

Table. PUFAs and CHD/CVD: Design Type 2 Studies

Author/ Year	De- sign Type	Class	Quality (+,-,Ø)	Purpose/ Population Sample Size	Regimen	Primary Outcome Measures Results	Author's Conclusions/ <i>Reviewer's Comments (Italicized)</i>
Laaksonen et al., 2005	Cohort	B	+	<p>Purpose: To assess assoc of dietary linoleic acid and PUFA intake with cardiovascular and overall mortality in pop-based cohort</p> <p>Sample: 1551 middle-aged men</p> <p>Inclusions: Participant in Kuopio Ischaemic Heart Disease Risk Factor study; resident of eastern Finland; 42, 48, 52 or 54 y old at baseline (bet 1984 and 1989)</p> <p>Exclusions: HX of CVD, cancer or diabetes at baseline; missing data for dietary or serum FA</p>	<p>Run-in Period: None</p> <p>TX/Duration: Blood sample collected at baseline</p> <p>Medical and family HX, socioeconomic status, lifestyle factors and BP assessed and wt measured</p> <p>Deaths ascertained by computer linkage to national death registry (death bet March 1984 and December 2001 included)</p> <p>Dietary Intake Assessment/Frequency: 4-d food record at baseline</p> <p>Follow-up: 15 y</p>	<p>Outcome Measures: Cardiovascular and overall mortality Dietary fat composition Serum FA composition</p> <p>Results: 78 men died of CVD and 225 of any cause during 22,645 person-y</p> <p>Men with lower dietary intake of linoleic ($P<0.05$), ALA ($P<0.05$) and PUFA ($P<0.01$, $P<0.05$) had higher cardiovascular and overall mortality, respectively, after adjustment for age and y of examination</p> <p>Proportions of esterified linoleic ($P<0.01$, $P<0.001$) and ALA (NS, $P<0.001$) and total PUFA ($P<0.001$) and proportions of nonesterified linoleic acid ($P<0.05$, $P<0.001$) inversely assoc with death from CVD or any cause, respectively</p> <p>Intake of total fat SFA, MUFA and chol not assoc with CVD</p> <p>Men with dietary linoleic acid in upper 3rd up to 61% less likely</p>	<p>Author's Conclusions: "We found strong inverse associations of dietary and serum linoleic acid and PUFA, but no association of dietary total fat intake, with CVD mortality. Dietary fat quality thus seems more important than fat quantity in the reduction of CVD mortality in middle-aged men. Carrying out recommendations to replace saturated fat with polyunsaturated fat in the primary prevention of cardiovascular disease may substantially decrease CVD and to a lesser degree overall mortality"</p> <p>Reviewer's Comments: <i>None</i></p>

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						<p>to die of CVD than their counterparts whose intake in lower 3rds after adjustment for age and y of examination (RR, 0.39 [95% CI, 0.21-0.71]; <i>P</i> for trend 0.01)</p> <p>Dietary PUFA intake in upper 3rd assoc with up to 62% lower risk of CVD mortality after adjustment for age and y of examination (RR, 0.38 [95% CI, 0.20-0.70]; <i>P</i> for trend 0.01)</p> <p>Assoc of dietary P/S ratio with CVD mortality somewhat weaker or similar (upper vs lower 3rd, model 1: RR, 0.46 [95% CI, 0.25-0.83])</p> <p>Dietary linoleic acid assoc with lower overall mortality during follow-up after adjustment for age and examination y (upper vs lower 3rd, model 1: RR, 0.66 [95% CI, 0.48-0.92], <i>P</i> for trend 0.06), but NS after adjustment for lifestyle or dietary factors</p> <p>Total PUFA intake NS assoc with overall mortality</p> <p>Nonesterified linoleic acid proportions assoc with CVD</p>	

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						<p>mortality, but gradient nonlinear, with lowest risk in middle 3rd (middle vs lower 3rd, model 1: RR, 0.40 [95% CI, 0.22-0.75])</p> <p>Mortality from CVD lower for men with proportion of serum esterified linoleic acid (RR, 0.42 [95% CI, 0.21-0.80]; <i>P</i> for trend <0.01) and PUFA (RR, 0.25 [95% CI, 0.12-0.50] <i>P</i> for trend <0.001) in upper vs lower 3rd</p> <p>Esterified linoleic acid proportions assoc with lower overall mortality (upper vs lower 3rd, model 1: RR, 0.44 (95% CI, 0.30-0.67) <i>P</i> for trend <0.001)</p> <p>Inverse assoc for proportions of n-6 FA and especially PUFA even stronger and sig in all models (<i>P</i> for trend <0.001 to 0.02</p>	
Hu et al., 1997	Cohort	B	+	<p>Purpose: To examine dietary fat intake and risk of CHD in women</p> <p>Sample: 80,082 female registered nurses</p>	<p>Run-in Period: None</p> <p>TX/Duration: Completed medical HX, lifestyle questionnaire and validated FFQ at baseline (1980) and 1984, 1986</p>	<p>Outcome Measures: Nonfatal MI or fatal coronary disease</p> <p>Results: 658 incident cases of nonfatal MI and 281 deaths from CHD</p>	<p>Author's Conclusions: "In this large, prospective study of women, we found that a higher dietary intake of saturated fat and <i>trans</i> unsaturated fat</p>

