XXIX GIORNATE CARDIOLOGICHE TORINESI
Turin, 27-28 October 2017

Palm oil and cardiovascolar disease: what scientific evidence ?

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IRCCS-ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI

OUTLINE

1. **Introduction**

   General information on palm oil

2. **Scientific evidence on palm oil consumption and cardiovascular diseases**

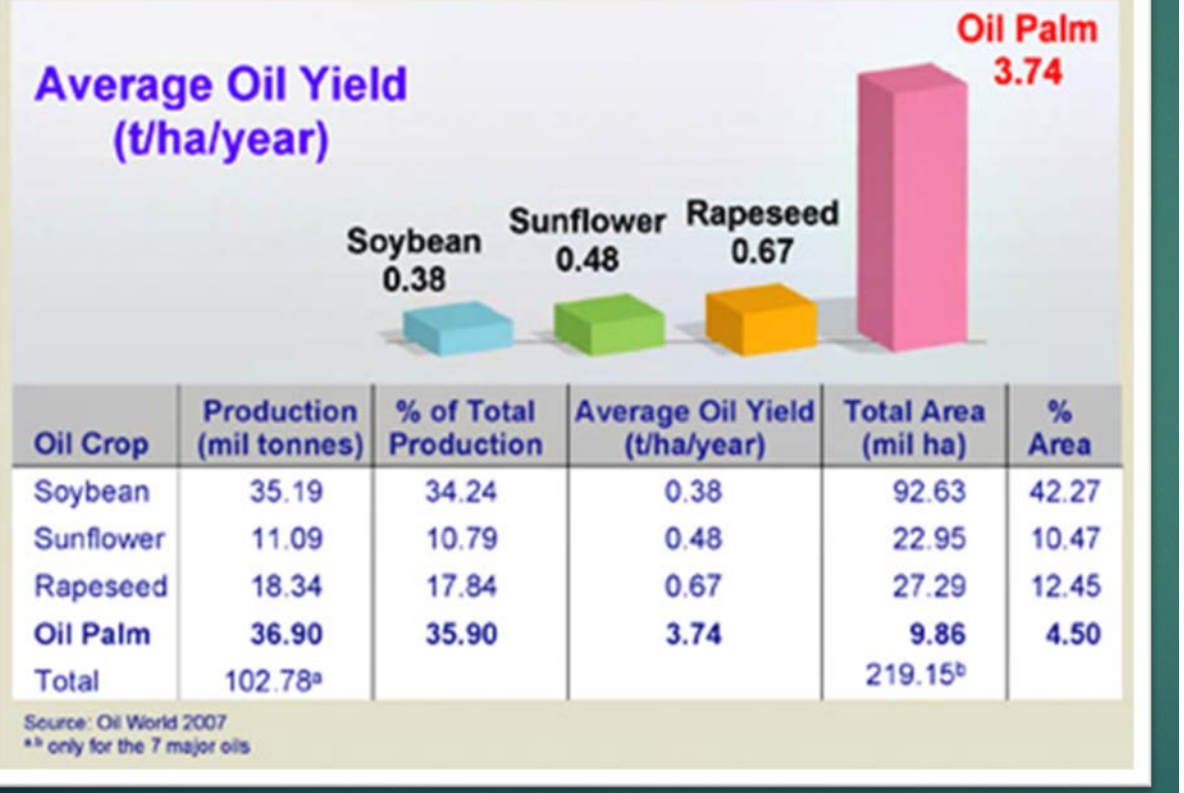
3. **Scientific evidence on saturated fatty acids and cardiovascular diseases – old and new studies**

4. **Conclusions**

Palm Oil

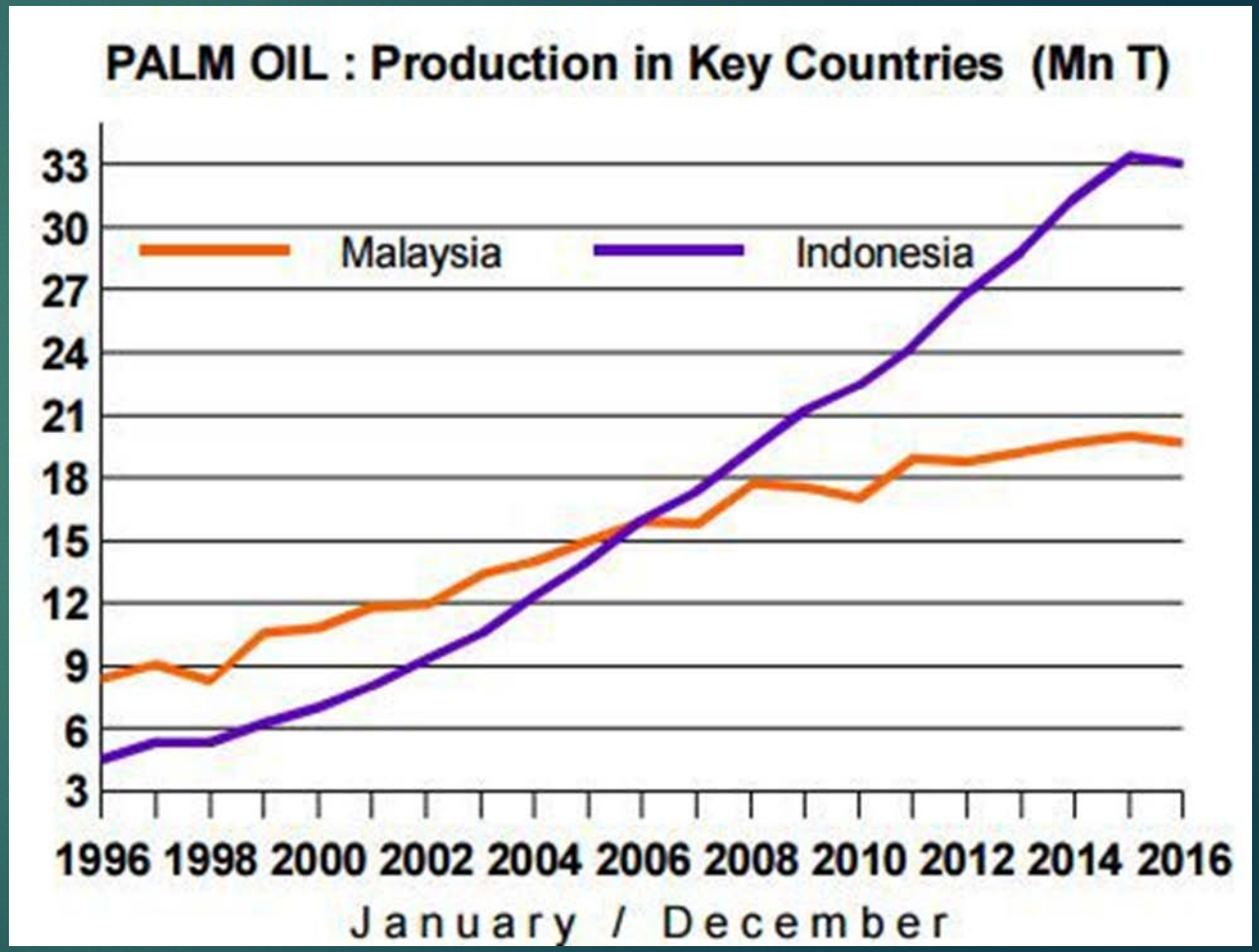
- Vegetable oil from the fruit of the palm tree (Elaeis guineensis) originating West Africa
- Widespread throughout the tropical areas of America and South East Asia.

Palm oil productivity



Oil Crop	Production (mil tonnes)	% of Total Production	Average Oil Yield (t/ha/year)	Total Area (mil ha)	% Area
Soybean	35.19	34.24	0.38	92.63	42.27
Sunflower	11.09	10.79	0.48	22.95	10.47
Rapeseed	18.34	17.84	0.67	27.29	12.45
Oil Palm	**36.90**	**35.90**	**3.74**	**9.86**	**4.50**
Total	102.78[a]			219.15[b]	

Source: Oil World 2007
[a,b] only for the 7 major oils



Fatty acid composition

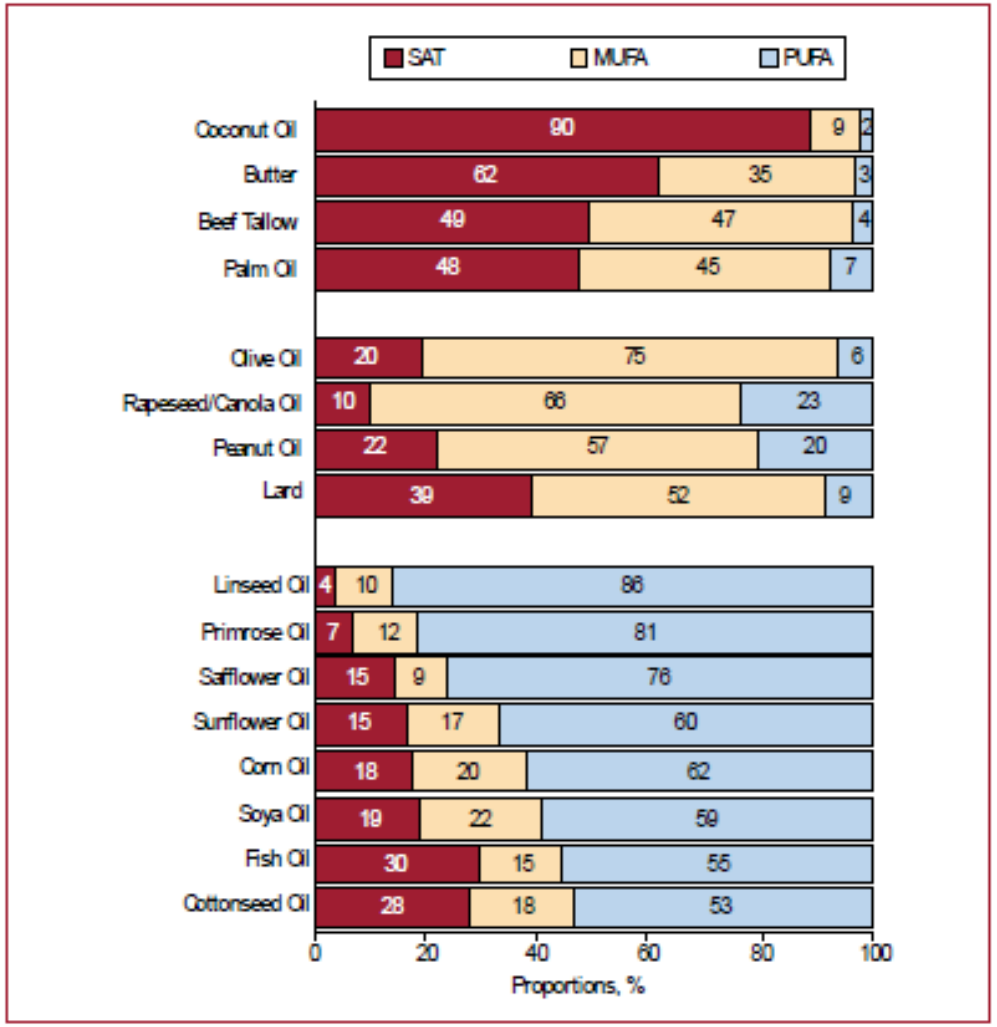


Figure 1. Percentage of the different types of fatty acids present in the different oils and fats. The most frequently consumed oils in the world are as follows: soybean (used by 28% of the world population), palm (18%), sunflower (13%), and colza/canola (12%). Adapted from Sunra et al,[13] with permission from the Spanish Society of Obesity. MUFA indicates monounsaturated fat; PUFA, polyunsaturated fat; SAT, saturated fat.


