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## Caffeine Intake During Pregnancy and Weight of Offspring in Childhood: A Systematic Review

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# Caffeine Intake During Pregnancy and Weight of Offspring in Childhood: A Systematic Review

## Abstract

**Background:** Childhood obesity currently affects one third of the United States' youth. Meeting criteria for overweight and obesity in childhood not only increases the risk of being overweight or obese in adulthood, but also increases the risk of comorbidities of obesity including: type 2 diabetes, metabolic syndrome, non-alcoholic steatohepatitis, hypertension, obstructive sleep apnea, and slipped capital femoral epiphysis. Several factors have been implicated to have a causal relationship or association with excessive weight gain; however, new studies are suggesting that a significant influence on the weight of the child is present *in-utero*. The current review explores the relationship between caffeine consumption during pregnancy and the weight of offspring in childhood. The purpose of this review is to organize and critically appraise the current data in order to realign our standard of care with the most recent information. Preventing childhood obesity is our best line of defense for our children and the health of our nation.

**Method:** A comprehensive search of MEDLINE-PubMed, Web of Science, CINAHL-EBSCO, and MEDLINE-Ovid was conducted using the following key words: maternal, pregnant women, caffeine, and childhood obesity. The search produced five articles of which four were relevant to the topic and met all eligibility criteria. The four applicable articles were then reviewed using GRADE criteria.

**Results:** Three of the 4 eligible studies suggest that there is an association between higher levels of caffeine intake in pregnancy and increased weight in childhood compared to lower levels of maternal caffeine intake. One study even suggests complete avoidance of caffeine may be advisable after findings reveal increased BMI from infancy to childhood were associated with any amount of caffeine intake during pregnancy. In contrast, a study by the Research Institute at Nationwide Children's Hospital did not support the theory that increasing maternal caffeine consumption during pregnancy increases the risk of childhood obesity.

**Conclusion:** The use of caffeine during pregnancy may be linked to childhood obesity. Providers should consider giving stricter recommendations than the current ACOG guidelines of <200mg/day and may even educate pregnant mothers to eliminate caffeine altogether.

**Keywords:** Maternal, pregnant women, caffeine, childhood obesity

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# **Caffeine Intake During Pregnancy and Weight of Offspring in Childhood: A Systematic Review**

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*A Clinical Graduate Project Submitted to the Faculty of*

*the School of Physician Assistant Studies*

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## **|| Biography ||**

Evelyn Evans hails from San Luis Obispo, California. She attended the University of California, Davis earning a Bachelor of Arts in Studio Art with a minor in Human Physiology in 2014. Evelyn's medical background includes work as an emergency department scribe, physical therapy aide, and volunteer medical assistant in free clinics in both Sacramento and San Francisco. She is excited to assume the role of provider in a variety of fields throughout her career as a PA.

Gina McCoy is from Overland Park, Kansas. She received a Bachelor of Arts in Psychology from Central College of Pella, Iowa in 2014. Part of Gina's clinical background involves working with the pediatric population at Rocky Mountain Hospital for Children in Denver, CO. She is interested in pursuing a career in either pediatrics or obstetrics & gynecology.

## || Abstract ||

**Background:** Childhood obesity currently affects one third of the United States' youth. Meeting criteria for overweight and obesity in childhood not only increases the risk of being overweight or obese in adulthood, but also increases the risk of comorbidities of obesity including: type 2 diabetes, metabolic syndrome, non-alcoholic steatohepatitis, hypertension, obstructive sleep apnea, and slipped capital femoral epiphysis. Several factors have been implicated to have a causal relationship or association with excessive weight gain; however, new studies are suggesting that a significant influence on the weight of the child is present *in-utero*. The current review explores the relationship between caffeine consumption during pregnancy and the weight of offspring in childhood. The purpose of this review is to organize and critically appraise the current data in order to realign our standard of care with the most recent information. Preventing childhood obesity is our best line of defense for our children and the health of our nation.

