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# Does Pet-Keeping Modify the Association of Delivery Mode with Offspring Body Size?

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## Abstract

**Objectives—**Caesarean-section (CS) delivery increases risk of childhood obesity, and is associated with a distinct early-life gut microbiome, which may contribute to obesity. Household pets may alter human gut microbiome composition. We examined if pet-keeping modified the association of CS with obesity at age 2 years in 639 Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS) birth cohort participants.

**Methods—**Pet-keeping was defined as having a dog or cat (indoors ≥1 hour/day) at child age 2 years. We used logistic regression to test for an interaction between CS and pet-keeping with obesity (BMI≥95$^{th}$ percentile) at age 2 years, adjusted for maternal obesity.

**Results—**A total of 328 (51.3%) children were male; 367 (57.4%) were African American; 228 (35.7%) were born by CS; and 55 (8.6%) were obese. After adjusting for maternal obesity, CS-born children had a non-significant (*P*=0.25) but elevated 1.4 (95% CI: 0.8, 2.5) higher odds of obesity compared to those born vaginally. There was evidence of effect modification between current pet-keeping and delivery mode with obesity at age 2 years (interaction *P*=0.054). Compared to children born vaginally without a pet currently in the home, children born via CS without a pet currently in the home had a statistically significant (*P*=0.043) higher odds (odds ratio=2.00; 95% CI: 1.02, 3.93) of being obese at age 2 years.

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**Conclusions—**Pets modified the CS-BMI relationship; whether the underlying mechanism is through effects on environmental or gut microbiome requires specific investigation.

**Keywords**

Birth cohort; childhood obesity; delivery mode; companion animals

## Introduction

The epidemic of pediatric obesity and overweight in the United States has burgeoned in recent decades [1]. Data from the National Health and Nutrition Examination Survey (NHANES) demonstrated that between NHANES I (years 1971-1974) and NHANES 1999-2000, the rate of obesity in 2-5 year olds significantly increased from 5.0% to 10.4% [2]; in 2009-2010, 12.1% of US children aged 2-5 years were obese [1]. Over this same time period, rates of caesarean-section (CS) delivery also steeply increased [3, 4]. Several studies in different populations have demonstrated that delivery mode may increase the risk of childhood obesity/overweight [5-8]; not surprisingly, results have been inconsistent across different study groups [9-13]. A recent meta-analysis summarized the association between CS and childhood (ages 3-8 years) overweight/obesity, estimating a moderate association with an overall pooled odds ratio (OR) of 1.32 (95% CI: 1.15, 1.51) for CS on risk of offspring overweight/obesity [14]. While this is a moderate-sized association, given that CS delivery is common, Li et al (2012) suggest that CS delivery may have significant implications for public health with respect to obesity risk [15].

Mechanistically, the association between delivery mode and childhood overweight/obesity is postulated to at least partially be explained through differences in establishment of the gut microbiome [5, 6, 14]. Newborns delivered vaginally have bacterial communities resembling their mother's vaginal microbiome whereas those born by CS have compositionally distinct bacterial communities more closely resembling maternal skin [16]. These differences in microbiome composition by delivery mode persist into infancy [17]. Work in animal models has demonstrated that the gut microbiome composition and function influences body size [18, 19]. A small number of human studies have also demonstrated a plausible link between selected bacteria of the gut microbiome and childhood obesity [20-23].

Studies focusing on the role of pet-keeping in early-life have largely focused on allergic/asthmatic disease. Pet-keeping in early-life is considered a potential protective factor for development of allergic disease [24] potentially through modification of the home microbial environment and a resident's own microbiome. Pet-keeping increases house dust bacterial community richness and diversity, with dog-ownership in particular leading to introduction of additional bacterial types into house dust [25]. Dog-ownership is associated with greater bacterial diversity on adult skin [26] and infants living with pets have increased gut microbiota richness and diversity [27]. Ingestion of dog-associated house dust results in a distinct gut microbiome composition in mice [28]. As with obesity, CS is also associated with increased risk of childhood allergic disease [29]. The association between delivery mode and a measure of allergic disease risk, total immunoglobin E, is modified by early-life

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pet keeping, with indoor pet exposure having a significantly greater protective effect on children born via CS [30]. To our knowledge, no studies have examined if there is a similar modification of the relationship between delivery mode and childhood obesity by early-life pet keeping.

Although a growing body of literature implicates delivery type in future obesity risk [5, 6, 14], much less is known regarding postnatal exposures that could modify this association. We therefore examined the association of CS delivery with childhood body size at age 2 years in the racially and socioeconomically diverse Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS) birth cohort [30, 31]. Our primary objective was to examine if the association between delivery mode and childhood body size at age 2 years was modified by pet-keeping.

