RESEARCH
Review

Effects of Medium-Chain Triglycerides on Weight Loss and Body Composition: A Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

Background Medium-chain triglycerides (MCTs) may result in negative energy balance and weight loss through increased energy expenditure and lipid oxidation. However, results from human intervention studies investigating the weight reducing potential of MCTs, have been mixed.

Objective To conduct a systematic review and meta-analysis of randomized controlled trials comparing the effects of MCTs, specifically C8:0 and C10:0, to long-chain triglycerides (LCTs) on weight loss and body composition in adults. Changes in blood lipid levels were secondary outcomes.

Methods Randomized controlled trials >3 weeks' duration conducted in healthy adults were identified searching Web of Knowledge, Discover, PubMed, Scopus, New Zealand Science, and Cochrane CENTRAL until March 2014 with no language restriction. Identified trials were assessed for bias. Mean differences were pooled and analyzed using inverse variance models with fixed effects. Heterogeneity between studies was calculated using I^2 statistic. An I^2>50% or P<0.10 indicated heterogeneity.

Results Thirteen trials (n=749) were identified. Compared with LCTs, MCTs decreased body weight (−0.51 kg [95% CI−0.80 to −0.23 kg]; P<0.001; I^2=35%); waist circumference (−1.46 cm [95% CI −2.04 to −0.87 cm]; P<0.001; I^2=0%), hip circumference (−0.79 cm [95% CI −1.27 to −0.30 cm]; P=0.002; I^2=0%), total body fat (standard mean difference −0.39 [95% CI −0.57 to −0.22]; P<0.001; I^2=0%), total subcutaneous fat (standard mean difference −0.46 [95% CI −0.64 to −0.27]; P<0.001; I^2=20%), and visceral fat (standard mean difference −0.55 [95% CI −0.75 to −0.34]; P<0.001; I^2=0%). No differences were seen in blood lipid levels. Many trials lacked sufficient information for a complete quality assessment, and commercial bias was detected. Although heterogeneity was absent, study designs varied with regard to duration, dose, and control of energy intake.

Conclusions Replacement of LCTs with MCTs in the diet could potentially induce modest reductions in body weight and composition without adversely affecting lipid profiles. However, further research is required by independent research groups using large, well-designed studies to confirm the efficacy of MCT and to determine the dosage needed for the management of a healthy body weight and composition.
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OBESITY CONTINUES TO BE ONE OF THE BIGGEST global challenges in the 21st century, with at least 2.8 million adults dying each year from conditions resulting from being overweight or obese.[1] In addition, 44% of diabetes burden, 23% of ischemic heart disease burden, and between 7% and 41% of certain cancer burdens are attributable to overweight and obesity.[1] The rising obesity rates can be ascribed to changing dietary patterns and lifestyle that have led to energy-dense diets with reduced physical activity.[1] High-fat diets are often blamed for increased obesity rates; however, fats are diverse and respond differently in vivo.

Medium-chain triglycerides (MCTs) may counteract fat deposition in adipocytes by increasing thermogenesis and satiety.[2] The MCTs contain 8 to 12 carbon atoms and include caprylic acid (C8:0, octanoic acid), capric acid (C10:0, decanoic acid), and lauric acid (C12:0, dodecanoic acid). Foods high in MCTs include coconut oil (58%), palm kernel oil (54%), desiccated coconut (37%), and raw coconut meat (19%) (US Department of Agriculture National Nutrient Database). Average intakes of 1.35 g/day (0.7% of total energy intake) MCTs have been reported in the United States[3] and 0.2 g/day in Japan.[4] MCT is cleaved into glycerol and medium-chain fatty acids in the gut lumen.[5] The medium chain length

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makes a smaller, more soluble molecule compared with a long-chain fatty acid, giving it a preferential absorption and metabolic route in the body.[6] This physicochemical nature of medium-chain fatty acids allows them to pass into the portal vein on route to the liver to be rapidly metabolized via β oxidation with no requirement of reesterification in intestinal cells, incorporation into chylomicrons,[7] or the rate limiting enzyme carnitine acyltransferase for intramitochondrial transport.[5] In comparison, long-chain fatty acids have a slower route, being re-esterified in the small intestine and transported by chylomicrons via the lymphatic and vascular system before being oxidized for energy or stored.[7] Thus, rapid metabolism of MCTs reduces their opportunity of adipose tissue uptake.[8]

Studies in animals and human beings have shown increased energy expenditure and lipid oxidation with MCTs, specifically C8:0 and C10:0, compared with long-chain triglycerides (LCTs).[5,9-16] Increased satiety, resulting in reduced food intake, is another possible benefit from the fast oxidation of MCT through the formation of ketones,[7] although studies in humans have been inconsistent with some showing no effect,[7,9,17,18] whereas others showed increased satiety.[19,20] Replacement of MCT with LCT in the diet, therefore, has the potential to result in negative energy balance and weight loss over the long term.

Several human intervention studies have been conducted investigating the weight-reducing potential of MCT, with mixed results.[21] If weight loss attributes are confirmed for MCT, its incorporation into the diet could have important clinical application for healthy body weight management. MCTs may be included into the diet through the development of food products, such as oils, where proportions of LCT are replaced with MCT for commercial and domestic use or weight loss products (eg, meal replacements). The availability of modern fat technologies enables the production of food products containing higher amounts of MCT that are suitable for cooking and other purposes.

The association between dietary fats and low-density lipoprotein (LDL) cholesterol is well established[22]; therefore, it is important to consider the effects of MCT on blood lipid profiles to ensure no adverse effects. Results from intervention trials with MCT on lipid profiles have been inconsistent, with some reporting unfavorable changes[23-25] and others no change.[24,25]

The primary aim of our study was to conduct a systematic review and meta-analysis of randomized controlled trials (RCTs) comparing the effects of MCT, specifically C8:0 and C10:0, to LCT on weight loss and body composition in healthy adults. Subgroup analyses were conducted to determine whether sex, baseline body weight status, length of intervention, or dosage affected the outcomes. The primary outcome measures were body mass, waist and hip circumference, total body fat, and subcutaneous and visceral fat. Secondary outcomes were blood lipids, including triglycerides (TG), total cholesterol, high-density lipoprotein (HDL) cholesterol, and LDL cholesterol.

METHODS

Eligibility Criteria

We reviewed RCTs, both parallel and crossover, published until March 2014 with no language restrictions. Only studies >3 weeks' duration were reviewed. All studies were peer reviewed and conference abstracts were excluded. In addition, the participants were required to be healthy and older than age 18 years. A body weight measurement was required at baseline and at the end point. Both ad libitum, weight maintaining, and reduced-calorie diets were included, but any exercise intervention studies were excluded. The interventions were to include C8:0 and C10:0 acids with the control containing a longer-chain fatty acid. A formal review protocol was not published.

Literature Search

A systematic search was performed for all studies published before March 31, 2014, through several journal databases, including Web of Knowledge, Discover, PubMed, Scopus, New Zealand Science, and Cochrane CENTRAL. Reference lists of included trials were scanned for further relevant studies. A pilot literature search tested suitability of search words. The final search terms included *medium-chain fatty acid*, *medium-chain triglyceride*; *octanoic*, *decanoic*, *dodecanoic*, *caprylic*, *capric*, *or lauric*; *obesity*, *weight loss*, *overweight*, *body composition*, or *energy expenditure*; and *trial*, *intervention*, or *study*. Results from each database were downloaded into EndNote (version X4.0.2, 2010, Thomson Reuters). Duplicates were removed and abstracts were screened. Where an abstract met the eligibility requirements, the full article was read to ensure inclusion and exclusion criteria were met.

