



Original Contribution

Longitudinal Associations Between Fish Consumption and Depression in Young Adults

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Few studies have examined longitudinal associations between fish consumption and depression; none have defined depression using a diagnostic tool. We investigated whether fish consumption was associated with fewer new depression episodes in a national study of Australian adults. In 2004–2006, 1,386 adults aged 26–36 years (38% males) completed a 127-item (9 fish items) food frequency questionnaire. Fish intake was examined continuously (times/week) and dichotomously (reference group: <2 times/week). During 2009–2011, the lifetime version of the Composite International Diagnostic Interview was administered by telephone. New episodes of major depression/dysthymic disorder (since baseline) were defined using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. During follow-up, 160 (18.8%) women and 70 (13.1%) men experienced depression. For women, each additional weekly serving of fish consumed at baseline decreased the risk of having a new depressive episode by 6% (adjusted relative risk = 0.94, 95% confidence interval: 0.87, 1.01). Women who ate fish ≥ 2 times/week at baseline had a 25% lower risk of depression during follow-up than those who ate fish <2 times/week (adjusted relative risk = 0.75, 95% confidence interval: 0.57, 0.99). Reverse causation was also suggested but appeared to be restricted to persons with recent depression. Fish consumption was not associated with depression in men. These findings provide further evidence that fish consumption may be beneficial for women's mental health.

depression; depressive disorders; diet; fish; longitudinal studies

Abbreviations: CDAH, Childhood Determinants of Adult Health; CIDI, Composite International Diagnostic Interview; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FFQ, food frequency questionnaire.

Depression affects approximately 340 million people worldwide and is the second leading cause of years lived with disability (1). The onset of depression increases with age through adolescence, with the highest prevalence in young adulthood (2). Because of low compliance with antidepressant medications and some undesirable side effects (3), there is increasing interest in how modifiable lifestyle factors may help prevent depression (4).

There is emerging evidence that fish and fish oils are beneficial for mental health. In cross-sectional studies, the prevalence of depression is lower in countries with higher apparent fish consumption (5) and among persons with higher fish intake (6–13). Interestingly, studies that have stratified

analyses by sex have found significant associations in only women (7, 8) or only men (13). Some cross-sectional studies have found no association between fish consumption and depression (14–16). Very few longitudinal studies exist. In a national study of 5,068 adults aged 25–74 years from the United States, baseline fish consumption appeared protective against severely depressed mood 10 years later among men but not women (17). However, depression was assessed using a screening tool, not a diagnostic tool, which may have overestimated the effect.

Omega-3 fatty acids are the component of fish believed to be beneficial for mental health. Persons with depression tend to have lower serum ω -3 fatty acid concentrations than those

without depression (18). In a recent study of French adults, lower intake of ω -3 polyunsaturated fatty acids was associated with fewer depressive symptoms in men at baseline but not with incident depression at the 13-year follow-up (19).

A recent meta-analysis of randomized controlled trials showed that ω -3 supplementation was associated with a decline in depressed mood (20). However, there was evidence of publication bias (20). Trials published since this review have shown that supplementation with eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) has benefits for depressive symptoms in menopausal women and older adults (21–25). Supplementation with fish oil has limitations, as components of fish other than ω -3 fatty acids may be beneficial for mental health or may be synergistic.

Major limitations of previous studies have included the cross-sectional study design and the use of depression measures that have relied on self-reporting or screening tools rather than diagnostic instruments. Because benefits of ω -3 fatty acids may only be evident in cases of more severe depression (20), diagnostic specificity is important. Longitudinal studies provide stronger evidence for causation than cross-sectional studies. However, the few studies that have prospectively examined associations between fish consumption and depression onset have not investigated the possibility of reverse causation—for example, whether there is an association between depression at baseline and fish consumption at follow-up. This is important, because changes in appetite are a common symptom of depression (26). Most studies have not adjusted for important confounding factors such as physical activity and healthier diets (20), which are known to be associated with fish consumption (27).

