sacn

Scientific Advisory Committee on Nutrition

Annexes to draft SACN report on saturated fats and health

Scientific consultation: 8 May to 3 July 2018

CONTENTS

ANNEX 1: Search terms

	Embase	**Medline**	**Cochrane**	**Scopus**
fats	*SATURATED FAT/ OR *SATURATED FATTY ACID/ saturate* AND (fat* or "fatty acid*" or lipid*)	saturate* AND (fat* or "fatty acid*" or lipid*)	saturated AND (fat* or "fatty acid*" or lipid*)	saturated AND (fat* or "fatty acid*" or lipid*)
sources	(saturat* OR type* OR source* OR animal OR dairy) ADJ2 (fat* OR lipid* OR "fatty acid*")	(saturat* OR type* OR source* OR animal OR dairy) ADJ2 (fat* OR lipid* OR "fatty acid*")	(saturat* OR type* OR source* OR animal OR dairy) NEAR (fat* OR lipid* OR "fatty acid*")	(saturat* OR type* OR source* OR animal OR dairy) W/2 (fat* OR lipid* OR "fatty acid*")
study type filters (terms)	SYSTEMATIC REVIEW/ systematic ADJ2 (review* or overview*)	systematic ADJ2 (review* or overview*)		systematic W/2 (review* or overview*)
	META-ANALYSIS/ "meta analys*" or meta-analys* pooled ADJ (analys* OR mean OR estimate*)	"meta analys*" or meta-analys* pooled ADJ (analys* OR mean OR estimate*)		"meta analys*" or meta-analys* pooled W/0 (analys* OR mean OR estimate*)
study type filters (database)			Cochrane reviews other reviews	
date filter	1991-current	1991-current	1991-current	1991-current

ANNEX 2: Characteristics of meta-analyses and systematic reviews

Cardiovascular diseases

Table A2.1 Characteristics of meta-analyses and systematic reviews

Study	Research methods	Analysis	Results	Comments
Harcombe et al. (2016a) (Systematic review) <u>Funding source</u> None declared. <u>Declarations of interest</u> Z Harcombe: receives income from writing and from two small self-employment businesses: The Harcombe Diet Co and Columbus Publishing.	<u>Research question</u> Assess if the published prospective cohort studies available to the dietary committees supported their recommendations on dietary fat. <u>Selection criteria</u> *Search dates:* Up to 5 September 1983. *Study design:* PCS. *Inclusion criteria:* Participants were human adults; primary study outcome was CHD mortality; data related to dietary fat consumption were available; data on CHD mortality and serum cholesterol measurements were available. *Exclusion criteria:* Clinical trials, cross-sectional studies, case-control studies. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Available data did not allow a meta-analysis. <u>Evaluation of study quality</u> Author judgement for each study on whether: cohort appropriately reflected wider population; blinding of outcome assessment; incomplete outcome data; selective reporting.	6 PCS; n=31,445 (range 337 – 12,770); duration: 4-20y (mean 7.5±6.2y (weighted mean [person years by participants] 5.6±0.8y)); age: 30-67y; gender: M (6); health at baseline: without previous heart disease (5), with previous heart disease (1); country: USA (2), UK (1), Puerto Rico (1), multi-country (2). <u>CHD mortality</u> 360 deaths from CHD (1.14%), mean follow-up 7.5±6.2y. 1 PCS found statistically significant association between CHD deaths and saturated fat intake.	No prospective cohort study available to dietary guideline committees found any association between saturated fat intake and deaths from heart disease in the same population. <u>Limitations</u> All evidence was undertaken on men. Evidence available at the time could not be generalised to women.

Study	Research methods	Analysis	Results	Comments
Harcombe et al. (2016b) (Systematic review with meta-analysis) <u>Funding source</u> None to declare. <u>Declarations of interest</u> None to declare.	<u>Research question</u> To extend the Harcombe et al. (2015) report, and re-examine the totality of RCT evidence relating to the current dietary fat guidelines. <u>Selection criteria</u> *Search dates:* Not specified. *Study design:* RCTs *Inclusion criteria:* Randomised dietary intervention study; study hypothesis relating to a reduction or modification of dietary fat; participants were human adults; study was a minimum of 1 year in duration; primary study outcome was all-cause and CHD mortality; data on all-cause mortality, CHD mortality, and cholesterol measurements were available. *Exclusion criteria:* Study being observational; non-randomised and/or multi factorial in design. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Random-effects meta-analysis. Heterogeneity and bias: I^2 and T^{-2} calculations. Publication bias: Funnel plot methodology and Effer's regression intercept were calculated. <u>Evaluation of study quality</u> Risk of bias assessed using the Cochrane Collaboration assessment tool for selection bias, performance/detection bias, attrition bias, and reporting bias. Sensitivity analysis of the exclusion of any one study.	10 RCTs; n=62,421; duration: 2-11y (mean 4.7±3.3y(weighted mean [person years by participants] 6.8±2y)); age: 30-70y; gender: M(8), F(1), M/F(1); health at baseline: primary and secondary prevention (2), primary prevention (1), secondary prevention (7); country: USA (3), UK (5), Norway (1), Australia (1). 6 RCTs did not examine total fat or saturated fat intakes of 30% and 10% of total energy respectively. 4 RCTs examined vegetable oil. 2 RCTs examined a diet of 10% energy as saturated fat (higher incidence of total and CHD mortality in intervention group in 1 RCT; no difference in total and CHD mortality in 1 RCT). <u>CHD mortality</u> 1218 deaths from CHD. RR 0.98 (95% CI 0.88, 1.08); Q-value=9.173; I^2=0.000; T^2=0.000. Excluding Women's Health Initiative (78% of the total participants, n=13,586), RR 0.96 (95% CI 0.85, 1.09)	RCT evidence does not support the current dietary fat guidelines. The reduction in serum cholesterol does not appear to translate into an improved survival from CHD.

Study	Research methods	Analysis	Results	Comments
Ramsden et al. (2016) (Systematic review and meta-analysis) <u>Funding source</u> US Public Health Service; National Heart Institute; The Intramural Program of the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health; University of North Carolina Program on Integrative Medicine (National Institutes of Health). <u>Declarations of interest</u> None to declare.	<u>Research question</u> Does replacement of saturated fat with linoleic acid rich vegetable oils decrease CHD and all-cause mortality by reducing serum LDL and total cholesterol? <u>Selection criteria</u> *Search dates:* 1950 to September 2015. *Study design:* RCTs. *Inclusion criteria:* Serum cholesterol-lowering RCTs published in English that: randomised participants; provided linoleic acid rich vegetable oil intervention in place of saturated fats, compared to usual care control diet; not confounded by addition of large quantities of n-3 EPA and DHA or other major concomitant interventions (e.g. complex dietary pattern changes) or unequal intensity of medical management (e.g. smoking cessation advice or blood pressure control); reported deaths due to CHD or all causes. *Exclusion criteria*: Excluded from main analysis, studies that: provided large quantities of EPA and DHA or advice only without provision of linoleic acid rich oils; only provided biochemical or intermediate endpoints. Sensitivity analyses included studies in: 1) exclusion criteria that otherwise met the inclusion and exclusion criteria. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Pooled risk estimates calculated for CHD death using random effects model. Heterogeneity: I^2 statistic and Tau-squared, and stratification by study oil. Publication bias: funnel plot visual inspection of treatment effect vs standard error. Sources of heterogeneity explored using stratified fixed effects meta-analysis (PUFA) and inverse variance weighted meta-regression (between group cholesterol reduction and increases in dietary linoleic acid). <u>Evaluation of study quality</u> Considerations included: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessments; selective reporting; systematic differences in between-group medical care; study-specific sources of potential bias.	5 RCTs; n=10,808; duration: ≤2 - ≤7y; age: not reported; gender: M (4), F (0), M/F (1); health at baseline: with or without CHD (2), history of CHD (3); country: USA (2), UK (2), Australia (1). <u>↑linoleic acid and ↓saturated fats</u> The mean change in serum cholesterol concentration in RCTs ranged from 7.8-13.8% lower in the intervention vs. the control groups. *CHD Mortality* (5 RCTs) No evidence of benefit on CHD mortality HR 1.13 (95% CI 0.83, 1.54) I^2 = 45.1% *Provision or advice to replace saturated fats with linoleic acid rich oils, with or without confounding by n-3 EPA+DHA* (8 RCTs) CHD mortality: HR 1.00 (95% CI 0.81, 1.24) I^2 = 37.5%	Replacement of saturated fat in the diet with linoleic acid lowers serum cholesterol but does not lower risk of death from CHD. <u>Limitations</u> Small number of RCTs; one trial (Minnesota Coronary Experiment) accounted for about 80% of participants; differences in methodological quality and design and population characteristics of individuals in trials.

Study	Research methods	Analysis	Results	Comments
de Souza et al. (2015) (Systematic review with meta-analysis) <u>Funding source</u> World Health Organization. <u>Declarations of interest</u> RJ de Souza: received a Canadian Institutes for Health Research postdoctoral fellowship. V Ha: received a Province of Ontario graduate scholarship and research support from the Canadian Institutes for Health Research. AI Cozma: received a Province of Ontario graduate scholarship.	<u>Research question</u> Systematically review associations between saturated fat and trans fats intake and total mortality, CVD and associated mortality, CHD and associated mortality, ischemic stroke, type 2 diabetes. <u>Selection criteria</u> *Search period*: Up to 1 May 2015. *Study design:* observational studies. *Inclusion criteria*: Observational studies in humans; report a measure of association between intakes of saturated fats or trans fats (measured by self-report or a biomarker) and total mortality, CVD and associated mortality, CHD and associated mortality, ischemic stroke, T2DM (measured by self-report and/or confirmed by medical records or registry linkage). *Exclusion criteria*: None reported. <u>Dietary assessment methods</u> FFQ, SQFFQ, 24 hr recall, dietary recall, 7 day food diary, weighted food diary, diet history, 4 day prospective diet record, cross check diet history method.	<u>Analysis</u> Principle association measures were RRs between highest and lowest intakes. ≥ 2 studies a random effects meta-analysis was performed. ≤ 3 studies fixed effect estimates also considered. Heterogeneity: Cochran's Q test (significant at P<0.10), quantified with the I^2 statistic. If ≥ 10 studies and substantial heterogeneity (I^2 > 60% or P_Q < 0.10) Meta-regression was used to explore heterogeneity. <u>Evaluation of study quality</u> The Newcastle-Ottawa scale was used to measure the risk of bias of included studies. The GRADE approach was used to assess confidence in the effect estimates derived from the body of evidence.	41 PCS; n= 90,501–339,090; duration: 1–32y; age 15-89y; gender: not reported; health at baseline: healthy; country: US (17), UK (4), Japan (4), Sweden (4), Israel (1), Finland (3), Denmark (1), Canada (1), China (1), Greece (1), Australia (1). <u>Highest vs lowest saturated fat intake</u> *CVD mortality* (3 cohorts) Most adjusted RR 0.97 (95% CI 0.84, 1.12) p=0.69; I^2=19%, P_{het}=0.29. Least adjusted RR 0.97 (95% CI 0.84, 1.12) p=0.69; I^2=19%, P_{het}=0.29. *CHD* (15 cohorts - 3 could not be included in analysis) Most adjusted RR 1.06 (95% CI 0.95, 1.17) p=0.29; I^2=47%, P_{het}= 0.02. Least adjusted RR 1.12 (95% CI 1.00, 1.26) p=0.05; I^2=63%, P_{het}<0.001. Risk estimates for 3 comparisons could not be extracted and so those reported in another meta-analysis were used; when removed RR 1.08 (95% CI 0.97, 1.20) p=0.18; I^2=51%, P_{het}=0.01. *CHD mortality* (11 cohorts) Most adjusted RR 1.15 (95% CI 0.97, 1.36) p=0.10; I^2=70%, p_{het}=<0.0001) Least adjusted RR 1.20 (95% CI 1.02, 1.41; P=0.02; I^2=74%, P_{het}=<0.00001) Risk estimates for 4 comparisons could not be extracted and so those reported in another meta-analysis were used; when removed RR 1.26 (95% CI 0.98, 1.62) p=0.07; I^2=74%, P_{het}<0.001. RR shifted to 1.20 (95% CI 1.01, 1.42) p=0.04; I^2=68%, P_{het}<0.001; when 2 comparisons were removed.	Saturated fat intake is not associated with total mortality, CVD, CHD, stroke or type 2 diabetes, but the evidence considered is heterogeneous with methodological limitations. <u>Limitations</u> Comparison of higher fat and lower fat obscures the importance of reciprocal and possibly heterogeneous decreases in other macronutrients that accompany high saturated fat intake. Most studies did not model the effect of nutrient substitution.

Study	Research methods	Analysis	Results	Comments
Harcombe et al. (2015) (Systematic review with meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Examine the evidence from RCTs available to US and UK regulatory committees when making dietary fat recommendations in the 1970's and 1980's respectively. <u>Selection criteria</u> *Search period*: Inception to 1983. *Study designs:* RCTs. *Inclusion criteria*: RCTs in human adults; hypothesis relating to a reduction or modification of dietary fat or cholesterol; ≥ 1 year duration; data on total and CHD mortality and cholesterol level. *Exclusion criteria*: Study being observational; non-randomised and/or multifactorial in design. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Overall pooled effect calculated using random effects meta-analysis. Heterogeneity evaluated using the Q-value, I^2 and T^2 calculations. Publication bias: Funnel plot methodology and Egger's regression intercept were calculated. <u>Evaluation of study quality</u> PEDro scale – all RCTs scored 4 or 5 (moderate quality).	6 RCTs; n=2467 (intervention n=1227; control n= 1240); duration: 2-11y (mean 5.4±3.5 y (weighted mean [person years by participants] 6.5±1 y)); age: 30-70y; gender: M(6); health at baseline: subjects with CHD (5), mixture of healthy and with CHD (1); country: USA (1), UK (3), Norway (1), Australia (1). 5 RCTs did not examine total fat and saturated fat intakes of 30% and 10% of total energy respectively. 4 RCTs examined vegetable oil. 3 RCTs examined replacement of saturated fats with vegetable oil (no significant differences in total mortality). 1 RCT examined a diet of 10% energy as saturated fat (higher incidence of total and CHD mortality in intervention group). <u>Intervention vs control</u> *CHD mortality* RR 0.99 (95% CI 0.78, 1.25); Q-value=8.649; I^2=30.632; T^2=0.028.	No difference in CVD mortality between intervention and control groups despite significantly greater reductions in serum cholesterol levels in the intervention group. <u>Limitations</u> Limitations of included RCTs: 1 RCT had open enrolment; 5 relied on dietary advice with meetings and periodical dietary analysis to monitor adherence; 3 involved additional dietary restrictions; difference between control and intervention groups at baseline; 2 didn't measure weight change; no information on saturated fat, MUFA or PUFA content of control or intervention diets.

Study	Research methods	Analysis	Results	Comments
Hooper et al. (2015) (Systematic review and meta-analysis) Funding source L Hooper: Studentship, Systematic Reviews Training, Institute of Child Health, University of London, UK. Declarations of interest None to declare.	Research question What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? Selection criteria *Search dates:* July 2010 to March 2014 (plus search from Hooper 2012 – inception to June 2010). *Study design:* RCTs only. *Inclusion criteria:* >18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet; duration ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions. *Exclusion criteria*: Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials. Dietary assessment methods Not reported.	Analysis Random effects meta-analysis to assess risk ratios. Low vs high % of energy from saturated fats. Incremental changes in % of energy from saturated fats. *Subgroup analysis* Saturated fat substitution with PUFA, MUFA, and carbohydrate. Evaluation of study quality Cochrane 'risk of bias' tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction. Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using I^2 test.	12 RCTs; n=59,000; duration: 2->8y; age: 45-66y; gender: M(7), F(3), M/F(5); health at baseline:: with or without CVD; country: USA (7), Europe (8), Australia/New Zealand (2). Lowest saturated fat compared with usual saturated fat *CVD mortality* (10 RCTs) RR 0.95 (95% CI 0.80, 1.12) *Combined CV events* (11 RCTs) RR 0.83 (95% CI 0.72, 0.96) *Myocardial infarctions* (11 RCTs) RR 0.90 (95% CI 0.80, 1.01) *Non-fatal MI* (9 RCTs) RR 0.95 (95% CI 0.80, 1.13) *CHD mortality* (10 RCTs) RR 0.98 (95% CI 0.84, 1.15) *CHD events* (12 RCTs) RR 0.87 (95% CI 0.74, 1.03) Subgroup analysis Analysis suggested reductions in CV events in studies where saturated fat intake was greater than 9% of energy in control groups and less than 9% of energy in intervention groups. Reduction in CV events was seen in studies that primarily replaced calories from saturated fats with PUFA; no effect was seen in studies that replaced saturated fats with carbohydrate or protein. Effects in studies replacing with MUFA were unclear.	Findings suggest a small but potentially important reduction in risk of CVD on reduction of saturated fat intake. Replacing energy from saturated fats with PUFA appears to be a useful strategy but replacement with carbohydrate appears to be less useful. Effects of replacement with MUFA unclear due to inclusion of only one trial. Limitations Although the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE). .

Study	Research methods	Analysis	Results	Comments
Chowdhury et al. (2014) (Systematic review and meta-analysis) <u>Funding source</u> British Heart Foundation (BHF); Medical Research Council (MRC); Cambridge National Institute for Health Research Biomedical Research Centre; Gates Cambridge. <u>Declarations of interest</u> Grants: Nestle; Metagenics; Pfizer; Merck Sharp & Dohme; Novartis; MRC; BHF; Cancer Research UK; British United Provident Association Foundation; diaDexus; European Research Council; European Union; Evelyn Trust; Fogarty International	<u>Research question</u> What is the association between fatty acids and coronary disease? *Specific*: What is the association between saturated fats and coronary disease? <u>Selection criteria</u> *Search dates:* Inception to end June 2013. *Study design:* PCS and RCTs. *Inclusion criteria:* Studies reporting on association of dietary fatty acid intake, fatty acids biomarkers or fatty acids intervention (dietary or supplement) with risk of coronary disease; observational studies with at least 1y follow-up; intervention studies – randomised and recorded coronary outcomes endpoint of interest; observational studies: participants from general populations or with stable CVD at study entry (defined as diagnosis made at least 30 days prior to baseline sampling). *Exclusion criteria:* Not reported.	<u>Analysis</u> Highest vs lowest 1/3 of saturated fat intake compared. Where RR adjusted, version not adjusting for blood lipids and/or circulating fatty acids was used. Random-effects model including between study heterogeneity used to pool RRs. Spearman's correlation coefficients using random-effects meta-analysis calculated for dietary fatty acid intake and circulating fatty acids. Heterogeneity: between studies, chi-squared and I^2 statistic. Newcastle-Ottawa Scale score using meta-regression. Publication bias: funnel plots and Egger tests. <u>Evaluation of study quality</u> Newcastle-Ottawa Scale for PCS. Cochrane Collaboration's tool for assessing risk of bias for RCTs. <u>Dietary assessment method</u> FFQs, 7-day food diary, 7-day weighted food record, 24-hour dietary recall, 4-day food record, 7-day food record, diet-history interview.	72 studies in total (45 PCS, 27 RCTs) across all fat classes; duration: not reported; age: not reported; gender: not reported; health at baseline: healthy (40), with CVD (22), with elevated risk factors for CVD (10); country: North America (19), Europe (42), Asia-Pacific region (9), multinational (2). <u>Dietary fats and coronary disease – highest vs lowest intake (32 PCS)</u> *Saturated fats* RR 1.02 (95% CI 0.97, 1.07) *MUFA* RR 0.99 (95% CI 0.89, 1.09) *Long chain n-3 PUFA* RR 0.93 (95% CI 0.84, 1.02) *n-6 PUFA* RR 1.01 (95% CI 0.96, 1.07) *Trans fats* RR 1.16 (95% CI 1.06, 1.27) <u>Fatty acid biomarkers and coronary disease - highest vs lowest intake (17 PCS)</u> *Saturated fats* RR 1.06 (95% CI 0.86, 1.30) *MUFA* RR 1.06 (95% CI 0.97-1.17) *Long chain n-3 PUFA* RR 0.84 (95% CI 0.63, 1.11) *n-6 PUFA* RR 0.94 (95% CI 0.84, 1.06) *Trans fats* RR 1.05 (95% CI 0.76, 1.44)	Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of PUFAs and low consumption of total saturated fats. <u>Limitations</u> Lack of repeat assessments of dietary intake; inability to adjust consistently for potential confounding factors across all studies.

Study	Research methods	Analysis	Results	Comments
Centre; GlaxoSmithKline; National Heart, Lung and Blood Institute; National Institute of Neurological Disorders and Stroke; National Health Service Blood and Transplant; University of British Columbia; University of Sheffield; Wellcome Trust; UK Biobank. Personal fees: Roche Pharmaceuticals; Bunge; Pollock Institute; Quaker Oats; Life Sciences Research Organization; Foodminds; Nutrition Impact; Amarin; AstraZeneca; Winston & Strawn; Unilever North American Scientific Advisory Board; UpToDate online chapter; Merck Sharp & Dohme UK Atherosclerosis Advisory Board;			<u>Fatty acid supplementation and coronary disease – intervention vs control group (27 RCTs)</u> *α-linoleic acid* RR 0.97 (95% CI 0.69, 1.36) *Long chain n-3 PUFA* RR 0.94 (95% CI 0.86, 1.03) *n-6 PUFA* RR 0.89 (95% CI 0.71, 1.12)	

Study	Research methods	Analysis	Results	Comments
Novartis Cardiovascular & Metabolic Advisory Board; Pfizer Population Research Advisory Panel; Sanofi Advisory Board. Royalties: Elsevier (France).				

Study	Research methods	Analysis	Results	Comments
Farvid et al. (2014) (Systematic review and meta-analysis) <u>Funding source</u> National Institutes of Health grants. <u>Declarations of interest</u> Received research support from California Walnut Commission.	<u>Research question</u> *General*: does dietary linoleic acid intake reduce CHD risk? *Specific*: does replacement of dietary saturated fat with dietary linoleic acid reduce CHD risk? <u>Selection criteria</u> *Search dates:* Inception to June 2013. *Study design:* PCS. *Inclusion criteria:* Studies provided multivariate adjusted risk estimates (RR or HR) for dietary linoleic acid consumption as the exposure and CHD endpoints; *Exclusion criteria:* Retrospective, cross-sectional or ecological studies; studies in non-adults (< 19 years old); non-original papers (reviews, editorials, letters), meeting abstracts and duplicated publications; studies conducted in patients with known CHD at baseline. <u>Dietary assessment method</u> FFQ (9); diet/7-day weighed food record (1); diet history (1); diet/24-hour recall (1); FQ/7-day menu book (1).	<u>Analysis</u> RR calculated using fixed-effect models; random effects models for sensitivity analysis. Heterogeneity: I^2 statistic, stratified analysis and meta-regression. Multivariate model included: total energy, age, smoking, BMI, education level, alcohol intake, hypertension, fibre intake, % of energy from saturated fats, trans fats, MUFAs, α-linoleic acid, PUFAs other than linoleic acid and α-linoleic acid and protein intake. Publication bias: visual inspection of funnel plot and Begg test. <u>Evaluation of study quality</u> No information provided; however the "study quality score" was used to assess heterogeneity between studies.	13 PCS; n=310,602 (range 1643 – 84,566); duration: 5.3–30y; age 20-75y; gender: M(4), F(3), M/F(6); health at baseline: without known CHD; country: USA (6), Finland (2), Sweden (2), The Netherlands (1), Denmark (1),Israel (1). <u>Highest vs lowest linoleic acid intake</u> *CHD events* (10 PCS) RR 0.85 (95% CI 0.78, 0.92) I^2=35.5% *CHD mortality* (11 PCS) RR 0.79 (95% CI 0.71, 0.89) I^2=0.0% <u>5% lower energy intake from saturated fats and higher energy intake from linoleic acid</u> *CHD events* (8 PCS) RR 0.91 (95% CI 0.87, 0.96); I^2=55.9% *CHD mortality* (10 PCS) RR 0.87 (95% CI 0.82, 0.94); I^2=0.0%	Dietary linoleic acid is inversely associated with CHD risk in a dose-response manner. These data provide support for current recommendations to replace saturated fats with PUFA for primary prevention of CHD. <u>Limitations</u> Most studies used FFQs to assess dietary intake, thus measurement errors may be introduced by under- or over-reporting of the amounts of food groups usually eaten by day; intake levels of linoleic acid may be underestimated in some studies that did not query brand names of some linoleic acid containing foods in the FFQ.

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) Funding source Supported by the Nordic Council of Ministers. Declarations of interest None to declare.	Research question What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? Selection criteria *Search dates:* January 2000- February 2012. *Study designs:* RCT and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); ≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration ≥ 4 weeks (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6 months, <40% on 12 months, <50% in 24 months; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority; study aim outside scope of review; exposure food pattern or a whole food; included non-healthy subjects, obese	Analysis Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-suggestive, and limited-no conclusion. Evaluation of study quality Primary evidence assessed for quality but method not stated. Quality categories included: A) high quality with very low risk of bias; B) good quality, some risk of bias but not enough to invalidate results; C) low quality with significant bias and weaknesses which may invalidate results.	5 PCS (6 publications); n=185,049; duration: 7-22y; age: 30-84y; gender: M (1), F (2), M/F (3); health at baseline: healthy (6); country: USA (4), Denmark (2). 1 RCT; n=48,835; duration: 8.1y; age: 50-79y; gender: F; health at baseline: healthy; country: USA. Majority of PCS – no association between intake of saturated fats and risk of CVD outcomes (grade B evidence). *Secondary analysis* RCT: Lower saturated fat intake associated with decreased risk of CHD in women (men not included in RCT), (grade B evidence). 2 PCS: saturated fats reduced, and replaced with carbohydrate: associated with increased risk of CVD outcomes (grade B evidence). 1 PCS: Increased risk of CVD outcomes with simple carbohydrate (high glycaemic index) but not complex carbohydrate (low glycaemic index) (grade B evidence).	Limitations Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included, however several systematic reviews and meta-analyses included in previous publications. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence. Many questions remain unresolved due to conflicting results from studies and lack of high quality controlled studies.

Study	Research methods	Analysis	Results	Comments
	subjects. Dietary assessment methods Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Ramsden et al. (2013) (Meta-analysis) Funding source The Life Insurance Medical Research Fund of Australia and New Zealand; The Intramural Program of the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health. Declarations of interest None to declare	Research question Are longitudinal dietary changes in PUFAs and saturated fats associated with mortality outcomes? Selection criteria *Search dates:* Not specified. *Study design:* RCTs *Inclusion criteria:* RCTs in which PUFA were increased in place of saturated fats; CHD mortality, CVD mortality and/or total mortality reported. *Exclusion criteria*: No randomisation; disproportionate CHD risk factors reported in different arms; dietary information necessary to classify experimental diets as either n-6 specific PUFA or mixed n-3/n-6 PUFA was not available. Dietary assessment method Not reported.	Analysis Fixed effects meta-analyses for linoleic acid-selective and mixed n-3/n-6 PUFA intervention datasets for CHD mortality, CVD mortality and total mortality. Test of heterogeneity performed to determine whether effects of linoleic acid-selective and mixed n-3/n-6 PUFA intervention datasets should be evaluated separately. Potential for publication bias assessed by visual inspection of a funnel plot of the treatment effect versus standard error. Sensitivity analysis performed. Evaluation of study quality Not systematically assessed.	7 RCTs; n=11,275; duration: 2-≤8y; age: not reported; gender: M(7), F(1); health at baseline: with CHD (5), with or without CHD (3); country: USA (3), UK (3), Norway (1), Australia (1). Increased n-6 linoleic acid-selective PUFA vs decreased saturated fats *CHD Mortality (4 datasets)* HR 1.33 (95% CI 0.99, 1.79) p=0.056; I^2=7.5% *CVD Mortality (4 datasets)* HR 1.27 (95% CI 0.98, 1.65) p=0.07; I^2=22% Increased n-3/n-6 PUFA vs decreased saturated fats *CHD Mortality (4 datasets)* HR 0.81 (95% CI 0.64, 1.03) p=0.08; I^2=0% *CVD Mortality (4 datasets)* HR 0.79 (95% CI 0.63, 0.99) p=0.04; I^2=0%	An updated meta-analysis of linoleic acid intervention trials showed no evidence of CV benefits. Selective substitution of n-6 PUFA for saturated fats is unlikely to be beneficial particularly in patients with established heart disease. Limitations Relatively small number of trials investigating PUFA interventions and differences in design and population characteristics of each trial.

Study	Research methods	Analysis	Results	Comments
Micha and Mozaffarian (2010) (Narrative review) <u>Funding source</u> Searle Funds at The Chicago Community Trust; the Bill & Melinda Gates Foundation/World Health Organization Global Burden of Diseases, Injuries, and Risk Factors Study. <u>Declarations of interest</u> Consulting honoraria (modest) from Nutrition Impact, Unilever and SPRIM.	<u>Research question</u> Elucidate effects of saturated fat consumption on CVD risk based on the most current evidence. <u>Selection criteria</u> *Search period*: Inception to September 2009. *Study design*: RCT and PCS. *Inclusion*: Adults; evaluating saturated fat intake and risk of CHD, stroke, type 2 diabetes, related risk pathways including lipids and lipoproteins, systemic inflammation, vascular function, insulin resistance. *Exclusion*: A priori animal studies, ecological studies, commentaries, general reviews, case reports. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Narrative review. <u>Evaluation of study quality</u> Not reported.	Characteristics of identified studies not summarised. <u>CHD risk and saturated fats replaced with:</u> *PUFA* Consistent evidence that this modestly ↓ CHD risk, with ~10% reduction for a 5% energy substitution. RR 0.90 (95% CI 0.83, 0.97) *MUFA* Effect/association on CHD risk uncertain. *Carbohydrate* No benefit effect on CHD risk.	Substantial evidence indicating that health effects of reducing saturated fats vary depending on the replacement nutrient: Replacement with PUFA lowers CHD risk. Replacement with carbohydrate has no benefit. Replacement with MUFA has uncertain effects. Advice to reduce saturated fat intake without considering the replacement may have little or no effects on disease risk.

Study	Research methods	Analysis	Results	Comments
Mozaffarian et al. (2010) (Systematic review and meta-analysis) <u>Funding source</u> National Heart, Lung and Blood Institute, National Institute of Health; Searle Scholar Award from the Searle Funds at the Chicago Community Trust. <u>Declarations of interest</u> Research grants: US National Institutes of Health; Searle Funds at the Chicago Community Trust; Genes and Environment Initiative; Gates Foundation/WHO Global Burden of Diseases, Injuries and Risk Factors Study; GlaxoSmithKline;	<u>Research question</u> What is the impact of increased PUFA consumption, as a replacement for saturated fats, on CHD endpoints? <u>Selection criteria</u> *Search dates:* Inception to June 2009. *Study design:* RCTs. *Inclusion criteria:* Interventions that randomised adults to increased total or n-6 PUFA consumption for at least 1y without other major concomitant interventions; an appropriate control group; sufficient data to calculate risk estimates with SE for effects on occurrence of "hard" CHD events; primary or secondary prevention trials; feeding trials and trials that utilised dietary advice. *Exclusion criteria*: Observational or non-randomised studies; tested mainly n-3 rather than total or n-6 PUFAs; studies that evaluated only intermediate endpoints (e.g. angina); or were commentaries, reviews or duplicate publications from the same study. <u>Dietary assessment method</u> Direct analysis of provided food (4), multiple serial weighted diet records (1), 7-14 day weighed diet records in a subset (1), questionnaire validated against 7-day weighed diet records (1), clinical interviews about dietary compliance (1).	<u>Analysis</u> The overall pooled effect was calculated using random effects meta-analysis. Heterogeneity between studies was evaluated using the I^2 statistic and meta-regression. Pre-specified potential sources of heterogeneity were explored using stratified inverse-variance weighted random effects meta-analysis and inverse-variance weighted meta-regression including trial duration, study population and overall quality score. <u>Evaluation of study quality</u> The validated Jadad score was used to assess quality, which includes criteria relating to randomisation, blinding, and withdrawals and dropouts that are together summed to generate an overall quality score between 0 and 5.	8 RCTs; n=13,614; duration: 2-8y; age: not reported; gender: M(6), F(1), M/F(1); health at baseline: with or without CHD (1), without CHD (3), history of CHD (4); country: USA (2), UK (3), Finland (2), Norway (1). <u>PUFA intake and CHD</u> RR 0.81 (95% CI 0.70, 0.95) p=0.008 <u>For each 5% of energy greater PUFA consumption</u> RR 0.90 (95% CI 0.83, 0.97) A number of sub-group analyses were performed, none of which were significantly different from the main pooled result.	Consuming PUFA in place of saturated fats reduces CHD events in RCTs. <u>Limitations</u> Many of the included RCTs had important design limitations: some provided all or most meals limiting generalisability while others only provided dietary advice; some trials were not double-blinded; the methods of estimating and reporting saturated fats and PUFA varied between trials; some trials included sources of marine n-3 PUFA.

Study	Research methods	Analysis	Results	Comments
Sigma Tau and Pronova. Honoraria and travel expenses: US Food and Drug Administration; International Life Sciences Institute; Aramark; Unilever; SPRIM; Nutrition Impact, WHO; UpToDate.				