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				<p>Inclusions: Participant in Nurses' Health Study; 34-59 y of age</p> <p>Exclusions: ≥10 items on FFQ blank; implausibly low or high scores for total food or energy intake [ie, <2094 kJ (500 kcal) or >14,650 kJ (3500 kcal); previously diagnosed DM, angina, MI, stroke or other CVD; high serum chol conc</p>	<p>and 1990</p> <p>Medical records of subj reviewed by study physicians when nonfatal MI</p> <p>MI confirmed using World Health Organization criteria</p> <p>Deaths identified from state vital records and National Death Index or reported by next of kin or postal system</p> <p>Dietary Intake Assessment/Frequency: 61-item FFQ (1980) and 116-item FFQ (1984, 1986 and 1990); FFQ included info on types of fat or oil used for frying, baking and at table and type of margarine used</p> <p>Follow-up: 14 y</p>	<p>In multivariate analyses, RR for 5% increment in energy from total fat and chol NS; from MUFA 0.81 (95% CI: 0.65 to 1.00; $P=0.05$); from PUFA 0.62 (95% CI: 0.46 to 0.85; $P=0.003$)</p> <p>Risk lowest with lowest intake of trans unsaturated FA and highest intake of PUFA (RR=0.31; 95% CI: 0.11 to 0.88; $P=0.01$)</p> <p>Replacing 5% energy from SFA with unsaturated FA assoc with 42% lower risk (95% CI: 23 to 56%; $P<0.001$); replacing 2% energy from trans unsaturated FA with unhydrogenated, unsaturated FA assoc with 53% lower risk (95% CI: 34 to 67%; $P<0.001$)</p> <p>Use of incr veg fat assoc with reduced CHD risk (RR=0.84 for each incr of 5% energy; 95% CI: 0.76 to 0.94; $P=0.001$); animal fat assoc NS</p>	<p>was associated with an increased risk of coronary disease, whereas a higher intake of monounsaturated and polyunsaturated fats was associated with a decreased risk. Because of the opposite effects of different fats on incidence, total fat intake was not significantly related to the risk of coronary disease"</p> <p>Reviewer's Comments: <i>Women who reported CVD or cancer on previous questionnaires excluded from subsequent follow-up; results adjusted for dietary and non-dietary factors; Linoleic acid comprised 81% of total PUFA in pop</i></p>

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Keys, 1997	Cohort	B	+	<p>Purpose: To evaluate imp of fats in diet by examining death rates and FA in diet</p> <p>Actual Sample: 12,763 men</p> <p>Inclusions: Men who completed entry examination in Seven Countries Study</p> <p>Exclusions: Not provided</p>	<p>Run-in Period: None</p> <p>TX/Duration: Cardiovascular risk factors assessed at y 0 and 10; CHD and non-CHD death rate established</p> <p>Dietary Intake During Study: Ave of 16 cohorts: Total fat (% TE): 32.4 SFA (% TE): 11.3 Chol (mg/d): not reported Calories: not reported</p> <p>Dietary Intake Assessment/Frequency: Methods not described in detail; American cohort used 24-h recall, Italian cohort used 7-d food diaries, other cohorts used 7-d food wt of sub-sample of men</p>	<p>Outcome Measures: Death rate from all-causes and CHD</p> <p>Results: Death rate from CHD closely related to dietary SFA and to SFA/unsaturated FA ratio ($r=0.82$ for both)</p> <p>Total fat NS related to CHD death, but negative PUFA/SFA ratio sig ($r=-0.54$)</p> <p>Non-CHD death NS related to any dietary variables</p> <p>Multiple regression analysis showed SFA sig for all-causes ($t=2.8$) and CHD ($t=5.8$) deaths. MUFA ($t=1.9$) and PUFA ($t=1.8$) negatively related to all-cause deaths. When all FA considered together with all-cause death rate, $r=0.72$</p> <p>Correlation bet cohort means for BP and TC sig ($r=0.69$)</p>	<p>Author's Conclusions: "The present data are consistent with the hypothesis that saturated fats in the diet not only promote an increase in the cholesterol in the serum...but also increase the probability of early death"</p> <p>Reviewer's Comments: Diet assessment of sub-sample only and with inconsistent methods; lifestyle not discussed; stat analyses not complete</p>
Ascherio et al., 1996	Cohort	B	+	<p>Purpose: To examine assoc bet fat intake and incidence of CHD in U.S. men of middle-</p>	<p>Run-in Period: None</p> <p>TX/Duration: Dietary and medical HX</p>	<p>Outcome Measures: Incidence of acute MI or coronary death</p> <p>Results:</p>	<p>Author's Conclusions: "In this large prospective study, we found strong and</p>

