Fish, Shellfish, and Children’s Health: An Assessment of Benefits, Risks, and Sustainability

Aaron S. Bernstein, MD, MPH, FAAP, Emily Oken, MD, MPH, Sarah de Ferranti, MD, MPH, FAAP

COUNCIL ON ENVIRONMENTAL HEALTH, COMMITTEE ON NUTRITION

American children eat relatively little fish and shellfish in comparison with other sources of animal protein, despite the health benefits that eating fish and shellfish may confer. At the same time, fish and shellfish may be sources of toxicants. This report serves to inform pediatricians about available research that elucidates health risks and benefits associated with fish and shellfish consumption in childhood as well as the sustainability of fish and shellfish harvests.

Fish and shellfish are, in general, good sources of low-fat protein rich in several essential vitamins and minerals as well as, in certain instances, the essential nutrients omega-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs). Some guidance is available and accessible to pediatric health care providers or families to assist them with navigating fish and shellfish choices, but most sources focus on consumption by adults or pregnant women and do not directly address childhood consumption. This report provides an overview of the potential risks and benefits associated with childhood consumption of fish and shellfish. Whenever possible, it draws on research performed with children. However, in instances when such evidence is not available, it will examine prenatal and adult evidence.

This report also addresses the sustainability of fish and shellfish choices. Approximately 90% of fisheries worldwide are exploited at or above maximum sustainable yield. As a result, any guidance on fish consumption must consider sustainability to protect the viability of fisheries.

An overview of the report can be found in Table 1.

NUTRIENT VALUE OF FISH CONSUMPTION
All fish are protein dense and have little or no sugar or saturated fat. Many species contain high levels of vitamin D and calcium. Some shellfish
species have high iron content. Other trace nutrients, such as selenium and iodine, are present in many fish and shellfish species as well. The health benefits of consumption of these nutrients have been documented extensively elsewhere²–⁷ and will not be reviewed here, but a summary table describing which fish and shellfish species provide various nutrients is provided in Table 2.

Some fish are a rich source of the n-3 LCPUFAs, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). n-3 LCPUFAs are essential nutrients and, as such, must be consumed in the diet. Humans also can elongate and desaturate short-chain “parent” polyunsaturated fatty acids such as linoleic acid, present in nuts and seeds, into LCPUFAs, but this process is inefficient and unlikely to result in sufficient levels for optimal health among most individuals.⁸ Fish are the primary natural dietary source for DHA and EPA. These fatty acids can also be concentrated from algal sources and in this form have been added to infant formula and foods such as milk, yogurt, and pasta and increasingly are taken as supplements. n-3 LCPUFAs are structural components of neurons in the brain and eye and have anti-inflammatory and immunomodulatory properties, and many researchers have investigated the potential benefits of fish or n-3 LCPUFA consumption in early life for neurodevelopmental and atopic outcomes, which are summarized in later sections of this report.

STUDIES OF FISH CONSUMPTION

Prevention of Allergic Disease

The majority of observational studies conducted to date have shown that maternal fish consumption likely...
TABLE 2 Nutritional and Toxicant Contents for Various Animal Based Foods (Per 100 g Raw, Unless Otherwise Specified)

| Kcal | Protein (g) | Total fat (g) (rounded to nearest whole No.) | Sat fat (g) (rounded to nearest whole No.) | Cholesterol (mg) | DHA + EPA omega-3 (mg) | Calcium (mg) | Vitamin D (IU) | Iron (mg) | Mercury mean\(^a\) (CV) (mg/kg (ppm))\(^b\) |
|------|-------------|---------------------------------------------|------------------------------------------|-----------------|------------------------|------------|--------------|---------|----------------|----------------|
| Fish |             |                                              |                                          |                 |                        |            |              |         |                |                |
| Catfish | 95          | 16                                           | 3                                        | 1               | 58                     | 364        | 14           | 500     | 0.3             | 0.118 (4.97)   |
| Atlantic cod | 82          | 18                                           | 1                                        | 0               | 43                     | 184        | 16           | 36      | 0.4             | 0.070 (3.70)   |
| Flounder | 70          | 12                                           | 2                                        | 0               | 45                     | 245        | 21           | 113     | 0.2             | 0.119 (3.42)   |
| Haddock | 74          | 16                                           | 1                                        | 0               | 54                     | 131        | 11           | 18      | 0.2             | 0.164 (4.59)   |
| Halibut (Pacific) | 91     | 19                                           | 1                                        | 0               | 49                     | 194        | 7            | 190     | 0.8             | 0.261 (4.32)   |
| Pangasius, swai, or basa\(^c\) | 74   | 15                                           | 2                                        | 0               | 36                     | 0          | 10           | 54      | 0.1             | 0.395 (6.95)   |
| Pollock, Alaskan\(^d\) | 70   | 17                                           | 0                                        | 0               | 61                     | 62         | 15           | 73      | 0.22            | 0.58 (5.35)    |
| Rainbow trout (wild) | 119  | 20                                           | 3                                        | 1               | 59                     | 587        | 67           | 265     | 0.7             | 0.344 (5.00)   |
| Salmon (farmed Atlantic) | 208  | 20                                           | 13                                       | 3               | 55                     | 1866       | 9            | 441     | 0.3             | 0.026 (2.91)   |
| Salmon (wild Alaskan Chinook or King) | 187 | 20                                           | 12                                       | 2               | 61                     | 1150       | 42           | 425     | 0.8             | 0.067 (1.59)   |
| Sardine, Atlantic canned in oil, with bone | 208 | 25                                           | 11                                       | 2               | 142                    | 1480       | 382          | 193     | 2.9             | 0.079 (2.56)   |
| Swordfish | 144         | 20                                           | 7                                        | 2               | 66                     | 754        | 5            | 556     | 0.4             | 0.893 (2.30)   |
| Tilapia | 96          | 20                                           | 2                                        | 1               | 50                     | 91         | 10           | 124     | 0.6             | 0.019 (4.99)   |
| Tuna (albacore, canned in water) | 128 | 24                                           | 3                                        | 1               | 42                     | 862        | 14           | 80\(^a\) | 1.0             | 0.328 (2.92)   |
| Tuna (light or skipjack, canned in water) | 116 | 26                                           | 1                                        | 0               | 30                     | 281        | 11           | 47      | 1.5             | 0.118 (2.55)   |
| Tuna (yellowfin) | 109 | 24                                           | 1                                        | 0               | 39                     | 100        | 4            | 69      | 0.8             | 0.143 (4.80)   |
| Shellfish |             |                                              |                                          |                 |                        |            |              |         |                |                |
| Blue crab | 87          | 18                                           | 1                                        | 0               | 78                     | 549        | 89           | 0       | 0.7             | 0.110 (5.40)   |
| Clams\(^f\) | 86        | 15                                           | 1                                        | 0               | 30                     | 107        | 39           | 1       | 1.6             | 0.028          |
| Lobster | 77          | 17                                           | 1                                        | 0               | 127                    | 176        | 84           | 0       | 0.3             | 0.153 (2.08)   |
| Scallops | 68          | 12                                           | 3                                        | 0               | 24                     | 106        | 6            | 1       | 0.4             | 0.40 (3.65)    |
| Shrimp | 85          | 20                                           | 1                                        | 0               | 161                    | 61         | 64           | 0       | 1.62            | 0.053 (4.03)   |
| Other animal protein |             |                                              |                                          |                 |                        |            |              |         |                |                |
| Bologna (beef) | 299       | 11                                           | 26                                       | 10              | 57                     | 4          | 21           | 28      | 1.3             | ND             |
| Chicken breast with skin | 172     | 21                                           | 9                                        | 3               | 64                     | 30         | 11           | 16      | 0.7             | 0\(^f\)         |
| Chicken leg with skin | 214    | 16                                           | 16                                       | 4               | 79                     | 14         | 8            | 2       | 0.7             | 0\(^f\)         |
| Eggs | 143          | 6                                            | 5                                        | 3               | 186                    | 58         | 56           | 82      | 1.8             | 0\(^f\)         |
| Milk, whole (with vitamin D supplemented) | 61 | 3                                            | 3                                        | 2               | 10                     | 0          | 113          | 51      | 0\(^f\) (NA)   |
| Pork chops, meat and fat | 170        | 20                                           | 9                                        | 3               | 69                     | 0          | 19           | 21      | 0.63            | ND             |
| Sirloin steak, trimmed to 1/8\(^b\) fat | 201 | 20                                           | 13                                       | 5               | 75                     | 0          | 24           | 7\(^b\) | 1.61            | ND             |

Nutritional data from US Department of Agriculture Food Composition Database unless otherwise noted (https://ndb.nal.usda.gov/ndb/foods). Typical seafood serving size (84 g/3 oz). Recommended daily allowances: Vitamin D: 600 IU, ages 1–18 years, male or female. Calcium: 0–6 months, 200 mg; 7–12 months, 260 mg; 1–3 years, 700 mg; 4–8 years, 1 g; 9–18 years, 1.3 g; iron: 0–6 months, 0.27 mg; 7–12 months, 11 g; 1–3 years, 7 mg; 4–8 years, 10 mg; 9–15 years, 14 mg; 11–15 mg (male or female); pregnant women, 27 mg; lactating women, 10 mg; CV, coefficient of variation; NA, not applicable; ND, no data.

\(^a\) Mercury data from Karimi R, Fitzgerald TP, Fisher NS. A quantitative synthesis of mercury in commercial seafood and implications for exposure in the United States. Environ Health Perspect. 2012;120(11):1512–1519. The FDA has set an action level of 1 ppm per edible portion. Fish that exceed this level may be pulled from the marketplace by the FDA.