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**Results:** Three of the 4 eligible studies suggest that there is an association between higher levels of caffeine intake in pregnancy and increased weight in childhood compared to lower levels of maternal caffeine intake. One study even suggests complete avoidance of caffeine may be advisable after findings reveal increased BMI from infancy to childhood were associated with any amount of caffeine intake during pregnancy. In contrast, a study by the Research Institute at Nationwide Children's Hospital did not support the theory that increasing maternal caffeine consumption during pregnancy increases the risk of childhood obesity.

**Conclusion:** The use of caffeine during pregnancy may be linked to childhood obesity. Providers should consider giving stricter recommendations than the current ACOG guidelines of <200mg/day and may even educate pregnant mothers to eliminate caffeine altogether.

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## List of Abbreviations

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<b>ACOG</b>	American Congress of Obstetricians and Gynecologists
<b>CDC</b>	Centers for Disease Control and Prevention
<b>GRADE</b>	Grading of Recommendations, Assessment, Development, and Evaluations
<b>SGA</b>	Small-for-Gestational Age



## **BACKGROUND**

It is no secret that childhood obesity has swiftly reached epidemic proportions as nearly a third of our nation's youth now qualifies as being overweight or obese.<sup>1</sup> The issue of increased weight in childhood is especially problematic given that those who meet criteria for overweight and obesity in childhood are much more likely to be overweight and obese in adulthood and to suffer the systemic consequences of obesity including increased morbidity and mortality.<sup>2</sup> Therefore, the etiology and prevention of obesity among our pediatric population ought to be of critical importance to health care providers in order to promote health and wellness throughout the lifespan.

Initial strategies for remedying the issue of obesity in the pediatric population have focused on modifying environmental factors such as the child's diet, exercise, and access to healthy food. However, these strategies may have failed to rectify the issue at its source; new research suggests that the earliest environmental factors impacting weight in childhood emerge from inside the womb.<sup>3</sup> The theory of fetal programming argues that threats to a fetus in utero may cause permanent physiological changes that predispose the individual to diseases in adulthood.<sup>3</sup> Caffeine is widely recognized as a threat to fetal development due to its connection with increased risk of spontaneous abortion, preterm delivery and small-for-gestational age (SGA) newborns.<sup>4</sup> However, current studies are now suggesting that the consumption of caffeine during pregnancy may have implications well beyond the postnatal period. The current review compiles evidence from four studies that explore an association between maternal caffeine intake and childhood obesity.

## **METHODS**

The initial literature search was conducted via MEDLINE-PubMed and Web of Science online databases using the keywords: pregnant women, caffeine and childhood obesity. Both search engines produced the same three articles<sup>5,5,6</sup>, all three of which matched the eligibility criteria. Eligibility required human studies published in English no earlier than 2008 with abstracts that contained 1 or more of the key search terms identified (See Abstract). A subsequent search of CINAHL-EBSCO using the aforementioned keyword search produced zero articles. A follow-up search was conducted using the keywords: maternal, caffeine and childhood obesity using MEDLINE-PubMed, Web of Science and MEDLINE-Ovid. Of the five articles produced by this search, three were the same articles produced by the initial literature search, one article was not relevant to the current review of literature and one additional article met eligibility criteria.

## **RESULTS**

The online literature searches produced a total of 6 unique articles, 4 of which were relevant and met eligibility criteria. These articles included 3 prospective cohort studies<sup>6,7,8</sup> and 1 case control study.<sup>5</sup>

### **Klebanoff et al**

This case-control study<sup>5</sup> which was part of the Collaborative Perinatal Project, assessed the relationship between maternal serum caffeine metabolite levels and body mass index of offspring at ages 4 and 7 years. Pregnant women were recruited from 1 site in the U.S between 1959 and 1965 and tracked from pregnancy to delivery. Paraxanthine, caffeine's primary metabolite, was measured in women's serum to objectively quantify maternal caffeine intake.