In the current study, we attempted to overcome some of these limitations. Using a large, population-based national sample of Australian adults, we aimed to examine longitudinal associations between fish consumption and onset of depression, defined using a diagnostic tool. We also investigated whether depression was prospectively associated with a lower intake of fish.

METHODS

The Childhood Determinants of Adult Health (CDAH) Study is a follow-up of the 8,498 children who participated in the 1985 Australian Schools Health and Fitness Survey, a nationally representative sample of Australian schoolchildren aged 7–15 years (28). During 2002–2004, a total of 6,840 participants were traced and 5,170 agreed to participate in the CDAH Study (Figure 1). During 2004–2006, when the participants were aged 26–36 years, 2,881 participants completed questionnaires and 2,410 participants also attended one of 34 study clinics that were held in each state and territory of Australia for physical measurements (CDAH-1, referred to as “baseline”). The second follow-up (CDAH-2) was conducted during 2009–2011, when the participants were aged 31–41 years. Participants completed a postal questionnaire and a computer-assisted telephone interview ($n = 1,548$). The Southern Tasmanian Health and Medical Ethics Committee approved the study protocol. Written informed consent was obtained at both time points.

Fish consumption

Diet was assessed at both time points using a 127-item food frequency questionnaire (FFQ) and a food habits questionnaire. The FFQ was a modified version of the one used in the 1995 National Nutrition Survey and was based on an existing validated questionnaire developed for Australian populations (29). The number of fish items was increased to reflect current consumption patterns. Nine types of fish and seafood items were included (canned fish, fresh fish, frozen fish, fried fish, mussels/oysters, lobster/crayfish/yabbies (small lobsters), calamari/squid, prawns, and other seafood). Participants were asked to estimate their intake over the previous 12 months by choosing one of 9 response options ranging from “never/less than once per month” to “6 or more times per day.” Weekly equivalents were calculated for each item, assuming that 1 serving was consumed on each eating occasion (29). Total weekly fish consumption was calculated by summing the weekly equivalents for all fish and seafood items. Participants were excluded from the analysis if they did not answer all of the fish questions ($n = 79$), because it was not known whether they had simply missed that item or had not consumed that particular type of fish. An exception was made if the participant was only missing a response for “other seafood” ($n = 27$), since the “other” item at the end of each section was commonly skipped (e.g., the number of participants missing responses for “other” items was 214 for “other vegetables”).

Depression

During CDAH-2, participants completed the computerized lifetime version of the Composite International Diagnostic Interview (CIDI), CIDI-Auto 2.1, as a computer-assisted telephone interview (26). The CIDI was developed by the World Health Organization and the US National Institutes of Health for use by trained nonclinical interviewers in a range of different community populations. Computerized diagnostic instruments have been shown to be more reliable, to be more comprehensive, and to have lower bias than routine clinical interviews (30). The lifetime version of the CIDI collects information on age at first onset and age at the most recent episode. Age at the most recent episode was used to determine whether an episode of depression or dysthymia had occurred since CDAH-1. Participants who had experienced an episode of major depression or dysthymic disorder (hereafter referred to as “depression”) as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), since baseline were compared with those who had not. The prevalence of lifetime depression in the study sample was compared with that in the general Australian population.

Covariates

Information on sociodemographic variables was self-reported at baseline and included age, marital status, education, and employment status. Accessibility/Remoteness Index of Australia (ARIA) classifications (major city, inner regional, outer regional/remote) were assigned to participants