Study	Research methods	Analysis	Results	Comments
Siri-Tarino et al. (2010) (Meta-analysis) <u>Funding source</u> National Dairy Council; National Center for Research Resources; National Institutes of Health; National Institute of Health Roadmap for Medical Research; Postdoctoral Fellowship from Unilever Corporate Research. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What is the evidence related to the association of dietary saturated fat with risk of CHD, stroke and CVD in prospective epidemiological studies? <u>Selection criteria</u> *Search dates:* Inception to 17 September 2009. *Study design: PCS.* *Inclusion criteria:* Data available on dietary consumption of saturated fats; specifically investigating association of saturated fat with fatal or non-fatal CVD events; participants were generally healthy adults. *Exclusion criteria*: Investigating CVD risk factors. <u>Dietary assessment method</u> FFQs, 24-hour recalls, interview and multiple daily food records (1day, 7day).	<u>Analysis</u> RRs and 95% CIs were log transformed to derive corresponding SEs for β-coefficients by using Greenland's formula. Risk estimates for the most fully adjusted models used to estimate pooled RR. Meta-analyses performed with a random effects model. Influence of individual studies on the pooled estimated were examined. Examined whether the size of the effect depended on characteristics of each study, including age, gender, sample size, duration of follow-up, whether disease outcomes were confirmed by medical record and a score evaluating overall study quality. *Secondary analysis*: age and gender effects; effects of replacing saturated fats with carbohydrate or PUFA. <u>Study quality</u> Studies were given a quality score derived from the dietary assessment method, the number of dietary assessments and the number of adjusted established risk factors for CVD.	21 PCS (16 CHD, 8 Stroke); n=347,747 (total) (range: 266-85,764); duration: 6-23y; age: ~30-89y; gender: M(11), F(2), M/F(8); health at baseline: healthy; country: North America (12), Europe (6), Japan (2), Israel (1). <u>Highest vs lowest saturated fat intake</u> *CHD* (16 cohorts) RR 1.07 (95% CI 0.96, 1.19) p=0.22; I^2=41%, P_{het}=0.04 *Stroke* (8 cohorts) RR 0.81 (95% CI 0.62, 1.05) p=0.11; I^2=61%, P_{het}=0.11 *CVD mortality* (21 cohorts) RR 1.00 (95% CI 0.89, 1.11) p=0.95; I^2=56%, P_{het}=0.0004 <u>CVD by gender</u> *Men* (14 cohorts) RR 0.97 (95% CI 0.87, 1.08) p=0.60; I^2=34%, P_{het}=0.10 *Women* (6 cohorts) RR 1.06 (95% CI 0.86, 1.32) p=0.57; I^2=1%, P_{het}=0.40 <u>CVD by age</u> *<60y* (15 cohorts) RR 0.98 (95% CI 0.84, 1.13) p=0.77; I^2=50%, P_{het}=0.01 *≥60y* (10 cohorts) RR 0.98 (95% CI 0.86, 1.10) p=0.69; I^2=0%, P_{het}=0.78 <u>Adjusted for total energy intake and energy from protein, carbohydrate and fats (except PUFA)</u> *CHD* (4 cohorts) RR 0.98 (95% CI 0.86, 1.13) p=0.83; I^2=0%, P_{het}=0.57 *Stroke* (3 cohorts) RR 0.93 (95% CI 0.71, 1.21) p=0.58; I^2=0%; P_{het}=0.60 *CVD* RR 0.97 (95% CI 0.86, 1.10) p=0.66; I^2=0%; P_{het}=0.79	There is insufficient evidence from prospective epidemiological studies to conclude that dietary saturated fat is associated with an increased risk of CHD, stroke or CVD. <u>Limitations</u> The meta-analysis relies on the accuracy of dietary assessments of the component studies. Only a limited number of studies provided data that enabled the evaluation of the effects of isoenergetically replacing saturated fats with carbohydrate or PUFA and therefore the statistical power was diminished for the secondary analysis restricted to these studies. The funnel plot analysis suggests publication bias; studies with significant associations tended to be received more favourably for publication.

Study	Research methods	Analysis	Results	Comments
Jakobsen et al. (2009) (Pooled analysis) Funding source National Heart, Lung and Blood Institute, National Institutes of Health; Danish Heart Foundation. Declarations of interest None to declare.	Research question Should energy from unsaturated fatty acids or carbohydrate replace energy from saturated fats to prevent CHD? Selection criteria *Search dates:* Not reported. *Study design:* PCS. *Inclusion criteria:* Published follow-up study with ≥ 150 incident coronary events; availability of usual dietary intake; a validation or repeatability study of the diet-assessment method used. *Exclusion criteria*: Age < 35 years; history of CVD, diabetes or cancer (other than non-melanoma skin cancer); and extreme energy intake (i.e. > or < 3 SDs form the study-specific log-transformed mean energy intake of the population). Dietary assessment method FFQs and diet history interview.	Analysis HRs with 95% CI for the incidence of a coronary event and of mortality from CHD were calculated using Cox proportional hazards regression. Studies with follow-up periods >10y were truncated to reduce possible effect modification by time. Two models were used to investigate whether energy intake from unsaturated fatty acids or carbohydrate should replace energy intake from saturated fats to prevent coronary events: *Model 1* included intakes of MUFAs, PUFAs, trans fats, carbohydrate and protein expressed as percentages of total energy intake. *Model 2* included variables in model 1 and CHD risk factors measured at baseline: smoking, BMI, physical activity, highest attained educational level, alcohol intake, history of hypertension and energy adjusted quintiles of fibre intake (g/day) and cholesterol (mg/day). A random effects model was used to provide a pooled estimate of HRs. Between study heterogeneity was assessed using the Q statistic. Evaluation of study quality Not described.	11 PCS; n=344,696 (range 3324 – 143,121); duration: 4-10y; age: 47-61y (median at baseline); gender: M(3), F(3), M/F(5) (71% of total participants were women); health at baseline: healthy, no history of CVD, diabetes or cancer; country: USA (6), Finland (2), Sweden (1), Denmark (1), Israel (1). 5% lower energy intake from saturated fats and a concomitant higher energy intake from PUFAS *Coronary events* HR = 0.87 (95% CI 0.77,0.97), heterogeneity p=0.70 *Coronary mortality* HR 0.74 (95% CI 0.61,0.89), heterogeneity p=0.40 5% lower energy intake from saturated fats and a concomitant higher energy intake from carbohydrates *Coronary events* HR 1.07 (95% CI 1.01, 1.14), heterogeneity p=0.51 *Coronary mortality* HR 0.96 (95% CI 0.82, 1.13), heterogeneity p=0.05 5% lower energy intake from saturated fats and a concomitant higher energy intake from MUFAs *Coronary events* HR 1.19 (95% CI 1.00, 1.42), heterogeneity p=0.32 *Coronary mortality* HR 1.01 (95% CI 0.73, 1.41), heterogeneity p=0.18 No effect modification by gender or age was found.	The associations suggest that replacing saturated fats with PUFAs rather than MUFAs or carbohydrate prevent CHD over a wide range of intakes. Limitations Although the study suggests that to lower the risk of CHD, saturated fats should not be replaced with carbohydrate, the authors acknowledged that the effect of substitution may vary depending on the type of carbohydrate consumed as the study did not consider different types of carbohydrate. Only baseline information was available regarding dietary habits.

Study	Research methods	Analysis	Results	Comments
Mente et al. (2009) (Systematic review) Funding source Heart and Stroke Foundation of Canada Postdoctoral Research Fellowship; Canadian Institutes of Health Research Clinician-Scientist Phase 2 Award; Heart and Stroke Foundation of Ontario Michael G. DeGroote Research Chair in Population Health Research; Canadian Institutes of Health Research Canada Graduate Scholarship Doctoral Award. Declarations of interest None declared.	Research question Systematically evaluate dietary exposures and CHD using the Bradford Hill criteria; determine which dietary exposures have been studied sufficiently in RCTs and found to support the findings of PCS; identify dietary exposures deemed to have insufficient evidence to be conclusive. Selection criteria *Search period*: 1950 – June 2007. *Study designs:* PCS and RCTs. *Inclusion criteria*: English language; investigating dietary exposures in relation to CHD, with ≥ 1 year follow-up; PCS include estimates of dietary intake measured using conventional dietary assessment tools; RCTs randomised and compare dietary exposure with control diet or placebo. *Exclusion criteria*: Crossover trials that did not evaluate plasma biomarkers or atherosclerotic indicators. Dietary assessment methods FFQ, food records, 24-hour diet recall.	Analysis Summary estimates were calculated using a general variance-based method (random-effects model) with 95% CIs. Evaluation of study quality Not reported.	146 PCS (describing 361 sub-cohorts; 86% primary prevention); n=160,673 (saturated fat cohorts); median duration: 11y (range 2.8–28y); mean age: 53 y; gender: 41% female; country: USA (201), Europe (130), Asia (12). 43 RCTs (involving 51 sub-groups; 74% secondary prevention); n=7204 (average for each dietary exposure); median duration: 3.7y (range 1–12y); mean age: 58 y; gender: 34% female. Highest vs lowest intake of saturated fats *Coronary outcomes (11 sub-cohorts)* RR = 1.06 (95% CI 0.96, 1.15) *Coronary and secondary outcomes (11 sub-cohorts)* RR = 1.06 (95% CI 0.96, 1.15) Higher intake of PUFA relative to saturated fats not significantly associated with CHD. Bradford Hill Criteria Weak evidence (≤ 2 criteria) for association between saturated fats and CHD.	Strong evidence for a causal association for protective factors including intake of vegetables, nuts, monounsaturated fatty acids, Mediterranean and high quality dietary patterns, and harmful factors including foods with a high glycaemic index, trans fats and a western dietary pattern. Among these factors, only a Mediterranean dietary pattern was associated with CHD in RCTs. Limitations Created arbitrary definitions for evidence and scoring system, but has been validated. Derived RR cut-off points to define a strong association from the distribution of RR values in cohort studies because the true cut-off points for defining clinically meaningful effects are not known. Heterogeneity of cohort studies may have influenced results.

Study	Research methods	Analysis	Results	Comments
Skeaff and Miller (2009) (Meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> Funding received from Unilever and Fonterra.	<u>Research question</u> What is the relationship between dietary fat and risk of CHD? <u>Selection criteria</u> *Search dates:* Not reported. *Study design:* PCS and RCTs. *Inclusion criteria:* Studies in which dietary fat exposure was assessed by dietary assessment measures or fatty acid biomarkers. *Exclusion criteria*: Cohort studies that did not report a RR associated with intake of dietary fats; studies where MUFA exposure was assessed using fatty acid biomarkers. <u>Dietary assessment method</u> 24-hour recall, diet records, diet histories and FFQs.	<u>Analysis</u> *PCS*: random effects meta-analysis to calculate summary estimates of RR of CHD in high vs low exposure to dietary fat or its components. Separate meta-analysis performed for summary estimates of risk for 5% energy increments for saturated fats. *RCTs: meta-analysis* of results from RCTs based on diets involving a change in the PUFA to saturated fats ratio of the diet, with or without reduction in total fat intake. <u>Evaluation of study quality</u> Not systematically assessed. Commentary in discussion section.	<u>PCS: highest vs lowest intake.</u> 8 PCS; n=415-78,778; duration: 5-20y; age: 30-79y; gender: M (3), F (1), M/F (4); health at baseline: healthy (5), high risk (smokers) (1), clinically established coronary artery disease (1), not reported (1); country: USA (4), UK (1), Finland (2), Denmark (1). *CHD Mortality* (6 PCS) RR 1.14 (95% CI 0.82, 1.60) p=0.431; I^2 = 72.1% *CHD Events* (5 PCS) RR 0.93 (95% CI 0.83, 1.05) p=0.269; I^2 = 0.09% <u>Per 5% total energy increment in saturated fat intake</u> *CHD Mortality* (2 PCS) RR 1.11 (95% CI 0.75, 1.65) p=0.593; I^2 = 62.8% *CHD Events* (3 PCS) RR 1.03 (95% CI 0.87, 1.22) p=0.723; I^2 = 34.3% <u>RCTs: Increased PUFA and decreased saturated fat</u> 8 RCTs; n=90-9057; duration: 2-6y; age: 30-64y; gender: M (6), F (1), M/F (1); health at baseline: previous MI (3), with CHD (1), hospitalised patients (3), not reported (1); country: USA (2), UK (4), Norway (1), Finland (1). *CHD Mortality* (5 RCTs) RR 0.84 (95% CI 0.62, 1.12) p=0.867; I^2 = 12.4% *CHD Events* (8 RCTs) RR 0.83 (95% CI 0.69, 1.00), p=0.050; I^2 = 44.2% *Only trials where mean serum cholesterol concentration was significantly lowered in the intervention group* *CHD Mortality* (3 RCTs) RR 0.52 (95% CI 0.30, 0.87), p=0.014; I^2 = 0.0% *CHD Events* (5 RCTs) RR 0.68 (95% CI 0.49, 0.94), p=0.020; I^2 = 40.3%	The available evidence from PCS and RCTs is unsatisfactory and unreliable to make judgement about and substantiate the effects of dietary fat on risk of CHD. The null results of observational studies reflect the combined effects of limitations of dietary assessment methods, inadequate numbers of participants studied and the prolonged follow-up of individuals.

Study	Research methods	Analysis	Results	Comments
Van Horn et al. (2008) (Systematic narrative review) Funding source None declared. Declarations of interest None declared.	Research question Review of the evidence associated with key dietary factors and risk of CVD. Selection criteria *Search period:* First review 1991-2001; update review 2001-2004; supplementary search in 2006. *Study Design:* Not detailed. *Inclusion criteria:* Human subjects; English language; articles in ADA evidence analysis library. *Exclusion criteria:* Sample size <10 in each treatment group; drop-out rate >20%. Provided more than 1000 papers, additional criteria applied but not detailed. Dietary assessment method Not reported.	Analysis Expert panel identified and evaluated current research, limited details provided. Evaluation of study quality Not reported.	Original review: 67 primary and 30 review articles 83 primary and 19 review articles, supplementary search provided additional 50 articles Summary of characteristics of identified studies not provided Evidence from RCTs reported that dietary saturated fat (<7% energy) resulted in reduced LDL-C and reduced risk of CHD, stroke and CVD.	To reduce the risk of CVD, dietary saturated fats should be replaced isoenergetically with complex carbohydrate and/or unsaturated fatty acids including both MUFA (<20% of energy) and PUFA (<10% of energy).

Table A2.2 RCTs and PCS assessing the relationship between dietary saturated fat intake and cardiovascular diseases in each review article

Study name[1] / first author **Publication year**	**Harcombe et al. (2016a)**	**Harcombe et al. (2016b)**	**Ramsden et al. (2016)**	**de Souza et al. (2015)**	**Harcombe et al. (2015)**	**Hooper et al. (2015)[2]**	**Chowdhury et al. (2014)**	**Farvid et al. (2014)**	**Schwab et al. (2014)[3]**	**Ramsden et al. (2013)**	**Micha and Mozaffarian (2010)[4]**	**Mozaffarian et al. (2010)**	**Siri-Tarino et al. (2010)**	**Jakobsen et al. (2009)**	**Mente et al. (2009)**	**Skeaff and Miller (2009)**	**Van Horn et al. (2008)**
A, cardiovascular disease; B, coronary heart disease; C, stroke; d number of deaths; t number of events.																	
Total primary studies (publications)	6	10	5 (20)	27 (30)	6	12	20 (25)	13	5 (6)	7 (23)	18	8	21	11	9	18 (20)	1
De Goede 2015				C													
Japan Collaboration Cohort Study																	
Wakai 2014				A^{d}													
Yamagishi 2013				B^{t} C													
Yamagishi 2010							B										
Virtanen 2014				B^{dt}													
Pientinen 1997				B^{dt}			B	B^{dt}			B^{t}		B^{t}	B^{dt}	B^{d}	B^{d}	
De Oliveira 2012									A								
European Prospective Investigation into Cancer and Nutrition (EPIC)																	
Misirli 2012				C													
Trichopoulou 2006							B										
De Goede 2012								B^{t}									
Malmo Diet and Cancer Study																	
Wallstrom 2012							B	B^{dt}									
Leosdottir 2007				B^{t} C			B						B^{dt} C				
Leosdottir 2005				A^{d}							B^{t}						
Yaemsiri 2012				C													
Caerphilly Prospective Study																	

Study name[1] / first author Publication year	Harcombe et al. (2016a)	Harcombe et al. (2016b)	Ramsden et al. (2016)	de Souza et al. (2015)	Harcombe et al. (2015)	Hooper et al. (2015)[2]	Chowdhury et al. (2014)	Farvid et al. (2014)	Schwab et al. (2014)[3]	Ramsden et al. (2013)	Micha and Mozaffarian (2010)[4]	Mozaffarian et al. (2010)	Siri-Tarino et al. (2010)	Jakobsen et al. (2009)	Mente et al. (2009)	Skeaff and Miller (2009)	Van Horn et al. (2008)
A, cardiovascular disease; B, coronary heart disease; C, stroke; d number of deaths; t number of events.																	
Atkinson 2011				C													
Fehily 1993				B^{t}			B						B^{t}				
Vedtofte 2011								B^{t}									
Jakobsen 2010									A								
Wang 2010									A								
Ding 2006											$B^{t}C$						
Howard 2006		B^{d}		B^{t}		$A^{dt}B^{dt}$					$AB^{t}C$						B^{t}
Wiberg 2006				C													
Xu 2006				B^{dt}			B						B^{t}			B^{d}	
Health Professionals Follow-up Study																	
Mozaffarian 2005							B										
He 2003							B		A		$B^{t}C$						
Ascherio 1996				B^{dt}			B	B^{dt}					B^{t}	B^{dt}	B^{dt}	B^{dt}	
Laaksonen 2005							B										
Nurses' Health Study																	
Albert 2005							B										
Oh 2005				B^{t}			B	B^{dt}			B^{t}		B^{t}		B^{t}	B^{t}	
Iso 2001							B										
Hu 1997														B^{dt}			
Tucker 2005				B^{d}			B						B^{dt}		B^{dt}	B^{dt}	
Jakobsen 2004				B^{t}			B		A				B^{t}	B^{dt}		B^{t}	
Ley 2004						$A^{dt}B^{dt}$											
Sauvaget 2004				$A^{dt}C$									C				

Study name[1] / first author Publication year	Harcombe et al. (2016a)	Harcombe et al. (2016b)	Ramsden et al. (2016)	de Souza et al. (2015)	Harcombe et al. (2015)	Hooper et al. (2015)[2]	Chowdhury et al. (2014)	Farvid et al. (2014)	Schwab et al. (2014)[3]	Ramsden et al. (2013)	Micha and Mozaffarian (2010)[4]	Mozaffarian et al. (2010)	Siri-Tarino et al. (2010)	Jakobsen et al. (2009)	Mente et al. (2009)	Skeaff and Miller (2009)	Van Horn et al. (2008)
A, cardiovascular disease; B, coronary heart disease; C, stroke; d number of deaths; t number of events.																	
Erkkila 2003							B								B^{d}	B^{t}	
Hallmans 2003								B^{dt}						B^{dt}			
He 2003				C									C				
Iso 2003											$B^{t}C$		C				
Sydney Diet-Heart Study																	
Woodhill 1978		B^{d}	B^{d}							$A^{d}B^{d}$							
Ramsden 2010			B^{d}														
Enig 1990										$A^{d}B^{d}$							
Woodhill 1978					B^{d}	$A^{t}B^{d}$											
Woodhill 1975										$A^{d}B^{d}$							
Woodhill 1973			B^{d}							$A^{d}B^{d}$							
Woodhill 1969			B^{d}							$A^{d}B^{d}$							
Boniface and Tefft 2002				B^{d}			B						B^{dt}		B^{d}	B^{dt}	
Liu 2002								B^{dt}						B^{dt}			
Iso 2001									A		$B^{t}C$		C				
Moy 2001						$A^{t}B^{dt}$											
Keys 1970	B^{d}																
Folsom 1997								B^{dt}						B^{dt}			
Gillman 1997				C							C		C				
Mann 1997				B^{d}			B						B^{dt}		B^{t}	B^{d}	
Seino 1997				C							C						
Esrey 1996				B^{d}			B						B^{dt}				
Kushi 1996								B^{d}									

Study name[1] / first author Publication year	Harcombe et al. (2016a)	Harcombe et al. (2016b)	Ramsden et al. (2016)	de Souza et al. (2015)	Harcombe et al. (2015)	Hooper et al. (2015)[2]	Chowdhury et al. (2014)	Farvid et al. (2014)	Schwab et al. (2014)[3]	Ramsden et al. (2013)	Micha and Mozaffarian (2010)[4]	Mozaffarian et al. (2010)	Siri-Tarino et al. (2010)	Jakobsen et al. (2009)	Mente et al. (2009)	Skeaff and Miller (2009)	Van Horn et al. (2008)
A, cardiovascular disease; B, coronary heart disease; C, stroke; d number of deaths; t number of events.																	
Black 1994						C^{td}											
Knekt 1994								B^{dt}						B^{dt}			
Goldbourt 1993				B^{d} C			B	B^{d}					B^{dt} C	B^{dt}			
Dolecek 1992								B^{d}									
Fraser 1992														B^{dt}			
Watts 1992		B^{d}				C^{dt}					B^{t}	B^{t}				B^{t}	
Framingham Heart Study																	
Posner 1991				B^{t}			B						B^{t}		B^{t}	B^{d}	
Gordon 1970	B^{d}																
DART Study																	
Burr 1989						$A^{dt}B^{dt}$					B^{t}	B^{t}				B^{t}	
Burr 1968		B^{d}															
Minnesota Coronary Experiment																	
Frantz 1989		B^{d}	B^{d}							$A^{d}B^{d}$	B^{t}	B^{t}				B^{t}	
Broste 1981			B^{d}														
Brewer 1975			B^{d}														
Dawson 1975			B^{d}														
Frantz 1975			B^{d}							$A^{d}B^{d}$							
Honolulu Heart Programme																	
McGee 1985				B^{t} C													
Kagan 1974	B^{d}																
Kushi 1985				B^{d}			B						B^{dt}	B^{d}	B^{d}		
McGee 1984							B						B^{t} C				

Study name[1] / first author Publication year	Harcombe et al. (2016a)	Harcombe et al. (2016b)	Ramsden et al. (2016)	de Souza et al. (2015)	Harcombe et al. (2015)	Hooper et al. (2015)[2]	Chowdhury et al. (2014)	Farvid et al. (2014)	Schwab et al. (2014)[3]	Ramsden et al. (2013)	Micha and Mozaffarian (2010)[4]	Mozaffarian et al. (2010)	Siri-Tarino et al. (2010)	Jakobsen et al. (2009)	Mente et al. (2009)	Skeaff and Miller (2009)	Van Horn et al. (2008)
A, cardiovascular disease; B, coronary heart disease; C, stroke; d number of deaths; t number of events.																	
Miettinen 1983											B^{t}	B^{t}					
Shekelle 1981				B^{dt}			B						B^{dt}				
Houtsmuller 1979						A^{t} B^{dt}											
Finnish Mental Hospital Study																	
Turpeinen 1983																B^{dt}	
Turpeinen 1979											B^{t}	B^{t}				B^{dt}	
Morris 1977	B^{d}																
Oslo Diet-Heart Study																	
Leren 1970		B^{d}			B^{d}					$A^{d}B^{d}$	B^{t}	B^{t}				B^{t}	
Leren 1966						$A^{dt}B^{dt}$				$A^{d}B^{d}$						B^{dt}	
Los Angeles Veterans Admin																	
Dayton. *Lancet* 1970			B^{d}							$A^{d}B^{d}$							
Dayton. *Ann Intern Med* 1970										$A^{d}B^{d}$							
Dayton. *Am J Med* 1969		B^{d}	B^{d}							$A^{d}B^{d}$						B^{t}	
Dayton. *Circulation* 1969					B^{d}	$A^{dt}B^{dt}$											
Dayton. *Pub Med PMID* 1969			B^{d}														
Dayton. *Minn Med* 1969										$A^{d}B^{d}$							
Dayton. *Pub Med PMID* *1968*			B^{d}														
Dayton. *Lancet* 1968			B^{d}							$A^{d}B^{d}$	B^{t}	B^{t}					
Dayton 1967										$A^{d}B^{d}$							
Dayton 1966										$A^{d}B^{d}$							
Dayton 1965										$A^{d}B^{d}$							
Dayton 1962			B^{d}							$A^{d}B^{d}$							
Hiscock 1962			B^{d}							$A^{d}B^{d}$							

Study name[1] / first author Publication year	Harcombe et al. (2016a)	Harcombe et al. (2016b)	Ramsden et al. (2016)	de Souza et al. (2015)	Harcombe et al. (2015)	Hooper et al. (2015)[2]	Chowdhury et al. (2014)	Farvid et al. (2014)	Schwab et al. (2014)[3]	Ramsden et al. (2013)	Micha and Mozaffarian (2010)[4]	Mozaffarian et al. (2010)	Siri-Tarino et al. (2010)	Jakobsen et al. (2009)	Mente et al. (2009)	Skeaff and Miller (2009)	Van Horn et al. (2008)
A, cardiovascular disease; B, coronary heart disease; C, stroke; d number of deaths; t number of events.																	
Pearce 1971			B^{d}							$A^{d}B^{d}$							
Garcia-Palmieri 1969	B^{d}																
Medical Research Council Soy Study																	
Clarke 1969			B^{d}							$A^{d}B^{d}$							
Medical Research Council 1968		B^{d}	B^{d}		B^{d}	$A^{dt}B^{dt}$				$A^{d}B^{d}$	B^{t}	B^{t}				B^{dt}	
Research Committee 1965		B^{d}			B^{d}												
Rose 1965		B^{d}	B^{d}		B^{d}	$A^{dt}B^{dt}$				$A^{d}B^{d}$						B^{t}	
Paul 1963	B^{d}																

Outcomes measured by study: A, cardiovascular disease; B, coronary heart disease; C, stroke; [d] number of deaths; [t] number of events.

[1] Study name is only provided when two or more publications for that study are used in any of the reviews.

[2] Hooper et al. (2015) presents publications used in the analyses by study name and identifies a main study publication along with all supplementary publications for the study. It is not possible to know which exact publication the data has come from, therefore, the main study publication has been used in the table above.

[3] Schwab et al. (2014) also discusses the reviews by Jakobsen et al. (2009), Mozaffarian et al. (2010), and Hooper et al. (2015), however, these are included as separate reviews in this report.

[4] Micha and Mozaffarian (2010) also discusses the reviews by Jakobsen et al. (2009), Mente et al. (2009), Siri-Tarino et al. (2010), and Mozaffarian et al. (2010), however, these are included as separate reviews in this report.

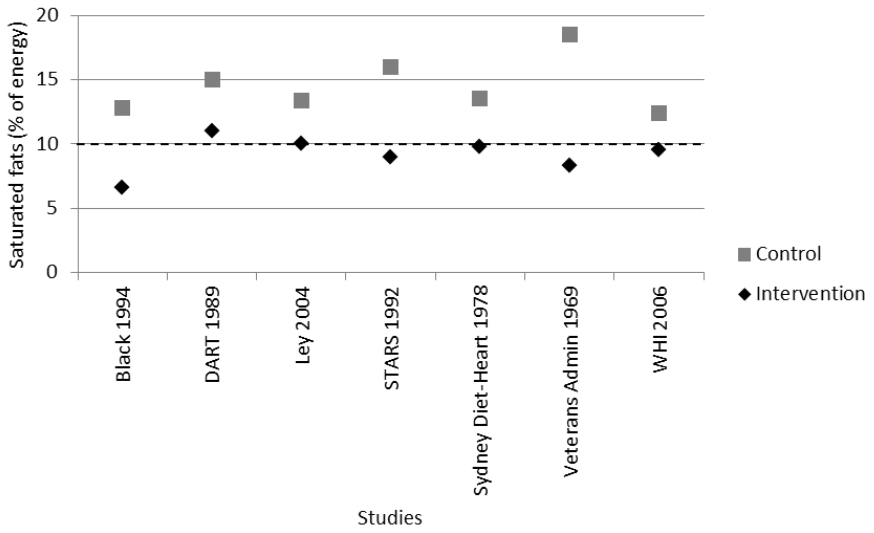


Figure A2.1 Mean intakes of saturated fat from individual RCTs that examined the effect of reduced intake of saturated fats on CVD mortality

Note:

- Data on mean intakes of saturated fat obtained from individual RCTs included in the Hooper et al (2015) review
- Hooper et al., 2015 examined 10 RCTs; 7 RCTs reported mean intakes of saturated fat
- Intakes of saturated fat ranged from 6.6-11.0% of energy (intervention) and 12.4-18.5% of energy (control)

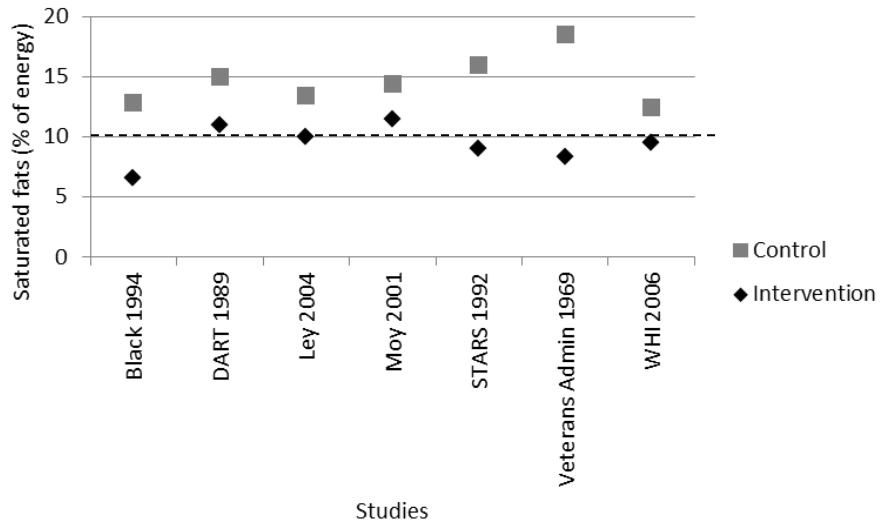


Figure A2.2 Mean intakes of saturated fat from individual RCTs that examined the effect of reduced intakes of saturated fats on CVD events

Note:

- Data on mean intakes of saturated fat obtained from individual RCTs included in the Hooper et al (2015) review
- Hooper et al., 2015 examined 11 RCTs ; 7 RCTs reported mean intakes of saturated fat
- Intakes of saturated fat ranged from 6.6-11.5% of energy (intervention) and 12.4-18.5% of energy (control)

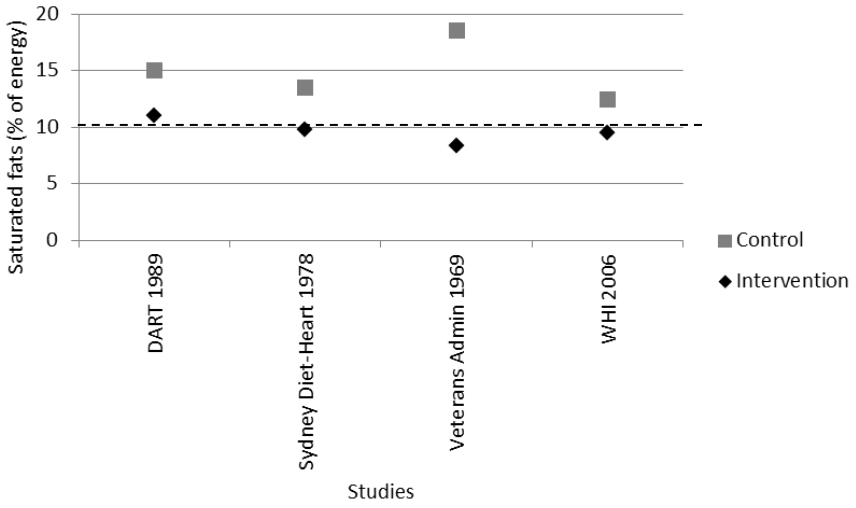


Figure A2.3 Mean intakes of saturated fat from individual RCTs that examined the effect of reduced intakes of saturated fats on CHD mortality

Note:

- Data on mean intakes of saturated fat obtained from individual RCTs included in the Hooper et al (2015) review
- Hooper et al., 2015 examined 10 RCTs; 4 RCTs reported mean intakes of saturated fat
- Intakes of saturated fat ranged from 8.3-11.0% of energy (intervention) and 12.4-18.5% of energy (control)

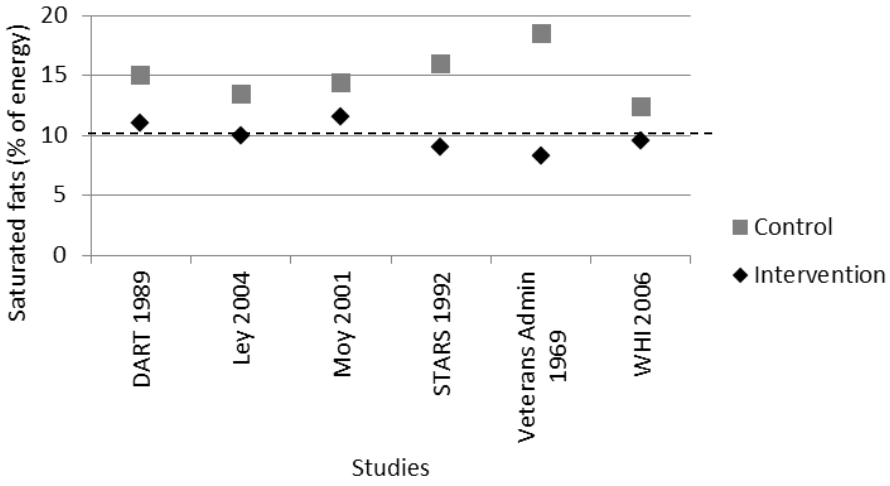


Figure A2.4 Mean intakes of saturated fat from individual RCTs that examined the effect of reduced intakes of saturated fats on CHD events