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				<p>age and older</p> <p>Sample: 43,757 male health professionals</p> <p>Inclusions: Participant in Health Professionals Follow-up study; daily energy intake bet 3.34 and 17.56 MJ</p> <p>Exclusions: HX of CVD or diabetes at baseline; >70 blanks on FFQ</p>	<p>questionnaires completed in 1986 and every 2 y through January 1992</p> <p>Medical records of subj reporting MI reviewed</p> <p>Dietary Intake Assessment/Frequency: 131 item FFQ completed at baseline and in 1988, 1990 and 1992</p> <p>Follow-up: 6 y</p>	<p>734 coronary events (505 nonfatal MI and 229 deaths) during 236,782 person-y of follow-up</p> <p>For men in top vs lowest 5th of SFA intake (median, 14.8% vs 5.7% TE), multivariate RR for MI 1.22 (95% CI, 0.96 to 1.56; <i>P</i>=0.14) and for fatal CHD 2.21 (95% CI, 1.38 to 3.54; <i>P</i>=0.0016); after adjustment for fiber intake, RR 0.96 (0.73 to 1.27; <i>P</i>=0.68) and 1.72 (1.01 to 2.90; <i>P</i>=0.09), respectively</p> <p>Intakes of linoleic and linolenic acids NS assoc with risk of MI</p> <p>Inverse assoc bet linoleic acid and fatal coronary disease after adjustment for total fat intake (RR 0.68, 0.34 to 0.99; <i>P</i><0.05)</p> <p>Linolenic acid inversely assoc with risk of coronary disease; RR for 1% incr in linolenic acid intake 0.53 (0.30 to 0.95; <i>P</i><0.05) after adjustment for risk factors</p> <p>In regression models, corrected RR of MI 0.54 (0.26 to 1.14) for 5% incr in SFA intake, 0.91</p>	<p>highly significant age adjusted associations between intakes of saturated fat, cholesterol, and <i>trans</i> fatty acids with risk of coronary disease.... We also found an independent inverse relation between intake of linolenic acid and risk of coronary disease....In our study, the proportion of energy intake contributed by linoleic acid was not significantly associated with risk of coronary heart disease. A significant inverse association with fatal coronary disease, however, became apparent after adjustment for total fat intake. This result and the inverse association with the polyunsaturated fat to saturated fat ratio, is consistent with a benefit of replacing saturated fat with</p>

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						(0.66 to 1.27) for 100 mg/4 MJ incr in chol intake and 0.80 (0.31 to 2.03) for 5% incr in PUFA intake	polyunsaturated fat" Reviewer's Comments: <i>None</i>
Kromhout et al., 1995	Cohort	B	Ø	<p>Purpose: To study assoc bet ave intake of individual fatty acids and dietary chol in 16 cohorts in relation to ave serum chol and 25-y ave pop mortality rates from CHD</p> <p>Sample: 12,763 middle-aged men; 16 cohorts</p> <p>Inclusions: Participant in Seven Countries Study (resident of Finland, Italy, Greece, Croatia, Japan, USA, Netherlands); 40-59 y of age</p> <p>Exclusions: Not provided</p>	<p>Run-in Period: NA</p> <p>TX/Duration: 25-y follow-up</p> <p>Dietary Intake Assessment/Frequency: Dietary survey (weighed record method) completed at baseline (bet 1959 and 1964 for 14 cohorts and in 1970 for 2 cohorts)</p> <p>Study Visits/ Measurements: Serum chol determined at baseline</p> <p>Vital status follow-up every 5 y</p> <p>Chemical analyses of food 25 y from baseline</p>	<p>Outcome Measures: Mortality rates from CHD</p> <p>Results: Ave intake of oleic and linoleic acids and sum of EPA and DHA not assoc with 25 y mortality rates from CHD</p> <p>In multivariate model, SFA major determinant of diff in CHD mortality rates and explained 73% of total variance</p>	<p>Author's Conclusions: "...the results of these cross cultural analyses suggest that dietary saturated and <i>trans</i> fatty acids and dietary cholesterol are important determinants of differences in population rates of coronary heart disease death"</p> <p>Reviewer's Comments: <i>None</i></p>
Posner et al., 1991	Cohort	B	Ø	<p>Purpose: To examine</p>	<p>Run-in Period: None</p>	<p>Outcome Measures: Incidence of CHD</p>	<p>Author's Conclusions:</p>