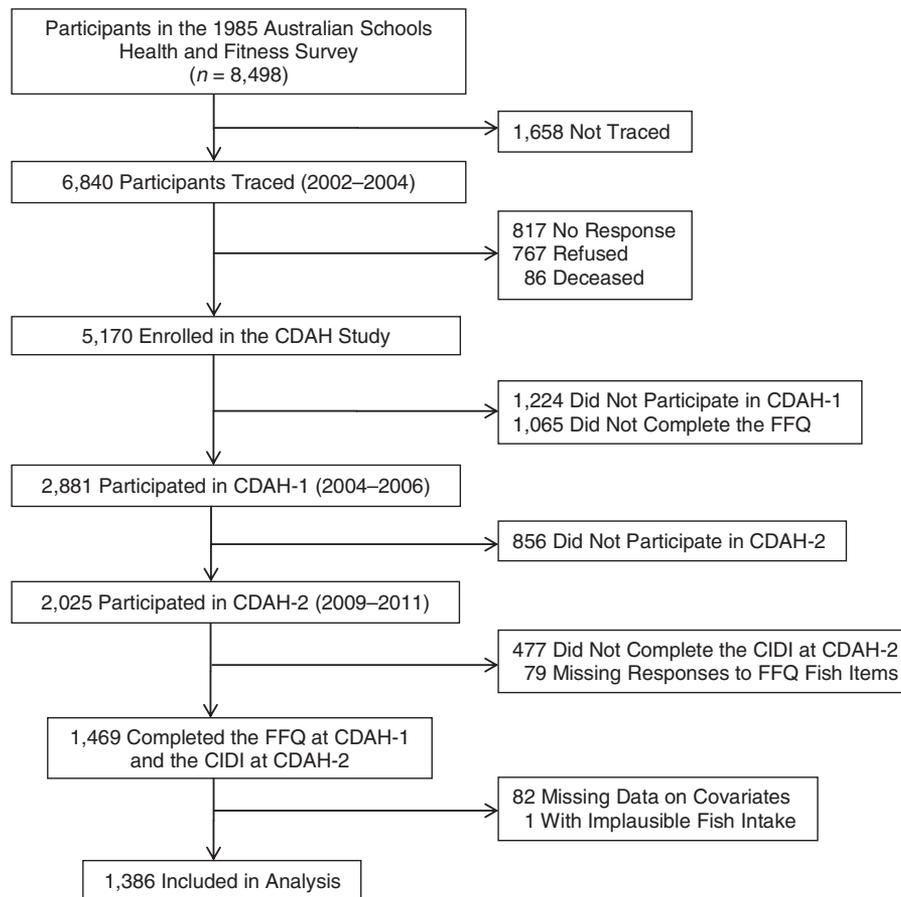


Figure 1. Selection of participants for the Childhood Determinants of Adult Health (CDAH) Study, Australia, 1985–2011. Participants who were initially nonresponders were given the option of completing a shorter protocol by telephone interview, which included shorter versions of the questionnaires (no food frequency questionnaire (FFQ)) at baseline (CDAH-1) and follow-up (CDAH-2) and excluded administration of the Composite International Diagnostic Interview (CIDI) at CDAH-2. Participants were excluded from the analysis if they did not answer all of the fish items in the FFQ at baseline.

based on residential address and census collection district. Smoking status and medication use were self-reported. For women, parity was defined as the number of livebirths.

170 The number of standard alcoholic drinks (10 g of ethanol) consumed per week was estimated from 9 alcoholic beverages listed in the FFQ and their average alcohol concentration. Usual fruit and vegetable consumption were assessed using short questions (29). Information from the FFQ and the food habits questionnaire was used to assess diet quality using a dietary guideline index based on the Australian Guide to Healthy Eating (31). The score included 15 components that were scored from 0 to 10, with 10 indicating optimal intake (total range, 0–150). Proportional scores were given for participants who consumed intermediate amounts. This score has been shown to be a valid measure of diet quality (32, 33). The FFQ also asked about supplement use, including use of fish oil/evening primrose oil supplements (the question combined these 2 supplements), and included questions on use of ω -3 fatty acid-fortified margarine for cooking and as a spread on breads and savory biscuits. Leisure-time physical activity

and time spent sitting were assessed using the long version of the International Physical Activity Questionnaire (34).

