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Title

Projected Long-Chain n-3 Fatty Acid Intake Post-Replacement of Vegetables Oils with SDA-Modified Varieties: Results from a NHANES 2003-2008 Analysis

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Abstract

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) intake is well below the amount recommended by the 2015-2020 Dietary Guidelines for Americans (0.25 g/d), supporting the need for alternative dietary sources. Stearidonic acid (SDA)-enriched soybeans have been bioengineered to endogenously synthesize SDA, which can be readily metabolized to EPA in humans; thus, incorporating the derived SDA-enriched soybean oil into the food supply is a potential strategy to increase EPA. We performed a dietary modeling exercise using National Health and Nutrition Examination Survey 2003-2008 repeat 24-hour dietary recall data (n=24,621) to estimate the potential contribution of SDA-enriched oils to total long-chain n-3 fatty acid intake (defined as EPA + DHA + EPA-equivalents) following two hypothetical scenarios: (1) replacement of regular soybean oil with SDA soybean oil and (2) replacement of four common vegetable oils (corn, canola, cottonseed, and soybean) with respective SDA-modified varieties. Estimated median daily intakes increased from 0.11 g/d to 0.16 g/d post-replacement of regular soybean oil with SDA-modified soybean oil, and to 0.21 g/d post-replacement of four oils with SDA-modified oil; corresponding mean intakes were 0.17, 0.27, and 0.44 g/d, respectively. The percent of the population who met the 0.25 g/d recommendation increased from at least 10% to at least 30% and 40% in scenarios 1 and 2, respectively. Additional strategies are needed to ensure the majority of the US population achieves EPA and DHA recommendations. Future modeling analyses would benefit from statistical approaches designed to estimate the distribution of usual intake of these episodically consumed nutrients.

Abbreviations and Acronyms

ALA, alpha-linolenic acid

DGA, Dietary Guidelines for Americans

DHA, docosahexaenoic acid

EPA, eicosapentaenoic acid

LNA, linoleic acid

NCHS, National Center for Health Statistics

NHANES, National Health and Nutrition Examination Survey

PUFA, polyunsaturated fatty acid(s)

SDA, stearidonic acid

USDA, United States Department of Agriculture

Introduction

Numerous authoritative agencies have issued dietary recommendations for seafood (e.g., fish and shellfish) and the long-chain n-3 polyunsaturated fatty acids (PUFA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) because of their expected cardiovascular health benefits (Bowen et al., 2016). The 2015-2020 Dietary Guidelines for Americans (DGA) recommend that the general population consume 8 ounces/week of a variety of seafood, providing an average of 0.25 grams/day (g/d) of EPA and DHA, to reduce the risk of cardiac death among those with and without cardiovascular disease (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015a). Dietary recall data from the National Health and Nutrition Examination Survey (NHANES) collectively indicate that a considerable proportion of Americans do not meet intake recommendations (Papanikolaou et al., 2014; U.S. Department of Agriculture & Agricultural Research Service, 2014; Keim & Branum, 2015; U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015a; Nordgren et al., 2017; Richter et al., 2017). For instance, we recently assessed NHANES 2003-2008 data and reported that over 80% of the total population did not meet the 0.25 g/d target for EPA and DHA (median intake of 0.11 g/d from foods), with further disparities in race/ethnicity and age and sex subgroups (Richter et al., 2017). In particular, median intakes were lowest among Mexican-Americans (0.09 g/d) and groups with higher EPA and DHA requirements [e.g., children (0.06-0.09 g/d) and women who were pregnant/lactating or of childbearing age (0.09-0.11 g/d)] (Richter et al., 2017).

One potential strategy to address the problem of insufficient EPA and DHA intake is to incorporate genetically modified vegetable oils into the food supply that have been bioengineered to endogenously produce n-3 fatty acids (Kris-Etherton et al., 2001). Whereas oily fish are a concentrated source of preformed EPA and DHA, plants and their respective oils (e.g., flaxseed, walnut, canola, soybean) provide the shorter chain n-3 fatty acid alpha-linolenic acid (ALA). ALA is the metabolic precursor of EPA; however, increasing the consumption of

ALA-containing foods is not a viable means of increasing EPA because ALA to EPA conversion is highly inefficient in humans due to the rate-limiting preceding conversion of ALA to stearidonic acid (SDA) by the Δ^6 desaturase enzyme. Oilseed crops, such as soybean (Sato et al., 2004; Eckert et al., 2006) and rapeseed (Ursin, 2003), have been bioengineered to contain the Δ^6 desaturase gene, thereby achieving this ALA to SDA conversion in the plant. The resulting oils are enriched with SDA (15-30%) (2009b), which is then more efficiently metabolized to EPA in humans after oil consumption and subsequently incorporated into cells and tissues (James et al., 2003; Krul et al., 2012). These crops were also modified to enhance the flux of the n-6 fatty acid linoleic acid (LNA) to ALA via the Δ^{15} desaturase enzyme, thus providing a more abundant substrate pool of ALA for the Δ^6 desaturase enzyme to act upon (Ursin, 2003; Eckert et al., 2006). Replacing commonly consumed vegetable oils with SDA-enriched oils may be a viable strategy for increasing long-chain n-3 fatty acids via more efficient endogenous conversion; however, the extent to which this theoretical strategy could be effective is unknown.

