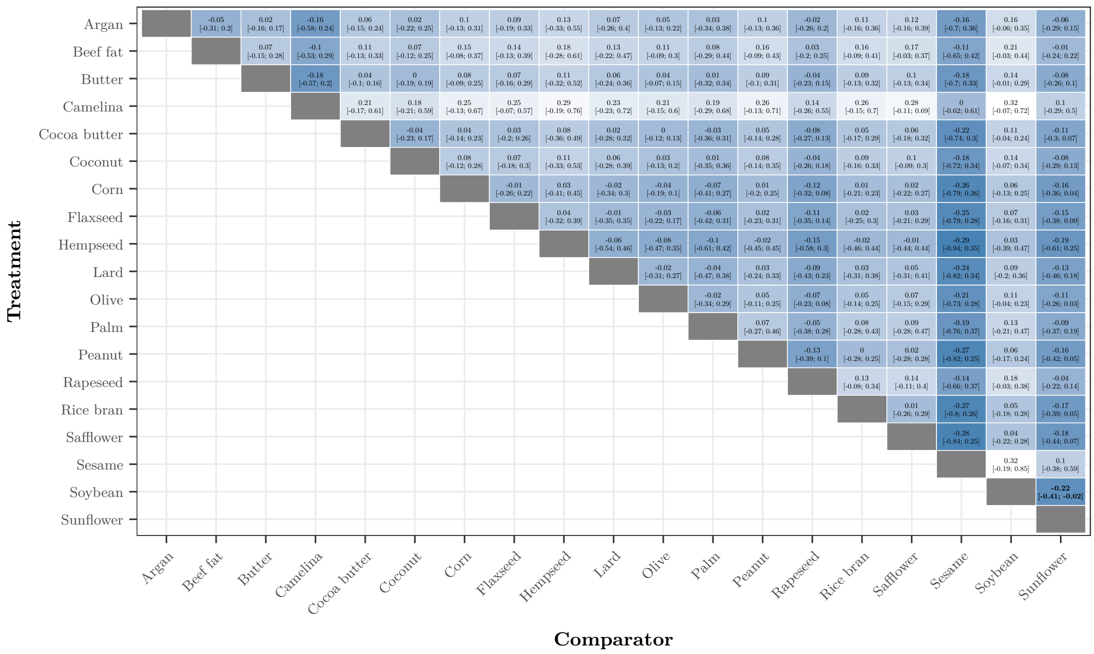

Figure A.16: Relative effect estimates - TG (Bayesian sensitivity analysis)

Table A.6: Inconsistency analysis for LDL-C (Bayesian analysis)

Comparison	Direct	Indirect	Network	p
Argan - Butter	0.440 (0.200, 0.680)	0.160 (-0.320, 0.630)	0.390 (0.160, 0.600)	0.286
Argan - Olive	-0.260 (-0.700, 0.180)	0.028 (-0.270, 0.310)	-0.056 (-0.310, 0.190)	0.282
Beef fat - Coconut	0.310 (-0.110, 0.740)	-0.220 (-0.730, 0.270)	0.081 (-0.240, 0.390)	0.105
Beef fat - Corn	-0.380 (-0.890, 0.130)	0.110 (-0.370, 0.580)	-0.130 (-0.470, 0.200)	0.165
Beef fat - Olive	-0.200 (-0.710, 0.320)	0.240 (-0.200, 0.690)	0.017 (-0.300, 0.330)	0.196
Beef fat - Rapeseed	-0.360 (-0.860, 0.140)	-0.020 (-0.520, 0.500)	-0.220 (-0.580, 0.140)	0.341
Beef fat - Rice bran	-0.450 (-0.960, 0.044)	0.120 (-0.420, 0.650)	-0.200 (-0.570, 0.160)	0.126
Beef fat - Safflower	-0.210 (-0.630, 0.210)	-0.460 (-1.100, 0.150)	-0.280 (-0.640, 0.074)	0.502
Butter - Cocoa butter	-0.360 (-0.570, -0.130)	-0.340 (-0.610, -0.077)	-0.350 (-0.520, -0.160)	0.948
Butter - Coconut	-0.420 (-0.960, 0.100)	-0.350 (-0.640, -0.067)	-0.380 (-0.640, -0.130)	0.811
Butter - Corn	-0.460 (-0.830, -0.088)	-0.650 (-0.920, -0.380)	-0.590 (-0.810, -0.370)	0.405
Butter - Olive	-0.350 (-0.560, -0.130)	-0.580 (-0.860, -0.310)	-0.440 (-0.600, -0.290)	0.173
Butter - Soybean	-0.710 (-0.970, -0.450)	-0.460 (-0.720, -0.190)	-0.590 (-0.780, -0.400)	0.172
Cocoa butter - Olive	-0.120 (-0.340, 0.097)	-0.043 (-0.340, 0.250)	-0.097 (-0.270, 0.067)	0.673
Cocoa butter - Soybean	-0.380 (-0.630, -0.120)	-0.088 (-0.370, 0.190)	-0.250 (-0.440, -0.056)	0.135
Coconut - Corn	-0.220 (-0.740, 0.280)	-0.200 (-0.490, 0.100)	-0.210 (-0.470, 0.047)	0.937
Coconut - Olive	-0.080 (-0.400, 0.250)	-0.018 (-0.340, 0.310)	-0.064 (-0.280, 0.170)	0.790
Coconut - Safflower	-0.450 (-0.790, -0.096)	-0.230 (-0.910, 0.460)	-0.360 (-0.660, -0.052)	0.572
Coconut - Soybean	0.440 (-0.140, 1.000)	-0.370 (-0.640, -0.089)	-0.210 (-0.470, 0.054)	0.015
Corn - Flaxseed	-0.260 (-0.860, 0.330)	0.049 (-0.270, 0.370)	-0.017 (-0.310, 0.260)	0.360
