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Association of *n*-3 long-chain PUFA and fish intake with depressive symptoms and low dispositional optimism in older subjects with a history of myocardial infarction

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Individuals with CHD are at increased risk of poor mental well-being. Dietary intake of EPA and DHA, the main *n*-3 fatty acids from fish, may be beneficial to mental well-being. We examined the association of EPA + DHA and fish intake with mental well-being in 644 participants, aged 60–80 years, with a history of myocardial infarction. Habitual food intake was assessed with a 203-item FFQ. Depressive symptoms were assessed with the self-report geriatric depression scale, and dispositional optimism was assessed with the revised life orientation test (LOT-R) and a four-item questionnaire (4Q). In Cox-regression models modified for cross-sectional analyses, we adjusted for sex, age, energy intake, BMI, family history of depression, education, marital status, smoking, physical activity and intake of saturated fat, alcohol and fibre. Compared with the lower tertile, subjects in the higher tertile of EPA + DHA intake had a lower prevalence of depressive symptoms, but this association was not statistically significant (prevalence ratio (PR) 0·78; 95 % CI 0·50, 1·22, *P*-trend 0·27). The higher tertile of EPA+DHA intake was positively associated with dispositional optimism measured with the 4Q (PR 0·69; 95 % CI 0·46, 1·03, *P*-trend 0·05), but not according to the LOT-R. Fish intake was not related to either depressive symptoms or dispositional optimism. In conclusion, intake of EPA+DHA was positively associated with dispositional optimism assessed with the 4Q, but not with optimism assessed with the LOT-R or with depressive symptoms.

Fish: EPA + DHA: Depression: Dispositional optimism: Elderly

Poor mental well-being and CHD often co-occur. Depression is a strong risk factor for the development of CHD and is associated with a worse prognosis of CHD[1]. In post-myocardial infarction patients, the risk of depression is three times as high as compared to the general healthy population[2]. Therefore, the American Heart Association recommends to routinely screen for depressive disorders in coronary patients[3].

A low intake of fish and marine *n*-3 PUFA, especially of EPA (C20 : 5*n*-3) and DHA (C22 : 6*n*-3), could increase the risk of CHD[4] and may also predispose to depression. Because *n*-3 PUFA are a major component of neural membranes and act as precursors of compounds involved in immune and inflammatory responses, it is biologically plausible that these PUFA could play a role in mood and behavioural disorders[5]. Appleton *et al.* [6] reviewed the clinical and epidemiological evidence of *n*-3 PUFA and fish with depression until the beginning of 2008 and concluded that in both clinical and observational studies depression may be associated with *n*-3 PUFA and fish intake and *n*-3 PUFA status, but results are inconclusive. A meta-analysis of randomised controlled trials on *n*-3 PUFA supplementation and depression, which were mainly performed in depressed patients, pointed towards a beneficial effect, although the pooling of results was hampered by the heterogeneity of populations and the type of interventions[7]. More recently, the results of a trial performed in 302 Dutch older subjects provided with 400 or 1800 mg/d of EPA + DHA for 26 weeks have been published, and they did not show an effect on mental well-being[8]. Studies that focused on the association between *n*-3 PUFA and depression in coronary patients showed that depression was associated with lower plasma or membrane *n*-3 PUFA levels, in particular of DHA[9–13].

Depression is not simply the reverse of optimism, but both affect mental well-being, and because the intake of fish or *n*-3 PUFA may alleviate depressive symptoms, it may also enhance optimism. Dispositional optimism is defined in terms of generalised positive expectancies for one's future[14] and has been associated with more healthy dietary and other lifestyle habits[15,16] and also with less cardiovascular mortality[17]. In a prospective study in 773 community-dwelling elderly men, it was shown that dispositional optimism was associated with healthy lifestyle and dietary habits, including eating ≥400 mg EPA + DHA/d[16]. Another study in 8690 men and women aged 31 years showed that lack of optimism

Abbreviations: GDS-15, geriatric depression scale; LOT-R, life orientation test-revised; PR, prevalence ratio; 4Q, four-item questionnaire.

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was associated with unhealthy dietary and other habits in general, including a low fish intake, but only in women[15].

In the present study, we examined the association of mental well-being, based on the lack of depressive symptoms and on the presence of dispositional optimism, with EPA + DHA and fish intake in an older population with a history of CHD.

