



Cod Liver Oil consumption assessed using repeated measures is associated with a lower risk of Coronary Heart Disease mortality in a general population-based cohort

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For older age groups, supplement use appears to have increased over time at the population level according to national survey data^(1,2). In the Norfolk-based European Prospective Investigation into Cancer (EPIC-Norfolk), a general population-based cohort, repeated measures of supplement use are available to investigate changes over time in an individual's supplement use behaviour and associate these with health outcomes. Cod liver oil (CLO) is the most commonly consumed supplement in the UK^(1,2) and can contribute 50 % to the essential polyunsaturated fatty acids (n-3 PUFA) intake⁽³⁾. N-3 PUFA intake above 250 mg/d has been associated with lower risk of CHD mortality⁽⁴⁾; an intake which was not met by fish consumption in the UK in 2000/01^(1,5), but could be met when supplement sources are included⁽³⁾. We studied associations between n-3 PUFA containing supplements (mainly CLO) and CHD mortality, using baseline only as well as repeated measures of supplements.

EPIC-Norfolk recruited men and women, aged 39–79 y (N = 25,639) between 1993–1998. Anthropometry was measured. Participants completed three questionnaires (Q1: 1993–1998; Q2: 2002–2004; Q3: 2004–2011) that assessed supplement use in the past week. Participants were grouped (for each Q) into three mutually exclusive groups: non-supplement users (NSU), supplement users with n-3 PUFA supplements [or combined with any other] (SU + n3) and supplement users without n-3 PUFA (SU-n3). Questionnaires also ascertained following characteristics: social class, education, smoking, physical activity, marital status, alcohol consumption and prevalent diseases. Multivariable Cox proportional hazards regression was used to ascertain associations between supplement use and CHD mortality (ICD 410–414/I20–25, follow-up until March 2015), from three different time origins defined by completion of the three questionnaires: Q1 (1562 CHD over median of 19 years, N = 22,035), Q2 (742 CHD over 12 years, N = 15,932) and Q3 (241 over 6 years, N = 10,119) adjusted for participants' characteristics assessed at respective time points. Lastly, a single Cox regression analysis was fitted using a time-varying supplement use variable.

With increasing age, the percentage of SU + n3 increased over time (Q1: 25 %, Q2: 33 %, Q3: 36 %), with 16 % (Q1 to Q2) and 23 % (Q2 to Q3) being consistent SU + n3. Characteristics of the SU + n3 group remained similar at all three time points. Being in the SU + n3 group was significantly associated with a lower risk of CHD mortality using Q2 (HR 0.81, 95 %CI: 0.69–0.97) and Q3 (HR 0.71 95 %CI: 0.52–0.96), but not using Q1. Associations were stronger when follow-up time was restricted to the first 2–4 years after Q completion, which is consistent with there being unobserved changes in supplement use over longer periods. In time-varying regression, current use of n-3 PUFA containing supplements was associated with a lower risk of CHD mortality (HR 0.74 95 %CI: 0.65–0.83).

Supplement use was a variable behaviour, with current use of n-3 PUFA supplements being significantly associated with lower CHD mortality. The attenuation over time might reflect the infrequent assessments, the short-term effect of n-3 PUFA⁽⁴⁾, and hence the potential of interactions between supplement use and follow-up time. Frequent assessments of supplement use are recommended to ascertain associations with disease endpoints.

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