Corn - Olive	0.190 (-0.025, 0.400)	0.041 (-0.380, 0.480)	0.150 (-0.031, 0.330)	0.545
Corn - Rapeseed	0.017 (-0.420, 0.460)	-0.150 (-0.490, 0.190)	-0.086 (-0.350, 0.180)	0.559
Corn - Rice bran	-0.080 (-0.520, 0.360)	-0.009 (-0.380, 0.370)	-0.066 (-0.350, 0.220)	0.810
Flaxseed - Olive	0.082 (-0.310, 0.470)	0.230 (-0.095, 0.560)	0.170 (-0.078, 0.420)	0.552
Flaxseed - Safflower	-0.084 (-0.660, 0.500)	-0.160 (-0.630, 0.310)	-0.130 (-0.490, 0.230)	0.835
Flaxseed - Sunflower	0.041 (-0.350, 0.440)	0.110 (-0.250, 0.470)	0.079 (-0.180, 0.340)	0.799
Lard - Olive	-0.200 (-0.640, 0.250)	-0.530 (-1.100, 0.012)	-0.330 (-0.680, 0.014)	0.347
Lard - Peanut	-0.430 (-0.980, 0.110)	-0.046 (-0.590, 0.500)	-0.240 (-0.630, 0.140)	0.317
Lard - Soybean	-0.630 (-1.200, -0.055)	-0.350 (-0.830, 0.140)	-0.480 (-0.850, -0.120)	0.459
Olive - Peanut	0.150 (-0.160, 0.450)	-0.021 (-0.420, 0.370)	0.093 (-0.150, 0.330)	0.480
Olive - Rapeseed	-0.220 (-0.500, 0.064)	-0.230 (-0.690, 0.240)	-0.230 (-0.450, -0.012)	0.976
Olive - Rice bran	-0.260 (-0.700, 0.180)	-0.140 (-0.470, 0.190)	-0.220 (-0.460, 0.032)	0.661
Olive - Soybean	-0.200 (-0.470, 0.075)	-0.094 (-0.300, 0.110)	-0.150 (-0.320, 0.023)	0.550
Olive - Sunflower	-0.032 (-0.260, 0.200)	-0.210 (-0.540, 0.120)	-0.089 (-0.270, 0.095)	0.374
Palm - Rice bran	-0.780 (-1.300, -0.250)	-0.490 (-1.300, 0.280)	-0.690 (-1.100, -0.280)	0.560
Palm - Soybean	-0.690 (-1.200, -0.170)	-0.450 (-1.200, 0.300)	-0.630 (-1.000, -0.230)	0.611
Palm - Sunflower	-0.400 (-1.100, 0.300)	-0.650 (-1.200, -0.140)	-0.570 (-0.980, -0.160)	0.570
Peanut - Soybean	-0.190 (-0.580, 0.200)	-0.300 (-0.660, 0.070)	-0.240 (-0.490, 0.025)	0.659
Rapeseed - Rice bran	-0.033 (-0.370, 0.310)	0.001 (-0.490, 0.500)	0.020 (-0.260, 0.300)	0.907
Rapeseed - Sunflower	0.140 (-0.190, 0.460)	0.150 (-0.220, 0.530)	0.150 (-0.096, 0.380)	0.942
Rice bran - Soybean	0.110 (-0.260, 0.490)	0.023 (-0.330, 0.380)	0.064 (-0.190, 0.320)	0.726
Rice bran - Sunflower	-0.380 (-0.940, 0.190)	0.270 (-0.035, 0.580)	0.130 (-0.150, 0.400)	0.046

Table A.7: Inconsistency analysis for TC (Bayesian analysis)

