

# preconception2infancy (p2i)<sup>TM</sup>

FROM THE EXECUTIVE COMMITTEE OF THE FORUM<sup>TM</sup>

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## The Science that Supports P2i

*The Forum has reviewed the scientific literature and collected peer-reviewed articles that support and elucidate P2i's vision of improving pregnancy outcomes.*

PARTICIPANTS: David Humphrey,  
Chair, Gleason Eakin, John DeHoney,  
Matt Pamuku, David Cheveallier,  
Sarah Mensah; Jonathan Staebler,  
consultant.

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DRAFT

# The Science that Supports P2i

The Forum has reviewed the scientific literature and collected peer-reviewed articles that support and elucidate P2i's vision of improving pregnancy outcomes. Here we summarize selected, published, scientific studies – publications that can be easily accessed by laypersons for the purpose of education and raising public awareness.

## Preconception as a Policy

Several important public health organizations have emphasized the importance of preconception health as a tool in preventing chronic disease. The Centers for Disease Control and Prevention (CDC) has summarized evidence of the effectiveness of preconception care (PCC) in a report (Recommendations to Improve Preconception Health and Health Care)<sup>1</sup> which concludes that preconception and prenatal care can make a significant difference in birth outcomes. PCC concepts have been discussed for over two decades and standards for PCC have been promulgated by the CDC's Select Panel of Preconception Care.<sup>2</sup> However, many barriers to the implementation of PCC remain. There is a need for a fundamental shift that incentivizes well-woman care and preventive visits that include health promotion, risk assessment, and counseling within primary care. This new model of care emphasizes a primary care medical home that accepts responsibility for delivering such services, and that is linked to new information technologies, which allow for such care to be conveniently and comprehensively provided. Although changes in clinical practice are necessary to ensure that women receive PCC, such changes cannot and will not occur without important modifications to public policy, health care financing, and incentivization.

The Environmental Working Group (EWG), a non-profit American environmental organization that specializes in research and advocacy in the areas of toxic chemicals, agricultural subsidies, public lands, and corporate accountability collaborated with Rachel's Network, a group of impassioned women leaders to do research on children's exposure to toxic chemicals. They commissioned five laboratories in the U.S., Canada, and Europe to analyze the umbilical cord blood collected from minority infants born in 2007 and 2008. The laboratories identified up to 232 industrial compounds and pollutants from the blood of these babies and found complex mixtures of compounds in each infant, demonstrating that industrial chemicals absorbed by the mother cross the placenta in large numbers to contaminate a baby before the moment of birth.<sup>3</sup> The published results were replicated by the CDC, which tested the core blood of thousands of infants and their mothers and published their findings in *Pediatrics*, the official journal of the American Academy of Pediatrics, recommending that chemical management policy in the United States be revised to protect children and pregnant women and to better protect other populations.<sup>4</sup>

Hundreds of studies show that various environmental chemicals and pollutants can sow health hazards even before a child is conceived until he reaches full maturity. It is now generally accepted that much has to be done by clinicians, researchers, lay people, and government authorities to improve birth outcomes and the general health of the population with regards to exposure to toxic substances. The

evidence of both the need and the ability is overwhelming, and we have selected some of these to highlight our point.

## **Environmental Impact on Children's Health: Evidences**

Scientific advancements that aid in determining the role of environmental factors in causation of disease are rapidly growing, showing more evidence that biologic factors such as genetics may not be the only major influence in many childhood disorders. A lot of research has been done on environmental as well as lifestyle factors that could affect the outcome of pregnancy and childhood, including the effects of tobacco smoking, alcohol ingestion, excess sugar and fat intake, drug use, and many more. For many years, physicians and other health care professionals have increased their efforts, addressing these lifestyle factors to improve prenatal care and childcare based on the recommendations set by national and medical standards, but the incidence of many chronic childhood diseases continues to rise.

Changing patterns of disease have been documented among children over the recent decades, with a shift in trend from acute infectious diseases to chronic diseases, which could be mild to debilitating. Viral epidemics are now seen to be more controllable than childhood obesity, which in turn is leading more children to develop type 2 diabetes early (once considered an adult-onset type of disease).

Strong evidence linking certain environmental toxicants to serious childhood disorders compels the scientific community to identify these and look deeper into their impact on child health. To this end, the science of environmental pediatrics has grown exponentially in the past decade, and scientific initiative from many sectors has emerged.