Note:

- Data on mean intakes of saturated fat obtained from individual RCTs included in the Hooper et al (2015) review
- Hooper et al., 2015 examined 12 RCTs; 6 RCTs reported mean intakes of saturated fat
- Intakes of saturated fat ranged from 8.3-11.5% of energy (intervention) and 12.4-18.5% of energy (control)

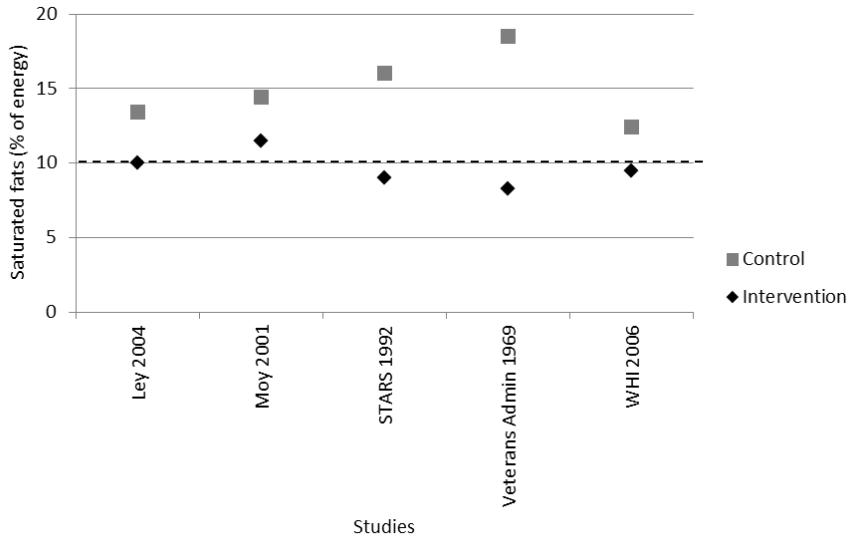


Figure A2.5 Mean intakes of saturated fat from individual RCTs that examined the effect of reduced intakes of saturated fats on strokes

Note:

- Data on mean intakes of saturated fat obtained from individual RCTs included in the Hooper et al (2015) review
- Hooper et al., 2015 examined 7 RCTs; 5 RCTs reported mean intakes of saturated fat
- Intakes of saturated fat ranged from 6.6-11.0% of energy (intervention) and 12.4-18.5% of energy (control)

Blood lipids

Table A2.3 Characteristics of meta-analyses and systematic reviews

Study	Research methods	Analysis	Results	Comments
Hooper et al. (2015) (Systematic review and meta-analysis) <u>Funding source</u> L Hooper: Studentship, Systematic Reviews Training, Institute of Child Health, University of London, UK. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? <u>Selection criteria</u> *Search dates:* July 2010 to March 2014 (plus search from Hooper 2012 – inception to June 2010). *Study design:* RCTs only. *Inclusion criteria:* >18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet; duration ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions. *Exclusion criteria*: Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Random effects meta-analysis to assess risk ratios. Low vs high %of energy from saturated fats. Incremental changes in % of energy from saturated fats. *Subgroup analysis* Saturated fat substitution with PUFA, MUFA, carbohydrate. <u>Evaluation of study quality</u> Cochrane 'risk of bias' tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction. Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using I^2 test.	15 RCTs; n=56,568; duration: 1.6-8.1y; age 46-66y; gender: M(8), F(3), M/F(4); health at baseline: high risk of CVD (4), previous MI (6), diabetic / impaired glucose intolerance (3), angina (2), breast cancer (1), siblings of people with CHD, with at least one CVD risk factor (1); country: USA (5), UK (6), The Netherlands (1), Norway (1), New Zealand (1), Australia (1). <u>Reduced saturated fats compared to usual diet</u> TC: ↓ with reduced saturated fats (13 RCTs; n=7115) MD -0.24mmol/L (95% CI -0.36, -0.13) I^2=60% No clear differential effect on TC depending on the replacement for saturated fats. LDL-C:↓ with reduced saturated fats (5 RCTs; n=3291) MD -0.19mmol/L (95% CI -0.33, -0.05) I^2=37% No clear differential effect on LDL-C depending on the replacement for saturated fats. HDL-C: no effect (7 RCTs; n=5147) MD -0.01mmol/L (95% CI -0.02, 0.01) I^2=0% No clear differential effect on HDL-C depending on the replacement for saturated fats. TC:HDL-C ratio: no effect (3 RCTs; n=2985) MD -0.10mmol/L (95% CI -0.33, 0.13) I^2=24% No clear differential effect on TC:HDL ratio depending on the replacement for saturated fats. TAG: no effect (7 RCTs; n=3845) MD -0.08mmol/L (95% CI -0.21, 0.04) I^2=51% No clear differential effect on TAG depending on the replacement for saturated fats.	Findings suggest reducing saturated fat intake reduces TC and LDL-C but not HDL-C, TC:HDL-C ratio or TAG. No differential effect of replacement type was observed. <u>Limitations</u> Although the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE).

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates:* January 2000- February 2012. *Study designs:* RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); ≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration ≥ 4 weeks (RCTs), ≥6 months (BW and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6 months, <40% on 12 months, <50% in 24 months; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority; study aim outside scope of review; exposure food pattern or a whole food;	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-suggestive, and limited-no conclusion. <u>Evaluation of study quality</u> Primary evidence assessed for quality but method not stated. Quality categories included: A) high quality with very low risk of bias; B) good quality, some risk of bias but not enough to invalidate results; C) low quality with significant bias and weaknesses which may invalidate results.	9 RCTs; n=976; duration: 5-18wks; age 18-65y; gender: M(2), F(0), M/F(7); health at baseline: healthy (6), diabetic (1), obese/overweight (2); country: USA (3), UK (2), The Netherlands (2), Sweden (1), Czech Republic (1). <u>High MUFA and/or PUFA diet compared with high saturated fat diet</u> Saturated fat vs MUFA diet: saturated fat 13-19% of energy, MUFA 14-21% of energy. Saturated fat vs PUFA diets: saturated fat 20% of energy or 52% of total fat in diet, PUFA 9% of energy or 41% of total fat in diet. *Fasting plasma/serum TC* (9 RCTs, n=476) All RCTs: ↓TC. Convincing evidence of an effect; grade B evidence. *Fasting plasma/serum LDL-C* (9 RCTs, n=not stated). 8 RCTs: ↓ LDL-C. 1 RCT: no effect. Convincing evidence of an effect; grade B evidence. *Fasting plasma/serum HDL-C* (9 RCTs, n=476) 3 RCTs: ↓ HDL-C 1 RCT: ↑ HDL-C. 5 RCTs: no effect. Limited evidence-no conclusion; grade B evidence. *Fasting plasma/serum total TAGs* (8 RCTs, n=456) 2 RCTs: ↓ total TAGs. 6 RCTs: no effect. Effect unlikely; grade B evidence.	Substitution of saturated fats with MUFA and/or PUFA convincingly decreases concentration of total and LDL-C but is unlikely to affect total triglycerides. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included, however several systematic reviews and meta-analyses included in pervious publications. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence. Many questions remain unresolved due to conflicting results from studies and lack of high quality controlled studies.

Study	Research methods	Analysis	Results	Comments
	included non-healthy subjects, obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Micha and Mozaffarian (2010) (Narrative review) Funding source Searle Funds at The Chicago Community Trust; the Bill & Melinda Gates Foundation/WHO Global Burden of Diseases, Injuries, and Risk Factors Study. Declarations of interest Consulting honoraria (modest) from Nutrition Impact; Unilever; SPRIM.	Research question Elucidate effects of saturated fat consumption on CVD risk based on the most current evidence. Selection criteria *Search period*: Inception to September 2009. *Study design*: RCTs and PCS. *Inclusion criteria*: Adults; evaluating saturated fat intake and risk of CHD, stroke, type 2 diabetes, related risk pathways including lipids and lipoproteins, systemic inflammation, vascular function, insulin resistance. *Exclusion criteria*: A priori animal studies, ecological studies, commentaries, general reviews, case reports. Dietary assessment methods Not reported.	Analysis Narrative review. Evaluation of study quality Not reported.	Number of publications not mentioned for this analysis; characteristics of identified studies not summarised. Compared with MUFA or PUFA, saturated fat intake ↓ TC, LDL-C, TC:HDL-C ratio; has little effect on TAG; PUFA slightly ↓ HDL-C. Compared with carbohydrate, saturated fat intake ↑ TC, LDL-C, HDL-C; ↓ TAG; has no effect on TC:HDL-C ratio. Compared with trans fats, saturated fat intake has a minimal effect on LDL-C; ↑ HDL-C, ↓ TAG, improves TC:HDL-C ratio.	Substantial evidence indicating that reducing saturated fat has varying effects depending on the replacement nutrient: Replacement with PUFA lowers CHD risk. Replacement with carbohydrate has no benefit. Replacement with MUFA has uncertain effects. Advice to reduce saturated fat intake without considering the replacement may have little or no effects on disease risk.

Study	Research methods	Analysis	Results	Comments
Van Horn et al. (2008) (Systematic narrative review) <u>Funding source</u> None declared. <u>Declarations of interest</u> None declared.	<u>Research question</u> Review of the evidence associated with key dietary factors and risk of CVD. <u>Selection criteria</u> *Search period:* First review 1991-2001; update review 2001-2004; supplementary search in 2006. *Study Design:* Not detailed. *Inclusion criteria:* Human subjects; English language; articles in ADA evidence analysis library. *Exclusion criteria:* Sample size <10 in each treatment group; drop-out rate >20%. Provided more than 1000 papers, additional criteria applied but not detailed. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Expert panel identified and evaluated current research, limited details provided. <u>Evaluation of study quality</u> Not reported.	*Saturated fat* 4 RCTs; n=25-290; duration: 4-8 wk; other study characteristics not reported. Low saturated fat diet (<7% of energy) reduced LDL-C by 9-12% (4 RCTs), and HDL-C (3 RCTs). Population studies (number and characteristics not reported): associations between diets high in saturated fats and increased TC, LDL-C, and HDL-C concentrations. *Isoenergetic replacement of saturated fat (2 RCTs)* Isoenergetic replacement of saturated fats with PUFA and MUFA decreases TC, LDL-C, and TC:HDL-C ratio.	To reduce the risk of CVD, dietary saturated fat should be replaced isoenergetically with complex carbohydrate and/or unsaturated fatty acids including both MUFA (<20% of energy) and PUFA (<10% of energy).

Study	Research methods	Analysis	Results	Comments
Mensink et al. (2003) (Meta-analysis) <u>Funding source</u> Maastricht University; Wageningen University; Wageningen Centre for Food Sciences. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Evaluate the effect of individual fatty acids on TC:HDL-C and on serum lipoproteins. <u>Selection criteria</u> *Search period:* January 1970- December 1998. *Study design:* Parallel, crossover or Latin-square design control trials. *Inclusion criteria:* Dietary fatty acids sole variable; controlled consistent dietary cholesterol intake; feeding period > 13 days; adult subjects >17 years; non disturbances of lipid metabolism or diabetes; English language only. *Exclusion criteria:* Very long chain PUFAs (n-3) e.g. fish oils; medium-chain fatty acids (too few studies to allow stats analysis); sequential study design; subjects with diabetes. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Data points: Independent variable – fatty acid composition of the diet; Dependent variable - mean serum TC:HDL-C, mean serum lipid, or apolipoprotein concentration; of a group of subjects, at end of dietary period. Regression coefficients are predicted change in TC:HDL-C, serum lipid, or apolipoprotein, concentrations, when carbohydrate intake decreases by 1% of energy and the fatty acid increases by the same amount. Model estimated effects on a particular outcome of all fatty acids (saturated fats, *cis* MUFAs, n-6 *cis* PUFAs). Dependent variable: absolute lipid or apolipoprotein concentrations during the diets rather than changes induced by diets. Cook's distances and visual inspection of plots used for validity. Random-effect model not used as standard error not provided in the studies. <u>Evaluation of study quality</u> Not reported.	60 RCTs; n=1672; duration: 13-91days; age: 21-72y (reported in 51 RCTs); gender: 70% male; health at baseline: trials on inpatients (11), used liquid formulas (6); country: USA (34), The Netherlands (8), Denmark (4), Canada (3), Finland (2), Israel (2), Malaysia (2), Norway (2), Germany (1), Italy (1), UK (1). 40 studies reported mean pre study TC, range: 3.7-6.5mmol/L. <u>Isoenergetic replacement of carbohydrate with saturated fats</u> *Increased:* TC (47 studies): 0.036mmol/L (95% CI 0.029, 0.043) LDL-C (43 studies): 0.032mmol/L (95% CI 0.025, 0.039) HDL-C (43 studies): 0.010mmol/L (95% CI 0.007, 0.013) Apo A-I (22 studies): 5.7mmol/L (95% CI 2.3, 9.1) *Decreased:* TAG (45 studies): -0.021 (95% CI -0.027, -0.015) *No effect:* TC:HDL-C (42 studies), Apo B (23 studies). <u>Replacement of saturated fats with cis MUFA</u> 1% of energy replaced, predicted to lower HDL-C concentrations by 0.002mmol/L. <u>Replacement of saturated fats with cis unsaturated fatty acids</u> TC:HDL-C ratio decreased.	Efficacy of replacing saturated fats with carbohydrate depends on the effect on body weight in the long term and effect is uncertain. Replacement of saturated fats with *cis* unsaturated fatty acids reduce coronary artery disease risk. <u>Limitations</u> Effect of gender could not be examined as many studies combine male and female results.

Study	Research methods	Analysis	Results	Comments
Yu-Poth et al. (1999) (Meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> None declared.	<u>Research question</u> Evaluate the effects of different dietary interventions (National Cholesterol Education programs Step 1 and Step 2 dietary interventions) on major CVD risk factors in healthy and high-risk subjects using meta-analysis. <u>Selection criteria</u> *Search dates:* 1981-1997. *Study design:* RCTs (sequential, randomised, parallel-arm). *Inclusion criteria:* Aim to lower blood cholesterol concentrations or reduce body weight for primary purpose of preventing CVD; a Step 1 diet (all intervention groups: total fat ≤30% of energy; saturated fats ≤10% of energy; ≤ 300mg dietary cholesterol/d), a Step 2 diet (saturated fats ≤7% of energy; ≤200mg dietary cholesterol/d) or both were part of dietary intervention; subjects free-living, prepared own food and counselled by dietitians/professionals about low-fat diets; intervention ≥3 weeks to stabilise plasma cholesterol concentrations. *Exclusion criteria:* Not reported. <u>Dietary assessment method</u> 24 hour recall, 3-7 day food record and FFQ.	<u>Analysis</u> Changes in plasma TC, LDL-C, HDL-C and TAG after Step 1 and Step 2 dietary interventions assessed. Analysis of variance to compare effects of Step 1 with Step 2. Changes in plasma TC, LDL-C, HDL-C and TAG with changes in saturated fats evaluated by regression analysis. <u>Evaluation of study quality</u> Not reported.	37 RCTs; n=9276 (intervention), n=2310 (control); duration: 3wk-4y; age: not reported; gender: M(9), F(7), M/F(21); health at baseline: healthy and high-risk subjects; country: not reported. Range of dietary interventions and experimental designs (% saturated fat of total energy <6% to <10%); had control group (19 RCTs) (maintained habitual lifestyle and food consumption during study); included exercise intervention (13 RCTs). *Step 1 intervention: lipids decreased by* Plasma TC: 0.63 ± 0.06mmol/L (10%) p<0.01 LDL-C: 0.49 ± 0.05mmol/L (12%) p<0.01 HDL-C: 0.04 ± 0.02mmol/L (1.5%) p not reported TAG: 0.17 ± 0.04mmol/L (8%) p<0.01 TC:HDL-C: 0.50 ± 0.11mmol/L (10%) p<0.01 *Step 2 intervention: lipids decreased by* Plasma TC: 0.81 ± 0.12mmol/L (13%) (p<0.01) LDL-C: 0.65 ± 0.09mmol/L (16%) (p<0.01) HDL-C: 0.09 ± 0.03mmol/L (7%) (p<0.01) TAG: 0.19 ± 0.14mmol/L (8%)(p<0.01) TC:HDL-C: 0.34 ± 0.12mmol/L (7%) (p<0.01) <u>Changes in lipids in males vs females</u> *Step 1 intervention* TAG: Females 0.01mmol/L (2.4%) Males -0.21mmol/L (-10.4%) *Step 2 intervention* HDL-C: Females -0.10mmol/L (-6.7%) Males -0.03mmol/L (-2.2%) p<0.05 TAG: Females 0.07mmol/L (5.4%) Males -0.03mmol/L (-1.5%)	Reduction in dietary fat and saturated fat has beneficial effects on CVD risk factors in free-living subjects. Plasma TC, LDL-C, and TAG concentrations and TC:HDL-C significantly decreased after both Step 1 and Step 2 diets. Weight loss and exercise combined can increase the effect.

Study	Research methods	Analysis	Results	Comments
			1% decrease in energy from saturated fats resulted in: TC: -0.056mmol/L (-0.77%) LDL-C: -0.056mmol/L (-1.07%) HDL-C: -0.012mmol/L (-0.6%)	

Study	Research methods	Analysis	Results	Comments
Tang et al. (1998) (Systematic review) <u>Funding source</u> Funded by a project grant from the nutrition programme phase 1 of the Department of Health and Medical Research Council. Authors supported by the British Heart Foundation and Imperial Cancer Research Fund. <u>Declarations of interest</u> None to declare.	<u>Research Question</u> Estimate the efficacy of dietary advice to lower blood TC concentration in free-living subjects and to investigate the efficacy of different dietary recommendations. <u>Selection criteria</u> *Search period:* Inception to 1996. *Study Design:* RCTs. *Inclusion criteria:* Two groups, one a control, treatment assignment by random allocation; intervention was a global dietary modification (changes to various food components of the diet to achieve desired targets); lipid concentration measured before and after intervention. *Exclusion criteria:* Specific supplementation diets (e.g. specific oils, garlic); multifactorial interventions trials; trials aimed primarily at lowering body weight or blood pressure; interventions that lasted <4 weeks; randomisation of workplace or general practice. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Absolute difference (mmol/L) in mean change in blood TC between control and intervention groups. % reduction cholesterol concentrations at end of trial or 12 months, whichever was earlier. SE of the difference for each comparison. Similar methods applied to changes in dietary intakes. Heterogeneity tested by comparing observed results in different categories of trials grouped according to type of diet, intensity of advice, and type of patients. <u>Evaluation of study quality</u> Not reported.	19 RCTs; n=40-2033; duration: 6wk-5y; age: not reported; gender: M(7), F(2), M/F(10); health at baseline: CHD patients with aim of secondary prevention (5), raised cholesterol (4), raised blood pressure (3), healthy adults (4), women at increased risk of breast cancer (2), children (1); country: not reported. Average baseline blood TC concertation 6.3mmol/L. <u>Overall effect of dietary advice on TC</u> *Weighted mean reduction in blood TC:* 5.7% (95% CI 5.2%, 6.3%). *For studies of at least 6 months duration:* 5.3% (95% CI 4.7, 5.9%). <u>Reduction in TC by category of diet</u> • American Heart Association Step 1 or equivalent diets: 3.0% (1.8%- 4.1%), no significant heterogeneity (X^2_4 = 6, P>0.1), but estimate heavily depends on one large trial. • American Heart Association Step 2 or equivalent diets: 5.6% (4.7%-6.5%), significant heterogeneity of effects of Step 2 diets (X^2_7= 45, p<0.001), includes one trial in children (aged 8-10y). • Diets increased ratio of PUFA to saturated fats, reduced blood cholesterol concentration by 7.6% (6.3%-9.0%), significant heterogeneity between effects (X^2_4 = 24, p<0.001). • Low fat diets:5.8% (3.8%-7.8%), no significant heterogeneity (no figure provided). <u>Reduction in TC by duration of intervention</u> Overall reduction in blood TC concentration attributable to dietary advice was 6.6% at about 6	Suggests that dietary advice to free-living subjects can be expected to reduce blood TC by only 3-6%. Step 1 diet only has a small cholesterol lowering effect even among those with evidence of CHD. <u>Limitations</u> Excluded trials in which dietary advice was given together with other interventions. Publication bias- unable to identify any unpublished trials. Limited analysis to published, tabulated data by approaching investigators and experts in the subject to obtain extra unpublished data or clarify areas of uncertainty, but was largely unsuccessful.

Study	Research methods	Analysis	Results	Comments
			weeks, 8.5% at about 3 months, 6.8% at 6 months, 5.5% at 112 months and 4.4% at 24 months. <u>Compliance with dietary advice</u> Fat intake of control groups ranged from 29 to 42% of total energy intake. Two trials of Step 1 diets met target for saturated fat (<10% of total fat), both achieved the largest reduction in blood TC concentration.	

Study	Research methods	Analysis	Results	Comments
Brunner et al. (1997) (Meta-analysis) Funding source Review undertaken as part of the Health Gain Project, which was jointly funded by the Health Education Authority and the North Thames (West) Regional Health Authority. Declarations of interest None declared.	Research Question Evaluation of the effectiveness of dietary advice in primary prevention of chronic disease Selection criteria *Search period:* Inception to July 1993. *Study Design:* RCTs. *Inclusion criteria:* Free living adults; trial involved primary prevention (<25% had diagnosed disease); invention group was encouraged to change fat consumption pattern; subjects were randomised to intervention or control group; trial lasted a minimum of 3 months. *Exclusion criteria:* Supplement diet used; any other difference between the groups other than dietary intervention; meal provided to subjects; cross over design; multiple intervention trials; diet vs exercise advice. Dietary assessment method FFQ, food dairies (3- 4 days), diet history taken by dietitian.	Analysis Intervention effects estimated by comparing mean changes in intervention and control groups, with SE. Estimated treatment effects and SE from graphs and comparison of follow-up values without baseline data. In trials involving 3 randomised groups, compared most intensive and least intensive interventions. Pooled intervention effects summarised by random effects meta-analysis (weighted by inverse of the sum of the between-studies variance and the variance of the study intervention effect). Heterogeneity assessed by Q statistic, a weighted between-studies sum of squares. Evaluation of study quality Not reported.	17 RCTs; n=6893 (n=3736 intervention; 3817 randomised individually, 3076 randomised by work place); duration: not reported; age: not reported; gender: M(49%); health at baseline: not reported; country: USA (10), UK (2), The Netherlands (2), Australia (1), Canada (1), Sweden (1). Dietary intake assessed in 9 trials. Reported dietary outcomes: dietary fat All 3-6 month trials (4 RCTs) showed effects favouring intervention. Effect sizes varied considerably, formal evidence of heterogeneity at 3- 6 and 9-18 months of follow-up (all p<0.0001). Biochemical outcomes: serum cholesterol *Estimated overall net reduction in serum cholesterol at 3-6 months (8 RCTs) :* -0.28 (95% CI -0.42, -0.15) mmol/L Heterogeneity significant (p<0.05). *Estimated overall net reduction in serum cholesterol at 9-18 months (5 RCTs) :* -0.22 (95% CI -0.39, -0.05) mmol/L Heterogeneity significant (p<0.02).	Individual dietary intervention would result in the reduction of CHD representing 35% of UK Health of the Nation target. Dietary advice from health care or health promotion personnel appears to be effective in achieving modest dietary change and accompanying CVD risk reduction. Limitations Evaluated the effects of dietary change on blood pressure and cholesterol, not mortality. Summary statistics may be misleading as a result of publication bias - funnel plots suggest not a serious problem.

Study	Research methods	Analysis	Results	Comments
Clarke et al. (1997) (Meta-analysis) <u>Funding source</u> British Heart Foundation and Medical Research Council. <u>Declarations of interest</u> None to declare.	<u>Research Question</u> Determine the quantitative importance of dietary fatty acids and dietary cholesterol to blood concentrations of TC, LDL-C and HDL-C. <u>Selection criteria</u> *Search period:* Not specified. *Study Design:* Metabolic ward studies. *Inclusion criteria:* Diets persisting for minimum 2 weeks; solid food studies (liquid diets considered separately); healthy volunteers. *Exclusion criteria:* Subjects selected for some disorder (e.g. diabetes or dyslipidaemia); dietary changes deliberately confounded by other interventions (e.g. weight reduction or exercise); no data available about dietary fatty acids or dietary cholesterol; poor compliance. <u>Dietary assessment method</u> Not reported.	<u>Analysis</u> Multilevel regression analyses (included: age, weight, dietary intake of nutrients, and one unique term per study to ensure people within any other one study were compared directly only with each other). Analyses assessed different sources of variability: (a) within group, between experiments; (b) within study, between matched groups; (c) within study, between unmatched groups; and (d) between studies. <u>Evaluation of study quality</u> Not reported.	No study characteristics reported. Blood HDL-C and LDL-C (227 trials). <u>Saturated fat (% of energy)</u> *Univariate analysis:* TC: 0.067 (0.003) *Multivariate analysis:* TC: 0.052 (0.003) LDL-C: 0.036 (0.0050) HDL-C: 0.013 (0.002) <u>Replacement of saturated fats equivalent to 10% of dietary calories by complex carbohydrates</u> TC: -0.52mmol/L (SE 0.03) LDL-C: -0.36mmol/L (SE 0.05) HDL-C: -0.13mmol/L (SE 0.02) Heterogeneity: all four types of saturated fat $X^2_3 = 18.1$ ($p<0.001$).	Reduction in blood cholesterol concentration when isoenergetic replacements of saturated fats by unsaturated fats appears within a few weeks and is greater than sometimes appreciated. <u>Limitations</u> Restricted to metabolic ward studies as non-experimental dietary studies in community subjects may chiefly reflect poor compliance.

Study	Research methods	Analysis	Results	Comments
Howell et al. (1997) (Meta-analysis) <u>Funding source</u> Supported by a grant-in-aid from the American Egg Board administered through the Egg Nutrition Center and by funds from The University of Arizona Agricultural Experiment Station. <u>Declarations of interest</u> None declared.	<u>Research Question</u> Investigate the extent to which study and subject characteristics, initial serum lipid concentrations, interactions of dietary manipulations, and the duration of treatment influenced the predictive models. Develop a more broadly applicable model, spanning a diversity of study designs and types of subjects, to predict more appropriately the extent to which meeting the National Cholesterol Education Program (NCEP) Steps 1 and 2 national dietary guidelines could be expected to affect changes in blood lipid concentrations of the American population. <u>Selection criteria</u> *Search period:* January 1966-February 1994. *Study Design:* Not stated. *Inclusion criteria:* English language; adults >18 years; studies reporting single-group or multiple-group repeated-measures comparisons; studies reporting quantitative measures of manipulated dietary components including one or more of the following: cholesterol, total fat (% of energy), saturated fats, PUFAs, and MUFAs (% of energy); studies reporting group means ± SDs or SEMs for quantitative measures of response variables including any or all of the following: serum TC, LDL-C, HDL-C, VLDL-C and serum TAG. *Exclusion:* Large clinical trials with multiple interventions; studies reporting data on weight reduction diets; fish oils, trans fat and hydrogenated fats were excluded.	<u>Analysis</u> Study groups were weighted proportionally to their size and inversely to the number of times observed. Difference between the final and initial values of dietary cholesterol (mg/day) and total fat, PUFA, MUFA and saturated fats (% of energy), computed to create dietary change variables. Bivariate Pearson correlations described relations between dietary variables and response variables. Stepwise-multiple-regression analysis used to identify best linear prediction equations for response measures, evaluating combined and independent contributions of specified dietary variables. Forward stepwise variable selection to describe relations and control for problems of linear dependence. Effects of dietary manipulations explored using modified linear predication model into a nonlinear. Nonlinear least squares estimates significantly different from 0 taken as indicative of a discernible treatment duration effect. <u>Evaluation of study quality</u> Internal validity was assed as high, medium or low; 9% of studies were rated as having high internal validity.	224 studies; 8143 subjects (in 366 independent groups including 878 diet-blood lipid comparisons were presented for the weighted least square regression analyses); duration: not reported; age: 18-69y: gender: M (70% in independent groups); health at baseline: healthy (81%), coronary artery disease (19%); country: not reported. 10% studies where blinded (7% double blinded, 3% single blinded). <u>Results related to saturated fats only</u> *Bivariate relations between variables* Serum TC and saturated fats (r=0.80, p<0.0005) Change in saturated fats associated with changes in LDL-C (r=0.79, p<0.0005) and HDL-C (r=0.60, p<0.0005) <u>Prediction equations</u> 1% alteration in total energy from saturated fats will result in 49.1µmol/L change in serum TC. 1% change in saturated fats (as % of energy) will result in a change in LDL-C of 46.5mmol/L.	Some individuals can lower their plasma cholesterol concentrations by decreasing dietary saturated fat and cholesterol intakes.

Study	Research methods	Analysis	Results	Comments
	Dietary assessment method Weighed/measured intake, subject reported intake records, subject recall.			

Table A2.4 RCTs and PCS assessing the relationship between dietary saturated fat intake and blood lipids in each review article

Study name[1] / first author **Publication year**	**Hooper et al. (2015)[2]**	**Schwab et al. (2014)**	**Van Horn et al. (2008)[3]**	**Mensink et al. (2003)[4]**	**Yu-Poth et al. (1999)**	**Tang et al. (1998)**	**Brunner et al. (1997)**
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Total primary studies (publications)	14 (15)	9	7	35	29	19 (21)	10
Guldbrand 2012							
Women's Health Initiative							
Howard 2010							
Howard 2006	C, H, L, T, R						
Bos 2010		C, H, L, T					
Elhayany 2010							
Foster 2010							
Iqbal 2010							
Klemsdal 2010							
Lim 2010							
Brehm 2009							
Brinkworth 2009							
Dale 2009							
Davis 2009							
Esposito 2009							
Frisch 2009							
Sacks 2009							
van Dijk 2009		C, H, L					
Wolever 2009							
Shai 2008							

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Lesna 2008		C, H, L, T					
Ebbeling 2007							
Gardner 2007							
Chlebowski 2006	C						
McAuley 2006							
Jenkins 2006							
Appel 2005			H, L, T				
Dansinger 2005							
Ebbeling 2005							
Lefevre 2005		C, H, L, T					
Stern 2004							
Ley 2004	C, H, L, T, R						
Foster 2003							
Jenkins 2003			L				
Vessby 2001		C, H, L, T					
Smith 2003		C, H, L, T					
Judd 2002			L				
Lichtenstein 2002			H, L, T				
Lovejoy 2002		C, H, L, T					
Summers 2002		C, H, L, T					
Dietary Intervention Study in Children (DISC) Obarzanek 2001 DISC Collaboration writing group 1995			C, H, L, T			C	

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Lanza 2001							
Lichtenstein 2001							
Moy 2001	H, L, T						
Denke 2000		C, H, L, T					
Yu-Poth 2000			L, H				
Singh 1993					C, H, L, T		
Ginsberg 1998			H, L, T	X			
Judd 1998				X			
Lee-Han 1998							
Muller 1998				X			
Aro 1997				X			
Cater 1997				X			
Knopp 1997					C, H, L, T		
Mazier 1997				X			
McCarron 1997					C, H, L, T		
Simon 1997 Simon 1997 Kasim 1993	C, H, L, T				C, H, L, T		
Walden 1997					C, H, L, T		
Davidson 1996					C, H, L, T		
Park 1996				X			
Almendingen 1995							
Dengel 1995					C, H, L, T		

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Dougherty 1995				X			
Fielding 1995				X			
Geil 1995					C, H, L, T		
Ginsberg 1995							
Katzel 1995					C, H, L, T		
Nelson 1995				X			
Zock 1995							
Cheung 1994							
de Lorderil 1994					C, H, L, T		
Burr 1989	C, H					C	
Denke 1994					C, H, L, T		
Haskell 1994					C, H, L, T		
Insull 1994							
Judd 1994							
Kris 1994							
Lichtenstein 1994				X			
Lopez-Miranda 1994							
Marckmann 1994							
Milne[5] 1994							
Sarkkinen 1994						C	
Sundram 1994				X			
Tholstrup (b) 1994				X			
Tholstrup (a) 1994				X			

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Zock 1994				X			
Baer 1993					C, H, L, T		
Derr 1993				X			
Hellenius 1993							C
Hunninghake 1993						C	
Kris-Etherton 1993				X			
Lichtenstein 1993							
Sabate 1993							
Wood 1993							
Anderson 1992						C	
Barnard 1992					C, H, L, T		
Barr 1992				X			
Berry 1992							
Denke 1992				X			
Marckmann 1992				X			
Mata 1992							
Ng 1992							
Schyler 1992					C, H, L, T		
Sciarrone 1992						C	
Seim 1992					C, H, L, T		
Singh (a) 1992					C, H, L, T		
Singh (b) 1992					C, H, L, T		
Valsta 1992							

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Wahrburg 1992							
Watts 1992	C, H, L, T, R					C	
White 1992							
Zock 1992							
Bae 1991					C, H, L, T		
Barnard 1991					C, H, L, T		
Berry 1991							
Bloemberg 1991						C	C
Brown 1991							
Iacano 1991							
Kwon 1991				X			
Masana 1991							
Ng 1991							
Nikolaus 1991					C, H, L, T		
Savolainen 1991							
Wardlaw 1991							
Wood 1991					C, H, L, T		
Baron 1990						C	C
Boyd 1990					C, H, L, T		C
Brinton 1990							
Denamark-Wahrenfreid 1990						C	
Dreon 1990						C	
Ginsberg 1990							

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Henderson 1990							C
Insull 1990						C	
Koopman 1990							C
Mensink 1990							
Ornish 1990					C, H, L, T		
Hockaday 1978	C						
Wardlaw 1990				X			
Frantz 1989							
Mensink 1989							
Oslo Diet-Heart Study							
Leren 1970						C	
Leren 1968						C	
Leren 1966	C					C	
Baggio 1988							
Bonanome 1988				X			
Boyd 1988						C	
Denke 1988							
Grundy 1988							
Judd 1988							
Katan 1988				X			
Weintraub 1988							
Jones 1987							
Mensink 1987							

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Crouch 1986							C
Grundy 1986				X			
Marshall 1986				X			
Arntzenius 1985					C, H, L, T		
Beynen 1985							
Hegsted 1985							
Kohlmeier 1985							
Kuusi 1985					C, H, L, T	C	
Lasserre 1985							
Mattson 1985				X			
Reiser 1985				X			
Weisweiler 1985							
Ehnholm 1984					C, H, L, T		
Masarei 1984							
Becker 1983				X			
Bruno 1983							C
Harris 1983							
Weisweiler 1983							
Wolf 1983				X			
Ehnholm 1982					C, H, L, T	C	
Laine 1982							
McMurry 1982							
Chenoweth 1981							

Study name[1] / first author Publication year	Hooper et al. (2015)[2]	Schwab et al. (2014)	Van Horn et al. (2008)[3]	Mensink et al. (2003)[4]	Yu-Poth et al. (1999)	Tang et al. (1998)	Brunner et al. (1997)
C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.							
Flaim 1981							
Hjermann 1981					C, H, L, T		
Lewis 1981				X			
Brussaard 1980				X			
Mojonnier 1980							C
Foreyt 1979							C
Houtsmuller 1979	C, T						
Woodhill 1978	C, T					C	
Anderson 1976				X			
MRC 1968	C						
Nestel 1973							
Grande 1972				X			
Grande 1970				X			
McGandy 1970							
Veterans Admin Dayton 1969 Dayton 1962	C						
American National Heart Study 1968						C	
Moore 1968							
Research Committee 1965						C	
Rose 1965	C						
Keys 1957							

Outcomes measured by study: C, total cholesterol (TC); H, high density lipoprotein cholesterol (HDL-C); L, low density lipoprotein cholesterol (LDL-C); T, triacylglycerol (TAG); R, TC to HDL-C ratio.