Comparison	Direct	Indirect	Network	p
Argan - Butter	0.720 (0.460, 0.980)	0.220 (-0.320, 0.750)	0.630 (0.380, 0.860)	0.095
Argan - Olive	-0.250 (-0.770, 0.240)	0.240 (-0.071, 0.550)	0.110 (-0.160, 0.370)	0.097
Beef fat - Coconut	0.340 (-0.007, 0.690)	-0.260 (-0.800, 0.270)	0.190 (-0.120, 0.460)	0.061
Beef fat - Corn	-0.620 (-1.100, -0.076)	0.140 (-0.260, 0.560)	-0.140 (-0.480, 0.190)	0.026
Beef fat - Olive	-0.320 (-0.860, 0.230)	0.230 (-0.150, 0.630)	0.018 (-0.290, 0.320)	0.097
Beef fat - Rapeseed	-0.600 (-1.200, -0.068)	-0.110 (-0.580, 0.340)	-0.330 (-0.680, 0.025)	0.178
Beef fat - Rice bran	-0.630 (-1.200, -0.092)	-0.140 (-0.630, 0.360)	-0.340 (-0.710, 0.019)	0.182
Beef fat - Safflower	-0.360 (-0.710, -0.017)	-0.920 (-1.500, -0.310)	-0.460 (-0.780, -0.180)	0.110
Butter - Cocoa butter	-0.420 (-0.610, -0.210)	-0.360 (-0.640, -0.082)	-0.390 (-0.570, -0.190)	0.734
Butter - Coconut	-0.190 (-0.770, 0.380)	-0.380 (-0.690, -0.094)	-0.350 (-0.610, -0.091)	0.565
Butter - Corn	-0.500 (-0.880, -0.110)	-0.750 (-1.000, -0.470)	-0.670 (-0.890, -0.440)	0.287
Butter - Olive	-0.410 (-0.630, -0.190)	-0.720 (-1.000, -0.430)	-0.520 (-0.680, -0.350)	0.085
Butter - Soybean	-0.870 (-1.100, -0.600)	-0.580 (-0.840, -0.290)	-0.740 (-0.920, -0.530)	0.122
Camelina - Flaxseed	0.061 (-0.500, 0.620)	0.290 (-0.250, 0.820)	0.180 (-0.210, 0.560)	0.556
Camelina - Olive	0.420 (-0.130, 0.950)	0.210 (-0.420, 0.830)	0.340 (-0.027, 0.720)	0.609
Camelina - Rapeseed	0.100 (-0.420, 0.620)	-0.160 (-0.820, 0.510)	-0.004 (-0.390, 0.390)	0.538
Cocoa butter - Olive	-0.150 (-0.380, 0.072)	-0.058 (-0.370, 0.240)	-0.130 (-0.310, 0.049)	0.596
Cocoa butter - Soybean	-0.550 (-0.770, -0.300)	-0.097 (-0.370, 0.180)	-0.350 (-0.550, -0.140)	0.022
Coconut - Corn	-0.370 (-1.000, 0.300)	-0.310 (-0.590, 0.002)	-0.320 (-0.580, -0.051)	0.869
Coconut - Olive	-0.230 (-0.560, 0.098)	-0.051 (-0.380, 0.280)	-0.170 (-0.390, 0.063)	0.434
Coconut - Safflower	-0.640 (-0.930, -0.340)	-0.850 (-1.400, -0.270)	-0.650 (-0.910, -0.390)	0.522
Coconut - Soybean	0.290 (-0.300, 0.890)	-0.550 (-0.830, -0.260)	-0.390 (-0.640, -0.110)	0.013