## Methods

### Study Population

WHEALS recruited pregnant women with due dates from September, 2003 through December 2007, and who were seeing a Henry Ford Health System (HFHS) practitioner at one of five clinics to establish a birth cohort [30, 31]. All women were in their second trimester or later, were aged 21-49 years, and were living in a predefined geographic area in western Wayne County that included the western portion of the city of Detroit as well as the suburban areas immediately surrounding the city. Post-partum interviewer-administered questionnaires were completed at child age 1, 6, 12, and 24 months. Children and their parent/guardian were invited to return for a clinic visit at child age 2 years for assessment of child health. All participants provided written, informed consent and study protocols were approved by the Institutional Review Board at HFHS.

### Body Size, Pet Exposure and Other Covariate Measurement

Delivery records for WHEALS women were abstracted to obtain delivery type (vaginal or CS), birthweight and gestational age at delivery. Maternal prenatal care records were abstracted to obtain body mass index (BMI) at first prenatal care visit; maternal obesity was defined as BMI≥30 kg/m$^2$. Gender- and gestational-age adjusted birthweight Z-scores were calculated using the US population as a reference [32]. Maternal race was self-reported.

At the 2 year clinic visit, trained field staff measured child height in stocking feet with a wall stadiometer. Child weight was measured with the child in light clothing using a balance beam physician scale. BMI was calculated as weight (in kg) divided by the square of height (m$^2$). Height Z-scores and BMI Z-scores and percentiles were calculated according to the 2000 Centers for Disease Control and Prevention age- and gender-specific growth charts [33]. Obesity was defined as BMI≥95th percentile [33].

At all interviews (pre-delivery and 1, 6, 12 or 24 months postpartum), the parent/guardian was asked if they had a pet in the home (inside ≥1 hour). As done elsewhere [30], for the primary analysis current pet-keeping was defined as report of having a cat or dog indoors at least part of the day at the 24 month visit. Some studies have attributed health benefits primarily to dog ownership [34-36]; current exposure only to dog was defined similarly.

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Since pet-keeping may change over time, whether the child ever had pet exposure was defined as a response at any interview that they kept a pet inside ≥1 hour.

### Statistical Analysis

For descriptive purposes, maternal, newborn and child characteristics were compared by delivery mode using a chi-square test for discrete characteristics and a t-test for continuous characteristics.

To examine the association between CS and the binary outcome of obesity (BMI≥$95^{th}$ percentile vs. BMI<$95^{th}$ percentile), we utilized logistic regression as the prevalence of obesity was relatively low (<10%) [37]. Linear regression was used for continuous BMI Z-score. Models were first fit unadjusted. Potential confounding factors were identified as any factor that when added to the model resulted in a ≥10% change in the parameter estimate for delivery mode on body size measure [38]. Potential confounders included: maternal age, maternal race, maternal education, maternal smoking during pregnancy, maternal obesity, ever breastfed, firstborn status, child gender, birthweight Z-score, and child age. Only maternal obesity was identified as a potential confounding variable.

Potential effect modification of the association between delivery mode and body size by pet-keeping, gender, birthweight or breast feeding was examined using interaction terms (product of selected factors). An interaction $P \leq 0.2$ was used as a threshold for identifying potentially important interaction terms [39]. To further evaluate effect modification by pet-keeping, we also estimated the joint effect of delivery mode and current pet-keeping on BMI measures. Children born via CS with and without pets and children born vaginally with pets were compared to vaginally-born children without pets. Finally, as pet-keeping [40], CS [41], and obesity [1] vary by race, a three-way interaction term between race, pet-keeping and delivery mode was fit to examine potential modification of the relationship of mode of delivery and BMI measures.

We also conducted several sensitivity analyses. Although we *a priori* examined obesity as the primary categorical outcome variable, there is potential loss of information by not examining all BMI category outcomes (i.e. underweight, normal weight, overweight and obese). We examined the joint effect of CS and current pet-keeping on BMI category using a multinomial logistic regression model with normal weight as the reference category. Models were also fit using a variable indicating whether the child ever had any pet exposure or with a variable indicating exposure specifically to dogs.

## Results

The WHEALS cohort included 1,258 babies; 706 children (56.1%) completed a 2 year follow-up visit in the clinic. We excluded 10 sets of twins (n=20 children). Seventeen children missing delivery mode and 30 children missing height and weight information at the 2 year visit were excluded. Our final sample size consisted of 639 children. We compared the 639 children included in the analytic sample to the 619 children not included in the analytic sample for selected factors. There was no difference in rates of CS comparing those who were (35.7%) and were not included (38.9%) ($P$=0.24). Mean maternal age at

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delivery was statistically significantly higher (*P*<0.001) in those included (30.1±5.2 years) compared to those not included (29.0±5.2 years). Statistically significantly fewer African-American children were in the included sample (57.4%) relative to those not included (67.2%).