The objective of this project was to estimate the potential contribution of SDA-enriched oils to total long-chain n-3 fatty acids via "EPA-equivalents", which account for the potential endogenous conversion of ALA and SDA to EPA. Using NHANES 2003-2008 data we modeled total long-chain n-3 fatty acid intake (i.e., EPA + DHA + EPA-equivalents) from foods and foods plus supplements prior to and following two hypothetical scenarios: (1) replacement of regular soybean oil with SDA-enriched soybean oil, and (2) replacement of four common oils (conventional corn, canola, cottonseed, and soybean) with respective SDA-modified oils (i.e., replace corn oil with SDA corn oil). This dietary modeling exercise allowed us to evaluate whether replacement of commonly consumed vegetable oils with SDA-enriched oils offers a realistic approach for addressing insufficient long-chain n-3 fatty acid intake.

Methods

Data from NHANES were analyzed by Exponent, Inc. at the request of PEW Charitable Trusts to assess the theoretical intake of total long-chain n-3 fatty acids if common dietary oils were replaced with oils modified to provide higher amounts of the n-3 fatty acid SDA (i.e., regular soybean oil replaced by SDA-enriched soybean oil). Intakes were estimated for the total US population and the following age/sex subpopulations: children 1-6 years, children 7-12 years, men 13-19 years, women 13-19 years (not pregnant/not lactating), men 20+ years, women 20+ years (not pregnant/not lactating), women 13+ years (pregnant/lactating), and seniors 55+ years. Intakes were also estimated for the following races/ethnicities: Mexican-Americans, non-Hispanic whites, non-Hispanic blacks, and other (including multi-racial). Data from the 2003-2004, 2005-2006, and 2007-2008 survey periods (NHANES 2003-2008) were used. The National Center for Health Statistics (NCHS) recommends analysis of the Mexican-American subgroup rather than the Hispanic subgroup for the 2003-2006 and 2005-2008 survey periods due to NHANES sampling methodology (i.e., oversampling of the Mexican-American subgroup from 1999-2006 with subsequent under sampling of non-Mexican-American Hispanics, and oversampling of all Hispanic persons from 2007-2010 (U.S. Department of Health and Human Services et al., 2011); therefore, the Hispanic subgroup is not presented in this report. The combined sample included 24,621 individuals.

Estimated daily intake of total long-chain n-3 fatty acids from foods and supplements

Total long-chain n-3 fatty acid intake was defined as the sum of EPA + DHA + EPA-equivalents. EPA-equivalents were estimated from the potential conversion of ALA (5%; (Brenna, 2002; Burdge & Calder, 2005; Plourde & Cunnane, 2007)) and SDA (33%; (James et al., 2003; Harris et al., 2008; Lemke et al., 2010; Krul et al., 2012; Lemke et al., 2013)) to EPA. A detailed description of the methods used to estimate total daily long-chain n-3 fatty acid intake from foods and supplements has been described previously (Richter et al., 2017) and is summarized herein. Briefly, intake from foods was calculated from 24-hour dietary recalls conducted as part of the "What We Eat in America" component of NHANES. Analyses were limited to participants who provided two complete and reliable 24-hour dietary recalls. The United States Department of Agriculture (USDA) National Nutrient Database for Standard Reference, Release 22, was used to determine the amount of n-3 fatty acids in each food or food component and the amount consumed per participant. Estimated intake from supplements was calculated based on 30-day dietary supplement use reported by participants. Intake was estimated using a database of the n-3 fatty acid content per serving of specified supplements. Supplement labels were used to determine the n-3 fatty acid content (i.e., mg or g of ALA, DHA, EPA, EPA/DHA, etc.) whenever possible. In cases where only the n-3 fatty acid containing ingredient (e.g., flaxseed oil, fish oil, cod liver oil, etc.) was provided with no breakdown of EPA or DHA content, n-3 fatty acid content was imputed based on a conservative estimate of the proportion of n-3 fatty acids in each ingredient (e.g., 0.2 g EPA+DHA per 1.0 g of fish oil, based on menhaden oil composition).