Corn - Flaxseed	-0.380 (-0.980, 0.210)	0.085 (-0.230, 0.400)	-0.005 (-0.290, 0.270)	0.174
Corn - Olive	0.190 (-0.015, 0.400)	-0.044 (-0.520, 0.440)	0.160 (-0.027, 0.330)	0.367
Corn - Rapeseed	-0.005 (-0.450, 0.450)	-0.280 (-0.630, 0.053)	-0.190 (-0.450, 0.080)	0.318
Corn - Rice bran	-0.023 (-0.460, 0.420)	-0.300 (-0.680, 0.073)	-0.200 (-0.480, 0.085)	0.345
Flaxseed - Olive	0.110 (-0.320, 0.540)	0.190 (-0.120, 0.490)	0.160 (-0.079, 0.410)	0.762
Flaxseed - Safflower	-0.510 (-0.960, -0.055)	-0.150 (-0.580, 0.290)	-0.320 (-0.640, -0.011)	0.271
Flaxseed - Sunflower	0.046 (-0.410, 0.500)	0.094 (-0.240, 0.450)	0.079 (-0.190, 0.350)	0.869
Lard - Olive	-0.240 (-0.820, 0.350)	-0.550 (-1.100, 0.001)	-0.400 (-0.800, -0.016)	0.454
Lard - Peanut	-0.500 (-1.000, 0.037)	-0.008 (-0.640, 0.650)	-0.280 (-0.690, 0.130)	0.232
Lard - Soybean	-0.620 (-1.200, -0.054)	-0.500 (-1.100, 0.110)	-0.630 (-1.000, -0.220)	0.767
Olive - Peanut	0.140 (-0.180, 0.460)	0.099 (-0.240, 0.470)	0.120 (-0.096, 0.360)	0.855
Olive - Rapeseed	-0.320 (-0.600, -0.040)	-0.390 (-0.840, 0.055)	-0.350 (-0.570, -0.120)	0.792
Olive - Rice bran	-0.310 (-0.770, 0.150)	-0.370 (-0.710, -0.037)	-0.360 (-0.610, -0.100)	0.798
Olive - Soybean	-0.300 (-0.560, -0.030)	-0.130 (-0.340, 0.066)	-0.220 (-0.390, -0.036)	0.305
Olive - Sunflower	-0.054 (-0.330, 0.220)	-0.130 (-0.440, 0.170)	-0.083 (-0.280, 0.120)	0.694
Palm - Peanut	0.140 (-0.580, 0.840)	-0.340 (-0.800, 0.120)	-0.220 (-0.610, 0.170)	0.273
Palm - Rice bran	-0.850 (-1.400, -0.320)	-0.440 (-0.980, 0.090)	-0.700 (-1.100, -0.330)	0.290
Palm - Soybean	-0.910 (-1.400, -0.370)	-0.280 (-0.790, 0.240)	-0.560 (-0.920, -0.210)	0.089
Palm - Sunflower	-0.290 (-0.760, 0.170)	-0.680 (-1.200, -0.160)	-0.430 (-0.780, -0.082)	0.265
Peanut - Soybean	-0.120 (-0.530, 0.280)	-0.500 (-0.830, -0.180)	-0.340 (-0.590, -0.092)	0.141
Peanut - Sunflower	-0.700 (-1.300, -0.110)	-0.071 (-0.380, 0.260)	-0.200 (-0.490, 0.071)	0.064
Rapeseed - Rice bran	0.003 (-0.360, 0.360)	-0.089 (-0.590, 0.430)	-0.013 (-0.300, 0.260)	0.767
