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Effects of Omega-3 Fatty Acids on Mental Health

Summary

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Introduction

The purpose of this study was to conduct a systematic review of the scientific-medical literature to identify, appraise, and synthesize the human evidence for the effects of omega-3 fatty acids on mental health. The review was requested and funded by the Office of Dietary Supplements, National Institutes of Health. It was undertaken as part of a consortium involving three Evidence-based Practice Centers (EPCs), which investigated the value of omega-3 fatty acid supplementation across 11 health/disease areas. The three EPCs are Southern California-RAND, Tufts-New England Medical Center, and the University of Ottawa. To ensure consistency of approach, the three EPCs collaborated on selected methodologic elements, including literature search strategies, rating of evidence, and data table design.

While the intention was to evaluate the spectrum of psychiatric disorders or conditions (i.e., behavior or symptoms which, while their consequences could be serious, do not warrant receipt of a formal psychiatric diagnosis), certain foci were beyond the scope of the review (see Methods). At the same time, a mental health disorder or condition did not require extant animal or basic science data or models to justify the investigation of their evidence. Nevertheless, justification for the study of two disorders exists in the literature: depression and schizophrenia.

The mechanism by which diet may affect health, including depression or cardiovascular disease, has been thought to involve low levels of omega-3 fatty acid content in biomarkers (e.g., red blood cells [RBCs]).[1,2] An omega-3 fatty acid deficiency hypothesis of depression has been put forward, which has helped justify treatment with omega-3 fatty acid supplementation.[3] The membrane phospholipid hypothesis of schizophrenia has been proposed in an attempt to develop a model explaining its etiology.[4] It describes the presumed biochemical dynamics underpinning a neurodevelopmental theory. Some of the evidence used to support this perspective suggests the existence of phospholipid and polyunsaturated fatty acid (PUFA) metabolic abnormalities in schizophrenia.[4-6] It has been posited that modifications to diet could mitigate or even aggravate an underlying abnormality of phospholipid metabolism.[4]

However, the present review was not conducted to test these hypotheses. Rather, the rationale for this 2-year project investigating the possible health benefits of omega-3 fatty acids was to systematically review the evidence to aid in the development of a research agenda. Nevertheless, these emerging models regarding depression and schizophrenia do suggest plausible bases for the use of omega-3 fatty acids to treat or prevent these psychiatric disorders.

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Key Questions

Four basic questions were investigated with respect to each psychiatric disorder or condition for which evidence meeting eligibility criteria could be identified. To illustrate, the questions pertaining to depression were:

- Are omega-3 fatty acids efficacious as (primary or supplemental) treatment for depression?
- Is omega-3 fatty acid intake, including diet and/or supplementation, associated with the onset, continuation, or recurrence of depression (i.e., primary or secondary prevention)?
- Is the onset, continuation, or recurrence of depression associated with omega-3 or omega-6/omega-3 fatty acid content of biomarkers (i.e., primary or secondary prevention)?
- What is the evidence in review-relevant studies concerning mental health that adverse events (e.g., side effects) or contraindications are associated with the intake of omega-3 fatty acids?

Where data permitted, the impact of effect modifiers (e.g., covariates) was investigated with respect to the following study characteristics:

- Population (e.g., primary diagnosis, disorder severity, smoker status, alcohol consumption).
- Intervention/exposure (e.g., source, type, dose or serving size, and method to deliver the omega-3 fatty acids; intervention length; dietary omega-6/omega-3 fatty acid content).
- Comparator/control (e.g., type of placebo material, a "gold standard" medication).
- Cointerventions (e.g., concurrent psychotropic medication, other supplement use).

Methods

A Technical Expert Panel (TEP) consisting of nine members was convened to provide advisory support to the project, including refining the questions and highlighting key variables requiring consideration in the evidence synthesis.

Study Identification

Several electronic databases were searched: MEDLINE®, EMBASE®, the Cochrane Library including the Cochrane Central Register of Controlled Trials, PsycINFO, and CAB Health®. Searches were not restricted by language of publication, publication type, or study design, except with respect to the MeSH® term "dietary fats," which was limited by study design to increase its specificity. Search elements included: scientific terms, with acronyms, as well as generic and trade names relating to the exposure and its sources (e.g., eicosapentaenoic acid (EPA), omega-3 fatty acids, MaxEPA®); and relevant population terms (e.g., depression). Additional published or unpublished literature was sought through manual searches of reference lists of included studies and key review articles, and from the files of content experts. A final set of 1,212 unique references was identified and posted to an Internet-based software system for review.