Replacement with SDA-modified oil

Total long-chain n-3 fatty acid intake was also estimated for two theoretical scenarios in which common dietary oils were replaced with oils modified to have higher SDA content. The two modeling scenarios were: (1) replacement of regular soybean oil with SDA-enriched soybean oil; and (2) replacement of four common oils (conventional canola, corn, cottonseed, and soybean) with respective SDA-enriched oils. The four oils in the latter scenario were selected for replacement because they are commonly consumed oils in the US, particularly used as fat sources in processed and packaged foods (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015a). In replacement scenario 1, the SDA content of the modified soybean oil was assumed to be 20%. This represents the lower end of SDA yield from genetically modified soybean oil and provides a minimum estimate for the potential increase in EPA-equivalents (2009b). The ALA content of modified soybean oil is also slightly higher than regular soybean oil (9-12% versus 5-10%) (2009b); hence, 10% ALA content was also assumed for the modified soybean oil in this replacement scenario. In replacement scenario 2, soybean oil was replaced with SDA modified soybean oil and the canola, corn, and cottonseed oils were replaced by theoretical SDA modified versions of those oils. In all cases, the modified oils were assumed to have an SDA content of 30%, which is the high end of SDA yield from genetically modified soybean oil (2009b). The modified soybean oil was again assumed to have an ALA content of 10% in this scenario. Because the ALA content of theoretical modified canola, corn, and cottonseed oils is uncertain, the ALA content of the conventional oils was used for calculations of EPA-equivalents. This scenario provided a maximum potential increase in EPA-equivalents with replacement by theoretical SDA-enriched oils. The estimated EPA-equivalents provided by the modified oils in both scenarios are provided in **Table 1**. Values are reported as total long-chain n-3 fatty acid intake, but it should be noted that reported changes in relative intake under these replacement scenarios reflect increases in EPA-equivalents due to the enhanced SDA pool for conversion, not increases in preformed EPA or DHA intake. In both scenarios 1 and 2, only the conventional versions of the oils were replaced to estimate intake, not partially hydrogenated or any other modified varieties of the oils.

Results

The estimated daily intake of total long-chain n-3 fatty acids (the sum of EPA + DHA + EPA equivalents; g/d) for the US population and subgroups are presented as the mean, median, maximum, and deciles of intake on a per person basis. Intake from foods and foods plus supplements has been described elsewhere (Richter et al., 2017). Including supplement use in the scenarios did not substantially alter median or percentile values due to infrequent supplement usage; thus, estimated daily intake from foods plus supplements prior to and following the two replacement scenarios is presented in **Supplemental Table 1**.

Total US population

Estimated daily intake of total long-chain n-3 fatty acids, including from potential conversation of plant-based n-3 fatty acids (i.e., EPA-equivalents), is presented in **Table 2**. Estimated median daily intake increased from 0.11 g/d to 0.16 g/d following replacement of regular soybean oil with SDA modified soybean oil, and to 0.21 g/d following replacement of all four common oils with SDA modified oils. Estimated mean intake increased from 0.17 g/d to 0.27 g/d and to 0.44 g/d following the two replacement scenarios. The percent of the total population who met the 0.25 g/d recommendation increased from at least 10% to at least 30% with the scenario that replaced soybean oil, and to at least 40% with the scenario that replaced all four dietary oils.

Population subgroups: age and sex

Estimated daily intake of total long-chain n-3 fatty acids in the US by age and sex subgroups is presented in **Table 3**. Median and mean intakes prior to and following replacement scenarios were lowest in children 1-6 years and highest in men 20+ years. In children 1-6 years, replacement of regular soybean oil and replacement of all four common oils increased the median intake by 0.02 and 0.04 g/d, respectively; and in men 20+ years, by 0.07 and 0.15 g/d, respectively. In children 1-6 years, the percent of individuals who met the 0.25 g/d target increased from <10% to at least 10% and at least 20% with the two replacement scenarios. Predicted changes in the percent of individuals meeting this 0.25 g/d target were equivalent for children 7-12 years and women 13-19 years who were not pregnant/not lactating (from <10% to at least 20% and at least 30%). In men 13-19 years, women 20+ years (not pregnant/not lactating), and seniors 55+ years, the percent of individuals consuming 0.25 g/d increased from at least 10% to at least 30% and at least 40% post the two replacement scenarios. The percent of men 20+ years and women 13+ years (pregnant/lactating) who met the 0.25 g/d recommendation increased to at least 40% with replacement of soybean oil and at least 50% with replacement of all four oils (up from at least 20% in men and at least 10% in women).

Population subgroups: race/ethnicity

Estimated daily intake of total long-chain n-3 fatty acids among race/ethnicity categories (Mexican-American, non-Hispanic white, non-Hispanic black, and other) is presented in **Table 4**. The two replacement scenarios had the greatest impact on the Mexican-American and other categories, with the replacement of soybean oil increasing the median intake by 0.07 g/d and 0.08 g/d, and the replacement of all four oils increasing the median intake by 0.16 g/d and 0.17 g/d, respectively. In the non-Hispanic white and black subgroups, the percent of individuals who consumed 0.25 g/d increased from at least 10% to at least 30% with the two replacement scenarios. The percent of individuals in the Mexican American and the other categories who met the 0.25 g/d recommendation increased to at least 30% with replacement of soybean oil and at least 50% with replacement of all four oils (up from at least 10% for Mexican Americans and at least 20% for other).