A review of literature shows strong associations between various childhood disorders and preconception/prenatal exposure to environmental chemicals and pollutants. Most notable of these associations include preterm births, birth defects, harms to the nervous system, developmental disorders, obesity and diabetes, asthma, cancer, and decline in fertility.

## Part 1

### Preterm Births

It has been reported that the number of babies being born prematurely or preterm has been increasing in recent years. According to March of Dimes, a non-profit organization that works to improve maternal and child health, preterm birth rate has increased by 33% in the last two decades.<sup>5</sup> Similar reports have been published by the Institute of Medicine and by the National Institutes of Health.

Babies who are born before they reach 37 weeks gestational age are usually predisposed to greater risk of low birth weight, severe physical and mental disabilities, and death. Prematurity and other adverse birth outcomes such as low birth weight and birth defects lead to significant increases in healthcare cost, tremendous stress for families and caregivers and decreased productivity in the workplace.<sup>6</sup> For preterm babies who survive the early years of infancy, studies have found the risk of death during early childhood (up to five years) is higher than full-term babies, although the risk becomes the same at 6 to 17 years of age. The increase in risk of premature death reappears during young adulthood (ages 19-36 years). Causes of deaths include congenital anomalies, endocrine disorders and heart disease.<sup>7</sup> Other consequences linked to preterm births relate to delayed brain development and poor academic performance.<sup>8</sup>

Various studies have suggested that aside from genetic anomalies the possible causes associated with preterm births include lifestyle factors and environmental influence. A large study involving almost 60,000 Danish pregnant women showed that regular intake of sweetened soft drinks increased the risk of preterm births.<sup>9</sup> Another study of more than 3000 pregnant women in Adelaide, Australia, and New Zealand looked into the most common risk factors for preterm birth and found that the use of marijuana more than doubles the risk of giving birth to a preterm baby.<sup>10</sup> The nutritional status of a woman before conception has also been found to correlate to the birth weight of her child. Energy, fatty acid, and micronutrient deficiencies in women either before conception or very early in pregnancy have all been implicated in causing low birth weight in infants.<sup>11</sup>

Some of the environmental factors that have been linked to premature births include living in areas with high levels of air pollution, with polycyclic aromatic hydrocarbons (PAHs), chemicals found in soot, being associated with the highest risk of preterm births.<sup>12</sup>

### Birth Defects

The CDC reports that one in 33 babies is born with a major birth defect<sup>12</sup> but the cause of 70% of birth defects is unknown.<sup>5</sup> Several studies involving farm families, however, show that parental occupational exposure to pesticides or endocrine disrupting chemicals (EDC) is associated with significant numbers of birth defects, including external genital malformations (hypospadias, cryptorchidism, and micropenis),<sup>13</sup> neural tube defects (anencephaly and spina bifida),<sup>14</sup> and reduced survival of male fetuses.<sup>16</sup> Data also show that babies from agricultural families who were conceived in springtime or April to July were more

likely to be born with defects compared to other babies. This coincides with the findings of the USGS National Water Quality Assessment (NAWQA), which indicate that concentrations of atrazine, nitrates, and other pesticides were higher during these months.<sup>17</sup>

## Nervous System Harms

Several studies show that exposure of women to many environmental toxins is associated with harm to the brain and nervous system, resulting in neurodevelopmental abnormalities. Toxins that are potentially harmful to the brain and nervous system development include pesticides,<sup>18,19</sup> flame retardants,<sup>20</sup> endocrine disrupting chemicals,<sup>21</sup> and tobacco smoke.

According to Dr. Philip J. Landrigan, Senior Advisor on Children's Health to the Administrator of the U.S. Environmental Protection Agency, exposure to these chemicals during early fetal development can cause brain injury at doses much lower than those affecting adult brain function. However, two main impediments to prevention of neurodevelopmental deficits of chemical origin are the great gaps in testing chemicals for developmental neurotoxicity and the high level of proof required for regulation.<sup>22</sup>

- **Autism**

Various studies demonstrate that maternal exposure to toxic chemicals in the form of pesticides and other environmental toxins is linked to pervasive developmental disorders such as autism. Autism is a childhood neurodevelopmental disorder that affects the brain's normal development of social and communication skills, accompanied by social withdrawal and repetitive hyper-focused behaviors.