Paluani
I Nuovi
Croissant
Senza Olio di Palma
Paluani Croissant Albicocca
Senza Olio di Palma
-30% di grassi*
Paluani Croissant Classico
Senza Olio di Palma


ANCHE LE FETTE...SENZA OLIO DI PALMA!
novità
senza olio di palma
MISURA
DOLCESENZA
MISURA
IPOSALE
senza sale
40 FETTE BISCOTTATE DORATE
MISURA
FIBREXTRA
con Fecolina Selezione Integrale Misura
40 FETTE BISCOTTATE INTEGRALI


IL GRANTURCHESE
Colussi
IL GRANTURCHESE
INZUPPO FORZA 10
SENZA olio di PALMA
dal 1911
Colussi
Biscuits
Net weight - Poids net
400 g e 14.11 oz


Plasmon
Scelto dalle mamme in Italia dal 1902
dal 6° mese
Oasi nella Crescita
Da sempre il Biscotto dei bambini
IL GUSTO
PLASMON
DI CRESCERE
Con 6 vitamine e sali minerali selezionati
Si scioglie in bocca e nel latte
Senza olio di palma
Senza uova, grassi idrogenati, coloranti* e conservanti*
PRODOTTO IN ITALIA
360g e


I Nostri Biscotti
Senza Olio di Palma
Mulino Bianco
Buongrano
Mulino Bianco
Cioccolato
Mulino Bianco
Nocciola
Mulino Bianco
Bosco
Mulino Bianco
Latte

2. Scientific evidence on palm oil consumption and cardiovascular diseases

The hierarchy of clinical evidence

The American Journal of Clinical Nutrition

Palm oil and blood lipid–related markers of cardiovascular disease: a systematic review and meta-analysis of dietary intervention trials[1–3]

Elena Fattore, Cristina Bosetti, Furio Brighenti, Carlo Agostoni, and Giovanni Fattore

Am J Clin Nutr 2014;99:1331–50. Printed in USA.

What evidence on the effect of palm oil on blood lipid markers of cardiovascular disease risk?

P = Population: general population (humans)

I = Intervention: diets rich in palm oil, palm olein or palmitic acid at the sn-1,3 position

C = Comparator: diets rich other dietary fats

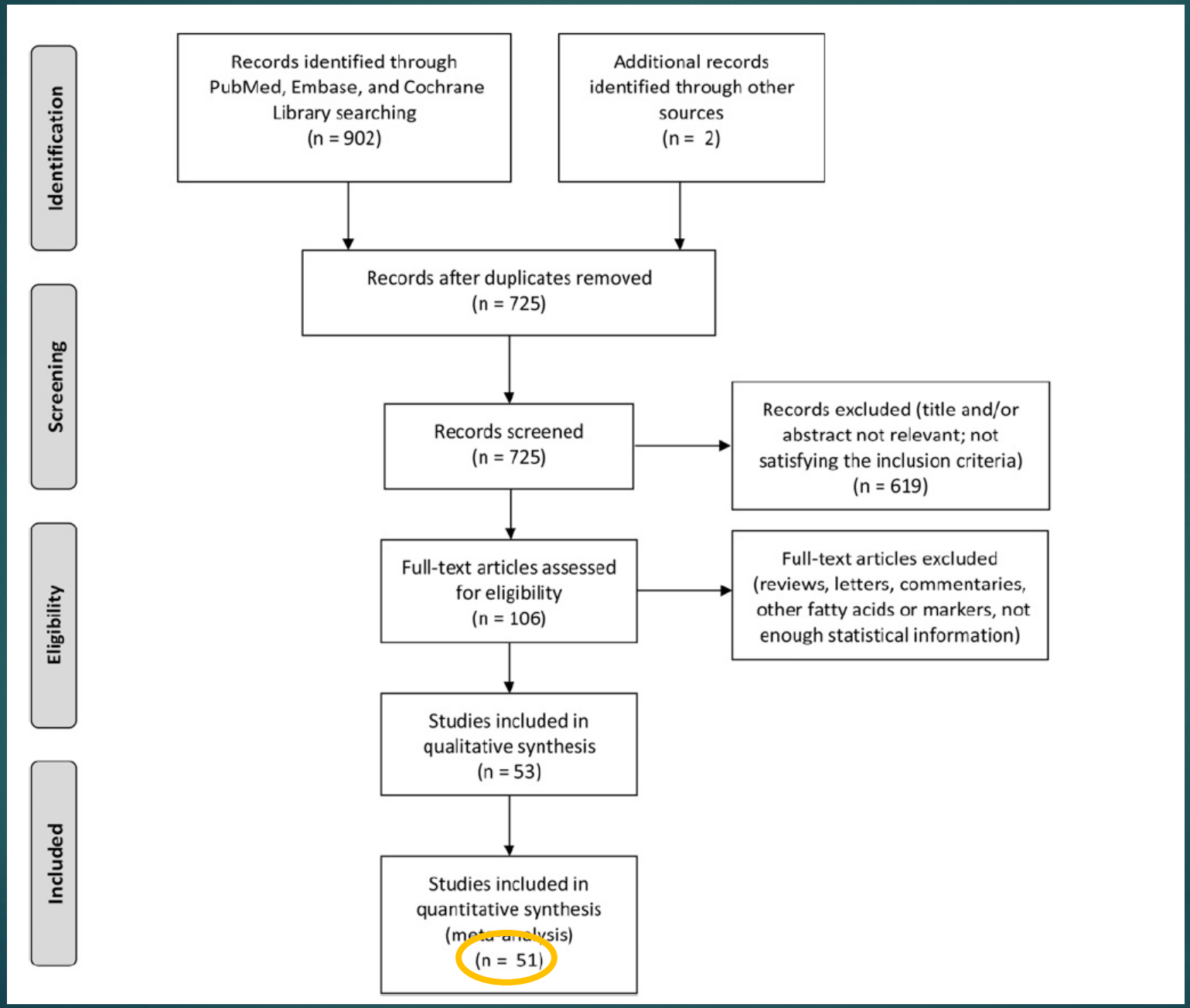
- •stearic acid
- •myristic and/or lauric acid
- •monounsaturated fatty acids (**MUFA)**, mainly in oleic acid
- •polyunsaturated fatty acids (**PUFA)**, mainly linoleic acid
- •partially hydrogenated fatty acids (**TRANS)**
- •interesterified (**IE**) palm oil or with palmitic acid occurring in sn-2 position

O = Outcomes TC, LDL-C , HDL-C TC/HDL-C ratio, LDL-C/HDL-C, TAG, Apo AI, Apo B, VLDL, Lp(a)

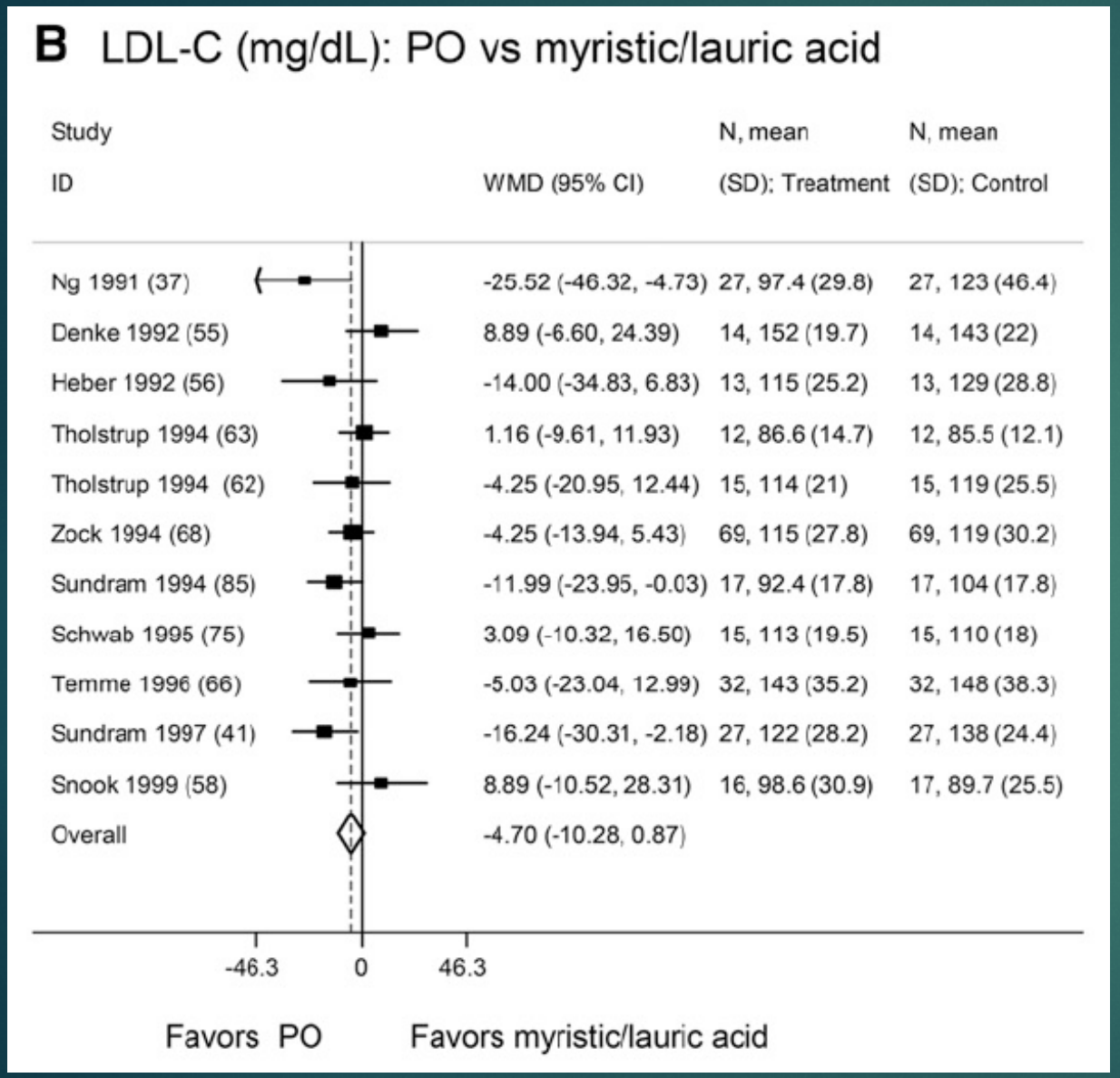
Inclusion Criteria:

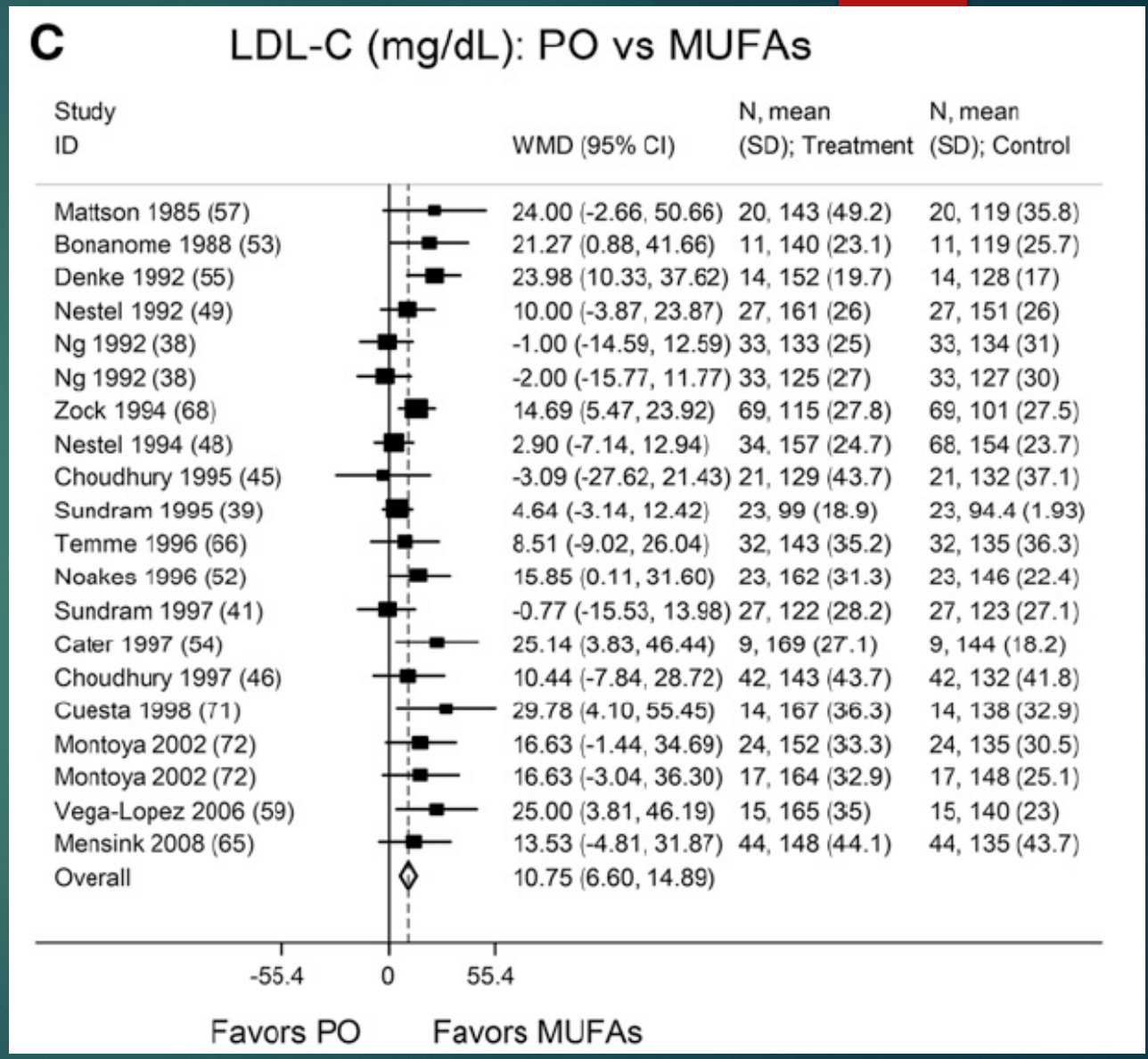
- **Control and intervention diets, and the exchange of the test fat, should be iso-energetic**
- **Estimate of mean values, and a corresponding measure of dispersion for the outcome**
- **Intervention duration over 2 weeks**

Flow chart study selection



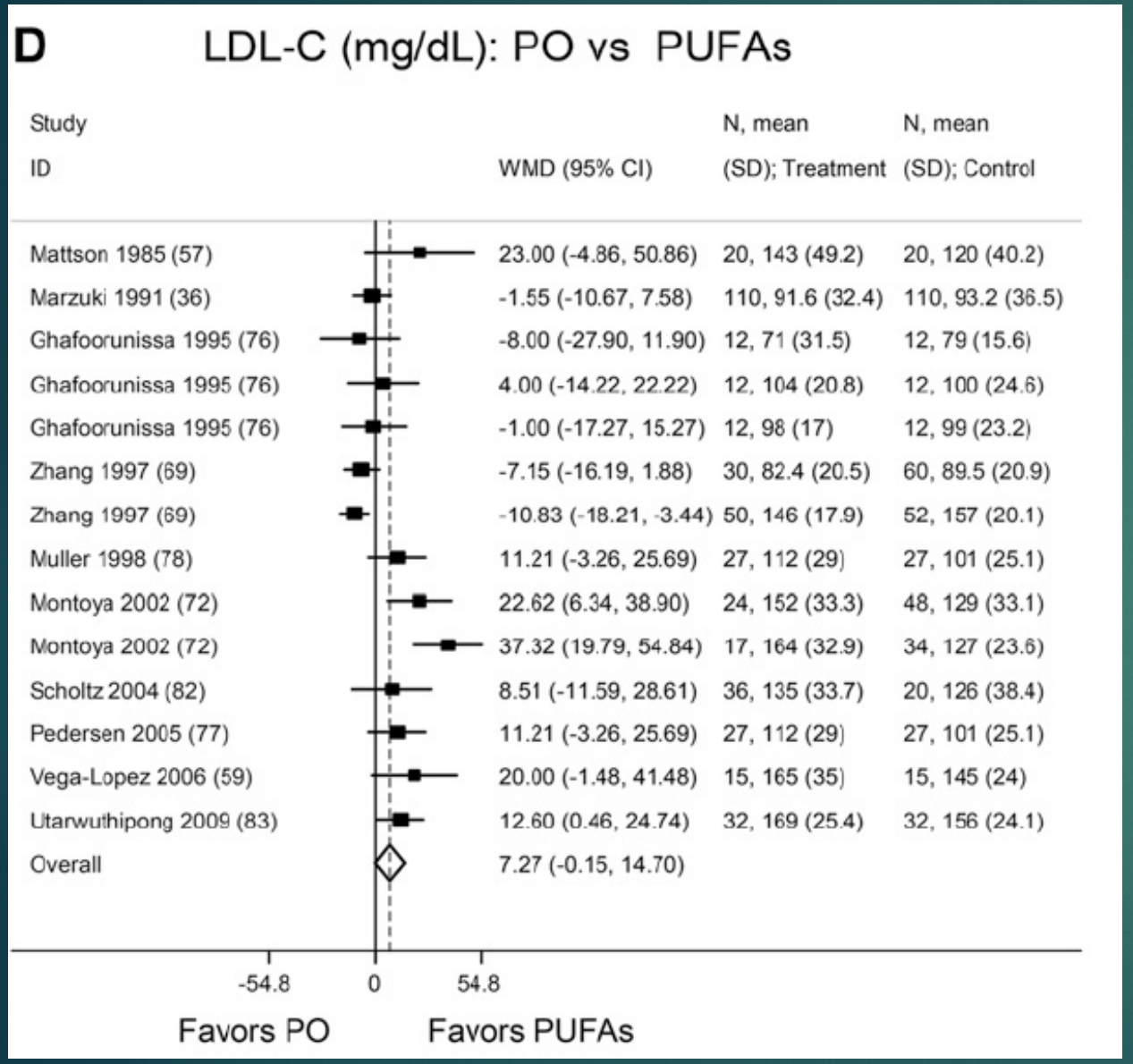
Results Palm Oil (PO) meta-analysis (1)

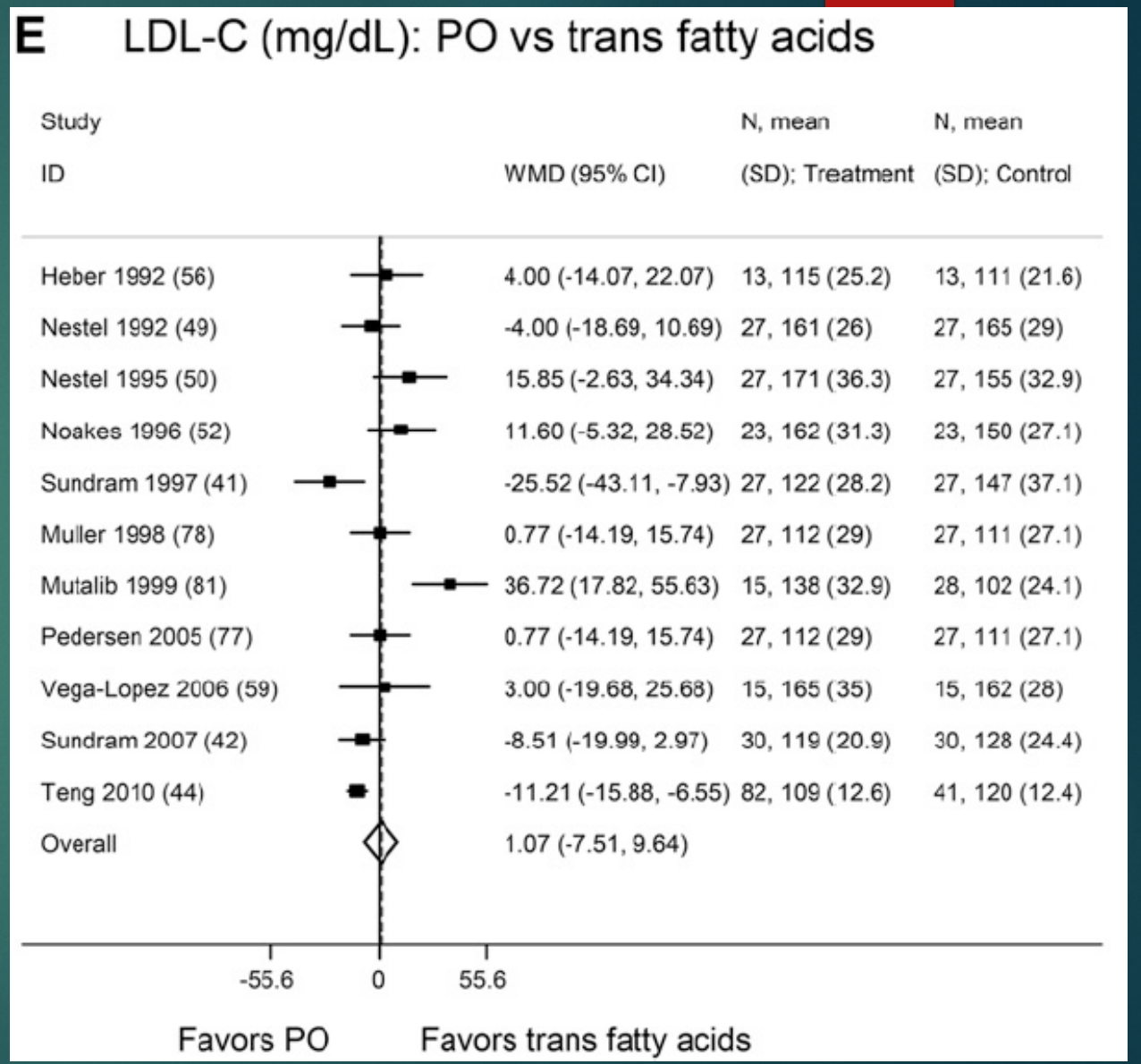




Am J Clin Nutr 2014;99:1331–50. Printed in USA. © 2014 American Society for Nutrition

Results Palm Oil (PO) meta-analysis (2)