Discussion

The present study investigates the predicted intake of total long-chain n-3 fatty acids (EPA + DHA + EPA-equivalents) following substitution of soybean oil and substitution of four commonly consumed vegetable oils (corn, canola, cottonseed, and soybean) with SDA-modified oils. In the total US population, replacing soybean oil only or replacing all four common oils increased the mean intake by 0.10 g/d and 0.27 g/d, respectively, and the median intake by 0.05 and 0.10, respectively. The percent of the total population who met the 2015-2020 DGA recommendation of 0.25 g/d of EPA and DHA increased from at least 10% to at least 30% with the replacement of soybean oil, and to at least 40% with the replacement of four oils. Analyses of age and sex subgroups showed that the proportion of pregnant/lactating women aged 13+ years who met the intake target increased from at least 10% to at least 40% and to at least 50% with the replacement of soybean oil only and all four oils, respectively. Among race/ethnicity subgroups, Mexican Americans exhibited the greatest improvement in the proportion of the population meeting the recommendation, increasing from at least 10% to at least 30% and at least 50% with the replacement scenarios. We underscore that the aforementioned shifts in the percentage of the population meeting the DGA EPA plus DHA recommendation reflect increases in EPA-equivalents, not DHA. Thus, the modeling exercise indicates that incorporating SDA-modified vegetable oils into the diet may result in modest elevations in long-chain n-3 fatty acid intake via EPA-equivalents. Additional strategies would be needed to increase the relative proportion of the total US population, and age and sex and race/ethnicity subgroups, that achieve the current EPA and DHA recommendation.

Fatty fish and fish oil are the richest sources of EPA and DHA, but low intakes are prevalent among Americans. The 2015-2020 DGA recommend 8 oz/week (or 2 servings) of a variety of seafood (estimated to provide ≈0.25 g/d of EPA + DHA) to reduce cardiovascular disease risk (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015a). Previous analyses of NHANES 2007-2010 data revealed that merely 10% of the US population consumed the 8 oz/week recommendation (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015b) and average weekly intakes of seafood for men and women of all ages were below recommended intake ranges (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015a). Further, the American Heart Association (Kris-Etherton et al., 2002, 2003) and the Academy of Nutrition and Dietetics (Vannice & Rasmussen, 2014) recommend consuming oily fish at least twice per week, which is estimated to provide ≈0.5 g/d of EPA + DHA. A 2018 update to the 2002 American Heart Association seafood intake guidelines recommended the consumption of non-fried seafood, especially species higher in long-chain n-3 fatty acids, 1 to 2 times per week for cardiovascular benefit (Rimm et al., 2018). We recently reported that over 90% of the total US population in NHANES 2003-2008 was below 0.5 g/d (mean from foods=0.17 g/d; mean from foods plus supplements=0.22 g/d) (Richter et al., 2017). Fatty fish is the preferred source of long-chain n-3 fatty acids, providing not only EPA and DHA but also other favorable nutrients that are often under consumed (i.e., vitamin D, vitamin B12) (Bowen et al., 2016) and also displacing other less healthy food choices such as those higher in saturated fat (Rimm et al., 2018). However, the consistently low EPA and DHA intake, as well as fish consumption, in the US population indicates a need to identify non-marine sources of EPA and DHA.

The food and agricultural industries have implemented a variety of approaches to increase n-3 fatty acids in the food supply, such as genetic modification of oilseed crops to produce desirable fatty acid profiles (Ursin, 2003; Sato et al., 2004; Eckert et al., 2006). SDA-enriched vegetable oils may be a plant-based alternative to fish and fish oil supplements, particularly for individuals who avoid, dislike, or have limited access to fish (Ursin, 2003). There is also an inadequate supply of EPA and DHA from fish and fish oils to meet global demand (Salem & Eggersdorfer, 2015), and SDA-enriched oils may help to address related concerns about overfishing and the sustainability of fisheries, as well as perceived risks of methyl mercury contamination from seafood (Ursin, 2003). Herein, we report that the predicted increase in mean intake reached 0.25 g/d with soybean oil replacement and approached 0.5 g/d when all four all oils were replaced. Median intakes remained below 0.25 g/d under both replacement scenarios. Additional strategies to address insufficient EPA and DHA intake could include fortification of foods (e.g., dairy (Martini et al., 2009; McCowen et al., 2010; Hughes et al., 2012), eggs (Shapira et al., 2008), meat (Meadus et al., 2013)), modification of animal feed to enrich the resulting animal products with n-3 fatty acids (Konieczka et al., 2017), or microbial fermentation for oil production (e.g., from algae) (Salem & Eggersdorfer, 2015).