[1] Study name is only provided when two or more publications for that study are used by the reviews. Micha and Mozaffarian (2010), Clarke et al. (1997), Howell et al. (1997): unclear which primary studies were included in reviews.
[2] Hooper et al. (2015) presents publications used in the analyses by study name and identifies a main study publication along with all supplementary publications for the study. It is not possible to know which exact publication the data has come from, therefore, the main study publication has been used in the table above.
[3] Van Horn et al. (2008) also includes the review by Yu-Poth (1999).
[4] Unclear in review which papers relate to each outcome measured.

Blood pressure

Table A2.5 Characteristics of meta-analyses and systematic reviews

Study	Research methods	Analysis	Results	Comments
Hooper et al. (2015) (Systematic review and meta-analysis) Funding source L Hooper: Studentship, Systematic Reviews Training, Institute of Child Health, University of London, UK. Declarations of interest None to declare.	Research question What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? Selection criteria *Search dates:* July 2010 to March 2014 (plus search from Hooper 2012 – inception to June 2010). *Study design:* RCTs only. *Inclusion criteria:* >18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet; duration ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions. *Exclusion criteria*: Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials. Dietary assessment methods Not reported.	Analysis Random effects meta-analysis to assess risk ratios. Low vs high % of energy from saturated fats. Incremental changes in % energy from saturated fats. *Subgroup analysis:* Saturated fat substitution with PUFA, MUFA, carbohydrate. Evaluation of study quality Cochrane 'risk of bias' tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction. Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using I^2 test.	5 RCTs; n=3812 participants; duration: 3.8-8.1y; age: 30-67y; gender: M(3), F(1), M/F(1); health at baseline: high risk of CVD (1), previous MI (3), diabetic/impaired glucose intolerance (1); country: USA (1), UK (1), Norway (1), Australia (1), New Zealand (1). Systolic blood pressure- no effect of reducing saturated fats MD = -0.19 mmHg, 95% CI -1.36 to 0.97, P=0.97, I^2 0% Diastolic blood pressure- no effect of reducing saturated fats MD = -0.36 mmHg, 95% CI -1.03 to 0.32, P=1.00, I^2 0%	Reducing saturated fats has no effect on systolic or diastolic blood pressure. Limitations Although the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE). Unable to tell which trials were included in the analysis.

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates:* January 2000- February 2012. *Study designs:* RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); ≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration ≥ 4 weeks (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6 months, <40% on 12 months, <50% in 24 months; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority; study aim outside scope of review;	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-suggestive, and limited-no conclusion. <u>Evaluation of study quality</u> Primary evidence assessed for quality but method not stated. Quality categories included: A) high quality with very low risk of bias; B) good quality, some risk of bias but not enough to invalidate results; C) low quality with significant bias and weaknesses which may invalidate results.	3 RCTs; n=647; duration: 8 wks-3 months; age: 30-70y; gender: M (0), F (0), M/F (3); health at baseline: healthy (2), impaired glucose tolerance but not diabetic (1); country: The Netherlands (1), Europe (1), Europe/Australia (1). 1 PCS; n=28,100; durations: 12.9y; age: ≥39y; gender: F; health at baseline: healthy; country: USA. 3 RCTs and 1 PCS compared MUFA and saturated fats. Saturated fats replaced with MUFA (20-21% of energy) resulted in lower blood pressure in two of the RCTs. 1 RCT found the response to a MUFA-enriched diet (21% of energy) was pronounced when total fat was <37% of energy, compared with total fat intake >37% of energy. PCS found no effect on blood pressure. 1 RCT found fish oil 12 g/day resulted in lower mean arterial blood pressure than saturated fats in an energy-restricted setting.	Evidence for an association between total fat, proportions of saturated fats, MUFA or total unsaturated fat and blood pressure was 'limited-no conclusion'. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included, however several systematic reviews and meta-analyses included in previous publications. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence. Many questions remain unresolved due to conflicting results from studies and lack of high quality controlled studies.

Study	Research methods	Analysis	Results	Comments
	exposure food pattern or a whole food; included non-healthy subjects, obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Micha and Mozaffarian (2010) (Narrative review) Funding source Searle Funds at The Chicago Community Trust; the Bill & Melinda Gates Foundation/WHO Global Burden of Diseases, Injuries, and Risk Factors Study. Declarations of interest Consulting honoraria (modest) from Nutrition Impact, Unilever and SPRIM.	Research question Elucidate effects of saturated fat consumption on CVD risk based on the most current evidence. Selection criteria *Search period*: Inception to September 2009. *Study design*: RCTs and PCS. *Inclusion criteria*: Adults; evaluating saturated fat intake and risk of CHD, stroke, type 2 diabetes, related risk pathways including lipids and lipoproteins, systemic inflammation, vascular function, insulin resistance. *Exclusion criteria*: A priori animal studies, ecological studies, commentaries, general reviews, case reports. Dietary assessment methods Not reported.	Analysis Narrative review. Evaluation of study quality Not reported.	Characteristics of identified studies not summarised. 7 out of the 9 RCTs observed no differences between diets that differed in saturated fat intakes and replacement nutrients. 2 of the 5 RCTs including a comparison to MUFA found an improvement (decrease) in blood pressure (3 RCTs found no effect). 1 of the 5 RCTs including a comparison to PUFA found an improvement (decrease) in blood pressure (4 RCTs found no effect). All of the 4 RCTs including a comparison to carbohydrate found no effect.	Varying saturated fat consumption intake has no clear effect on blood pressure.

Table A2.6 RCTs and PCS assessing the relationship between dietary saturated fat intake and blood pressure in each review article

Study name / first author Publication year	Hooper et al. (2015)[1]	Schwab et al. (2014)	Micha and Mozaffarian (2010)
Total primary studies	5	5	9
Bos 2010		X	
Gulseth 2010		X	
Wang 2010		X	
Sanders 2009			X
Howard 2006	X		
Rasmussen 2006		X	X
Dyerberg 2004			
Ley 2004	X		
Piers 2003			X
Lahoz 1997			X
Storm 1997			X
Uusitupa 1994			X
Sacks 1987			X
Margetts 1985			X
Puska 1985			X
Woodhill 1978	X		
MRC 1968	X		
Leren 1966	X		

[1] Hooper et al. (2015) presents publications used in the analyses by study name and identifies a main study publication along with all supplementary publications for the study. It is not possible to know which exact publication the data has come from, therefore, the main study publication has been used in the table above.

Type 2 diabetes and markers of glycaemic control

Table A2.7 Characteristics of meta-analyses and systematic reviews

Study	Research methods	Analysis	Results	Comments
Type 2 diabetes				
de Souza et al. (2015) (Systematic review with meta-analysis) <u>Funding source</u> World Health Organization. <u>Declarations of interest</u> Canadian Institutes for Health Research postdoctoral fellowship; Province of Ontario graduate scholarship; Canadian Institutes for Health Research.	<u>Research question</u> Systematically review associations between saturated fat and trans fats intake and total mortality, CVD and associated mortality, CHD and associated mortality, ischemic stroke, type 2 diabetes. <u>Selection criteria</u> *Search period*: Up to 1 May 2015. *Study design:* Observational studies. *Inclusion criteria*: Observational studies in humans; report a measure of association between intakes of saturated fats or trans fats (measured by self-report or a biomarker) and total mortality, CVD and associated mortality, CHD and associated mortality, ischemic stroke, type 2 diabetes (measured by self-report and/or confirmed by medical records or registry linkage). *Exclusion criteria*: None reported. <u>Dietary assessment methods</u> FFQ, SQFFQ, 24 hr recall, dietary recall, 7 day food diary, weighted food diary, diet history, 4 day prospective diet record, cross check diet history method.	<u>Analysis</u> The principle association measures were RRs between highest and lowest intakes. ≥ 2 studies a random effects meta-analysis was performed. ≤ 3 studies fixed effect estimates were also considered. Heterogeneity measured using Cochran's Q test (significant at P<0.10), quantified with the I^2 statistic. If ≥ 10 studies and substantial heterogeneity (I^2 > 60% or P_Q < 0.10) meta-regression was used to explore heterogeneity. <u>Evaluation of study quality</u> The Newcastle-Ottawa scale was used to measure the risk of bias of included studies. The GRADE approach was used to assess confidence in the effect estimates derived from the body of evidence.	8 PCS; n=522-84,204; duration: 5-14y; age: 34-75y; gender: M (3), F (4), M/F (1); health at baseline: not reported; country: USA (4), Finland (3), Australia (1). <u>Type 2 diabetes</u> (8 cohorts) *Highest vs lowest saturated fat intake* Most adjusted: RR 0.95 (95% CI 0.88, 1.03) p=0.20; I^2=0%, P_{het}=0.61 Least adjusted: RR 1.23 (95% CI 0.98, 1.52) p=0.07; I^2=91%, P_{het}<0.00001	Saturated fat intake is not associated with type 2 diabetes, but the evidence considered is heterogeneous with methodological limitations. <u>Limitations</u> Comparison of higher fat and lower fat obscures the importance of reciprocal and possibly heterogeneous decreases in other macronutrients that accompany high saturated fat intake. Most studies did not model the effect of nutrient substitution.

Study	Research methods	Analysis	Results	Comments
Hooper et al. (2015) (Systematic review and meta-analysis) <u>Funding source</u> L Hooper: Studentship, Systematic Reviews Training, Institute of Child Health, University of London, UK. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? <u>Selection criteria</u> *Search dates:* July 2010 to March 2014 (plus search from Hooper 2012 – inception to June 2010). *Study design:* RCTs only. *Inclusion criteria:* >18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet; duration ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions. *Exclusion criteria*: Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Random effects meta-analysis to assess risk ratios. Low vs high % of energy from saturated fats. Incremental changes in % of energy from saturated fats. *Subgroup analysis:* Saturated fat substitution with PUFA, MUFA, carbohydrate. <u>Evaluation of study quality</u> Cochrane 'risk of bias' tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction. Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using I^2 test.	<u>Type 2 diabetes, new diagnoses</u> 1 RCT reported on diagnosis. No clear effect of reducing saturated fat intakes (compared with usual diet) on diagnosis of diabetes RR: 0.96, (95%CI 0.90, 1.02, 48,835 participants, P_{effect} 0.21).	No clear effect of reducing saturated fats on diabetes diagnoses. <u>Limitations</u> Although the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE).

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates:* January 2000-February 2012. *Study designs:* RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); n≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration≥4w (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6m, <40% 12m, <50% 24m; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority; study aim outside scope of review; exposure food pattern or a whole food; included non-healthy subjects, obese subjects.	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-suggestive, and limited-no conclusion. <u>Evaluation of study quality</u> Primary evidence assessed for quality but method not stated. Quality categories included: A) high quality with very low risk of bias; B) good quality, some risk of bias but not enough to invalidate results; C) low quality with significant bias and weaknesses which may invalidate results.	<u>Type 2 diabetes</u> *Saturated fat intake (2 PCS)* No association *Substituting PUFA for saturated fats (3-6% of energy)* (2 PCS) 1 PCS reported reduced risk of type 2 diabetes: RR 0.84 (95% CI 0.71, 0.98) 1PCS reported no association with type 2 diabetes with changing the PUFA:saturated fat ratio (OR 0.91, 95% CI 0.81, 1.03), although the association was significant when model was not adjusted for BMI or waist:hip ratio (OR 0.88, 95% CI 0.78, 0.99). Evidence graded limited to draw conclusions between saturated fat intake and type 2 diabetes.	<u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included, however several systematic reviews and meta-analysis included in previous publications. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence. Many questions remain unresolved due to conflicting results from studies and lack of high quality controlled studies.

Study	Research methods	Analysis	Results	Comments
	Dietary assessment methods Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Alhazmi et al. (2012) (Systematic review with meta-analysis) Funding source A Alhazmi supported by scholarship from the government of Saudi Arabia. Declarations of interest None to declare.	Research question Association between macronutrient intake and type 2 diabetes risk. Selection criteria *Search dates*: Up to July 2012. *Study designs*: PCS. *Inclusion criteria*: Cohorts that examined the relationship between dietary macronutrient intake or macronutrient sub-types and type 2 diabetes and if included healthy participants at baseline with no history of type 2 diabetes at baseline assessment; studies that report RR, OR or HRs and 95%CIs for comparison of type 2 diabetes risk between the highest and lowest levels of macronutrient consumption were included; required a minimum score of 7 on JBI check list for quality; human studies only; no language restriction. *Exclusion criteria:* Reviews, case-control, case studies, editorial or statistical analysis. Dietary assessment methods FFQs.	Analysis RRs (95% CI) comparing type 2 diabetes risk between highest and lowest quintiles of macronutrient intake. A random effects meta-analysis model, which takes into account within- and between-study variations, was applied. Sub-group analysis conducted by length of follow-up period (<10y or ≥10y), gender and use of follow-up or baseline only FFQ. Heterogeneity between studies was measured using I^2 statistic. Evaluation of study quality JBI checklist.	7 PCS for saturated fat intake and type 2 diabetes risk; n=2724 – 84,360; duration: 6-14y; age: 34-75y; gender: M(1), F(5), M/F(1); health at baseline: healthy with no history of diabetes; country: USA (6), Europe (1). Saturated fat intakes and type 2 diabetes risk Saturated fat intake was not associated with type 2 diabetes risk. RR: 0.99 (95% CI 0.91, 1.07), I^2=0.0%, p=0.75	Saturated fat intake was not significantly associated with type 2 diabetes risk. Limitations It is possible that the observed effects between macronutrient intake and the risk of type 2 diabetes could be due to residual or unmeasured confounding factors in PCS.

Study	Research methods	Analysis	Results	Comments
Micha and Mozaffarian (2010) (Narrative review) Funding source Searle Funds at The Chicago Community Trust; the Bill & Melinda Gates Foundation/WHO Global Burden of Diseases, Injuries, and Risk Factors Study. Declarations of interest Consulting honoraria (modest) from Nutrition Impact, Unilever and SPRIM.	Research question Elucidate effects of saturated fat consumption on CVD risk based on the most current evidence. Selection criteria *Search period*: Inception to September 2009. *Study design*: RCTs and PCS. *Inclusion criteria*: Adults; evaluating saturated fat intake and risk of CHD, stroke, type 2 diabetes, related risk pathways including lipids and lipoproteins, systemic inflammation, vascular function, insulin resistance. *Exclusion criteria*: A priori animal studies, ecological studies, commentaries, general reviews, case reports. Dietary assessment methods Not reported.	Analysis Narrative review. Evaluation of study quality Not reported.	1 RCT, 4 PCS; study characteristics not summarised. Type2 diabetes *4 PCS: N*o association with saturated fat intake. *1 RCT* (Women's Health Initiative: n=45,887, saturated fat intake reduced from 12.7 to 9.5% of energy over 8 years, mainly replaced with carbohydrate, total fat also reduced): No effect on incident diabetes : RR = 0.95 (95% CI 0.90, 1.03)	Several long-term observational studies and one large RCT suggest no effect of saturated fat consumption on onset of diabetes.

Study	Research methods	Analysis	Results	Comments
Markers of glycaemic control				
Imamura et al. (2016) (Systematic review with meta-analysis) Funding source Support received from Medical Research Council Epidemiology Unit Core Support; The National Institute of Health. Declarations of interest Support received from Unilever R&D. Consulting honoraria from Boston Heart Diagnostics; Haas Avocado Board; Astra Zeneca; GOED; DSM; Life Sciences Research Organization. Chapter royalties from UpToDate; scientific advisory board Elysium Health. Listed on a	Research Question Quantify effects of isoenergetic replacement of major macronutrient intake, focusing on different types of fatty acids, on fasting glucose, fasting insulin and insulin resistance. Disease outcome/intermediate risk factors Isoenergetic exchange of saturated fats. Selection criteria *Search dates:* Up to 26th November 2015. *Study designs:* RCTs. *Inclusion criteria:* RCTs in adults (≥18y) of isoenergetic exchange of different types of dietary fat, carbohydrate or total protein; reporting different types of dietary fat intake and examining post-intervention values or changes in the values of fasting glucose ,fasting insulin or measures of insulin resistance as effects of dietary modification on glucose homeostasis. *Exclusion criteria:* Insufficient information on macronutrient composition or glycaemic outcomes; studies of supplements or dietary advice only; studies of acute (single meal) post-prandial effects only; pregnant women or children (aged <18years). Dietary assessment methods Not stated.	Analysis Evaluated post intervention values of trial arms as the primary outcomes. Between arms correlations in trials using either crossover or Latin-square design were estimated and incorporated in meta-analysis by using reported p values and outcome measures based on the function of within individual correlations, interventional effects, their standard error or deviations, and p values. Estimated dose-response effects of replacement among carbohydrate, saturated fat, MUFA and PUFA using multiple-treatment meta-regression. Heterogeneity was tested using the standard Q-statistics. Evaluation of study quality Examined using the Jadad scale.	102 RCTs; n=4220; duration: 3-168days (median 28 days); age <30y (18), 30-49.9y (29), ≥50y (55); gender: M (45%), F (55%); health at baseline: healthy and diabetics; country: USA and Canada (35), Europe, Australia, and New Zealand (57), Asia (7), Central or South America and Africa (3). Effect of isoenergetic replacement of 5% dietary energy *Glucose mmol/L* (99 RCTs, n=4144) Carbohydrate to saturated fat: 0.02 (95% CI -0.01,0.04) Saturated fat to MUFA: -0.02 (95% CI -0.04,0.00) Saturated fat to PUFA: -0.04 (95% CI -0.07,-0.01), p<0.05 *2 h glucose, mmol/L* (11 RCTs, n=615) Carbohydrate to saturated fat: -0.04 (95% CI -0.39, 0.31) Saturated fat to MUFA: -0.10 (95% CI-0.91, 0.70) Saturated fat to PUFA: 0.26 (95% CI -0.34, 0.85) *Haemoglobin A1c, %* (23 RCTs, n=618) Carbohydrate to saturated fat: 0.03 (95% CI -0.02, 0.09) Saturated fat to MUFA: -0.12 (95% CI -0.19, -0.05), p<0.001 Saturated fat to PUFA: -0.15 (95% CI -0.23, -0.06), p<0.001 *Insulin, pmol/L* (90 RCTs, n=3774) Carbohydrate to saturated fat: -1.1 (95% CI -1.7, -0.5), p<0.01 Saturated fat to MUFA: 1.2 (95% CI 0.6, 1.8), p<0.001 Saturated fat to PUFA: -0.5 (95% CI -2.0, 1.1)	Increasing MUFA in place of saturated fats has beneficial effects to improve glycaemia and insulin resistance, with possibly stronger effects among patients with type 2 diabetes. Increasing PUFA intake in the general population to improve long-term glycaemic control, insulin resistance, and insulin secretion capacity, in place of saturated fats. Limitations Data from feeding trails which is included in this data may not be generalisable to the effects of long term habitual diet. Not all RCTs were double blinded. This study showed that replacing saturated fats with MUFA was shown to lower fasting glucose, 2h glucose, 2h insulin and HOMA-IR in trials implementing blinding intervention but not in trials blinding for participants.

Study	Research methods	Analysis	Results	Comments
patent assigned to Harvard University for use of trans-palmitoleic acid in identifying and treating metabolic disease.			*2 hr insulin, pmol/L* (11 RCTs, n=598) Carbohydrate to saturated fat: 1.9 (95% CI -19.3, 23.1) Saturated fat to MUFA:-22.2 (95% CI -49.1, 4.6) Saturated fat to PUFA: -26.8 (95% CI -72.5, 18.9) *C-peptide, nmol/L* (7 RCTs, n=175) Carbohydrate to saturated fat: 0.03 (95%CI -0.00, 0.05) p<0.05 Saturated fat to MUFA: -0.01 (95%CI -0.03, 0.01) Saturated fat to PUFA: -0.07 (95%CI -0.14, -0.01) p<0.05 *HOMA-IR, % change* (30 RCTs, n=1801) Carbohydrate to saturated fat: 0.7 (95% CI -1.6, 3.1) Saturated fat to MUFA: -3.1 (95% CI -5.8, -0.4) p<0.01 Saturated fat to PUFA: -4.1 (95% CI -6.4, -1.6) p<0.05 *Insulin sensitivity index, 10^{-5}/(pmol/L)/min* (13 RCTs, n=1292) Carbohydrate to saturated fat: -0.10 (95% CI -0.21, 0.02) Saturated fat to MUFA: 0.08 (95% CI -0.01, 0.17) Saturated fat to PUFA: 0.24 (95% CI -0.13, 0.61) *Acute insulin response, pmol/L/min* (10 RCTs, n=1204) Carbohydrate to saturated fat: -0.02 (95% CI -0.11, 0.07) Saturated fat to MUFA: -0.01 (95% CI -0.08, 0.06) Saturated fat to PUFA: 0.51 (95% CI -0.20, 0.82) p<0.01	

Study	Research methods	Analysis	Results	Comments
Hooper et al. (2015) (Systematic review and meta-analysis) <u>Funding source</u> L Hooper: Studentship, Systematic Reviews Training, Institute of Child Health, University of London, UK. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? <u>Selection criteria</u> *Search dates:* July 2010 to March 2014 (plus search from Hooper 2012 – inception to June 2010). *Study design:* RCTs only. *Inclusion criteria:* >18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet; duration ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions. *Exclusion criteria*: Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Random effects meta-analysis to assess risk ratios. Low vs high % of energy from saturated fats. Incremental changes in %of energy from saturated fats. *Subgroup analysis:* Saturated fat substitution with PUFA, MUFA, carbohydrate. <u>Evaluation of study quality</u> Cochrane 'risk of bias' tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction. Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using I^2 test.	4 RCTs; n=3081; duration: 3-8.1y; age: 48-62y; gender: M(1), F(1), M/F(2); health at baseline: high risk of CVD (1), diabetic/impaired glucose intolerance (2), angina (1); country: USA (1), UK (1), The Netherlands (1), New Zealand (1). <u>Homeostatic model assessment (HOMA) (1 RCT, n=2832)</u> No clear effect of ↓saturated fat intake vs usual diet MD: 0.00 (95%CI -0.04, 0.04), I2=93%, p=1.00. <u>Glucose at two hours post-glucose tolerance test (3 RCTs, n=249)</u> Glucose ↓after saturated fat intakes ↓ vs usual diet. MD: -1.69mmol/L (95% CI -2.55, -0.82), I^2=45%, p_{effect}=0.0001.	No clear effect of reducing saturated fats on HOMA, but a suggestion of reduction in glucose two hours after a glucose load. <u>Limitations</u> Although the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE).

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates:* January 2000- February 2012. *Study designs:* RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); ≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration ≥ 4 weeks (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6 months, <40% on 12 months, <50% in 24 months; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority; study aim outside scope of review; exposure food pattern or a whole food; included non-healthy subjects, obese subjects.	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in relation to the posed research questions. The evidence for each exposure-outcome association was categorised according to predetermined categories: convincing, probable, limited-suggestive, and limited-no conclusion. <u>Evaluation of study quality</u> Primary evidence assessed for quality but method not stated. Quality categories included: A) high quality with very low risk of bias; B) good quality, some risk of bias but not enough to invalidate results; C) low quality with significant bias and weaknesses which may invalidate results. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.	<u>Insulin sensitivity</u> 9 RCTs; n=17-154; duration: 4wk (crossover) – 6m; age: 30-65y; gender: M/F (9); health at baseline; healthy (4), obese (4), diabetic or at risk (1); country: not reported. *MUFA vs saturated fats (4 RCTs)* 1 RCT: Insulin sensitivity better on MUFA diet. 3 RCTs: No effect. Limited evidence - no conclusion; grade B evidence. *PUFA vs saturated fats (1 RCT)* 1 RCT: Insulin sensitivity better on PUFA diet. Limited evidence - no conclusion; grade B evidence. *MUFA and carbohydrate vs saturated fats (4 RCTs)* 4 RCTs: Insulin sensitivity better on MUFA diet. 1 RCT: Insulin sensitivity better on carbohydrate diet than high saturated fat diet. Probable evidence of an effect; grade B evidence. <u>Plasma/serum glucose concentration</u> 8 RCTs; n=17-154; duration: 28days (crossover) – 6m; age: 18-65y; gender: M/F (8); health at baseline: healthy (4), obese subjects (3), diabetic or at risk (1); country: not reported. *MUFA vs saturated fats (3 RCTS)* 3 RCTs: no effect. Limited evidence – no conclusion; grade B evidence. *PUFA vs saturated fats (1 RCT)* 1 RCT: no effect. Evidence – considered unlikely; grade B evidence. *MUFA and carbohydrate vs saturated fats (4 RCTs)*	Substitution of saturated fats with MUFA and/or PUFA convincingly decreases concentration of total and LDL-C but is unlikely to affect total triglycerides. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included, however several systematic reviews and meta-analyses included in pervious publications. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence. Many questions remain unresolved due to conflicting results from studies and lack of high quality controlled studies.

Study	Research methods	Analysis	Results	Comments
			3 RCTs: no effect. 1 RCT: reported decreased fasting glucose. Limited evidence – no conclusion; grade B evidence. *Isoenergetic replacement of saturated fats with:* MUFA: 1 out of 3 favourable effect, 2 out of 3 no effect. PUFA: 1 no effect. Evidence - considered unlikely; grade B evidence.	

Study	Research methods	Analysis	Results	Comments
Micha and Mozaffarian (2010) (Narrative review) Funding source Searle Funds at The Chicago Community Trust; the Bill & Melinda Gates Foundation/WHO Global Burden of Diseases, Injuries, and Risk Factors Study. Declarations of interest Consulting honoraria (modest) from Nutrition Impact, Unilever and SPRIM.	Research question Elucidate effects of saturated fat consumption on CVD risk based on the most current evidence. Selection criteria *Search period*: Inception to September 2009. *Study design*: RCTs and PCS. *Inclusion criteria*: Adults; evaluating saturated fat intake and risk of CHD, stroke, type 2 diabetes, related risk pathways including lipids and lipoproteins, systemic inflammation, vascular function, insulin resistance. *Exclusion criteria*: A priori animal studies, ecological studies, commentaries, general reviews, case reports. Dietary assessment methods Not reported.	Analysis Narrative review. Evaluation of study quality Not reported.	Characteristics of the identified studies not summarised. Saturated fat consumption inconsistently affects insulin resistance in controlled trials and has not been associated with incident diabetes in PCS. Among healthy individuals, most RCTs show no difference in markers of glucose-insulin homeostasis comparing different intakes of saturated fats vs MUFA, PUFA, or carbohydrate. Findings mixed among individuals having or predisposed to insulin resistance: improvements in markers of glucose-insulin homeostasis were seen in 3out of 5 RCTs with comparison to MUFA, 1 out of 3 RCTs comparison to PUFA, 1 RCT including a comparison to carbohydrate. Limitation: majority of studies were short-term (up to several weeks) and <20 subjects. Two largest trials (n = 163 and 59) found saturated fats to worsen glucose-insulin homeostasis in comparison to MUFA (both) and carbohydrate (1 trial).	Some evidence from short-term RCTs that saturated fat consumption in place of MUFA may worsen glucose-insulin homeostasis, especially among individuals predisposed to insulin resistance. Limitations Further confirmatory results required in appropriately powered studies.

Table A2.8 RCTs and PCS assessing the relationship between dietary saturated fat intake and type 2 diabetes and markers of glycaemic control in each review article

Study name[1] / first author (publication dates) **Publication year**	**de Souza et al. (2015)**	**Hooper et al. (2015)[2]**	**Schwab et al. (2014)**	**Alhazmi et al. (2012)**	**Micha and Mozaffarian (2010)**
Total primary studies (publications)	8	4 (5)	14	7	15
Alhazmi 2014	G				
Korger 2011				G	
Women's Health Initiative					
Tinker 2008					D, G
Howard 2006		D, G			
Harding 2004			D		D
Ley 2004		G			
Song 2004	G			G	
Lovejoy 2002			G		G
Vessby 2001			G		G
Watts 1992		G			
Houtsmuller 1979		G			
Mahendran 2014	G				
Simila 2012	G				
Bos 2010			G		
Van Dijk 2009			G		
Sloth 2009			G		
Due 2009			G		
Due 2008 (a)			G		
Due 2008 (b)			G		
Lithander 2008					G
Paniagua 2007					G
Lindstrom 2006	G				
Vega-Lopez 2006					G
Summers 2002			G		G
van Dam 2002	G			G	D
Meyer 2001	G		D	G	D
Perez-Jimenez 2001			G		G
Salmeron 2001	G		D	G	D
Louheranta 2000			G		G
Christiansen 1997					G
Salmeron 1997				G	
Fasching 1995					G
Colditz 1992				G	
Vessby 1992					

Outcome measured by study: D, incident type 2 diabetes; G, markers of glycaemic control.

[1] Study name is only provided when two or more publications for that study are used in any of the reviews. Imamura et al. (2016): unclear which primary studies were included in review.

[2] Hooper et al. (2015) presents publications used in the analyses by study name and identifies a main study publication along with all supplementary publications for the study. It is not possible to know which exact publication the data has come from, therefore, the main study publication has been used in the table above.

Anthropometry

Table A2.9 Characteristics of meta-analyses and systematic reviews

Study	Research methods	Analysis	Results	Comments
Tielemans et al. (2016) (Systematic review) <u>Funding source</u> Supported by Nestle Nutrition, Metagenics Inc. and AXA. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Assess whether energy intake and macronutrient intake during pregnancy were associated with gestational weight gain. <u>Selection criteria</u> *Search dates*: Up to 12th August 2015. *Study design*: RCTs and PCS. *Inclusion criteria*: Studies recruited women with singleton pregnancy either healthy or diseased; protein, fat, carbohydrate or energy intake was measured or supplemented as the exposure or intervention; reported outcome was gestational weight gain (measured or self-reported) or the adequacy of gestational weight gain; studies that measured weight shortly after birth; any language. *Exclusion criteria*: Studies that included only mothers who had given birth to newborns with birth defects or to extremely preterm newborns (<28wk of gestation); studies restricted to adolescents and studies in which the mean age of the total population was <18y; intervention studies in which the exclusive effects of macronutrients could not be determined (e.g. intervention combined with micronutrients or physical activity); studies on dietary counselling when actual	<u>Analysis</u> Narrative review. Studies were stratified by the income level of the country in which the study was performed on the basis of the World Bank list of economies. <u>Evaluation of study quality</u> Quality of each study given a score based on: study design, population size, exposure measurement (or in intervention studies the adequacy of blinding), outcomes measurement and adjustment for confounders and energy adjustment (or in intervention studies the adequacy of random assignment). Studies were considered of high quality when the score was ≥7 (out of 10).	8 PCS (for saturated fat intake); n=39-3360; duration: not reported; age: 16-43y; gender: all female; health at baseline: healthy (6), obese women (1), women carrying newborns with increased risk of type 1 diabetes (1); country: USA (3), The Netherlands (1), Finland (1), Denmark (1), Australia (1), Brazil (1). <u>Saturated fat intake and gestational weight gain</u> *2 high quality PCS* 1 PCS reported marginally higher gestational weight gain with higher saturated fat intake. 1 PCS reported no association. *6 low quality PCS* 1 PCS reported a positive association. 5 PCS reported no association.	The effects of macronutrients on gestational weight gain are inconclusive and inconsistent. Higher intake of fat, mainly saturated fat, might be associated with higher gestational weight gain, however the included studies had a low quality. <u>Limitations</u> Overall low quality of studies and the insufficient adjustment for confounding factors in many of the included studies. Therefore, residual confounding might remain.