During CDAH-1, weight and height were measured at study clinics using a portable scale and stadiometer. Participants who did not attend a study clinic self-reported their height and weight, and a correction factor was applied (35). Body mass index was calculated as weight (kg) divided by the square of height (m^2). Health status was assessed using the 12-Item Short-Form Health Survey (36).

Statistical analyses

Baseline fish consumption was treated as a continuous exposure variable (times/week) and was also dichotomized, with <2 times/week used as the reference group. This cut-point was chosen to reflect current recommendations by the National Heart Foundation of Australia and the American Heart Association to eat fish at least 2 times/week. Relative risks were calculated using Poisson regression with robust standard errors. Reverse causation was examined by investigating

whether a diagnosis of depression since baseline was associated with fish intake reported at the CDAH-2 survey. Covariates included in the analyses were factors significantly associated with having experienced depression since baseline in the univariable analysis. Men and women were analyzed separately, because previous studies suggested sex differences in the relationship between fish consumption and depression (7, 8, 13).

Sensitivity analyses were conducted taking into consideration fish consumption at baseline and follow-up in order to provide a longer-term estimate of fish intake. The analysis was also repeated after excluding persons who had a history of depression at baseline (age of onset at or before CDAH-1), to examine incident depression. Statistical analyses were conducted with STATA software, version 12.0 (StataCorp LP, College Station, Texas).

RESULTS

In total, 544 men and 925 women completed the FFQ at baseline and the CIDI at follow-up. The different participation rates for men and women were due to a lower proportion of men responding to the postal questionnaire in CDAH-2 (37% men). Participants who were missing information on covariates included in the adjusted analyses (11 men, 71 women) and 1 woman with an implausibly high fish intake (107.5 times/week) were excluded, leaving 533 men and 853 women for the analysis. Table 1 shows the participants' baseline characteristics.

Table 1. Baseline Sociodemographic and Anthropometric Characteristics of Participants in the Childhood Determinants of Adult Health Study, Australia, 2004–2006^a

| Characteristic | Men (n = 533) | | Women (n = 853) | |
|------------------------------|-------------------------|------|-----------------|------|
| | No. | % | No. | % |
| Mean age, years | 31.8 (2.6) ^b | | 31.5 (2.6) | |
| Married or living as married | 362 | 67.9 | 637 | 74.7 |
| Education | | | | |
| University degree | 232 | 43.6 | 445 | 52.2 |
| Vocational school | 180 | 33.8 | 193 | 22.6 |
| High school only | 120 | 22.6 | 215 | 25.2 |
| Occupation | | | | |
| Professional or manager | 328 | 62.4 | 446 | 53.0 |
| Nonmanual | 40 | 7.6 | 203 | 24.1 |
| Manual | 137 | 26.0 | 30 | 3.6 |
| Not in the workforce | 21 | 4.0 | 163 | 19.4 |
| Body mass index ^c | | | | |
| Normal (<25) | 238 | 47.2 | 545 | 63.9 |
| Overweight (25–29.9) | 199 | 39.5 | 204 | 23.9 |
| Obese (≥30) | 67 | 13.3 | 104 | 12.2 |

^a Sample sizes varied (range, 479–504 for men and 753–764 for women) because of missing data.

^b Numbers in parentheses, standard deviation.

^c Weight (kg)/height (m)².

Compared with the Australian general population of adults aged 25–34 years, a higher percentage of the CDAH sample at baseline was married or living as married (57% of men and 64% of women in the Australian population (37)) and employed as professionals or managers (40% of men and 38% of women in the general population (38)). The percentage classified as being overweight or obese (body mass index ≥25) was similar to that of the general population of the same age (58% of men, 35% of women (39)).

Mean follow-up time was 4.96 (standard deviation, 0.34) years. During follow-up, 70 (13.1%) men and 160 (18.8%) women had a depressive episode. The prevalence of lifetime depression (ever having depression/dysthymia) was higher in the CDAH sample than in the general Australian population of 31- to 41-year-old men (18.1% vs. 13.5%, respectively) and women (29.4% vs. 21.8%, respectively). Participation in CDAH-2 was not affected by depression status in CDAH-1 (78.2% for persons who had 12-month depression in CDAH-1 and 78.6% for those who did not).