Subjects and methods

Subjects

We used baseline data of the Alpha Omega Trial, a randomised placebo-controlled double-blind intervention study designed to investigate the effect of the *n*-3 PUFA α-linolenic acid, EPA and DHA on cardiovascular mortality. Participants were free-living men and women aged 60–80 years with a documented history of myocardial infarction within the past 10 years. Main exclusion criteria were (1) habitual fish intake >150 g/d; (2) habitual alcohol intake >6 drinks/d; (3) recent (within 2 weeks before study entry) or current use of fish oil or other *n*-3 capsules; (4) dementia or severe cognitive impairment (mini-mental state examination score <22[18]). The Medical Ethics Committee South West Holland approved the study, and all participants gave written informed consent.

The sample examined in the present analysis comprised 791 participants who were enrolled in 2006 during the final part of the recruitment phase and who completed questionnaires on mental well-being. We excluded those with missing EPA + DHA intake data (*n* 97), and those who reported improbable energy intakes (*n* 10; <2093 or >14 654 kJ/d for women and <3349 or >16 747 kJ/d for men)[19]. Furthermore, we excluded current users of antidepressant medication (*n* 18) and subjects without complete data on all three measures of mental well-being (*n* 22). This resulted in a total of 644 subjects for the present analyses.

Assessment of mental well-being

Depressive symptoms were measured using the geriatric depression scale (GDS-15)[20]. The GDS-15 is a fifteen-item yes/no self-report questionnaire designed to screen for depressive symptoms during the past week in elderly subjects. The total score ranges from 0 to 15, with higher scores indicating more depressive symptoms. In elderly people, good sensitivity (0·88) and specificity (0·76) for depression were found for a cut-off point ≥4[21].

Dispositional optimism was assessed by using two questionnaires: the life orientation test-revised (LOT-R) and a four-item questionnaire (4Q). The LOT-R consists of ten coded items of which four statements are filler items not used in scoring[22]. Of the six items that are scored, three are keyed in a positive direction and three in a negative direction. There are five answer categories ranging from 'strongly disagree' (coded as 0) to 'strongly agree' (coded as 4). Negatively worded items (i.e. items 3, 7 and 9) are reversely coded before scoring. The total score ranges from 0 to 24, and higher scores indicate greater optimism. Because there is, to the best of our knowledge, no cut-off point for the LOT-R, we defined low dispositional optimism as the 20 % of the subjects with the lowest scores yielding <12 as a cut-off.

The 4Q was used previously in the Zutphen Elderly Study, and was predictive of both subsequent depressive symptoms[23] and cardiovascular mortality[17]. It consists of the following four questions: 'I still expect much from life'; 'I do not look forward to the years to come'; 'My days seem to pass by slowly'; 'I am still full of plans'. The response format is a three-point scale ranging from 'fully in agreement' (coded as 0) to 'not in agreement' (coded as 2). The additional answer category 'do not know' is also coded as the midpoint (coded as 1). The two negatively worded items (i.e. items 2 and 3) are reversely coded before scoring, so higher scores again indicate greater optimism. A score <6, as defined previously in the Zutphen Elderly Study[24], was used as a cut-off to indicate low dispositional optimism.

Assessment of diet, EPA + DHA and fish consumption

Habitual food intake during the previous month was estimated with a 203-item FFQ, which was specifically developed for the Alpha Omega Trial. This list is based on a previously validated FFQ that was designed to estimate the intake of total energy, total fat, cholesterol, and SFA, MUFA and PUFA in adults[25]. This questionnaire was updated, adapted for people aged 60–80 years and extended with questions to estimate intakes of α-linolenic acid, EPA and DHA. Questions on frequency, amount, type and cooking method of fish were also included.

Trained dietitians checked the returned questionnaires and obtained information by phone on important unclear or missing important items. The food consumption data were converted into nutrient intakes by using The Netherlands Food Composition Table 2001[26].

Assessment of lifestyle and health

Trained research nurses performed baseline examinations at the hospital or at the subjects' home. Body weight and height were measured, and BMI was calculated as weight (in kg) divided by height squared (m^2). Blood pressure was measured twice and the average was calculated. Blood samples were obtained for measurement of glucose, total cholesterol and HDL cholesterol. Self-administered questionnaires were used to collect information on medical history, medication use, smoking habits (current/former/never), educational level (low/intermediate/high) and marital status (living together with wife, partner or others/alone). Subjects were considered physically active when they reported 30 min of moderate or heavy exercise per day as assessed by the physical activity scale for the elderly questionnaire[27]. Hypercholesterolaemia was defined as total serum cholesterol ≥6·5 mmol/l or use of lipid-lowering medication. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of antihypertensive medication. Diabetes was assessed by self-report or serum glucose ≥11·1 mmol/l, or present treatment with oral antidiabetic medication or insulin.