Study	Research methods	Analysis	Results	Comments
	dietary intake was not measured. <u>Dietary assessment methods</u> FFQ, 24 hr recall, weighed food record, dietary interview.			

Study	Research methods	Analysis	Results	Comments
Hooper et al. (2015) (Systematic review and meta-analysis) <u>Funding source</u> L Hooper: Studentship, Systematic Reviews Training, Institute of Child Health, University of London, UK. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What is the effect of reducing saturated fat intake and replacing it with carbohydrate, PUFA, MUFA and/or protein on mortality and cardiovascular morbidity? <u>Selection criteria</u> *Search dates:* July 2010 to March 2014 (plus search from Hooper 2012 – inception to June 2010). *Study design:* RCTs only. *Inclusion criteria:* >18yrs at any risk of CVD, with/without existing CVD, using/not using lipid-lowering medication; aim to reduce saturated fat intake or alter dietary fats and achieve reduction in saturated fats; intervention dietary advice, supplementation of fats, oils or modified or low-fat foods or a provided diet and the control group usual diet, placebo or a control diet; duration ≥ 24 months; mortality or cardiovascular morbidity data available; no language restrictions. *Exclusion criteria*: Pregnant, acutely ill or breastfeeding subjects; allocation not truly randomised; multifactorial trials. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Random effects meta-analysis to assess risk ratios. Low vs high % of energy from saturated fats. Incremental changes in %of energy from saturated fats. *Subgroup analysis* Saturated fat substitution with PUFA, MUFA, carbohydrate. <u>Evaluation of study quality</u> Cochrane 'risk of bias' tool used. Additional characteristics assessed include: studies being free of systematic differences in care, a study aiming to reduce saturated fat intake, achieving saturated fats reduction, and achieving total serum cholesterol reduction. Evidence assessed using GRADE system, sensitivity analyses, and heterogeneity examined using I^2 test.	6 RCTs; n=194-2439; duration: 1.8-9.3y; age: 45-65y; gender: M(1), F(3), M/F(2); health at baseline: high risk of CVD (1), previous MI (1), diabetic/impaired glucose intolerance (1), breast cancer (2), siblings of people with CHD, with at least one CVD risk factor (1); country: USA (4), UK (1), Australia (1). <u>Reduced saturated fat intake</u> *Body weight* (6 RCTs, n=4541) Reducing saturated fat intake resulted in small reduction in body weight MD -1.97kg (95% CI -3.67, -0.27), I^2=72%. *BMI* (6 RCTs, n=5553) Reducing saturated fat intake resulted in small reduction in BMI MD -0.50 kg/m^2 (95% CI -0.82, -0.19), I^2=55%.	Small reductions in body weight and BMI with advice to reduce saturated fat intake. <u>Limitations</u> Although the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE were searched, due to limited resources, filters were applied to limit to core clinical journals (MEDLINE) and priority journals (EMBASE).

Study	Research methods	Analysis	Results	Comments
Fogelholm et al. (2012) (Systematic narrative review) <u>Funding source</u> Review was part of the Nordic Nutrition Recommendations 2012 project, with financial support from the Nordic Council of Ministers. <u>Declarations of interest</u> None declared.	<u>Research question</u> 1. Primary prevention of obesity The effect of different dietary macronutrient composition on long-term (≥1y) change in weight/waist circumference/body fat in adult population. 2. Prevention of weight regain after weight loss The effect of different dietary macronutrient composition on long-term (≥1y) change in weight/waist circumference/body fat in individuals who have deliberately reduced their weight by at least 5%. <u>Selection criteria</u> *Search period:* 2000 onwards. *Study design:* PCS, case-control studies, weight maintenance interventions (intentional mean weight loss at least 5%; at least 6 months follow up). *Inclusion criteria:* Adults 18-70 years, PCS with a minimum follow-up of 1y. *Exclusion criteria:* Cross-sectional studies, adults >70 years, studies without Caucasians or with Caucasians as a minority group. <u>Dietary assessment methods</u> FFQ.	<u>Analysis</u> Narrative review. <u>Evaluation of study quality</u> Principles of the Nordic Nutrition Recommendation 2012 working group was used to assess the quality of the papers. The papers were evaluated according to a 3-scale grading	<u>Saturated fats and change in weight or waist circumference</u> 2 PCS; n=89,432 – 130,950; duration: 3.7-10y; age: 41-68y; gender: M(0), F(1), M/F(1); health at baseline: healthy (2); country: USA (1), Europe (1). *Saturated fats and change in weight* 2 PCS: 1 PCS reported a positive association between saturated fats and weight gain 1 PCS reported no association between saturated fats and weight change *Saturated fats and change in waist circumference* 1 PCS found no association	Limited evidence, no conclusion can be drawn from the 2 studies, as 1 reported a positive association of saturated fat with body weight and 1 study found no significant association of saturated fat with body weight or waist circumference.

Study	Research methods	Analysis	Results	Comments
Micha and Mozaffarian (2010) (Narrative review) <u>Funding source</u> Searle Funds at The Chicago Community Trust and; the Bill & Melinda Gates Foundation/WHO Global Burden of Diseases, Injuries, and Risk Factors Study. <u>Declarations of interest</u> Consulting honoraria (modest) from Nutrition Impact, Unilever and SPRIM.	<u>Research question</u> Elucidate effects of saturated fat consumption on CVD risk based on the most current evidence. <u>Selection criteria</u> *Search period*: Inception to September 2009. *Study design*: RCTs and PCS. *Inclusion criteria*: Adults; evaluating saturated fat intake and risk of CHD, stroke, type 2 diabetes, related risk pathways including lipids and lipoproteins, systemic inflammation, vascular function, insulin resistance. *Exclusion criteria*: A priori animal studies, ecological studies, commentaries, general reviews, case reports. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Narrative review. <u>Evaluation of study quality</u> Not reported.	2 PCS; characteristics of identified studies not summarised. *Waist circumference* Male cohort, 9y follow-up. Positive association with saturated fat intake. *Body weight* Female cohort, 8y follow-up; adjusted for other risk factors, lifestyle and dietary behaviours. Positive association with saturated fat intake compared with carbohydrate intake.	Limited evidence for independent effects of saturated fats on weight gain or adiposity.

Table A2.10 RCTs and PCS assessing the relationship between dietary saturated fat intake and anthropometry in each review article

Study name / first author / Publication year	Tielemans et al. (2016)	Hooper et al. (2015)[1]	Fogelholm et al. (2012)	Micha and Mozaffarian (2010)
Total primary studies	8 PCS	6 RCTs	2 PCS	2 PCS
Blumfield 2015	GWG			
Renault 2015	GWG			
Shin 2014	GWG			
Maple-Brown 2013	GWG			
Costa 2011	GWG			
Howard 2006		BMI, WC		
Martins and Benicio 2011	GWG			
Althuizen 2009	GWG			
Forouhi 2009			WC, C	
Stuebe 2009	GWG			
Field 2007			WC	WC
Chlebowski 2006		BMI, WC		
Koh-Banerjee 2003				C
Moy 2001		BMI		
Simon 1997		WC		
Hockaday 1978		BMI		
Woodhill 1978		BMI, WC		

Outcomes measured by study: BMI, body mass index; C, waist circumference; GWG, gestational weight gain; WC, weight change.

[1] Hooper et al. (2015) presents publications used in the analyses by study name and identifies a main study publication along with all supplementary publications for the study. It is not possible to know which exact publication the data has come from, therefore, the main study publication has been used in the table above.

Cancers

Table A2.11 Characteristics of meta-analyses and systematic reviews

Study	Research methods	Analysis	Results	Comments
Colorectal Cancer				
Liu et al. (2011) (Meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Evaluate the association between total dietary fat and risk of colorectal cancer. <u>Selection criteria</u> *Search dates*: Up to 1st May 2009. *Study designs*: PCS. *Inclusion criteria*: PCS that reported an association between total dietary fat and risk of colorectal cancer; reported RR and 95% CI according to highest vs. lowest level of intake. *Exclusion criteria*: No details of inclusion and exclusion criteria in studies; data were repeatedly reported; the study was a review, comment, editorial or letter. <u>Dietary assessment methods</u> FFQ (ranged from 50 to 276 items).	<u>Analysis</u> Combined RR and 95% CI used to measure the impact of the highest vs. lowest level of fat and colorectal cancer risk. RR and 95% CI for each study transferred into a logarithm for combined analysis. Random-effects model used to analyse statistical significance. Stratified analyses were performed for types of fat (including saturated fats). Heterogeneity assessed using Q test and I^2. Publication bias evaluated by visual inspection of funnel plots, Begg rank correlation and Egger weighted regression method. <u>Evaluation of study quality</u> Not assessed.	13 PCS; n= 459,910 participants (3635 cases of colorectal cancer); duration: 3-32y; age: not reported; health at baseline: not reported; country: USA (5), UK (1), Finland (2), The Netherlands (1), Norway (1), Japan (2), Singapore (1). <u>Highest vs lowest intake of saturated fat and risk of colorectal cancer (12 PCS)</u> RR 1.00 (95% CI 0.90, 1.12);I^2=0%, p=0.89 Stratified analysis according to gender, ethnicity, country, tumour location, follow-up duration, number of items included in FFQ and age showed that saturated fat intake was not associated with the risk of colorectal cancer.	No associations between saturated fat intake and risk of colorectal cancer found. <u>Limitations</u> Probable bias caused by measurement error, needs to be adjusted in the future studies. Ten out of 13 studies performed in Europe and USA, therefore extrapolation to Asian populations difficult.

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates*: January 2000- February 2012. *Study designs*: RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); n≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration≥4w (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6m, <40% 12m, <50% 24m; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority. Aim of study outside scope of review. The studied exposure was a food pattern or a whole food. Included non-healthy subjects,	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in related tot the posed research questions. The evidence for each exposure-outcome association was categorising according to pre demented categories: convincing, probable, limited-suggestive, and limited- no conclusion. <u>Evaluation of study quality</u> The primary evidence was assessed for quality but method not stated. Quality categories included A: high quality with very low risk of bias; B: good quality, some risk of bias but not enough to invalidate results; C: low quality with significant bias and weaknesses which may invalidate results.	<u>Colorectal cancer</u> 1 PCS; n=37,547; duration: 8.7y: age: ≥45y; gender: F. No significant association with saturated fat intake. Limited evidence – no conclusion; grade B evidence.	Limited evidence, no conclusion. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence.

Study	Research methods	Analysis	Results	Comments
	obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Pancreatic Cancer				
Yao and Tian (2015) (Meta-analysis) <u>Funding source</u> None to declare. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Role of different fatty acids on the risk of pancreatic cancer. <u>Selection criteria</u> *Search dates*: Until end of June 2014. *Study designs*: PCS. *Inclusion criteria*: Study had to be a cohort/case-cohort/nested case-control/case-control study design; exposure was dietary saturated fat, MUFA or PUFA intake; the outcome was the incidence of pancreatic cancer; provided RR, OR, HR with 95% CI. *Exclusion criteria*: Not provided. <u>Dietary assessment methods</u> FFQs.	<u>Analysis</u> Random or fixed effects models were used to estimate RR with 95% CI. Galbraith plot used to depict heterogeneity, I^2 statistics to evaluate heterogeneity among studies, Higgins and Thompson fixed-effects model where non-significant heterogeneity. DerSimonian and laird random-effects model if significant heterogeneity. <u>Evaluation of study quality</u> Scoring system with 9-star on the strength of the Newcastle-Ottawa Scale.	7 PCS; n = 1,130,815 participants (3072 cases of pancreatic cancer); duration: 8-22y; age: not stated; gender: M (1), F (1), M/F (5); health at baseline: not stated; country: USA (5), The Netherlands (1), Finland (1). <u>Highest vs lowest saturated fat intake and risk of pancreatic cancer (6 PCS)</u> RR 1.04 (95% CI 0.81, 1.35); I^2 = 74.2%	No statistically significant relationship between saturated fat intake and pancreatic cancer risk. <u>Limitations</u> Could not control for confounders not adjusted for in the individual studies. A few studies adjusted for BMI and alcohol intake, the majority adjusted for age, cigarette smoking and total energy intake, however, residual or unmeasured confounding cannot be excluded. Some degree of misclassification of fatty acids intake could be prone to overestimation of the range of intake and underestimation of the magnitude of the association between dietary intake and risk of cancer.

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates*: January 2000- February 2012. *Study designs*: RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); n≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration≥4w (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6m, <40% 12m, <50% 24m; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority. Aim of study outside scope of review. The studied exposure was a food pattern or a whole food. Included non-healthy subjects,	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in related tot the posed research questions. The evidence for each exposure-outcome association was categorising according to pre demented categories: convincing, probable, limited-suggestive, and limited- no conclusion. <u>Evaluation of study quality</u> The primary evidence was assessed for quality but method not stated. Quality categories included A: high quality with very low risk of bias; B: good quality, some risk of bias but not enough to invalidate results; C: low quality with significant bias and weaknesses which may invalidate results.	<u>Pancreatic cancer</u> 4 PCS; n=831,931; duration: 6.3-18y; age: 30-75y; gender: M (1), F (1), M/F (2). 2 PCS: found no significant associations with saturated fat intake. 2 PCS: found positive associations with saturated fat intake. Limited evidence – no conclusion; grade B evidence.	Limited evidence, no conclusion. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence.

Study	Research methods	Analysis	Results	Comments
	obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Lung Cancer				
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates*: January 2000- February 2012. *Study designs*: RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); n≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration≥4w (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6m, <40% 12m, <50% 24m; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority. Aim of study outside scope of review. The	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in related tot the posed research questions. The evidence for each exposure-outcome association was categorising according to pre demented categories: convincing, probable, limited-suggestive, and limited- no conclusion. <u>Evaluation of study quality</u> The primary evidence was assessed for quality but method not stated. Quality categories included A: high quality with very low risk of bias; B: good quality, some risk of bias but not enough to invalidate results; C: low quality with significant bias and weaknesses which may invalidate results.	<u>Lung cancer</u> *1 pooled analysis (Smith-Warner et al., 2002); this pooled analysis was identified in this review, the results are described in the lung cancer table.*	*(Lung: association with saturated fats unlikely)* <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence.

Study	Research methods	Analysis	Results	Comments
	studied exposure was a food pattern or a whole food. Included non-healthy subjects, obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Smith-Warner et al. (2002) (Pooled analysis) Funding source National Institutes of Health. Declarations of interest None declared.	Research Question Examine the relationship between lung cancer and intakes of total and specific types of fat and cholesterol. Selection criteria *Search dates:* Not specified. *Study designs:* PCS. *Inclusion criteria:* At least 200 incident breast cancer cases; assessment of long term dietary intake; validation of the diet assessment method or a closely related instrument; at least 50 incident lung cancer cases; assessment of smoking history at baseline. *Exclusion criteria:* Excluded data on participants that had reported energy intakes greater or less than 3 SDs from the study specific $\log_e$-transformed mean energy intake of the baseline population; reported a history of cancer (except non-melanoma skin cancer) at baseline; no information on smoking habits. Dietary assessment methods FFQ (the number of items included in the questionnaires ranged from 45 to 276; portion sizes not given in 2 PCS; specified by participants in 3 PCS; specified on the questionnaire in 3 PCS).	Analysis Cox proportional hazards model used to calculate study-specific RRs. Analysed associations for intakes of saturated fats as a percentage of total calories. In the multivariate analyses smoking habits, education, BMI, alcohol consumption, fruit and vegetable consumption, and energy intake included as covariates. Two sided 95% CIs were calculated. Pooled RRs were calculated using a random effects model. Heterogeneity among studies assessed using asymptotic DerSimonian and Laird Q statistics. Analyses for specific types of fat were conducted by including saturated fat, MUFA and PUFA, protein and alcohol intakes in the same multivariate model, in addition to the other covariates. In this model, the RRs for the specific types of fat are adjusted for each other and have the interpretation of being compared with an identical decrease in the % of energy from carbohydrates. Evaluation of study quality Not reported.	8 PCS; n = 280,419 women, n =149,862 men, 3188 cases of lung cancer (1395 in women, 1793 in men); duration: 6-16y; age: 15-107y; gender: M(2), F(3), M/F(3); country: USA/Canada (6), The Netherlands (1), Finland (1). *RR of lung cancer by quartile of saturated fat intake* Q1 vs Q2: RR 0.94 (95% CI 0.81, 1.10) Q1 vs Q3: RR 0.99 (95% CI 0.87, 1.11) Q1 vs Q4: RR 1.01 (95% CI 0.89, 1.14) P, test for trend = 0.57 P, test for between study heterogeneity = 0.40 *RR of lung cancer for saturated fat (5% of energy increase)* Age adjusted: RR 1.21 (95% CI 1.08, 1.36), p=0.001 (when adjusted for education, BMI, alcohol consumption, fruit and vegetable consumption and energy intake the association were attenuated but still statistically significant). Multivariate-adjusted: RR 1.03 (95% CI 0.96, 1.11), p=0.35. (P, test for between study heterogeneity = 0.60) *RR of lung cancer for intake of saturated fats (5% of energy increase) by smoking status* Current: RR 1.02 (95% CI 0.92, 1.13) Past: RR 1.10 (95% CI 0.91, 1.33) Never: RR 0.97 (95% CI 0.74, 1.27) Greater saturated fat intakes not significantly associated with higher risk of lung cancer in any of the individual cohorts in the multivariate analysis. When intakes of saturated fat, MUFA and PUFA were mutually adjusted by including them simultaneously in	No evidence of an association between saturated fat intake and risk of lung cancer risk. Findings consistent with evidence from cohort studies but not case-control studies which indicate positive associations between saturated fat intake and lung cancer risk. Limitations Fat intake measurement error induced by use of FFQ compared with other studies where fat intake has been measured more precisely, thereby resulting in an underestimate of association.

Study	Research methods	Analysis	Results	Comments
			the multivariate model as continuous variables, there was no significant association between saturated fat and lung cancer risk.	

Study	Research methods	Analysis	Results	Comments
Breast Cancer				
Cao et al. (2016) (Meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> L Hou received a grant from the Natural Science Foundation of Shandong Province.	<u>Research question</u> Assess the association between dietary total fat and fatty acids intake and breast cancer risk. <u>Selection criteria</u> *Search dates:* Inception to September 2015. *Study designs:* PCS. *Inclusion criteria:* PCS or nested case-control study in which total fat and fatty acids consumption precedes breast cancer incidence; exposure of interest was dietary total fat, fatty acids intake or serum fatty acids; the outcome of interest was breast cancer; RR, HR, ORs with 95% CI provided. *Exclusion criteria:* Not reported. <u>Dietary assessment methods</u> FFQ (22), food record and 24 hour recall (2).	<u>Analysis</u> Pooled measure was calculated as the inverse variance weighted mean of the logarithm of RR with 95% CI to assess the strength of association. A random-effect model was used as the pooling method, which considers both within and between study variations. I^2 statistic was used to evaluate heterogeneity. <u>Evaluation of study quality</u> 9-star Newcastle-Ottawa Scale was used to evaluate study quality.	24 PCS (20 for saturated fat); n=1,387,366 subjects (38,262 breast cancer cases); duration: 2-25y; age: 20-74y; gender: female only; health at baseline: not specified; country: USA (11), Canada (1), Sweden (3), The Netherlands (1), Finland (1), Norway (1), Italy (1), France (1), Japan (2), China (1), multinational (1). <u>Highest vs lowest dietary saturated fat intake and breast cancer (20 PCS)</u> RR 1.08 (95% CI 0.99, 1.18);I^2= 58.81%, p=0.003 <u>Sub-group analysis</u> Positive association between saturated fat intake and breast cancer for: *Estrogen receptor positive breast cancer (3 PCS)* RR 1.29 (95% CI 1.04, 1.60); I^2=0.00% *Studies conducted in Europe (8 PCS)* RR 1.16 (95% CI 1.06, 1.26); I^2=0.00% *Studies with follow-up duration <10y (12 PCS)* RR 1.13 (95% CI 1.02, 1.24); I^2=16.28% *Studies with subjects with mean age >50y (14 PCS)* RR 1.09 (95% CI 1.00, 1.19); I^2=43.67% *Studies that did not adjust for family history of breast cancer (9 PCS)* RR 1.15 (95% CI 1.08, 1.23); I^2=0.00%	No association was observed between saturated fat intake and risk of breast cancer. <u>Limitations</u> Some of the sub-group analyses included data from a limited number of studies; adjustment of several covariates could influence the fat-breast cancer association.

Study	Research methods	Analysis	Results	Comments
Brennan et al. (2015) (Systematic review with meta-analysis) <u>Funding source</u> SF Brennan: PhD studentship from the Department of Employment and Learning, Northern Ireland. <u>Declarations of interest</u> None declared.	<u>Research question</u> Clarify the association between dietary fat and breast cancer mortality. <u>Selection criteria</u> *Search dates:* Up to March 2012. *Study designs*: PCS. *Inclusion criteria:* English language; reported risk estimates (HRs, ORs and RRs); measures of variability (SEs, 95% CIs); all-cause and/or breast cancer mortality according to total fat and/or saturated fat intake. *Exclusion criteria*: not reported. <u>Dietary assessment methods</u> FFQs (3), diet histories (1).	<u>Analysis</u> All data converted to g/day by calculation or by requesting the results from the authors. Meta-analyses were conducted to evaluate the risk of all-cause or breast cancer specific death in women, comparing highest and lowest intakes of fat and saturated fat. Regression analysis of HRs, to calculate linear increase in risk of breast cancer and all-cause death per percentile increase in total fat and saturated fat. Multivariable adjusted HRs, ORs or RR with 95% CIs from individual studies were weighted and combined using an inverse-variance weighted random-effects model to produce pooled estimates. Heterogeneity was tested with the chi-squared test and measured using the I^2 statistic. Sub-group analyses were conducted for studies which did and did not have energy intake adjusted and type of dietary assessment method, pre vs post-diagnosis diet. <u>Evaluation of study quality</u> Not stated.	15 PCS (4 for saturated fat); n=149-11,302; duration: 3-26y; age: 19-79y; gender: female only; health at baseline: not reported; country: USA (8), Canada (4), Australia (1), Denmark (1), Belgium (1). *Highest vs lowest saturated fat intake and breast cancer mortality (4 PCS)* HR 1.51 (95% CI: 1.09, 2.09); I^2=15%, p=0.317 *Breast cancer specific mortality with 20g increase in saturated fat intake (4 PCS)* HR 1.03 (95%CI 0.77, 1.38), p=0.80; I^2=75%, p<0.01	Saturated fat intake negatively impacts upon breast cancer survival. <u>Limitations</u> Adjustment for confounders was inconsistent between studies resulting in the potential for residual confounding.

Study	Research methods	Analysis	Results	Comments
Xia et al. (2015) (Meta-analysis) <u>Funding source</u> None to declare. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Determine the quantitative relations between dietary saturated fat intake and incidence of breast cancer. <u>Selection criteria</u> *Search dates*: Up to April 2015. *Study designs*: Cohort, case-control. *Inclusion criteria*: Published in English; human studies only; published openly; evaluated the association between saturated fat intake from food and the incidence of female breast cancer only; specified diagnosis of breast cancer; containing ORs, RRs or HRs with corresponding 95%CIs or data could be estimated; selected when data were most sufficient if they were from the same population. *Exclusion criteria:* Animal or vitro experiments; review articles, repeated literatures, or mechanism studies; not related to human subjects; not of appropriate control groups; without analysis method provided; and were excluded when lack of access to full texts. <u>Dietary assessment methods</u> FFQs, diet history, 24 hour recall.	<u>Analysis</u> Used RR as an approximate for HR in the cohort studies. Adjusted ORs or RRs comparing highest versus lowest category of dietary saturated fat intake were gathered with the corresponding 95% CIs as possible and meanwhile were calculated by the logarithmic transformation of RRs and ORs with the corresponding 95% CIs. Fixed effects model was used when I^2 was lower than 50% and P of the value of heterogeneity was ≥ 0.05. Otherwise the random-effects model was used. <u>Evaluation of study quality</u> Assessed using the Newcastle-Ottawa scale.	24 PCS; n=1,786,537 subjects (35,651 breast cancer cases);duration: 3.3-20y; age: not reported; gender: female only; health at baseline: not stated; country: USA (14), Sweden (2), UK (1), Finland (1), Norway (1), The Netherlands (2), Canada (1), Japan (1), Europe-multi country (1). <u>Pooled RR of breast cancer incidence for highest vs lowest saturated fat intake (24 PCS)</u> Pooled RR 1.04 (95%CI 0.97, 1.11); I^2=59.9% <u>Sub-group analysis</u> *Menopause status:* Pre-menopausal (5 PCS) Pooled RR 1.01 (95%CI 0.92, 1.10); I^2= 0% Post-menopausal (13 PCS) Pooled RR 1.04 (95%CI 0.95, 1.13); I^2=63.4% *Recruit source:* Population (17 PCS) RR 1.11(95% CI 1.01, 1.21); I^2=48.3% Hospital (7 PCS) RR 0.96 (0.91, 1.00); I^2=35%	No association was found between saturated fat intake and breast cancer in PCS.

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates*: January 2000- February 2012. *Study designs*: RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); n≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration≥4w (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6m, <40% 12m, <50% 24m; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority. Aim of study outside scope of review. The studied exposure was a food pattern or a whole food. Included non-healthy subjects,	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in related tot the posed research questions. The evidence for each exposure-outcome association was categorising according to pre demented categories: convincing, probable, limited-suggestive, and limited- no conclusion. <u>Evaluation of study quality</u> The primary evidence was assessed for quality but method not stated. Quality categories included A: high quality with very low risk of bias; B: good quality, some risk of bias but not enough to invalidate results; C: low quality with significant bias and weaknesses which may invalidate results.	<u>Breast cancer</u> 6 PCS; n=659,782; duration: 7.8-20y; age: 25-75y; gender: F (6). 5 PCS: no significant associations with saturated fat intake. 1 PCS: found a positive association among menopausal women who did not use hormone replacement therapy. Limited evidence – no conclusion; grade B evidence.	Limited evidence, no conclusion. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence.

Study	Research methods	Analysis	Results	Comments
	obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Makarem et al. (2013) (Systematic narrative review) <u>Funding source</u> Financial support from the American Cancer Society and the National Cancer Institute. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Assess epidemiological evidence on the impact of total dietary fat and fat subtypes, measured pre- and/or post cancer diagnosis, in relation to breast cancer-specific and all-cause mortality among breast cancer survivors. <u>Selection criteria</u> *Search dates:* Up to 30th May 2012. *Study designs:* Cross-sectional, case-control, cohort and experimental studies *Inclusion criteria:* English language; sample size ≥200 subjects; presented HR/RR for recurrence, disease specific mortality, or all-cause mortality among breast cancer patients; conducted follow-up in cancer cases; presented multivariate analysis. *Exclusion criteria:* Univariate analysis. <u>Dietary assessment methods</u> FFQ.	<u>Analysis</u> Narrative review. <u>Evaluation of study quality</u> Not documented.	4 PCS; n=212-678; duration: not stated; age: 19-75y; gender: female only; health at baseline: not stated; country: Canada (3), Japan (1). <u>Saturated fat intake</u> *Evaluation of association between saturated fat intake assessed before diagnosis and breast cancer mortality (2 PCS)* Significant increased risk of breast cancer mortality when treated as a continuous variable and when comparing highest vs lowest quartile of saturated fat intake. Statistically significant linear trend across the quartiles of intakes were observed in a Canadian cohort for saturated fat expressed as % of total fat and as % of total energy. <u>5% increase in saturated fat intake as a % of total energy</u> Associated with approx. 65% increased risk of breast cancer mortality in models including estrogen receptor status as a covariate (HR 1.65, 95%CI 1.07, 2.56), and the association was borderline significant in models excluding estrogen receptor status (HR 1.55, 95% CI 1.00, 2.37). <u>Post diagnostic saturated fat intake and breast cancer mortality</u> 2 PCS suggested an increased risk of 55% and 65% increased risk, albeit confidence intervals included the null. 1 PCS showed a non-significant 23% increased risk when comparing women with the highest consumption of saturated fat to the lowest. 1 PCS reported a statistically significant 41% elevation in risk of death.	Inconsistent and limited evidence warrants research to assess the impact of consumption of fat subtypes on breast cancer recurrence and mortality. <u>Limitations</u> One issue relates to the measurements of dietary fat intake using different dietary assessment methods. Deaths from breast cancer may have been miss-reported as other causes. Selection bias may have occurred.

Study	Research methods	Analysis	Results	Comments
			1 PCS reported a non-significant increase in risk with lowest intake compare to the highest intake of saturated fat.	

Study	Research methods	Analysis	Results	Comments
Turner (2011) (Meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> None declared.	<u>Research question</u> Identify relationships between dietary fat and fat subtypes, with risk of breast cancer in women. <u>Selection criteria</u> *Search dates:* Up to May 2010. *Study designs*: Cohort and case-control studies. *Inclusion criteria*: Human subjects only. *Exclusion criteria*: Not specified. <u>Dietary assessment methods</u> FFQ (17), diet history (1), serum fatty acid analysis (1).	<u>Analysis</u> Inverse variance method was used for pooling and subsequent random effects meta-analysis. Additional sub-grouping and regression analyses were conducted to identify significant difference between studies. Heterogeneity identified significant variability between studies. <u>Evaluation of study quality</u> Not stated.	19 PCS for saturated fat; n=1,379,666 (24,257 cases of breast cancer); duration: not stated; age: pre-menopausal (2), post-menopausal (12), both pre- and post-menopausal (5); gender: female only; health at baseline: not stated; country: USA (13), Sweden (2), Singapore (1), Netherlands (1), Italy (1), multiple (1). <u>RR of breast cancer for highest vs lowest quartile of saturated fat intake</u> RR 0.99 (95% CI 0.94, 1.05)	Data from cohort studies suggest that intakes of saturated fats were associated with decreased risk of breast cancer, but not significantly. <u>Limitations</u> Small sample of pre-menopausal studies. Study results were based on estimated RR extracted from published studies.

Study	Research methods	Analysis	Results	Comments
Boyd et al. (2003) (Meta-analysis) <u>Funding source</u> Supported by Department of Medical Biophysics, University of Toronto; Institute of Medical Sciences, University of Toronto. <u>Declarations of interest</u> None declared.	<u>Research question</u> Examine the association of dietary fat or fat containing foods with risk of breast cancer. <u>Selection criteria</u> *Search dates*: From January 1966 up to July 2003. *Study designs*: Cohort and case-control studies. *Inclusion criteria:* Not specified. *Exclusion criteria*: Not specified. <u>Dietary assessment methods</u> Diet history (12), FFQs (32), 24 hour diet recall (1), food records and food frequency questionnaire (1). *Cohort only:* FFQ (10), diet history (3), 24 hour diet recall (1).	<u>Analysis</u> Data for case-control and cohort were analysed separately and together. To account for sources of variation in this meta-analysis, the method of DerSimonian and Laird was used. The magnitude of the heterogeneity was estimated, and accounted for by assigning a greater variability to the estimate of the overall effect. Regression analysis was used to examine independent factor contributions. <u>Evaluation of study quality</u> Calculated for each study independently by 4 investigators using predetermined methodological standards and any difference resolved by discussion. Quality scores were used to divide studies into groups for stratified analysis.	14 PCS; n=568,549 (8735 breast cancer cases); duration: not stated; age: not stated; gender: female only; health at baseline: not stated; country: USA (7), UK (1), Canada (1), Finland (1), France (1), Sweden (1), The Netherlands (1), Norway (1). <u>RR of breast cancer and saturated fat intake (12 PCS)</u> RR 1.15 (95% CI 1.02, 1.30)	Saturated fat intake was significantly associated with breast cancer risk in cohort studies. <u>Limitations</u> Homogeneity of fat intake within population, error in measurement of fat intake, as FFQ may lead to overestimation of the range of intakes.