Serum levels were measured at 2 points during pregnancy, <20 weeks' and  $\geq 26$  weeks' gestation. The blood samples were frozen at -20 degrees Celsius and analyzed between 1997 and 1999.<sup>5</sup>

Height and weight measurements were taken at study visits when children were ages 4 and 7 years. The Centers for Disease Control 2000 growth charts were utilized to calculate sex and age specific BMIs. Children with an average z-score, percent BMI  $\geq 85^{\text{th}}$  percentile, and percent BMI  $\geq 95^{\text{th}}$  percentile for age and sex, were considered important outcomes. Furthermore persistent obesity was characterized as a BMI  $\geq 95^{\text{th}}$  percentile at ages 4 and 7 years.<sup>5</sup>

Adjustments were made for a variety of possible confounders including maternal age, race, education, weight prior to pregnancy, smoking at enrollment, gestation at blood draw, and diabetes during pregnancy. Upon analysis, it was recognized that paraxanthine levels tended to be higher in women who were older, had smoked heavily at registration, were less educated, and were Caucasian. Children at both ages were observed to have higher BMIs with increasing maternal age, amount of maternal smoking, and increased maternal prepregnant weight. Ultimately a significant relationship was not demonstrated between maternal serum paraxanthine and increased risk of childhood obesity. A connection between serum paraxanthine was observed with increased risk of elevated BMI in offspring but only up to about 1000  $\mu\text{g/liter}$ . The association flattened or fell at increased paraxanthine concentrations. Adjusting for confounders greatly decreased any associations that were found (Figure 1).<sup>5</sup>

Limitations of the study include not gathering information on the diet or exercise of mothers and their children, nor the incidence of breastfeeding after birth. Another flaw of the study is the difference in caffeine consumption, prevalence of maternal smoking, incidence of prepregnant obesity, and nutritional supplementation for mothers and babies between the population in the 1960s and present day. Lastly, paraxanthine was only measured at 2 points

during pregnancy, and using it as a proxy for caffeine consumption may have skewed the results.<sup>5</sup>

### **Li et al**

This prospective cohort study<sup>6</sup> assessed *in-utero* caffeine exposure and the risk of childhood obesity of offspring over a 15-year follow up period. One thousand sixty-three women with positive pregnancy tests in the San Francisco area were incorporated into a study of the risk factors for miscarriage on patients from Kaiser Permanente Northern California (KPNC) from 1996 to 1998. Of the 1063 women who were early in their pregnancies, 829 of them birthed live children who were included in the study, and 28 children were excluded due to failure to receive pediatric care in the KPNC system. Ultimately 615 mother-child pairs were included in the study. To determine caffeine consumption for the first or early second trimesters of their pregnancies, women reported all beverages consumed since their last menstrual period during in-person interviews. They were questioned on type, timing, frequency, amount, and patterns of beverage consumption since becoming pregnant. Caffeine consumption was reported on a daily or weekly basis including caffeine from coffee, tea, 17 kinds of soda, and hot chocolate. Total daily caffeine intake was calculated using conversion factors. The caffeine in decaffeinated tea proved difficult to calculate, leading the authors to exclude 46 participants who drank decaffeinated teas exclusively. Women were grouped into the following categories of caffeine consumption during pregnancy for data analysis: 0mg, <150mg per day, and  $\geq$ 150mg per day.<sup>6</sup>

Weight and height of offspring from birth onward were obtained using paper and electronic medical records. For those children that stayed in the KPNC system, data was collected for over 15 years until the end of the study on May 31<sup>st</sup>, 2013. BMI was calculated if both height and weight had been recorded on the same day. Almost 100% of mother and baby

pairs had multiple BMI measurements with the average number of child measurements being 17. Children were considered obese if they had a BMI at or above the 95<sup>th</sup> percentile after age 2, per the 2000 Centers for Disease Control definition of obesity. Furthermore, children were considered to have persistent obesity rather than temporary/transitory obesity if more than half of their BMIs during follow up met criteria for obesity, or if after age 11 years their final measurement was over the 95<sup>th</sup> percentile.<sup>6</sup>

When set against women who did not consume caffeine during pregnancy, it was found that women who consumed greater than 150mg of caffeine per day were more likely to be older, Caucasian, smokers, multiparous, and tended not to breastfeed their offspring. Multiple factors were controlled for including gender and age of children at weight measurements, prepregnancy BMI and race/ethnicity, and maternal age and smoking. The study observed an 87% increased risk of obesity in children of women consuming any amount of caffeine during pregnancy compared to the children of women whose caffeine consumption was 0. Daily maternal caffeine intake  $\geq 150$ mg showed a more than doubled risk of offspring obesity and daily maternal caffeine consumption  $< 150$ mg was associated with a 77% increase in offspring obesity risk. After analyzing children with persistent obesity separately from children with transitory obesity, a statistically significant linear dose-response relationship between amount of daily maternal caffeine intake and obesity in offspring was found in female children with persistent obesity. Caffeine source as well as factors such as preexisting maternal conditions and lifestyle patterns of offspring did not appear to alter the results.<sup>6</sup>