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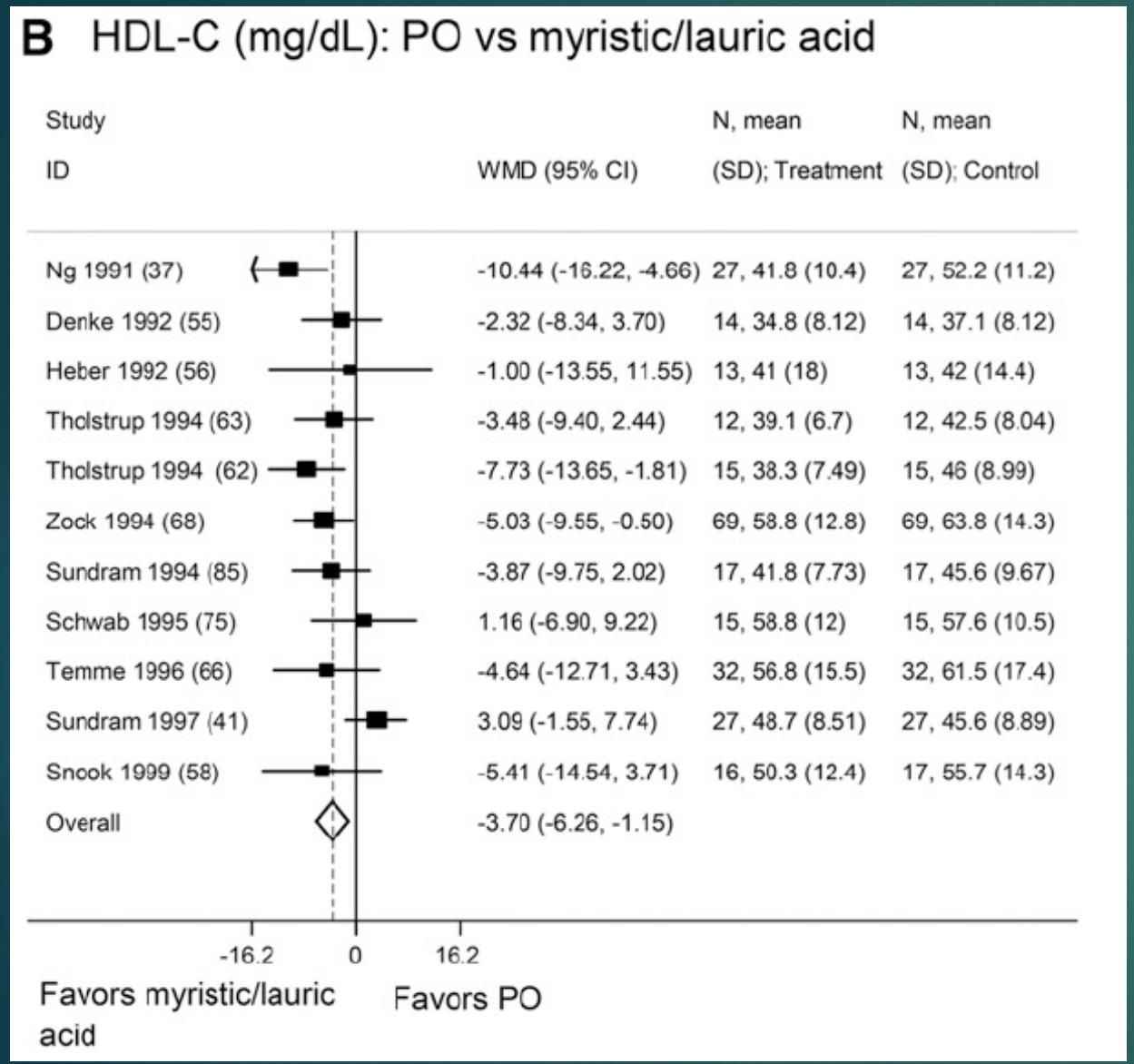
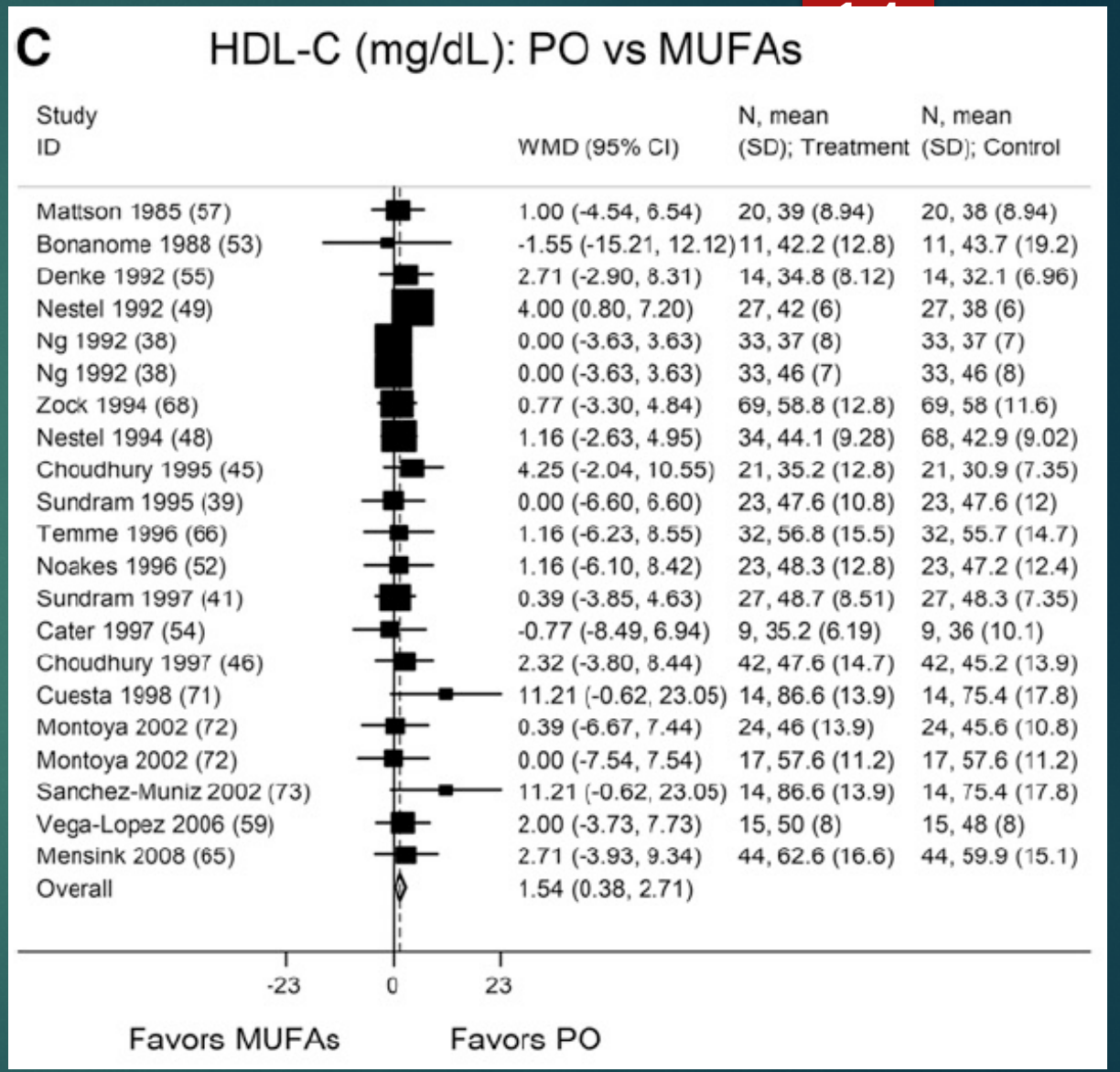
Results Palm Oil (PO) meta-analysis (3)





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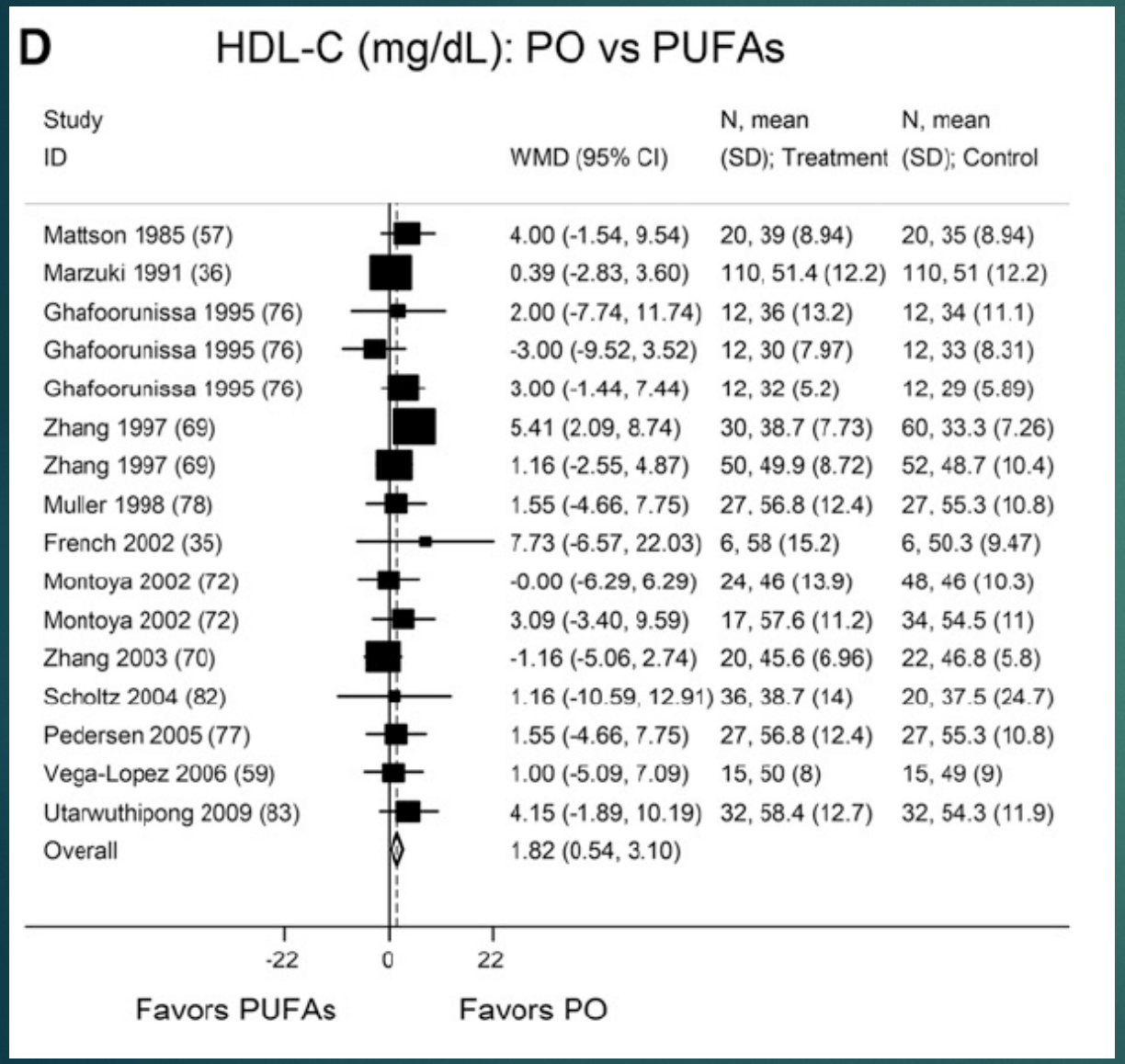
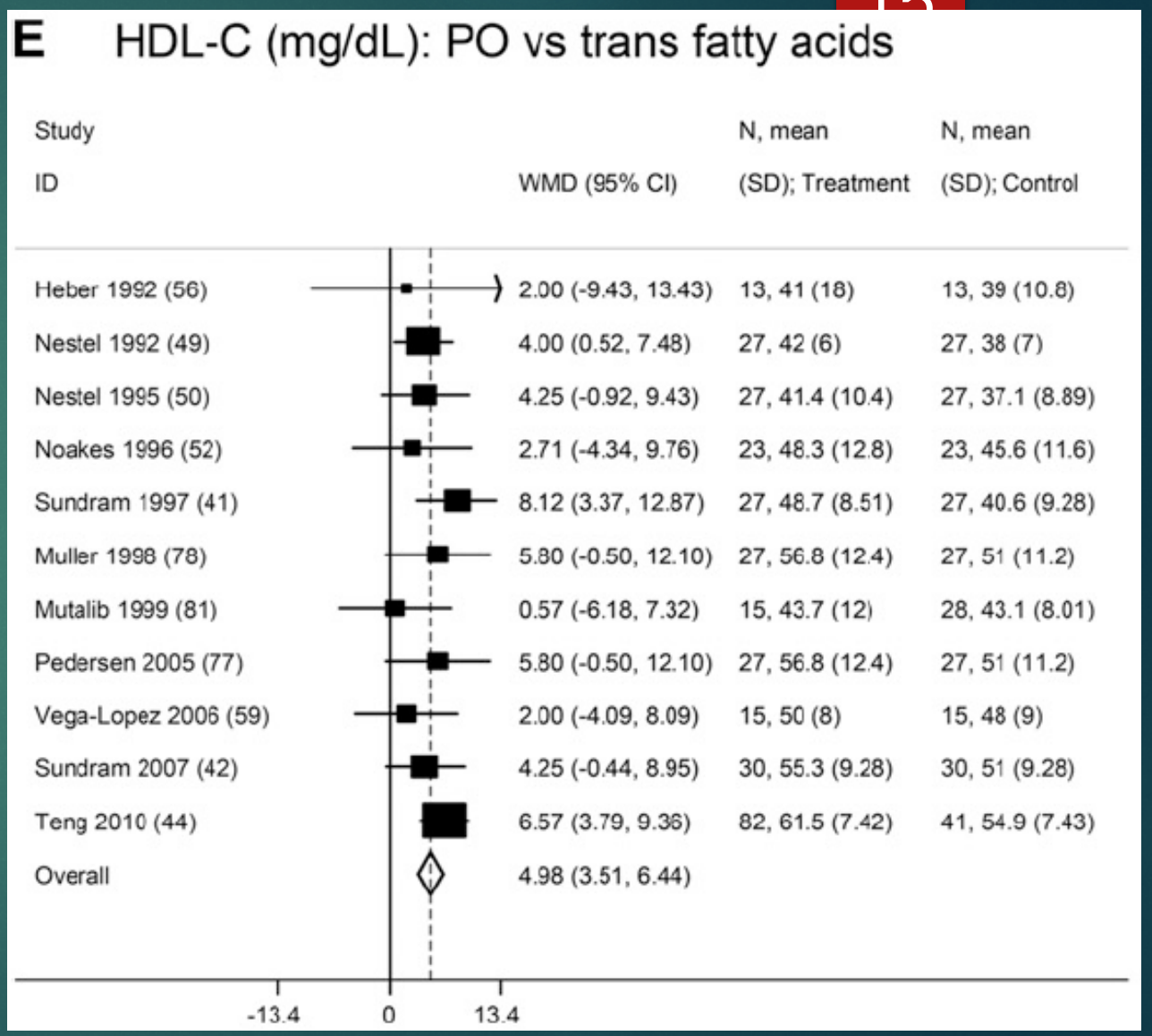
Results Palm Oil (PO) meta-analysis (4)