Data Extraction and Quality Assessment

An extraction form was drafted to collect study details on authors; sources of funding; aim, objective, and hypothesis; study design and setting; population; intervention and delivery methods; possible confounders; outcomes; results; conclusions; and assessment of bias risk. The extraction table was piloted on one article independently by the authors and adapted to exclude any sources of discrepancies. Outcome results were collected in Excel (version 14.0.6129.5000, 2010, Microsoft Corp) for further calculation if required. Blood lipid results were converted, where necessary, to milligrams per deciliter from millimoles per liter using a conversion factor of 88.57 for TG and 38.6 for cholesterol.

A bias assessment was performed following the Cochrane risk of bias assessment[26] to assess the validity of studies. Selection, performance, detection, attrition, and reporting bias were reviewed and assessed at the study level. Crossover trials underwent a further assessment of bias risk to consider whether the effects of the first dietary intervention could be reversed during the washout period, whether any carryover effects could bias the second treatment period, whether the treatment order was randomized, and whether a paired statistical analysis was used.[26] In addition, commercial bias was identified where one or more of the authors were employees of the supplier of MCT trial products, there was a conflict of interest, and the control of data and publishing of results were not clearly stated.

Where a study had more than two arms, only relevant arms were selected for comparison and care was taken not to double count participants in the meta-analysis. Where a trial registration number was provided, the registry file was searched to determine reporting bias. Data for each study were extracted independently by one author and verified by the other. Any differences were resolved by discussion.

Statistical Analysis

Data were analyzed using Review Manager (version 5.2.11, 2012, The Nordic Cochrane Centre, The Cochrane Collaboration). A fixed-effects model and inverse variance method was used to calculate the forest plot with a 95% CI. A random effects model was applied in subgroupings to minimize the risk of a false positive result.[26] The fixed-effect estimate gives the best estimate of the intervention effect, whereas the random-effect estimate gives an average intervention effect.[26]

For each outcome, the mean difference of change scores from baseline between intervention groups was used plus the standard deviation (SD). If the SD was not given, it was calculated from the standard error. If the SD or standard error was not available, it was imputed from the mean correlation coefficient for an outcome from other studies in the meta-analysis.[26] For outcomes using differing units of measure that could not be converted (eg, subcutaneous and visceral body fat were measured in kilograms and centimeters^3), the standardized mean difference (SMD) was calculated.

Heterogeneity between studies was calculated using the I^2 statistic. Heterogeneity was identified when $I^2>50\%$ or $P<0.10$.[26] If heterogeneity was identified in any outcome, the reasons were explored or a random effects model was used.[26] If the heterogeneity could not be rectified, the meta-analysis for that particular outcome was not completed.

Where there were 10 or more studies for an outcome, publication bias was calculated using the Egger linear regression method.[27] Subgroup analysis was done a priori on study duration (<12 weeks or ≥12 weeks), sex, and MCT intake (<8%, 8% to 16%, and >16% energy). It was not possible to do a subgroup analysis by baseline body weight status due to the overlapping of groups. Post hoc analysis was done on commercial- vs noncommercial-biased studies. Subgroup differences were assessed using χ^2 test. Sensitivity analysis was done on trials with a high bias (two or more high-risk assessment), trials with imputed data, crossover trials, and trials with high commercial bias. Results are shown as weighted mean difference or SMD with 95% CIs. Statistical significance was set at $P<0.05$.

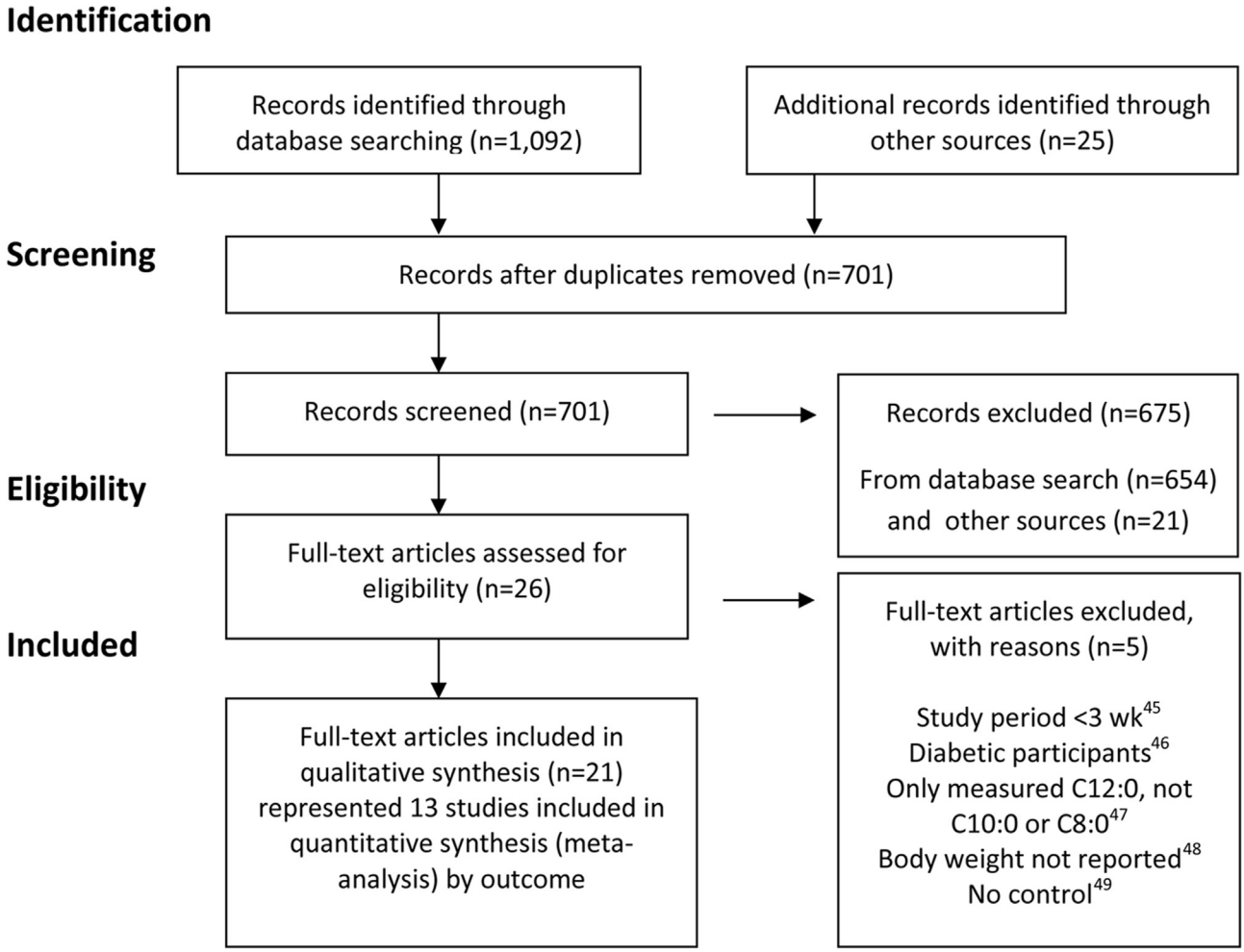

Figure 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram for search of randomized controlled trials used in meta-analysis. Databases searched included Web of Knowledge, Discover, PubMed, Scopus, New Zealand Science, and Cochrane CENTRAL. Other sources of literature included reference lists of full-text articles included in meta-analyses.