Most children were born vaginally (64.3%). Table 1 presents maternal, newborn and child characteristics by delivery mode. The only maternal characteristics significantly associated with delivery mode were age at delivery (*P*<0.001), maternal BMI at first prenatal care visit (*P*<0.001) and maternal obesity (*P*<0.001). Birth order was significantly (*P*=0.027) associated with delivery mode; 43% of CS births were first-born, compared to 35% of vaginal births. Mean BMI, BMI Z-score and BMI percentile at age 2 years were each statistically significantly (all *P*<0.05) higher in children born via CS compared to vaginal birth. There were no other statistically significant differences in selected characteristics by mode of delivery.

Of the 228 born via CS, type of CS (i.e. planned/scheduled vs. unplanned/emergent) was available on 224 deliveries; 106 (47.3%) were planned and 118 (52.7%) were unplanned. Among those born via CS, comparing those with planned vs. unplanned CS, there was no difference in obesity (*P*=0.943) or BMI Z-score (*P*=0.391); data not shown.

### Association of Delivery Mode with Body Size at Age 2 years

CS was associated with an elevated but not statistically significant OR for obesity at age 2 years (Table 2). After adjustment for maternal obesity, CS was marginally associated (*P*=0.080) with BMI Z-score; compared to those born vaginally, children born via CS had a 0.17 unit higher BMI Z-score at age 2 years (Table 2). There was no evidence that the association between delivery mode and body size was modified by gender, birthweight or breast feeding (all interaction *P*>0.34 for all body size metrics).

### Association of Delivery Mode with Body Size at Age 2 years is Modified by Pet-Keeping

At age 2 years, 204 children (31.9%) were living in a home with a pet. Prevalence of obesity and mean BMI Z-score of children in pet-keeping homes were 7.8% (n=16) and 0.16±1.14, respectively, and of children in non-pet homes were 9.0% (n=39) and 0.07±1.11, respectively; they did not differ significantly (*P*=0.64 and *P*=0.35, respectively).

There was evidence of effect modification between current pet-keeping and delivery mode with obesity at age 2 years (interaction *P*=0.054). There was no significant interaction between pet-keeping and delivery mode with BMI Z-score (interaction *P*=0.25). Table 3 presents the joint effect of delivery mode and pet-keeping on BMI measures. Compared to vaginally-born children without a pet in the home, children born via CS without a pet in the home had statistically significantly greater odds of obesity (OR=2.00; 95% CI: 1.02, 3.92; *P*=0.043) and a statistically significantly greater BMI Z-score (0.24±0.11; *P*=0.037) at age 2 years.

There was no evidence that race modified the delivery mode by pet-keeping interaction (race-delivery mode-CS interaction *P*>0.65 for all body size metrics).

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### Sensitivity Analysis

Inferences from the multinomial logistic regression model were similar. After adjusting for maternal obesity, children born via CS without a pet in the home had statistically significantly greater odds of being obese than normal weight compared to children vaginally-born without a pet in the home (OR=2.00; 95% CI: 1.02, 3.94; *P*=0.046).

Although pet-keeping was relatively stable (i.e. 173 of the 328 (52.7%) who ever had a pet had pets at all time points queried), there was loss and gain of pets over the study time period. We reran our final models using a variable for a child ever being exposed to a pet during the first two years of life, and all inferences were the same. Finally, we examined the effect of current dog-keeping on the association between delivery mode and body size, excluding 60 homes with cats but no dogs and results were similar.

## Conclusions

In the current study, we found evidence suggesting that CS was associated with body size at age 2 years, which is consistent with previous studies [5, 6, 13, 15]. Given that approximately one-third of all US births are via CS [4] and a substantial number of those may be avoidable [42], continued efforts to reduce CS in the absence of medical indications may positively impact rates of obesity [43]. Additionally, we found new evidence to suggest that this association may be modified by pet-keeping behavior in the first two years of life, with pet-keeping potentially providing children born by CS some protection against a larger body size. A potential mechanism by which pets may offer this protection is through alterations in the gut microbiome [28]. CS is associated with distinct offspring gut microbiome profiles compared to vaginal delivery [16, 17]; living with a pet may expose a child born via CS to bacterial communities with similar structure or function that they would have been exposed to during vaginal birth.