Dr. Jill James, Director of the Metabolic Genomics Laboratory at Arkansas Children's Hospital Research Institute (ACHRI) and a collaborator of the Arkansas Center for Birth Defects Research and Prevention conducts research focused on understanding the metabolic and genetic factors involved in the etiology of autism. Her team measures genetic polymorphisms and plasma levels of metabolites that are predictive of impaired methylation capacity and oxidative stress. They discovered that abnormal metabolic and genetic profiles indicate that autistic children may be more vulnerable to environmental factors that increase oxidative stress. Evidence shows that both genetic and environmental factors interact and adversely affect neurologic and immunologic functions during prenatal and postnatal development in children with autism. Recent evidence presented by Dr. James suggests that autism may involve inherited metabolic aberrations that secondarily affect these functions during prenatal and postnatal development.<sup>23</sup>

Research indicates that mothers who were exposed to the organochlorine pesticides endosulfan and dicofol early in pregnancy because they lived within 500 feet from agricultural fields where the chemicals were often sprayed, were more likely to have autistic babies.<sup>24</sup> The finding of organophosphate metabolites in the mothers' urine also predicted the rate of autism in their babies.<sup>25</sup> However, it was found that even babies of families who lived in the inner city of New York were prone to develop autism when their mothers were exposed to chlorpyrifos (an organophosphate insecticide) during pregnancy.<sup>26</sup>

Researchers have also explored the interaction of exposure to organophosphate pesticides, gene expression, and dietary factors as potential contributors to autism.<sup>27</sup> In addition, researchers found that

older fathers are more likely to transmit spontaneous gene mutations that occur over a lifetime in response to environmental stressors to their offspring, which increases the risk of autism.<sup>28</sup>

Autism Advocate<sup>29</sup>, which is the Autism Society's flagship publication, issued a magazine published in 2006 and introduced the scientific community and the public to the connection between autism and the environment. A distinguished Environmental Board chaired by Martha Herbert, MD PhD, and David Humphrey Esq. presented a collection of articles that established the environmental connection with autism. This publication was circulated to more than 150,000 individuals and organizations as well as achieving an internet distribution of over 500,000 copies. Shortly after this publication, research institutions and government agencies began to fund numerous and critical projects to establish the role of the environment with Autism.

- **ADHD**

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common neurobehavioral disorders that is usually first diagnosed in childhood and often lasts into adulthood. Affected children have trouble paying attention and controlling impulsive behaviors, or may be overly active. Studies have shown that children who have organophosphate metabolites in their urine are more likely to have ADHD than children who do not have them.<sup>30,31</sup> It has also been shown that prenatal exposure of women to organophosphates and findings of organophosphate metabolites in a pregnant woman's urine were associated with increased risk of ADHD in their children.<sup>32,33</sup>

Symptoms of ADHD such as inattention, hyperactivity and impulsive behavior were also noted in children whose mothers were exposed to mercury through their consumption of fish before they became pregnant.<sup>34</sup>

- **Cognitive Function**

Pesticide exposure during pregnancy can have dramatic effects on a child's cognitive development. A wide range of animal research and clinical studies tracking the intellectual development of children over time demonstrate evidence pointing squarely at prenatal pesticide exposures as significantly harming the development and functioning of the brain. These harms can then lead to both lower IQ (intellectual quotient) levels and neurodevelopmental delays.

Research by Dr. Philip Landrigan et al found that toxic injury to the fetal brain caused by mercury emitted from coal-fired power plants resulted in significant human and economic consequences on American children. They found downward shifts in children's IQ resulting from prenatal exposure to methylmercury, which were associated with many cases of mental retardation (MR) annually. The costs associated with decreases in IQ in these children amount to about \$2.0 billion/year.<sup>35</sup> It is estimated that between 316,000 and 637,200 children are born each year with umbilical cord blood mercury levels linked to IQ loss, which causes diminished economic productivity over their entire lifetime.<sup>36</sup>

Prenatal exposure to organophosphate insecticides and pesticides has been associated with lower intelligence scores at age 7 by research at the University of California, Berkeley's School of Public Health.<sup>37</sup> Researchers found that every tenfold increase organophosphates detected during a mother's

pregnancy corresponded to a 5.5 point drop in overall IQ scores in their 7-year-olds. Investigator Brenda Eskenazi, UC Berkeley professor of epidemiology and of maternal and child health believes that the difference could mean “more kids being shifted into the lower end of the spectrum of learning, and more kids needing special services in school.” Other researchers have observed that mothers’ exposure to chlorpyrifos (organophosphate) was associated with significant abnormal changes in areas of their children’s brain, which were related to attention, language, reward systems, emotions, and control.<sup>38</sup>

