Table. PUFAs and CHD/CVD: Design Type 3 Studies

Author/ Year	De-sign Type	Class	Quality (+,-,Ø)	Purpose/ Population Sample Size	Regimen	Primary Outcome Measures Results	Author's Conclusions/ *Reviewer's Comments (Italicized)*
Kark et al., 2003	**Case-CNTL**	**C**	**+**	**Purpose:** To assess assoc bet adipose tissue n-6 FA and acute MI **Sample:** Jewish pop in Jerusalem 180 cases; 25-64 y of age with acute MI 492 CNTL subj; 25-64 y of age with no IHD **Inclusions:** Jerusalem residents hospitalized with first acute MI **Exclusions:** Prior diagnosis of IHD; institutionalized; within 6 mo of termination of pregnancy	**TX/Duration:** FFQ administered Subcutaneous gluteal tissue biopsy measured adipose tissue FA **Dietary Intake During Study:** Reported for CNTL group only Total fat (% TE): 36.6 PUFA (% TE): 10.1±3.2 SFA (% TE) 11.1 **Dietary Intake Assessment/Frequency:** FFQ by trained interviewers; 145-item FFQ tailored to Israeli foods; used photographed food models; adipose tissue FA measurement	**Outcome Measures:** Adipose tissue composition **Results:** Correlation of dietary PUFA with adipose tissue linoleic acid (r=0.43, P<0.001); weaker assoc with ALA (r=0.16, P=0.001); NS assoc with arachidonic acid; and inverse assoc with adipose tissue oleic acid (r=-0.18, P<0.001) and palmitoleic acid (r=-0.16, P<0.001) Dietary SFA inversely assoc with adipose tissue linoleic acid (r=-0.38, P<0.001) and ALA (r=-0.16, P=0.005) Dietary MUFA not assoc with adipose tissue n-6 FA NS assoc of linoleic acid, γ-linolenic acid or ALA with acute MI; arachidonic acid sig positive assoc with acute MI (P=0.025); inverse assoc of acute MI with stearic acid (P=0.054) and oleic acid (P=0.097) Ratio of n-3 to n-6 FA assoc with acute MI NS	**Author's Conclusions:** "A very high linoleic acid intake does not appear to confer increased risk of nonfatal AMI. Nonetheless, the increased risk associated with arachidonic acid, a finding that requires confirmation, tempers an inference that diets rich in n-6 fatty acids are safe vis-à-vis coronary health" ***Reviewer's Comments:*** *Long-term dietary intake assessed via biopsy; weekly exercise energy expenditure assessed; pop-based design with good response rate*

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						Inverse assoc of adipose tissue linoleic acid with acute MI when adjusted for mystiric, palmitoleic, oleic and arachidonic acids sig only when linoleic acid continuous variable (age- and sex-adjusted *P*=0.033 and multivariate-adjusted *P*=0.026) γ-linolenic acid NS assoc with acute MI	
Tell et al., 1994	**Pop-based longi-tudinal study**	**C**	**+**	**Purpose:** To examine assoc bet dietary fat and atherosclerosis **Sample:** 13,148 men and women; age 45-64 y **Inclusions:** Middle-aged black and middle-aged white men and women from 4 U.S. communities **Exclusions:** Not provided	**TX/Duration:** FFQ administered Carotid artery intima-media wall thickness measured by ultrasound **Dietary Intake During Study:** Not reported **Dietary Intake Assessment/Frequency:** FFQ to define food intake over previous y; administered by trained interviewers; 66-item Willett et al. FFQ modified to include specific fish items	**Outcome Measures:** Carotid artery wall thickness **Results:** Incr animal fat intake sig incr wall thickness in: White women (*P*<0.0001) Black women (*P*=0.047) White men (*P*=0.009) Incr veg fat intake sig decr wall thickness in: White women (*P*=0.004) Black women (*P*=0.041) White men (*P*=0.001) NS trend of PUFA inversely related to wall thickness No trend seen for MUFA	**Author's Conclusions:** "The results are consistent across all four sex and race groups, are biologically plausible, and are consistent with metabolic and animal studies. They therefore lend support to the evidence that a diet high in saturated fat and cholesterol may contribute to atherosclerotic disease and give additional credence to current public health-oriented efforts to