Table. Characteristics of randomized controlled trials examining the effect of medium-chain triglycerides on weight, body composition, and blood lipid levels selected for this meta-analysis

Study[a]	Methods and duration	Participants	Diet		Outcomes
			Intervention	Control	
Yost and Eckel 1989[34]	DB[b] P[c] 4-12 wk	16 obese women, aged 29-44 y in Colorado	800 kcal/d via formula containing 47% energy from CHO[d], 22% energy from protein, 6% energy from LCT[e] and 24% energy from MCT[f] (~21 g/d)	800 kcal/d via formula containing 47% energy from CHO, 22% energy from protein, 31% energy from LCT (soy oil)	BW[g]
Temme and colleagues 1997[28]	SB[h] P 6 wk	60 adults, BMI[i] 20-30, in the Netherlands	Margarine and foods, 10% energy from MCT (~24 g/d)	i) Margarine and foods, 10% energy from myristic acid (C14:0) ii) Margarine and foods, 17% energy from oleic acid	BW, TG[j], total cholesterol, HDL[k] cholesterol, LDL[l] cholesterol
Feldheim 2001[36]	C-O[m] 2×4 wk + 2 wk washout	35 women, aged 19-24 y, normal BMI, in Prague	Fat provided, 5% energy from MCT (~12.5 g/d)	Unknown LCT	BW
Krotkiewski 2001[19]	DB P 4 wk	66 obese, perimenopausal women in Sweden	579 kcal/d via Adinax[n] powder; 13% energy from MCT (9 g/d), 21% energy from CHO, 20% energy from protein, mixed with nonfat milk (45% of energy)	579 kcal/d via Adinax powder; 13% energy from LCT, 21% energy from CHO, 20% energy from protein, mixed with nonfat milk (45% of energy)	BW, body fat, TG, total cholesterol
			3 liquid meals per day		
Matsuo and colleagues 2001[30,o]	P 12 wk	13 men aged 18-20 y, normal BMI, in Japan	Liquid formula supplement, 20 g SMLCT[p], <1% energy from MCT	Liquid formula supplement, 20 g soybean oil	BW, total adipose, TG, total cholesterol, HDL cholesterol, LDL cholesterol
			plus other ad libitum food		
Tsuji and colleagues 2001[33,o]	DB P 12 wk	78 adults in Japan	Breakfast bread containing ~4% energy from MCT (10 g/d)	Breakfast bread containing 10 g/d LCT (70% rapeseed, 30% soybean oil)	BW, body composition, TG and total cholesterol
			Pre-packaged lunch, dinners provided plus 250 g fruit and vegetables/day		

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Table. Characteristics of randomized controlled trials examining the effect of medium-chain triglycerides on weight, body composition, and blood lipid levels selected for this meta-analysis (*continued*)

Study[a]	Methods and duration	Participants	Diet		Outcomes
			Intervention	Control	
Kasai and colleagues 2003[4,o]	DB P 12 wk	82 adults, mean BMI=25, in Japan	Breakfast bread containing 14 g MLCT[q], providing 1.7 g MCT, <1% energy Pre-packaged lunch, dinners provided plus 250 g fruit and vegetables/day	Breakfast bread containing 14 g LCT (70% rapeseed, 30% soybean oil)	BW, body composition, TG, total cholesterol, HDL cholesterol, and LDL cholesterol
Nosaka and colleagues 2003[31,o]	DB P 12 wk	64 adults, mean BMI=25, in Japan	14 g margarine/d containing <2% energy from MCT (5 g/d) Prepackaged lunch, dinners provided plus 250 g fruit and vegetables/d	14 g margarine/d containing LCT (70% rapeseed, 30% soybean oil) (5 g/d)	BW, body composition, TG, and total cholesterol
St Onge and colleagues 2003[10] Bourque and colleagues 2003[38]	C-O 2×27 d, 4-8 wk washout	17 obese women, mean age 44 y, mean BMI=32, in Montreal	30% from fat mixture containing 20% energy from MCT (~54 g/d) plus 22 mg/kg/BW stanol/sterol mixture 3 isoenergetic meals 40% energy from fat, 45% energy from CHO, and 15% energy from protein	30% energy from beef tallow	BW, body composition, TG, total cholesterol, HDL cholesterol, and LDL cholesterol
St Onge and colleagues 2003[9] St Onge and colleagues 2003[39] St-Onge and Jones 2003[40]	C-O 2×4 wk, 4-wk washout	25 overweight men, mean age 43 y, in Montreal	30% energy from structured oil containing 20% energy from MCT plus 3% stanol/sterol mixture 3 isoenergetic meals 40% energy from fat, 45% energy from CHO, and 15% energy from protein	30% energy from olive oil	BW, body composition, and blood lipid levels

(*continued on next page*)

Table. Characteristics of randomized controlled trials examining the effect of medium-chain triglycerides on weight, body composition, and blood lipid levels selected for this meta-analysis (*continued*)

Study[a]	Methods and duration	Participants	Diet		Outcomes
			Intervention	Control	
Roynette and colleagues 2008[35,o] Rudkowska and colleagues 2006[41,o]	SB C-O 2×6 wk, 4-8 wk washout	32 hypercholesterolemic, overweight men, 18-45 y, in Montreal	30% energy from structured oil containing 13% energy from MCT (48 g/d) plus 6%-10% sterol esters	30% energy from olive oil	BW and body composition
			3 isoenergetic meals 40% energy from fat, 45% energy from CHO, and 15% energy from protein		
St Onge and Bosarge 2008[32] St Onge and colleagues 2008[42]	DB P 16 wk	49 overweight adults, 19-50 y, in Birmingham, AL	12% energy from MCT, women: 18 g/d; men: 24 g/d	12% energy from olive oil	BW, body composition, TG, total cholesterol, HDL cholesterol, LDL cholesterol
			Study muffins (10 g) and cooking oil (8-14 g)		
Xue 2009[29,o] Xue 2009[43,o] Liu 2009[37,o] Zhang 2010[44,o]	DB P 8 wk	101 adults, BMI >22, high triglycerides, China	25-30 g/d MLCT oil containing <2% energy from MCT, 3.25-3.9 g/d	25-30 g/d LCT oil	BW, body composition, TG, total cholesterol, HDL cholesterol, and LDL cholesterol

[a]Where >1 article is published for the study, the primary study is listed first.
[b]DB: double-blind.
[c]P=parallel.
[d]CHO=carbohydrate.
[e]LCT=long-chain triglycerides.
[f]MCT=medium-chain triglycerides.
[g]BW=body weight.
[h]SB=single blind.
[i]BMI=body mass index.
[j]TG=triglycerides.
[k]HDL=high-density lipoprotein.
[l]LDL=low-density lipoprotein.
[m]C-O=crossover.
[n]Norovital.
[o]Risk of commercial bias, where authors are also employees of the company supplying the MCT and ownership of data and publishing is not declared.
[p]SMLCT=structured medium long-chain triglycerides.
[q]MLCT=medium long-chain triglycerides.