Prenatal exposure to breakdown products of DDT (an organochlorine insecticide) is also associated with neurodevelopmental delays in children, particularly the psychomotor skills linking movement or muscular activity with mental processes. Exposure to DDT itself has been associated with reduced cognitive functioning, memory and verbal skills among preschoolers.<sup>39</sup>

## Obesity and Diabetes

One of the most important health problems in developed countries is that of childhood obesity, which has often been linked to genetic and lifestyle factors. However, scientists believe that overeating and inactivity do not fully explain the current trend in obesity. An examination of environmental causes has led to findings that numerous widely used synthetic chemicals induce weight gain, including pesticides (specifically organochlorines and organophosphates). Researchers explain that these toxins disrupt major weight controlling hormones, alter levels and sensitivity to neurotransmitters, interfere with metabolic processes, and cause widespread damage to body tissues. These effects are believed to change appetite, food efficiency, and the metabolism of fats, proteins, and carbohydrates.<sup>40,41,42</sup> Aside from increased body weight, exposure to organophosphates has also been associated with an increased risk of dyslipidemia, insulin resistance, and diabetes.<sup>43,44</sup>

## Asthma

Asthma is the most common chronic childhood health problem, which affects nearly 9 million children or one in seven US kids. Since children have smaller airways than adults, asthma is especially a serious problem for them. Factors such as pollen, cold weather, respiratory infection, and exercise are some of the factors known to trigger asthma attacks, but a review of clinical and epidemiological studies links exposure to pesticides to asthma attacks and an increased risk of developing asthma.<sup>45</sup>

Researchers from the University of Southern California found that children exposed to herbicides and pesticides early in life have a significantly increased risk for developing asthma compared to children who were never exposed to these chemicals.<sup>46</sup> Researchers from Spain and the United Kingdom also found that prenatal exposure to organochlorine compounds was linked to development of asthma at age four years.<sup>47</sup>

## Fertility

Scientists do not fully understand the role of industrial chemicals in infertility, but many studies suggest a link exists between common pollutants and reproductive system disorders, including low sperm count, sperm damage, and damage to the ovaries and uterus. Scientists have measured significant regional differences in sperm count that cannot be explained by differences in genetic factors.<sup>48</sup> About 12 percent of American women reported having difficulty in getting pregnant or carrying a baby to full term in

2002, which reflects an increase of 20 percent over 1995.<sup>49</sup> Girls may be reaching puberty earlier by 6 to 12 months from the 1960's to the 1990's.<sup>50</sup> EWG studies have identified 149 chemicals that interfere with the delicate cycles of the reproductive system.<sup>51</sup> Several studies also show that developmental exposure to environmental contaminants is associated with increasing incidences of hypospadias (a physical deformity of the penis), undescended testicles (cryptorchidism) and testicular cancer.

## Cancer

The National Cancer Institute (NCI) reported in its "Annual Report to the Nation on the Status of Cancer, 1975-2002" that cancer incidence has steadily increased over the decades for many forms of the disease, including breast, prostate, and testicular.<sup>52</sup> The incidence of childhood cancer increased by 27.1 percent during this period, with the sharpest rise estimated for brain and other nervous system cancers (56.5%) and acute lymphocytic leukemia (68.7%). The incidence of testicular cancer also steadily rose by 66 percent. According to the 2004 report of the American Cancer Society (ACS), the probability that a U.S. resident will develop cancer at some point in his/her lifetime is one in two for men and one in three for women. A broad array of environmental factors plays a pivotal role in the initiation and promotion of cancer and only 5 to 10 percent of all cancers are directly linked to inherited or genetic factors.

Recent studies continue to support the previous findings regarding trends reflecting the rising incidence of childhood cancers. A 2011 meta-analysis of several epidemiological studies published recently shows positive links between parental pesticide exposure and risk of childhood cancer.<sup>53</sup> Researchers found that the risk of lymphoma and leukaemia increased significantly in children when their mothers were exposed to pesticides through household use or professional exposure during the prenatal period. On the other hand, they found that the incidence of brain cancer in children was influenced by the father's exposure to pesticides.