Three primary mechanisms linking the microbiome with obesity have been described from work in animal studies and include alterations in energy intake, fatty acid metabolism and fat storage, and inflammation and are described in detail in several recent review papers [44-46]. For example, gut microbes may differentially break down food sources such as carbohydrates leading to altered availability of nutrients for absorption in the digestive tract [45]. In the inflammatory model, differential microbiome inhabitants, for example, could lead to alterations in gut permeability and a subsequent metabolic endotoxemia, and may influence signaling of appetite and satiety between the gut and the brain [45].

In additional to a microbial-mediated pathway, pets may alter a child's risk of overweight/obesity through other means. For example, in a study of 5-6 and 10-12 year olds conducted in Melbourne, Australia, dog ownership was significantly associated with increased parental-reported total walking frequency/week in all children and with increased accelerometer-measured physical activity levels in 5-6 year old girls (but not boys) [47]. In this same study population, dog ownership was associated with reduced prevalence of overweight/obesity in children at age 5-6 years [48]. However, the association between dog-ownership and overweight/obesity persisted even after adjustment for dog-walking, and coupled with relatively low rates of dog-walking in the sample, the authors suggest that dogs

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may protect against early child obesity at least partially independently of dog-walking frequency [48]. A microbial-mediated pathway may be an alternative means of protection.

Maternal obesity is a risk factor for CS [49] and independently increases risk of offspring obesity [50]. Gut microbiomes of pre-pregnancy overweight and normal weight mothers differ and maternal weight gain over pregnancy is associated with gut microbial composition [51, 52]; these maternal factors appear to similarly influence differences in the offsprings' gut microbial composition [53]. In the current study, even after adjustment for maternal obesity the association between CS and early childhood body size remained statistically significant in the non-pet group. Huh et al (2012) similarly demonstrated that the association between delivery mode and childhood obesity remained even when controlling for maternal body size [5].

There is evidence that early-life intervention with microbial modulators can impact childhood body size. In a randomized double-blind trial conducted in Finland, 159 pregnant women were assigned to probiotics at 4 weeks before expected delivery; post-partum, probiotics were given to either the breast-feeding mother or mixed in water and directly fed to formula-fed infants [54]. Infants in the probiotic arm of the study had slower weight gain between the fetal period and 2-4 years of age, with reduced birth-weight-adjusted BMI at age 4 years. We speculate that pet exposure in early life may similarly alter the gut microbiome postnatally and impact body size in childhood by affecting rates of weight gain.

There are several limitations to the current study. Approximately 44% of the cohort did not complete a study visit at age 2 years potentially increasing risk of selection bias; however, our primary factor of interest, delivery mode, did not differ between these groups. Loss-to-follow up for the 2 year visit was greater for African-American children, reinforcing the need for optimizing retention strategies for racial and ethnic minority participants [55]. Maternal obesity was defined based on the BMI at entry into prenatal care; if women entered prenatal care later in pregnancy, this may reflect both pre-pregnancy weight and weight gain during pregnancy. In the overall sample, after adjusting for maternal obesity, there was a marginally statistically significant association of CS with the continuous BMI Z-score but not with risk of obesity. We may have been underpowered to detect a moderate sized association of CS with obesity risk in the overall cohort. However, our effect size (OR=1.40) is similar to the previously reported meta-analysis OR of 1.32 (95% CI: 1.15, 1.51) for CS on risk of offspring overweight/obesity [14].

Strengths of the current study include use of medical records to obtain data on maternal obesity, delivery mode and birthweight and measurement of child body size at a research clinic visit, thus our results are not subject to recall bias. Our study population includes a large number of African-American maternal-child pairs, a population at higher-risk for obesity [1] but typically understudied. We examined very early childhood body size (i.e. mean age of 2.2±0.2 years). Children who are overweight at age 2 years are at increased risk of future overweight [56]. Identification of risk factors for very early-life obesity may provide an opportunity for intervention for prevention in early-life, during critical stages of development, [56, 57], when risk may be most readily mitigated. Additional longitudinal studies examining the association of CS with trajectories of weight gain during the entire

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childhood period are needed. CS was associated with higher BMI over childhood (through age 15 years) in one study [58], but in another study CS was associated with obesity risk at age 2 years but not at ages 6 or 10 years [13].

In summary, this study provides further evidence that CS is associated with larger body size, as measured by BMI Z-score, in early childhood. We provide new evidence suggesting that early-life pet-keeping may modify the relationship between delivery mode and obesity risk, perhaps by increasing gut microbial diversity of children born by CS; however, this requires specific investigation.