Although total long-chain n-3 fatty acid (EPA + DHA + EPA-equivalents) intake was predicted to increase following replacement of soybean oil and four common oils, it should be noted that this reflected an elevation of EPA-equivalents due to estimated conversion of SDA rather than preformed EPA. Modification of oilseed crops through introduction of the Δ^6 desaturase gene allows for bioconversion of ALA to SDA, and subsequent conversion to EPA, at a more efficient rate (≈33%; (James et al., 2003; Harris et al., 2008; Lemke et al., 2010; Krul et al., 2012; Lemke et al., 2013) compared to ≈5%; (Brenna, 2002; Sato et al., 2004; Burdge & Calder, 2005; Plourde & Cunnane, 2007)); however, this does not address the limited conversion of EPA to DHA. For instance, Lemke et al. reported that 12-week supplementation of SDA soybean oil (4.2 g/d SDA) significantly increased red blood cell EPA content compared to regular soybean oil, with no effect on DHA content (Lemke et al., 2010). Similar findings were reported in trials of SDA soybean oil (3.7 g/d SDA) (Harris et al., 2008), encapsulated SDA (0.75 – 5.2 g/d SDA (James et al., 2003; Krul et al., 2012)), and baked goods and beverages with SDA soybean oil (1.6 g/d SDA) (Lemke et al., 2013). DHA is essential for the neural and visual development of infants and children, and intake in these age groups and women who are pregnant or lactating is far below the recommended amount (Joint FAO/WHO Expert Consultation, 2010). Given the importance of DHA for human health, recent plant biotechnology research efforts have been directed toward endogenous accumulation of both EPA and DHA, with successful production in the minor oilseed crop *Camelina sativa* (Ruiz-Lopez et al., 2014; Usher et al., 2017) and the major oilseed crop *Brassica napus* (rapeseed) (Walsh et al., 2016). Such an approach would simultaneously address limited consumption of both EPA and DHA.

Incorporation of n-3 modified oils into the food supply raises the possibility of excess consumption. However, a threshold at which adverse effects may occur is not quantitatively well defined, and theoretical concerns regarding potential bleeding or other risks with elevated n-3 fatty acid intakes have not been demonstrated in clinical settings (Wachira et al., 2014). The Institute of Medicine has deemed that there is insufficient evidence to establish a tolerable upper intake level for EPA and DHA (Institute of Medicine of the National Academies, 2002). The US Food and Drug Administration concluded that up to 3 g/d of total EPA and DHA from foods and supplements is generally recognized as safe (U. S. Food and Drug Administration, 2000), and the European Food Safety Authority reported no safety concerns up to 5 g/d (Eurpoean Food Safety Authority Panel on Dietetic Products Nutrition and Allergies, 2012). Guidelines for maximum intake of SDA have not been proposed, presumably due to minor intakes from naturally occurring marine (i.e., mackerel, seaweed) and plant (i.e., echium oil, currant seed oil) sources of SDA (Whelan, 2009). Numerous safety assessments of SDA intake in humans report no adverse treatment-related effects, including following 12 weeks of 4.2 g/d of SDA oil (Lemke et al., 2010) and 5.2 g/d of SDA capsules (Krul et al., 2012). SDA-modified soybean oil also received generally recognized as safe status by the Food and Drug Administration (2009a). Herein, men 20+ years and women 13+ years (pregnant/lactating) had the greatest value in the 90th decile of total long-chain n-3 fatty acid intake post-replacement of four common oils (1.33 g/d). Thus, neither replacement scenario exceeded maximum long-chain n-3 fatty acid consumption guidelines for at least 90% of the total population and subgroups.