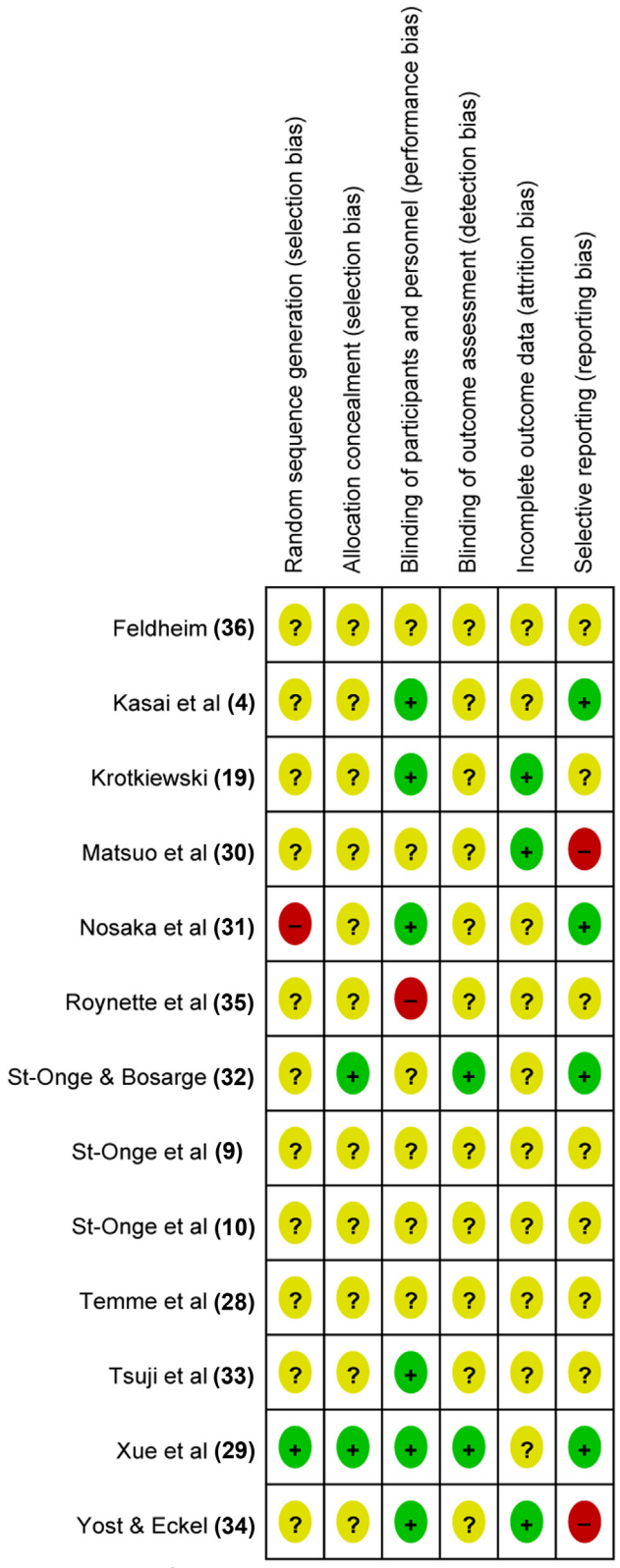

Figure 2. Risk of bias table showing judgments on each risk factor for each primary study included in meta-analysis. +=low risk (green). ?=unclear risk (yellow). −=high risk (red).

RESULTS

The literature search identified 701 possible studies, 675 were eliminated based on title and abstract because they did not meet the inclusion criteria (Figure 1). A full-text assessment was completed on 26 articles: 21 articles represented 13 RCTs that met the inclusion criteria and are described in the Table. The five excluded studies are referenced in Figure 1.

The final analysis included 239 and 250 individuals in the intervention or control diet, respectively, for nine parallel studies[4,19,28-34] and 90 participants in four crossover trials.[9,10,35,36] Eight studies provided information by sex: four crossover studies[9,10,35,36] with 42 women and 48 men, and four parallel studies[19,29,30,37] of 94 women and 80 men. Study length ranged from 27 days to 16 weeks, equating to 10 diet weeks/person. Body mass index ranged from 20 to >30. Intake of MCT ranged from <1% to 24% of energy intake. Body fat was assessed in nine studies using a variety of methods: air-displacement method,[4,31,33] bioelectrical impedance analyzer,[29] computed tomography,[4,29,31-33] dual-energy x-ray absorptiometry,[19,32] and magnetic resonance imaging.[9,10,35] Eleven RCTs measured blood lipid levels.[4,9,10,19,28-33,35] Differing controls were used but the primary controls were monounsaturated fatty acid and polyunsaturated fatty acid sources; for example, soybean oil, rapeseed oil, and olive oil containing 18 carbon atoms.[4,9,28-35] Two studies used saturated fatty acid sources, including myristic acid (C14:0)[28] and beef tallow (C15:0, C16:0),[10] and a further two studies described the control as an LCT[19,36] (see the Table).

Quality Assessment of Studies

No studies were excluded based on quality of study, although many studies did not report sufficient information for a clear bias assessment. The risk of bias for each study is summarized in Figure 2. A major possible source of bias was selection bias. Only one study detailed a method through random numbers[29]; other studies mentioned randomization, but no method was given. Allocation concealment was seen in two using central allocation[29] and opaque containers.[32] Performance bias had the best result: six studies had double-blinding,[4,19,29,31,33,34] one study was single-blind,[35] and remaining studies did not discuss blinding[9,10,30,36] or there was a possibility the blinding could have been broken[32] or unclear.[28] Detection bias was eliminated in two studies[29,32] and not mentioned in 11 studies.[4,9,10,19,28,30,31,33-36] Attrition bias was low in three studies with no dropouts.[19,30,34] The remaining studies did a completers analysis and it is unlikely the results would substantially depart from original allocation.[4,9,10,28,29,31-33,35,36] Selective reporting bias was seen in two studies: one study failed to report subgroups of in- and outpatients with differing study durations[34]; another study did not report hip and waist circumference measurements taken and provided insufficient information for body weight to be included in the meta-analysis.[30] Low risk of reporting bias was seen in four studies where all expected outcomes were reported.[4,29,31,32] The remaining studies had unclear risk because some expected outcomes might not have been reported.[9,10,19,28,33,35,36] Commercial bias was found in six studies.[4,29-31,33,35]

The risks of bias from four crossover trials were assessed.[9,10,35,36] Study design was considered suitable for weight maintenance and the washout period was sufficient at

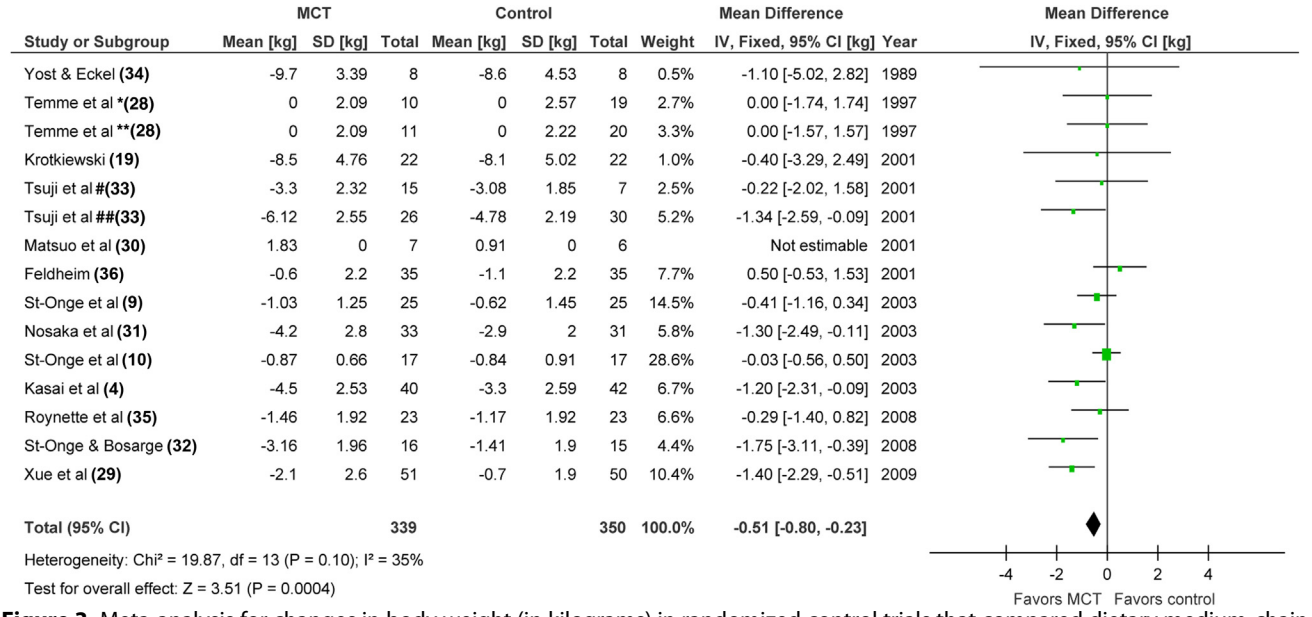

Figure 3. Meta-analysis for changes in body weight (in kilograms) in randomized control trials that compared dietary medium-chain triglycerides (MCTs) with a longer-chain triglyceride (control) shows a favorable effect of MCT intervention on body weight. *Oleic acid as control. **Myristic acid as control. #Body mass index <23. ##Body mass index ≥23. IV=inverse variance. SD=standard deviation. NOTE: Information from this figure is available online at www.andjrnl.org as part of a PowerPoint presentation.