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Conclusions

The American Journal of Clinical Nutrition

Palm oil and blood lipid–related markers of cardiovascular disease: a systematic review and meta-analysis of dietary intervention trials[1–3]

Elena Fattore, Cristina Bosetti, Furio Brighenti, Carlo Agostoni, and Giovanni Fattore

ABSTRACT

Background: Palm oil (PO) may be an unhealthy fat because of its high saturated fatty acid content.

Objective: The objective was to assess the effect of substituting PO for other primary dietary fats on blood lipid–related markers of coronary heart disease (CHD) and cardiovascular disease (CVD).

Design: We performed a systematic review and meta-analysis of dietary intervention trials. Studies were eligible if they included original data comparing PO-rich diets with other fat-rich diets and analyzed at least one of the following CHD/CVD biomarkers: total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, TC/HDL cholesterol, LDL cholesterol/HDL cholesterol, triacylglycerols, apolipoprotein A-I and B, very-low-density lipoprotein cholesterol, and lipoprotein(a).

Results: Fifty-one studies were included. Intervention times ranged from 2 to 16 wk, and different fat substitutions ranged from 4% to 43%. Comparison of PO diets with diets rich in stearic acid, monounsaturated fatty acids (MUFAs), and polyunsaturated fatty acids (PUFAs) showed significantly higher TC, LDL cholesterol, apolipoprotein B, HDL cholesterol, and apolipoprotein A-I, whereas most of the same biomarkers were significantly lower when compared with diets rich in myristic/lauric acid. Comparison of PO-rich diets with diets rich in *trans* fatty acids showed significantly higher concentrations of HDL cholesterol and apolipoprotein A-I and significantly lower apolipoprotein B, triacylglycerols, and TC/HDL cholesterol. Stratified and meta-regression analyses showed that the higher concentrations of TC and LDL cholesterol, when PO was substituted for MUFAs and PUFAs, were not significant in young people and in subjects with diets with a lower percentage of energy from fat.

Conclusions: Both favorable and unfavorable changes in CHD/CVD risk markers occurred when PO was substituted for the primary dietary fats, whereas only favorable changes occurred when PO was substituted for *trans* fatty acids. Additional studies are needed to provide guidance for policymaking. *Am J Clin Nutr* 2014;99:1331–50.

morbidity and mortality (5). These recommendations were put forward because dietary SFAs increase blood total cholesterol (TC) and LDL cholesterol, which are known risk factors for CHD and CVD (6). However, not all studies have supported the relation between SFAs and CHD or CVD (7–11), and research on individual dietary fats has shown that different SFAs can exert different effects on cholesterolemia (12) and not only the type of fatty acid, but also the triacylglycerol structure, plays a role (13). In addition, conflicting results have recently emerged regarding the benefit of substituting SFAs with PUFAs on major cardiovascular outcomes (14–16).

Overall, during the past several years, a more complex picture concerning the risk factors for CVD has been developed. In addition to the major traditional serum/plasma markers of CHD risk (ie, TC, LDL cholesterol, HDL cholesterol, and triacylglycerols), other lipid-related biomarkers, such as apolipoprotein A-I and -B, which are the main protein components of HDL cholesterol and LDL cholesterol, respectively, and lipoprotein(a), have been suggested to be valid, if not better, risk predictors (17–20).

Palm oil (PO), a vegetable oil obtained from the fruit of the palm tree (*Elaeis guineensis*), is composed of ~50% palmitic acid, 40% oleic acid, and 10% linoleic acid. Palmitic acid, in addition to being the most abundant constituent of PO, is the main SFA that naturally occurs in animal and vegetable fats and is the main component of human milk fats (21). Over the past few years, PO use has significantly increased, despite debates over whether it is a potential unhealthy fat because of its relatively high palmitic

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Palm Oil Consumption Increases LDL Cholesterol Compared with Vegetable Oils Low in Saturated Fat in a Meta-Analysis of Clinical Trials[1–3]

Ye Sun,[4,7] Nithya Neelakantan,[4] Yi Wu,[4] Rashmi Lote-Oke,[4] An Pan,[4] and Rob M van Dam[4–7]*

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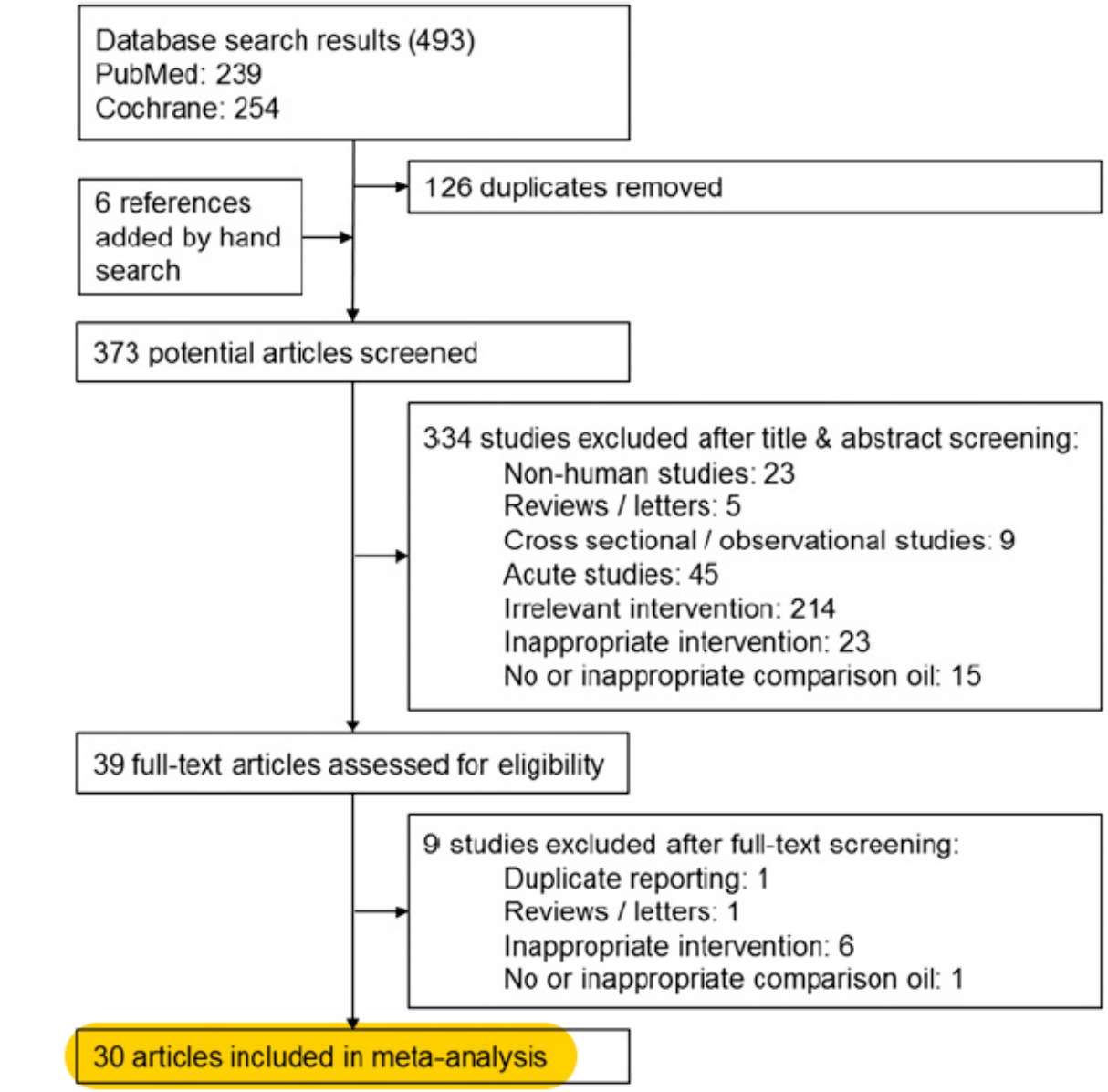
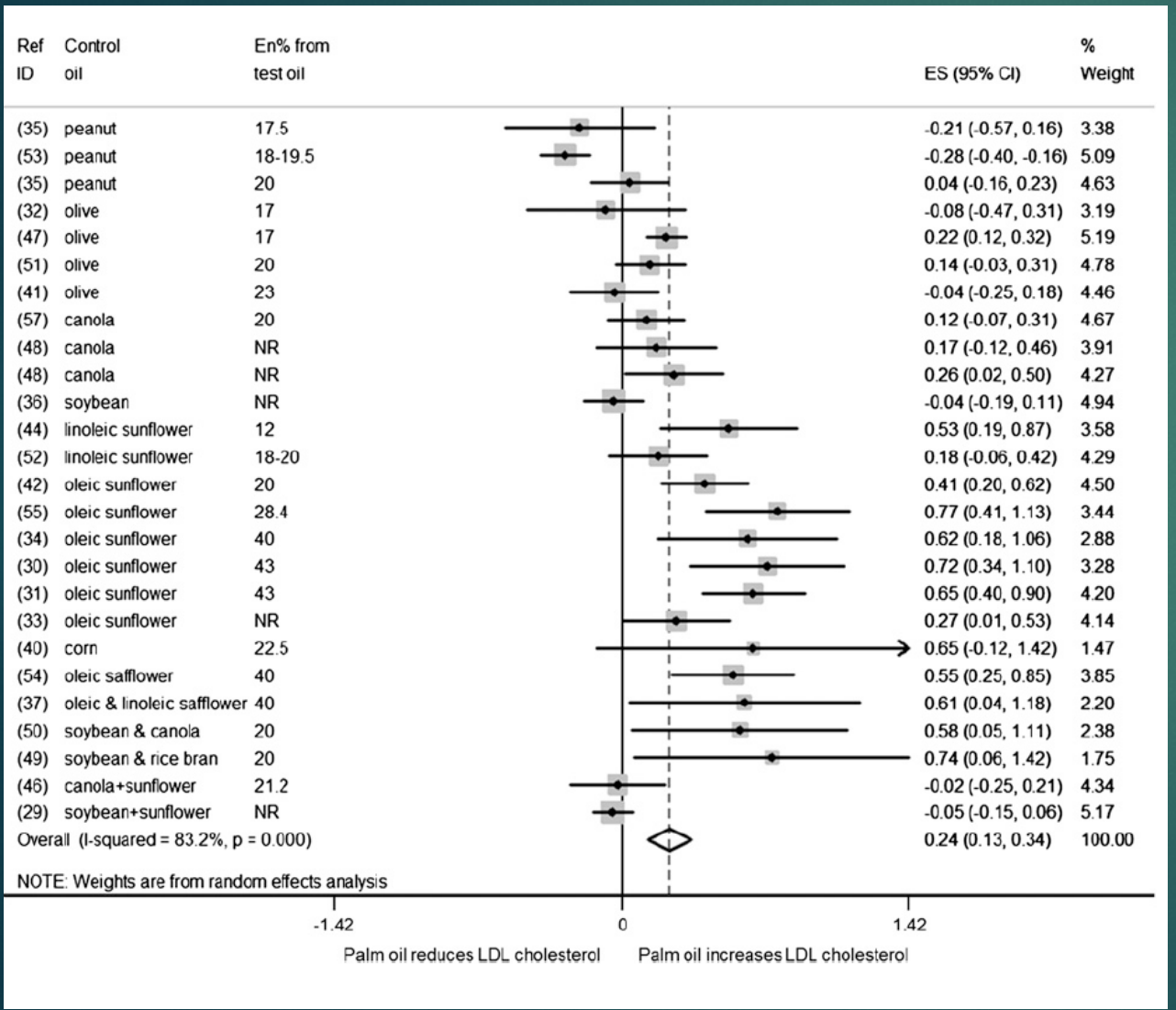


FIGURE 1 Flow diagram for selection of studies for meta-analysis.