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						Incr SFA intake sig incr wall thickness in white women only (*P*=0.006) Incr chol intake sig incr wall thickness in: White women (*P*<0.0001) Black women (*P*=0.004)	modify the dietary intake patterns toward a less atherogenic one" ***Reviewer's Comments:*** *FFQ administered 1x/subj; limitations of FFQ discussed; subj info not used if reported daily energy intake very high or low; stat adjusted for age, smoking, HTN; consistent FFQ findings found across 4 race/sex groups*
Artaud-Wild et al., 1993	**Pop-based des-crip-tive study**	**C**	**+**	**Purpose:** To examine relations of coronary mortality to intakes of foods and nutrients in 40 countries, focusing specifically on France and Finland **Sample:** Men and women in 40 countries **Inclusions:** All countries with pop	**Run-in Period:** None **TX/Duration:** CHD mortality data collected from World Health Organization reports for 1977 **Dietary Intake Assessment/Frequency:** Ave food disappearance data collected from Food Balance Sheets of Food and Agriculture	**Outcome Measures:** CHD mortality **Results:** Mortality from CHD in Finland 3-5x higher than in France From 1960 to 1987, mean ratio of coronary mortality/100,000 men 55 to 64 y old in Finland vs France 4.6±0.4 MUFA, PUFA and total fats negatively assoc with CHD mortality (*r*= -0.33, -0.33, -0.34,	**Author's Conclusions:** "In our study, however, the negative correlation between polyunsaturated fat and CHD mortality was significant after adjusting for cholesterol and saturated fat intakes. This observation may help account for the divergent rates of CHD mortality. There

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				>1 million for which both CHD mortality rates and food supply data could be obtained **Exclusions:** None listed	Organization of United Nations for 1977 CSI equation [(1.01 x sat fat) + (0.05 x mg chol)] used to compute lipid score **Follow-up:** Data representative of 1950s through 1980s	respectively; *P*<0.05) Consumption of liquid veg oils, rich in MUFA and PUFA, 8x greater in France	was a marked difference between the consumption of liquid vegetable oils between France and Finland" ***Reviewer's Comments:*** *None*
Joossens et al., 1989	**Pop-based des-crip-tive study**	**C**	**Ø**	**Purpose:** To assess nutrition and cardiovascular mortality in Belgian citizens **Sample:** 5,264,948 Belgian citizens; age 25-74 y **Inclusions:** Not provided **Exclusions:** Not provided	**TX/Duration:** Not specified **Dietary Intake During Study:** Total fat (% TE) North Belgium: Men: 41.6 Women: 42.7 South Belgium: Men: 42.6 Women: 43.3 SFA (% TE): not reported Chol (mg/d) North Belgium: Men: 410 Women: 330 South Belgium: Men: 460 Women: 360 Calories: not reported	**Outcome Measures:** All-cause mortality Cardiovascular mortality **Results:** All-cause mortality in subj sig incr as SFA incr (*P*<0.001); and decr as PUFA incr (*P*<0.001). Higher in southern region consistent with decr P/S ratio Total cardiovascular mortality in subj incr as SFA incr (*P*<0.001); and decr as PUFA incr (*P*<0.001 males, *P*<0.01 females). Higher in southern region consistent with decr P/S ratio	**Author's Conclusions:** "All causes, total cardiovascular… mortality are higher in the south, consistent with the regional distribution of fat intake. However, within each region there is no correlation between these mortality patterns and fat intake. This phenomenon can be explained by the presence of confounding factors: salt intake from processed foods, fish, alcohol intake and smoking habits…."