4 or 8 weeks, although one study only had a 2-week washout.[36] The risk of a carryover effect was not clear, nor were data from the first period available. In two cases, the SD of the mean difference had to be imputed.[10,36]

All studies, except one,[30] had methods to check dietary compliance. Ten studies provided some or all food to participants.[4,9,10,19,31-36] One study monitored physical activity levels,[31] whereas eight studies advised participants to maintain current activity levels.[4,9,10,28,29,33-35] Four studies limited alcohol consumption.[4,31,33,34] Three studies were hypocaloric.[19,32,34] Three studies added phytosterols to the intervention oil[9,10,35] and one added psyllium.[34]

Effect of MCTs on Body Composition in Adults

Body Weight. Twelve studies—eight parallel[4,19,28,29,31-34] and four crossover trials[9,10,35,36]—recorded body weight outcomes (Figure 3). The weighted mean difference for body weight significantly favored MCT with small effect (−0.51 kg [95% CI −0.80 to −0.23 kg]). Moderate heterogeneity was seen in the meta-analysis for body weight (I^2=35%; P=0.10). There did not appear to be one study driving the moderate heterogeneity. Sensitivity analyses did not change this result except for study design where parallel vs crossover trials removed the significance for all the subgroup analyses, perhaps due to loss of statistical power. Furthermore, a post hoc sensitivity analysis of hypocaloric studies[19,32,34] did not alter the results. Subgroup analysis identified significant differences between duration, dose, and commercial biased groups. Studies ≥12 weeks showed greater weight loss than those <12 weeks (P=0.004). More weight was lost with doses <8% energy compared with doses >16% energy (P=0.03). More weight was lost in the commercially biased trials compared with the noncommercially biased trials (P=0.001).

Waist and Hip Circumference. Waist[4,29,31-33] and hip circumferences[4,29,31] were recorded in five and three parallel studies as shown in Figure 4. The weighted mean difference significantly favored MCT in waist circumference with medium effect (−1.46 cm [95% CI −2.04 to −0.87 cm]) and hip circumference with small effect (−0.79 cm [95% CI −1.27 to −0.30 cm]). Heterogeneity was not present for either waist (I^2=0%; P=0.71) or hip circumference (I^2=0%; P=0.87) (Figure 4). A subgroup analysis did not show any intergroup differences and results were not affected by a sensitivity analysis.

Total body, Subcutaneous, and Abdominal Visceral Fat. Nine studies—six parallel[4,19,29,31-33] and three crossover trials[9,10,35]—recorded outcomes for total body fat. Seven studies—four parallel[4,29,31,33] and three crossover trials[9,10,35]—measured outcomes for total subcutaneous fat. Six studies—five parallel studies[4,29,31-33] and one crossover trial[35]—recorded outcomes for visceral fat. Studies are detailed in Figure 5. The SMD significantly favored MCT in total body fat with small effect (SMD=−0.39 [95% CI −0.57 to −0.22]), total subcutaneous fat with medium effect (SMD=−0.46 [95% CI −0.64 to −0.27]) and visceral fat with medium effect (SMD=−0.55 [95% CI −0.75 to −0.34]). Heterogeneity was not present in total body fat (I^2=0%; P=0.62), total subcutaneous fat (I^2=20%; P=0.27), or visceral fat (I^2=0%; P=0.53). A subgroup analysis did not show any intergroup differences and results were not affected by a sensitivity analysis.

Effect of MCTs on Blood Lipid Levels in Adults

Three crossover studies[9,10,35] included phytosterols in the intervention oil; they have been excluded from analysis of blood lipids because phytosterols may confound results.[42]

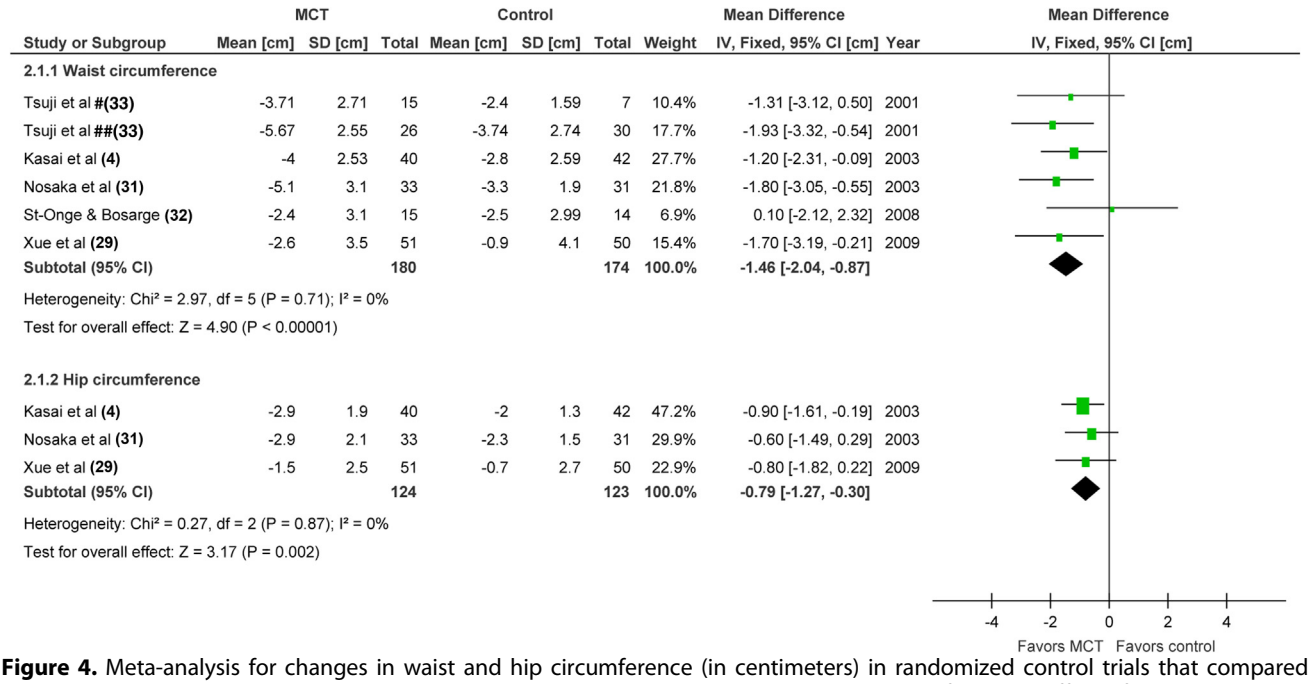

Figure 4. Meta-analysis for changes in waist and hip circumference (in centimeters) in randomized control trials that compared dietary medium-chain triglycerides (MCTs) with a longer-chain triglycerides (control) shows a favorable effect of MCT intervention on waist and hip circumference. #Body mass index <23. ##Body mass index ≥23. IV=inverse variance. SD=standard deviation.

Similarly, baseline lipid levels may affect lipid responses to dietary interventions[50]; because the study by Xue and colleagues[29] was the only study conducted on patients with hypertriglyceridemia this study was excluded from the blood lipids analysis.