Studies were considered relevant if they described live human populations of any age with any or no comorbidity, exhibiting a psychiatric status consistent with one of the above-noted research questions concerning treatment or prevention (i.e., with or without [a known elevated risk to develop] a psychiatric diagnosis or condition). Studies also had to investigate at least one pertinent clinical outcome (e.g., symptom improvement, incidence of a disorder).

As markers of omega-3 fatty acid metabolism, the following fatty acid compositions or concentrations, from any source (e.g., plasma phospholipids), were considered relevant as possible predictors of the onset, continuation, or recurrence of psychiatric disorders or conditions: EPA, docosahexaenoic acid (DHA), arachidonic acid (AA)/EPA, AA/DHA, and AA/EPA+DHA. Studies exclusively evaluating the role of other biomarkers (e.g., cytokine production, eicosanoid levels) were not included. Populations with degenerative (e.g., Alzheimer's) and peroxisomal (e.g., Zellweger's) disorders were excluded since each was addressed in Southern California-RAND's year-2 review of the evidence concerning omega-3 fatty acids in neurology.

Treatment studies, as well as those investigating the possible association between omega-3 fatty acid intake and the onset, continuation, or recurrence of psychiatric disorders or conditions, had to investigate foods or supplements known to contain omega-3 fatty acids of any type (e.g., EPA), from any source (e.g., walnuts), any serving size or dose, delivered in any

fashion (e.g., capsules, PUFA-rich diet), and for any length of time. In all studies, some method had to have been employed to suggest the presence of omega-3 fatty acid content in the exposure, if not its actual amount (e.g., g/d). Studies investigating "PUFAs" or " long-chain PUFAs," or even types of diet one might presume would contain marine or land sources of omega-3 fatty acids (e.g., "Mediterranean diet") at minimum had to highlight at least one source of the omega-3 fatty acid content (e.g., oily fish servings). No restrictions were placed on the types or doses of pre- or on-study cointerventions (e.g., psychotropic medication, omega-6 fatty acid intake).

Controlled studies employing any control were required to address questions of intervention efficacy (or effectiveness), with randomized controlled trials (RCTs) being the gold standard method to investigate these questions.[7] Any type of research design other than noncomparative case series or case studies was deemed appropriate for questions concerning the possible association between the intake of omega-3 fatty acids and the onset, continuation, or recurrence of psychiatric disorders or conditions. A special interpretative emphasis was placed on results from prevention RCTs and other controlled prospective designs. Controlled studies involving any control were required to address the questions of the possible association between the fatty acid content of biomarkers and the onset, continuation, or recurrence of psychiatric disorders or conditions. These decisions were made with the assistance of our TEP.

Two initial levels of screening for relevance, and two reviewers per level, were directed at bibliographic records and then full articles. A third dual-assessor relevance screening identified and thereby excluded uncontrolled studies with respect to questions of intervention efficacy or the possible protective role of lipid biomarker content. Calibration exercises preceded each step of the screening process. Excluded studies were noted as to the reason for their ineligibility using a modified QUOROM format.[8] Disagreements were resolved by forced consensus and, if necessary, third party intervention.

Data Abstraction

Following a calibration exercise, seven reviewers independently abstracted the contents of each included study using an electronic data abstraction form. A second reviewer verified these data. Data included the characteristics of the report (e.g., publication status), study (e.g., research design), population (e.g., diagnosis), intervention/exposure (e.g., omega-3 fatty acid type), comparator group(s), cointerventions (e.g., medications), withdrawals or dropouts, and outcomes (i.e., symptom improvement, biomarker status, adverse events).

After calibration exercises, each study's quality (internal validity) and applicability (external validity) were formally assessed. Dual-review appraised RCTs' quality while only single-assessor evaluations could be conducted for other research designs. For the RCTs, disagreements were resolved by forced consensus and, if necessary, third party intervention. RCTs' reporting of randomization, double blinding, withdrawals and dropouts, and the concealment of allocation, were evaluated using Jadad's[9] and Schulz's validated instruments.[10] The validated Newcastle-Ottawa Scale (NOS) assessed case-control and cohort study designs, while all other designs were evaluated using modifications of the NOS,[11] Jadad's instrument,[9] or items from Downs and Black's validated 27-item tool.[12] Applicability was defined as the extent to which a given study's sample population was representative of a "typical" North American population. The method of diagnosis and the omega-6/omega-3 fatty acid ratio in the background diet were the key variables defining the reference population of North Americans identified with a psychiatric disorder. The omega-6/omega-3 fatty acid ratio in the background diet defined the reference population of North Americans who did not exhibit a psychiatric disorder.