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				<p>relationship bet dietary lipids and 16-y incidence of CHD morbidity and mortality</p> <p>Sample: 2 cohorts – 420 men 45-55 y of age; 393 men 56-65 y of age</p> <p>Inclusions: Participant in Framingham Study; male; 45-65 y of age</p> <p>Exclusions: Not provided</p>	<p>TX/Duration: Assessed dietary intake</p> <p>Panel of 3 investigators reviewed health info to determine development of CHD</p> <p>Dietary Intake Assessment/Frequency: Single 24 h recall at initiation of follow-up visit</p> <p>Study Visits/ Measurements: Serum TC, systolic BP, glucose intolerance, left ventricular hypertrophy and wt measured at time of 10th and 11th examinations</p> <p>Follow-up: 16 y</p>	<p>Dietary lipid intake</p> <p>Results: 99 men in younger cohort and 114 in older cohort developed CHD during 16 y follow-up</p> <p>Mean proportion of energy intake from total fat 39.7% in younger group and 38.3% in older group ($P<0.05$)</p> <p>Both groups consumed 15% SFA energy intake, 5% PUFA energy intake, 16% MUFA energy intake and about 530 mg dietary chol</p> <p>Sig positive assoc bet CHD and proportion of energy intake from total dietary fat ($P=0.16$) and MUFA ($P=0.21$) in younger cohort</p> <p>SFA marginally sig positive assoc with CHD incidence ($P=0.85$ and 0.50 for g intake and percentage of energy intake, respectively)</p> <p>None of dietary lipid variables assoc with CHD incidence in men ≥ 56 y; β coefficients approached 0 for all nutrients</p>	<p>"The present study demonstrated statistically significant associations between dietary total fat and monounsaturated fatty acid intakes and CHD morbidity and mortality during 16 years in men aged 45 to 55 years....We were unable to detect an independent effect of polyunsaturated fat and cholesterol intakes on CHD incidence in our samples of Framingham men"</p> <p>Reviewer's Comments: <i>None</i></p>

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						<p>except energy intake ($P=0.67$)</p> <p>Persons who consumed 30% energy as fat (vs samples mean intake of 39.7%) 29% lower risk of CHD (RR 0.71; 95% CI, 0.56-0.90) in younger group</p> <p>In younger group, RR assoc with MUFA intake of 10% of total energy intake (0.64; 95% CI, 0.48-0.87), compared with mean level of 16.2%</p> <p>RR for CHD assoc with higher PUFA intake NS higher (95% CI, 0.95-1.90) in younger group</p>	
Shekelle et al., 1981	Cohort	B	+/Ø	<p>Purpose: To investigate assoc of dietary SFA, PUFA and chol with serum chol level and risk of death from CHD</p> <p>Sample: 1900 middle-aged men</p> <p>Inclusions: Participant in Western Electric Study; male 40-55 y of age; employed ≥ 2 y at</p>	<p>Run-in Period: NA</p> <p>TX/Duration: 20-y follow-up</p> <p>Dietary Intake Assessment/Frequency: Obtained at baseline and 1 y examinations by standardized interviews and questionnaires</p> <p>Keys and Hegsted diet scores calculated</p>	<p>Outcome Measures: Serum chol Dietary intake of SFA, PUFA and chol Risk of death from CHD</p> <p>Results: Serum chol conc varied positively with dietary SFA and chol; tended to vary inversely with PUFA</p> <p>Coefficient for change in intake of PUFA negative in sign but NS</p>	<p>Author's Conclusions: "...the present observations support the conclusion that the lipid composition of the diet affects the level of serum cholesterol and the long-term risk of death from CHD in middle-aged American men"</p> <p>Reviewer's Comments: <i>None</i></p>

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				<p>Western Electric Company's Hawthorne Works in Chicago area</p> <p>Exclusions: Evidence of CHD at 1st examination; missing data from initial or follow-up exam for diet, ht, wt or serum chol; absence from 2nd examination because of death; leaving company's employment or transfer to another plant</p>	<p>Study Visits/ Measurements: Vital status at 20 y ascertained</p> <p>Study Visits/ Measurements: Serum chol and wt measured</p>	<p>Risk of death from CHD inversely related to intake of PUFA (logistic regression coefficient, -0.258; $P=0.010$) and positively related to intake of chol (0.003; $P=0.008$)</p>	

APPENDIXM2PUFAType2Table