Strengths and limitations

We used a dietary modeling framework with NHANES data to evaluate the potential change in total long-chain n-3 fatty acid intake. The strengths and limitations of using NHANES data for estimation of population level intake of n-3 fatty acids have been discussed previously (Richter et al., 2017). Similar exercises substituting dietary oils to increase or decrease the intake of targeted fatty acids for improved dietary guideline compliance have been reported (Johnson et al., 2007; Lefevre et al., 2012). These 2003-2008 NHANES data provide an important benchmark of intake prior to federal EPA and DHA guidelines, as the 2005-2010 DGA did not include specific recommendations for these nutrients (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2005). Future substitution analyses would benefit from re-evaluating n-3 PUFA consumption using the most recent NHANES data to assess implementation and impact of the 0.25 g/d recommendation introduced in the 2010-2015 DGA (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2010) and maintained in the 2015-2020 DGA (U.S. Department of Agriculture & U.S. Department of Health and Human Services, 2015a). Future analyses would also benefit from statistical approaches designed to estimate the distribution of usual intake of episodically consumed nutrients, such as the National Cancer Institute method. The use of repeat 24-hour dietary recall assessments to estimate usual intake of long chain n-3 fatty acids is limited by within-individual variability across days of intake, which can overestimate the spread of the distribution around the mean. Further modeling of shifts in other fatty acids, such as ALA and LNA, following introduction of modified oils to the food supply is also of interest. Oil produced from SDA-enriched soybean plants is comprised of 15-30% SDA (2009b), which is the basis for the estimated SDA content in the theoretical n-3 modified oils. The scenario in which only regular soybean oil was replaced assumed 20% SDA oil (i.e., 20 g SDA per 100 g soybean oil) to provide a conservative estimate of total long-chain n-3 fatty acid intake (EPA + DHA + EPA-equivalents) if a modified oil entered the food supply and replaced its conventional counterpart. For the second scenario, reflecting maximal potential impact, estimation of EPA-equivalents following replacement of four common oils assumed a 30% SDA oil content (i.e., 30 g SDA per 100 g oil). This substitution model represents a theoretical situation in which 100% of the traditional soybean, corn, canola, and cottonseed oils are replaced with SDA-modified oils. This approach was chosen to represent a "maximum levels" scenario in which additional, theoretical SDA-modified oils had been developed and used to replace the conventional version of these four commonly consumed oils. This scenario is unlikely as it is neither practical nor is there strong scientific evidence to support such a drastic modification of the food supply. Rather, we present this simulation as a study about the potential impacts of SDA-modified vegetable oils and the extent by which they may increase EPA-equivalents via endogenous conversion of

SDA. The calculation of EPA-equivalents used the upper end of reported conversion efficiencies for estimating the conversion of ALA to EPA (5%) and SDA to EPA (33%); however, the accuracy of these metabolic conversion rates should be interpreted with caution. Evidence suggests that the methodologies used to estimate conversion of ALA to longer-chain n-3 fatty acids may under estimate the true synthetic capacity and do not capture tissue-dependent variation in conversion (Barcelo-Coblijn & Murphy, 2009; Domenichiello et al., 2015). Further, SDA conversion to longer-chain n-3 fatty acids in children has not been assessed and, thus, interpretation of estimated intake in the respective age and sex subgroups is limited. Additional limitations of this modeling include the practicality of directly exchanging dietary oils. Testing of commercial products containing SDA-modified oil and consumer acceptability is ongoing (Whittinghill & Welsby, 2010; Pande et al., 2012); however, genetically modified foods have traditionally faced consumer resistance (Yang & Chen, 2016). While SDA-modified oil has better oxidative stability compared to EPA and DHA-containing oils due to the lower unsaturation and higher antioxidant content, SDA-modified oil is susceptible to lipid oxidation (Decker et al., 2012). Thus, it may be a challenge to replace conventional oils comprised of fatty acids with a lesser degree of unsaturation, particularly those used in food products requiring high-heat and shelf stability. As such, current efforts in the edible oils industry have shifted toward the development of high-monounsaturated fatty acid, low-PUFA oils with enhanced oxidative stability (Huth et al., 2015); however, this will not address insufficiency of EPA and DHA intake. In addition, future research is needed to determine if there are independent biological effects of SDA intake in humans, apart from serving as a precursor to EPA.

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supplements prior to and following the replacement scenarios for the US population and age, sex, and race/ethnicity subgroups.

Conflicts of Interest

KJB reports a travel grant from the Global Organization for EPA and DHA Omega-3s (GOED). CKR and ACS-R have no conflict of interest. DM reports honoraria or consulting from Astra Zeneca, Acasti Pharma, GOED, DSM, Haas Avocado Board, Nutrition Impact, Pollock Communications, and Boston Heart Diagnostics; scientific advisory board, Omada Health and Elysium Health; chapter royalties from UpToDate; and research funding from the National Institutes of Health and the Gates Foundation. PMK-E reports research funding from the California Walnut Commission and serves without compensation on the scientific advisory board for the Seafood Nutrition Partnership.

Table 1. EPA-equivalents provided by four common dietary oils at baseline and under theoretical scenarios in which the conventional oils were replaced by oils modified to provide higher amounts of the n-3 fatty acid SDA (g EPA-equivalents /100 g oil).

Oil	Baseline	Replacement Scenario 1 [a]	Replacement Scenario 2 [b]
Soybean	0.34	7.10	10.4
Cottonseed	0.01	-	9.91
Corn	0.06	-	9.96
Canola	0.46	-	10.36

[a] This scenario replaces regular soybean with n-3 modified soybean oil and assumes 20% SDA content in the modified oil. This provides a minimum estimate for the potential increase in EPA-equivalents using n-3 modified soybean oil.
[b] This scenario replaces soybean, cottonseed, corn, and canola oil with hypothetical oils modified to provide 30% SDA content. This provides a maximum estimate for the potential increase in EPA-equivalents if n-3 modified oils were used to replace the conventional forms of these oils.