Data Synthesis

A summary table provided a question-specific overview of included studies' relevant data presented in greater detail in evidence tables. A question-specific summary matrix situated each study in terms of its quality and applicability ratings. Question-specific qualitative syntheses of the evidence were derived. A dearth of studies best suited to address a particular kind of question (i.e., RCTs, prospective and controlled observational studies), as well as limitations on, or the strong clinical heterogeneity of, available studies (e.g., divergent intervention-comparator contrasts, use of complex interventions where it was impossible to tease out the possible specific benefit of omega-3 fatty acids, failure to control for key confounders), made it impossible to perform meta-analysis for any question other than the supplemental treatment for schizophrenia.

Results

Literature Search

Of 1,212 records entered into the initial screening for relevance, 955 were excluded. All but seven of the remaining 257 reports were then retrieved and subjected to a more detailed relevance assessment.[13-21] A second relevance screening then excluded 137 reports. A third screening excluded 27 reports of uncontrolled studies. In total, 86 reports, describing 79 unique studies, were deemed relevant for the systematic review, with six studies each described by more than one report. To simplify matters, only one report per study is referred to in this summary. Yet, data from all of a study's documents were included in qualitative and quantitative syntheses. Some studies addressed more than one question.

Of the included studies, only one failed to be described by at least one published report.[22] It was reported in abstract format. Sixteen relevant studies were identified by manual search. One report required translation from Chinese.[23] All the other included reports were written in English.

Overall, depression (n=22 studies) and schizophrenia (n=28) were the most frequently studied disorders. Only the 10 studies investigating attention-deficit/hyperactivity disorder (AD/HD) enrolled pediatric populations. Many of the studies exhibited poor quality or weak applicability to North American populations. Synopses of evidence are presented according to seven cross-cutting topics:

Adverse Events

A number of study reports explicitly stated that no exposure-related adverse events had been observed.[24-32] Ten RCTs described at least one mild adverse event associated with an omega-3 fatty acid intervention/exposure.[2,33-41] Results from these studies suggest that the exposures were well tolerated. In spite of a small number of discontinuations presumed to have been instigated by an adverse event, it is unlikely that moderate or severe side effects were ever observed in relation to an omega-3 fatty acid exposure. Reported difficulties tended to be mild and transient, often involving gastrointestinal upset or nausea. Occasionally, adverse events were linked to the intake of oily substances, rather than to the omega-3 fatty acid contents in the oils. Aside from the mild adverse effects associated with Stoll et al.'s very high dose of 9.6 g/d EPA+DHA (i.e., three patients had to decrease the number of capsules swallowed per day, yet none were required to discontinue),[38] no other patterns were discerned regarding the impact of dose, type (e.g., DHA, EPA) or source (e.g., marine, plant) of omega-3 fatty acids on safety. In one study, a child with AD/HD in the active treatment group had to leave the study due to problems swallowing the capsules.[41] Few of the events described in two trials by Hamazaki et al., which enrolled healthy volunteers, suggested that the adverse effects had been directly related to the exposure.[39,40]

Primary Treatment

One RCT examined omega-3 fatty acids as primary treatment for depression.[34] It found no benefit for 2 g/d DHA as primary treatment despite an increase in the absolute RBC levels of DHA in the active treatment group.[34] Reasons for this null result could include the use of too small a dose, too short an intervention period, the "wrong" omega-3 fatty acid, broken blinding, low power, or failure to modify the on-study background intake of omega-6 fatty acids.

Notwithstanding the noncomparability of interventions, comparators, and populations (i.e., with[32,42,43] or without a formal diagnosis of AD/HD,[41] with[32] or without significant comorbidity[41,43]), the complex definitions of the intervention where it was impossible to tease out the possible specific benefit of omega-3 fatty acids,[41] evidence for selection bias,[43] or the failure to specify study enrollees' specific diagnostic subtype of AD/HD (e.g., inattentive),[44] the results of the three RCTs[32,41,42] and the comparative before-after study[43] addressing the question about the primary treatment of AD/HD were inconsistent. Thus, no definitive conclusions can be drawn about the value of omega-3 fatty acids as primary treatment for AD/HD.