Rapeseed - Sunflower	0.300 (-0.062, 0.670)	0.200 (-0.160, 0.560)	0.260 (0.010, 0.510)	0.689
Rice bran - Soybean	0.130 (-0.270, 0.550)	0.110 (-0.250, 0.480)	0.140 (-0.130, 0.410)	0.933
Rice bran - Sunflower	0.100 (-0.520, 0.720)	0.320 (-0.009, 0.650)	0.270 (-0.013, 0.560)	0.539

Table A.8: Inconsistency analysis for HDL-C (Bayesian analysis)

Comparison	Direct	Indirect	Network	p
Argan - Butter	-0.320 (-0.380, -0.250)	-0.005 (-0.140, 0.130)	-0.240 (-0.320, -0.160)	0.000
Argan - Olive	-0.011 (-0.130, 0.120)	-0.330 (-0.400, -0.240)	-0.210 (-0.290, -0.120)	0.000
Beef fat - Coconut	0.0001 (-0.130, 0.130)	0.087 (-0.093, 0.270)	0.029 (-0.072, 0.130)	0.435
Beef fat - Corn	-0.009 (-0.210, 0.190)	-0.065 (-0.210, 0.083)	-0.038 (-0.150, 0.075)	0.652
Beef fat - Olive	0.041 (-0.160, 0.240)	-0.063 (-0.200, 0.075)	-0.032 (-0.140, 0.072)	0.398
Beef fat - Rapeseed	-0.011 (-0.220, 0.200)	-0.068 (-0.220, 0.083)	-0.039 (-0.160, 0.077)	0.654
Beef fat - Rice bran	1e-04 (-0.200, 0.200)	-0.058 (-0.230, 0.110)	-0.031 (-0.160, 0.095)	0.661
Beef fat - Safflower	-0.150 (-0.280, -0.020)	-0.110 (-0.320, 0.100)	-0.140 (-0.250, -0.036)	0.736
Butter - Cocoa butter	-0.010 (-0.110, 0.094)	0.020 (-0.093, 0.130)	0.001 (-0.073, 0.074)	0.692
Butter - Coconut	0.290 (0.016, 0.560)	0.072 (-0.019, 0.160)	0.096 (0.012, 0.180)	0.134
Butter - Corn	-0.010 (-0.130, 0.110)	0.060 (-0.045, 0.170)	0.029 (-0.048, 0.110)	0.377
Butter - Olive	-0.003 (-0.082, 0.075)	0.081 (-0.011, 0.170)	0.035 (-0.024, 0.094)	0.165
Butter - Soybean	-0.045 (-0.140, 0.053)	0.002 (-0.100, 0.100)	-0.021 (-0.090, 0.047)	0.512
Cocoa butter - Olive	0.027 (-0.064, 0.120)	0.043 (-0.077, 0.170)	0.033 (-0.036, 0.100)	0.841
Cocoa butter - Soybean	0.008 (-0.110, 0.130)	-0.047 (-0.160, 0.059)	-0.022 (-0.100, 0.057)	0.499
Coconut - Corn	-0.010 (-0.200, 0.190)	-0.083 (-0.180, 0.016)	-0.067 (-0.150, 0.019)	0.498
Coconut - Olive	-0.150 (-0.280, -0.027)	-0.012 (-0.110, 0.084)	-0.061 (-0.140, 0.012)	0.078
Coconut - Safflower	-0.150 (-0.270, -0.027)	-0.200 (-0.380, -0.036)	-0.170 (-0.270, -0.076)	0.615
Coconut - Soybean	-0.090 (-0.220, 0.036)	-0.140 (-0.260, -0.033)	-0.120 (-0.200, -0.038)	0.523