Study	Research methods	Analysis	Results	Comments
Smith-Warner et al. (2001) (Pooled analysis) Funding source Supported by research grants from National Institute of health; Cancer Research Foundation of America; American Society of Preventive Oncology Research Fellowship; American Cancer Society. Declarations of interest None declared.	Research question Investigate the independent association between intakes of specific types of fat and breast cancer risk. Selection criteria *Search dates:* Not stated. *Study designs:* PCS. *Inclusion criteria:* At least 200 incident breast cancer cases; assessment of usual intake of foods and nutrients; a validation study of the diet assessment method or a closely related instrument. *Exclusion criteria:* Excluded data on participants if they reported energy intakes greater or less than 3 SDs from study specific $\log_e$-transformed mean energy intake of the baseline population, had missing alcohol intake data or reported history of cancer (expect non-melanoma skin cancer) at baseline. Dietary assessment methods FFQ (the number of items included in the questionnaires ranged from 45 to 150; portion sizes not given in 2 PCS; specified by participants (as small medium and large relative to a standard size) in 2 PCS; specified on the questionnaire in 3 PCS).	Analysis Holding total energy intake constant, RRs for increments of 5% of energy for each type of fat compared with an equivalent amount of energy from carbohydrates or from other types of fat were calculated. Study-specific RRs were combined using a random effects model. Evaluation of study quality Not specified.	8 PCS; n = 351,821 participants, 7329 cases of invasive breast cancer; duration: 6-16y; age: 28-93y; gender: female only; country: USA/Canada (6), The Netherlands (1), Sweden (1). Range of median total fat intake: 30-41% of total energy. Range of median saturated fat intake: 10-16% of total energy. Multivariate RR of breast cancer for 5% of energy increase from saturated fats (continuous model) RR 1.03 (95% CI 0.95, 1.10; p, test for heterogeneity = 0.04) Premenopausal: RR 1.10 (95% CI 0.91, 1.35) Postmenopausal: RR 1.07 (95% CI 0.93, 1.24) RR of breast cancer by quartile of saturated fat intake Q1 vs Q2: RR 0.99 (95% CI 0.91, 1.08) Q1 vs Q3: RR 0.95 (95% CI 0.87, 1.04) Q1 vs Q4: RR 1.01 (95% CI 0.89, 1.16) P, test for trend = 0.85 RR of breast cancer substituting 5% of energy from saturated fat with: Carbohydrate: RR 1.09 (95% CI 1.00, 1.19); p, test for heterogeneity = 0.25 MUFA: RR 1.18 (95% CI 0.99, 1.42) PUFA: 0.98 (95% CI 0.85, 1.12) RR of breast cancer substituting 5% of energy from MUFA with saturated fat RR 0.85 (95% CI 0.71, 1.02)	Pooled analyses are suggestive of only a weak positive association for substituting saturated fat consumption for carbohydrate consumption. Substituting MUFA for saturated fat associated with a nonsignificant lower breast cancer risk. Limitations Fat consumption is measured with error in cohort studies. Cohort studies frequently measure dietary intake using FFQs which lead to underestimation of fat intake.

Study	Research methods	Analysis	Results	Comments
Prostate Cancer				
Xu et al. (2015a) (Systematic review and meta-analysis) <u>Funding source</u> None to declare. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Assess relationship between fat intake and prostate cancer risk. <u>Selection criteria</u> *Search dates:* Up to 1st March 2015. *Study designs:* PCS. *Inclusion criteria:* PCS assessing the relationship between any stage of prostate cancer and total fat, saturated fat or unsaturated fat intake; studies reporting animal fat (expect for fish oil) categorised as saturated fats. *Exclusion criteria:* Secondary tumours from other organs not considered; vegetable and oils; grey literature; meeting papers; animal studies. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Dose response meta-analysis conducted in two steps: first, the generalised least squares method estimated the coefficient per unit increment of exposure within each study. Second, the regression coefficients were combined in a random-effect model with the weight calculated by inverse variance. Random-effects meta-regression was used to assess which covariates in the subgroup analysis influenced the intervention effect. Egger's test used to determine publication bias, I^2 statistic used to assess heterogeneity. <u>Evaluation of study quality</u> Quality assessed using the Newcastle-Ottawa Scale.	14 PCS; n=751,030 (37,349 prostate cancer cases); duration: 5-17.4y; age: 40-75y; gender: male only; health at baseline: not reported; country: USA/Canada (7), Finland (3), Sweden (1), The Netherlands (1), Norway (1), multi European countries (1). <u>Saturated fat intake and prostate cancer risk per 28.35g increment (9 PCS)</u> RR 1.00 (95% CI 1.00, 1.00); p = 0.72; I^2 = 14.3% <u>Saturated fat intake and advanced or high grade prostate cancer risk per 28.35g increment (6 PCS)</u> RR 0.96 (95%CI 0.84, 1.11);p = 0.61; I^2 = 70.4% <u>Sub-group analysis</u> *Area of country* America (6 PCS) RR 1.00 (95%CI 1.00, 1.00); p = 0.98, I^2 = 17.70% Europe (3 PCS) RR 1.00 (95%CI 1.00, 1.00); p = 0.29, I^2 = 0.00% *Adjusted for BMI* Adjusted (6 PCS) RR 1.00 (95% CI 1.00, 1.00); p=0.41; I^2=43.80% Non-adjusted (3 PCS) RR 1.00 (95% CI 1.00, 1.00); p=0.76; I^2=0.00% Confounders adjusted for in primary studies include age, race, family history of prostate cancer, education, marital status, prostate specific antigen (PSA) testing in past 3 years, physical activity, diabetes, socioeconomic status, BMI, age 21 BMI, waist circumference, birth country, vasectomy status, energy intake, intakes of calcium, fruit and vegetables, red meat, alcohol and tomatoes.	Current published cohort studies suggest no association between saturated fat intake and the risk of prostate cancer. <u>Limitations</u> Meta-analysis is on a limited number of studies and there is considerable heterogeneity; studies conducted in American and European populations only.

Study	Research methods	Analysis	Results	Comments
Schwab et al. (2014) (Systematic narrative review) <u>Funding source</u> Supported by the Nordic Council of Ministers. <u>Declarations of interest</u> None to declare.	<u>Research question</u> What are the effects of intake of total fat and various combinations and proportions of fatty acid classes in the diet, considering intake of other nutrients on: a. well-established indicators of clinical outcomes such as plasma or serum total lipids and lipoprotein concentrations, plasma or serum glucose and insulin concentrations and blood pressure? b. clinical outcomes including body weight, type 2 diabetes, CVD, and cancer? <u>Selection criteria</u> *Search dates*: January 2000- February 2012. *Study designs*: RCTs and PCS. *Inclusion criteria:* 18-70y, healthy (subjects with dyslipidaemia, glucose intolerance, or overweight (mean BMI of study population not exceeding 30kg/m^2) were included); n≥10 participants for RCTs; dietary assessment method: food record, FFQ, dietary recall, biomarkers; duration≥4w (RCTs), ≥6 months (body weight and body composition studies); PCS follow-up >4y, studies >5y for cancers; RCT dropout <30% in 6m, <40% 12m, <50% 24m; intervention: amount and/or quality of dietary fat; updated/relevant nutrient databases. *Exclusion criteria*: Studies without Caucasians or Caucasians a clear minority. Aim of study outside scope of review. The studied exposure was a food pattern or a whole food. Included non-healthy subjects,	<u>Analysis</u> Narrative review, results of the quality assessment of the individual studies were summarised to evaluate the quality and strength of the overall evidence in related tot the posed research questions. The evidence for each exposure-outcome association was categorising according to pre demented categories: convincing, probable, limited-suggestive, and limited- no conclusion. <u>Evaluation of study quality</u> The primary evidence was assessed for quality but method not stated. Quality categories included A: high quality with very low risk of bias; B: good quality, some risk of bias but not enough to invalidate results; C: low quality with significant bias and weaknesses which may invalidate results.	<u>Prostate cancer</u> 3 PCS; n=235,568; duration: 8-11y; age: 45-73y; gender: M. No significant associations with saturated fat intake observed. Limited evidence – no conclusion; grade B evidence.	Limited evidence, no conclusion. <u>Limitations</u> Focus on new evidence since previous edition of Nordic Nutrition Recommendations (NNR), hence why studies pre 2000 not included. Strict criteria for both study quality and evidence grading resulting in a relatively conservative estimate of the evidence.

Study	Research methods	Analysis	Results	Comments
	obese subjects. <u>Dietary assessment methods</u> Food record, FFQ, dietary recall, valid biomarkers.			

Study	Research methods	Analysis	Results	Comments
Dennis et al. (2004) (Meta-analysis) Funding source Research supported by the National Cancer Institute grants. Declarations of interest None declared.	Research question Examine both the strength and the consistency of the observed associations between aspects of dietary fat and prostate cancer. Selection criteria *Search dates*: 1966 to end of October 2003. *Study designs*: Case control and cohort studies. *Inclusion criteria*: Non-English language publications. *Exclusion criteria*: Animal and therapy studies; no relevant dietary intake data; included populations already reported on; studies that concentrated on % of fatty acids in adipose tissue or serum rather than on intake; ecological studies. Dietary assessment methods FFQs, 24 hour recall.	Analysis Examined RR where available across multiple ordinal categories of the exposures. Where multiple RRs were presented the most adjusted for greatest number of confounders were included. Pooled estimates of risk were then obtained from random-effects models applied to the study-specific slopes. Heterogeneity assessed using Cochran's chi-square test (Q) to assess consistency of associations. I^2 was calculated as the relative difference between Q statistic and its expected value. Evaluation of study quality Not assessed.	4 PCS for saturated fat; n = 130,875 participants (2536 cases prostate cancer); duration: 4-21y; age: 16-75y; health at baseline: not stated; country: USA (2), Netherlands (1), Norway (1). Risk of prostate cancer per 25g/day unit change in saturated fats (4 PCS) RR 1.00 (95%CI 0.87, 1.16); I^2 = 0%, p = 0.81 *Adjusted for energy (3 PCS)* RR 1.03 (95%CI 0.73, 1.46); I^2 = 0%, p = 0.63 Confounders adjusted for in primary studies include age; family history of prostate cancer; socioeconomic status; BMI; age 21 BMI; vasectomy status; energy intake; intakes of phosphorous, vitamin D, Vitamin E, lycopene, fructose and calcium.	No significant association between saturated fat intake and prostate cancer. Limitations Inconsistencies in assessments of dietary fat intake.

Table A2.12 RCTs and PCS assessing the relationship between dietary saturated fat intake and cancers in each review article

Study name[1] / first author (publication dates) **Publication year**	**Schwab et al. (2014)**	**Liu et al. (2011)**	**Yao and Tian (2015)**	**Schwab et al. (2014)**	**Smith-Warner et al. (2002)**	**Cao et al. (2016)**	**Brennan et al. (2015)**	**Xia et al. (2015)**	**Schwab et al. (2014)**	**Makarem et al. (2013)**	**Turner (2011)**	**Boyd et al. (2003)**	**Smith-Warner et al. (2001)**	**Xu et al. (2015a)**	**Schwab (2014)**	**Dennis et al. (2004)**
Cancer site	*Colorectal*		*Pancreatic*		*Lung*	*Breast*								*Prostate*		
Total primary studies (publications)	1	12	6	4	8	20	4	24	6	3 (4)	19	14	8	9	3	4
Boeke 2014						X		X								
Farvid 2014								X								
Sieri 2014						X										
Arem 2013			X													
NIH-AARP Diet and Health Study																
Pelser 2013														X		
Thiebaut 2009			X	X												
Park 2012						X		X	X							
Sczaniecka 2012						X		X								
Linos 2010									X		X					
Netherland's Cohort Study on Diet and Cancer																
Heinen 2009			X													
Kushi 1992												X	X			
Butler 2008		X														
European Prospective Into Cancer and Nutrition (EPIC)																
Crowe 2008														X	X	
Willett 1987											X					
Sieri 2008								X	X							
Lof 2007						X		X	X		X					

Study name[1] / first author (publication dates) Publication year	Schwab et al. (2014)	Liu et al. (2011)	Yao and Tian (2015)	Schwab et al. (2014)	Smith-Warner et al. (2002)	Cao et al. (2016)	Brennan et al. (2015)	Xia et al. (2015)	Schwab et al. (2014)	Makarem et al. (2013)	Turner (2011)	Boyd et al. (2003)	Smith-Warner et al. (2001)	Xu et al. (2015a)	Schwab (2014)	Dennis et al. (2004)
Cancer site	*Colorectal*		*Pancreatic*		*Lung*	*Breast*								*Prostate*		
Neuhouser 2007														X		
Park 2007														X	X	
Thiebaut 2007						X		X			X					
Wallstrom 2007														X	X	
Freedman 2006						X										
Kim 2006								X	X		X					
Oba 2006		X														
Nothlings 2005			X	X												
Wakai						X		X								
Borugian 2004							X			X						
Lin 2004	X	X														
Nurses' Health Study																
Frazier 2004								X								
Mills 1989													X			
Saadatian-Elahi 2004											X					
Bingham 2003								X				X				
Cho 2003								X	X		X	X				
Flood 2003		X														
Gago-Dominguez 2003											X					
Michaud 2003			X	X												
Byrne 2002								X			X					
New York University Women's Health Study																
Horn-Ross 2002						X					X					
Kato 1997		X														

Study name[1] / first author (publication dates) / Publication year	Schwab et al. (2014)	Liu et al. (2011)	Yao and Tian (2015)	Schwab et al. (2014)	Smith-Warner et al. (2002)	Cao et al. (2016)	Brennan et al. (2015)	Xia et al. (2015)	Schwab et al. (2014)	Makarem et al. (2013)	Turner (2011)	Boyd et al. (2003)	Smith-Warner et al. (2001)	Xu et al. (2015a)	Schwab (2014)	Dennis et al. (2004)
Cancer site	*Colorectal*		*Pancreatic*		*Lung*	*Breast*								*Prostate*		
Sieri 2002						X					X					
Stolzenberg-Solomon 2002			X	X												
Voorrips 2002						X		X			X					
Wirfalt 2002						X					X					
Jarvinen 2001		X														
Feskanaich 2000					X											
Rohan 2000					X											
Velie 2000						X		X			X	X				
Kristal														X		
Pietinen 1999		X														
Schuurman 1999																X
Holmes 1999					X		X	X			X	X	X			
Wolk 1998						X		X				X	X			
Jain and Milier 1997										X						
Jain 1994							X			X						
Veierod 1997														X		X
Gaard 1996		X														
Hunter 1996											X					
Gaard 1995						X		X				X				
Kushi 1995						X					X					
ATBC Cancer prevention Study Group 1994					X											
Bostick 1994		X														
Giovannucci 1994		X														
Goldbohm 1994		X														

Study name[1] / first author (publication dates) Publication year	Schwab et al. (2014)	Liu et al. (2011)	Yao and Tian (2015)	Schwab et al. (2014)	Smith-Warner et al. (2002)	Cao et al. (2016)	Brennan et al. (2015)	Xia et al. (2015)	Schwab et al. (2014)	Makarem et al. (2013)	Turner (2011)	Boyd et al. (2003)	Smith-Warner et al. (2001)	Xu et al. (2015a)	Schwab (2014)	Dennis et al. (2004)
Cancer site	*Colorectal*		*Pancreatic*		*Lung*	*Breast*								*Prostate*		
Toniolo* 1994						X		X			X	X	X			
Giovannucci 1993														X		X
van den Brandt (a) 1993					X											
Van den Brandt (b) 1993								X				X	X			
Rohan 1993							X									
Graham 1992					X							X	X			
Kushi 1992					X											
Kyogoku 1992										X						
Willett 1992								X			X					
Howe 1991						X		X				X	X			
Howe (b) 1991												X				
Knekt 1990						X		X				X				
Willett 1990		X														
Mills 1989					X											
Severson 1989														X		X
Jones 1987						X		X				X				

[1] Study name is only provided when two or more publications for that study are used in any of the reviews.

Cognitive impairment and dementias

Table A2.13 Characteristics of a meta-analysis and systematic reviews

Study	Research methods	Analysis	Results	Comments
Xu et al. (2015b) (Meta-analysis) <u>Funding source</u> None declared. <u>Declarations of interest</u> None to declare.	<u>Research question</u> To carry out the most extensive and comprehensive systematic review and meta-analysis to date, which employs a full-scale search of observational studies to calculate effect sizes of various modifiable risk factors for Alzheimer's disease. <u>Selection criteria</u> *Search dates:* Up to 15th July 2014. *Study designs:* PCS and retrospective case-control studies. *Inclusion criteria:* Original data concerning OR or RR of Alzheimer's disease; study population representative of the general population; exposures considered to be positively or negatively associated with later diagnosis of Alzheimer's disease are potentially modifiable. *Exclusion criteria:* Non English-written publications; about genetic risk factors; without dementia specification; statistically non-significant; special population or population not representing general people; relative of Alzheimer's disease patients or individuals with another disease as control; Alzheimer's disease progression or Alzheimer's disease has happened.	<u>Analysis</u> Where an exposure of interest was reported by 2 studies in a consistent way, these were combined. Pooled effect size calculated and 95% CI. Heterogeneity between studies: I^2 statistic, where significant ($p<0.05$), it was further analysed. When heterogeneity could not be explained, random effect model used. Publication bias: evaluated using Egger test, where significant, trim and fill method used. <u>Evaluation of study quality</u> Grade I evidence: pooled population >5000, lower heterogeneity $I^2<50\%$; Grade II-A evidence: pooled population >5000, higher heterogeneity $I^2\geq50\%$; Grade II-B evidence: pooled population <5000, lower heterogeneity $I^2\geq50\%$; Grade III evidence: pooled population <5000, higher heterogeneity.	3 PCS; n=7894 (244 cases); duration: 2.1-21y; age: 67.7y mean age in 1 PCS (not reported in 2 PCS); gender: M (2), F (0), M/F (1); health at baseline: not reported; country: USA (1), The Netherlands (1), Finland (1). <u>RR of Alzheimer's disease for highest vs lowest saturated fat intake</u> *Fixed effect analysis:* RR 1.35 (95% CI -0.03, 2.74), $I^2=0\%$, p=0.619. One cohort study adjusted for APOE status.	No association found.

Study	Research methods	Analysis	Results	Comments
	Dietary assessment methods FFQ, SQFFQ and structured questionnaire and interview.			

Study	Research methods	Analysis	Results	Comments
Barnard et al. (2014) (Narrative systematic review) <u>Funding source</u> None declared. <u>Declarations of interest</u> ND Barnard writes books and articles and gives lectures relayed to nutrition and health and has received royalties and honoraria from these sources. Authors affiliated with the Physicians Committee for Responsible Medicine, which promotes the use of low-fat, plant-based diets and discourages the use of animal-derived, fatty and sugary foods.	<u>Research question</u> Identify the strength of associations between saturated fat intake or trans fats intake and the risk of Alzheimer's disease and other forms of dementia. <u>Selection criteria</u> *Search dates*: Inception until July 2012. *Study designs*: PCS, RCTs. *Inclusion criteria*: Exposure to saturated or trans fats was quantified (at any adult age); endpoints included incident dementia, Alzheimer's disease or mild cognitive impairment; or cognitive decline; the outcome was identified in older age; in PCS, an interval of at least 1 year occurred between dietary assessment and determination of cognitive outcome or in studies assessing cognitive decline, between 2 or more assessments of cognitive status. *Exclusion criteria*: Case reports, case series, case-control studies, studies limited to individuals with medical conditions likely to influence cognitive status and intervention trials including non-dietary methods (e.g. exercise). <u>Dietary assessment methods</u> All used FFQ, except one study - shortened questionnaire specific to dairy products and spreads.	<u>Analysis</u> Narrative review, data not combined. <u>Evaluation of study quality</u> Study reports were examined for means of dietary assessment, diagnosis and cognitive assessment, sample size, baseline dietary variability, attrition, and statistical measures.	9 PCS (13 publications); n=278-6183; duration: 2.6-21y; age: mean 50.2-73.1y; gender: M (0), F (2), M/F (10); health at baseline: not reported; country: USA (6), Finland (2), Italy (2), The Netherlands (1), Australia (1). <u>Incident Alzheimer's disease and other forms of dementia (4 PCS)</u> *Alzheimer's disease:* 1 PCS reported high saturated fat intake was associated with an increased risk. 1 PCS reported high saturated fat was associated with a reduced risk. 2 PCS found no association. . *Total dementia:* 2 PCS found no association. 1 PCS found APOE e4 allele carriers at increased risk of dementia and Alzheimer's disease with moderate (second quartile) saturated fat intake: OR 3.16 (95% CI 1.12, 8.91). <u>Incident mild cognitive impairment (4 PCS)</u> 1 PCS found saturated fat intake was positively associated with risk of mild cognitive impairment limited to those with APOE e4 allele: OR 5.06 (95% CI 1.35, 18.94). 3 PCS found no association; did not test for APOE status or adjust for it in analysis. <u>Cognitive decline (4 PCS)</u> 2 PCS found higher saturated fat intake was associated with increased risk; APOE status not measured. 2 PCS found no association; APOE status reported in 1 PCS, no effect on association.	Several, although not all PCS indicate relationships between saturated fat intake and risk of cognitive problems. <u>Limitations</u> Limited number of studies and no RCTs reflect challenges of completing these studies and need for caution in drawing conclusions. Individuals with cognitive problems are more likely to be lost to follow-up.

Study	Research methods	Analysis	Results	Comments
Lee et al. (2010) (Narrative systematic review) <u>Funding source</u> Health Promotion Fund and partial support from the Clinical Research Center for Dementia, Ministry for Health, Welfare and Family Affairs, Republic of Korea. <u>Declarations of interest</u> None to declare.	<u>Research question</u> Provide an update on the evidence on major health behavioural factors affecting cognitive function, cognitive impairment, and dementia in older people living in the community. Five health behaviours considered: physical activity, smoking, alcohol drinking, BMI, diet and nutrition). <u>Selection criteria</u> *Search dates*: Inception until August 2008 *Study designs*: PCS *Inclusion criteria*: Predominantly aged over 65 years; from a community representative population; could include institutionalised patients as a minority in a larger community based sample. *Exclusion criteria*: Only involving those aged less than 65 years; non-representative samples; non-cognitive outcomes; cross sectional or retrospective study design; congress proceedings and abstracts. <u>Dietary assessment methods</u> Not reported.	<u>Analysis</u> Narrative review. <u>Evaluation of study quality:</u> Assessed based on a 'priori' internal and external validity criteria, incorporating representativeness of the study sample, sample size, follow-up rate and period, outcome and predictor measurements, and controlled confounders.	1 PCS (3 publications); n=1449-1589; duration: mean 20.9y (72.5% attrition rate); age: 39-64y; gender: M/F; health at baseline: not reported; country: Finland. Adjusted for sociodemographic, health-related variables, APOE status. <u>OR for mild cognitive impairment for highest vs lowest intake of saturated fats</u> *Saturated fat from milk, sour milk, and spreads* ↑SF ↑risk: OR 2.36 (95% CI 1.17, 4.74) <u>OR for total dementia and Alzheimer's disease for saturated fat intake (2nd quartile vs 1st quartile)</u> *Saturated fat from milk, sour milk, and spreads* Total dementia: OR 2.45 (95% CI 1.10, 5.47) Alzheimer's disease: OR 3.82 (95% CI 1.48, 9.87) *Saturated fat from spreads* ↑ saturated fat ↑ risk of total dementia and Alzheimer's disease: OR 2.54 (95% CI 1.13, 5.68) APOE $_e$4 carriers: OR 4.34 (95% CI 1.28, 14.68)	Saturated fat intake increased the risk of mild cognitive impairment and dementia.

Study	Research methods	Analysis	Results	Comments
Patterson et al. (2007) (Narrative systematic review) Funding source Financial support from the Institute of Advanced Studies, University of Bologna, Italy; CIHR New Investigator Award. Declarations of interest Support received from: Janssen-Ortho; Pfizer; Novartis; Lundbeck; Alzheimer Society of Nova Scotia; Voyager Pharmaceuticals; Myriad; Neurochem.	Research question To identify and quantify general (non-genetic) risk factors for all-cause dementia, Alzheimer's disease, and vascular dementia. Selection criteria *Search dates*: From 1966 to December 2005. *Study designs*: Longitudinal cohort studies. *Inclusion criteria*: Longitudinal cohort studies; population broadly representative of Canadian demographics; dementia, Alzheimer's disease, or vascular dementia as outcome; general risk factors identified (e.g. hypertension, educational status, occupation, chemical exposure). *Exclusion criteria*: Genetic risk factors. Dietary assessment methods Not reported.	Analysis Narrative review. Evaluation of study quality Categorised as good, fair, or poor based on a criteria considering: population characteristics, follow-up, exposure risk factors, outcomes, analysis.	Characteristics of identified studies not summarised. RR of all-cause dementia with total fat intake >85.5 g/day vs total fat intake <75.5 g/day (1 PCS) RR 2.4 (95% CI 1.1, 5.4) Increased amounts of saturated fat and cholesterol were not established as definite risk factors in 1PCS from The Netherlands (unclear if other studies were identified).	Limitations 1 PCS with very limited description.

Study	Research methods	Analysis	Results	Comments
Ernst (1999) (Narrative systematic review) <u>Funding source</u> None declared. <u>Declarations of interest</u> None declared.	<u>Research question</u> Summarise present knowledge of the relationship of dietary factors and dementias. <u>Selection criteria</u> *Search dates*: Inception to the end of 1997. *Study designs*: Cross-sectional or longitudinal. *Inclusion criteria*: Articles had to include either cross-sectional or longitudinal data on dietary factors and relate these to dementias of either vascular or degenerative type; human subjects. *Exclusion criteria*: Not reported. <u>Dietary assessment methods</u> FFQ.	<u>Analysis</u> Narrative review. <u>Evaluation of study quality</u> Not reported.	1 PCS for saturated fat; n=5386; duration: 2.1y; mean age: 67.7y; gender: not reported; health at baseline: not reported; country: The Netherlands. Adjustments made for age, gender, education, energy intake. Results suggested saturated fat intake was a risk factor for dementia RR 1.9 (95% CI not reported)	<u>Limitations</u> Saturated fat and dementia association found during post hoc analysis. Only one study looked into the association.

Table A2.14 RCTs and PCS assessing the relationship between dietary saturated fat intake and cognitive impairment and dementias in each review article

Study name[1] / first author (publication dates) **Publication year**	**Xu et al. (2015b)**	**Barnard et al. (2014)**	**Lee et al. (2010)**	**Patterson et al. (2007)**	**Ernst (1999)**
Total primary studies (publications)	3	9 (13)	1 (3)	1	1
Cherbuin and Anstey 2012		MCI			
Okereke 2012		CD			
Roberts 2012		MCI			
Naqvi 2011		CD			
Cardiovascular risk factors, Ageing and Dementia					
Eskelinen 2008		MCI	MCI		
Kivipelto 2008			AD, TD		
Laitenen 2006	AD	AD, TD	AD, TD		
Italian Longitudinal Study on Ageing					
Solfrizzi 2006		MCI			
Solfrizzi 2006		CD			
Chicago Health and Ageing Project					
Morris 2004		CD			
Morris 2003	AD	AD			
Luchsinger 2002		AD			
Rotterdam Study					
Engelhart 2002		AD, TD			
Kalmijin 1997	AD	AD, TD		TD	TD

Outcome measured by the study: AD, Alzheimer's disease; CD, cognitive decline; MCI, mild cognitive disorder; TD, total dementia.

[1] Study name is only provided when two or more publications for that study are used in any of the reviews.

ANNEX 3: Intakes and sources of dietary fats

Table A3.1 Average daily intake of saturated fats (g/day and % total energy) by sex and age in children and adults from 4 years of age

Aged 4 years and over *National Diet and Nutrition Survey Rolling Programme Years 5-6 (2012/13 - 2013/14)*

	Sex and age group (years)											
	Boys		**Men**		**Girls**		**Women**		**Total**			
	4-10	**11-18**	**19-64**	**65+**	**4-10**	**11-18**	**19-64**	**65+**	**4-10**	**11-18**	**19-64**	**65+**
Saturated fats (g/day)												
Mean	22.4	27.1	28.4	25.6	21.1	23.0	22.1	22.2	21.8	25.1	25.2	23.7
Median	21.0	26.7	27.3	24.0	20.6	22.0	21.6	21.1	21.0	24.0	24.2	22.3
SD	6.9	10.5	11.2	9.6	6.9	8.8	9.6	8.4	6.9	9.9	10.8	9.1
2.5th percentile	10.4	7.6	11.9	8.1	8.4	7.7	5.7	8.3	9.5	8.0	7.7	8.1
97.5th percentile	39.5	47.1	54.4	45.0	37.1	40.8	42.3	38.6	38.1	45.3	48.4	44.0
% total energy[1]												
Mean	13.2	12.5	12.0	12.5	13.5	12.6	12.3	13.3	13.3	12.5	12.1	12.9
Median	13.0	12.7	11.8	12.4	13.4	12.5	12.0	12.9	13.1	12.6	12.0	12.8
SD	2.6	2.7	3.0	3.2	3.0	2.6	3.5	3.4	2.8	2.7	3.3	3.3
2.5th percentile	8.4	5.6	6.6	6.7	7.6	7.7	5.9	6.8	7.9	7.1	6.0	6.8
97.5th percentile	18.9	18.0	18.4	18.4	19.7	17.5	19.5	20.9	19.0	18.0	18.8	20.4
% of people above DRV[2]	91.3	85.5	75.3	77.7	87.3	83.8	73.8	87.9	89.3	84.7	74.5	83.3
Bases Unweighted	*258*	*268*	*373*	*130*	*237*	*280*	*592*	*193*	*495*	*548*	*965*	*323*

Note:

[1] Total energy intake includes energy from alcohol.

[2] The dietary reference value for saturated fats is 10% of total dietary energy (11% of energy from food and drinks excluding alcohol) (COMA, 1994). All calculations weighted.

Source:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

Table A3.2 Percentage contribution of food groups to average daily saturated fats intake by sex and age in children and adults from 4 years of age

Aged 4 years and over *National Diet and Nutrition Survey Rolling Programme Years 5-6 (2012/13 - 2013/14)*

Food groups[a]	**Sex and age group (years)**													
	Boys		**Total**	**Men**		**Girls**		**Total**	**Women**		**Total**			
	4-10	**11-18**	**boys**	**19-64**	**65+**	**4-10**	**11-18**	**girls**	**19-64**	**65+**	**4-10**	**11-18**	**19-64**	**65+**
	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Cereals and cereal products	26	26	26	21	20	25	28	27	22	21	26	27	22	21
of which:														
Pasta, rice, pizza and other miscellaneous cereals	6	8	7	5	2	6	8	7	6	2	6	8	6	2
White bread	2	2	2	2	1	2	2	2	2	1	2	2	2	1
Wholemeal bread	1	0	0	0	1	0	0	0	0	1	0	0	0	1
Brown, granary and wheatgerm bread	0	0	0	0	1	0	0	0	0	0	0	0	0	0
High fibre breakfast cereals	1	1	1	1	2	1	0	1	1	2	1	1	1	2
Other breakfast cereals	1	0	0	0	0	0	0	0	0	0	1	0	0	0
Biscuits	7	7	7	4	4	7	7	7	5	5	7	7	5	5
Buns, cakes, pastries and fruit pies	7	6	6	5	7	6	8	7	5	7	7	7	5	7
Puddings	1	1	1	1	3	1	1	1	2	3	1	1	1	3
Milk and milk products	32	23	27	21	23	31	20	25	23	24	31	22	22	24
of which:														
Whole milk (3.8% fat)	9	3	6	2	2	8	3	5	2	2	8	3	2	2
Semi skimmed milk (1.8% fat)	5	5	5	4	5	6	3	5	5	6	5	4	4	6
Other milk and cream	2	1	2	1	2	3	2	2	2	2	2	2	2	2
Cheese	8	9	9	10	9	8	8	8	11	9	8	8	10	9
Cheddar cheese	6	7	6	7	6	5	5	5	7	6	5	6	7	6
Other cheese	3	2	3	3	3	3	3	3	4	3	3	2	3	3
Yoghurt, fromage frais and other dairy desserts	3	2	3	2	1	3	2	3	2	3	3	2	2	2
Ice cream	4	3	3	2	3	4	2	3	1	1	4	3	2	2
Eggs and egg dishes	2	2	2	3	3	2	2	2	4	4	2	2	4	4
Fat spreads[b]	8	7	8	10	14	9	9	9	10	14	9	8	10	14
of which:														
Butter	4	3	4	5	7	5	4	5	6	9	4	4	6	8
Reduced fat spread polyunsaturated (41-75% fat)	1	0	0	1	2	1	1	1	1	1	1	1	1	1
Reduced fat spread not polyunsaturated (41-75% fat)	3	3	3	3	4	3	3	3	3	3	3	3	3	4
Low fat spread polyunsaturated (18-39% fat)	0	0	0	0	1	0	0	0	0	1	0	0	0	1
Low fat spread not polyunsaturated (18-39% fat)	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 3.2 continued

Food groups[a]	Sex and age group (years)													
	Boys		Total	Men		Girls		Total	Women					
	4-10	11-18	boys	19-64	65+	4-10	11-18	girls	19-64	65+	4-10	11-18	19-64	65+
	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Meat and meat products	17	23	20	25	25	16	20	19	19	19	17	22	22	22
of which:														
Bacon and ham	1	3	2	2	3	1	2	1	1	2	1	2	2	3
Beef, veal and dishes	3	3	3	4	4	2	3	3	4	3	2	3	4	4
Lamb and dishes	1	1	1	2	2	1	2	1	2	2	1	1	2	2
Pork and dishes	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Coated chicken and turkey	1	2	1	1	1	1	2	1	1	0	1	2	1	0
Chicken, turkey and dishes	2	4	3	4	3	3	3	3	4	3	2	3	4	3
Liver and dishes	0	0	0	0	1	0	0	0	0	0	0	0	0	1
Burgers and kebabs	2	2	2	2	0	1	2	2	1	0	2	2	2	0
Sausages	5	4	4	3	3	3	4	3	2	2	4	4	3	3
Meat pies and pastries	2	3	2	4	5	3	3	3	2	3	2	3	3	4
Other meat, meat products and dishes	1	1	1	2	2	1	1	1	1	1	1	1	1	1
Fish and fish dishes	2	1	2	3	3	1	2	2	3	4	2	2	3	4
of which:														
White fish coated or fried including fish fingers	1	0	1	1	1	1	1	1	1	1	1	0	1	1
Other white fish, shellfish or fish dishes and canned tuna	1	0	0	1	0	0	1	0	1	1	0	0	1	1
Oily fish	0	1	1	1	2	0	1	0	1	2	0	1	1	2
Vegetables and potatoes	4	5	4	5	5	4	6	5	6	4	4	5	5	4
of which:														
Vegetables (not raw) including vegetable dishes	1	1	1	2	1	1	2	1	3	2	1	1	2	1
Chips, fried and roast potatoes and potato products	2	3	3	3	2	2	3	3	2	2	2	3	2	2
Other potatoes, potato salads and dishes	0	1	1	1	1	1	1	1	1	1	1	1	1	1
Savoury snacks	1	2	1	1	0	2	2	2	1	0	1	2	1	0
Nuts and seeds	1	0	1	1	1	0	0	0	1	1	1	0	1	1
Fruit	0	0	0	0	0	0	0	0	1	1	0	0	1	0

Table 3.2 continued

Food groups[a]	Sex and age group (years)													
	Boys		Total	Men		Girls		Total	Women		Total			
	4-10	11-18	boys	19-64	65+	4-10	11-18	girls	19-64	65+	4-10	11-18	19-64	65+
	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Sugar, preserves and confectionery	6	8	7	5	3	7	8	7	5	3	6	8	5	3
of which:														
Sugars, including table sugar, preserves and sweet spreads	0	0	0	0	0	1	1	1	0	0	1	0	0	0
Sugar confectionery	1	0	1	0	0	1	0	0	0	0	1	0	0	0
Chocolate confectionery	5	7	6	5	2	5	7	6	5	3	5	7	5	3
Non-alcoholic beverages[c]	0	0	0	1	0	0	0	0	1	1	0	0	1	1
of which:														
Tea, coffee and water	0	0	0	0	0	0	0	0	1	1	0	0	1	0
Alcoholic beverages	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Miscellaneous[d]	1	2	2	2	2	2	3	2	4	4	2	2	3	3
of which:														
Dry weight beverages	0	0	0	0	0	0	0	0	1	1	0	0	0	1
Soup, manufactured/retail and homemade	0	0	0	1	1	0	0	0	1	2	0	0	1	1
Savoury sauces, pickles, gravies and condiments	1	1	1	2	1	1	2	1	2	1	1	2	2	1
Commercial toddler foods	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Average daily saturated fatty acids intake g	22.4	27.1	24.9	28.4	25.6	21.1	23.0	22.1	22.1	22.2	21.8	25.1	25.2	23.7
Bases (unweighted)	*258*	*268*	*526*	*373*	*130*	*237*	*280*	*517*	*592*	*193*	*495*	*548*	*965*	*323*

Note:

[a] Sub food groups that contribute <0.5% to intake across all age/sex groups are excluded from the table. All other food groups are included.

