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Total (food and supplement) n-3 PUFA intake is associated with lower Coronary Heart Disease mortality, independently of fish intake

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Fish contains essential polyunsaturated fatty acids (n-3 PUFA) which increase n-3 PUFA concentrations in the cardiac membrane and influence cardio electrophysiology, which might have antiarrhythmic effects and so lower risk of fatal CHD.[1,2] Clinical trials of n-3 PUFA supplements conducted in high risk populations show no significant benefit,[3] results from observational studies on fish intake show heterogeneous results.[4] N-3 PUFA containing supplements, mainly cod liver oil, are widely used in the UK and by 24 % in the Norfolk-based European Prospective Investigation into Cancer (EPIC-Norfolk).[5,6] We studied the association between n-3 PUFA Total Nutrient Intake (TNI, *i.e.* intake from foods and supplements), n-3 PUFA supplement use and fatal CHD in a general population-based cohort.

EPIC-Norfolk recruited men and women, between 39–79 y (N = 25,639) between 1993–1997. Anthropometry was measured. Participants completed a 7-day diet diary, from which n-3 PUFA TNI, energy intake and disaggregated food consumption were determined. Participants were classified into three groups: non-supplement users (NSU), supplement users without n-3 PUFA supplements (SU-n3) and supplement users with n-3 PUFA supplements (SU+n3). General questionnaires ascertained social class, education, smoking, physical activity, alcohol consumption and prevalent diseases. Analyses were based on n = 22,137 with complete data. After a median follow-up of 18 years, 1393 participants died from CHD (ICD 410-414/I20-25). Cox proportional hazards regression was used to analyse differences between supplement groups as well as quintiles (Q5 *v* Q1) of TNI intake.

SU + n3 (compared to NSU) were more likely to be women, >60 years, and to be non-smokers and alcohol consumers. They reported fewer higher educational qualifications and less physical activity. SU + n3 and SU-n3 had lower self-reported history of myocardial infarction, diabetes or stroke. Differences in median (Med) n-3 sourced intake are shown in the top half of the table. SU + n3 did not have lower risk of fatal CHD; however higher n-3 PUFA intake was associated with a 22 % lower risk of fatal CHD, after adjusting for fish consumption, indicating that other sources than fish are associated with fatal CHD.

Case/N (1393/22,137)	NSU 899/13,490	SU-n3 161/3288		SU + n3 333/5359		Q1 TNI 254/4428	Q5 TNI 290/4427	
Med TNI n-3 PUFA (g/d)	0·12	0·13		0·31		0·04	0·82	
Med Food n-3 PUFA (g/d)	0·12	0·13		0·14		0·04	0·66	
Med White fish (g/d)	20	19		21		0	31	
Med Oily fish (g/d)	3	7		7		0	15	
	Ref	**HR**	**95 %CI**	**HR**	**95 %CI**	**Ref**	**HR**	**95 %CI**
1: age/sex adjusted	1·00	0·88	0·74, 1·04	*0·81*	*0·72, 0·92*	1·00	0·79	0·67, 0·94
2: adjusted for*	1·00	1·01	0·85, 1·20	0·98	0·87, 1·12	1·00	0·95	0·80, 1·13
3: adjusted for* and fish	1·00	1·01	0·85, 1·20	0·98	0·86, 1·12	1·00	*0·78*	*0·63, 0·99*

*sex, age, smoking, body mass index, alcohol, social class, education, season, physical activity, energy intake, fruit, vegetables, red meat, processed meat, white meat, prevalent diabetes/stroke/myocardial infarction.

Non-fish n-3 PUFA was negatively associated with fatal CHD. The negative confounding observed from fish might be explained by preparation methods[7] or UK dietary patterns (fish 'n chips); alternatively, contamination of fish with methylmercury might play a role.[8]

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