One RCT examined ethyl (E)-EPA as primary treatment for borderline personality disorder and observed significant clinical effects, as the E-EPA group had, at study end, significantly lower mean scores on both clinical outcomes compared with the placebo group.[31] Despite its strong applicability to the North American population, this is a small study requiring replication.

While the results of Peet et al.'s trial[37] indicate placebo-controlled benefits accruing to omega-3 fatty acids as primary treatment for schizophrenia, this was a small, albeit methodologically adequate, pilot trial with little applicability to a North American population. More work is required before we can determine omega-3 fatty acids' promise in this context.

Supplemental Treatment

Peet et al.'s dose-ranging RCT of E-EPA as supplemental treatment for depression found that only 1 g/d for 12 weeks had a significant impact on various clinical outcomes.[2] Two RCTs of shorter duration also showed significant benefits associated with 2 g/d E-EPA and 6.6 g/d of EPA+DHA, respectively;[27,33] the significant clinical effect reported by Su et al. was associated with a significant increase in RBC EPA exclusively in the active treatment group.[33] However, we decided to forego meta-analysis due to study differences on the basis of the intervention (i.e., type, dose, followup length) and comparator (i.e., placebo source). Also, unlike the other two trials, Peet et al.'s did not formally identify patients with a depressive disorder.[2] This may account for their finding that 1 g/d E-EPA had a beneficial effect on depressive symptomatology.[2] A low dose might not have helped the treatment-resistant depressive disorders investigated in the other RCTs. Yet, this likely cannot explain why Peet et al.'s higher doses (2 g/d, 4 g/d) did not likewise ameliorate depressive symptoms, or why more responders (i.e., 50 percent improvement) were found in the placebo group than in the 2 g/d E-EPA group. Su et al.'s trial may have been confounded by uncontrolled combinations of medication.[33] The question of omega-3 fatty acids as supplemental treatment for depression requires additional investigation.

Two studies, one a RCT[38] and one defined merely as "controlled,"[45] evaluated the supplemental treatment of bipolar disorder. Only the RCT report gave us an opportunity to assess its study parameters and results.[38] While it had to be stopped prematurely, their very high dose of 9.6 g/d EPA+DHA produced a significantly longer period of remission in the active treatment group compared with controls. This study's limitations (i.e., loss of power due to its stoppage, broken blind) require its replication. Therefore, the evidence base is too limited to allow us to conclude anything about the value of omega-3 fatty acids as supplemental therapy for bipolar disorder. Likewise, one underpowered and flawed crossover RCT, which failed to show that E-EPA is effective as supplemental treatment for obsessive-compulsive disorder, is insufficient to permit drawing a definitive conclusion.[25]

Inconsistencies in the results produced by three RCTs, the occasional use of a complex intervention making it impossible to tease out the possible specific benefit of omega-3 fatty acids,[46] the confirmation by parents—but not by professionals—of an AD/HD diagnosis,[46] interventions that did not last long enough,[30,42,46] and failures to weight-adjust doses of omega-3 fatty acids prevent us from identifying clear conclusions about their value as supplemental treatment for AD/HD.[30,42,46]

Three of four good quality placebo-controlled RCTs investigating the supplemental treatment of schizophrenia[26,35-37] reported significant clinical effects in favor of EPA using total Positive and Negative Syndrome Scale (PANSS) scores,[26,36,37] although Peet et al.'s study observed this effect only for those receiving clozapine as primary treatment.[36] Yet, the Emsley et al. study found a nonsignificant trend towards greater reduction in total PANSS scores in participants taking typical antipsychotic medication, compared with those receiving clozapine.[26] Results of our meta-analysis of two studies' PANSS total data revealed that dose influenced outcome. A or significant placebo-controlled effect was identified for 2 g/d EPA yet not for doses of at least 3g/d EPA.[36,37] However, these results might have been different had we been able to analyze data by type of psychotropic medication, had both studies used either the purified or unpurified form of EPA as well as the same placebo oils, had their intervention periods lasted longer, or had both trials employed capsules to deliver the omega-3 fatty acids. While the findings are suggestive, they remain inconclusive given that the data subjected to meta-analysis were derived from two small trials exhibiting certain limitations.