These findings support those of other studies that found a statistically significant increase in risk of childhood cancers among children whose parents experienced occupational pesticide exposure. A number of these studies found that maternal and paternal exposure to insecticides and herbicides up to five years before having a child increased the risk of all childhood brain tumors, astroglial tumors, primitive neuroectodermal tumors, glial tumors, non-Hodgkin's lymphoma, and Ewing's sarcoma.<sup>54,55,56,57</sup> Other studies also showed a link between parenteral home and occupational exposure to insecticides and leukaemia<sup>58</sup> and non-Hodgkin's lymphoma.<sup>59</sup>

## The Solution: Preconception and Prenatal Care

Improving preconception and prenatal care leads to reduction of risk for adverse health effects for women and their children. This can be achieved by optimizing the woman's health and knowledge before planning and conceiving a pregnancy. A woman's reproductive capacity spans almost four decades and optimizing their health before and between pregnancies should be an ongoing process that involves full participation of all segments of the health care system. Several national and international organizations and advocacy groups have emphasized the optimization of health before conception (preconception care), leading to the development of clinical recommendations and educational materials aimed at improving pregnancy-related outcomes.



CDC has developed recommendations based on a review of published research and the opinions of specialists from the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. One of the goals mentioned in the report was to assure that all women of childbearing age in the United States receive preconception care services (i.e., evidence-based risk screening, health promotion, and interventions) that will enable them to enter pregnancy in optimal health.<sup>60</sup> One of the recommendations to achieve their goals was to provide interventions for identified risks, although additional evidence may be needed regarding the effectiveness of interventions.

## The Role of Vitamin D

A report by the National Institutes of Health (“Nutrition Can Modulate the Toxicity of Environmental Pollutants: Implications in Risk Assessment and Human Health”) states there is a convincing body of evidence indicating that nutrition is a modulator of vulnerability to environmental insults and that it is reasonable to consider nutrition as a vital component of human risk assessment. The researchers conclude that healthful nutrition interventions might be a powerful approach to reduce disease risks associated with many environmental toxic insults, and should be considered a variable within the context of cumulative risk assessment, and where appropriate, a potential tool for subsequent risk reduction.<sup>61</sup>

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## Part 2

### The Effects of *In Utero* Nutrition on Adult Health

The importance of preconception and prenatal nutrition is a major concern for obstetricians and pediatricians who want to ensure good maternal and fetal outcomes. However, epidemiologists and other scientists are now looking into maternal nutrition as a factor in the development of chronic disease in the offspring. Studies suggest that perinatal nutrition influences pregnancy outcomes as well as subsequent health of babies in adult life.

#### Fetal Origins Hypothesis

Ever since Dr David J. Barker developed his fetal origins hypothesis stating that chronic, degenerative disease in adult life may be associated with *in utero* factors such as maternal and fetal nutrition, many epidemiologists and economists have investigated other possible factors that may impact health in adulthood.<sup>1</sup> It has been about two decades since the British physician discovered a link between small birth size and heart disease in middle age and evidence continues to grow, proving that many chronic conditions in adult life are not merely influenced by genetic and lifestyle factors. Science journalist Annie Murphy Paul states that fetal origins is an emerging science that is now investigating how various factors like chemical exposures, fetal stress, depression, drug and alcohol use, and nutrition could influence brain development and function.<sup>2</sup>

Dr David J. Barker specifically identified inadequate *in utero* nutrition as a trigger that programs changes in the fetuses' structure and metabolism, leading to a number of diseases in later life, including cardiovascular disease and noninsulin-dependent diabetes.<sup>3</sup> To date, several studies have been published, showing that maternal nutrition indeed has a significant impact on her child's life years after his birth. Because of the supporting evidence, dietary recommendations during pregnancy have emphasized maintaining adequate caloric intake and focusing on specific micronutrients, which can help optimize maternal and fetal outcomes, while avoiding substances that may harm the growing fetus.<sup>4</sup>

#### Prenatal Supplementation

Inadequate nutrition and being underweight have long been recognized as risks factor for unfavorable pregnancy outcomes, but more recently, maternal overweight and obesity have become more common and are now also considered as significant risk factors. Observational studies have suggested that a healthy diet may help modify these risks, and specific diets such as a Mediterranean-style diet have been linked with improved pregnancy outcomes. However, proving these findings by using randomized clinical trials has been difficult and research has focused instead on the role of multivitamins and specific micronutrient supplements in improving pregnancy outcomes.<sup>4</sup>