Statistical analyses

If mental well-being measures had one missing response, the missing item was assigned the mean value of the other items on that particular scale for that participant. When

more than one item on a particular questionnaire was missing, no total score was computed and the participant was not included in the analyses.

Baseline characteristics of the subjects were calculated for all subjects and for men and women separately. To examine the agreement between the LOT-R and the 4Q, we used Spearman rank correlation and cross-tabulations to examine whether subjects were categorised into the same tertile of dispositional optimism by the two questionnaires. The associations of the prevalence of depressive symptoms (GDS-15 ≥ 4) and the absence of dispositional optimism (4Q < 6 or LOT-R < 12) with tertiles of EPA + DHA and fish were examined using a Cox-regression model with robust error variance, modified for cross-sectional analyses[28,29]. Associations are presented as prevalence ratio (PR) with 95 % CI with the lower tertile of intake as reference group. Analyses were adjusted for sex, age and family history of depression in the first model, and in the second model, more socio-demographic, lifestyle and food intake factors were added, namely, BMI, education, marital status, smoking status, physical activity, energy intake, and intake of saturated fat, alcohol and fibre. Tests of linear trend across increasing tertiles of EPA + DHA and fish intake were performed by using the median values of intake for each tertile.

A two-sided P value $<0{\cdot}05$ was considered statistically significant, and the statistical analyses were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Population characteristics

The study population comprised 644 participants, 500 men with a mean age of 69 years and 144 women with a mean age of 70 years (Table 1). Based on GDS-15 scores with a cut-off point ≥ 4, 17 % of the subjects had depressive symptoms, and this was twice as high in women (29 %) compared to men (14 %). Based on LOT-R scores with a cut-off point <12, the percentage of low dispositional optimism was 15 %, and based on 4Q scores with a cut-off point <6, the percentage of low dispositional optimism was 22 %. Women were slightly less optimistic than men as measured with the LOT-R (16 *v.* 15 %) and as well as with the 4Q (32 *v.* 19 %). Median fish intake was 15 g/d, and 40 % of the participants consumed fish less than once per week, 40 % consumed fish once per week and 20 % consumed fish more than once per week. The median intake of EPA + DHA was 130 mg/d, with women consuming slightly less than men (120 *v.* 140 mg/d).

Depressive symptoms

Compared with the lowest tertile, subjects in the highest tertile of EPA + DHA intake had a significantly lower prevalence of depressive symptoms (PR 0·56; 95 % CI 0·36, 0·88, P-trend 0·009), which was no longer significant after adjustment for confounders (PR 0·78; 95 % CI 0·50, 1·22, P-trend 0·27; Table 2). For fish intake, the unadjusted PR of depressive symptoms for the highest tertile was 0·73 (95 % CI 0·48, 1·12, P-trend 0·14), and the multivariable adjusted PR was 0·94 (95 % CI 0·62, 1·42, P-trend 0·57; Table 3). Adding the eighteen users of antidepressant medication to the depressive symptoms group did not change these results (data not shown).

Dispositional optimism

Of the subjects, 46 % were categorised in the same tertile with the LOT-R and 4Q. Furthermore, 47 % were categorised in the adjacent tertile for the LOT-R and 4Q, and 7 % were categorised into the opposite tertile. Spearman rank correlation between the two questionnaires was 0·44 ($P<0{\cdot}0001$).

For dispositional optimism measured with the 4Q, the unadjusted PR for the highest tertile of EPA + DHA intake as compared to the reference group was 0·52 (95 % CI 0·35, 0·78, P-trend 0·003), and the statistical significant trend remained after adjustment for confounders (PR 0·69; 95 % CI 0·46, 1·03, P-trend 0·05; Table 2). However, dispositional optimism measured with the LOT-R was not associated with EPA+DHA intake. Fish intake was not related to dispositional optimism neither measured with the LOT-R or measured with the 4Q (Table 3).

Discussion

In the present study, in Dutch older subjects with established CHD, there was a significant positive association between EPA + DHA intake and dispositional optimism assessed with the 4Q, but not with the LOT-R. The inverse association of depressive symptoms with EPA + DHA intake was no longer statistically significant after adjusting for confounders.