Median fish consumption at baseline was the same for men and women: 2 times/week (interquartile range, 1–4). Fish was consumed ≥2 times/week by 320 (60.0%) men and 506 (59.3%) women. The most commonly consumed types of fish were canned fish (median, 0.5 times/week (interquartile range, 0–1) for both men and women) and fresh fish (median, 0.5 times/week (interquartile range, 0–0.5) for both men and women). Fish oil or evening primrose oil supplements were used at least once per month at baseline by 37 (6.9%) men and 119 (14.0%) women (see Web Table 1, available at <http://aje.oxfordjournals.org/>). Very few participants usually used ω-3 fatty acid-fortified margarine for cooking (10 men, 11 women) or as a spread (13 men, 25 women).

For women, baseline factors associated with having depression during the follow-up period were marital status (being single), smoking status (being a current smoker), being overweight or obese, and having poorer self-rated health (Web Table 1). For men, use of fish oil/evening primrose oil supplements was the only baseline characteristic associated with depression, with supplement use being higher in depressed men. These factors were included as covariates in the analyses.

For women, after adjustment for marital status, smoking status, weight status, and self-rated health, there was a trend for each additional weekly serving of fish at baseline to reduce the risk of having depression during follow-up by 6%. Women who ate fish ≥2 times/week at baseline had a 25% lower risk of having depression during follow-up than those who ate fish <2 times/week (Table 2). For men, baseline fish consumption was not associated with the risk of depression.

Reverse causation was also suggested, with women who had experienced an episode of depression since baseline being 15% less likely to eat fish ≥2 times/week at follow-up compared with women who had not had depression, after adjustment for marital status, smoking status, weight status, and self-rated health (adjusted relative risk = 0.85, 95% confidence interval: 0.71, 1.00). When persons who had depression during the 12 months prior to follow-up—that is, those whose symptoms were most recent—were excluded from the analysis, the association disappeared (adjusted relative risk = 0.98, 95% confidence interval: 0.81, 1.19). For men, depression

Table 2. Relative Risk of Having a New Episode of Depression Between Baseline and Follow-up, by Fish Consumption, Childhood Determinants of Adult Health Study, Australia, 2004–2011

| Baseline Fish Consumption | Depression Episode | | | Unadjusted RR | | | Adjusted RR ^a | | |
|---------------------------------|--------------------|-----------|------|---------------|------------|----------------------|--------------------------|------------|----------------------|
| | No. | Total No. | % | RR | 95% CI | P Value ^b | RR | 95% CI | P Value ^b |
| Women (<i>n</i> = 853) | | | | | | | | | |
| Continuous variable, times/week | 160 | 853 | 18.8 | 0.93 | 0.86, 1.01 | 0.07 | 0.94 | 0.87, 1.01 | 0.07 |
| Dichotomous variable | | | | | | | | | |
| <2 times/week | 79 | 347 | 22.8 | 1.00 | Reference | | 1.00 | Reference | |
| ≥2 times/week | 81 | 506 | 16.0 | 0.70 | 0.53, 0.93 | 0.01 | 0.75 | 0.57, 0.99 | 0.04 |
| Men (<i>n</i> = 533) | | | | | | | | | |
| Continuous variable, times/week | 70 | 533 | 13.1 | 1.03 | 0.96, 1.11 | 0.38 | 1.02 | 0.95, 1.10 | 0.54 |
| Dichotomous variable | | | | | | | | | |
| <2 times/week | 25 | 213 | 11.7 | 1.00 | Reference | | 1.00 | Reference | |
| ≥2 times/week | 45 | 320 | 14.1 | 1.20 | 0.76, 1.89 | 0.44 | 1.17 | 0.74, 1.86 | 0.49 |

Abbreviations: CI, confidence interval; RR, relative risk.