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## References

1. Ogden CL, Carroll MD, Kit BK, et al. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. JAMA. 2012; 307(5):483–90.10.1001/jama.2012.40 [PubMed: 22253364]
2. Ogden CL, Flegal KM, Carroll MD, et al. Prevalence and trends in overweight among US children and adolescents, 1999-2000. JAMA. 2002; 288(14):1728–32. [PubMed: 12365956]
3. Zahniser SC, Kendrick JS, Franks AL, et al. Trends in obstetric operative procedures, 1980 to 1987. Am J Public Health. 1992; 82(10):1340–4. [PubMed: 1415856]
4. Menacker F, Hamilton BE. Recent trends in cesarean delivery in the United States. NCHS Data Brief. 2010; 35:1–8. [PubMed: 20334736]
5. Huh SY, Rifas-Shiman SL, Zera CA, et al. Delivery by caesarean section and risk of obesity in preschool age children: a prospective cohort study. Arch Dis Child. 2012; 97(7):610–6. [PubMed: 22623615]
6. Goldani HA, Bettiol H, Barbieri MA, et al. Cesarean delivery is associated with an increased risk of obesity in adulthood in a Brazilian birth cohort study. Am J Clin Nutr. 2011; 93(6):1344–7. [PubMed: 21508088]
7. Li H, Ye R, Pei L, et al. Caesarean delivery, caesarean delivery on maternal request and childhood overweight: a Chinese birth cohort study of 181 380 children. Pediatric obesity. 2014; 9(1):10–6.10.1111/j.2047-6310.2013.00151.x [PubMed: 23512941]
8. Wang L, Alamian A, Southerland J, et al. Cesarean section and the risk of overweight in grade 6 children. Eur J Pediatr. 2013; 172(10):1341–7.10.1007/s00431-013-2043-2 [PubMed: 23708216]
9. Barros FC, Matijasevich A, Hallal PC, et al. Cesarean section and risk of obesity in childhood, adolescence, and early adulthood: evidence from 3 Brazilian birth cohorts. Am J Clin Nutr. 2012; 95(2):465–70. [PubMed: 22237058]
10. Ajslev TA, Andersen CS, Gamborg M, et al. Childhood overweight after establishment of the gut microbiota: the role of delivery mode, pre-pregnancy weight and early administration of antibiotics. Int J Obes. 2011; 35(4):522–9.
11. Lin SL, Leung GM, Schooling CM. Mode of delivery and adiposity: Hong Kong's "Children of 1997" birth cohort. Ann Epidemiol. 2013; 23(11):693–9.10.1016/j.annepidem.2013.06.090 [PubMed: 23880154]
12. Flemming K, Woolcott CG, Allen AC, et al. The association between caesarean section and childhood obesity revisited: a cohort study. Arch Dis Child. 2013; 98(7):526–32.10.1136/archdischild-2012-303459 [PubMed: 23680850]
13. Pei Z, Heinrich J, Fuertes E. Cesarean Delivery and Risk of Childhood Obesity. The Journal of pediatrics. 2014; 164(5):1068–73.10.1016/j.jpeds.2013.12.044 [PubMed: 24508442]