Seven parallel studies[4,19,28,30-33] recorded outcomes for TG with no heterogeneity (I^2=0%; P=0.77). MCTs did not affect TG (0.00 mg/dL; 95% CI −8.04 to 8.04 mg/dL [0.00 mmol/L; 95% CI −0.09 to 0.09 mmol/L]). Seven parallel[4,19,28,30-33] studies recorded outcomes for total cholesterol. MCT did not affect total cholesterol (−2.33 mg/dL; 95% CI −6.84 to 2.18 mg/dL [−0.06 mmol/L; 95% CI −0.18 to 0.06 mmol/L]) and no heterogeneity (I^2=0%; P=0.46) was present. Four parallel[4,28,31,32] studies recorded outcomes for LDL cholesterol with small heterogeneity (I^2=36%; P=0.18). MCT did not affect LDL cholesterol levels (−2.91 mg/dL; 95% CI −7.62 to 1.79 mg/dL [−0.08 mmol/L; 95% CI −0.20 to 0.05 mmol/L]). Five parallel studies[4,28,30-32] recorded outcomes for HDL cholesterol with no heterogeneity (I^2=0%; P=0.54). MCT did not affect HDL cholesterol levels (−1.35 mg/dL; 95% CI −3.02 to 0.31 mg/dL [−0.03 mmol/L; 95% CI −0.08 to 0.01 mmol/L]). Studies and results are summarized in Figure 6. Subgroup analyses did not show any intergroup differences and sensitivity analyses did not alter any results. Furthermore, a post hoc sensitivity analysis of studies using a saturated fatty acid as a control[10,28] did not alter the results.

Publication Bias

In this meta-analysis, publication bias was not detected for weight loss outcomes, but there was a trend for publication bias in total body fat outcomes (P=0.05) (Figure 7).

DISCUSSION

The findings from our meta-analysis suggest consuming MCTs as part of a diet compared with LCTs may result in a small average reduction in body weight of 0.51 kg (range=0.80 to 0.23 kg) over an average 10-week period. Waist and hip circumferences, total body fat, subcutaneous fat, and visceral fat were also significantly reduced and no changes were seen in TG, total cholesterol, LDL cholesterol, and HDL cholesterol when dietary MCT was compared with LCT. Although the reduction in body weight was small, it may be clinically relevant. When body weight is decreased by 1 kg, the associated risk of developing diabetes is reduced by 16%.[51] Nonetheless, several factors may have affected the quality of the meta-analysis results, which limits firm conclusions. The study designs in this meta-analysis were highly variable, including trials with very-low-calorie diets in obese women,[19,34] with normal-weight individuals,[29,33] or obese and overweight individuals where energy intake was highly controlled for weight maintenance[4,9,10,33,35] or on free-feeding weight-loss diets.[32] Dosages of MCT varied considerably from <1% percent energy (2 g/day) up to >20% energy (54 g/day) and duration of studies varied from 4 to 16 weeks. The reporting of studies was incomplete with few studies providing sufficient information to make a clear bias assessment. In addition, 6 out of 13 studies were identified with high risk of commercial bias.[4,29-31,33,35]

A recent systematic review of acute, short- and long-term studies published between 2000 and 2010 concluded that dietary intake of MCTs may be associated with improved body composition and increased energy expenditure without obvious effects on food intake.[21] The authors indicated that the results were inconclusive and further studies are

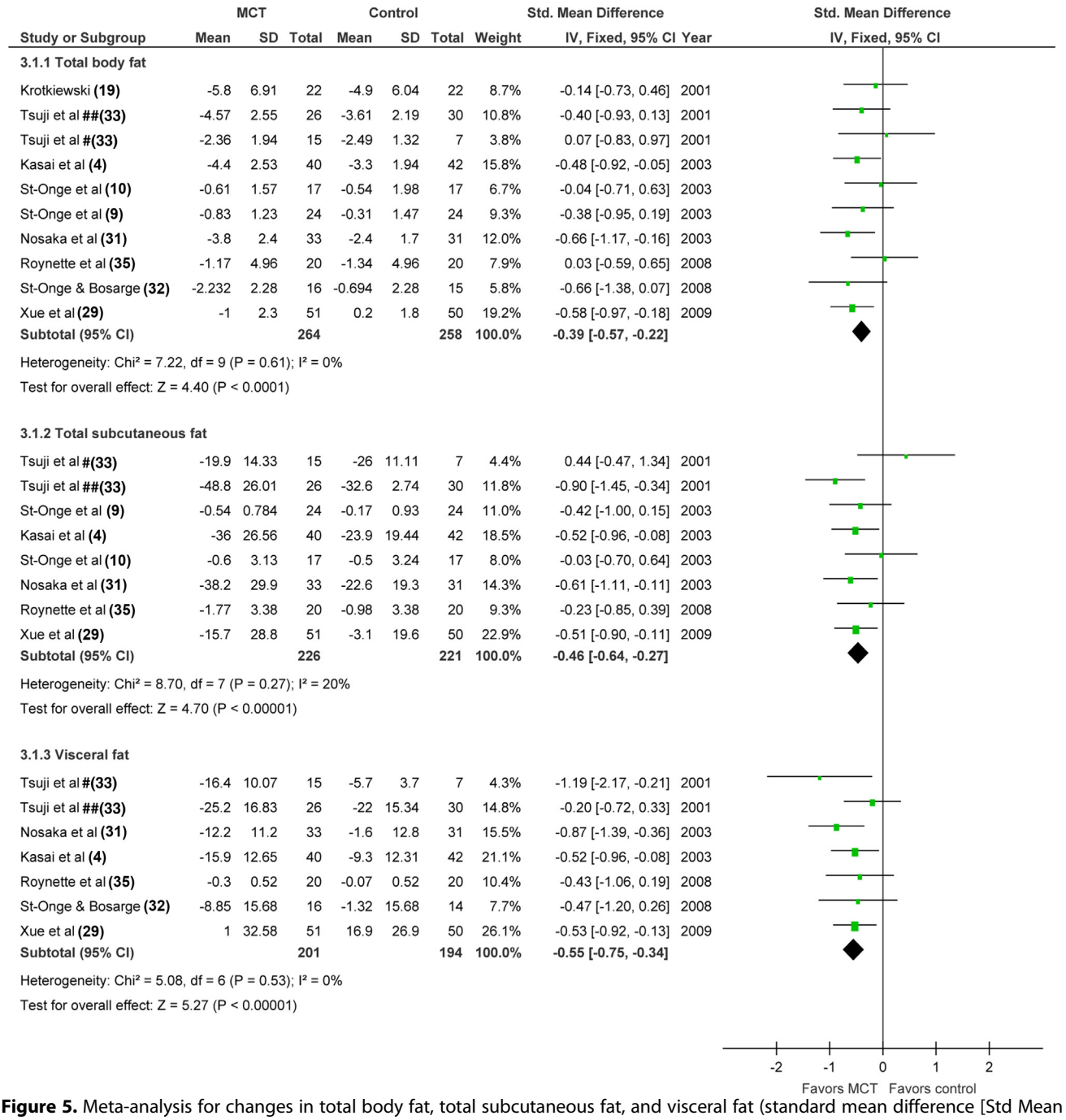

Figure 5. Meta-analysis for changes in total body fat, total subcutaneous fat, and visceral fat (standard mean difference [Std Mean Difference]) in randomized control trials that compared dietary medium-chain triglycerides (MCTs) with a longer-chain triglycerides (control) shows a favorable effect of MCT intervention on body fat. #Body mass index <23. ##Body mass index ≥23. IV=inverse variance. SD=standard deviation.

warranted to determine adequate amounts and long-term side effects of MCTs. Our systematic review focused on chronic (>3 weeks) RCTs published until March 2014 comparing MCT with LCT on weight loss, body composition, and lipid profiles as secondary outcomes and included a meta-analysis of the outcomes. Although no new studies have been published since 2010, our review identified six RCTs[28-31,34,36] that were not included in the previous systematic review. Our systematic review furthermore provides a comprehensive critical appraisal of the current evidence and aims to identify gaps and areas of further research needed before recommendations for intake of MCTs to facilitate body weight management can be made.