\(^b\) More detailed information on mercury content of seafood can be found in Table 3.


\(^d\) Omega 3, calcium, vitamin D, and iron data from Canada’s nutrient profile database, as values were unavailable from US Department of Agriculture. Available at: https://food.nutrition.canada.ca/cnf-fce/index-eng.jsp

\(^e\) Vitamin D data from Canada’s nutrient profile database, as values were unavailable from US Department of Agriculture. Available at: https://food.nutrition.canada.ca/cnf-fce/index-eng.jsp

\(^f\) Vitamin D content for wild Chinook salmon obtained from Nutrition Canada’s nutrient profile database, as values were unavailable from US Department of Agriculture. Available at: https://food.nutrition.canada.ca/cnf-fce/index-eng.jsp

\(^g\) US Department of Agriculture nutrition information based on “mixed” species. Mercury data for clams includes softshell, Pacific littleneck, cookie, geoduck, and hard.

\(^h\) Data from FDA Market Basket studies 1996–2011. Available at: http://www.fda.gov/downloads/Food/FoodScienceResearch/TotalDietStudy/UCM184301.pdf

\(^i\) Vitamin D data from Canada’s nutrient profile database, as values were unavailable from US Department of Agriculture. Available at: https://food.nutrition.canada.ca/cnf-fce/index-eng.jsp

\(^j\) US Department of Agriculture nutrition information based on “mixed” species. Mercury data for clams includes softshell, Pacific littleneck, cookie, geoduck, and hard.

\(^k\) Data from Nutrition Canada’s nutrient profile database, as values were unavailable from US Department of Agriculture. Available at: https://food.nutrition.canada.ca/cnf-fce/index-eng.jsp

\(^\) ND.

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TABLE 3 MeHg Content of Selected Fish (Adapted from Karimi et al)

<table>
<thead>
<tr>
<th>Seafood Item</th>
<th>Mean Hg (ppm)</th>
<th>Samples (Total)</th>
<th>SDw</th>
<th>SEw</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anchovies (all)</td>
<td>0.103</td>
<td>455</td>
<td>0.197</td>
<td>0.041</td>
</tr>
<tr>
<td>Bass (Chilean)</td>
<td>0.357</td>
<td>100</td>
<td>0.185</td>
<td>0.041</td>
</tr>
<tr>
<td>Bass (freshwater, all)</td>
<td>0.170</td>
<td>149</td>
<td>0.361</td>
<td>0.059</td>
</tr>
<tr>
<td>Bass (saltwater, black, white, striped)</td>
<td>0.288</td>
<td>1660</td>
<td>1.004</td>
<td>0.150</td>
</tr>
<tr>
<td>Bass, striped (all)</td>
<td>0.285</td>
<td>1367</td>
<td>1.155</td>
<td>0.140</td>
</tr>
<tr>
<td>Bass, striped (farmed)</td>
<td>0.028</td>
<td>15</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Bass, striped (wild)</td>
<td>0.285</td>
<td>1311</td>
<td>1.147</td>
<td>0.154</td>
</tr>
<tr>
<td>Bluefish</td>
<td>0.351</td>
<td>1019</td>
<td>0.963</td>
<td>0.145</td>
</tr>
<tr>
<td>Butterfish</td>
<td>0.054</td>
<td>109</td>
<td>0.112</td>
<td>0.021</td>
</tr>
<tr>
<td>Carp (all)</td>
<td>0.156</td>
<td>477</td>
<td>0.521</td>
<td>0.095</td>
</tr>
<tr>
<td>Catfish (all)</td>
<td>0.118</td>
<td>1757</td>
<td>0.586</td>
<td>0.067</td>
</tr>
<tr>
<td>Catfish (wild, all species)</td>
<td>0.144</td>
<td>1396</td>
<td>0.513</td>
<td>0.078</td>
</tr>
<tr>
<td>Catfish, channel (wild)</td>
<td>0.120</td>
<td>521</td>
<td>0.253</td>
<td>0.058</td>
</tr>
<tr>
<td>Catfish farmed, all species</td>
<td>0.012</td>
<td>320</td>
<td>0.073</td>
<td>0.008</td>
</tr>
<tr>
<td>Clams (all)</td>
<td>0.028</td>
<td>1027</td>
<td>0.177</td>
<td>0.032</td>
</tr>
<tr>
<td>Clams, hard</td>
<td>0.047</td>
<td>181</td>
<td>0.130</td>
<td>0.026</td>
</tr>
<tr>
<td>Clams, geoduck</td>
<td>0.030</td>
<td>11</td>
<td>0.049</td>
<td>0.021</td>
</tr>
<tr>
<td>Clams, cockle</td>
<td>0.054</td>
<td>122</td>
<td>0.404</td>
<td>0.073</td>
</tr>
<tr>
<td>Clams, Pacific littleneck</td>
<td>0.022</td>
<td>18</td>
<td>0.022</td>
<td>0.009</td>
</tr>
<tr>
<td>Clams, softshell</td>
<td>0.016</td>
<td>471</td>
<td>0.249</td>
<td>0.020</td>
</tr>
<tr>
<td>Cod (all)</td>
<td>0.087</td>
<td>2115</td>
<td>0.358</td>
<td>0.058</td>
</tr>
<tr>
<td>Cod, Atlantic (farmed)</td>
<td>0.034</td>
<td>24</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cod, Atlantic (wild)</td>
<td>0.070</td>
<td>1452</td>
<td>0.261</td>
<td>0.017</td>
</tr>
<tr>
<td>Cod, Pacific</td>
<td>0.144</td>
<td>431</td>
<td>0.260</td>
<td>0.058</td>
</tr>
<tr>
<td>Crab (all)</td>
<td>0.088</td>
<td>1584</td>
<td>0.453</td>
<td>0.086</td>
</tr>
<tr>
<td>Crab (blue, king, and snow)</td>
<td>0.091</td>
<td>1077</td>
<td>0.529</td>
<td>0.098</td>
</tr>
<tr>
<td>Crab, blue</td>
<td>0.110</td>
<td>864</td>
<td>0.594</td>
<td>0.103</td>
</tr>
<tr>
<td>Crab, Dungeness</td>
<td>0.120</td>
<td>264</td>
<td>0.225</td>
<td>0.057</td>
</tr>
<tr>
<td>Crab, king</td>
<td>0.027</td>
<td>203</td>
<td>0.154</td>
<td>0.032</td>
</tr>
<tr>
<td>Crab, snow</td>
<td>0.110</td>
<td>20</td>
<td>0.187</td>
<td>0.073</td>
</tr>
<tr>
<td>Crawfish (all)</td>
<td>0.034</td>
<td>206</td>
<td>0.104</td>
<td>0.019</td>
</tr>
<tr>
<td>Croaker (all)</td>
<td>0.092</td>
<td>856</td>
<td>0.308</td>
<td>0.058</td>
</tr>
<tr>
<td>Croaker, Atlantic</td>
<td>0.069</td>
<td>572</td>
<td>0.135</td>
<td>0.025</td>
</tr>
<tr>
<td>Croaker, white</td>
<td>0.169</td>
<td>193</td>
<td>0.344</td>
<td>0.066</td>
</tr>
<tr>
<td>Cuttlefish</td>
<td>0.134</td>
<td>156</td>
<td>0.275</td>
<td>0.085</td>
</tr>
<tr>
<td>Eel (all)</td>
<td>0.186</td>
<td>986</td>
<td>0.608</td>
<td>0.111</td>
</tr>
<tr>
<td>Eel (wild)</td>
<td>0.216</td>
<td>659</td>
<td>0.551</td>
<td>0.110</td>
</tr>
<tr>
<td>Eel (farmed)</td>
<td>0.086</td>
<td>220</td>
<td>0.163</td>
<td>0.027</td>
</tr>
<tr>
<td>Flatfish (Flounder, plaice, sole)</td>
<td>0.115</td>
<td>3070</td>
<td>0.417</td>
<td>0.079</td>
</tr>
<tr>
<td>Flounder (all)</td>
<td>0.119</td>
<td>1687</td>
<td>0.380</td>
<td>0.075</td>
</tr>
<tr>
<td>Flounder, summer</td>
<td>0.121</td>
<td>427</td>
<td>0.216</td>
<td>0.042</td>
</tr>
<tr>
<td>Flounder, windowpane</td>
<td>0.152</td>
<td>84</td>
<td>0.152</td>
<td>0.057</td>
</tr>
<tr>
<td>Flounder, winter</td>
<td>0.070</td>
<td>302</td>
<td>0.228</td>
<td>0.059</td>
</tr>
<tr>
<td>Freshwater perch (all)</td>
<td>0.141</td>
<td>1285</td>
<td>0.745</td>
<td>0.110</td>
</tr>
<tr>
<td>Groupers (all)</td>
<td>0.147</td>
<td>643</td>
<td>0.904</td>
<td>0.196</td>
</tr>
<tr>
<td>Haddock (all)</td>
<td>0.164</td>
<td>226</td>
<td>0.752</td>
<td>0.166</td>
</tr>
<tr>
<td>Hake (all)</td>
<td>0.146</td>
<td>739</td>
<td>0.489</td>
<td>0.090</td>
</tr>
<tr>
<td>Halibut (all)</td>
<td>0.254</td>
<td>3532</td>
<td>0.703</td>
<td>0.060</td>
</tr>
<tr>
<td>Halibut, Pacific</td>
<td>0.261</td>
<td>3111</td>
<td>1.127</td>
<td>0.053</td>
</tr>
<tr>
<td>Halibut, Greenland</td>
<td>0.183</td>
<td>138</td>
<td>0.630</td>
<td>0.120</td>
</tr>
<tr>
<td>Herring (all)</td>
<td>0.043</td>
<td>1277</td>
<td>0.174</td>
<td>0.026</td>
</tr>
<tr>
<td>Herring, Atlantic</td>
<td>0.037</td>
<td>973</td>
<td>0.119</td>
<td>0.015</td>
</tr>
<tr>
<td>Herring, Pacific</td>
<td>0.060</td>
<td>194</td>
<td>0.300</td>
<td>0.048</td>
</tr>
<tr>
<td>Lingcod</td>
<td>0.363</td>
<td>333</td>
<td>0.952</td>
<td>0.128</td>
</tr>
<tr>
<td>Lobster (all)</td>
<td>0.153</td>
<td>344</td>
<td>0.315</td>
<td>0.070</td>
</tr>
<tr>
<td>Lobster, American</td>
<td>0.200</td>
<td>142</td>
<td>0.367</td>
<td>0.075</td>
</tr>
<tr>
<td>Lobster, spiny</td>
<td>0.100</td>
<td>62</td>
<td>0.137</td>
<td>0.035</td>
</tr>
<tr>
<td>Mackerel (all)</td>
<td>0.586</td>
<td>2481</td>
<td>3.237</td>
<td>0.450</td>
</tr>
<tr>
<td>Mackerel, Atlantic</td>
<td>0.045</td>
<td>191</td>
<td>0.192</td>
<td>0.057</td>
</tr>
</tbody>
</table>