Limitations of this study include not ruling out all possible confounders such as added sugar in beverages. Caffeine intake was only reported in the first two trimesters, thus caffeine consumption could have changed in the third trimester leading to inaccurate estimations.<sup>6</sup>

## **Papadopoulou et al**

This was a prospective cohort study,<sup>7</sup> embedded in the Norwegian Mother and Child Cohort study, that looked for connections between caffeine intake in pregnant women and weight in offspring until age 8 years. Taking place across Norway, the study recruited mothers from 2002-2008. Exclusion criteria consisted of multiple gestations, stillbirths, fetal malformations and chromosomal abnormalities. Caffeine intake was self-reported during mid-pregnancy using the Food Frequency Questionnaire (FFQ) which was created for the study to assess diet during the first 4-5 months of pregnancy. Only mother-child pairs who had a completed FFQ and data on small for gestational age as well as offspring height and weight were included in the study, leaving 50 943 pairs as the study cohort. Using the FFQ, mean daily caffeine consumption was calculated from a variety of sources including coffee, black tea, soda, energy drinks, chocolate beverages, sandwich spread, desserts, and cocoa containing foods. Caffeine intake was grouped into the following categories: low (0-49mg/day), average (50-199mg/day), high (200-299mg/day), and very high ( $\geq 300$ mg/day).<sup>7</sup>

Body growth information including weight and length/height of singleton offspring were collected at the same 11 age points from 6 weeks to 8 years old. The study used a WHO weight gain z-score of  $>0.67$  to define excess infant growth and criteria from the International Obesity Task Force to define children as overweight.<sup>7</sup>

Statistical adjustments were made for maternal age, education, BMI, smoking, caloric intake and nausea and vomiting, as well as for paternal smoking. Gestational age and gender of offspring was accounted for. A negative control analysis was also performed to assess if paternal caffeine intake could be a possible confounder.

A comparison of pregnant women revealed that the more caffeine a woman consumed the more likely she was to be above 30 years, multiparous, have a higher energy intake, smoke, and not experience nausea or vomiting during pregnancy. She also tended to have lower education, be obese prior to pregnancy and have a partner who was obese and smoked. The study demonstrated that average, high, and very high caffeine intake were associated with higher risk of excess infant growth. Any amount of caffeine exposure proved to increase the risk of becoming overweight in offspring at ages 3 and 5, with a continued elevated risk at 8 years for children exposed to very high levels of caffeine *in-utero* (Table 2). Even exposure to small quantities of caffeine was related to higher BMIs from age 1 month to age 8 and very high exposure demonstrated an increased velocity of weight gain from infancy to age 8. The negative paternal control yielded very little change in the connection between maternal caffeine consumption and risk of excess infant growth and overweight at 3 years old.<sup>7</sup>

A limitation of this study is that not all participants could contribute anthropomorphic data at 8 years leading to possible outcome misclassification. Varying percentages of the population had either not reached 8 years old by the end of the study, could not contribute information, or were lost to follow up. Self-reporting of diet is another limitation.<sup>7</sup>

### **Voerman et al**

This population-based prospective cohort study,<sup>8</sup> performed in Rotterdam, the Netherlands, looked at the relationship between maternal caffeine consumption in pregnancy with growth patterns, body fat composition and insulin levels of offspring from birth to age 6 years. Nestled within the Generation R study which focused on fetal life through childhood, the study included pregnant women enrolled between 2001 and 2005. Originally 8879 women were

enrolled during pregnancy and ultimately 5562 were involved in the follow-up 6 years later, contributing information on the BMI, body composition, and insulin levels of their children.<sup>8</sup>