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					Dietary Intake Assessment/Frequency: Methods not reported		***Reviewer's Comments:*** *None*
Hegsted and Ausman, 1988	**Pop-based des-crip-tive study**	**C**	**-**	**Purpose:** To examine relation bet diet, alcohol and CHD in men **Sample:** Adult males from 18 countries (actual sample not reported) **Inclusions:** Not provided **Exclusions:** Not provided	**TX/Duration:** Diet and mortality data taken from Stamler study published in 1973 **Dietary Intake During Study:** Not reported **Dietary Intake Assessment/Frequency:** Methods not reported	**Outcome Measures:** CHD mortality **Results:** Correlations with CHD: Saturated fat: *r*=0.71 Polyunsaturated fat: *r*=-0.34 Correlation bet CHD and diet and alcohol, *r*=0.92	**Author's Conclusions:** "Indeed the size of the regression coefficients for saturated and polyunsaturated fats, that of saturated being about twice as large as that of polyunsaturated and opposite in sign, are similar to the metabolic effects on serum cholesterol" ***Reviewer's Comments:*** *None*
Kushi et al., 1985	**Pop-based des-crip-tive study**	**C**	**+**	**Purpose:** To examine relation bet retrospective dietary info and CHD mortality **Sample:** 1001 men; age 30-69 y	**TX/Duration:** Blood drawn for TC Diet HX collected 20 y prior **Dietary Intake Per Diet HX:** Total fat (% TE) Irish brothers: 37.6±0.31	**Outcome Measures:** TC CHD mortality **Results:** TC NS diff bet cohorts: Irish brothers: 215.9±2.21 Boston brothers: 218.5±1.95 1st generation: 215.1±2.93	**Author's Conclusions:** "Overall, these results tend to support the hypothesis that diet is related, albeit weakly, to the development of coronary heart disease"

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				Inclusions: Men of Irish descent enrolled in Ireland-Boston Diet-Heart Study: Irish brothers: brothers of Boston men; born and lived in Ireland Boston brothers: born in Ireland, lived in Boston 1st generation: born and lived in Boston; 1st generation Irish **Exclusions:** Lost to follow-up; no diet or TC info; no electrocardiogram readings; no smoking info	Boston brothers: 38.9±0.32 1st generation: 38.9±0.37 SFA (% TE) Irish brothers: 17.7±0.17 Boston brothers: 16.9±0.17 1st generation: 15.9±0.19 Chol (mg/1000 calories) Irish brothers: 233±3.6 Boston brothers: 273±3.9 1st generation: 240±5.0 Calories: Irish brothers: 4033±36 Boston brothers: 3099±38 1st generation: 2946±54 **Dietary Intake Assessment/Frequency:** Dietitian collected diet HX from each subj; info coded on food frequency forms; dietary lipid Keys scores, lipid Hegsted scores calculated	CHD mortality incr as: Chol intake incr (*P*=0.03) Hegsted dietary lipid scores incr (*P*=0.04) Keys dietary lipid scores incr (*P*=0.03) Upper 3rd with Keys dietary lipid score had sig incr risk of CHD mortality compared to lower 3rd (*RR* 1.60; 1.0-2.59) Subj whose Keys and Hegsted dietary lipid scores in middle 3rd of distribution had lowest risk of CHD death (*RR* 0.84 and 0.74, respectively) NS diff in CHD mortality bet cohorts	***Reviewer's Comments:*** *None*
Gordon et al., 1981	**Pop-based des-crip-**	**C**	**+**	**Purpose:** To assess dietary component effect on CHD in 3 pop	**TX/Duration:** 24-h diet recall **Dietary Intake Per Diet**	**Outcome Measures:** CHD CHD or MI mortality All-causes death	**Author's Conclusions:** "In all three studies there was a higher