Influences risk of atopy in offspring.9 Available research also suggests that eating fish early in life can prevent certain allergic diseases, including asthma, eczema, and allergic rhinitis. In more than a dozen observational studies, the associations of fish consumption in infancy and childhood with atopy risk have been evaluated. In a prospective observational study of more than 4000 Swedish infants who did not have eczema or recurrent wheeze in the first year of life, Kull et al10 found a dose-dependent association of greater fish consumption with lower risks for asthma, eczema, allergic rhinitis, and sensitization, even when controlling for smoking, maternal age, existence of parental allergies, and breastfeeding. They also found an inverse association between age at introduction of fish and atopy risk: children who consumed fish between 3 and 8 months of age had lower risks for asthma (adjusted odds ratio [OR], 0.73; 95% confidence interval [CI]: 0.55 to 0.97), eczema (adjusted OR, 0.77; 95% CI: 0.64 to 0.92), allergic rhinitis (adjusted OR, 0.77; 95% CI: 0.60 to 0.97), and allergic sensitization (adjusted OR, 0.78; 95% CI: 0.64 to 0.95) compared with children introduced to fish at 9 months or older. A subsequent study of this cohort found that the benefits of consuming 2 or more fish meals per month by age 1 extended to 12 years of age.11 Further research corroborates the potential for early fish consumption having durable protective effects. Goksör et al12 found that introduction of fish before 9 months of age independently reduced the risk (adjusted OR, 0.6; 95% CI: 0.4 to 0.96) of current atopic asthma (defined by respiratory symptoms plus positive skin prick test result) at school age. A 2013 meta-analysis of 3 studies found that fish consumption in infancy was inversely related to childhood asthma incidence, with children who ate the most fish having
a 25% lower risk of developing asthma than those who ate the least.\textsuperscript{13}

Another prospective cohort of Swedish infants found that introduction of fish between 6 and 8 months of age substantially reduced rates of infantile eczema (OR, 0.6; 95% CI: 0.5 to 0.7; \( P < .001 \)), and children who did not consume fish were 2.7 times more likely to have eczema than those who ate fish 3 or more times a week (95% CI: 1.80 to 4.13; \( P < .001 \)).\textsuperscript{14} Oien et al\textsuperscript{15} found that infants who ate fish once a week or more were 38% less likely to have eczema at 2 years. In this study, the mean age of introducing fish was 9 months. In contrast, in a trial among 123 pregnant women who were randomly assigned to consume 2 weekly servings of salmon or their usual diet low in fish, there was no difference in rates of infantile eczema at 6 months.\textsuperscript{16}

Results from other studies (eg, Hesselmar et al\textsuperscript{17}) support the potential for early introduction of fish to prevent other allergic disease, such as allergic rhinitis. Alm et al\textsuperscript{14} found that children who were given fish before 9 months were half as likely to develop allergic rhinitis by 4.5 years of age in a prospective cohort of Swedish children.

Of note, some evidence suggests that prenatal shellfish consumption (as opposed to finfish) may increase risk of food allergy. In their analysis of early childhood diet, Pelé et al\textsuperscript{18} found that maternal prenatal shellfish intake at least once a month was associated with a higher risk of any food allergy before age 2 (adjusted OR, 1.62; 95% CI: 1.11 to 2.37) compared with intake less than once per month while controlling for fish intake. Leermakers et al\textsuperscript{19} similarly found that 1 to 13 g of shellfish consumption per week, on average, during the first trimester of pregnancy marginally increased risk of childhood wheezing and eczema.

\begin{table}[h]
\centering
\begin{tabular}{lllll}
\hline
Seafood Item & Mean Hg & Samples & SDw & SEw \\
& (ppm) & (Total) & & \\
\hline
Mackerel, chub & 0.099 & 129 & 0.166 & 0.033 \\
Mackerel, king & 1.101 & 821 & 3.470 & 0.383 \\
Mackerel, Spanish & 0.440 & 1168 & 1.105 & 0.097 \\
Marlin (all) & 1.517 & 821 & 7.495 & 1.654 \\
Marlin, blue & 2.485 & 364 & 9.532 & 2.120 \\
Marlin, striped & 0.881 & 179 & 2.058 & 0.528 \\
Marlin, white & 0.685 & 56 & 0.518 & 0.120 \\
Monkfish & 0.174 & 92 & 0.117 & 0.024 \\
Mullet & 0.050 & 638 & 0.152 & 0.027 \\
Mussels (all) & 0.028 & 755 & 0.106 & 0.016 \\
Ocean perch & 0.117 & 262 & 0.421 & 0.082 \\
Orange roughy & 0.513 & 152 & 0.568 & 0.103 \\
Oysters (all) & 0.020 & 5310 & 0.178 & 0.013 \\
Oysters, Eastern & 0.018 & 4573 & 0.161 & 0.009 \\
Oysters, Pacific & 0.039 & 290 & 0.171 & 0.025 \\
Pike & 0.404 & 1374 & 1.328 & 0.101 \\
Plaice & 0.148 & 282 & 0.576 & 0.137 \\
Pollock (all) & 0.058 & 540 & 0.342 & 0.059 \\
Pollock, Atlantic & 0.160 & 79 & 0.330 & 0.053 \\
Pollock, Pacific/Alaska & 0.050 & 235 & 0.145 & 0.027 \\
Porgy & 0.085 & 169 & 0.143 & 0.027 \\
Sablefish & 0.243 & 477 & 0.620 & 0.080 \\
Salmon (all) & 0.048 & 2818 & 0.143 & 0.023 \\
Salmon, Atlantic (farmed) & 0.026 & 145 & 0.077 & 0.020 \\
Salmon, Atlantic (wild) & 0.058 & 95 & 0.083 & 0.015 \\
Salmon, Chinook, farmed & 0.017 & 4 & 0.024 & 0.017 \\
Salmon, Chinook, wild & 0.067 & 580 & 0.105 & 0.013 \\
Salmon, chum & 0.046 & 456 & 0.139 & 0.018 \\
Salmon, coho & 0.044 & 567 & 0.085 & 0.007 \\
Salmon, pink & 0.037 & 222 & 0.064 & 0.009 \\
Salmon, sockeye & 0.039 & 396 & 0.026 & 0.004 \\
Salmon (canned) & 0.035 & 61 & 0.042 & 0.012 \\
Sardine (all) & 0.079 & 1007 & 0.201 & 0.036 \\
Scallops (all) & 0.040 & 336 & 0.148 & 0.033 \\
Seabass, black & 0.120 & 139 & 0.118 & 0.032 \\
Shad (all) & 0.077 & 93 & 0.099 & 0.031 \\
Shad, American & 0.067 & 76 & 0.095 & 0.019 \\
Shark (all) & 0.882 & 3722 & 2.504 & 0.462 \\
Shark, blacktip & 0.882 & 250 & 1.249 & 0.274 \\
Shark, blue & 0.684 & 50 & 1.518 & 0.480 \\
Shark, mako & 1.259 & 168 & 1.955 & 0.464 \\
Shark, sandbar & 0.889 & 115 & 1.141 & 0.301 \\
Shark, thresher & 0.622 & 119 & 1.674 & 0.421 \\
Shrimp (all) & 0.053 & 935 & 0.212 & 0.059 \\
Shrimp, brown & 0.077 & 72 & 0.083 & 0.053 \\
Shrimp, pink & 0.083 & 49 & 0.079 & 0.024 \\
Shrimp, white & 0.057 & 113 & 0.136 & 0.016 \\
Skate (all) & 0.138 & 70 & 0.093 & 0.036 \\
Smelt & 0.025 & 175 & 0.086 & 0.019 \\
Snapper (all) & 0.230 & 1244 & 0.514 & 0.104 \\
Snapper, gray & 0.233 & 699 & 0.595 & 0.068 \\
Snapper, red & 0.243 & 279 & 0.725 & 0.168 \\
Sole & 0.086 & 1101 & 0.310 & 0.056 \\
Squid & 0.044 & 728 & 0.130 & 0.024 \\
Swordfish & 0.893 & 1726 & 2.052 & 0.296 \\
Tilefish (all) & 0.019 & 129 & 0.097 & 0.027 \\
Tilefish, Atlantic & 0.883 & 109 & 2.962 & 0.895 \\
Tilefish, Gulf of Mexico & 0.171 & 47 & 0.195 & 0.049 \\
\hline
\end{tabular}
\caption{Continued}
\end{table}
Randomized trials in which children are assigned to fish consumption or placebo are implausible, but such trials can be completed with n-3 LCPUFAs delivered via fish oil supplements. Such studies can help determine if n-3 LCPUFAs may account for allergy prevention as well as other health outcomes that may be associated with fish consumption.