Maternal caffeine ingestion was assessed by mail in questionnaire during all 3 trimesters of pregnancy with response rates over 75% in each trimester. Women provided information on the average number of daily cups of coffee and tea consumed, and the caffeine content was then calculated using standard caffeine amounts for coffee and tea in the Netherlands. Caffeine intake was divided into 4 categories: <2 units, 2-3.9 units, 4-5.9 units,  $\geq 6$  units, with each unit equal to 90mg of caffeine (a standard cup of coffee).<sup>8</sup>

Children's height and weight were collected using medical records from birth, subsequently measured at 6 months and then in 12-month intervals until age 3 years. Body mass index (BMI) was calculated beginning at 6 months of age and then sex and age appropriate standard deviation scores (SDS) were made for study participants utilizing North-European and Dutch growth charts. At age 3 children were described as overweight or obese according to The Obesity Task Force definition of obesity for girls and boys specifically. Dual-Energy X-ray absorptiometry (DXA) was used to calculate total body fat mass and android/gynoid fat mass ratios in children at age 6 years. Additionally, abdominal ultrasound was utilized to ascertain pre-peritoneal fat mass in place of visceral fat. Insulin and C-peptide levels were measured using fasting venipuncture blood draws in children at 6 years old.<sup>8</sup>

Questionnaires aided in gathering information such as maternal demographics, smoking and alcohol consumption during pregnancy, sources of nutrition in offspring during infancy, and the amount of TV watched by 6-year-old children. Hospital and midwife registries provided data on pregnancy disorders like gestational diabetes and hypertension.<sup>8</sup>



Women with caffeine intakes  $\geq 6$  units per day tended to have higher education levels, have never given birth before, and be European. Mothers were excluded from analysis due to failure to report all caffeine consumption during pregnancy or from loss to follow up, though the difference in their caffeine intake compared to women included in the analysis was minimal. When analyzing the results of the study, standard 95% confidence intervals were utilized and P values of  $< 0.05$  were considered significant. Compared with the offspring of pregnant women who consumed  $< 2$  units of caffeine per day, children of women consuming  $\geq 6$  units of daily caffeine had increased weight gain from birth to 3 years old as well as increased BMI from 6 months to 3 years old. Additionally, the children of mothers consuming 4-5.9 and  $\geq 6$  units of daily caffeine had increased childhood BMI and total body fat mass. Elevated android/gynoid fat mass ratio was solely observed in offspring of women with  $\geq 6$  units of daily caffeine intake. The completely adjusted model revealed a greater risk of being overweight in the children of women who consumed  $\geq 6$  units of caffeine during pregnancy set against the children of women who consumed  $< 2$  units (odds ratio: 1.25 (95% CI: 0.68, 2.30)). No association was found with caffeine consumption in pregnancy and childhood insulin or c-peptide levels.<sup>8</sup>

Though a large population of pregnant women and their children were studied, there was a 30% loss to follow up at 6 years. Other limitations include the study's inability to fully adjust for specific diets of pregnant women and their children, and the exclusion of dietary sources of caffeine beyond coffee and tea. Because questionnaires were used to establish caffeine intake, results could be subject to underreporting. Lastly it was assumed that a cup of coffee was 125mL, potentially causing a mis-categorization of maternal caffeine consumption if volumes strayed from the expected value.<sup>8</sup>

## DISCUSSION

Caffeine is the most commonly used psychoactive drug in the world. It can be found in a wide variety of foods and beverages including coffee, tea, soda, chocolate, weight loss pills, and certain types of pain medication.<sup>9</sup> Caffeine's ability to cross the placenta and blood-brain barrier allows entry of the drug into the fetal blood supply. Exposure of the fetus to caffeine is further augmented during pregnancy as a result of prolonged elimination of the drug.<sup>10</sup> Animal studies yield several biological postulates that may explain how fetal caffeine exposure can lead to weight gain by altering: (1) adenosine regulation,<sup>11</sup> which plays an important role in development, (2) leptin levels<sup>12</sup>, which regulates feelings of hunger, and (3) the hypothalamus-pituitary-axis<sup>13</sup>, which increases metabolic syndrome susceptibility.