To assess depressive symptoms, we used the self-administered GDS-15 which has good sensitivity (0·88) and specificity (0·76) to screen for depression in an older population[21]. To assess dispositional optimism, two questionnaires were used. The LOT-R assesses respondents' expectations for the future and is considered the standard psychological optimism test with good psychometric properties[22]. The other optimism test, the 4Q, was shown to represent a rather stable personality measure over time, and was predictive of subsequent depressive symptoms and cardiovascular mortality in the Zutphen Elderly Study[17,23], but has not been validated against other measures of mental well-being.

Dietary intake of the previous month was assessed by a FFQ that was based on a validated FFQ for estimating total energy and fatty acid intake[25]. A general disadvantage of FFQ is that they are memory based, which could result in over- or underestimation of intake. Fish consumption may also be subject to reporting bias due to the known possible health benefits of fish. However, FFQ are suitable for ranking individuals according to their intake. Fish consumption was assessed including the frequency, amount and type of fish, but our sample size and the range of intake were too small to separately analyse different types of fish in relation to mental well-being. We observed that associations between fish intake and mental well-being were weaker than associations between EPA + DHA and mental well-being, which supports the idea that EPA + DHA, as the major nutrient in fish, attributed mostly to the beneficial association with mental well-being.

Other observational studies showed that both depression[30] and lack of dispositional optimism are associated with unhealthy lifestyle and dietary habits[15,16]. Fish and

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Table 1. Characteristics of 644 Dutch subjects aged 60–80 years with a history of myocardial infarction

(Mean values and standard deviations; median and interquartile range (Q1–Q3) for skewed data or percentages)

	Total (*n* 644)				Men (*n* 500)				Women (*n* 144)			
	Mean	SD	Median	Interquartile range	Mean	SD	Median	Interquartile range	Mean	SD	Median	Interquartile range
Age (years)	69	6			69	6			70	6		
Score GDS-15 (0–15)*			1	0–3			1	0–3			2	1–4
Score ≥4 (%)	17				14				29			
Score LOT-R (0–24)†			15	13–17			15	13–17			14	12–16
Score ≥12 (%)	85				85				84			
Score 4Q (0–8)‡			7	6–8			7	6–8			6	5–8
Score ≥6 (%)	78				81				68			
Family history depressive symptoms (%)	16				16				16			
Previous treatment for depressive symptoms (%)	13				12				17			
Living alone (%)	17				10				44			
MMSE score (0–30)§			28·5	27–29			29	27–30			28	27–29
BMI (kg/m^2)	28	4			28	4			28	5		
Physical activity (%)‖	66				68				60			
Education (%)												
Low/intermediate/high¶	55/33/12				52/35/14				66/27/7			
Smoking status (%)												
Current/former/never	15/67/18				13/74/13				20/44/36			
Hypercholesterolaemia (%)**	87				86				90			
Blood pressure (mmHg)												
Systolic	139	22			138	21			140			
Diastolic	78	11			79	11			75	12		
Hypertension (%)††	93				93				90			
Diabetes mellitus (%)‡‡	20				18				27			
Dietary intake												
Energy intake (kJ/d)	8002	2090			8330	2086				1669		
Saturated fat (g/d)	26	10			28	10			21	6		
EPA (mg/d)			50	20–80			50	20–80			50	20–90
DHA (mg/d)			80	40–130			90	50–130			70	40–145
Fibre (g/d)	22	7			22	7				7		
Daily alcohol intake												
0 Glasses (%)	28				20				54			
0·1–2·9 Glasses (%)	65				70				44			
≥ 3 Glasses (%)	8				9				1			
Total fish consumption (g/d)			15	8–17			15	8–18			15	5–17
Fish intake (%)												
< 1 per week	40				40				41			
1 per week	40				41				36			
> 1 per week	20				19				23			

GDS-15, geriatric depression scale-15; LOT-R, life orientation test-revised; 4Q, four-item questionnaire; MMSE, mini-mental state examination; Q, quartile.

* Higher scores indicate poorer mental well-being[20].

† Higher scores indicate greater optimism[22].

‡ 4Q on dispositional optimism; higher scores indicate greater optimism[23].

§ Higher scores indicate better cognitive function[18].

‖ Defined as ≥30 min/d of physical activity.

¶ Low, primary education or less; intermediate, secondary general or vocational education; high, higher vocational education, university.