The results of all fish oil trials carry caveats. First, although the studies cited here used fish oil supplements in which the contents were standardized (although substantially different doses of EPA and DHA were used across studies), no assurance exists that over-the-counter supplements sold in the United States contain fatty acids in the amounts and types specified on the labels. Second, studies tend to use high doses of n-3 LCPUFAs, which may not be well tolerated by children. A recent review of 75 fish oil supplement studies in children found dropout rates of 17% and adherence rates of 85%, although most studies lacked adequate data on measures of compliance.22 Last, adverse events are not routinely reported. Although generally thought to be benign, fish oil supplements may carry certain risks, such as elevated low-density lipoprotein (LDL) cholesterol.24 Among possible side effects, weight gain has most often not been a consequence of fish oil supplementation, although some longitudinal studies, especially of children born prematurely, have documented greater weight in those receiving supplements (for example, Kennedy et al24).

A Cochrane systematic review analyzed data from 8 randomized controlled trials of pre- and postnatal fish oil supplementation for effects on childhood allergy. These studies evaluated food allergy, eczema, allergic rhinitis, and/or asthma (or wheeze). The metaanalysis conducted found that among children born to women who consumed fish oil supplements, immunoglobulin E (IgE)-mediated food allergy was less likely in children younger than 1 year (relative risk [RR] 0.13; 95% CI: 0.02 to 0.95), and any IgE-mediated allergy was less likely in children 12 to 36 months of age (RR 0.66; 95% CI: 0.44 to 0.98). No benefit was observed for eczema, allergic rhinitis, or asthma between birth and 3 years of age. Findings did not differ based on maternal history of asthma or prenatal or postnatal supplementation of the mother.25

Since that review, 2 randomized trials have been published. The first is a follow-up to one of the trials included in the Cochrane review. The original study began in 199026 and randomly assigned 533 women to consume a fish oil supplement, olive oil, or no oil capsules after 30 weeks gestation. At 24 years’ follow-up, adults born to mothers who received supplementation were less likely to need medications for asthma as compared with individuals born to mothers who received olive oil supplements (hazard ratio, 0.54; 95% CI: 0.32 to 0.90).27 A second randomized trial of n-3 LCPUFA

**TABLE 3 Continued**

<table>
<thead>
<tr>
<th>Seafood Item</th>
<th>Mean Hg</th>
<th>Samples</th>
<th>SDw</th>
<th>SEw</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trout (freshwater, wild and unknown status)</td>
<td>0.344</td>
<td>2804</td>
<td>1.030</td>
<td>0.087</td>
</tr>
<tr>
<td>Trout, lake</td>
<td>0.349</td>
<td>2748</td>
<td>1.268</td>
<td>0.080</td>
</tr>
<tr>
<td>Trout (freshwater, farmed)</td>
<td>0.029</td>
<td>178</td>
<td>0.066</td>
<td>0.015</td>
</tr>
<tr>
<td>Tuna (fresh/frozen, all)</td>
<td>0.450</td>
<td>3780</td>
<td>1.619</td>
<td>0.340</td>
</tr>
<tr>
<td>Tuna, albacore</td>
<td>0.317</td>
<td>296</td>
<td>0.475</td>
<td>0.103</td>
</tr>
<tr>
<td>Tuna, Atlantic bonito</td>
<td>0.499</td>
<td>263</td>
<td>2.200</td>
<td>0.399</td>
</tr>
<tr>
<td>Tuna, bigeye</td>
<td>0.582</td>
<td>376</td>
<td>1.113</td>
<td>0.222</td>
</tr>
<tr>
<td>Tuna, blackfin</td>
<td>0.856</td>
<td>159</td>
<td>0.972</td>
<td>0.251</td>
</tr>
<tr>
<td>Tuna, bluefin (farmed)</td>
<td>0.455</td>
<td>108</td>
<td>0.540</td>
<td>0.158</td>
</tr>
<tr>
<td>Tuna, bluefin (wild)</td>
<td>0.796</td>
<td>514</td>
<td>2.408</td>
<td>0.542</td>
</tr>
<tr>
<td>Tuna, skipjack</td>
<td>0.198</td>
<td>341</td>
<td>0.320</td>
<td>0.083</td>
</tr>
<tr>
<td>Tuna, yellowfin</td>
<td>0.270</td>
<td>1183</td>
<td>0.540</td>
<td>0.125</td>
</tr>
<tr>
<td>Tuna, albacore (canned)</td>
<td>0.328</td>
<td>1362</td>
<td>0.955</td>
<td>0.113</td>
</tr>
<tr>
<td>Tuna, light (canned or packed)</td>
<td>0.118</td>
<td>972</td>
<td>0.300</td>
<td>0.058</td>
</tr>
<tr>
<td>Tuna, yellowfin (canned)</td>
<td>0.143</td>
<td>298</td>
<td>0.688</td>
<td>0.098</td>
</tr>
<tr>
<td>Weakfish/seatrout (all)</td>
<td>0.361</td>
<td>2105</td>
<td>1.348</td>
<td>0.193</td>
</tr>
<tr>
<td>Whitefish (all)</td>
<td>0.106</td>
<td>2721</td>
<td>0.707</td>
<td>0.051</td>
</tr>
<tr>
<td>Whiting</td>
<td>0.040</td>
<td>27</td>
<td>0.058</td>
<td>0.015</td>
</tr>
</tbody>
</table>


(OR, 1.20; 95% CI: 1.04 to 1.40; OR, 1.18; 95% CI: 1.01 to 1.37, respectively) after controlling for fish intake.

Regarding the timing of introduction of fish and the risks related to atopic disease, a 2008 American Academy of Pediatrics clinical report revised previous guidance, which had recommended delaying consumption until 3 years for infants and children with a strong family history of allergic disease.20 The 2008 guidance states that the evidence is not adequate to delay introduction of foods beyond 4 to 6 months.21 More research is needed to clarify the effects of earlier introduction of fish and shellfish, particularly to at-risk infants.

**STUDIES OF N-3 LCPUFA SUPPLEMENTATION**

**Prevention of Allergic Disease**

Results of observational studies, such as those cited previously, have suggested that fish consumption in early childhood may protect against allergic disease, but they are subject to unmeasured confounding.
supplementation among more than 700 women in the third trimester of pregnancy found that supplementation reduced symptoms of asthma at 3 years of age (hazard ratio, 0.69; 95% CI: 0.49 to 0.97) and especially among children born to women who had the lowest serum n-3 LCPUFA levels at study entry.28

If a protective effect against asthma and allergy of n-3 LCPUFAs or of fish consumption exists, an outstanding question is when the optimal time of introduction may be. Studies suggest that introduction before 9 months of age may be preferable to postponing until 1 year.12,14,29

**Treatment of Allergic Disease**

The potential of fish and fish oil to prevent allergic disease raises the question as to whether they may be effective treatments for allergic disease. Few studies have investigated these questions. Hodge et al30 found that among a group of 39 children 8 to 12 years of age, supplementation with n-3 LCPUFA did not affect lung function, day or night symptoms, peak flow rates, or medication use at 3 or 6 months after the start of the intervention. Similarly, no effect on allergic outcomes including sensitization, eczema, asthma, or food allergy was found in a randomized study of 420 infants born to Australian women with history of atopy.31 In this study, infants received daily supplements from birth to 6 months and dropout rates were substantially higher in the fish oil supplement arm as compared with the placebo arm of the study (28.4% vs 16.8%).

In a study of 29 Japanese children with prolonged hospitalization for severe asthma, fish oil supplementation over 10 months reduced sensitivity to acetylcholine and induced bronchospasm as well as asthmatic symptoms based on a standardized asthma severity scale. Despite the small size of this study, it had several unique strengths. The children in this study largely received the same diet, air to breathe, and other potential exposures because they shared the same environment. They were also monitored by nurses and physicians in the hospital who assessed them with standardized outcome measures.32

**Inflammatory Bowel Disease**

The anti-inflammatory properties of n-3 LCPUFAs have prompted research on whether they may ameliorate or prevent inflammatory diseases, including Crohn disease and ulcerative colitis. A recent Cochrane review evaluated 6 studies on the use of fish oil supplements to maintain remission in Crohn disease. When all studies were considered, a benefit was observed of n-3 LCPUFA therapy for maintenance of remission at 12 months (RR, 0.77; 95% CI: 0.61 to 0.98). However, these 6 studies had heterogenous results (I² = 0.58), leading the reviewers to perform an analysis of the 2 most robust studies that had less potential bias. With just these 2 studies, the point estimate of the RR remained below 1, but the 95% CI crossed the null.33 Of note, in the studies reviewed, only 1 was conducted with children. In this study, 38 children were randomly assigned to receive acetylsalicylic acid along with n-3 LCPUFAs or acetylsalicylic acid with an olive oil supplement every day for a year. Children receiving n-3 LCPUFAs had lower relapse rates at 1 year (61 vs 95%).34

Costea et al35 recently published an observational study of 182 children with Crohn disease in which they assessed whether dietary intake of n-3 and omega-6 (n-6) fatty acids may interact with variants of genes that regulate fatty acid metabolism to affect susceptibility to Crohn disease. They found that children who consumed a higher dietary ratio of n-6/n-3 fatty acids were more susceptible to Crohn disease if they were also carriers of specific variants of CYP4F3 and FADS2 genes, which are both involved in the metabolism of polyunsaturated fatty acids.35

Metanlyses have not found clinical benefit of fish oil supplementation for ulcerative colitis, either for induction therapy or maintenance of remission,36–38 although the data in these analyses come exclusively from adult studies.