In light of the potential teratogenic effect of caffeine on fetal development, several recommendations have been put forth to limit in utero caffeine exposure. The American Congress of Obstetricians and Gynecologists (ACOG) suggests that pregnant women limit caffeine to no more than 200mg/day.<sup>14</sup> Despite this recommendation, Weng et al found that 75% of U.S. pregnant women continue to consume caffeine during pregnancy and 15% of U.S. pregnant women report consuming 200mg of caffeine or more per day while pregnant. Considering the prevalence of caffeine consumption in pregnancy and its possible association with increased weight in childhood, there exists a window of opportunity for the prevention of childhood obesity as it relates to environmental exposures in the womb.

Despite the conflicting results presented in the aforementioned articles, 3 of the 4 studies<sup>6,7,8</sup> reviewed found an association between maternal caffeine intake and increased weight in childhood. Of the 3 articles<sup>6,7,8</sup> that showed a statistically significant correlation between *in-utero* caffeine exposure and increased weight in childhood, 2 studies<sup>6,7</sup> found that any caffeine

intake led to adverse effects on childhood weight. Bearing in mind that ACOG recommends limiting caffeine consumption to less than or equal to 200mg/day during pregnancy,<sup>14</sup> consideration should be taken to create stricter guidelines and possibly to recommend complete elimination of caffeine intake during pregnancy.

Each study measured caffeine intake differently. Voerman et al<sup>8</sup> limited their study of 7857 mothers by collecting information on maternal caffeine intake solely from caffeinated and decaffeinated coffee and tea. Voerman et al<sup>8</sup> reasoned that from 2002-2006, when their data was collected, coffee and tea accounted for 96% of overall caffeine consumption.<sup>8</sup> However, the Papadopoulou et al<sup>7</sup> study was conducted between 2002-2008 with a larger sample size of 50943 pregnant mothers and the results showed “adverse effects on child’s growth even at low caffeine intakes, in the range of the recommendations, that are mostly due to consumption of foods and drinks other than coffee (chocolate, black tea, caffeinated sodas)”. Li et al<sup>13</sup> measured caffeine intake from coffee, tea, soda, energy drinks and hot chocolate and found similar effects of caffeine exposure as Papadopoulou et al.<sup>14</sup> These results are not surprising as many foods and beverages contain caffeine that consumers may not be aware of and these sources of caffeine may play a larger role on *in-utero* exposure to caffeine than previously suspected.

All 3 of the prospective cohort studies<sup>6,7,8</sup> in this review used self-report to measure maternal caffeine intake. There are several factors that can reduce the accuracy of these measurements. The studies that used self-report were conducted in different countries: the United States,<sup>6</sup> Norway,<sup>7</sup> and the Netherlands.<sup>8</sup> A coffee serving in the Netherlands is typically 125mL and contains about 90mg of caffeine, assuming the coffee is caffeinated. However, a standard U.S coffee mug holds 350mL of fluid, which equates to 142mg of caffeine. A U.S. coffee mug is often referred to as a “cup” of coffee, while the US customary unit, cup, is a unit of volume equal

to 8oz. Furthermore, espresso-containing drinks which are commonly referred to as coffee drinks are now a prominent source of caffeine in the United States. In fact, “gourmet” espresso drinks now account for 59% of coffee consumed daily in the United States.<sup>15</sup> Compared to coffee which averages 12-16mg of caffeine per ounce, one ounce of espresso contains 63mg of caffeine.<sup>16</sup> However, the amount of caffeine in coffee or espresso varies by brand, type of bean, roasting method and preparation technique.<sup>16</sup> Depending on how the researchers educated mothers on how to self-report their intake of caffeine-containing beverages, the self-reported measurements may not accurately represent maternal caffeine consumption.

Klebanoff et al<sup>5</sup> attempted to quantify maternal caffeine intake more objectively by measuring serum paraxanthine, the primary metabolite of caffeine. Using a biomarker for caffeine may have limited reporting errors that influenced the results of the other studies in this review. However, Klebanoff et al drew maternal serum from 1959-1966, nearly 5 decades before the remaining studies in this review collected their data.<sup>5</sup> This difference is not to be taken lightly. During World War II, the United States began rationing coffee available to the general public. In 1946, just as WWII ended, the supplies of coffee increased, and the annual per capita coffee consumption peaked to an all-time high. Klebanoff et al consider increased maternal intake to be a strength of their study<sup>5</sup>; however, this unique time in U.S. history leads to a multitude of confounding factors that may limit this study’s validity including: lack of prenatal vitamin recommendations, higher prevalence of smoking, wide usage of synthetic chemical pesticides, etc. Furthermore, several factors determine how fast an individual can metabolize food, namely pregnancy, smoking, regulation of TSH, exercise, etc. Anything that can change an individual’s metabolism will also affect the amount of paraxanthine in the serum. For these

reasons, the quality of evidence was downgraded and provided very low quality evidence based on GRADE criteria.