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14. Li H, Zhou Y, Liu J. The impact of cesarean section on offspring overweight and obesity: a systematic review and meta-analysis. Int J Obes. 2013; 37(7):893–9.
15. Li HT, Zhou YB, Liu JM. Cesarean section might moderately increase offspring obesity risk. Am J Clin Nutr. 2012; 96(1):215–6. [PubMed: 22718776]
16. Dominguez-Bello MG, Costello EK, Contreras M, et al. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. Proc Natl Acad Sci U S A. 2010; 107(26):11971–5.10.1073/pnas.1002601107 [PubMed: 20566857]
17. Azad MB, Konya T, Maughan H, et al. Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months. CMAJ. 2013; 185(5):385–94. [PubMed: 23401405]
18. Ridaura VK, Faith JJ, Rey FE, et al. Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice. Science. 2013; 341(6150):1241214.10.1126/science.1241214 [PubMed: 24009397]
19. Turnbaugh PJ, Ley RE, Mahowald MA, et al. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature. 2006; 444(7122):1027–31. [PubMed: 17183312]
20. Kalliomaki M, Collado MC, Salminen S, et al. Early differences in fecal microbiota composition in children may predict overweight. Am J Clin Nutr. 2008; 87(3):534–8. [PubMed: 18326589]
21. Luoto R, Kalliomaki M, Laitinen K, et al. Initial dietary and microbiological environments deviate in normal-weight compared to overweight children at 10 years of age. J Pediatr Gastroenterol Nutr. 2011; 52(1):90–5. [PubMed: 21150648]
22. Karlsson CL, Onnerfalt J, Xu J, et al. The microbiota of the gut in preschool children with normal and excessive body weight. Obesity. 2012; 20(11):2257–61. [PubMed: 22546742]
23. Balamurugan R, George G, Kabeerdoss J, et al. Quantitative differences in intestinal Faecalibacterium prausnitzii in obese Indian children. Br J Nutr. 2010; 103(3):335–8.10.1017/s0007114509992182 [PubMed: 19849869]
24. Wegienka G, Johnson CC, Havstad S, et al. Lifetime dog and cat exposure and dog- and cat-specific sensitization at age 18 years. Clin Exp Allergy. 2011; 41(7):979–86. [PubMed: 21668818]
25. Fujimura KE, Johnson CC, Ownby DR, et al. Man's best friend? The effect of pet ownership on house dust microbial communities. J Allergy Clin Immunol. 2010; 126(2):410–2. 2. [PubMed: 20633927]
26. Song SJ, Lauber C, Costello EK, et al. Cohabiting family members share microbiota with one another and with their dogs. eLife. 2013; 2:e00458.10.7554/eLife.00458 [PubMed: 23599893]
27. Azad MB, Konya T, Maughan H, et al. Infant gut microbiota and the hygiene hypothesis of allergic disease: impact of household pets and siblings on microbiota composition and diversity. Allergy, asthma, and clinical immunology. 2013; 9(1):15.10.1186/1710-1492-9-15
28. Fujimura KE, Demoor T, Rauch M, et al. House dust exposure mediates gut microbiome Lactobacillus enrichment and airway immune defense against allergens and virus infection. Proc Natl Acad Sci U S A. 2014; 111(2):805–10.10.1073/pnas.1310750111 [PubMed: 24344318]
29. Bager P, Wohlfahrt J, Westergaard T. Caesarean delivery and risk of atopy and allergic disease: meta-analyses. Clin Exp Allergy. 2008; 38(4):634–42.10.1111/j.1365-2222.2008.02939.x [PubMed: 18266879]
30. Havstad S, Wegienka G, Zoratti EM, et al. Effect of prenatal indoor pet exposure on the trajectory of total IgE levels in early childhood. J Allergy Clin Immunol. 2011; 128(4):880–5. [PubMed: 21820714]
31. Wegienka G, Havstad S, Joseph CL, et al. Racial Disparities in Allergic Outcomes in African Americans Emerge as Early as Age 2 Years. Clinical & Experimental Allergy. 2011; 42(6):909–17.10.1111/j.1365-2222.2011.03946.x [PubMed: 22909162]
32. Oken E, Kleinman KP, Rich-Edwards J, et al. A nearly continuous measure of birth weight for gestational age using a United States national reference. BMC Pediatr. 2003; 3:6. [PubMed: 12848901]
33. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States: methods and development. Vital Health Stat. 2002; 11(246):1–190.
34. Rabinowitz P, Conti L. Links among human health, animal health, and ecosystem health. Annu Rev Public Health. 2013; 34:189–204.10.1146/annurev-publhealth-031912-114426 [PubMed: 23330700]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

35. Wells DL. Domestic dogs and human health: an overview. British journal of health psychology. 2007; 12(Pt 1):145–56.10.1348/135910706x103284 [PubMed: 17288671]

36. Levine GN, Allen K, Braun LT, et al. Pet ownership and cardiovascular risk: a scientific statement from the American Heart Association. Circulation. 2013; 127(23):2353–63.10.1161/CIR. 0b013e31829201e1 [PubMed: 23661721]

37. Lovasi GS, Underhill LJ, Jack D, et al. At Odds: Concerns Raised by Using Odds Ratios for Continuous or Common Dichotomous Outcomes in Research on Physical Activity and Obesity. The open epidemiology journal. 2012; 5:13–7.10.2174/1874297101205010013 [PubMed: 23002407]

38. Greenland S. Modeling and variable selection in epidemiologic analysis. Am J Public Health. 1989; 79(3):340–9. [PubMed: 2916724]

39. Selvin, S. Statistical Analysis of Epidemiologic Data. 2nd. New York: Oxford University Press; 1996.

40. Ezell J, Cassidy-Bushrow A, Joseph C, et al. Prenatal Dog-Keeping Practices Vary By Race – Speculations on Implications for Disparities in Childhood Health and Disease. Ethnicity & disease. 2014; 24(1):104–9. [PubMed: 24620456]

41. Bryant AS, Washington S, Kuppermann M, et al. Quality and equality in obstetric care: racial and ethnic differences in caesarean section delivery rates. Paediatric and perinatal epidemiology. 2009; 23(5):454–62.10.1111/j.1365-3016.2009.01059.x [PubMed: 19689496]