**Neurologic and Cognitive Development**

LCPUFAs, especially DHA, are essential structural components of the brain and eye. Animal studies have shown that severe deprivation can result in blindness and impaired cognitive development.59 Only 1 study has directly assessed the value of childhood consumption of fish or shellfish consumption in childhood neurodevelopment. In that study, 232 Norwegian kindergarteners were randomly assigned to consume fatty fish (herring or mackerel) or meat (chicken, lamb, and/or beef) 3 times a week for 16 weeks. When controlling for the amount of fish or meat the children otherwise ate, children randomly assigned to consume fish scored higher on the Wechsler Preschool and Primary Scale of Intelligence, third edition (WPPSI-III) (fish 20.4; 95% CI: 17.5 to 23.3, vs meat 15.2; 95% CI: 12.4 to 18.0; P = .0060).40 A separate randomized study evaluated the effect of fish consumption on attention and processing speed among adolescents but the study had poor compliance.41 No trials have evaluated longer-term effects of childhood fish intake.

Some observational studies suggest that maternal prenatal consumption of fish may benefit neurodevelopment. Hibbeln et al.42 for example, investigated a cohort of 11,875 women who had seafood consumption assessed at 32 weeks’ gestation. After controlling for confounders, including prenatal smoking and psychosocial stressors...
via a family adversity index,* these investigators found that seafood intake during pregnancy of less than 340 g per week was associated with higher risk of children being in the lowest quartile for verbal IQ (no seafood consumption compared with mothers who consumed more than 340 g per week: OR, 1.48; 95% CI: 1.16 to 1.90; 1–340 g seafood consumption per week compared with no seafood consumption: OR, 1.09; 95% CI: 0.92 to 1.29, a nonsignificant result, but for the overall trend in consumption, \( P = .004 \)). Low maternal seafood intake was also associated with increased risk of worse outcomes for prosocial behavior, fine motor, communication, and social development scores.42

In addition, Oken et al\textsuperscript{43} found among a cohort of 25,446 Danish children that higher maternal prenatal fish intake and greater duration of breastfeeding were each independently associated with improved development in multiple domains at 18 months after controlling for socioeconomic status, smoking, maternal depression, and other relevant covariates.

In the US-based Project Viva cohort, Oken et al\textsuperscript{44,45} have found that maternal prenatal fish consumption above 2 weekly servings was associated with better cognition during infancy and early childhood. The best cognitive test scores were seen among children of mothers who ate more fish but had lower mercury levels. More recently, they followed the same cohort to midchildhood (6–10 years) and saw no evidence of either benefit from prenatal fish intake or harm from prenatal mercury exposure, suggesting perhaps that intervening factors during childhood might attenuate the influence of these prenatal exposures.\textsuperscript{46}

Several other studies have investigated the effects of n-3 LCPUFA supplementation on neurodevelopment and cognitive skills and whether they may be of use to improve academic performance.\textsuperscript{47–53} Results of such research are mixed and have been summarized by Joffre et al.\textsuperscript{54}

A study of 154 Arctic Quebecois Inuit children 10 to 13 years of age found that those with higher cord blood n-3 LCPUFA concentrations had shorter FN400 latency and larger late positive component amplitude,\textsuperscript{5} findings that suggest these children had more robust memory responses to stimuli.\textsuperscript{55}

A randomized controlled crossover trial of 409 Aboriginal Australian children aged 6 to 12 years found that fish oil supplement administered over 40 weeks resulted in more advanced drawings in the Draw-A-Person test (a global measure of cognitive maturity and intellectual ability) compared with administration of a placebo containing palm oil and a trace of fish oil to provide odor and taste consistent with the experimental treatment.\textsuperscript{56}

Another study evaluated 183 second-grade children from Northern Cape Province of South Africa randomly assigned to consume fish flour-based spread or placebo made from pulverized rusk (twice-baked bread) over 6 months. Dropout rates were similar (about 10%) in both groups. In an intention-to-treat analysis, those children who consumed the fish flour spread containing DHA and EPA had better recognition and discrimination of words as assessed by the Hopkins Verbal Learning Test (estimated effect size, 0.80; 95% CI: 0.15 to 1.45; and estimated effect size, 1.10; 95% CI: 0.30 to 1.91, respectively). They also performed better on the spelling portion of the Hopkins Verbal Learning Test (estimated effect size, 2.81 points; 95% CI: 0.59 to 5.02).\textsuperscript{57}

This study contrasts with findings from a randomized trial of 183 children from Jakarta, Indonesia, and Adelaide, South Australia, which found no effect of DHA and EPA supplementation on similar outcomes.\textsuperscript{58} Such opposing results may reflect the baseline levels of DHA and EPA in the population studied, with greater benefit to those with lower levels at baseline.

Richardson et al\textsuperscript{59} have found in a randomized trial that supplementation with n-3 LCPUFA (derived from algae) improved reading skills in a cohort of 74 healthy children 7 to 9 years of age from the United Kingdom through supplementation with n-3 LCPUFA (derived from algae) whose baseline reading performance was in the lowest quintile.

In a notable study that did not show a benefit of supplementation, Makrides et al\textsuperscript{60} conducted a double-blind, multicenter, randomized controlled trial of 2399 Australian women to determine if increasing DHA during the last half of pregnancy affects maternal depression or the neurodevelopment of their children. Mothers received fish oil capsules providing 800 mg/day of DHA or matched vegetable oil placebo without DHA from study entry to birth. Children were assessed at 18 months by using the Bayley Scales of Infant and Toddler Development. Maternal supplementation neither improved depressive symptoms nor early childhood language or cognitive development.\textsuperscript{60} Follow-up of this cohort at 7 years of age likewise found no effect of supplementation in infancy.\textsuperscript{61,62}

\textsuperscript{1} The FN400 latency refers to a finding on EEG associated with the brain’s response to an external stimulus. A shorter latency implies faster processing of stimuli input. The late positive component on EEG assesses explicit recognition memory with larger amplitude associated with better memory retrieval.

* The index is a 38-point battery of questions that cover a broad array of psychosocial variables including housing security, exposure to crime and violence, substance abuse, maternal mental health, and income.
Behavioral and Mental Health

Ample evidence from animal studies makes clear that extreme deficiencies in n-3 LCPUFA during gestation or early life can profoundly and adversely affect the developing brain, and several observational studies in children have identified low levels of n-3 PUFAs to be associated with cognitive and/or behavioral problems.63–65 Despite these findings, studies of whether n-3 LCPUFA may be of value in the management or treatment of a variety of conditions, including attention-deficit/hyperactivity disorder (ADHD), Tourette disorder,66 or depression, have found supplementation to be, at best, of limited value.

ADHD

In 2011, Bloch and Qawasmi67 conducted a meta-analysis to estimate the potential effect of n-3 LCPUFA supplementation on ADHD symptoms. They included 10 trials involving 699 children and identified a small effect of n-3 LCPUFA supplementation for ADHD (standardized mean difference [SMD], 0.31; 95% CI: 0.16 to 0.47), with higher doses of EPA yielding greater improvement in ADHD symptoms (β = .36; 95% CI: 0.01 to 0.72; t = 2.30; P = .04, R² = 0.37). These benefits were modest in comparison with those observed with standard pharmacotherapy. However, a 2012 Cochrane review that evaluated 13 trials with more than 1000 participants found no benefit of n-3 LCPUFA supplementation on ADHD symptoms in children.68 Bloch and Qawasmi’s67 meta-analysis and the Cochrane review evaluated much of the same evidence.

In a 2014 double-blind randomized controlled trial of 95 children with ADHD diagnoses based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria, participants were assigned to n-3 LCPUFA supplementation or placebo over 16 weeks. Supplementation resulted in an improvement in working memory (prettrial, 97.51 ± 10.04; posttrial, 101.78 ± 11.47; F = 5.54; P = .019) and digit span (prettrial, 12.46 ± 2.42; posttrial, 14.11 ± 2.78; F = 9.73; P = .003) compared with placebo, as assessed by the HAWIK-IV scale.69

Several other more recent studies, including randomized trials, have produced conflicting results, making firm conclusions about the efficacy of supplementation for management of ADHD difficult.70–72

Depression

n-3 LCPUFAs have been studied in the prevention and treatment of depression in both adults and children. The rationale behind n-3 LCPUFAs use is that their anti-inflammatory effects, their importance to neuroplasticity and neurogenesis, and their ability to affect serotonin and dopamine signaling in the brain, which might influence mood.73 A recent meta-analysis by Grosso et al74 of 11 randomized controlled trials enrolling mostly adult patients with major depression or depressive symptoms showed that DHA and EPA supplementation resulted in a pooled (DHA and EPA) SMD of 0.38 (95% CI: 0.18 to 0.59), which suggests a beneficial effect of n-3 fatty acids on depressed mood compared with placebo. Other meta-analyses have not found a beneficial effect and suggest that positive results are attributable to publication bias and methodologic shortcomings.75 Grosso et al74 suggest that such findings may relate to heterogeneity in symptoms and/or diagnoses in research subjects and formulations of fatty acid supplements, which they assert were better addressed in their study.