Despite several limitations, the highest quality evidence available suggests a link between maternal caffeine intake and increased weight in childhood. The World Health Organization considers obesity a top public health challenge of the 21<sup>st</sup> century, yet, over 75% of U.S. pregnant women consume caffeine on a daily basis.<sup>6</sup> This is an area where providers can use patient education and motivational interviewing in order to prevent serious implications throughout a lifespan. Providers should consider more stringent caffeine intake recommendations or complete abstinence from maternal caffeine intake to all pregnant women and those attempting to become pregnant in order to prevent childhood obesity and its comorbidities.

## **CONCLUSION**

The articles in this review were contradictory regarding the association between maternal caffeine intake and childhood obesity. Two articles found that any amount of caffeine intake during pregnancy had an adverse effect on weight of offspring in childhood. Voerman et al found that higher levels of caffeine are linked to increased weight gain from birth to 6 years and a higher BMI from 6 months to 6 years. Only one article found no association with maternal caffeine intake and weight in childhood; however this study had very low quality evidence and studied women who were pregnant in the 1950s and 60s.

Despite the contradictory nature of these articles and the poor quality of evidence provided, there is sufficient evidence to suggest a link between maternal caffeine intake and increased weight in childhood. As childhood obesity rates are quickly rising and the majority of pregnant mothers throughout the U.S. are still consuming caffeine, this should be an area of

concern for providers. This review seeks to encourage providers to recommend pregnant patients limit caffeine intake below ACOG guidelines and, perhaps, eliminate the use of caffeine entirely.

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**Table 1: Quality Assessment of Reviewed Articles**

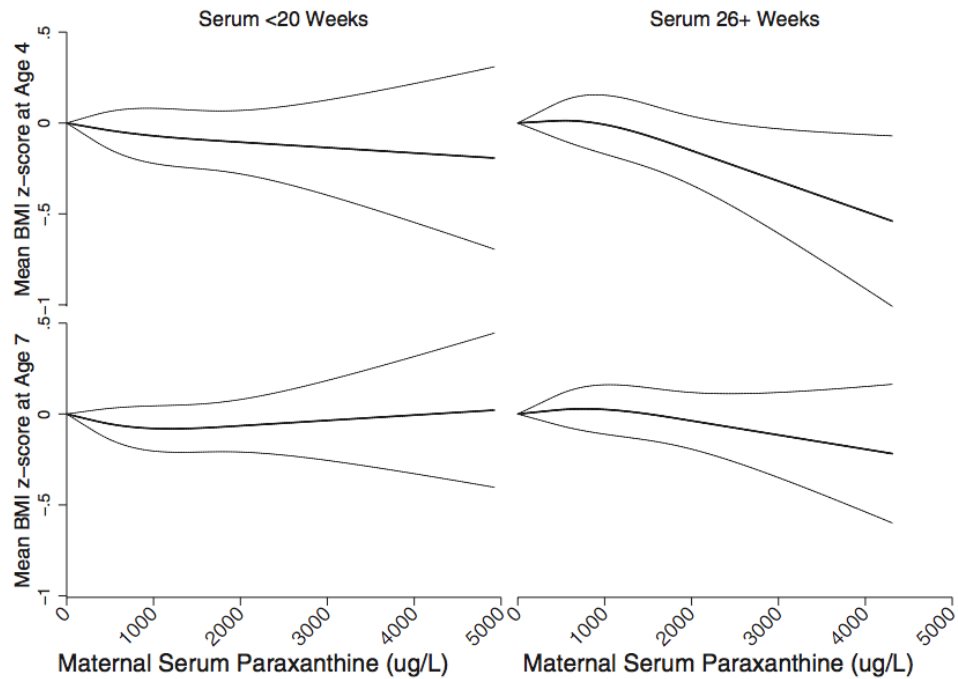
Study	Design	Downgrade Criteria					Upgrade Criteria	Quality
		Limitations	Indirectness	Inconsistency	Imprecision	Publication bias		
Klebanoff et al <sup>5</sup>	Case Control Study	Serious <sup>a</sup>	Serious	Not Serious	Not Serious	Likely	None	Very low
Li et al <sup>6</sup>	Prospective Cohort	Serious <sup>b</sup>	Not Serious	Not Serious	Not Serious	Unlikely	Dose Response	Very low
Papadopoulou et al <sup>7</sup>	Prospective Cohort	Serious <sup>b,c</sup>	Not Serious	Not Serious	Serious	Unlikely	None	Very low
Voerman et al <sup>8</sup>	Prospective Cohort	Serious <sup>b,c</sup>	Not Serious	Not Serious	Not Serious	Unlikely	None	Very low