^a Analyses for women adjusted for baseline marital status, smoking status, weight status, and self-reported health. Analyses for men adjusted for the use of fish oil/evening primrose oil supplements.

^b *P* values were calculated using Poisson regression with robust standard errors.

was not associated with fish intake at follow-up (adjusted for fish oil/evening primrose oil supplementation, adjusted relative risk = 1.12, 95% confidence interval: 0.91, 1.38).

In sensitivity analyses (Web Appendix), similar results were observed when fish intake at baseline and fish intake at follow-up were averaged. When persons who had a history of depression at baseline were excluded, the magnitude of the association remained the same, but the association was no longer statistically significant, probably because of the smaller sample size (Web Table 2). For consistency, we repeated the analysis for men using the same model as that used for women; this did not significantly change the results (Web Table 3). Additional adjustment for use of fish oil/evening primrose oil or antidepressant medication did not change the results for women, nor did replacing weight status with body mass index.

DISCUSSION

In this longitudinal study of Australian adults, higher fish consumption was associated with a significantly lower risk of having a depressive episode in women, but not in men, during approximately 5 years of follow-up. While there was also a suggestion of reverse causation, this appeared to be restricted to persons who had experienced depression relatively recently, and their lower fish intake at follow-up may have been a result of disturbed eating patterns associated with depressive symptoms. To our knowledge, this was the first study to examine longitudinal associations between fish consumption and depression using a diagnostic tool to define depression.

Our findings are consistent with those of previous cross-sectional studies that showed a lower risk of depression in healthy adults with higher fish consumption (6, 9–11).

Similar sex-specific results were reported in 2 cross-sectional studies conducted in Finland (7, 8), which found that depression prevalence, measured using a screening tool or a self-reported physician's diagnosis, was significantly lower in women who ate fish ≥1 time/week. Authors in both studies reported no significant associations between fish consumption and depression in men. In the Coronary Artery Risk Development in Young Adults (CARDIA) Study, baseline fish consumption was not associated with depressive symptoms at the 3-year follow-up (40). However, at the 13-year follow-up, there was a dose-response relationship between baseline fish consumption and chronicity of depression, with women who consumed more fish having depressive symptoms at fewer of the 3 follow-up visits (40).

The observed protective association for women but not for men may have been due to men consuming more ω-3 fatty acids from other dietary sources, particularly from meat. Fish is the best source of ω-3 fatty acids, but in Australia, pasture-fed meat, poultry, and game contribute similar amounts of ω-3 fatty acid to the diet, because they are consumed about 6 times more than fish and seafood (41). Alternatively, interactions between sex hormones and ω-3 fatty acids might provide another explanation. A study examining the association between ω-3 fatty acids and platelet aggregation found that men benefited more from EPA supplementation, while females responded better to DHA (42). The results may also be explained by differential reporting of fish intake between men and women, leading to exposure misclassification, or consumption of different types of fish by men and women, which would not be detected in the FFQ.

In contrast to our findings, several studies have observed beneficial associations only in men. In 2 Finnish cross-sectional studies, higher fish consumption was associated with lower depression prevalence in men but not in women

(13). In a large national US sample, men who ate fish ≥ 2 times/week at baseline were significantly less likely to have severely depressed mood at the 10-year follow-up than those who ate fish ≤ 1 time/week (17). The reasons for these sex differences are not clear, but they may reflect use of different methods to sample the study populations or to determine fish intake and depression, the different ages of the samples (i.e., older adults or having a large age range), or possibly residual confounding.