42. Kabir AA, Pridjian G, Steinmann WC, et al. Racial differences in cesareans: an analysis of U.S. 2001 National Inpatient Sample Data. Obstet Gynecol. 2005; 105(4):710–8.10.1097/01.AOG. 0000154154.02581.ce [PubMed: 15802395]

43. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 559: Cesarean delivery on maternal request. Obstet Gynecol. 2013; 121(4):904–7.10.1097/01.AOG. 0000428647.67925.d3 [PubMed: 23635708]

44. Kaplan JL, Walker WA. Early gut colonization and subsequent obesity risk. Curr Opin Clin Nutr Metab Care. 2012; 15(3):278–84. [PubMed: 22327336]

45. Wolf KJ, Lorenz RG. Gut Microbiota and Obesity. Current obesity reports. 2012; 1(1):1–8.10.1007/s13679-011-0001-8 [PubMed: 23106036]

46. Musso G, Gambino R, Cassader M. Obesity, diabetes, and gut microbiota: the hygiene hypothesis expanded? Diabetes Care. 2010; 33(10):2277–84.10.2337/dc10-0556 [PubMed: 20876708]

47. Salmon J, Timperio A, Chu B, et al. Dog ownership, dog walking, and children's and parents' physical activity. Res Q Exerc Sport. 2010; 81(3):264–71. [PubMed: 20949846]

48. Timperio A, Salmon J, Chu B, et al. Is dog ownership or dog walking associated with weight status in children and their parents? Health Promot J Austr. 2008; 19(1):60–3. [PubMed: 18481934]

49. Chu SY, Kim SY, Schmid CH, et al. Maternal obesity and risk of cesarean delivery: a meta-analysis. Obesity reviews. 2007; 8(5):385–94.10.1111/j.1467-789X.2007.00397.x [PubMed: 17716296]

50. Pham MT, Brubaker K, Pruett K, et al. Risk of childhood obesity in the toddler offspring of mothers with gestational diabetes. Obstet Gynecol. 2013; 121(5):976–82.10.1097/AOG. 0b013e31828bf70d [PubMed: 23635733]

51. Collado MC, Isolauri E, Laitinen K, et al. Distinct composition of gut microbiota during pregnancy in overweight and normal-weight women. Am J Clin Nutr. 2008; 88(4):894–9. [PubMed: 18842773]

52. Santacruz A, Collado MC, Garcia-Valdes L, et al. Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. Br J Nutr. 2010; 104(1):83–92.10.1017/s0007114510000176 [PubMed: 20205964]

53. Collado MC, Isolauri E, Laitinen K, et al. Effect of mother's weight on infant's microbiota acquisition, composition, and activity during early infancy: a prospective follow-up study initiated in early pregnancy. Am J Clin Nutr. 2010; 92(5):1023–30.10.3945/ajcn.2010.29877 [PubMed: 20844065]

54. Luoto R, Kalliomaki M, Laitinen K, et al. The impact of perinatal probiotic intervention on the development of overweight and obesity: follow-up study from birth to 10 years. Int J Obesity (2005). 2010; 34(10):1531–7.10.1038/ijo.2010.50

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55. Yancey AK, Ortega AN, Kumanyika SK. Effective recruitment and retention of minority research participants. Annu Rev Public Health. 2006; 27:1–28.10.1146/annurev.publhealth.27.021405.102113 [PubMed: 16533107]

56. Flores G, Lin H. Factors predicting overweight in US kindergartners. Am J Clin Nutr. 2013; 97(6):1178–87.10.3945/ajcn.112.052019 [PubMed: 23553169]

57. Lawlor DA, Chaturvedi N. Treatment and prevention of obesity—are there critical periods for intervention? Int J Epidemiol. 2006; 35(1):3–9.10.1093/ije/dyi309 [PubMed: 16396899]

58. Blustein J, Attina T, Liu M, et al. Association of caesarean delivery with child adiposity from age 6 weeks to 15 years. Int J Obes. 2013; 37(7):900–6.10.1038/ijo.2013.49

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## Table 1

Maternal, newborn and child characteristics by delivery mode among 639 WHEALS participants.