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	tive study			**Sample:** 16,349 men; age 45-64 y **Inclusions:** Men enrolled in Framingham Study (N=859), Honolulu Heart Study (N=7272), Puerto Rico Heart Health Program (N=8218) with no CHD at start of study **Exclusions:** Not provided	**Recall:** Total fat (% TE) Framingham: 39 Honolulu: 34 Puerto Rico: 36 SFA (% TE) Framingham: 15 Honolulu: 13 Puerto Rico: 13 Chol (mg/d) Framingham: 528±279 Honolulu: 549±315 Puerto Rico: 414±314 Calories Framingham: 2643±700 Honolulu: 2286±711 Puerto Rico: 2372±851 **Dietary Intake Assessment/Frequency:** Diet recall; food models and standard serving utensils used	**Results:** NS correlation bet CHD and fat, SFA or PUFA intake in Framingham and Honolulu samples In Puerto Rico sample: PUFA intake sig incr in subj with CHD (P<0.05) and MI or CHD death (P<0.01) vs no CHD P/S ratio sig incr in subj with MI or CHD death vs subj with no CHD (P<0.05) PUFA sig incr with all-causes death vs survivors at end of follow-up (P<0.01)	P/S ratio in those men developing CHD, particularly MI or CHD death, but this was statistically significant only in the Puerto Rico study" ***Reviewer's Comments:*** *None*
Garcia-Palmieri et al., 1980	**Pop-based des-crip-tive study**	**C**	**+**	**Purpose:** To investigate relationship of diet to CHD incidence **Sample:** 8218 men (45-64 y of age) **Inclusions:**	**TX/Duration:** Diet HX **Dietary Intake Per 24-h Recall:** Total fat (% TE) Rural: 33 Urban: 32 SFA (% TE) Rural: 13	**Outcome Measures:** TC CHD MI and CHD death **Results:** % change not reported for TC; TC sig diff bet rural (195 mg/dl) and urban (205 mg/dl) pop (P<0.01); TC not sig related to	**Author's Conclusions:** "When percent calories from total fat is used, there is a small but positive association with CHD in the urban cohort, although this is primarily from high

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				Urban and rural Puerto Rican men; CHD-free at study entry **Exclusions:** Not provided	Urban: 14 Chol (mg/d) Rural: 356 Urban: 439 Calories Rural: 2345 Urban: 2384 **Dietary Intake Assessment/Frequency:** 24-h diet recall at study entry	nutrient variables PUFA sig incr in urban men with CHD vs non-CHD (P<0.01) PUFA sig incr in urban men with MI or CHD death vs non-CHD (P<0.01) SFA sig incr in rural men with MI or CHD death vs non-CHD (P<0.05)	polyunsaturated fatty acids" ***Reviewer's Comments:*** *None*
Keys et al., 1957	**Non-ran-dom-ized trial**	**C**	**Ø**	**Purpose:** To predict serum chol responses to changes in fats in diet **Sample:** 84 men (66 hospitalized U.S. men, age 32-62 y; 18 Japanese men, age 22-54 y) **Inclusions:** U.S. sample: hospitalized schizophrenic men Japanese sample: healthy men **Exclusions:** U.S. sample: ill or	**Run-in Period:** 4 wk on fixed "normal" diet **TX/Duration:** 1) "House" diet: similar to U.S. diet (37-42% calories from fat, 13-15% from PRO) 2) "Low fat base" diet: decr fat and calories Fat/oil content of each diet not specified **Dose/Form:** Subj on each diet for approx 4 wk, with 4-wk washout period on "normal" diet No supplements given	**Outcome Measures:** TC **Results:** % change not reported; *P* values not reported Change in TC compared to House diet: Low fat base diet: After 1 wk: -24.6 mg/dl After 2 wk: -37.1 mg/dl After 1 mo: -33.8 mg/dl (NS) After 2 mo: -35.9 mg/dl (NS)	**Author's Conclusions:** "The experiments reported here clearly indicate that the saturated fatty acids, at least those of chain length longer than 10 carbons, have about twice as much effect in raising the serum-cholesterol level as the cholesterol depressing effect of an equal amount of polyethenoids or linoleic acid" ***Reviewer's Comments:*** *None*

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				otherwise deviated; those whose body wt changed up to 3 kg Japanese sample: none listed	**Dietary Intake During Study:** Total fat (% TE) House: 39 Low fat: 15 SFA (% TE) House: 19.5 Low fat: 6.3 Chol (mg/d) House: 740 Low fat: 300 Calories House: 3183/d Low fat: 2311/d **Dietary Intake Assessment/Frequency:** Calorie requirements estimated by measuring food intake at constant body wt during run-in period and adjusted weekly; subj under 24-h surveillance; fixed recipes used; food servings measured; plate waste recorded		

APPENDIXN2PUFAType3Table