Table 2. Estimated daily intake of total long-chain n-3 fatty acids (g/d) from foods and under the replacement scenarios in the total US population [a]

Description	Sample size	Mean	Median	Max	Percentiles								
					10th	20th	30th	40th	50th	60th	70th	80th	90th
Intake from foods [b]	24536	0.17	0.11	4.28	0.04	0.06	0.07	0.09	0.11	0.13	0.16	0.21	0.34
Intake from foods post-replacement of soybean oil	24536	0.27	0.16	4.66	0.05	0.07	0.10	0.12	0.16	0.21	0.28	0.39	0.64
Intake from foods post-replacement of four common oils	24536	0.44	0.21	8.25	0.05	0.08	0.11	0.15	0.21	0.30	0.43	0.67	1.13

[a] Intake of total long chain n-3 fatty acids is defined as EPA + DHA + EPA-equivalents (5% of ALA converted to EPA, 33% of SDA converted to EPA). Changes under the replacement scenarios reflect increases in EPA-equivalents due to the enhanced SDA pool for conversion, not increases in preformed EPA or DHA intake.
[b] Data from Richter et al. reproduced with permission for direct comparison with the two oil replacement scenarios (Richter et al., 2017).

Table 3. Estimated daily intake of total long-chain n-3 fatty acids (g/d) from foods and under the replacement scenarios for US age and sex subgroups [a]

Description	Sample size	Mean	Median	Max	Percentiles								
					10th	20th	30th	40th	50th	60th	70th	80th	90th
Children 1-6 years													
Intake from foods [b]	3354	0.08	0.06	1.38	0.03	0.04	0.05	0.05	0.06	0.07	0.08	0.10	0.14
Intake from foods post-replacement of soybean oil	3354	0.13	0.08	1.73	0.04	0.05	0.06	0.07	0.08	0.10	0.13	0.18	0.27
Intake from foods post-replacement of four common oils	3354	0.21	0.10	4.05	0.04	0.05	0.06	0.08	0.10	0.14	0.20	0.29	0.46
Children 7-12 years													
Intake from foods [b]	2846	0.12	0.09	1.52	0.04	0.05	0.06	0.08	0.09	0.10	0.11	0.15	0.20
Intake from foods post-replacement of soybean oil	2846	0.19	0.12	3.20	0.05	0.06	0.08	0.10	0.12	0.15	0.19	0.27	0.39
Intake from foods post-replacement of four common oils	2846	0.30	0.15	7.86	0.05	0.07	0.09	0.11	0.15	0.21	0.30	0.43	0.71
Men 13-19 years													
Intake from foods [b]	2125	0.16	0.11	2.70	0.04	0.06	0.08	0.09	0.11	0.13	0.16	0.19	0.28
Intake from foods post-replacement of soybean oil	2125	0.26	0.15	3.26	0.05	0.08	0.10	0.13	0.15	0.19	0.25	0.35	0.62
Intake from foods post-replacement of four common oils	2125	0.43	0.18	8.04	0.05	0.09	0.11	0.14	0.18	0.25	0.37	0.58	1.12
Women 13-19 years (not pregnant/not lactating)													
Intake from foods [b]	2071	0.12	0.09	1.88	0.04	0.05	0.06	0.07	0.09	0.10	0.12	0.15	0.23
Intake from foods post-replacement of soybean oil	2071	0.24	0.13	3.50	0.04	0.06	0.08	0.10	0.13	0.17	0.23	0.33	0.56
Intake from foods post-replacement of four common oils	2071	0.44	0.16	8.25	0.05	0.06	0.09	0.12	0.16	0.24	0.38	0.61	1.04
Men 20+ years													
Intake from foods [b]	6113	0.23	0.14	4.10	0.06	0.08	0.10	0.12	0.14	0.17	0.21	0.28	0.47