** Defined as total serum cholesterol concentrations ≥6·5 mmol/l or use of lipid-lowering medication.

†† Defined as systolic ≥140 mmHg or diastolic ≥90 mmHg or use of antihypertensive medication.

‡‡ Defined by self-report as serum glucose ≥11·1 mmol/l or as treatment with oral antidiabetic medication or insulin.

Table 2. Prevalence ratios (PR)* for the association of EPA + DHA intake with depressive symptoms† and dispositional optimism‡ in older subjects with a history of myocardial infarction

(Prevalence ratios and 95% confidence intervals)

	EPA + DHA (mg/d)§					
	Cut-off	Median	Interquartile range	*n*		*P*-trend‖
	≤90	40	10–70	221		
	90– < 180	140	120–160	214		
	≥180	360	220–460	209		
		PR	95 % CI	PR	95 % CI	
Depressive symptoms on the GDS-15						
Crude association	1	0·86	0·59, 1·25	0·56	0·36, 0·88	0·009
Model 1¶	1	0·92	0·64, 1·34	0·60	0·39, 0·94	0·02
Model 2**	1	1·07	0·74, 1·56	0·78	0·50, 1·22	0·27
Low optimism on the 4Q						
Crude association	1	0·93	0·67, 1·28	0·52	0·35, 0·78	0·003
Model 1¶	1	0·98	0·72, 1·33	0·57	0·39, 0·85	0·003
Model 2**	1	1·05	0·76, 1·44	0·69	0·46, 1·03	0·05
Low optimism on the LOT-R						
Crude association	1	0·84	0·54, 1·30	0·86	0·55, 1·34	0·57
Model 1¶	1	0·84	0·54, 1·31	0·88	0·57, 1·37	0·65
Model 2**	1	0·92	0·59, 1·42	1·13	0·72, 1·79	0·53

GDS-15, geriatric depression scale-15; 4Q, four-item questionnaire; LOT-R, life orientation test-revised; Q, quartile.
* PR and 95 % CI obtained using Cox regression with robust error variance.
† Depressive symptoms are defined as a score ≥4 on the GDS-15.
‡ Low optimism is defined as a score <6 on the 4Q or a score <12 on LOT-R.
§ Cut-off and median (Q1–Q3) per tertile.
‖ *P*-trend refers to a linear trend in regression coefficients across tertiles of intake using the median values of each tertile.
¶ Adjusted for sex, age and family history of depression.
** Adjusted for BMI, education, marital status, smoking status, physical activity, energy intake, and intake of saturated fat, alcohol and fibre (*n* 636).

EPA + DHA intake may be considered part of a healthy diet and lifestyle, which may explain why our associations between mental well-being and EPA + DHA intake and fish were attenuated after adjusting for many important lifestyle and dietary variables in the multivariable-adjusted models. Appleton *et al.* [30] concluded that depression was associated with fish intake both directly and indirectly as a result of the absence of fish in a diet associated with depressed mood and

Table 3. Prevalence ratios (PR)* for the association of fish intake with depressive symptoms† and dispositional optimism‡ in older subjects with a history of myocardial infarction

(Prevalence ratios and 95% confidence intervals)

	Fish (g/d)§					
	Cut-off	Median	Interquartile range	*n*		*P*-trend‖
	≤9·8	4·3	0·0–7·7	214		
	9·8– < 16·2	15·0	11·8–15·5	214		
	≥16·2	36·8	17·4–40·5	216		
		PR	95 % CI	PR	95 % CI	
Depressive symptoms on the GDS-15						
Crude association	1	0·91	0·61, 1·34	0·73	0·48, 1·12	0·14
Model 1¶	1	0·94	0·64, 1·39	0·75	0·50, 1·14	0·13
Model 2**	1	1·19	0·81, 1·75	0·94	0·62, 1·42	0·57
Low optimism on the 4Q						
Crude association	1	0·80	0·57, 1·13	0·71	0·49, 1·01	0·07
Model 1¶	1	0·84	0·60, 1·16	0·74	0·52, 1·04	0·09
Model 2**	1	0·93	0·66, 1·30	0·85	0·60, 1·21	0·37
Low optimism on the LOT-R						
Crude association	1	1·00	0·65, 1·55	0·85	0·54, 1·34	0·44
Model 1¶	1	1·02	0·66, 1·57	0·86	0·54, 1·35	0·47
Model 2**	1	1·13	0·73, 1·76	1·03	0·65, 1·63	0·96