Primary Prevention (i.e., Onset) Via Omega-3 Fatty Acid Intake

Inconsistent results, in addition to too few studies exhibiting sound methodologies or research designs that are ideally suited to investigate this question (e.g., prospective, controlled, with subject-level data), suggest that it is too early to conclude whether or not the intake of omega-3 fatty acids protects against the onset of depressive disorders or symptomatology.[1,24,28,47-55] The same issues prevent us from concluding whether or not the intake of omega-3 fatty acids protects against the onset of suicidal ideation or behavior.[51,55] Given the inability of any cross-national ecological analysis to provide meaningful subject-level data, and the failure to control for key confounders (i.e., socioeconomic status, urban/rural ratio, educational level, marital status, alcohol consumption, smoker status, or family history), we cannot conclude anything about the value of seafood consumption as protection against the onset of bipolar disorder.[56]

Two RCTs failed to clarify the protective value of omega-3 fatty acid intake with respect to the onset of symptoms, not disorders, of anxiety.[28,47] However, these small studies do not constitute optimal tests of this potential. Based on one cross-sectional study, which controlled for age, income, smoking, alcohol consumption, and eating patterns, mental health difficulties were more prevalent in those consuming no fish.[57] However, this design precludes inferring a causal link between fish consumption and the onset of mental health difficulties.

Four RCTs,[28,39,40,58] three of which enrolled healthy volunteers, one single population cross-sectional survey[59] and one cross-national ecological analysis[60] studied the possible association between omega-3 fatty acid intake and the onset of tendencies or behavior with the potential to harm others. Overall, their findings are too inconsistent and involve too few research designs permitting the drawing of causal inferences or too many different definitions of the exposure, population, or outcome to permit us to draw a consistent, individual/patient-level conclusion regarding the value of omega-3 fatty acid intake to protect against tendencies or behavior with the potential to harm others.

We could not identify the research designs which, due to their prospective and controlled nature, are most appropriate for addressing the question of the possible relationship between intake of omega-3 fatty acids (e.g., via breastfeeding) and the onset of schizophrenia. Five case-control designs,[22,61-64] one single prospective cohort,[65] and three cross-national ecological analyses[50,56,66] were found. The only prospective study was not controlled, and its followup was very short.[65] Moreover, failure to control for confounders was common (e.g., maternal feeding patterns, sex of children, maternal age, socioeconomic status, early mother-infant contact). Thus, nothing definitive can be asserted about a reliable association between omega-3 fatty acid intake and the onset of schizophrenia.

Secondary Prevention (i.e., Continuation, Recurrence) Via Omega-3 Fatty Acid Intake

One small, multiple-group cross-sectional study revealing that, relative to healthy controls, AD/HD children consumed significantly lesser amounts of linoleic acid and alpha linolenic acid (ALA) is insufficient to permit us to conclude anything definitive regarding the potential of these PUFAs to alter the course, or continuation, of AD/HD.[23] Likewise, a single RCT demonstrating that a complex intervention including omega-3 fatty acids—whose independent effect could not be ascertained—provided young adult prisoners with some protection against committing new offences[29] is insufficient to determine its capacity to prevent the recurrence of tendencies or behavior with the potential to harm others (i.e., antisocial behavior).[29]

Primary Prevention (i.e., Onset) Via Lipid Biomarker Content

Inconsistent results as well as too few studies exhibiting sound methodologies (e.g., protection against selection bias; control for smoking, alcohol use, and psychotropic medication) or research designs (e.g., prospective, controlled) that are ideally suited to investigate this question suggest that it is too early to conclude whether or not omega-3 fatty or omega-6/omega-3 acid content in biomarkers protects against the onset of depressive disorders or symptomatology. One RCT[24] and seven multiple-group cross-sectional studies[1,67-72] were included.

The inconsistency in findings across two multiple-group cross-sectional studies,[73,74] which is potentially attributable to the fact that the studies obtained their PUFA samples from different biomarker sources, in addition to the recognition that this type of research design is less than an ideal test of the research question, and the observation that the studies failed to control for different key confounders together indicate that nothing definitive can be concluded about the ability of specific lipid biomarker content to protect against the onset of bipolar disorder. Irrespective of the limited agreement in observing that both ALA and total omega-6 fatty acid levels in plasma phospholipids were significantly lower in anorexic patients compared with controls, the use of cross-sectional designs in two small studies prevent the drawing of causal inferences regarding the role of lipid biomarker content in the onset of anorexia nervosa.[75,76] Inconsistent findings from three multiple-group cross-sectional studies whose designs are of limited use in investigating the research question,[77-79] the failures to control for dietary intake,[77] to formally rule out the presence of psychopathology in the control subjects, or to employ formal diagnostic criteria (i.e., DSM-III) to identify their hyperactive subjects,[78] made it impossible to draw causal inferences about the role of omega-3 or omega-6/omega-3 fatty acid content in biomarkers to prevent the onset of AD/HD.