Cross-sectional pediatric studies have demonstrated lower erythrocyte DHA levels in patients with major depression.76,77 Trials that have explored whether fish consumption was associated with depressive symptoms have had mixed results,78,79 as have trials in which n-3 LCPUFAs were used in treatment of depression in children.77,80

Sickle Cell Disease

LCPUFAs have been shown to improve the membrane flexibility of red blood cells in animals and humans,81,82 prompting interest in whether they may be of benefit to patients with sickle cell disease. Two studies have examined the potential of n-3 LCPUFAs to ameliorate symptoms of sickle cell disease. Tomer et al83 conducted a randomized controlled trial in 2001, showing that supplementation reduced the number of pain crises from 7.8 to 3.1 per year in a small sample of sickle cell patients. A larger study of 128 Sudanese children and adults ranging from 2 to 24 years found that n-3 LCPUFA supplementation more than halved pain episodes (4.6 to 2.7 per year; P < .01) and decreased hospitalization for pain crisis from a median of 1 to 0 per year (P < .0001). Severe anemia was reduced from 16.4% to 3.2% per year and transfusion from 16.4% to 4.5% per year.84

Lipids

A substantial body of research in adults has evaluated the potential of n-3 LCPUFA supplementation to affect lipid profiles and has generally found modest effects of n-3 LCPUFA consumption on lipid profiles, especially on triglycerides. A 2006 meta-analysis by Balk et al85 including 21 randomized controlled trials of fish oil found that triglycerides decreased 27 mg/dL (95% CI: 20 to 33), high-density lipoprotein increased 1.6 mg/dL (95% CI: 0.8 to 2.3), and LDL increased 6 mg/dL (95% CI: 3 to 8) in those who received fish oil versus controls.

Research on children has been much more limited. A study involving 201 fifth- and sixth-graders with obesity...
from Campeche, Mexico, assigned participants to metformin or n-3 LCPUFA supplement (360 mg of EPA and 240 mg of DHA) 3 times a day for 12 weeks. Those receiving the fish oil supplement had increases in high-density lipoprotein (2.12 mg/dL; 95% CI: 0.61 to 3.63) and decreases in triglycerides (−26.35 mg/dL; 95% CI: −40.78 to −11.91). No change in LDL or total cholesterol was observed. Another randomized placebo controlled trial of 4 g of n-3 LCPUFA daily in 29 adolescents with hypertriglyceridemia, although underpowered, showed decreases in triglyceride levels that were not significantly different from placebo (experimental group, −54 ± 27 mg/dL; placebo, −34 ± 26 mg/dL). A recent randomized, double-blind, crossover trial comparing 4 g of fish oil daily for 8 weeks with placebo by Gidding et al similarly found that in a group of 42 adolescents with elevated LDL and triglycerides, those who received supplementation had lower triglycerides than those who received placebo, but the difference was not significant (−52 ± 16 vs −16 ± 16 mg/dL). No difference was found in LDL levels. Given these results, changes in lipids are likely to be at best modest and may require large (eg, 1000 mg or more) doses of n-3 LCPUFAs.

Effects of n-3 LCPUFAs for children with nonalcoholic fatty liver disease have also been studied. In a randomized trial of 40 children with biopsy-proven nonalcoholic liver disease, children who received the supplement had improvements in liver steatosis, improved insulin sensitivity, and, consistent with some of the studies presented above, lower triglycerides.

**Blood Pressure**

Dozens of randomized controlled trials have evaluated fish oil supplementation effects on blood pressure in middle-aged adults and found that high-dose (eg, ≥3 g/day) n-3 LCPUFA supplementation results in modest decreases in systolic and diastolic blood pressure. A 2014 meta-analysis of 70 randomized controlled trials found that when compared with placebo, EPA and DHA supplementation reduced systolic blood pressure (−1.52 mm Hg; 95% CI: −2.25 to −0.79) and diastolic blood pressure (−0.99 mm Hg; 95% CI: −1.54 to −0.44). This is consistent with another previous meta-analysis of 36 double-blinded randomized trials of fish oil and blood pressure in which high levels of fish oil consumption (3.7 g/day) lowered systolic blood pressure by 1.7 mm Hg (95% CI: 0.3–3.1) and diastolic blood pressure by 1.5 mm Hg (95% CI: 0.6–2.3). Given the size of blood pressure change, these effects are unlikely to be clinically relevant.

Effects of n-3 LCPUFA in childhood on blood pressure have been less well studied and results have not been consistent, although several have suggested that supplementation may elevate blood pressure, especially for boys. This evidence comes from observational studies as well as randomized trials of fish oil supplementation to infants. The studies have revealed elevations in blood pressure. Asserhøj et al recruited 122 Danish mothers and randomly assigned their offspring to receive fish oil or olive oil during the first 4 months of lactation. In a follow-up of 98 children at 7 years, boys who received fish oil had unexpectedly higher diastolic and mean arterial blood pressure (6 mm Hg) than those who received olive oil. No difference was found among girls. Higher diastolic blood pressure (−3 mm Hg) was observed at 10 years of age in girls, but not boys, from a group of children born at less than 35 weeks’ gestation and with birth weight <2000 g who were randomly assigned to receive a formula supplemented with n-3 LCPUFA (from tuna oil) and γ linoleic acid or a formula without fatty acid supplement through 9 months postterm. The difference between boys and girls became insignificant, however, after controlling for current weight, which suggests that the observed blood pressure difference may be mediated through weight. Of note, in the Asserhøj et al study, children receiving fish oil supplements had higher BMI at 2.5 years, but the higher BMI did not persist at 7 years.

A multicenter European study, in which 147 children born between 37 and 42 weeks’ gestation with birth weight between 2500 and 4000 g were randomly assigned to receive formula supplemented with n-3 and n-6 LCPUFAs (DHA, EPA, and α-linoleic acid, all sourced from egg yolks) or placebo through age 4 months yielded contrary results. At age 6 years, supplemented infants had lower mean blood pressure (mean difference, −3.0 mm Hg; 95% CI: −5.4 to −0.5 mm Hg) and diastolic blood pressure (mean difference, −3.6 mm Hg; 95% CI: −6.5 to −0.6 mm Hg) than the control group. These results, and those from the Asserhøj et al study, which compared n-3 with n-6 LCPUFA supplementation, raise the question as to whether n-6 LCPUFAs may be responsible for a greater effect than n-3 LCPUFAs on blood pressure in children. Although this specific question has not been addressed by other well-designed studies, Ryttet et al followed 180 children born to mothers randomly assigned to receive fish oil or olive oil supplements in the last trimester of pregnancy at 19 years of age and found no effect on blood pressure from prenatal supplementation.

**Potential Harms of Eating Fish and Shellfish**

Methylmercury (MeHg) pollution is a primary reason for parents to avoid feeding their children some fish and for expectant mothers to avoid consumption of some fish during

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**References**

1. Gidding et al.:
2. A recent randomized, double-blind, crossover trial comparing 4 g of fish oil daily for 8 weeks with placebo.
3. A multicenter European study, in which 147 children born between 37 and 42 weeks’ gestation with birth weight between 2500 and 4000 g were randomly assigned to receive formula supplemented with n-3 and n-6 LCPUFAs (DHA, EPA, and α-linoleic acid, all sourced from egg yolks) or placebo through age 4 months yielded contrary results.
4. At age 6 years, supplemented infants had lower mean blood pressure (mean difference, −3.0 mm Hg; 95% CI: −5.4 to −0.5 mm Hg) and diastolic blood pressure (mean difference, −3.6 mm Hg; 95% CI: −6.5 to −0.6 mm Hg) than the control group.
5. These results, and those from the Asserhøj et al study, which compared n-3 with n-6 LCPUFA supplementation, raise the question as to whether n-6 LCPUFAs may be responsible for a greater effect than n-3 LCPUFAs on blood pressure in children. Although this specific question has not been addressed by other well-designed studies, Ryttet et al followed 180 children born to mothers randomly assigned to receive fish oil or olive oil supplements in the last trimester of pregnancy at 19 years of age and found no effect on blood pressure from prenatal supplementation.

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**POTENTIAL HARM OF THE EATING FISH AND SHELLFISH**

Methylmercury (MeHg) pollution is a primary reason for parents to avoid feeding their children some fish and for expectant mothers to avoid consumption of some fish during
mercury exposure in utero.97

Mercury bioaccumulates in marine and freshwater food chains. Most of the mercury found in humans comes from contaminated fish. Elemental mercury enters the environment primarily through coal combustion and artisanal and small-scale gold mining as well as natural emissions, for example, from volcanoes. Bacteria convert elemental to organic (methyl) mercury, a form that is readily absorbed after ingestion. Given the increased use of coal for energy in recent decades, especially in Asia, mercury levels in the world’s oceans have increased and are expected to increase substantially, with a possible doubling by 2050 from 1995 levels.101

The US Food and Drug Administration (FDA) and Environmental Protection Agency have provided fish consumption guidance in the United States aimed at preventing harmful exposure to mercury that is intended for the average American consumer and not necessarily for populations that may have higher consumption of freshwater fish.102 These recommendations are based on cohort studies in the Faroe Islands, Seychelles Islands, and New Zealand in which health consequences from prenatal mercury exposure have been examined, although the diets of these populations do not represent the typical American diet. The Faroese, for instance, consume large amounts of whale blubber, and the Seychellois eat 12 meals with fish per week. In addition, the primary analysis in the Seychelles and New Zealand studies did not control for fish consumption, so any benefit of n-3 LCPUFAs on neurodevelopment may have masked harmful mercury effects.103 This was demonstrated in the Faroe Islands cohort, which had neurodevelopmental outcomes assessed while controlling for maternal fish consumption and found that beneficial effects of fish consumption concealed the deleterious effects of MeHg.103 These analyses of the Faroe Island data also confirmed the beneficial association of fish consumption with child neurocognitive outcomes.