[b] Some oils which are used as a condiment on bread or salads are included in this food group; however this food group does not include oils or fats used in cooking.

[c] Non-alcoholic beverages are reported as consumed with diluent water.

[d] In addition to dry weight beverages; soup, manufactured/retail and homemade; savoury sauces, pickles, gravies and condiments; and commercial toddler foods, Miscellaneous also includes nutrition powders and drinks.

Source:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

Table A3.3 Average daily intake of polyunsaturated fats (g/day and % total energy) by age and sex in children and adults from 4 years of age

Aged 4 years and over

National Diet and Nutrition Survey Rolling Programme Years 1, 2, 3 and 4 (2008/09 - 2011/12)

	Sex and age group (years)													
	Boys		Total	Men		Girls		Total	Women		Total			
	4-10	11-18	boys	19-64	65+	4-10	11-18	girls	19-64	65+	4-10	11-18	19-64	65+
***Cis* n-3 polyunsaturated fats (g/day)**														
Mean	1.4	1.9	1.7	2.2	2.3	1.3	1.6	1.5	1.8	1.8	1.4	1.8	2.0	2.0
Median	1.3	1.7	1.5	2.0	2.1	1.2	1.5	1.4	1.6	1.6	1.3	1.6	1.8	1.8
SD	0.6	0.9	0.8	1.1	1.2	0.6	0.8	0.8	1.0	1.0	0.6	0.8	1.1	1.1
Upper 2.5 percentile	2.7	4.2	3.6	4.9	5.7	2.9	3.4	3.3	4.2	4.4	2.8	3.8	4.7	4.5
Lower 2.5 percentile	0.6	0.6	0.6	0.7	0.8	0.6	0.5	0.5	0.5	0.7	0.6	0.6	0.6	0.7
% total energy[a]														
Mean	0.8	0.9	0.8	0.9	1.1	0.8	0.9	0.9	1.0	1.1	0.8	0.9	1.0	1.1
Median	0.8	0.8	0.8	0.9	0.9	0.7	0.9	0.8	0.9	0.9	0.8	0.8	0.9	0.9
SD	0.3	0.3	0.3	0.4	0.5	0.3	0.4	0.3	0.4	0.5	0.3	0.3	0.4	0.5
Upper 2.5 percentile	1.5	1.7	1.5	1.9	2.3	1.4	1.8	1.7	2.1	2.4	1.5	1.8	2.0	2.3
Lower 2.5 percentile	0.4	0.4	0.4	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
***Cis* n-6 polyunsaturated fats (g/day)**														
Mean	7.6	10.0	8.9	11.2	10.1	7.4	8.5	8.0	8.8	7.7	7.5	9.2	10.0	8.7
Median	7.3	9.3	8.4	10.6	9.4	6.7	8.0	7.5	8.2	7.3	7.0	8.8	9.2	8.1
SD	2.7	3.7	3.5	4.7	4.4	3.1	3.5	3.4	3.9	3.0	2.9	3.7	4.5	3.9
Upper 2.5 percentile	13.9	18.2	16.9	23.3	20.5	16.4	16.8	16.8	17.4	13.9	14.2	17.3	20.7	19.0
Lower 2.5 percentile	3.6	3.9	3.8	3.8	3.5	3.1	3.1	3.1	2.7	3.2	3.3	3.4	3.1	3.3
% total energy[a]														
Mean	4.4	4.6	4.5	4.8	4.7	4.4	4.8	4.6	4.9	4.6	4.4	4.7	4.8	4.6
Median	4.3	4.4	4.4	4.6	4.5	4.2	4.7	4.5	4.6	4.4	4.2	4.5	4.6	4.4
SD	1.2	1.2	1.2	1.5	1.4	1.3	1.3	1.4	1.6	1.7	1.3	1.3	1.6	1.6
Upper 2.5 percentile	7.2	7.1	7.1	8.2	8.1	7.6	8.1	8.0	8.6	7.5	7.5	7.6	8.4	7.7
Lower 2.5 percentile	2.5	2.7	2.6	2.4	2.4	2.6	2.7	2.6	2.4	2.4	2.5	2.7	2.4	2.4
Bases (unweighted)	*665*	*744*	*1409*	*1126*	*317*	*612*	*753*	*1365*	*1571*	*436*	*1277*	*1497*	*2697*	*753*

Note:

[a] Total energy intake includes energy from alcohol.

Source:

National Diet and Nutrition Survey. Results from Years 1,2,3 and 4 (combined) of the Rolling Programme (2008/09 – 2011/12).

Table A3.4 Average daily intake of monounsaturated fats (g/day and % total energy) by age and sex in children and adults from 4 years of age

Aged 4 years and over

National Diet and Nutrition Survey Rolling Programme Years 1, 2, 3 and 4 (2008/09 - 2011/12)

	Sex and age group (years)													
	Boys		Total	Men		Girls		Total	Women		Total			
	4-10	11-18	boys	19-64	65+	4-10	11-18	girls	19-64	65+	4-10	11-18	19-64	65+
***Cis* monounsaturated fats (g/day)**														
Mean	21.0	27.6	24.6	28.5	25.8	20.0	22.7	21.5	21.7	19.6	20.5	25.2	25.1	22.3
Median	20.5	27.2	23.4	27.4	25.0	19.6	22.0	20.4	20.9	18.7	20.0	24.2	23.6	21.4
SD	6.1	9.3	8.6	11.3	9.4	6.6	8.4	7.7	8.7	6.8	6.3	9.2	10.6	8.6
Upper 2.5 percentile	34.7	49.8	43.2	53.9	45.4	34.7	39.4	37.9	41.5	33.2	34.7	45.3	48.3	42.7
Lower 2.5 percentile	10.6	12.7	11.1	9.8	10.1	9.9	9.1	9.2	6.9	8.6	9.9	9.7	7.5	9.4
% total energy[a]														
Mean	12.0	12.5	12.3	12.0	11.9	12.0	12.8	12.5	11.9	11.5	12.0	12.7	12.0	11.7
Median	11.8	12.5	12.2	12.0	11.6	11.9	12.7	12.4	11.8	11.5	11.9	12.6	11.9	11.6
SD	2.0	2.3	2.2	2.8	2.6	2.2	2.6	2.5	2.9	2.6	2.1	2.5	2.8	2.6
Upper 2.5 percentile	15.9	17.2	16.9	17.5	17.2	16.5	18.3	17.7	17.7	16.8	16.1	17.7	17.7	16.8
Lower 2.5 percentile	8.2	7.8	8.1	6.5	7.4	7.5	8.0	7.7	6.1	6.6	7.9	7.9	6.4	7.1
Bases (unweighted)	*665*	*744*	*1409*	*1126*	*317*	*612*	*753*	*1365*	*1571*	*436*	*1277*	*1497*	*2697*	*753*

Note:

[a] Total energy intake includes energy from alcohol.

Source:

National Diet and Nutrition Survey. Results from Years 1,2,3 and 4 (combined) of the Rolling Programme (2008/09 – 2011/12).

Table A3.5 Average daily intake of saturated fats (g/day and % total energy) adults (16-64 years) at five NDNS time points

	NDNS Year				
	1986/87[a]	**2000/01**	**2008/09 - 2009/10**	**2010/11 - 2011/12**	**2012/13 - 2013/14**
	16-64 years	19-64 years	19-64 years	19-64 years	19-64 years
Saturated fats (g/day)					
Mean	36.6	27.3	26.0	24.5	25.2
Median	35.6	26.0	24.7	22.6	24.2
SD	11.9	12.6	12.1	10.7	10.8
2.5th percentile	15.5	8.0	7.5	7.7	7.7
97.5th percentile	62.0	56.1	52.8	48.7	48.4
% total energy[1]					
Mean	16.0	12.6	12.2	11.9	12.1
Median	15.9	12.5	12.0	11.8	12.0
SD	3.2	3.4	3.4	3.2	3.3
2.5th percentile	10.0	6.3	5.6	6.4	6.0
97.5th percentile	22.3	19.6	19.4	18.9	18.8
Bases (unweighted)	*2197*	*1724*	*1254*	*1443*	*965*

Note:

[a] Standard deviation (sd) was calculated from the Standard Error of the Mean (SE) where sd=SE x √N. sd shown is the average of published figures for men and women.

[1] Total energy intake includes energy from alcohol.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 - 2011/12).

National Diet and Nutrition Survey: Adults aged 19 to 64, 2000/01.

The Dietary and Nutritional Survey of British Adults, 1986/87.

Table A3.6 Average daily intake of saturated fats (g/day and % total energy) in adults aged 65+ years at four NDNS time points

	NDNS Year			
	1994/95	**2008/09 - 2009/10**	**2010/11 - 2011/12**	**2012/13 - 2013/14**
	65+ years	65+ years	65+ years	65+ years
Saturated fats (g/day)				
Mean	27.2	26.6	24.3	23.7
Median	25.4	25.7	22.0	22.3
SD	10.7	10.5	10.7	9.1
2.5th percentile	9.5	9.1	9.7	8.1
97.5th percentile	52.4	48.6	48.5	44.0
% total energy[1]				
Mean	15.0	13.8	12.8	12.9
Median	14.7	13.9	12.7	12.8
SD	3.9	3.6	3.4	3.3
2.5th percentile	8.2	6.6	7.6	6.8
97.5th percentile	23.2	20.4	20.0	20.4
Bases	*1275*	*359*	*394*	*323*

Note:

[1] Total energy intake includes energy from alcohol.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 - 2011/12).

National Diet and Nutrition survey: People aged 65 years and over, 1994/95.

Table A3.7 Percentage contribution of food groups to average daily saturated fat intake in adults (16-64 years) by survey year using NDNS data at five time points

Food groups	NDNS Year				
	1986/87	2000/01	2008/09 - 2009/10	2010/11 - 2011/12	2012/13 - 2013/14
	16-64 years	19-64 years	19-64 years	19-64 years	19-64 years
Cereals and cereal products	18	18	19	20	22
of which:					
Biscuits	4	4	4	5	5
Buns, cakes, pastries and fruit pies	6	4	4	5	5
Milk and milk products	23	24	22	22	22
of which:					
Whole milk (3.8% fat)	11	4	2	2	2
Cheese	9	10	10	11	10
Eggs and egg dishes	3	3	4	3	4
Fat spreads [a]	17	11	10	10	10
of which:					
Butter	10	6	5	5	6
Meat and meat products	23	22	25	24	22
of which:					
Bacon and ham	3	2	2	2	2
Beef, veal and dishes	4	4	5	4	4
Meat pies and pastries	4	4	3	3	3
Fish and fish dishes	2	2	3	3	3
Vegetables, potatoes and savoury snacks	6	9	6	6	5
Nuts and seeds	0	1	1	1	1
Fruit	0	0	0	0	1
Sugar, preserves and confectionery	4	5	5	4	5
Non-alcoholic beverages [b]	0	2	1	0	1
Miscellaneous [c]	3	3	3	3	3
Average daily saturated fat intake g	36.6	27.3	26.0	24.5	25.2
Bases (unweighted)	*2197*	*1724*	*1254*	*1443*	*965*

Note:

[a] Some oils which are used as a condiment on bread or salads are included in this food group; however this food group does not include oils or fats used in cooking.

[b] Non-alcoholic beverages are reported as consumed with diluent water.

[c] In addition to dry weight beverages; soup, manufactured/retail and homemade; savoury sauces, pickles, gravies and condiments; and commercial toddler foods, Miscellaneous also includes nutrition powders and drinks.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 - 2011/12).

National Diet and Nutrition Survey: Adults aged 19 to 64, 2000/01.

The Dietary and Nutritional Survey of British Adults, 1986/87.

Table A3.8 Percentage contribution of food groups to average daily saturated fat intake in adults (65+ years) by survey year using NDNS data at four time points

Food groups	NDNS Year			
	1994/95	2008/09 - 2009/10	2010/11 - 2011/12	2012/13 - 2013/14
	65+ years	65+ years	65+ years	65+ years
Cereals and cereal products	19	18	19	21
of which:				
Biscuits	5	5	5	5
Buns, cakes, pastries and fruit pies	6	6	6	7
Milk and milk products	27	26	25	24
of which:				
Whole milk (3.8% fat)	10	4	2	2
Cheese	8	10	10	9
Eggs and egg dishes	3	4	3	4
Fat spreads[a]	20	15	16	14
of which:				
Butter	13	10	10	8
Meat and meat products	19	20	19	22
of which:				
Bacon and ham	2	2	2	3
Beef, veal and dishes	3	4	4	4
Meat pies and pastries	5	4	2	4
Fish and fish dishes	2	4	5	4
Vegetables and potatoes	5	5	5	4
Nuts and seeds	0	1	1	1
Fruit	0	0	0	0
Sugar, preserves and confectionery	2	2	2	3
Beverages	0	0	0	1
Miscellaneous[b]	3	3	4	3
Average daily saturated fatty acids intake g	27.2	26.6	24.3	23.7
Bases (unweighted)	*1275*	*359*	*394*	*323*

Note:

[a] Some oils which are used as a condiment on bread or salads are included in this food group; however this food group does not include oils or fats used in cooking.

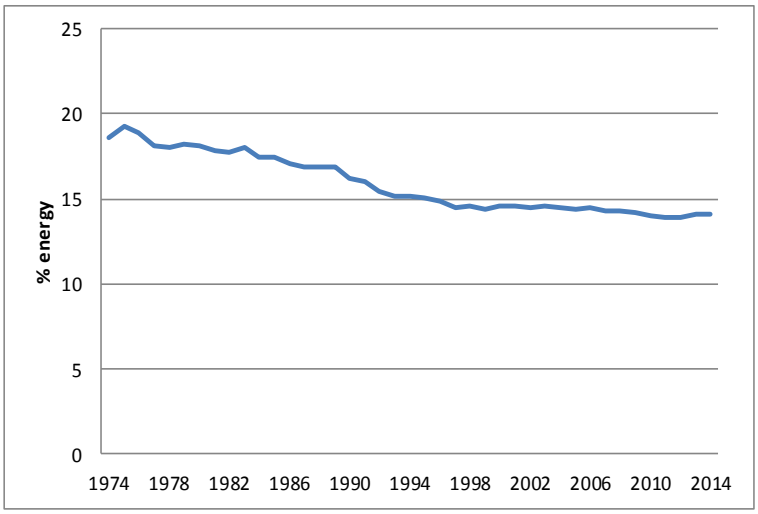
[b] In addition to dry weight beverages; soup, manufactured/retail and homemade; savoury sauces, pickles, gravies and condiments; and commercial toddler foods, Miscellaneous also includes nutrition powders and drinks.

Sources:

National Diet and Nutrition Survey. UK Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

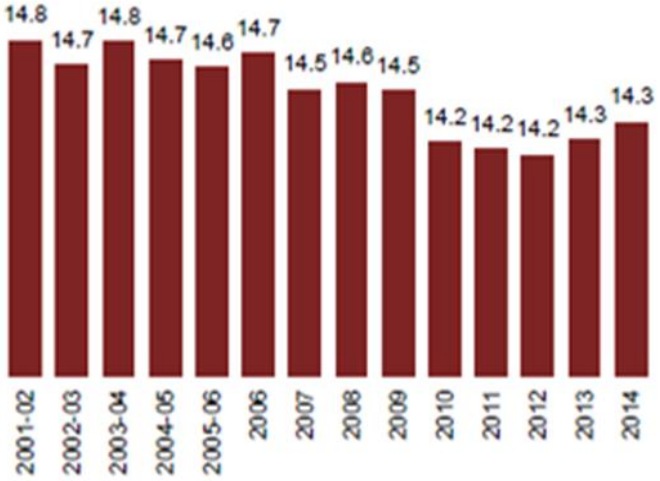
National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 - 2011/12).

National Diet and Nutrition survey: People aged 65 years and over, 1994/95.



Note: Pre-1992 energy intakes excluded alcohol, soft drinks and confectionery
Source: https://www.gov.uk/government/statistical-data-sets/family-food-datasets

Figure A3.1 Long term trend in the percentage of energy derived from saturated fats from household food and drink purchases



Source: Family food 2014

Figure A3.2 Recent trend in the percentage of food energy derived from saturated fats from household and eating out food and drink

Table A3.9 Trans fats intake (g/day and % total energy) in adults (16-64 years) by survey year using NDNS data at five time points

	NDNS Year				
	1986/87[a]	**2000/01**	**2008/09 - 2009/10**	**2010/11 -2011/12**	**2012/13 - 2013/14**
	16-64 years	19-64 years	19-64 years	19-64 years	19-64 years
***Trans* fats (g/day)**					
Mean	4.8	2.4	1.5	1.0	1.0
Median	4.5	2.2	1.4	1.0	0.9
SD	2.3	1.5	0.8	0.6	0.5
2.5th percentile	1.5	0.5	0.3	0.2	0.2
97.5th percentile	10.1	6.0	3.5	2.4	2.3
% total energy[1]					
Mean	2.1	1.1	0.7	0.5	0.5
Median	2.0	1.1	0.7	0.5	0.5
SD	0.7	0.5	0.3	0.2	0.2
2.5th percentile	0.9	0.3	0.2	0.1	0.1
97.5th percentile	3.9	2.2	1.3	1.0	1.0
Bases (unweighted)	*2197*	*1724*	*1254*	*1443*	*965*

Note:

[a] Standard deviation (sd) was calculated from the Standard Error of the Mean (SE) where sd=SE x√N. sd shown is the average of published figures for men and women.

[1] Total energy intake includes energy from alcohol.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 - 2011/12).

National Diet and Nutrition Survey: Adults aged 19 to 64, 2000/01.

The Dietary and Nutritional Survey of British Adults, 1986/87.

Table A3.10 Trans fats intake (g/day and % total energy) in adults (65+ years) by survey year using NDNS data at four time points

	NDNS Year			
	1994/95	**2008/09 - 2009/10**	**2010/11 - 2011/12**	**2012/13 - 2013/14**
	65+ years	65+ years	65+ years	65+ years
***Trans* fats (g/day)**				
Mean	2.8	1.6	1.0	1.0
Median	2.6	1.5	1.0	0.9
SD	1.3	0.8	0.6	0.5
2.5th percentile	0.9	0.4	0.3	0.3
97.5th percentile	5.6	3.2	2.4	2.2
% total energy[1]				
Mean	1.5	0.8	0.6	0.5
Median	1.5	0.8	0.5	0.5
SD	0.5	0.3	0.2	0.2
2.5th percentile	0.6	0.3	0.2	0.2
97.5th percentile	2.7	1.5	1.1	1.1
Bases (unweighted)	*1275*	*359*	*394*	*323*

Note:

[1] Total energy intake includes energy from alcohol.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).
National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 - 2011/12)
National Diet and Nutrition survey: People aged 65 years and over, 1994/95.

Table A3.11 Percentage contribution of food groups to trans fats intake in adults (16-64 years) by survey year using NDNS data at five time points

Food group[a]	NDNS Year				
	1986/87	**2000/01**	**2008/09 - 2009/10**	**2010/11 -2011/12**	**2012/13 - 2013/14**
	16-64 years	19-64 years	19-64 years	19-64 years	19-64 years
Cereals and cereal products	27	26	17	16	18
of which:					
Biscuits	7	9	3	1	1
Buns, cakes, pastries and fruit pies	14	8	4	4	5
Milk and milk products	10	16	23	30	31
of which:					
Whole milk (3.8% fat)	4	1	1	2	2
Cheese	4	8	12	16	16
Eggs and egg dishes	2	3	3	2	2
Fat spreads[b]	30	18	9	8	9
of which:					
Butter	5	4	5	6	7
Meat and meat products	18	21	25	28	27
of which:					
Meat pies and pastries	7	7	3	2	1
Fish and fish dishes	1	3	4	3	2
Vegetables, potatoes and savoury snacks	6	7	9	6	5
Sugar, preserves and confectionery	3	4	3	2	2
Miscellaneous[c]	2	3	5	4	3
Average daily *trans* fatty acids intake g	4.8	2.4	1.5	1.0	1.0
Bases (unweighted)	*2197*	*1724*	*1254*	*1443*	*965*

Note:

[a] Standard deviation (sd) was calculated from the Standard Error of the Mean (SE) where sd=SE x√N. sd shown is the average of published figures for men and women.

[b] Some oils which are used as a condiment on bread or salads are included in this food group; however this food group does not include oils or fats used in cooking.

[c] In addition to dry weight beverages; soup, manufactured/retail and homemade; savoury sauces, pickles, gravies and condiments; and commercial toddler foods, Miscellaneous also includes nutrition powders and drinks.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

National Diet and Nutrition Survey. Results from Years 1, 2, 3, and 4 (combined) of the Rolling Programme (2008/09 - 2011/12).

National Diet and Nutrition Survey: Adults aged 19 to 64, 2000/01.

The Dietary and Nutritional Survey of British Adults, 1986/87.

Table A3.12 Trans fats content of fat spreads analysed in 1991, 1992 and 2009

Composite samples analysed 2009/10[1]	**Examples of products included**	**Total fat g/100g**	**Trans fat g/100g**
Low fat spreads (26-39%) not polyunsaturated (including dairy type)	I can't believe it's not butter light; own brand equivalents	39.0	0.12
Low fat spread (26-39%) not polyunsaturated, olive oil	Bertolli Light; own brand equivalents	38.9	0.14
Low fat spread (26-39%) polyunsaturated	Flora Light; own brand equivalents	36.9	0.05
Hard block margarine	Stork margarine block. Own brand equivalents	76.4	0.07
Compound cooking fat, not polyunsaturated	Cookeen, Crisp n dry, Trex	100.0	0.06
Ghee from vegetable oil	Khanum, Taj Mahal, Pride	100.0	0.08
Reduced fat spread (41-62%) polyunsaturated	Flora Original, Vitalite; own brand equivalents	59.2	0.13
Reduced fat spread (41-62%) not polyunsaturated	I can't believe it's not butter, Utterly Butterly; Stork; own brand equivalents	60.6	0.15
Reduced fat spread (41-62%) not polyunsaturated, olive oil	Bertoli; Own brand equivalents	59.1	0.11
Reduced fat spread (62-75%) not polyunsaturated	Clover; own brand equivalents	73.2	0.14
Composite samples analysed 1992[2]			
Reduced fat spread 70-80% fat polyunsaturated	I can't believe it's not butter	77.0	5.9
Reduced fat spread 60% fat made with olive oil	Olivio and own brand equivalents	62.7	6.1
Vegetable ghee	Khanum, Pride	99.4	1
Catering margarine	Chef's Choice, Family Choice	81.7	12.6
Samples analysed 1991[3]			
Soft margarine not polyunsaturated	own brands; Stork SB, Blue Band	79-83	7-4-11.7
Soft margarine polyunsaturated (sunflower)	own brands; Vitalite	81-82	3.3-5.6
Hard margarine	Echo	79.4	14.4
Compound cooking fat	White Flora, Cookeen, White Cap	99.9	7.5-17.0
Reduced fat spreads 70% fat not polyunsaturated	Krona, Clover, Summer County	70-74	1.8-7.6
Reduced fat spreads 60% fat not polyunsaturated	Mello, Stork Light Blend	60	4.4-7.2
Reduced fat spreads 60% fat polyunsaturated	Vitalite Light	60.8	3.3
Low fat spread polyunsaturated	Flora Extra Light, Shape Sunflower	38-39	2.2-2.8
Low fat spread not polyunsaturated	Gold, Clover Light, Delight	39-41	3.4-4.4
Very low fat spread not polyunsaturated	Outline, Gold Lowest	23-28	1.9-2.9

References

1 Department of Health. Nutrient analysis of processed foods with special reference to trans fatty acids. Analysis of composite samples of different brands. https://www.gov.uk/government/publications/nutrient-analysis-of-processed-foods-including-trans-fats

2 Ministry o fAgriculture , Fisheries and Food . Fatty acids in foods. Nutrient analysis project. RHM. 1992. Analysis of com posite samples of different brands

3 Ministry of Agriculture, Fisheries and Food. Fat, fatty acids, fat soluble vitamins and sodium composition of yellow fats . 1990/91. Laboratory of the Government Chemist. Analysis of single brands. Analytical values are shown as a range of the products analysed in each category

Table A3.13 Average daily intake of cholesterol (mg/day) in adults (16-64 years) by survey year using NDNS data at three time points

	NDNS Year		
	1986/87[a]	**2000/01**	**2012/13 - 2013/14**
	16-64 years	19-64 years	19-64 years
Cholesterol (mg/day)			
Men under 65 years			
Mean	390	304	25
Median	375	285	263
SD	148	128	235
2.5th percentile	151	95	126
97.5th percentile	741	606	92
			559
Bases (unweighted)	*1087*	*766*	*373*
Women under 65 years			
Mean	280	213	219
Median	269	201	199
SD	107	95	113
2.5th percentile	98	60	35
97.5th percentile	511	427	472
Bases (unweighted)	*1110*	*958*	*592*

Note:

[a] Standard deviation (sd) was calculated from the Standard Error of the Mean (SE) where sd=SE x √N. sd shown is

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 – 2013/14).

National Diet and Nutrition Survey: Adults aged 19 to 64, 2000/01.

The Dietary and Nutritional Survey of British Adults, 1986/87.

Table A3.14 Blood lipids analysis among adults (16-64 years) by sex and age using NDNS data at five time points

Analyte	NDNS Year									
	1986/87[a,b]		2000/01[a,b]		2008/09 - 2009/10[d]		2010/11 - 2011/12[d]		2012/13 - 2013/14[d]	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
	16-64 years		19-64 years		19-64 years		19-64 years		19-64 years	
Serum total cholesterol (mmol/L)										
Mean	5.8	5.8	5.2	5.3	5.1	5.2	5.2	5.2	4.9	5.0
Median	5.8	5.6	5.1	5.2	5.0	5.2	5.1	5.0	4.9	4.9
SD	1.2	1.4	1.2	1.2	1.0	1.1	1.1	1.1	1.1	1.1
2.5th percentile	*	*	3.2	3.3	3.4	3.2	3.4	3.4	2.8	3.4
5th percentile	4.0	4.0	*	*	*	*	*	*	*	*
95th percentile	8.0	8.1	*	*	*	*	*	*	*	*
97.5th percentile	*	*	7.6	8.0	7.7	7.7	7.3	7.5	6.7	7.1
% below 5.2mmol/L	32.0	36.0	52.0	52.0	*	*	*	*	*	*
% between 5.2mmol/L and 6.4mmol/L	*	*	*	*	35.9	39.7	3.3	31.6	38.0	31.2
% between 6.5mmol/L and 7.8mmol/L	*	*	*	*	8.3	9.3	12.7	13.4	5.9	8.9
% above 7.8mmol/L	*	*	*	*	1.6	2.2	1.1	2.3	0.0	0.7
Serum high density lipoprotein-cholesterol (mmol/L)										
Mean	1.2	1.4	1.1	1.3	1.3	1.6	1.3	1.6	1.3	1.5
Median	1.1	1.4	1.0	1.3	1.3	1.6	1.3	1.5	1.2	1.5
SD	0.3	0.3	0.3	0.4	0.3	0.4	0.4	0.5	0.4	0.4
2.5th percentile	*	*	0.6	0.7	0.8	1.0	0.8	0.9	0.7	0.8
5th percentile	0.7	0.9	*	*	*	*	*	*	*	*
95th percentile	1.8	2.1	*	*	*	*	*	*	*	*
97.5th percentile	*	*	1.7	2.3	2.1	2.6	2.2	2.6	2.2	2.5

Table 3.14 continued

Serum low density lipoprotein-cholesterol (mmol/L)[c]										
Mean	4.7	4.4	4.2	4.0	3.1	3.1	3.2	3.1	3.0	3.0
Median	4.6	4.2	4.1	3.8	3.1	3.1	3.2	3.0	3.1	3.0
SD	1.2	1.4	1.2	1.2	0.9	1.0	1.0	1.0	0.9	0.9
2.5th percentile	*	*	2.1	2.1	1.5	1.4	1.6	1.6	1.2	1.7
5th percentile	2.8	2.7	*	*	*	*	*	*	*	*
95th percentile	6.9	6.8	*	*	*	*	*	*	*	*
97.5th percentile	*	*	6.6	6.8	5.1	5.2	5.3	5.3	4.9	4.9
Bases (unweighted)										
[1] Serum total cholesterol (mmol/L)	*923*	*809*	*618*	*659*	*252*	*344*	*308*	*445*	*210*	*327*
[2] Serum high density lipoprotein-cholesterol (mmol/L)	*919*	*806*	*617*	*659*	*252*	*344*	*308*	*445*	*210*	*327*
[3] Serum low density lipoprotein-cholesterol (mmol/L)	*919*	*806*	*618*	*659*	*243*	*340*	*299*	*438*	*208*	*327*

1986/87 and 2000/01 notes:

[a] Blood samples were **not** fasting samples.

[b] LDL was calculated by subtracting HDL from total cholesterol uncorrected for plasma triglycerides (not measured).

* Data not available.

2008/12 and 2012/14 notes:

[c] LDL was calculated using the Friedewald equation: LDL (mmol/L) = Total Cholesterol – HDL Cholesterol – (triglycerides/2.2). LDL was not calculated for samples with triglyceride values greater than 4.5mmol/L.

[d] Blood samples were fasting samples.

* Data not available.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 - 2013/14).

National Diet and Nutrition Survey. Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/09 – 2011/12).

National Diet and Nutrition Survey: Adults aged 19 to 64, 2000/01.

The Dietary and Nutritional Survey of British Adults, 1986/87.

Table A3.15 Blood lipids analysis among adults (65+ years) by sex using NDNS data at four time points

Analyte	NDNS Year							
	1994/95		2008/09 - 2009/10		2010/11 - 2011/12		2012/13 - 2013/14	
	65+ years							
	Men	Women	Men	Women	Men	Women	Men	Women
Serum total cholesterol (mmol/L)								
Mean	5.6	6.2	4.6	5.4	4.7	5.6	4.6	5.3
Median	5.6	6.1	4.2	5.7	4.7	5.4	4.4	5.3
SD	1.1	1.5	1.2	1.1	1.1	1.2	1.2	1.1
2.5th percentile	3.3	3.5	2.6	3.6	2.9	3.6	2.6	3.4
97.5th percentile	8.0	9.3	7.1	7.3	7.0	8.2	7.1	7.6
% below 5.2mmol/L	34.0	24.0	*	*	*	*	*	*
% between 5.2mmol/L and 6.4mmol/L	*	*	24.2	50.6	24.2	30.4	16.2	36.6
% between 6.5mmol/L and 7.8mmol/L	*	*	10.2	10.6	6.1	24.7	7.6	17.4
% above 7.8mmol/L	*	*	0.0	1.9	2.0	4.5	2.2	1.1
Serum high density lipoprotein-cholesterol (mmol/L)								
Mean	1.2	1.4	1.3	1.6	1.3	1.7	1.3	1.6
Median	1.1	1.3	1.3	1.5	1.2	1.7	1.3	1.5
SD	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4
2.5th percentile	0.5	0.7	0.8	0.9	0.8	1.1	0.6	0.8
97.5th percentile	2.3	2.5	2.1	2.4	2.3	2.6	2.0	2.5
Serum low density lipoprotein-cholesterol (mmol/L)[a]								
Mean	4.4	4.8	2.8	3.2	2.9	3.4	2.8	3.2
Median	4.4	4.8	2.5	3.5	2.8	3.4	2.7	3.0
SD	1.1	1.5	1.2	1.0	0.9	1.1	1.0	1.0
2.5th percentile	2.0	2.2	0.8	1.2	1.4	1.9	1.2	1.5
97.5th percentile	6.9	8.1	5.0	5.0	4.8	6.1	5.2	5.1
Bases (unweighted)								
[1] Serum total cholesterol (mmol/L)	*458*	*428*	*69*	*98*	*76*	*104*	*71*	*102*
[2] Serum high density lipoprotein-cholesterol (mmol/L)	*458*	*428*	*69*	*98*	*76*	*104*	*71*	*102*
[3] Serum low density lipoprotein-cholesterol (mmol/L)	*458*	*428*	*68*	*95*	*75*	*104*	*71*	*101*

Note:

Surveys collected fasting blood samples.