| | Vaginal Mean±std or N (%) | Caesarean-Section Mean±std or N (%) | *P* |
|---|---|---|---|
| N (%) | 411 (64.3%) | 228 (35.7%) | |
| **Maternal Characteristics** | | | |
| Age at Delivery (years) | 29.5±5.1 | 31.1±5.3 | <0.001 |
| >High school education | 327 (79.6%) | 186 (81.6%) | 0.54 |
| Married | 269 (65.4%) | 159 (69.7%) | 0.27 |
| Smoking during pregnancy | 44 (10.7%) | 17 (7.5%) | 0.18 |
| Total household income <$40,000[a] | 136 (37.9%) | 73 (36.7%) | 0.78 |
| Race | | | 0.065 |
| African-American | 227 (55.2%) | 140 (61.4%) | |
| White | 135 (32.9%) | 55 (24.1%) | |
| Other | 49 (11.9%) | 33 (14.5%) | |
| BMI at first prenatal care visit (kg/m$^2$) [b] | 28.9±7.7 | 32.0±8.4 | <0.001 |
| Maternal obesity | 141 (35.2%) | 120 (53.6%) | <0.001 |
| **Newborn Characteristics** | | | |
| Male | 200 (48.7%) | 128 (56.1%) | 0.07 |
| Gestational age at birth (weeks)[c] | 39.0±1.6 | 38.7±1.8 | 0.11 |
| Birthweight (g)[d] | 3367±519 | 3392±650 | 0.62 |
| Birthweight Z-score[e] | -0.06±0.92 | 0.06±1.07 | 0.19 |
| First Born | 142 (34.6%) | 99 (43.4%) | 0.027 |
| **Child Characteristics at age 2 clinic visit** | | | |
| Age at clinic visit (months) | 26.8±3.1 | 26.4±2.7 | 0.16 |
| Ever Breastfed | 331 (80.5%) | 178 (78.1%) | 0.46 |
| Ever Any Pet | 221 (53.8%) | 107 (46.9%) | 0.097 |
| Current Pet | 133 (32.4%) | 71 (31.1%) | 0.75 |
| Current Dog | 92 (22.4%) | 52 (22.8%) | 0.90 |
| Height (cm) | 89.8±4.6 | 89.7±4.3 | 0.95 |
| Height Z-score | 0.52±1.04 | 0.56±1.04 | 0.649 |
| BMI (kg/m$^2$) | 16.5±1.6 | 16.9±1.8 | 0.009 |
| BMI Z-score | 0.02±1.09 | 0.24±1.17 | 0.018 |
| BMI percentile | 50.7±29.3 | 57.8±28.9 | 0.004 |
| BMI category | | | 0.29 |
| Underweight (BMI<5$^{th}$ percentile) | 28 (6.8%) | 14 (6.1%) | |
| Normal Weight (BMI≥5$^{th}$ and <85$^{th}$ percentile) | 319 (77.6%) | 165 (72.4%) | |
| Overweight (BMI≥85$^{th}$ and <95$^{th}$ percentile | 34 (8.3%) | 24 (10.5%) | |
| Obese (BMI≥95$^{th}$ percentile) | 30 (7.3%) | 25 (11.0%) | |

std, standard deviation; BMI, body mass index

[a] n=81 with missing or refused income information;

[b] n=14 with missing data;

[c] n=15 with missing data;

[d] n=32 with missing data;

[e] n=40 with missing data

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## Table 2

**Association of caesarean-section (CS) delivery compared to vaginal delivery (referent) with body mass index (BMI) measures at age 2 years in WHEALS, unadjusted (Model 1) and adjusted for maternal obesity (Model 2)**

| Delivery Mode | BMI≥95th percentile (Obese) | | BMI Z-score | |
|---|---|---|---|---|
| | **OR (95% CI)** | ***P*** | **β (se)** | ***P*** |
| **Model I** | | | | |
| CS | 1.56 (0.90, 2.73) | 0.12 | 0.22 (0.09) | 0.018 |
| **Model 2** | | | | |
| CS | 1.40 (0.79, 2.47) | 0.25 | 0.17 (0.09) | 0.080 |
| Maternal Obesity | 1.80 (1.02, 3.18) | 0.042 | 0.24 (0.09) | 0.012 |

OR, odds ratio; CI, confidence interval; β, parameter estimate; se, standard error

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## Table 3

**Joint effect of delivery mode and current pet-keeping with body mass index (BMI) measures at age 2 years in WHEALS adjusted for maternal obesity**

| | BMI≥95$^{th}$ percentile (Obese) | | BMI Z-score | |
|---|---|---|---|---|
| **Delivery Mode/Pet Keeping** | **OR (95% CI)** | ***P*** | **β (se)** | ***P*** |
| Vaginally-born/No Pet | REFERENCE | | REFERENCE | |
| Vaginally-born/Pet | 1.50 (0.70, 3.24) | 0.30 | 0.19 (0.12) | 0.12 |
| CS-born/No Pet | 2.00 (1.02, 3.93) | 0.043 | 0.24 (0.11) | 0.037 |
| CS-born/Pet | 0.80 (0.26, 2.45) | 0.69 | 0.20 (0.15) | 0.19 |

OR, odds ratio; CI, confidence interval; β, parameter estimate; se, standard error; CS, caesarean-section