Largely based on findings from the Faroe Islands study, the US Environmental Protection Agency’s reference dose (RfD) for MeHg is 0.1 µg/kg of body weight per day.104 The RfD for mercury is an estimated daily intake likely to be without appreciable risk of harm over a lifetime, even for the most sensitive populations, and employs an uncertainty factor of 10 based on variability in concentrations of cord blood and maternal blood and for differences in how MeHg may be metabolized in different people. The MeHg RfD was calculated with the intent of preventing fetal neurologic harm from maternal consumption. The RfD assumes that the fetal brain is the organ most sensitive to the effects of MeHg, and thus the RfD should protect everyone, including children, from harm. As a result, no governmental guidance for MeHg in other populations, including children and nonpregnant adults, has been given.

On the basis of representative data from the NHANES, the number of women in the United States with MeHg blood levels reflecting intake above the RfD has decreased considerably since 1990, and, as a result, the number of potentially adversely affected children has decreased as well.105 An analysis by Mahaffey et al106 based on NHANES data from 1990 to 2000 found that each year more than 300,000 children are born in the United States with in utero exposure to MeHg at levels that may cause neurologic harm. The same analysis using data from the 2000–2010 NHANES found that only 75,000 children might have been exposed in utero to mercury at levels above the RfD.107 Of note, neither of these analyses accounted for observed trends in maternal blood mercury with increasing age, with older women having higher blood mercury concentrations.107 In subsequent NHANES research, researchers have also identified that women living on the Atlantic and Pacific coasts, and to a lesser extent Gulf coast, are likely to have higher blood mercury concentrations (see Fig 1).108

Beyond this, little research is available to inform specific recommendations for fish consumption in young children to prevent harms from mercury exposure.

Persistent Organic Pollutants

Aside from mercury, several other pollutants commonly found in fish and shellfish have raised concern for their detrimental health effects. These include a large group of chemicals known as persistent organic pollutants (POPs). POPs are organic compounds that resist breakdown and are lipid soluble. These properties make it possible for long-range transport of POPs after they are released into the environment and also enable them to bioaccumulate within animals and humans and biomagnify within food chains. As a result, some of the animals with the highest POP burdens live in the Arctic circle (for example, polar bears, which are at the apex of the marine food chain).

Polychlorinated Biphenyls

Polychlorinated biphenyls (PCBs) are POPs that comprise a group of
chemicals that have a biphenyl structure with between 1 and 10 chlorine atoms. Roughly 130 different PCB molecules, known as congeners, have been used commercially, and most commercial preparations contained mixtures of these congeners. They most often can be found near industrial sites where they were produced or disposed of and can contaminate fish in the surrounding rivers and harbors. Studies over several decades have found that PCBs can adversely affect the developing fetus and young children. In utero PCB exposure has been associated with lower birth weight, acute lymphoblastic leukemia and non-Hodgkin’s lymphoma, obesity, immune system dysfunction and impairment, asthma, motor and cognitive developmental deficits as assessed on the Bayley Scale and other instruments, and lowered IQ. Research on postnatal exposure is limited. Exposure through breastfeeding may both increase and decrease IgE-mediated allergy. Children with higher blood levels of PCBs may have impairments in gonadal and pubertal development. Studies on the effects of PCB blood levels on growth have yielded conflicting results.

Because of health concerns, PCBs were banned in the United States in 1977. However, they have persisted in the environment, contaminating water, soil, and air and have made their way into fish and, as a result, humans, albeit at declining levels with the passage of time.

Fish concentrations of PCBs vary widely. They tend to be highest in freshwater fish at the top of their local ecosystem’s food chain. The Environmental Protection Agency maintains a Web site that provides information on local fish advisories across the United States that can identify local water bodies and species with potentially high levels of PCBs (http://fishadvisoryonline.epa.gov/General.aspx).

Although fish can be a significant source of dietary PCBs, most exposure for Americans is from red meat and dairy consumption. On a per-weight basis, butter and processed meats may have as much PCBs as fish, if not more.

Of note, several studies have investigated concentrations of PCBs in fish oil supplements, and 1 recent study examined pediatric supplements in particular. Ashley et al analyzed PCBs in 13 over-the-counter children’s fish oil supplements. Every supplement analyzed contained PCBs, with a mean concentration of 9 ± 8 ng PCBs/g, resulting in a mean daily exposure of 2.5 to 50.3 ng PCBs/day depending on suggested serving size. The trophic level of the fish species or purification method used to produce the supplement did not predict the amount of PCB it contained, although the sample sizes were limited. The Environmental Protection Agency has established RfDs for several PCB mixtures, including Aroclor 1016 at 0.00007 mg/kg of body weight per day. Based on the supplements in the Ashley et al study, several of them, if taken as directed, would result in exposures that exceed this RfD. Also, given the wide range of PCB and n-3 LCPUFA content in the samples, they might provide more or less PCB/g n-3 LCPUFA than wild-caught salmon, a fish that usually has high n-3 LCPUFA and low PCB content.

Dioxins

A dioxin is a member of a class of organochlorine chemicals that originate from, among other sources, waste incineration, paper bleaching, pesticide production, metal smelting, and production of polyvinyl chloride plastics. Dioxins are highly toxic POPs known to cause reproductive and developmental problems, damage to the immune system, and cancer. Dioxin levels in the US population have declined substantially in recent years because of regulations and are expected to continue to fall. Compared with other pollutants, dioxins are rarely a cause for freshwater fish advisories from the

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**FIGURE 1**


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In 2010, for example, only 2 of 533 fish consumption advisories were made on the basis of dioxins (not including dioxin-like PCBs) in the United States. These advisories were for the Hudson River of New York and Trinity River of Texas. Dioxins are present in fish and can be at high concentrations in freshwater fish; however, the levels are often lower than in beef, butter, and cheese.

Toxicant Avoidance
In general, PCBs and other POPs, because they are fat soluble, are found at higher concentrations in fatty fish and are concentrated in fatty tissue. Removing the fatty skin and broiling or baking rather than frying fish may decrease exposure. MeHg, in contrast, tends to be stored in protein rather than in fat and is distributed throughout the flesh of the fish. Thus, removing the skin or fatty tissue does not reduce mercury exposure. For both POPs and mercury, the trophic level of the species on the food web is a major determinant of pollution burdens aside from where the fish or shellfish was raised or lived.

Mercury levels in fish are proportional to their age, size, and trophic level, as well as the amount of mercury contamination in the water where the fish lived and ate. Although certain species have generally been considered to have higher mercury concentrations in their flesh than others, variability in mercury levels even within the same species can be marked. For example, the median concentration of mercury in canned light tuna is 0.128 ppm (µg/g), with a range from 0 to 0.889 ppm; the concentration in canned albacore tuna is 0.338 ppm, ranging from 0 to 0.853 ppm. A 25-kg child consuming 4 oz (113 g) of canned light tuna (a whole can is 5 oz) would, on average, consume 0.08 µg of mercury/kg of body weight (approximately 80% of the RfD) but could get none or as much as 0.57 µg/kg (>5 times RfD) depending on the size, source, and trophic level of the particular fish included in the can.

Increasingly, guidance is available that provides information on nutrients, toxicants, and sustainability by fish species. See Resources for examples.

Fish and Shellfish Poisoning
Fish and shellfish, and in particular bivalve shellfish, such as oysters, clams, scallops, and mussels, can become contaminated with toxins produced by algae. If these toxins are ingested by humans, they can cause several syndromes, some of which may be life-threatening, including amnesic shellfish poisoning, diarrheal shellfish poisoning, neurotoxic shellfish poisoning, paralytic shellfish poisoning, and ciguatera fish poisoning. Because all of these toxins are heat stable, cooking does not prevent intoxication. In recent decades, coastal harmful algal blooms that contained the toxins that cause these syndromes occurred nationwide more than 60 times annually. Although shellfish poisoning syndromes were only rarely reported to the Centers for Disease Control and Prevention between 1990 and 2008, estimates of the true incidence are likely 15,000 cases per year or more in the United States for ciguatera alone. Most ciguatera cases from fish harvested in US waters originate from fisheries in the eastern Gulf of Mexico and around the southern coast of Florida as well as Hawaii. Caribbean fisheries also may be affected. Recent research has suggested that climate change may increase the risk of ciguatera fish poisoning.

Freshwater Fish and Vulnerable Populations
Consuming freshwater fish captured from US waters carries unique risks compared with seafood, given the high concentrations of pollutants that can be found in certain water bodies, particularly POPs and MeHg. The Environmental Protection Agency maintains a database of local fish advisories (see Resources) that provide guidance on when toxicants may be present in lakes and rivers around the nation. Most states have similar databases available on the Internet as well.

For some children, freshwater fish may be a large part of their diets; therefore, fish consumption may carry heightened risk. Some American Indian children, for instance, have been found to have high exposure to PCBs, other POPs, and mercury through eating freshwater fish.

SUSHI
Sushi has become an increasingly popular part of the American diet, including for children. Raw fish and shellfish in sushi carry increased risk for transmitting foodborne illnesses. On the basis of data reported to the Centers for Disease Control and Prevention, sushi accounted for 0.3% of all foodborne illnesses in the United States between 1998 and 2015 (see https://wwwn.cdc.gov/foodboreneoutbreaks/). No evidence supports guidance on the right age to introduce raw fish and shellfish. In places where sushi consumption is more common than in the United States, parents may introduce sushi containing raw fish as early as children can eat solid foods or delay until children enter elementary school.