* Data not available.

1994/95 notes:

LDL was calculated by subtracting HDL from total cholesterol uncorrected for serum triglycerides.

2008/12 notes:

[a] LDL was calculated using the Friedewald equation: LDL (mmol/L) = Total Cholesterol – HDL Cholesterol – (triglycerides/2.2). LDL was not calculated for samples with triglyceride values greater than 4.5mmol/L.

Sources:

National Diet and Nutrition Survey. Results from Years 5 and 6 (combined) of the Rolling Programme (2012/13 - 2013/14).

National Diet and Nutrition Survey. Results from Years 1,2,3 and 4 (combined) of the Rolling Programme (2008/2009 – 2011/12).

National Diet and Nutrition survey: People aged 65 years and over, 1994/95.

The British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, endorsed by the British Diabetic Association, have issued guidance published in the article 'Joint British recommendations on prevention of coronary heart disease in clinical practice'. Heart, 1998; 80: 1–29.

ANNEX 4: AMSTAR assessment summary tables for all included meta-analyses and systematic reviews

Study	**Was an 'a priori' design provided?**	**Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?**	**Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched**	**Was the status of publication (i.e. grey literature) used as an inclusion criterion?**	**Was a list of 1) included studies and 2) excluded studies provided?**	**Were the characteristics of the included studies provided?**	**Was the scientific quality of the included studies 1) assessed and 2) documented?**	**Was the scientific quality of the included studies used appropriately in formulating conclusions?**	**Were the methods used to combine the findings of studies appropriate?**	**1) Was the likelihood of publication bias assessed? 2) how was it assessed?**	**1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?**
Cao et al. (2016) (Meta-analysis)	No	1) Yes 2) Yes 3) No	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes- in online supplement. 6) Yes	No	1) Yes 2) No	Yes- in online supplement	1) Yes - Newcastle Ottawa Scale 2) No	No	Two stage random effects dose-response meta-analysis. Heterogeneity: I^2 statistic.	1) Yes 2) Egger regression test.	1) Yes 2) No 3) Not stated.
Harcombe et al. (2016a) (Systematic review)	Yes	1) Yes 2) No 3) No	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) No	No	1) Yes 2) No	Yes	1) Yes – Cochrane Collaboration assessment 2) Yes	No	Narrative systematic review – available data did not allow for a meta-analysis.	1) No 2) N/A	1) Yes 2) Z Harcombe receives income from 2 small self-employment businesses: The Harcombe Diet Co and Columbus Publishing. 3) Not stated
Harcombe et al. (2016b) (Systematic review with meta-analysis)	Yes	1) Yes 2) No 3) No	Yes 1) Yes 2) No 3) Yes 4) Yes 5) Yes 6) No	No	1) Yes 2) **No**	Yes	1) Yes – Cochrane Collaboration assessment 2) Yes	No	Random-effects meta-analysis. Heterogeneity and bias: I^2 and T^2 calculations.	1) Yes 2) Funnel plots and Egger's test.	1) Yes 2) No 3) No funding support
Imamura et al.	Yes	1) No	Yes	Yes	1) Yes	Yes - in online	1) Yes-	Yes	Primary outcome:	1) Yes	1) Yes

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) >2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
(2016) (Systematic review with meta-analysis)		2) Yes 3) No	1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes		2) No	supplement.	2) Yes- in online supplement.		post intervention values. Meta-analysis: between arm correlations from crossover/Latin-square design – p-values and outcome measures, within individual correlations, interventional effects (SD or SE). Dose-response replacement nutrient estimated multiple treatments meta-regression. Heterogeneity: Q-statistics.	2) Examined plots and Egger's test.	2) Yes - support/consulting : Hass Avocado board Boston Heart Diagnostics, GOED, DSM, Life Science Research Organization, Elysium Health, Astra Zeneca, Unilever R&D 3) Medical Research Council Epidemiology Unit Core Support, National Institute of Health in the US
Ramsden et al. (2016) (Systematic review and meta-analysis) (all information provided in the supplementary	Can't answer	1) Yes 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	Yes	1) Yes 2) Yes	Yes	1) Yes 2) Yes	Yes	Pooled risk estimates calculated for CHD death and all-cause mortality using a random effects model. Heterogeneity: I^2 statistic and Tau-squared.	1)Yes 2) Visual inspection of a funnel plot. Trim and fill analysis then performed.	1) Yes 2) No 3) US Public Health Service, National Heart Institute, National Institute of Alcohol Abuse and Alcoholism, National Institute of Health, University of North Carolina.

Study	**Was an 'a priori' design provided?**	**Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?**	**Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched**	**Was the status of publication (i.e. grey literature) used as an inclusion criterion?**	**Was a list of 1) included studies and 2) excluded studies provided?**	**Were the characteristics of the included studies provided?**	**Was the scientific quality of the included studies 1) assessed and 2) documented?**	**Was the scientific quality of the included studies used appropriately in formulating conclusions?**	**Were the methods used to combine the findings of studies appropriate?**	**1) Was the likelihood of publication bias assessed? 2) how was it assessed?**	**1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?**
material)											
Tielemans et al. (2016) (Narrative systematic review)	Yes	1) Yes 2) No 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes- in supplement. 5) Yes-in supplement. 6) Yes but only in the 20% most recent publications.	Yes	1) Yes 2) No	Yes	1) Yes 2) Yes- in supplement.	Yes	N/A - narrative systemic review.	1) No 2) N/A	1) Yes 2) Yes (funding source) 3) Nestle Nutrition, Metagenics and AXA.
Brennan et al. (2015) (Systematic review with meta-analysis)	No	1) Yes 2) No 3) No	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) No 6) Yes	No	1) Yes 2) No included a list of some excluded studies.	Yes	1) No 2) N/A	N/A	Meta-analysis and variance weighted least squares linear regression analysis of HRs. Heterogeneity: X^2 and I^2 statistic.	1) Yes 2) Inspection, funnel plots, Begg's and Egger's tests.	1) Yes 2) No 3) PhD studentship funding from Department of Employment and Learning.
de Souza et al. (2015) (Systematic review with meta-analysis)	Yes	1) No 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes - in supplement. 5) Yes - in supplement. 6) Yes	No	1) Yes 2) No	Yes - in supplement.	1) Yes 2) Yes	Yes	Risk ratios (highest and lowest intakes). ≥ 2 studies random effects meta-analysis performed. ≤ 3 studies fixed effect estimates also considered. Heterogeneity:	1) only if ≥ 10 studies 2) Funnel plots Egger's and Begg's tests.	1) Yes 2) Yes 3) World Health Organization

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
									Cochran's Q test (significant at P<0.10), and I^2 statistic. If ≥ 10 studies and I^2 > 60% or P_Q < 0.10, meta-regression used.		
Harcombe et al. (2015) (Systematic review with meta-analysis)	Yes	1) Yes 2) No 3) No	Yes - *although only searched for primary evidence up to 1983.* 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) No	No	1) Yes 2) No	Yes	1) Yes 2) No	No	Pooled effect calculated using random effects meta-analysis. Heterogeneity: Q-value, I^2, and T^2 calculations.	1) Yes 2) Funnel plots and Egger's test.	1) Yes 2) No 2) Not stated.
Hooper et al. (2015) (Systematic review with meta-analysis)	Yes	1) Two authors for search dates 06/2010 – 03/2014. One author for studies in Hooper et al., 2012 2) Two authors for latest search. One author for studies in	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	Yes	1) Yes 2) Yes	Yes	1) Yes 2) Yes	Yes	Risk ratios: random-effects meta-analysis. Heterogeneity: I^2 statistic.	1)Yes 2) Funnel plot	1) Yes 2) No 3) Institute of Child Health, University of London, UK – to support the first systematic review.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
		Hooper et al., 2012. 3) Yes									
Xia et al. (2015) (Meta-analysis)	Yes	1) Yes 2) No 3) No	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) No 6) Yes	No	1)Yes 2) No	Yes	1) Yes 2) Yes-Newcastle-Ottawa scale.	Yes	Random and fixed effect model meta-analysis. Heterogeneity: I^2.	1) Yes 2) Begg funnel-plot and Egger test.	1) Yes 2) No 3) National Natural Science Foundation.
Xu et al. (2015a) (Systematic review with meta-analysis)	Yes	1) Yes 2) Yes 3) Yes	1) Yes 2) yes 3) Yes 4) Yes 5) Yes 6) Yes	No	1) Yes 2) No	Yes	1) Yes 2) Yes – Newcastle Ottawa Scale	N/A	Dose-response meta-analysis calculated by generalised least-squares method, and then random-effect model. Fixed effect model used to pool subgroups before inclusion in overall analysis. Heterogeneity: I^2 statistic. Random-effects meta-analysis assessed influence of subgroup covariates on intervention effect.	1) Yes 2) Egger's test	1) Yes 2) No 3) No support of funding to report
Xu et al. (2015b)	No	1) Can't answer 2) Can't answer	Yes	Yes	1) Yes 2) Yes	Yes – in supplement	1) Yes 2) No	Yes	Where an exposure of interest was	1) Yes 2) Egger	1) Yes 2) No

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) >2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
(Meta-analysis)		3) Can't answer	1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes						reported by 2 studies in a consistent way, these were combined. Pooled effect size calculated and 95% CI. Heterogeneity between studies: I2 statistic. Where significant ($p<0.05$) it was further analysed. When heterogeneity could not be explained, random effect model used.	test – where significant trim and fill method used.	3) None stated
Yao and Tian (2015) (Meta-analysis)	No	1) Yes 2) Yes 3) No	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	No	1) Yes - in supplement. 2) No	Yes – in supplement.	1) Yes - Newcastle Ottawa Scale 2) Yes - in supplement.	Yes	Random or fixed effects models (RRs and 95% CI). Heterogeneity: I^2.	1) Yes 2) Egger's and Begg's method and visual inspection of funnel plots.	1) Yes 2) No 3) Not stated.
Barnard et al. (2014) (Narrative systematic review)	Yes	1) Yes 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes	No	1) Yes 2) No	Yes	1) Yes 2) No	N/A	Narrative systematic review- data not combined. Heterogeneity not assessed.	1) No 2) N/A	1) Yes 2) Yes - authors affiliated with the Physicians Committee for Responsible

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
			5) Yes 6) Yes								Medicine. 3) Not stated.
Chowdhury et al. (2014) (Systematic review and meta-analysis)	Yes	1) No 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	No	1) Yes 2) No	Yes	1) Yes 2) Yes	Yes	Random-effects model and parallel analysis - fixed effects models (RR). Heterogeneity: Within studies - X^2 and I^2 statistic; between studies – meta-regression.	1) Yes 2) Funnel plots and Egger tests	1) Yes 2) Yes 3) British Heart Foundation, MRC, Cambridge National Institute for Health Research Biomedical Research Centre, Gates Cambridge.
Farvid et al. (2014) (Systematic review and meta-analysis)	No	1) Yes 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Fixed-effects models (RR). Random-effects models: sensitivity analysis. Heterogeneity: I^2 statistic, stratified analysis and meta-regression.	1) Yes 2) Visual inspection of funnel plot; Begg's test.	1) Yes 2) Yes 3) National Institute of Health grant.
Schwab et al. (2014) (Systematic narrative review)	Yes	1) Yes 2) Not reported 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes - in Appendix 1. 5) Yes - in Appendix 1. 6) Yes	No	1) Yes - in appendix 3. 2) Yes - in appendix 2.	Yes - In appendix 3	1) Yes 2) Yes in appendix 3-6.	Yes	N/A – narrative review.	1) No 2) N/A	1) Yes 2) No 3) Yes- Nordic Council on Ministers.

Study	**Was an 'a priori' design provided?**	**Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?**	**Was a comprehensive literature search performed?** **1) ≥2 electronic databases searched** **Reported:** **2) Search period** **3) Databases searched** **4) Key words / MESH terms** **5) Search strategy** **6) Reference lists searched**	**Was the status of publication (i.e. grey literature) used as an inclusion criterion?**	**Was a list of 1) included studies and 2) excluded studies provided?**	**Were the characteristics of the included studies provided?**	**Was the scientific quality of the included studies 1) assessed and 2) documented?**	**Was the scientific quality of the included studies used appropriately in formulating conclusions?**	**Were the methods used to combine the findings of studies appropriate?**	**1) Was the likelihood of publication bias assessed? 2) how was it assessed?**	**1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?**
Makarem et al. (2013) (Systematic review)	No	1) No 2) No 3) N/A	No 1) No 2) Yes 3) Yes 4) Yes 5) Yes 6) yes	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Narrative review.	1) No 2) No	1) Yes 2) No 3) American Cancer Society; The National cancer Institute.
Ramsden et al. (2013) (Meta-analysis) (information provided in the supplementary material and Ramsden et al., 2010[1])	Yes	1) No 2) No 3) can't answer	Yes 1) Yes 2) No 3) Yes 4) Yes 5) No 6) Yes	No	1) Yes 2) No	Yes - *limited data provided in the supplementary material; more comprehensive data available in Ramsden 2010.*	1) No 2) N/A	N/A	Fixed effects meta-analysis performed for linoleic acid-selective and mixed n-3/n-6 PUFA intervention datasets for CHD death, CVD death and total deaths. Heterogeneity: Q-statistic to determine whether effects of linoleic acid-selective and mixed n-3/n-6 PUFA intervention datasets should be evaluated separately.	1)Yes 1) Funnel plot	1) Yes 2) No 2) Life Insurance Medical Research Fund of Australia and New Zealand and Intramural Program of the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health.
Alhazmi et al.	Yes	1) Yes	Yes	Yes	1) Yes	Yes	1) Yes - JBI	Yes	RRs (95% CI)	1) Yes	1) Yes

[1] Ramsden CE, Hibbeln JR, Majchrzak SF, Davis JM (2010) n-6 fatty acid-specific and mixed polyunsaturated dietary interventions have different effects on CHD risk: a meta-analysis of randomised controlled trials. *Br J Nutr* 104; 1586-600.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) >2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
(2012) (Systematic review with meta-analysis)		2) Yes 3) Yes	1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes		2) No		checklist 2) Yes		comparing type 2 diabetes risk between highest and lowest quintiles of macronutrient intake. Random effects meta-analysis, (within- and between- study variations taken into account). Subgroup analysis conducted by length of follow-up, gender and follow-up or baseline only FFQ. Heterogeneity (between studies): I^2 statistic.	2) Visual inspection of funnel plots and Egger's test	2) No 3) One author has a scholarship from the government of Saudi Arabia.
Fogelholm et al. (2012) (Systematic narrative review)	No	1) Yes 2) Yes 3) No	Yes 1) Yes 2) Yes 3)Yes 4) Yes – in Appendix 1 5) Yes 6)No	No	1) Yes 2) Yes – in Appendix 2	Yes	1) Yes 2) Yes – in Appendices	Yes	N/A – narrative review	1) No 2) N/A	1) None declared 2) N/A 3) Nordic Council of Ministers
Liu et al. (2011)	No	1) No 2) Yes 3) Yes	Yes 1) Yes	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Random effects model: RR (95% CI). Heterogeneity: Q-	1) Yes 2) Inspection	1) Yes 2) No 3) Not stated.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) >2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
(Meta-analysis)			2) Yes 3) Yes 4) Yes 5) No 6) Yes						test and I^2 statistic.	of funnel plots, Begger rank correlation and Egger weighted regression model.	
Turner (2011) (Meta-analysis)	No	1) No 2) No 3) N/A	Yes 1) Yes 2) Yes 3) Yes 4) No 5) No 6) Yes	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Random effects meta-analysis. Heterogeneity assessment not reported.	1) No 2) N/A	1) No 2) N/A 3) None stated.
Lee et al. (2010) (Narrative systematic review)	No	1) Yes 2) Did not report. 3) Did not report.	No 1) Yes 2) Yes 3) Yes 4) Yes 5) No 6) No	No	1) Yes 2) No	Yes	1) Yes 2) No	N/A	N/a - narrative review.	1) No 2) N/A	1) Yes 2) No 3) Health Promotion Fund and Clinical Research Centre for Dementia; both Ministry for Health, Welfare and Family Affairs, Republic of Korea.
Micha and Mozaffarian (2010)	No	1) Yes 2) Yes 3) Yes	No 1) No 2) Yes	No	1) No 2) No	No	1) No 2) N/A	N/A	N/A – narrative review.	1) No 2) N/A	1) Yes 2) Yes 3) Searle Funds, Bill and Melinda Gates

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
(Systematic review)			3) Yes 4) Yes 5) No 6) Yes								Foundation/ World Health Organisation Global Burden of Diseases, Injuries and Risk Factors Study.
Mozaffarian et al. (2010) (Systematic review and meta-analysis)	Yes - *protocol in supplementary material*	1) Yes 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	Yes	1) Yes 2) Yes	Yes	1) Yes 2) Yes	Yes	Pooled effect calculated using random effects meta-analysis. Heterogeneity (between studies):Q-statistic, I^2 statistic, and meta-regression.	1) Yes 2) Visual inspection of funnel plot and Begg's test.	1) Yes 2) Yes 3) National Heart, Lung and Blood Institute, National Institute of Health and Searle Funds at the Chicago Community Trust.
Siri-Tarino et al. (2010) (Meta-analysis)	Can't answer	1) Yes 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) No 6) Yes	No	1) Yes 2) No	Yes	1) Yes 2) Yes - in supplement.	Yes	RR (95% CI) log transformed to derive corresponding SEs for β-coefficients using Greenland's formula. Otherwise used p-values to drive SE where possible. Random effects meta-analysis: pooled RR.	1) Yes 2) Funnel plots	1) Yes 2) Yes – *one author supported by postdoctoral fellowship from Uniliver Corporate Research* 3) National Dairy Council; grant from National Centre for Research Resources.
Jakobsen et al. (2009)	Can't answer	1) No 2) No 3) No	No 1) No	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Study-specific logs of hazard ratios weighted by inverse	1) No 2) N/A	1) Yes 2) No 3) National Heart,

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
(Pooled analysis)			2) No 3) No 4) No 5) No 6) No						of variances and pooled estimate of hazard ratios computed using random-effects model. Heterogeneity (between-studies): Q statistic.		Lung and Blood Institute, National Institute of Health and the Danish Heart Foundation.
Mente et al. (2009) (Systematic review)	Can't answer	1) Yes 2) Can't answer 3) Yes	No 1) No 2) Yes 3) Yes 4) No 5) No 6) Yes	No	1) No 2) No	Yes - in supplement.	1) Yes 2) Yes	No	Bradford Hill criteria used to evaluate evidence of causal relationship between dietary exposures and CHD. Heterogeneity (between studies): Q statistic. Random effects-effects model: summary statistics.	1) No 2) N/A	1) Yes 2) No 3) None
Skeaff and Miller (2009) (Meta-analysis)	Can't answer	1) No 2) No 3) No	Can't answer 1) Yes 2) No 3) Yes 4) No 5) No 6) Yes	No	1) No 2) No	Yes	1) No 2) N/A	N/A	Random effects meta-analysis: summary estimates of CHD RR high vs low exposure to dietary fat or fat classes. Heterogeneity: I^2 statistic.	1) Yes 2) Funnel plots	1) Yes 2) Yes - Dr Skeaff has conducted clinical research trials funded through the University of Unilever and Fonterra. 3) Not stated.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
Van Horn et al. (2008) (Systematic narrative review)	No	1) No 2) No 3) No	Yes 1) Yes 2) Yes 3) Yes 4) No 5) No 6) Yes	No	1) Yes 2) No	Yes	1) Yes 2) Yes	Yes	N/A – narrative review.	1) No 2) N/A	1) No 2) Can't answer 3) Can't answer
Patterson et al. (2007) (Narrative systematic review)	No	1) Yes 2) Yes 3) Yes	No 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes (in appendix) 6) Yes	No	1) No 2) No	No	1) Yes 2) No	N/A	Narrative review: Risk factors and RR. Heterogeneity not assessed.	1) No 2) N/A	1) Yes 2) Yes (Authors received support from Pfizer, Lundbeck, Novartis, Voyage Pharmaceuticals, Neurochem, Myriad) 3) Institute of Advanced studies, Uni of Bologna, CIHR.
Dennis et al. (2004) (Meta-analysis)	No	1) No 2) No 3)N/A	No 1) No 2) Yes 3) Yes 4) Yes 5) No 6) Yes	No	1) Yes 2) No	Yes- in online supplement	1) No 2) N/A	N/A	RR examined, selecting those with the greatest number of potential confounders. Pooled estimates of risk from random effects obtained. Heterogeneity: Cochran's X^2 and I^2	1) No 2) N/A	1) No 2) N/A 3) National Cancer Institute grant.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
									statistic.		
Boyd et al. (2003) (Meta-analysis)	No	1) No 2) No 3) N/A	Yes 1) Yes 2) Yes 3) Yes 4) No 5) No 6) Yes	No	1) Yes 2) No	Yes	1) Yes 2)Yes	Yes	Random effects model of DerSimonian and Laird. Also employed subgroup and regression analysis.	1) No 2) N/A	1) No 2) N/A 3) University of Toronto.
Mensink et al. (2003) (Meta-analysis)	No	1) No 2) No 3) No	No 1) Can't answer 2) Yes 3) No 4) No 5) No 6) Yes	No	1) Yes 2) No	Yes	1) No 2) No	N/A	Estimated regression coefficients calculated.	1) No 2) N/A	1) Yes 2) No 3) Maastricht University, Wageningen University and Wageningen Centre for Food Sciences.
Smith-Warner et al. (2002) (Pooled analysis)	No	1) No 2) No 3) N/A	No 1) No 2) No 3) No 4) No 5) No 6) No	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Cox proportional hazards model: RRs (adjusted for smoking history, education, BMI, alcohol consumption, fruit and vegetable consumption, E intake). Two sided 95% CIs calculated. Random effects model: pooled RR. Heterogeneity	1) No 2) N/A	1) No 2) No 3) Supported by Grants NIH CA55075 and CA78548. Article considered an advertisement as defrayed in part by payment of page charges.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
									(between studies): asymptotic DerSimonian and Laird Q statistics.		
Smith-Warner et al. (2001) (Pooled analysis)	No	1) No 2) No 3) N/A	No 1) No 2) No 3) No 4) No 5) No 6) No	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Analysed primary data using a standardized approach. Holding total energy intake constant, RR calculated for increments of 5% of energy for each type of fat compared with an equivalent amount of energy from carbohydrates or other types of fat. Random effects model: study-specific RR combined. Heterogeneity (between studies): asymptotic DerSimonian and Laird Q Statistic.	1) No 2) N/A	1) No 2) N/A 3) National Institutes of health, Cancer Research foundation of America/America Society of Preventive Oncology, American Cancer Society.
Ernst (1999) (Narrative systematic	No	1) No 2) No 3) No	Yes 1) Yes 2) Yes	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	N/A - narrative review.	1) No 2) N/A	1) No 2) N/A. 3) Not reported.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
review)			3) Yes 4) No 5) No 6) Yes								
Yu-Poth et al. (1999) (Meta-analysis)	No	1) No 2) No 3) No	No 1) No 2) Yes 3) Yes 4) No 5) No 6) Yes	No	1) Yes 2) No	Yes	1) No 2) No	N/A	Analysis of variance compared effects of Step I with Step II dietary interventions. Changes in plasma TC, LDL-C, HDL-C and TAG in response to ΔSFA evaluated by regression analysis.	1) No 2) N/A	1) No 2) No 3) Not reported.
Tang et al. (1998) (Systematic review)	No	1) No 2) Yes 3) Yes	Yes 1) Yes 2) Yes 3) Yes 4) No 5) No 6) Yes	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Percentage reduction in cholesterol concentrations in each trial calculated and compared. SE of difference for each comparison calculated. Same methods applied to changes in dietary intakes. Heterogeneity: comparing observed results in different categories of trials grouped according	1) No – although it is considered. 2) The authors comment on it in the discussion.	1) Yes 2) No 3) Department of Health and Medical Research Council.

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
									to type of diet, intensity of advice, and type of patients.		
Brunner et al. (1997) (Meta-analysis)	No	1) One author screened abstracts, four authors screened full publications. 2) No 3) No	No 1) No 2) Yes 3) No 4) No 5) No 6) No	No	1) Yes 2) No	Yes	1) No 2) N/A	N/A	Intervention effects: mean changes intervention and control (and SE). Most and least intensive interventions compared where >3 randomised groups. Random effects meta-analysis: weighted by inverse of sum of between-studies variance and study intervention effect. Heterogeneity - Q statistic.	1) Yes 2) Funnel plots (data not shown).	2) No 3) Health Education Authority and North Thames Regional Health Authority.
Clarke et al. (1997) (Meta-analysis)	No	1) No 2) No 3) N/A	No 1) No 2) No 3) Yes 4) No 5) Available on request. 6) Yes	No	1) No 2) No	No	1) No 2) N/A	N/A	Multilevel regression analyses (age, weight and nutrient dietary intake, 1 unique term/study to ensure people within one study were compared directly only with each other).	1) No 2) N/A	1) Yes 2) No 3) British Heart Foundation and Medical Research Council

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
									Assessed sources of variability: within group, between experiments; within study, between matched groups; within study, between unmatched groups; between studies.		
Howell et al. (1997) (Meta-analysis)	No	1) No 2) No 3) No	Yes 1) Yes 2) Yes 3) Yes 4) Yes 5) Yes 6) Yes	No	1) No 2) No	Yes	1) Yes 2) Yes	Yes	Dietary change variables: difference final and initial dietary TC and TF, PUFA, MUFA, SFA (% of energy). Bivariate Pearson correlations - between dietary variables and between dietary variables and response variables. Stepwise-multiple-regression: linear prediction equations for each response measures, evaluating combined and independent contributions of specified dietary variables.	1) No 2) N/A	1) No 2) N/A 3) Yes- American Egg Board and Agricultural Experiment station (University of Arizona).

Study	Was an 'a priori' design provided?	Was there 1) duplicate study selection 2) duplicate data extraction? 3) was a consensus procedure for disagreement in place?	Was a comprehensive literature search performed? 1) ≥2 electronic databases searched Reported: 2) Search period 3) Databases searched 4) Key words / MESH terms 5) Search strategy 6) Reference lists searched	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Was a list of 1) included studies and 2) excluded studies provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies 1) assessed and 2) documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	1) Was the likelihood of publication bias assessed? 2) how was it assessed?	1) Was the conflict of interest included? 2) Was there a conflict or potential conflict of interest? 3) Funding source?
									Modified linear predication model into a nonlinear, used for effects of dietary manipulation. Heterogeneity testing not reported.		

ANNEX 5: Summary table of the evidence on the relationship between dietary saturated fats and health outcomes, intermediate markers and risk factors.

Outcome	Saturated fats intake		Saturated fats substitution with PUFA		Saturated fats substitution with MUFA		Saturated fats substitution with carbohydrate		Saturated fats substitution with protein	
	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence
Cardiovascular diseases (RCTs)										
CVD mortality	-	Adequate	-	Adequate	n/a	Insufficient	-	Limited	-	Limited
CVD events	↓	Adequate	↓	Adequate	n/a	Insufficient	-	Limited	-	Limited
CHD mortality	-	Adequate	-	Adequate	n/a	Insufficient	-	Limited	-	Limited
CHD events	↓	Moderate	↓	Limited	n/a	Insufficient	-	Moderate	-	Limited
Strokes	-	Adequate	n/a	Insufficient	n/a	No evidence	-	Limited	-	Limited
Peripheral vascular disease	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Cardiovascular diseases (PCS)										
CVD mortality	-	Adequate	↓	Limited	n/a	No evidence	n/a	Insufficient	n/a	No evidence
CVD events	n/a	Insufficient	n/a	No evidence	n/a	No evidence	n/a	Insufficient	n/a	No evidence
CHD mortality	↓	Moderate	↓	Adequate	-	Limited	-	Adequate	n/a	No evidence
CHD events	↓	Moderate	↓	Adequate	↑	Limited	↑	Adequate	n/a	No evidence
Strokes	-	Adequate	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Peripheral vascular disease	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Blood lipids (RCTs)										
Serum total cholesterol	↓	Adequate	↓	Adequate	↓	Adequate	↓	Adequate	n/a	No evidence
Serum LDL cholesterol	↓	Adequate	↓	Adequate	↓	Adequate	↓	Adequate	n/a	No evidence
Serum HDL cholesterol	↓	Adequate	↓	Moderate	↓	Moderate	↓	Moderate	n/a	No evidence
Serum total:HDL cholesterol	n/a	No evidence	↓	Moderate	↓	Moderate	-	Adequate	n/a	No evidence
Serum lipid triacylglycerol	↓	Adequate	-	Moderate	-	Moderate	n/a	Inconsistent	n/a	No evidence
Blood lipids (PCS)										
Serum total cholesterol	n/a	Insufficient	n/a	Insufficient	n/a	Insufficient	n/a	Insufficient	n/a	No evidence
Serum LDL cholesterol	n/a	Insufficient	n/a	Insufficient	n/a	Insufficient	n/a	Insufficient	n/a	No evidence
Serum HDL cholesterol	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Serum total:HDL cholesterol	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Serum lipid triacylglycerol	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence

Outcome	Saturated fats intake		Saturated fats substitution with PUFA		Saturated fats substitution with MUFA		Saturated fats substitution with carbohydrate		Saturated fats substitution with protein	
	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence
Blood pressure (RCTs)										
Blood pressure	-	Limited	-	Limited	-	Limited	-	Limited	n/a	No evidence
Blood pressure (PCS)										
Blood pressure	n/a	No evidence	n/a	No evidence	n/a	Insufficient	n/a	No evidence	n/a	No evidence
Type 2 diabetes and markers of glycaemic control (RCTs)										
Type 2 Diabetes	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	Insufficient	n/a	No evidence
Fasting glucose	n/a	No evidence	↓	Adequate	-	Adequate	-	Adequate	n/a	No evidence
Fasting insulin	n/a	No evidence	-	Adequate	↑	Adequate	↑	Adequate	n/a	No evidence
HbA1c	n/a	No evidence	↓	Adequate	↓	Adequate	-	Adequate	n/a	No evidence
Glucose tolerance	n/a	Insufficient	-	Adequate	-	Adequate	-	Adequate	n/a	No evidence
Insulin resistance HOMA	n/a	No evidence	↓	Adequate	↓	Adequate	-	Adequate	n/a	No evidence
Insulin resistance by infusion	n/a	No evidence	-	Adequate	-	Adequate	-	Adequate	n/a	No evidence
Type 2 diabetes and markers of glycaemic control (PCS)										
Type 2 Diabetes	-	Adequate	n/a	Insufficient	n/a	No evidence	n/a	No evidence	n/a	No evidence
Fasting glucose	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Fasting insulin	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
HbA1c	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Glucose tolerance	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Insulin resistance HOMA	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Insulin resistance by infusion	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Weight change (RCTs)										
Anthropometric measurements	↓	Limited	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Gestational weight gain	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Weight change (PCS)										
Anthropometric measurements	n/a	Insufficient	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Gestational weight gain	n/a	Insufficient	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence

Outcome	Saturated fats intake		Saturated fats substitution with PUFA		Saturated fats substitution with MUFA		Saturated fats substitution with carbohydrate		Saturated fats substitution with protein	
	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence	Direction of effect/ association	Strength of evidence
Cancers (RCTs)										
Colorectal cancer	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Pancreatic cancer	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Lung cancer	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Breast cancer	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Prostate cancer	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Cancers (PCS)										
Colorectal cancer	-	Adequate	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Pancreatic cancer	-	Adequate	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Lung cancer	-	Adequate	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Breast cancer	-	Adequate	-	Adequate	-	Adequate	-	Adequate	n/a	No evidence
Prostate cancer	-	Adequate	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Dementias and cognitive function (RCTs)										
Cognitive decline	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Mild cognitive impairment	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Alzheimer's disease	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Dementias	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Demetias and cognitive function (PCS)										
Cognitive decline	n/a	Inconsistent	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Mild cognitive impairment	-	Limited	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Alzheimer's disease	n/a	Inconsistent	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence
Dementias	n/a	Insuffcient	n/a	No evidence	n/a	No evidence	n/a	No evidence	n/a	No evidence

n/a- not enough evidence to draw conclusions

Direction of effect for reported outcomes: ↑increased; ↓decreased; - no effect/association