Description	Sample size	Mean	Median	Max	Percentiles								
					10th	20th	30th	40th	50th	60th	70th	80th	90th
Intake from foods post-replacement of soybean oil	6113	0.34	0.21	4.66	0.07	0.10	0.13	0.17	0.21	0.27	0.36	0.50	0.76
Intake from foods post-replacement of four common oils	6113	0.54	0.29	6.92	0.07	0.11	0.15	0.21	0.29	0.40	0.57	0.82	1.33
Women 20+ years (not pregnant/not lactating)													
Intake from foods [b]	6139	0.17	0.11	4.28	0.04	0.06	0.07	0.09	0.11	0.12	0.15	0.21	0.34
Intake from foods post-replacement of soybean oil	6139	0.28	0.16	4.66	0.05	0.07	0.10	0.12	0.16	0.21	0.29	0.41	0.65
Intake from foods post-replacement of four common oils	6139	0.45	0.22	7.77	0.05	0.08	0.11	0.15	0.22	0.32	0.46	0.70	1.13
Women 13+ years (pregnant/lactating)													
Intake from foods [b]	723	0.17	0.11	1.66	0.05	0.07	0.09	0.09	0.11	0.12	0.15	0.23	0.34
Intake from foods post-replacement of soybean oil	723	0.30	0.20	2.27	0.07	0.09	0.11	0.15	0.20	0.25	0.37	0.43	0.69
Intake from foods post-replacement of four common oils	723	0.51	0.30	5.49	0.07	0.10	0.13	0.20	0.30	0.42	0.57	0.77	1.33
Seniors 55+ years													
Intake from foods [b]	5326	0.19	0.11	3.66	0.05	0.06	0.08	0.09	0.11	0.14	0.17	0.24	0.40
Intake from foods post-replacement of soybean oil	5326	0.29	0.17	3.69	0.05	0.08	0.10	0.13	0.17	0.22	0.30	0.43	0.65
Intake from foods post-replacement of four common oils	5326	0.44	0.22	6.92	0.06	0.08	0.11	0.15	0.22	0.32	0.45	0.69	1.11

[a] Intake of total long chain n-3 fatty acids is defined as EPA + DHA + EPA-equivalents (5% of ALA converted to EPA, 33% of SDA converted to EPA). Changes under the replacement scenarios reflect increases in EPA-equivalents due to the enhanced SDA pool for conversion, not increases in preformed EPA or DHA intake.

[b] Data from Richter et al. reproduced with permission for direct comparison with the two oil replacement scenarios (Richter et al., 2017).

Table 4. Estimated daily intake of total long-chain n-3 fatty acids (g/d) from foods and under the replacement scenarios for US race and ethnicity subgroups [a]

Description	Sample size	Mean	Median	Max	Percentiles								
					10th	20th	30th	40th	50th	60th	70th	80th	90th
Mexican-American [b]													
Intake from foods [c]	6027	0.16	0.09	2.68	0.04	0.05	0.07	0.08	0.09	0.11	0.14	0.18	0.30
Intake from foods post-replacement of soybean oil	6027	0.27	0.16	3.48	0.05	0.07	0.10	0.13	0.16	0.21	0.28	0.40	0.62
Intake from foods post-replacement of four common oils	6027	0.48	0.25	8.04	0.05	0.09	0.13	0.18	0.25	0.37	0.51	0.76	1.23
Non-Hispanic White													
Intake from foods [c]	10044	0.17	0.11	4.10	0.04	0.06	0.07	0.09	0.11	0.13	0.16	0.21	0.34
Intake from foods post-replacement of soybean oil	10044	0.27	0.15	4.66	0.05	0.07	0.09	0.12	0.15	0.20	0.27	0.39	0.64
Intake from foods post-replacement of four common oils	10044	0.43	0.20	8.25	0.05	0.08	0.10	0.14	0.20	0.29	0.42	0.65	1.11
Non-Hispanic Black													
Intake from foods [c]	5960	0.18	0.11	4.28	0.04	0.06	0.08	0.09	0.11	0.14	0.17	0.23	0.36
Intake from foods post-replacement of soybean oil	5960	0.27	0.16	4.66	0.05	0.07	0.10	0.12	0.16	0.21	0.28	0.38	0.64
Intake from foods post-replacement of four common oils	5960	0.43	0.19	7.86	0.05	0.08	0.10	0.14	0.19	0.28	0.40	0.60	1.07
Other													
Intake from foods [c]	1035	0.23	0.12	3.66	0.04	0.06	0.08	0.10	0.12	0.15	0.18	0.27	0.51
Intake from foods post-replacement of soybean oil	1035	0.34	0.20	3.69	0.05	0.08	0.12	0.16	0.20	0.24	0.34	0.50	0.71
Intake from foods post-replacement of four common oils	1035	0.52	0.29	5.21	0.06	0.09	0.15	0.20	0.29	0.40	0.56	0.79	1.23

[a] Intake of total long chain n-3 fatty acids is defined as EPA + DHA + EPA-equivalents (5% of ALA converted to EPA, 33% of SDA converted to EPA). Changes under the replacement scenarios reflect increases in EPA-equivalents due to the enhanced SDA pool for conversion, not increases in preformed EPA or DHA intake.
[b] Analysis of the Mexican-American subgroup rather than the Hispanic subgroup is strongly recommended by NCHS for NHANES 2003-2006 and 2005-2008 survey periods due to sampling methodology used during those time periods (U.S. Department of Health and Human Services et al., 2011).
[c] Data from Richter et al. reproduced with permission for direct comparison with the two oil replacement scenarios (Richter et al., 2017).

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