<sup>a</sup> Study published more than 50 years ago, did not collect diet or exercise information, and used paraxanthine to measure caffeine consumption  
<sup>b</sup> Strong use of self-reported data  
<sup>c</sup> High rate of lost to follow up or ineligible data

**Table 2** Maternal caffeine intake in pregnancy and risk of overweight/obesity at age 3 years, 5 years and 8 years (recreated from Papadopoulou et al<sup>7</sup>)

<b>Risk of overweight and/or obesity*</b>							
<b>All children (n=50 943)</b>							
<b>Age 3 years</b>		<b>Age 5 years</b>		<b>Age 8 years</b>			
<b>OR</b>	<b>95% CI</b>	<b>OR</b>	<b>95% CI</b>	<b>OR</b>	<b>95% CI</b>		
<b>Maternal daily caffeine intake</b>							
Low (<50mg)	1.00		1.00		1.00		
Average (50–199mg)	1.05	0.99 to 1.12	1.00	0.95 to 1.06	0.95	0.86 to 1.04	
High (200–299mg)	1.17	1.05 to 1.30	1.12	1.02 to 1.23	1.11	0.94 to 1.31	
Very high (≥300 mg)	1.44	1.24 to 1.67	1.29	1.13 to 1.47	1.29	1.04 to 1.61	
<b>After excluding smokers during pregnancy (n=47 036)</b>							
Low (<50mg)	1.00		1.00		1.00		
Average (50–199mg)	1.05	0.99 to 1.12	1.00	0.95 to 1.06	0.92	0.84 to 1.02	
High (200–299mg)	1.17	1.04 to 1.32	1.10	1.00 to 1.23	1.08	0.89 to 1.29	
Very high (≥300 mg)	1.50	1.25 to 1.79	1.31	1.12 to 1.54	1.30	1.00 to 1.70	
<b>After excluding SGA neonates (n=46 718)</b>							
Low (<50mg)	1.00		1.00		1.00		
Average (50–199mg)	1.06	0.99 to 1.12	1.01	0.95 to 1.06	0.96	0.87 to 1.05	
High (200–299mg)	1.18	1.05 to 1.32	1.14	1.03 to 1.25	1.11	0.94 to 1.32	
Very high (≥300 mg)	1.48	1.28 to 1.72	1.32	1.15 to 1.51	1.36	1.09 to 1.69	

The same population was included at each age since the outcome was defined using model-derived anthropometrics.  
 All models adjusted for maternal age, parity, parental education, prepregnancy BMI, total energy intake, nausea and/or vomiting during pregnancy, paternal BMI, parental smoking during pregnancy, gestational age and gender.  
 \*Overweight and/or obesity in children, according to the International Obesity Task Force definition.  
 BMI, body mass index; SGA, small for gestational age.



**FIGURE 1.** Mean difference in BMI z-score at ages 4 and 7 years by maternal serum paraxanthine (micrograms/liter) at <20 and 26+ weeks, adjusted for maternal age, prepregnant weight, smoking, education, gestation at blood draw, and diabetes. Lines indicate estimate (dark line) and 95% CI (lighter line).

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