The biological mechanism linking fish consumption and depression is not well understood, but it has been postulated that ω -3 fatty acids may alter the phospholipid composition of cell membranes or cause changes to the membrane microstructure and the function of membrane-associated proteins (17). Although ω -3 fatty acids are hypothesized to be the beneficial component of fish, the results from randomized controlled trials examining the association between ω -3 supplements and depressive symptoms have been inconclusive (20). The associations between fish consumption and depression might be due to confounding by healthier diet and lifestyle and better psychosocial circumstances (10). In our adjusted models, when we included marital status, smoking status, weight status, and health status, the results were only slightly attenuated and remained statistically significant. Other lifestyle factors considered to be important in previous studies, such as physical activity, other dietary components, and alcohol consumption, were not associated with depression in this sample and therefore could not be confounders. However, residual confounding by lifestyle or socioeconomic factors not measured in this study is possible.

Fish consumption was fairly high, with about 60% of men and women consuming fish ≥ 2 times/week. Canned fish and fresh fish were the most common types of fish consumed. Canned fish is a relatively cheap dietary option in Australia, but fresh fish is expensive unless self-caught. Participants in the CDAH sample were of higher socioeconomic status than the general Australian population, which may mean that participants could afford to eat fish frequently. There are no recently published national data on fish consumption in Australia, but in a population health survey of approximately 3,500 18- to 75-year-olds conducted in 2009–2010 in Victoria, the second most populated state in Australia, the mean intake of fish and seafood was 38.3 g/day for men and 32.3 g/day for women (43). When converted to servings/week (1 serving = 120 g (44)), men were consuming 2.2 servings/week and women were consuming 1.9 servings/week, on average. Fish consumption may have been higher in the CDAH sample because of different socioeconomic status levels, age ranges, and methods used to assess fish consumption between the studies. Alternatively, fish consumption may have been overestimated because of the large number of items (9 items) included in this variable. However, in an Australian study, Mina et al. (45) found that an aggregate measure of 71 fish items was a valid measure of fish consumption when compared with erythrocyte membrane EPA levels.

Several limitations need to be taken into consideration when interpreting these results. The prevalence of lifetime depression was higher in the CDAH Study sample than in participants of similar age in the 2007 Australian National Survey of Mental Health and Wellbeing (46), the most recent

national survey. However, the National Survey used the CIDI 3.0, which has a different structure and includes some different questions in the depression section. Therefore, the prevalences derived from the 2 different versions of the CIDI may not be directly comparable. Consistent with the national data, the prevalence of depression was higher among women than among men in the CDAH Study. The CIDI does not gather information on the timing of every episode of depression; therefore, we were unable to examine associations of fish consumption with individual episode occurrence. Participation in CDAH-2 was not affected by depression status in CDAH-1.

The questionnaire did not differentiate between fatty fish and lean fish, which is a limitation, since the concentrations of ω -3 fatty acids are much higher in fatty fish. However, this would result in underestimation of the effect estimate, since consumption of only fatty fish may have an even stronger association with reduced risk of depression. Information on portion size was not collected; therefore, it is not known how many servings of fish participants were actually consuming on each eating occasion. The use of fish oil supplements may have been overestimated, since fish oil supplements and evening primrose oil supplements were combined in the questionnaire, and this may have underestimated the true effect. Information on energy intake was not available. However, the analysis was stratified by sex, and other key determinants of energy intake (age and physical activity) were not associated with fish consumption.

The environmental impact of recommending increased intake of fish for mental and physical health should be considered. Concerns have been raised regarding the potential overfishing of wild fish stocks and the use of wild fish to feed farmed fish (47). It is important to identify sustainable sources of fish to ensure long-term viability and affordability. In the CDAH Study, use of fish oil supplements and ω -3-fortified foods was low. Eating fish rather than taking supplements can provide benefits other than ω -3 fatty acids, since fish is also a good source of high-quality protein, vitamins, and minerals.

In summary, this study advanced on previous work in this area by using a “gold standard” diagnostic tool (the CIDI), rather than a screening tool or self-reports, to define depression. Findings from this longitudinal study suggest that, for women, fish consumption may be protective against depression. Depression was also associated with lower intake of fish around the time of the depressive episode. Data were available for a wide range of potential confounders. The findings add to the growing evidence that fish consumption may be beneficial for women’s mental health.

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