Three multiple-group cross-sectional studies examined the possible association of the onset of tendencies or behavior with the potential to harm others with the omega-3 or omega-6/omega-3 fatty acid content of biomarkers.[80-82] Inconsistent results, small sample sizes, and the exclusive use of cross-sectional designs preclude deriving clear inferences regarding

etiology. Two multiple-group cross-sectional studies investigated the possible association of the onset of alcoholism with the omega-3 or omega-6/omega-3 fatty acid content of biomarkers.[83,84] However, conflicting results and the use of cross-sectional designs do not allow us to draw conclusions regarding this possible etiology of alcoholism.

Medication status may have had somewhat of an influence on between-group differences in RBC or plasma phospholipid fatty acid content when the comparison group was healthy controls. However, because these data were obtained exclusively from twelve multiple-group cross-sectional studies[74,85-95] or two single prospective cohort studies with methodologic flaws,[96,97] no meaningful possibility exists to permit drawing causal inferences regarding patterns of lipid biomarker content and the onset of schizophrenia. The same criticism relating to cross-sectional designs applies to the single study examining biomarkers data with respect to the onset of autism.[98]

Secondary Prevention (i.e., Continuation, Recurrence) Via Lipid Biomarker Content

This question could not be evaluated since studies meeting eligibility criteria were not identified.

Discussion

A notable safety profile (i.e., beyond occasional and mild discomfort) for any type or dose of omega-3 fatty acid supplementation was not observed. Overall, other than for the topics of schizophrenia and depression, few efficacy or safety studies were identified.

Only with respect to the supplemental treatment of schizophrenia is the evidence even somewhat suggestive of omega-3 fatty acids' potential as short-term intervention. However, these meta-analytic results exclusively pertaining to 2 g/d EPA require replication using design and method refinements. Additional research might reveal the short-term or long-term therapeutic value of omega-3 fatty acids.

One study demonstrating a significant placebo-controlled clinical effect related to 1 g/d E-EPA given over 12 weeks to 17 patients with depressive symptoms—rather than depressive disorders—cannot be taken to support the view of the utility of this exposure as a supplemental treatment for depressive symptomatology or disorders. Nothing can yet be concluded concerning the clinical utility of omega-3 fatty acids as supplemental treatment for any other psychiatric disorder or condition, or as a primary treatment for all psychiatric disorders or conditions examined in our review. Primary treatment studies were rare.

Much more research, implementing design and methods improvements, is needed before we can begin to ascertain the possible utility of (foods or supplements containing) omega-3 fatty acids as primary prevention for psychiatric disorders or conditions. Studies of omega-3 fatty acids' primary protective potential in mental health could be "piggybacked" onto longitudinal studies of their impact on general health and development.

Overall, almost nothing is known about the therapeutic or preventive potential of each source, type, dose, or combination of omega-3 fatty acids. Likewise, limitations within the evidence base prevented us from identifying the influence of key covariables (e.g., smoking, alcohol use, psychotropic medication) on the relationship between omega-3 fatty acid content and clinical outcomes.

Because of limited study designs, little is known about the relationship between PUFA biomarker profiles and the onset of any psychiatric disorder or condition. Studies examining the possible association between the intake of omega-3 fatty acids, or the PUFA content of biomarkers, and the continuation or recurrence of psychiatric disorders or conditions were virtually nonexistent.

If future research is going to produce data that are unequivocally applicable to North Americans, it will need to enroll either North American populations or populations exhibiting a high omega-6/omega-3 fatty acid intake ratio similar to what has been observed in the diet of North Americans. Furthermore, if a reasonable view is that omega-3 fatty acids may play a role in mental health, then given the observed or proposed inter-relationships among omega-3 and omega-6 fatty acid contents both in the human diet and metabolism, researchers should likely consider taking into account the possible therapeutic or preventive influence of the dietary omega-6/omega-3 fatty acid intake ratio.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the University of Ottawa Evidence-based Practice Center under Contract No. 290-02-0021. It is expected to be available in July 2005. At that time, printed

copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 116, *Effects of Omega-3 Fatty Acids on Mental Health*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

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