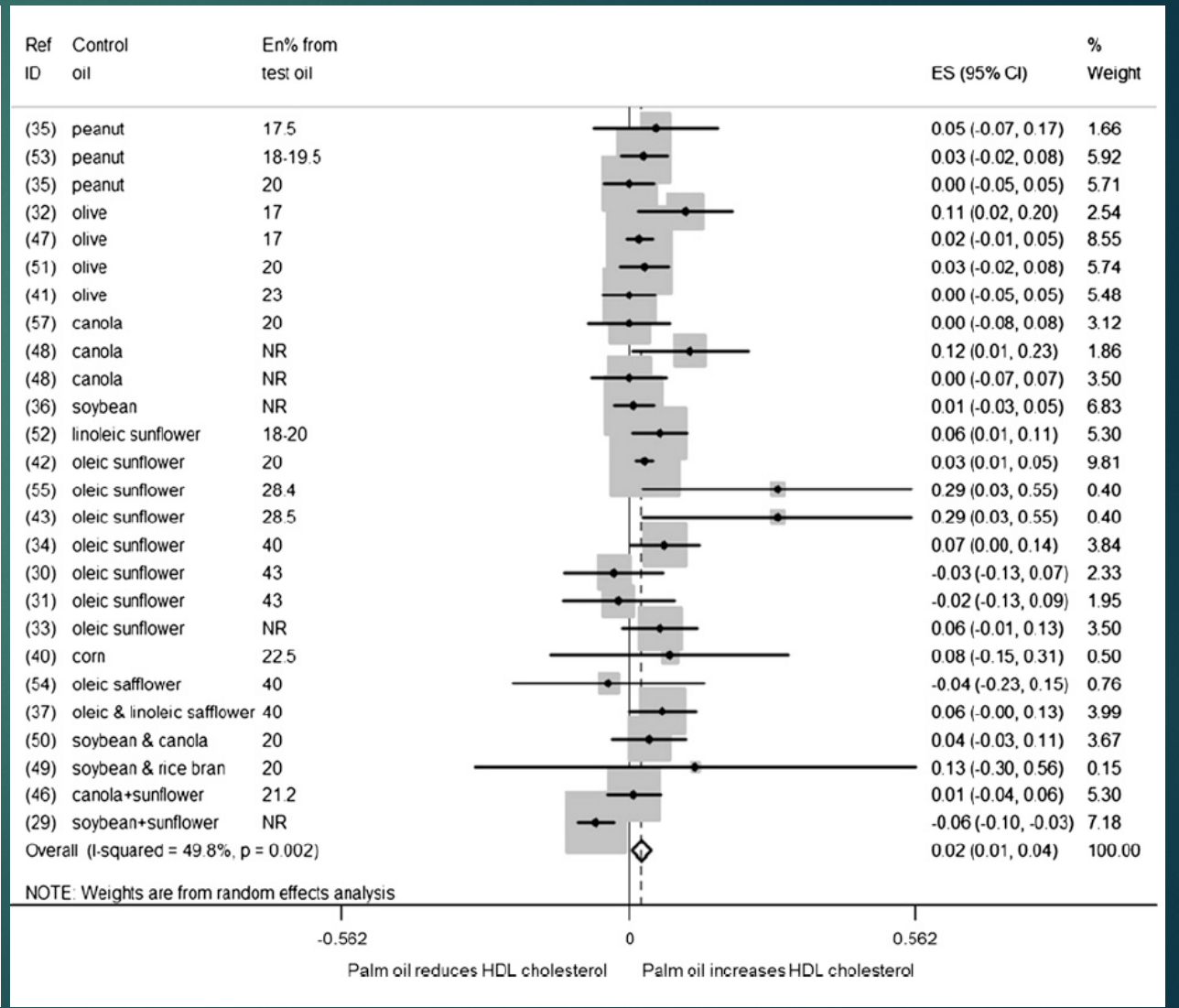
Sun et al., Journal of Nutrition 2015

Results (Sun et al., Journal of Nutrition 2015) (1)

LDL-C PO vs vegetable oils

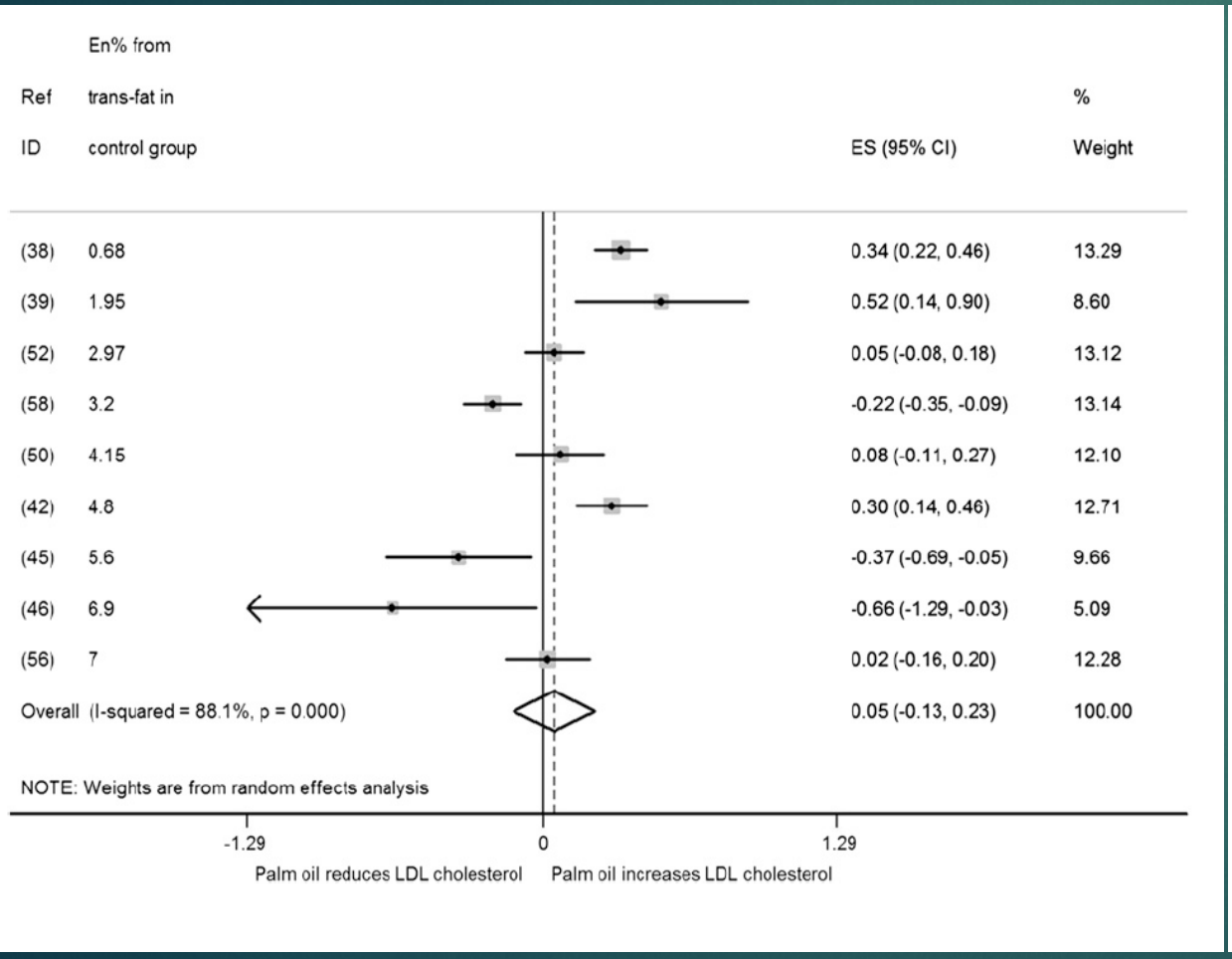


HDL-C PO vs vegetable oils

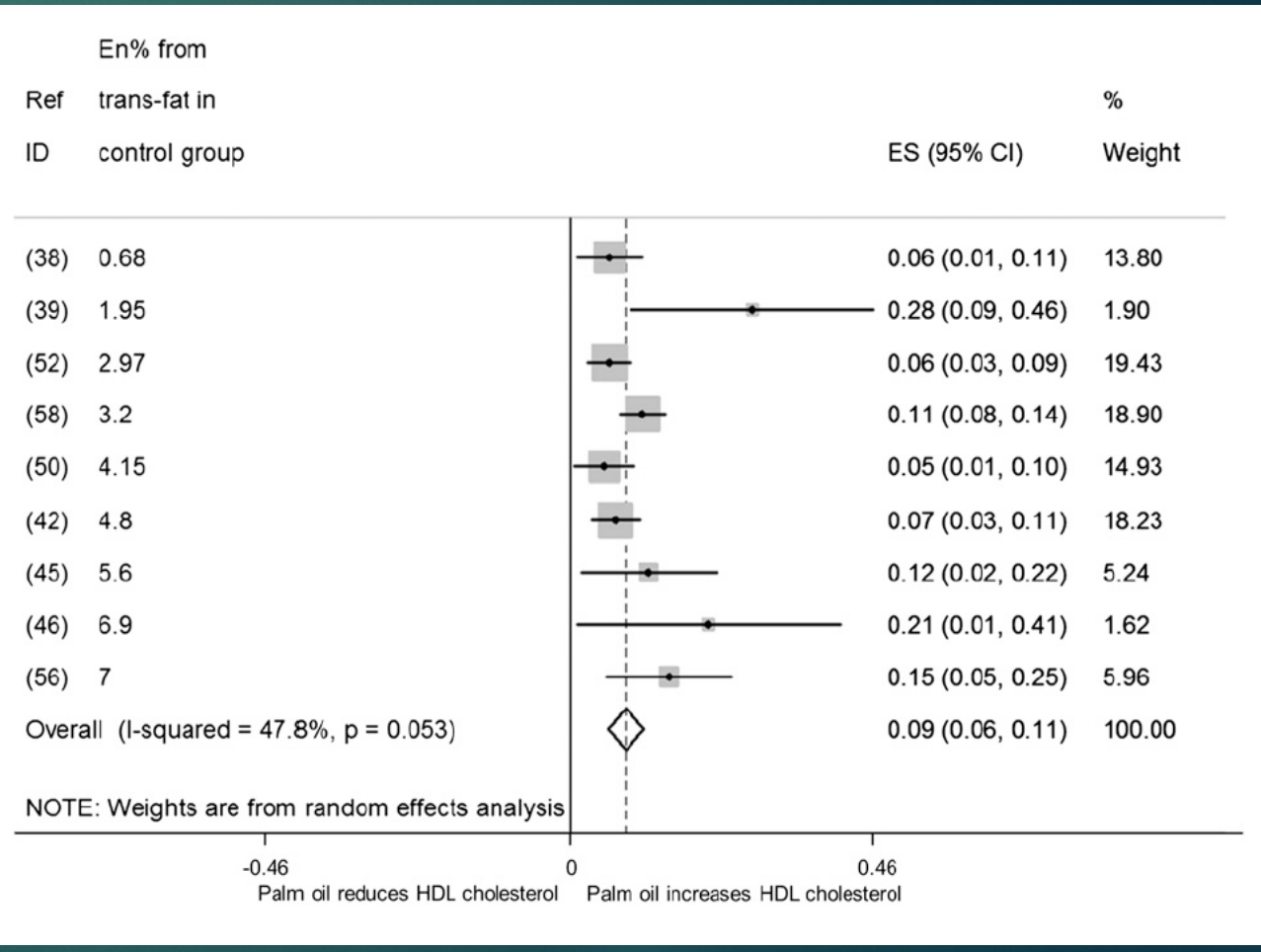


Results (Sun et al., Journal of Nutrition 2015) (1)

LDL-C PO vs partially hydrogenated vegetable oils



HDL-C PO vs partially hydrogenated vegetable oils



Conclusions

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Palm Oil Consumption Increases LDL Cholesterol Compared with Vegetable Oils Low in Saturated Fat in a Meta-Analysis of Clinical Trials[1–3]

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[4]Saw Swee Hock School of Public Health and [5]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore; [6]Department of Nutrition, Harvard School of Public Health, Boston, MA; and [7]NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore

Abstract

Background: Palm oil contains a high amount of saturated fat compared with most other vegetable oils, but studies have reported inconsistent effects of palm oil on blood lipids.