All research is susceptible to bias, but industry-funded trials tend to report results favoring their own products[52] and possibly lead to publication bias. Industry funding is

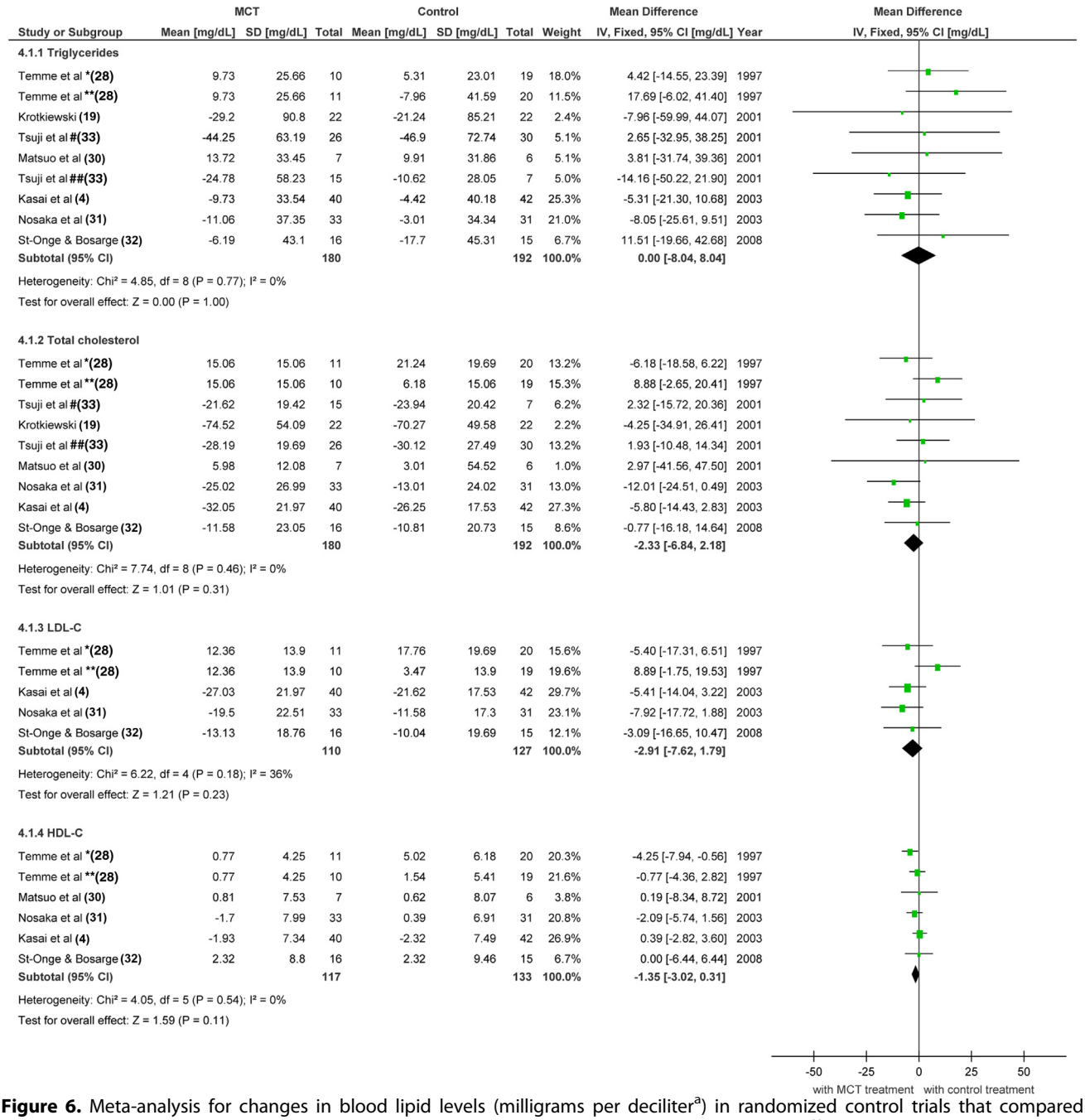

Figure 6. Meta-analysis for changes in blood lipid levels (milligrams per deciliter[a]) in randomized control trials that compared dietary medium-chain triglycerides (MCT) with a longer chain triglyceride (control) shows no differences with MCT intervention. Four studies were excluded from the analysis: three contained phytosterols in the intervention oil and one had participants with hyperlipidemia. [a]To convert mg/dL triglycerides to mmol/L, multiply mg/dL by 0.0113. To convert mmol/L triglyceride to mg/dL, multiply mmol/L 88.6. Triglyceride of 159 mg/dL=1.80 mmol/L. To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.0259. To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.6. Cholesterol of 193 mg/dL=5.00 mmol/L. *Oleic acid as control. **Myristic acid as control. #Body mass index <23. ##Body mass index ≥23. IV=inverse variance. SD=standard deviation.

critical for the advancement of nutrition science and not all industry-funded trials are biased, particularly if parties follow the guiding principles for industry-funded research,[53] including (but not exhaustively) the conduct of transparent and objectively designed research according to accepted principles of scientific inquiry, the control of both study design and research remaining with the scientific investigators, freedom and obligation to publish the findings, and full disclosure of all financial interest. The six trials identified were cowritten by employees of the suppliers of the MCT trial products. As coauthors, it is assumed they contributed substantially to the design of the research; the

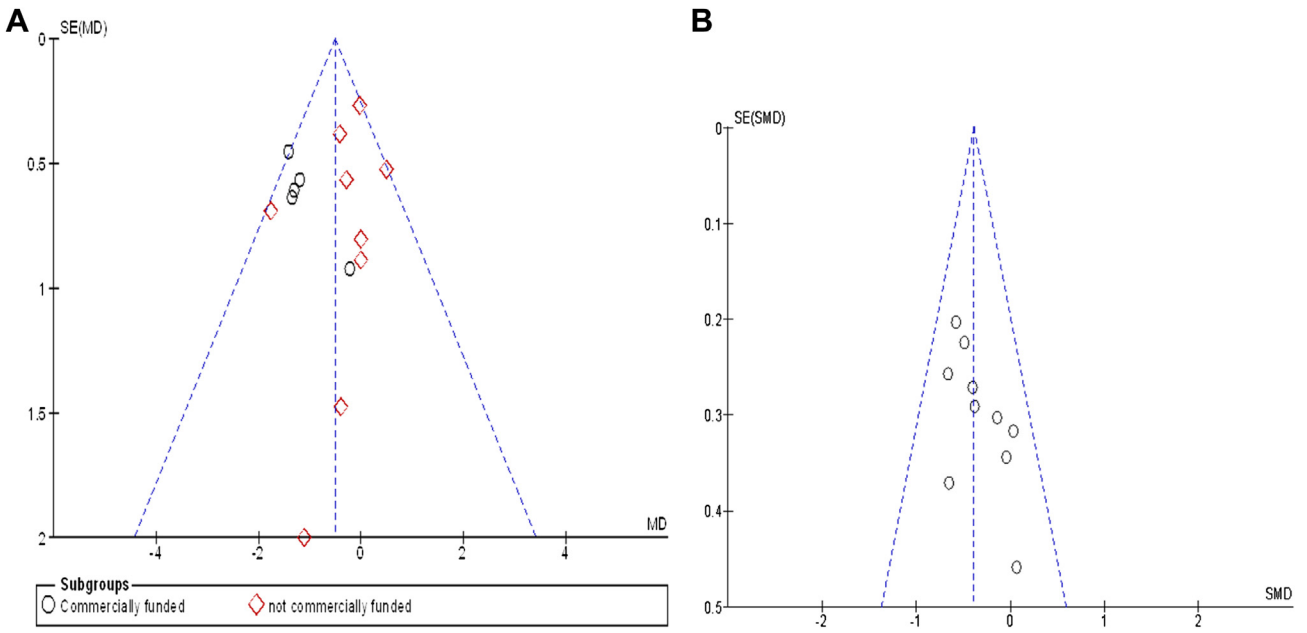

Figure 7. (A) Funnel plot of 12 randomized controlled trials (differentiated by funding) recording body weight outcomes when dietary medium-chain triglycerides were compared with a longer-chain triglyceride (control). An Egger linear regression analysis showed a symmetrical funnel plot (P=0.35). (B) Funnel plot of 10 randomized controlled trials recording total body fat outcomes when dietary medium-chain triglycerides were compared with a longer-chain triglyceride (control). An Egger linear regression analysis showed a trend toward an asymmetrical funnel plot (P=0.05).