### **Multivitamin/Minerals**

The influence of taking multivitamins and minerals as prenatal supplements on the outcome of pregnancy has been widely studied. Researchers from the Department of Obstetrics and Gynecology, University of Medicine and Dentistry of New Jersey found that in low income, urban women who took these dietary supplements during the first and second trimesters of their pregnancy, the risks for preterm delivery and low birth weight were significantly reduced compared to women who did not take the supplements. They concluded that the use of multivitamin/mineral prenatal supplements has the potential to reduce the risk of infant mortality and morbidity.<sup>5</sup> A later study involving a large group of Danish women showed that regular use of periconceptual multivitamins resulted in reduced risk of small-for-gestational-age (SGA) and preterm births in nonoverweight women. The findings showed that women who regularly took multivitamins before conception and during pregnancy were more likely to give birth to full-term babies who were of adequate or normal birth weights, supporting previous studies which involved smaller groups of women.<sup>6</sup>

Aside from unfavorable pregnancy outcomes associated with poor fetal nutrition, the fetal origins hypothesis suggests that *in utero* events could later lead to disease, even if some infants were born apparently healthy. Animal and human studies provide some observational data describing the latent effects of poor *in utero* nutrition including chronic degenerative diseases like non-insulin dependent diabetes mellitus and cardiovascular disease. The programming of insulin responses to glucose, cholesterol metabolism, blood pressure, blood coagulation, and hormonal functions are currently areas of active research.<sup>7</sup> However, some authors feel that there is too little data showing associations between birth size and consequences of chronic diseases and available data still have to demonstrate whether these associations are causal.<sup>8</sup>

### **Folic Acid**

Experts recommend eating a healthy, balanced diet that includes a variety of foods to support the growth and development of a fetus *in utero*. However, studies show that many pregnant women are malnourished, either underweight or overweight/obese, or deficient in certain nutrients. The Institute of Medicine's (IOM) Food and Nutrition Board and the American College of Obstetricians and Gynecologists (ACOG) have published the recommended daily allowances (RDAs) on important nutrients such as vitamins, folic acid, calcium, and iron for pregnant women. These dietary reference intakes (DRIs) were based on studies showing strong evidence that these nutrients were essential to the health of the mother and the normal growth and development of the fetus, and deficiencies of which could result in serious health consequences.

For instance, folic acid (folate), a naturally occurring, water-soluble vitamin, is believed to be important in DNA synthesis and maintenance, amino acid metabolism, red blood cell production, and fetal and placental growth. Although it is found abundantly in foods like green, leafy vegetables, most women do not consume the recommended daily allowance of folic acid, so dietary supplementation is recommended.<sup>9</sup> Other important nutrients that most pregnant women are at risk for deficiency include calcium, iron, omega-3 fatty acids, and vitamin D.

### **Vitamin D**

Recent studies have shown that both black and white pregnant women and neonates living in the northern portion of US are at high risk of vitamin D insufficiency, even when mothers are compliant with prenatal vitamin intake. This suggests that higher-dose supplementation with the vitamin is needed to improve maternal and neonatal vitamin D levels.<sup>10</sup> Researchers from University of Montreal recently reviewed literature on maternal vitamin D status and adverse pregnancy outcomes and performed a meta-analysis of these observational studies. After screening 2,406 papers they found 24 rigorous studies and found that pregnant women with 25(OH)D levels lower than 20 ng/ml had an increased risk of preeclampsia, gestational diabetes mellitus, preterm birth, and small-for-gestational age.<sup>11</sup> Another systematic review and meta-analysis involving 31 studies was recently published in *British Medical Journal* and showed similar results.<sup>12</sup>

### **Iron**

The US Preventive Services Task Force<sup>38</sup> and ACOG recommend screening pregnant women for iron deficiency anemia because studies show that the condition is associated with preterm delivery, low birth weight, perinatal mortality, as well as maternal depression. Adequate intake of elemental iron is important during pregnancy to support the increase in volume of red blood cells and meet oxygen requirements of uteroplacental circulation.<sup>13</sup>

### ***Omega-3 Fatty Acids***

*Omega-3 fatty acids are important natural components in fetal neurodevelopment. In contrast to other nutrients, omega-3 long chain polyunsaturated fatty acids (LCPUFAs) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have not been definitively recommended during pregnancy because of lack of data proving the benefits of supplementation. Although mothers' fish and fish oil consumption as well as omega-3 fatty acid supplementation have been linked with improved cognitive function in their children, more research is needed to show the benefits of supplementation versus consumption of a healthy diet. DRIs for DHA have thereby not been established in the United States, although a recommendation for at least two meals of fish per week is advised.*<sup>4</sup>

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