Objective: We systematically reviewed the effect of palm oil consumption on blood lipids compared with other cooking oils using data from clinical trials.

Methods: We searched PubMed and the Cochrane Library for trials of at least 2 wk duration that compared the effects of palm oil consumption with any of the predefined comparison oils: vegetable oils low in saturated fat, *trans* fat–containing partially hydrogenated vegetable oils, and animal fats. Data were pooled by using random-effects meta-analysis.

Results: Palm oil significantly increased LDL cholesterol by 0.24 mmol/L (95% CI: 0.13, 0.35 mmol/L; I^2 = 83.2%) compared with vegetable oils low in saturated fat. This effect was observed in randomized trials (0.31 mmol/L; 95% CI: 0.20, 0.42 mmol/L) but not in nonrandomized trials (0.03 mmol/L; 95% CI: −0.15, 0.20 mmol/L; *P*-difference = 0.02). Among randomized trials, only modest heterogeneity in study results remained after considering the test oil dose and the comparison oil type (I^2 = 27.5%). Palm oil increased HDL cholesterol by 0.02 mmol/L (95% CI: 0.01, 0.04 mmol/L; I^2 = 49.8%) compared with vegetable oils low in saturated fat and by 0.09 mmol/L (95% CI: 0.06, 0.11 mmol/L; I^2 = 47.8%) compared with *trans* fat–containing oils.

Conclusions: Palm oil consumption results in higher LDL cholesterol than do vegetable oils low in saturated fat and higher HDL cholesterol than do *trans* fat–containing oils in humans. The effects of palm oil on blood lipids are as expected on the basis of its high saturated fat content, which supports the reduction in palm oil use by replacement with vegetable oils low in saturated and *trans* fat. This systematic review was registered with the PROSPERO registry at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42012002601#.VU3wvSGeDRZ as CRD42012002601. *J Nutr* 2015;145:1549–58.

3. Scientific evidence on saturated fatty acids and cardiovascular diseases – old and new studies

Ancel Keys

The Seven Countries Study

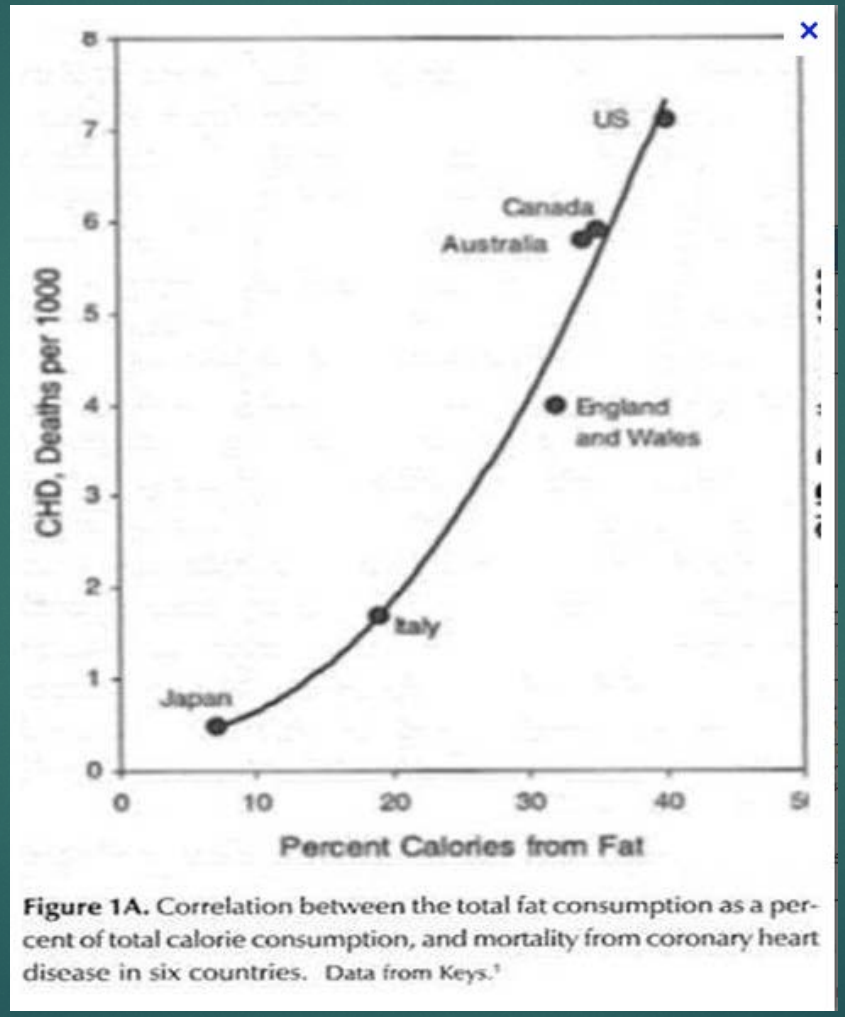
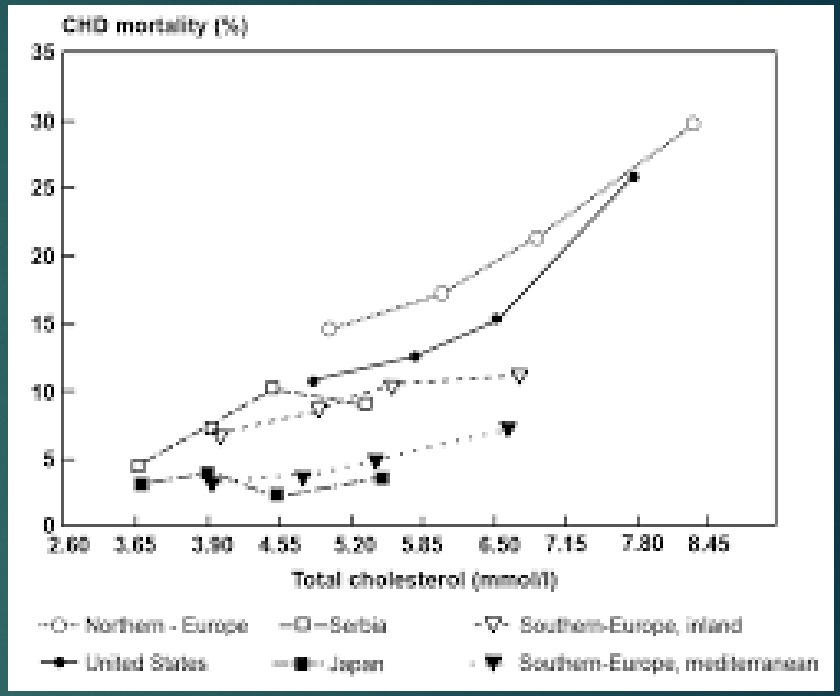


Figure 1A. Correlation between the total fat consumption as a percent of total calorie consumption, and mortality from coronary heart disease in six countries. Data from Keys.[1]



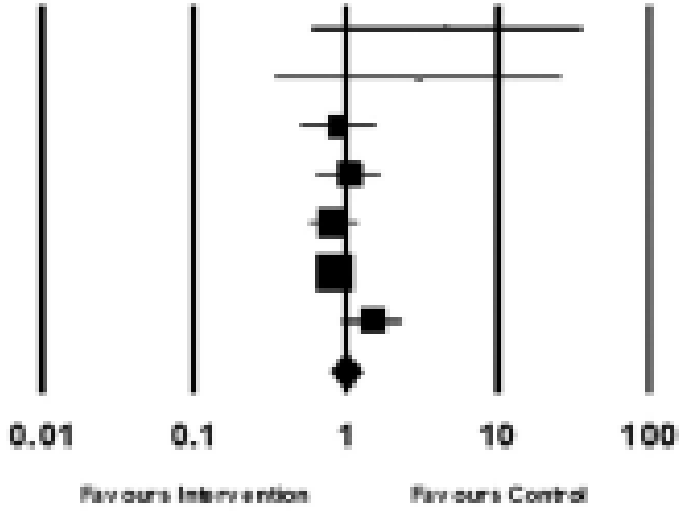
The Lipid Theory

openheart

Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977

Dietary Intervention & Heart Deaths

Study name	Risk ratio	Lower limit	Upper limit	Heart Deaths / Total Intervention	Control
Rose Corn Oil (1965)	4.643	0.580	37.149	5 / 28	1 / 26
Rose Olive Oil (1965)	3.000	0.333	26.992	3 / 26	1 / 26
Research Committee Low-Fat (1965)	0.891	0.490	1.620	17 / 123	20 / 129
MRC Soybean Oil (1968)	1.053	0.634	1.748	27 / 199	25 / 194
LA Veterans Dayton (1969)	0.816	0.552	1.206	41 / 424	50 / 422
Leren, Oslo heart study (1970)	0.840	0.669	1.056	79 / 206	94 / 206
Woodhill, Sydney heart study (1978)	1.501	0.930	2.425	35 / 221	25 / 237
	0.969	0.794	1.247		



Meta Analysis Random Effects Method

Figure 3 Estimates of CHD mortality (95% CIs) from meta-analysis.

University of the West of Scotland, Hamilton, Lanarkshire, UK
[2]Cardiff School of Sport, Cardiff Metropolitan University, Cardiff, UK
[3]University of South Wales,

were untested in any trial prior to being introduced.
Conclusions: Dietary recommendations were introduced for 220 million US and 56 million UK citizens by 1983, in the absence of supporting evidence from RCTs.

sumption to 30% of total energy intake and (2) reduce saturated fat consumption to 10% of total energy intake.

The recommendations were an attempt to address the incidence of coronary heart

Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73)

Christopher E Ramsden,[1,2] Daisy Zamora,[3] Sharon Majchrzak-Hong,[1] Keturah R Faurot,[2] Steven K Broste,[4] Robert P Frantz,[5] John M Davis,[3,6] Amit Ringel,[1] Chirayath M Suchindran,[7] Joseph R Hibbeln[1]

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Accepted: 19 February 2016

ABSTRACT

OBJECTIVE

To examine the traditional diet-heart hypothesis through recovery and analysis of previously unpublished data from the Minnesota Coronary Experiment (MCE) and to put findings in the context of existing diet-heart randomized controlled trials through a systematic review and meta-analysis.

DESIGN

The MCE (1968-73) is a double blind randomized controlled trial designed to test whether replacement of saturated fat with vegetable oil rich in linoleic acid reduces coronary heart disease and death by lowering serum cholesterol. Recovered MCE unpublished documents and raw data were analyzed according to hypotheses prespecified by original investigators. Further, a systematic review and meta-analyses of randomized controlled trials that lowered serum cholesterol by providing vegetable oil rich in linoleic acid in place of saturated fat without confounding by concomitant interventions was conducted.