GDS-15, geriatric depression scale-15; 4Q, four-item questionnaire; LOT-R, life orientation test-revised; Q, quartile.
* PR and 95 % CI obtained using Cox regression with robust error variance.
† Depressive symptoms are defined as a score ≥4 on the GDS-15.
‡ Low optimism is defined as a score <6 on the 4Q or a score <12 on LOT-R.
§ Cut-off and median (Q1–Q3) per tertile.
‖ *P*-trend refers to a linear trend in regression coefficients across tertiles of intake using the median values of each tertile.
¶ Adjusted for sex, age and family history of depression.
** Adjusted for BMI, education, marital status, smoking status, physical activity, energy intake, and intake of saturated fat, alcohol and fibre (*n* 636).

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in a lifestyle associated with depressed mood. Thus, it is possible that mental well-being is more influenced by a healthy dietary pattern and lifestyle than exclusively by fish or EPA + DHA intake. Conversely, myocardial infarction patients with depression were found to be less likely to adhere to dietary and lifestyle recommendations than myocardial infarction patients without depression[31]. Thus, more optimal mental well-being might lead one to use a healthy diet.

The present results, though NS, pointed to the same direction as other studies on depression in coronary heart patients, which all showed that depression was associated with lower plasma or membrane levels of *n*-3 PUFA, in particular DHA[9–13]. However, one study also observed that the effect was no longer significant after adjustment for confounders, whereas only two of these studies adjusted for lifestyle confounders and none for other nutritional confounders. EPA + DHA intake is associated with blood levels of moderate strength[32]. The correlation between EPA + DHA intake and EPA + DHA concentrations in plasma cholesteryl esters in the present study was 0·37 (J de Goede, JM Geleijnse and D Kromhout, unpublished results). The present results are consistent with some cross-sectional studies in general populations that also found no association between intake and depression[33–35]. Yet, several other cross-sectional studies did observe an inverse association[30,36–39]. The present study population predominantly comprised men, and some studies observed an association between fish and EPA + DHA intake and depressive symptoms only in women[36,37,40]. Contrarily, Astorg *et al.*[41] observed stronger associations of fatty fish or *n*-3 PUFA intake with (recurrent) depressive episodes in men compared to women. Sex may thus interact with the association between depression and EPA + DHA and fish. In a stratified analysis in male participants only (data not shown), we observed weaker associations between EPA + DHA and fish intake compared to the present whole study population so a sex difference may indeed be an explanation for the fact that we did not observe a significant association in our total population.

To the best of our knowledge, there is only one other study that found an association between dispositional optimism and EPA + DHA intake[16]. In the present study, dispositional optimism was also measured with the 4Q, and higher mean dispositional optimism scores were only observed with EPA + DHA intakes $\geq$ 400 mg/d compared with EPA + DHA intakes $<$ 400 mg/d. However, we did not observe an association of EPA + DHA intake and dispositional optimism measured with the LOT-R. These questionnaires may differ because the 4Q also captures life engagement, vitality, motivation and feeling a purpose in life[17] rather than generalised positive outcome expectancies which is the focus of the LOT-R[22]. Nevertheless, 46 % of the participants were classified into the same tertile with both the LOT-R and 4Q, and Spearman rank correlation was 0·44 indicating a reasonable agreement between the two questionnaires.

The present study also has some limitations that need to be considered. First, we performed a cross-sectional analysis from which causality cannot be inferred. As pointed out by Kamphuis *et al.*[39], reverse causality is an alternative explanation because depression may induce loss of appetite, decreased food consumption and weight loss. Second, although we adjusted our analyses for the most important potential confounders, residual confounding cannot be completely ruled out. Third, the differences in intakes of fish and EPA + DHA between the tertiles may have been too small to find an association. Fourth, we did not assess clinical depressive disorders through structured clinical interviews based on the Diagnostic and Statistical Manual of Mental Disorders criteria. Finally, selection bias could be an issue in the present study since depressive subjects could be less willing to participate in a 3-year intervention study, questioning generalisability.

In conclusion, in the population of Dutch older subjects with a history of CHD, there was a significant positive association between EPA + DHA intake and dispositional optimism assessed with the 4Q, but not with the LOT-R. There was also a tendency for less depressive symptoms with a higher EPA + DHA or fish intake, but after adjustment for confounders these associations were no longer significant. We recommend performing longitudinal and additional large intervention studies in high-risk populations with low EPA + DHA biochemical status and with different states of mental well-being.

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