Corn - Flaxseed	-0.150 (-0.380, 0.081)	-0.001 (-0.110, 0.110)	-0.027 (-0.130, 0.070)	0.247
Corn - Olive	0.019 (-0.053, 0.093)	-0.095 (-0.260, 0.067)	0.001 (-0.058, 0.068)	0.205
Corn - Rapeseed	5.6e-05 (-0.200, 0.200)	-0.004 (-0.110, 0.094)	-0.001 (-0.090, 0.087)	0.969
Corn - Rice bran	0.008 (-0.190, 0.200)	0.007 (-0.120, 0.130)	0.007 (-0.098, 0.110)	0.985
Flaxseed - Olive	-0.020 (-0.190, 0.150)	0.051 (-0.050, 0.150)	0.033 (-0.053, 0.120)	0.470
Flaxseed - Safflower	-0.084 (-0.190, 0.023)	-0.057 (-0.220, 0.110)	-0.076 (-0.160, 0.011)	0.774
Flaxseed - Sunflower	0.058 (-0.077, 0.190)	0.047 (-0.080, 0.170)	0.053 (-0.038, 0.140)	0.897
Lard - Olive	-0.020 (-0.190, 0.150)	-0.046 (-0.180, 0.093)	-0.037 (-0.140, 0.067)	0.808
Lard - Peanut	-0.140 (-0.270, -0.017)	-0.041 (-0.250, 0.160)	-0.110 (-0.210, -0.001)	0.412
Lard - Soybean	-0.059 (-0.200, 0.079)	-0.093 (-0.270, 0.088)	-0.092 (-0.200, 0.014)	0.767
Olive - Peanut	-0.021 (-0.140, 0.094)	-0.140 (-0.280, -0.008)	-0.070 (-0.160, 0.016)	0.168
Olive - Rapeseed	-0.026 (-0.110, 0.055)	0.039 (-0.100, 0.180)	-0.007 (-0.076, 0.061)	0.429
Olive - Rice bran	-0.040 (-0.240, 0.160)	0.004 (-0.100, 0.110)	0.001 (-0.090, 0.093)	0.689
Olive - Soybean	-0.110 (-0.240, 0.025)	-0.041 (-0.120, 0.031)	-0.055 (-0.120, 0.008)	0.395
Olive - Sunflower	0.013 (-0.070, 0.098)	0.020 (-0.089, 0.130)	0.020 (-0.046, 0.086)	0.924
Palm - Rice bran	-0.070 (-0.320, 0.170)	-0.018 (-0.400, 0.360)	-0.083 (-0.280, 0.120)	0.814
Palm - Soybean	-0.200 (-0.460, 0.051)	-0.069 (-0.450, 0.310)	-0.140 (-0.330, 0.058)	0.555
Palm - Sunflower	-0.008 (-0.380, 0.350)	-0.088 (-0.320, 0.150)	-0.065 (-0.260, 0.130)	0.717
Peanut - Soybean	0.079 (-0.057, 0.220)	-0.052 (-0.190, 0.084)	0.015 (-0.079, 0.110)	0.167
Rapeseed - Rice bran	-0.017 (-0.130, 0.097)	0.058 (-0.160, 0.280)	0.008 (-0.085, 0.100)	0.550
Rapeseed - Sunflower	0.026 (-0.071, 0.130)	0.029 (-0.098, 0.160)	0.026 (-0.049, 0.100)	0.969
Rice bran - Soybean	-0.094 (-0.290, 0.110)	-0.043 (-0.170, 0.077)	-0.057 (-0.160, 0.045)	0.671
Rice bran - Sunflower	-0.009 (-0.150, 0.130)	0.017 (-0.120, 0.160)	0.018 (-0.077, 0.110)	0.792