SETTING

One nursing home and six state mental hospitals in Minnesota, United States.

PARTICIPANTS

Unpublished documents with completed analyses for the randomized cohort of 9423 women and men aged 20-97; longitudinal data on serum cholesterol for the 2355 participants exposed to the study diets for a year or more; 149 completed autopsy files.

INTERVENTIONS

Serum cholesterol lowering diet that replaced saturated fat with linoleic acid (from corn oil and corn oil polyunsaturated margarine). Control diet was high in saturated fat from animal fats, common margarines, and shortenings.

MAIN OUTCOME MEASURES

Death from all causes; association between changes in serum cholesterol and death; and coronary atherosclerosis and myocardial infarcts detected at autopsy.

RESULTS

The intervention group had significant reduction in serum cholesterol compared with controls (mean change from baseline −13.8% *v* −1.0%; P<0.001). Kaplan Meier graphs showed no mortality benefit for the intervention group in the full randomized cohort or for any prespecified subgroup. There was a 22% higher risk of death for each 30 mg/dL (0.78 mmol/L) reduction in serum cholesterol in covariate adjusted Cox regression models (hazard ratio 1.22, 95% confidence interval 1.14 to 1.32; P<0.001). There was no evidence of benefit in the intervention group for coronary atherosclerosis or myocardial infarcts. Systematic review identified five randomized controlled trials for inclusion (n=10 808). In meta-analyses, these cholesterol lowering interventions showed no evidence of benefit on mortality from coronary heart disease (1.13, 0.83 to 1.54) or all cause mortality (1.07, 0.90 to 1.27).

CONCLUSIONS

Available evidence from randomized controlled trials shows that replacement of saturated fat in the diet with linoleic acid effectively lowers serum cholesterol but does not support the hypothesis that this translates to a lower risk of death from coronary heart disease or all causes. Findings from the Minnesota

Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73)

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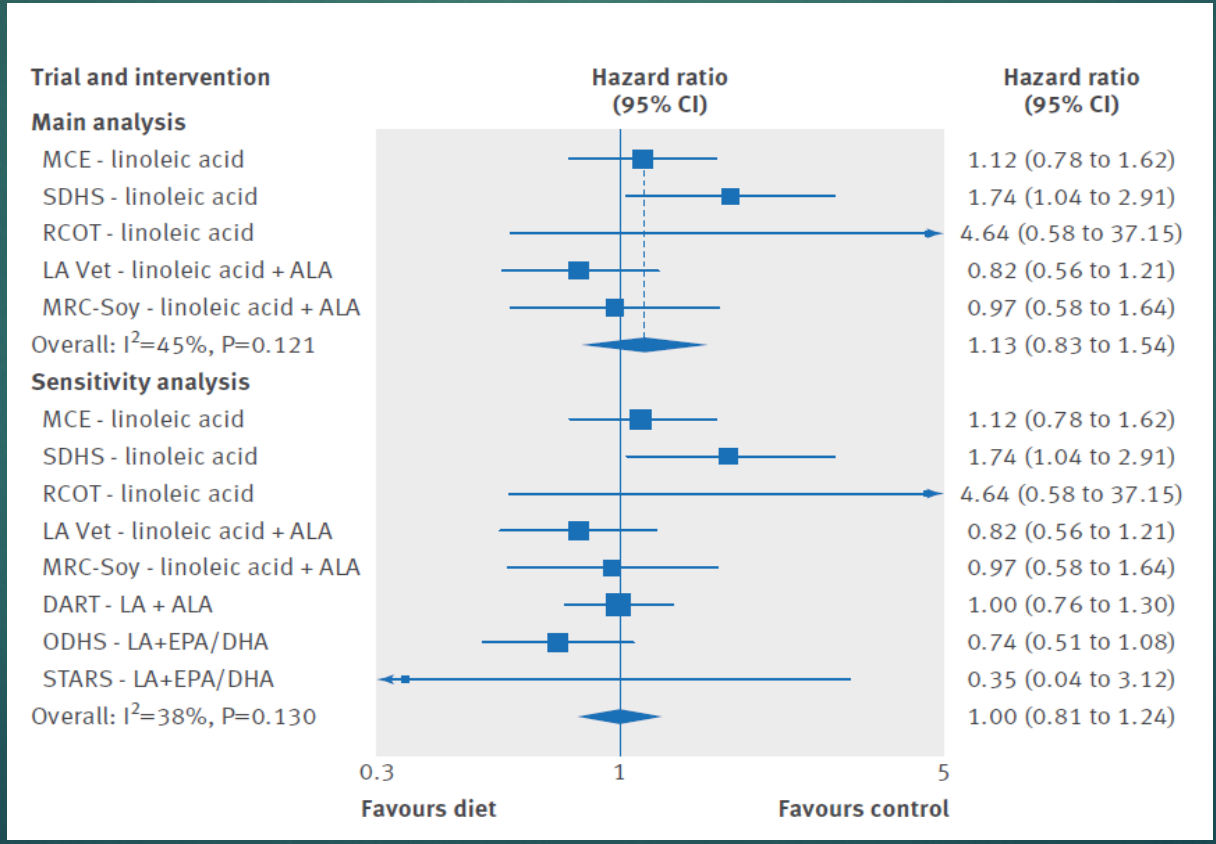

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Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study

Interpretation High carbohydrate intake was associated with higher risk of total mortality, whereas total fat and individual types of fat were related to lower total mortality. Total fat and types of fat were not associated with cardiovascular disease, myocardial infarction, or cardiovascular disease mortality, whereas saturated fat had an inverse association with stroke. Global dietary guidelines should be reconsidered in light of these findings.

Association of dietary nutrients with blood lipids and blood pressure in 18 countries: a cross-sectional analysis from the PURE study

Interpretation Our data are at odds with current recommendations to reduce total fat and saturated fats. Reducing saturated fatty acid intake and replacing it with carbohydrate has an adverse effect on blood lipids. Substituting saturated fatty acids with unsaturated fats might improve some risk markers, but might worsen others. Simulations suggest that ApoB-to-ApoA1 ratio probably provides the best overall indication of the effect of saturated fatty acids on cardiovascular disease risk among the markers tested. Focusing on a single lipid marker such as LDL cholesterol alone does not capture the net clinical effects of nutrients on cardiovascular risk.

Conclusions

- There is not a scientific evidence on advantage/disadvantage from substitution of palm oil by other main dietary fats (trans fatty acids excluded)
- A more complex picture has emerged about the lipid biomarkers related to cardiovascular diseases: total serum cholesterol or LDL-cholesterol seem to be not valid predictors.
- The soundness of the scientific evidence underpinning current and previous dietary advice on dietary fat intake for total fats and SFA has been questioned (no causal relation)

Thank you
for your attention !

REVIEW | Annals of Internal Medicine

Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk

A Systematic Review and Meta-analysis

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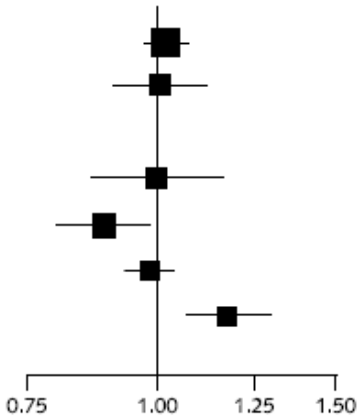
Figure 1. RRs for coronary outcomes in prospective cohort studies of dietary fatty acid intake.

Fatty Acid Intake	Studies, *n*	Participants, *n*	Events, *n*	RR (95% CI)*
Total saturated fatty acids	20	276 763	10 155	1.03 (0.98–1.07)
Total monounsaturated fatty acids	9	144 219	6031	1.00 (0.91–1.10)
Total ω-3 fatty acids				
α-Linolenic	7	157 258	7431	0.99 (0.86–1.14)
Total long-chain ω-3	16	422 786	9089	0.87 (0.78–0.97)
Total ω-6 fatty acids	8	206 376	8155	0.98 (0.90–1.06)
Total trans fatty acids	5	155 270	4662	1.16 (1.06–1.27)



RR (95% CI) Comparing Top vs. Bottom Thirds of Baseline Dietary Fatty Acid Intake

Size of the data marker is proportional to the inverse of the variance of the RR. RR = relative risk.
* Pooled estimate based on random-effects meta-analysis. Corresponding forest plots, I^2 estimates, and pooled RRs based on fixed-effects meta-analysis are provided in **Supplement 1**, available at www.annals.org.

Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

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ABSTRACT

OBJECTIVE
To systematically review associations between intake of saturated fat and trans unsaturated fat and all cause mortality, cardiovascular disease (CVD) and associated mortality, coronary heart disease (CHD) and associated mortality, ischemic stroke, and type 2 diabetes.

DESIGN
Systematic review and meta-analysis.

DATA SOURCES
Medline, Embase, Cochrane Central Registry of Controlled Trials, Evidence-Based Medicine Reviews, and CINAHL from inception to 1 May 2015, supplemented by bibliographies of retrieved articles and previous reviews.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES
Observational studies reporting associations of saturated fat and/or trans unsaturated fat (total, industrially manufactured, or from ruminant animals) with all cause mortality, CHD/CVD mortality, total CHD, ischemic stroke, or type 2 diabetes.

DATA EXTRACTION AND SYNTHESIS
Two reviewers independently extracted data and assessed study risks of bias. Multivariable relative risks were pooled. Heterogeneity was assessed and quantified. Potential publication bias was assessed and subgroup analyses were undertaken. The GRADE approach was used to evaluate quality of evidence and certainty of conclusions.

RESULTS
For saturated fat, three to 12 prospective cohort studies for each association were pooled (five to 17 comparisons with 90 501-339 090 participants). Saturated fat intake was not associated with all cause mortality (relative risk 0.99, 95% confidence interval 0.91 to 1.09), CVD mortality (0.97, 0.84 to 1.12), total CHD (1.06, 0.95 to 1.17), ischemic stroke (1.02, 0.90 to 1.15), or type 2 diabetes (0.95, 0.88 to 1.03). There was no convincing lack of association between saturated fat and CHD mortality (1.15, 0.97 to 1.36; P=0.10). For trans fats, one to six prospective cohort studies for each association were pooled (two to seven comparisons with 12 942-230 135 participants). Total trans fat intake was associated with all cause mortality (1.34, 1.16 to 1.56), CHD mortality (1.28, 1.09 to 1.50), and total CHD (1.21, 1.10 to 1.33) but not ischemic stroke (1.07, 0.88 to 1.28) or type 2 diabetes (1.10, 0.95 to 1.27). Industrial, but not ruminant, trans fats were associated with CHD mortality (1.18 (1.04 to 1.33) *v* 1.01 (0.71 to 1.43)) and CHD (1.42 (1.05 to 1.92) *v* 0.93 (0.73 to 1.18)). Ruminant *trans*-palmitoleic acid was inversely associated with type 2 diabetes (0.58, 0.46 to 0.74). The certainty of associations between saturated fat and all outcomes was "very low." The certainty of associations of trans fat with CHD outcomes was "moderate" and "very low" to "low" for other associations.

CONCLUSIONS
Saturated fats are not associated with all cause mortality, CVD, CHD, ischemic stroke, or type 2 diabetes, but the evidence is heterogeneous with methodological limitations. Trans fats are associated with all cause mortality, total CHD, and CHD mortality, probably because of higher levels of intake of industrial trans fats than ruminant trans fats. Dietary guidelines must carefully consider the health effects of recommendations for alternative macronutrients to replace trans fats and saturated fats.

WHAT IS ALREADY KNOWN ON THIS TOPIC
Contrary to prevailing dietary advice, authors of a recent systematic review and meta-analyses claim that there is no excess cardiovascular risk associated with intake of saturated fat, and the US has recently taken policy action to remove partially hydrogenated vegetable oils from its food supply

No associations between saturated fatty acids and cardiovascular outocomes
Positive association with partially hydrogenated fatty acids