acquisition, analysis, and interpretation of data; decision to publish and the drafting; revision; and approval of the final manuscript for submission, which may conflict with the guiding principles described above. Although these studies were generally well designed (randomized, controlled, blind, and sufficient duration), the reporting was poor resulting in unclear bias assessments for all, except Xue and colleagues.[29] It is interesting to note these studies were most likely to show a significant improvement in body weight despite being conducted on normal/overweight samples (four of five studies). They also provided the smallest doses, ≤4% energy from MCT, and were the longest in duration (four studies being 12 weeks' duration),[4,30,31,33] both factors shown in subgroup analysis to most favorably affect body weight.

The studies using the smallest doses[4,29,31,33] of ≤4% of energy (1.7 to 10 g/day), showed significant improvements in body weight (~−1.2 kg), body fat (~−1.0 kg), subcutaneous fat (~−10.3 cm^2), and visceral fat (~−8.9 cm^2) over 8 to 12 weeks compared with LCT and were conducted in Japanese[4,31,33] and Chinese[29] participants of normal weight. However, Tsuji and colleagues[33] only showed significant improvements in participants with body mass index ≥23. According to Kasai and colleagues,[4] 2 g/day MCT was small, yet 8 to 50 times the usual intake by Japanese people (0.2 g/day), and perhaps sufficient to accelerate lipid metabolism in human beings. Feldheim,[36] with young European women of normal body mass index, also used a small dosage of approximately 12.5 g/day (~5% energy) MCT in an ad libitum diet, but did not see significant changes in body weight. However, the energy and fat consumption were greater (P<0.01 and P<0.001) and protein consumption lower (P<0.05) in the MCT group compared with the LCT group, which could have confounded the results.

In contrast, St Onge and colleagues showed that large doses of 20% energy from MCT (~54 g/day), as part of a strictly controlled weight maintenance diet in Canadian overweight men[9] and obese women,[10] resulted in increased energy expenditure and fat oxidation in both men and women, although weight loss was not significant compared with LCT. Similarly, Roynette and colleagues,[35] using the same study design as St Onge and colleagues[9,10] but a reduced dose (13% energy, 48 g/day), did not show significant differences in body weight and body composition between MCT and LCT in overweight men. The differences in weight loss between MCT and LCT in these trials may have been greater if the energy intake of the diets were not strictly controlled to maintain weight; instead, free feeding may allow the satiety effects of MCT to operate. The total fat intake in these studies were high at 40% energy compared with recommended intakes of 30% energy (US Department of Agriculture National Nutrient Database), which may have affected the outcomes. In addition, olive oil was used as control in two of these studies.[9,35] Olive oil consumption has been shown to increase fat oxidation[54] and lead to beneficial body composition changes[55,56] and could, therefore, have diminished the differences between MCT and control. St Onge and Bosarge[32] conducted a follow-up weight-loss trial in overweight men and women with a moderate amount of MCT (~12% energy: 18 g/day for women, 24 g/day for men). This dose was used by Dulloo and colleagues,[11] who showed 15 to 30 g/day significantly enhanced energy expenditure. St Onge and Bosarge[32] presented a decrease in body weight (−1.75 kg [95% CI −3.11 to −0.39 kg]) over 16 weeks compared with olive oil. In this trial, participants were allowed free feeding to capture the satiety effect of MCTs. However, the authors did not report dietary intake data to determine whether the energy intake was reduced in the MCT group. Temme and colleagues[28]

conducted an ad libitum dietary study in the Netherlands on healthy adults (body mass index ranged from 20 to 30) with 10% energy from MCT (23.7 g/day) compared with either myristic acid margarine or sunflower oil margarine and failed to show weight loss effects in either trial arm, but the study's primary aim was to investigate the effects of MCT on lipid profiles.

Two studies[19,34] involving very-low-calorie diets (800 kcal/day and 579 kcal/day) containing MCT doses of 24% energy (21 g/day) and 13% energy (9 g/day) in obese women were unable to show any effects on body weight and the results were highly variable with wide 95% CIs (Figure 3). Krotkiewski[19] showed greater reductions in body weight and body fat, a sparing effect on lean mass, and decreased hunger feelings that paralleled higher increases in ketone bodies with MCT compared with LCT after 2 weeks, but not after 4 weeks. They argued the effects of MCT might be transient, which is disputed by the results of our meta-analysis. The role of MCTs in very-low-calorie liquid diets; therefore, needs further investigation.

It is important to consider effects on lean mass and whether MCT could prevent or reduce the reduction in lean mass typically associated with weight-reducing diets. However, few studies have measured the effects of MCT on lean mass with inconsistent effects. St Onge and Bosarge[32] in their weight loss study showed lean mass was higher in the olive oil control group than in the MCT group at the end of the study (-0.93 ± 0.41 kg), whereas Krotkiewski[19] showed reduced loss of lean mass with MCT compared with LCT with their very-low-calorie diet.

With regard to the investigation of MCT on lipid profiles, it must be noted that blood lipid levels were a secondary outcome and not included as a search term; therefore, some key studies may have been omitted and firm conclusions cannot be drawn from this meta-analysis. This analysis has at least illustrated high doses of MCT do not adversely affect lipid profiles. This should be further investigated in a meta-analysis specifically designed to answer this research question.

One consistent quality from the studies is the method of dietary intervention. Many studies provided food to control energy and dietary fat intake, minimizing confounders and the risk of blinding being broken. Another strength of the trials included assessment of body composition to support body weight loss, although few studies measured lean mass. However, a limitation of the studies included the large variation of body mass index within studies and a failure to control for baseline body weight in many studies. In addition, the study of dietary MCT and weight loss has centered principally around two research groups: one in Japan[4,30,31,33] and the other from Canada[9,10,35]; thus, outcomes may not be applied to the general population. Subgroup analyses are observational only as they are not based on randomized comparisons,[26] so subgroup results should be used with caution. A limitation of this meta-analysis was that the retrieval, extraction, and bias analyses of the studies was conducted by one author and verified by the second author. However, the verification involved rigorous scrutiny of the information and it is unlikely to have affected the quality of the meta-analysis.

The replacement of LCT with MCT in the diet could potentially result in small decreases in body weight and composition without adversely affecting lipid profiles. However, several factors affected the quality of the meta-analysis results: inadequate reporting made it difficult to assess the quality of the trials; several studies were at high risk of commercial bias; and the study designs varied considerably with regard to dosage, duration, and control of energy intake. Further research is required by other independent research groups using large, robustly designed studies of sufficient duration (at least 12 weeks), with different MCT doses in different food matrixes, different populations, different body weight status groups (normal weight vs overweight/obese), sex, and age groups also capturing pre- and postmenopausal women. The effect of MCT on the fat:lean mass also needs to be investigated, particularly in weight loss studies and older adults. The long-term safety of MCT-enriched foods also need to be ascertained. Finally, all studies should be reported according to the Consolidated Standards of Reporting Trials guidelines (http://www.consort-statement.org/), which provides a set of evidence-based recommendations for reporting randomized trials in a standard way that facilitates transparent and complete reporting that aids in their critical appraisal and interpretation.[57]

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

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