Table A.9: Inconsistency analysis for TG (Bayesian analysis)

Comparison	Direct	Indirect	Network	p
Argan - Butter	0.046 (-0.099, 0.200)	0.110 (-0.160, 0.390)	0.060 (-0.063, 0.200)	0.646
Argan - Olive	0.060 (-0.180, 0.310)	-0.008 (-0.190, 0.190)	0.014 (-0.130, 0.170)	0.646
Beef fat - Coconut	-0.110 (-0.340, 0.120)	0.006 (-0.320, 0.340)	-0.072 (-0.250, 0.110)	0.560
Beef fat - Corn	-0.088 (-0.420, 0.240)	-0.190 (-0.500, 0.130)	-0.140 (-0.350, 0.081)	0.661
Beef fat - Olive	-0.051 (-0.370, 0.270)	-0.160 (-0.440, 0.120)	-0.110 (-0.300, 0.081)	0.608
Beef fat - Rapeseed	-0.080 (-0.400, 0.250)	-0.027 (-0.360, 0.300)	-0.036 (-0.260, 0.190)	0.823
Beef fat - Rice bran	-0.049 (-0.370, 0.280)	-0.270 (-0.620, 0.079)	-0.160 (-0.390, 0.077)	0.359
Beef fat - Safflower	-0.180 (-0.410, 0.051)	-0.160 (-0.650, 0.310)	-0.170 (-0.370, 0.031)	0.954
Butter - Cocoa butter	-0.074 (-0.240, 0.089)	0.028 (-0.190, 0.250)	-0.038 (-0.160, 0.087)	0.444
Butter - Coconut	0.037 (-0.480, 0.550)	-0.013 (-0.220, 0.190)	-0.007 (-0.190, 0.180)	0.863
Butter - Corn	-0.061 (-0.350, 0.230)	-0.066 (-0.270, 0.140)	-0.070 (-0.230, 0.093)	0.980
Butter - Olive	-0.032 (-0.180, 0.120)	-0.058 (-0.250, 0.140)	-0.046 (-0.150, 0.063)	0.829
Butter - Soybean	-0.120 (-0.300, 0.070)	-0.120 (-0.320, 0.084)	-0.130 (-0.250, 0.008)	0.988
Cocoa butter - Olive	0.004 (-0.150, 0.160)	-0.022 (-0.250, 0.200)	-0.008 (-0.130, 0.110)	0.843
Cocoa butter - Soybean	-0.180 (-0.340, -0.029)	0.100 (-0.110, 0.310)	-0.089 (-0.220, 0.047)	0.036
Coconut - Corn	-0.097 (-0.660, 0.480)	-0.062 (-0.280, 0.150)	-0.063 (-0.260, 0.130)	0.909
Coconut - Olive	-0.058 (-0.290, 0.170)	-0.008 (-0.270, 0.250)	-0.039 (-0.200, 0.120)	0.770
Coconut - Safflower	-0.060 (-0.280, 0.170)	-0.260 (-0.740, 0.220)	-0.097 (-0.300, 0.097)	0.458
Coconut - Soybean	-0.360 (-0.950, 0.240)	-0.094 (-0.290, 0.120)	-0.120 (-0.310, 0.076)	0.401
Corn - Flaxseed	-0.150 (-0.620, 0.310)	0.052 (-0.180, 0.290)	0.010 (-0.200, 0.220)	0.433
Corn - Olive	0.060 (-0.110, 0.220)	-0.089 (-0.480, 0.300)	0.024 (-0.120, 0.160)	0.485