A NUTRITIONAL COMPARISON
Although some potential toxicants may be more likely to come from consumption of certain forms of fish, most fish, with some notable exceptions, have favorable nutritional and overall health qualities compared with other forms of animal protein. In the United States, red meat and chicken represent the majority of childhood animal protein.
consumption. On average, less than 10% of children's animal protein intake comes from fish. PCBs and dioxins may be found in beef and other animal products in much higher concentrations than in most fish, with the possible exception of farmed salmon or certain freshwater fish.

**SUSTAINABILITY**

Just under 60% of fisheries worldwide are harvested at their maximum sustainable yield, and 30% are overexploited. Several recent and notable instances of complete collapses of fisheries include the Northwest Atlantic cod fishery off the coast of New England and Canada. The depletion of fish stocks has had major consequences for the nutrition of coastal populations, especially in resource-limited nations, where the void left by declining fish stocks has resulted in increased consumption of other animal proteins that may have less healthful profiles, including bushmeat.

Fishery practices also have implications for those who work in them. In the United States, fishers and those working at sea to catch fish have the second-highest on-the-job mortality rate. Research has also shown that children may be trafficked into labor in the fisheries workforce, with dire consequences. One study found that 19% of boys trafficked in the Mekong region of southeast Asia were forced to labor in fisheries. Many of these children were found to have witnessed or experienced violence and exposure to violence, and this was associated with increased risk for depression, anxiety, and posttraumatic stress disorder as well as suicidality. Shrimp, the most consumed seafood in the United States, with the average American consuming approximately 4 lb per year; 94% of shrimp are imported, and almost all are farm raised. Shrimp farms in Southeast Asia and Central and South America have resulted in the loss of millions of hectares of mangrove forest, and shrimp farms account for roughly one-third of mangrove forest loss worldwide. Mangrove forests serve many functions to coastal ecosystems, including providing breeding grounds for wild fish and shellfish. Mangrove forests also are vital contributors to the health of coral reefs and seagrass beds, both among the greatest repositories of marine biodiversity. Shrimp farms have also been the sources of severe nutrient and chemical pollution as crowded pens generate tremendous amounts of waste and require chemical inputs, such as antibiotics and disinfectants, that can harm people exposed to these pollutants. In contrast to shrimp farming, much of the other farm-raised shellfish, such as mussels and oysters, are some of the most sustainably raised seafood available.

**Farmed Salmon**

Salmon is the most widely consumed noncanned fish in the United States,
and over the past 35 years, the majority of salmon eaten has shifted from wild to farm raised. An influential 2004 study in *Science* reported that farmed salmon had levels of PCBs, dioxins, and other POPs several fold higher than wild-caught salmon. However, critics have argued that the potential health harms of consuming the PCBs in farm-raised salmon are more than offset by the health benefits of salmon’s nutritional profile. In addition, among other concerns, farmed salmon has been a source of local pollution from chemical additives (eg, antibiotics) and nutrient overload as well as disease spread, given high animal density and escapes of nonnative salmon species into local ecosystems. Salmon, as carnivores, have also historically been fed fishmeal when farmed, requiring 1.5 to 3 lb of feed for every pound of salmon.

Progress has been made in recent years to address problems associated with salmon farming. Some operations now approximate 1:1 fish-in to fish-out ratios (ie, 1 lb of wild fish in salmon feed produces 1 lb of farmed salmon), scarcely use chemicals, and have greatly reduced disease spread and escapes through better monitoring and lower-density farming. Experiments with vegetarian feeds and other fishmeal and oil substitutes have shown promise at further reducing reliance on wild fish stocks for long-chain omega-3 fatty acids. Experiments with vegetarian feeds and substituting a yeast for anchovies as a source of omega-3 fatty acids have shown promise in further reducing reliance on wild fish stocks. (Note that the original source of all n-3 LCPUFAs in the oceans are phytoplankton.)

Most salmon farms do not yet meet cutting-edge standards for production that limit undesirable environmental and health impacts. Guidance on identifying those operations engaged in best practices can be found from a variety of sources (see Resources). Many major retail outlets have embraced selling seafood that is recommended by major ocean conservation groups.

The Sustainability of Aquaculture Compared With Beef, Poultry, and Pork

Comparing the resource intensity of aquaculture to other animal protein sources, most farmed fish and seafood has a comparable, if not favorable, profile. On a per-calorie basis, beef is by far the most resource-intensive animal protein: it takes about 10 times more irrigated water and 4 times more nitrogen fertilizer and produces about 10 times more greenhouse gas emissions when compared with pork or poultry. Many species of farmed seafood have a carbon footprint roughly equivalent to or less than pork and poultry, although it can vary greatly, especially with long-distance transit. Shrimp eaten in America mostly comes from Southeast Asian nations (Indonesia, India, and Thailand, in particular) and has a disproportionately large carbon footprint, in part because of transport but largely because of mangrove forest loss. Shrimp sourced from these regions can have a carbon footprint an order of magnitude greater than beef.

Fifty percent or more of salmon is farm raised. Farmed salmon comes mostly from Canada, Chile, or Norway. Studies of farmed salmon from these countries have found farmed salmon to have a carbon footprint of approximately 2 kg carbon dioxide equivalent/1000 kcal salmon, which is similar to pork or poultry.

Sustainably Raised and Caught Fish and Shellfish

The United States has some of the best-managed fisheries (wild or farmed) in the world, and although all are not sustainably harvested, all are managed toward that direction even if they have not achieved sustainable harvests to date. The Magnuson Stevens Act (Pub Law No. 109–479 [2006]) serves as the foundation of the US regulation of fisheries and has established a framework to promote the application of the best available science to fisheries management. As a result, identifying the products of American fisheries may be the best first pass assessment of sustainability. Thorough sustainability assessments of fish and shellfish have been conducted by several nongovernmental organizations for many years. These initiatives are summarized in the Resources section of this report.

CONCLUSIONS

Despite the favorable nutritional and, in many cases, sustainability profile of fish and shellfish, children in the United States eat relatively little of them as compared with other animal protein sources, and seafood consumption by children has declined every year since 2007 to levels not seen since the early 1980s. Some evidence suggests that federal mercury advisories on fish consumption may have pushed people away from eating fish in general and canned tuna in particular. Evidence-based expert guidance has largely advised that seafood should have a larger place in the American diet. The recent Scientific Report of the 2015 Dietary Guidelines Advisory Committee, for instance, stated, “The Committee concurs with the Joint WHO/FAO Consultancy that, for the majority of commercial wild and farmed species, neither the risks of mercury nor organic pollutants outweigh the health benefits of seafood consumption, such as decreased cardiovascular disease risk and improved infant neurodevelopment. However, any assessment evaluates evidence within a time frame and contaminant composition can change
rapidly based on the contamination conditions at the location of wild catch and altered production practices for farmed seafood.176

Even if fish and shellfish have a favorable nutritional profile compared with other forms of animal protein, available research to substantiate specific health benefits from fish and shellfish consumption in children remains limited. Further research is needed to clarify the value of fish and shellfish consumption in childhood to health.

RESOURCES

An Interactive Map of Freshwater Fish Advisories in the United States
https://fishadvisoryoneline.epa.gov/GeneraL.aspx (Note that results can be limited to active advisories. In some instances, the last update may be >10 years ago. If this is the case, there is often a link to a state database to look for newer information.)

Environmental Protection Agency Fish and Shellfish Advisories and Safe Eating Guidelines

Monterrey Bay Aquarium Seafood Watch
Seafoodwatch.org

Mercury in Seafood: A Guide for Health Care Professionals

LEAD AUTHORS
Aaron S. Bernstein, MD, MPH, FAAP
Emily Oken, MD, MPH
Sarah de Ferranti, MD, MPH, FAAP

COUNCIL ON ENVIRONMENTAL HEALTH, 2017–2018
Jennifer Ann Lowry, MD, FAAP, Chairperson
Samantha Ahdoot, MD, FAAP
Carl R. Baum, MD, FACMT, FAAP
Aaron S. Bernstein, MD, FAAP
Aparna Bole, MD, FAAP
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Mary Ellen Mortensen, MD, MS – Centers for Disease Control and Prevention/National Center for Environmental Health
Mary H. Ward, PhD – National Cancer Institute

STAFF
Paul Spire

COMMITTEE ON NUTRITION
Steven A. Abrams, MD, FAAP
George J. Fuchs, III, MD, FAAP
Jae Hong Kim, MD, PhD, FAAP
C. Wesley Lindsey, MD, FAAP
Sheela Natesh Magge, MD, MSCE, FAAP

ABBREVIATIONS
ADHD: attention-deficit/hyperactivity disorder
CI: confidence interval
DHA: docosahexaenoic acid
EPA: eicosapentaenoic acid
FDA: US Food and Drug Administration
IgE: immunoglobulin E
LCPUFA: long-chain polyunsaturated amino acid
LDL: low-density lipoprotein
MeHg: methylmercury
n-3: omega-3
n-6: omega-6
OR: odds ratio
POPB: polychlorinated biphenyl
POP: persistent organic pollutant
RfD: reference dose
RR: relative risk

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Fish, Shellfish, and Children's Health: An Assessment of Benefits, Risks, and Sustainability
Aaron S. Bernstein, Emily Oken, Sarah de Ferranti, COUNCIL ON ENVIRONMENTAL HEALTH and COMMITTEE ON NUTRITION

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