Corn - Rapeseed	0.009 (-0.310, 0.330)	0.160 (-0.089, 0.410)	0.099 (-0.093, 0.300)	0.462
Corn - Rice bran	0.037 (-0.280, 0.350)	-0.082 (-0.350, 0.180)	-0.021 (-0.220, 0.180)	0.565
Flaxseed - Olive	0.079 (-0.160, 0.320)	-0.069 (-0.320, 0.190)	0.014 (-0.160, 0.190)	0.406
Flaxseed - Safflower	-0.130 (-0.530, 0.270)	0.005 (-0.300, 0.320)	-0.045 (-0.290, 0.200)	0.589
Flaxseed - Sunflower	-0.079 (-0.450, 0.290)	0.190 (-0.043, 0.430)	0.110 (-0.085, 0.310)	0.222
Lard - Olive	0.036 (-0.450, 0.520)	0.017 (-0.270, 0.310)	0.022 (-0.220, 0.270)	0.954
Lard - Peanut	-0.160 (-0.460, 0.150)	0.022 (-0.500, 0.530)	-0.057 (-0.320, 0.190)	0.553
Lard - Soybean	0.020 (-0.270, 0.310)	-0.068 (-0.570, 0.430)	-0.058 (-0.300, 0.190)	0.759
Olive - Peanut	0.030 (-0.160, 0.220)	-0.290 (-0.550, -0.037)	-0.079 (-0.260, 0.075)	0.048
Olive - Rapeseed	0.052 (-0.140, 0.250)	0.170 (-0.130, 0.470)	0.076 (-0.080, 0.240)	0.524
Olive - Rice bran	0.001 (-0.310, 0.310)	-0.110 (-0.320, 0.110)	-0.045 (-0.220, 0.120)	0.579
Olive - Soybean	-0.099 (-0.280, 0.100)	-0.050 (-0.210, 0.120)	-0.080 (-0.200, 0.043)	0.696
Olive - Sunflower	0.120 (-0.042, 0.300)	0.056 (-0.160, 0.270)	0.098 (-0.030, 0.230)	0.615
Palm - Peanut	-0.210 (-0.680, 0.250)	-0.018 (-0.300, 0.250)	-0.070 (-0.320, 0.160)	0.481
Palm - Rice bran	0.0004 (-0.320, 0.320)	-0.077 (-0.400, 0.240)	-0.035 (-0.250, 0.190)	0.729
Palm - Soybean	-0.013 (-0.350, 0.330)	-0.120 (-0.410, 0.180)	-0.071 (-0.280, 0.140)	0.644
Palm - Sunflower	0.120 (-0.140, 0.380)	0.150 (-0.180, 0.480)	0.110 (-0.087, 0.310)	0.878
Peanut - Soybean	0.180 (-0.120, 0.480)	-0.096 (-0.290, 0.140)	-0.001 (-0.170, 0.200)	0.155
Peanut - Sunflower	0.550 (-0.160, 1.300)	0.140 (-0.067, 0.370)	0.180 (-0.014, 0.390)	0.273
Rapeseed - Rice bran	-0.091 (-0.320, 0.140)	-0.200 (-0.560, 0.160)	-0.120 (-0.310, 0.068)	0.601
Rapeseed - Sunflower	-0.006 (-0.250, 0.240)	0.060 (-0.190, 0.320)	0.022 (-0.150, 0.200)	0.716
Rice bran - Soybean	0.035 (-0.250, 0.330)	-0.075 (-0.320, 0.170)	-0.035 (-0.220, 0.150)	0.563
Rice bran - Sunflower	0.220 (-0.150, 0.590)	0.110 (-0.110, 0.330)	0.140 (-0.042, 0.330)	0.619